

THE PARADOX OF CORONARY HEART DISEASE IN AFRICAN-AMERICAN WOMEN

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Coronary heart disease is the leading cause of death in the United States in both men and women. Much has been written on the ill effects of this disease in the general population; however, its ramifications in African-American women have been overlooked. Without a doubt, this group has a higher mortality and morbidity than African-American men and white women below the age of 55. Despite the lower angiographic prevalence of disease, when symptomatic coronary heart disease develops, the outlook is dismal. Today's research must concentrate on the ramifications of coronary heart disease in this population to improve the health standard of the general populace. (*J Natl Med Assoc.* 2000;92:327-333.)

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Coronary heart disease is the leading cause of death in the United States. However, it is inappropriate to discuss coronary heart disease without addressing its effect on subgroups. Coronary heart disease is the leading cause of death in African-American and women groups. Epidemiologic studies have shown African-American women to have a higher coronary heart disease mortality risk than their white counterparts in multiple studies.^{1,2} In fact, among women between the ages of 25 and 44, relative to similarly matched white women, the coronary heart disease mortality risk ratio is approximately 2.5.³ Yet, a dearth of information exists addressing the natural history, diagnosis, and treatment of coronary heart disease in this subpopulation. Vital statistics data have shown African-American women to have a higher coronary heart

disease mortality risk in comparison to white women since the 1940s. This mortality gap continues into the present day. However, mortality rate is not a measure of disease prevalence. Coronary artery disease prevalence, based on angiographic surveys, is lower in the African-American women population than in the white women population; yet mortality rates are higher.^{1,2,4,5} The expression of coronary artery disease in the form of first infarct occurs at an earlier age in the African-American population.⁶ The African-American population has a higher out-of-hospital mortality rate, higher incidence of sudden cardiac death, and higher in-hospital mortality rate after first infarct.^{7,8} In fact, African-American women have a higher postinfarct mortality rate than the other three gender/race groups. Despite this higher risk, African-American women are least likely to be referred for cardiac catheterization with appropriate symptoms and an abnormal noninvasive study.⁹⁻¹¹ Physician referral bias is the biggest hurdle to overcome. A grave need exists to study the clinical characteristic profile of this high-risk subgroup, analyze present methods of diagnosis, and determine areas for further research. In part I of this series, we will explore the characteristics of coronary heart disease in the African-American women population and examine methods of diag-

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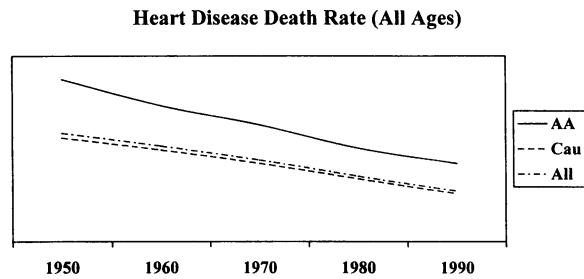


Figure 1. Heart disease death rate (all ages). Data are from the National Center for Health Statistics.⁴⁰

nosis from the present data. In addition, we will also review interventional treatment options. In part II, methods of primary and secondary prevention through risk factor modification, and other medical treatment regimens will be discussed.

EPIDEMIOLOGY

Historically, African-American women have always had a higher age-adjusted coronary heart disease death rate than do white women (Figure 1). Myocardial infarctions occur earlier in young African Americans and with greater severity and more complications. In the 35- to 44-year age group, the relative risk in African-American women is 2.1 (when compared to white women). The relative risk increases to 2.3 in the 45- to 54-year age group for African-American women.¹ In a national observational study with long-term epidemiologic follow-up, overall relative risk for African-American women between the ages of 25 and 54 was found to be 1.76 for coronary heart disease, 1.0 for acute myocardial infarction, and 2.25 for death from coronary heart disease.¹² The survivor effect or force of mortality⁸ suggests a more aggressive natural history of coronary heart disease for this young African-American population (Figures 2 and 3). The full expression of coronary artery disease is experienced at an earlier age with an earlier death from coronary artery disease. Therefore, Darwinian laws of preselection would dictate that the subjects remaining represent a subpopulation with a lower predisposition for coronary artery disease, and hence a lower mortality rate. Unfortunately, the crossover, when the African-American mortality rate becomes lower than that of the general population, is occurring at a later decade than in the past. Whereas, in the 80s, the crossover occurred in the eighth decade of life,

Heart Disease Mortality Rate (1985)

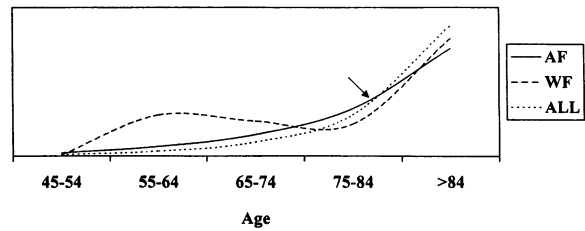


Figure 2. Heart disease mortality rate (1985). Data are from the National Center for Health Statistics.⁴⁰

Heart Disease Mortality (1995-1997)

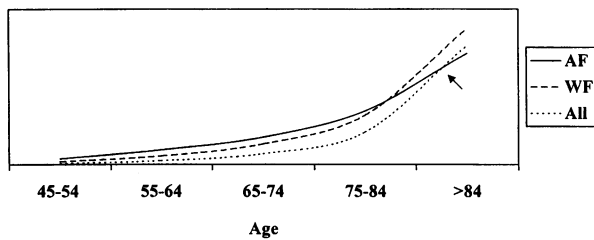


Figure 3. Heart disease mortality (1995 through 1997). Data are from the National Center for Health Statistics.⁴⁰

we do not see this crossover in mortality rate until the ninth decade in the late 90s.

The first census in the 1940s uncovered evidence of a mortality gap between African-American women and white women. The Census Bureau counted the "nonwhite" population and grouped all minorities into this "nonwhite" group. Yet African Americans comprised 80% of this group. Therefore, "nonwhite" was considered a surrogate marker of African-American vital statistics from that era. A trend of declining coronary heart disease deaths in white women paralleled the explosion in cardiac technology and research in the 60s and 70s. African-American women notably failed to reap similar benefits until almost 10 years later.¹ Although the 80s saw this declining trend in African-American mortality rates, the 90s witnessed a plateau in mortality among African Americans coincident with a continued decline in the white women population. The overall effect is a mortality gap that continues to widen today (Figure 4). In fact, the ethnic African-American ratio in women is increasing as of 1997 (Figure 5). The human tendency to underappreciate the continued need for preventive health behaviors can partially explain these figures. In addition, the present social environment of today is markedly

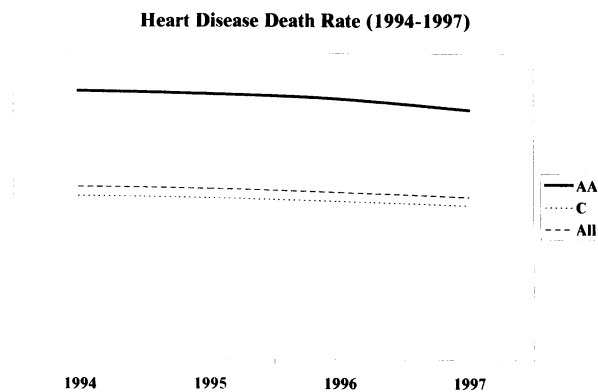


Figure 4. Heart disease death rate (1994 through 1997). Data are from the National Center for Health Statistics.⁴⁰

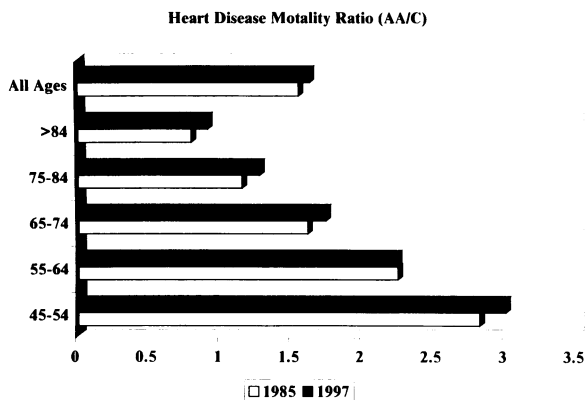


Figure 5. Heart disease mortality ratio of coronary heart disease in African Americans to whites. Data are from the National Center for Health Statistics.⁴⁰

different from the politically active and socially conscious era of the 1960s and early 1970s. Therefore, it is conceivable that less emphasis is placed on the healthcare of the “minority” population by the country as a whole.

ANGIOGRAPHIC PREVALENCE

Angiographic prevalence of coronary artery disease is lower in African-American women than the general population. The Coronary Artery Surgery Study (CASS) registry had 573 African Americans out of almost 23,000 subjects. Maynard et al.¹³ evaluated the African-American subgroup in the CASS population and found a high rate of normal coronary arteries in the African-American women category. This group had the highest incidence of normal coronary arteries at 63%. In addition, African-American women had the lowest incidence of

single, two-vessel, and three-vessel disease in comparison to all other race/gender subgroups. Left main coronary artery disease prevalence was equally low in African-American men and African-American women at 1.9%.

Other analyses of coronary artery disease prevalence in the African-American population corroborate the high percentage of normal coronary arteries in African-American women.^{4,5}

A meta-analysis of three studies of angiographic disease prevalence demonstrated the prevalence of three-vessel coronary artery disease in the African American females to be 19.4%. This is higher than the 12% prevalence shown for African American women shown in the Coronary Artery Surgery Study (CASS) study and similar to the almost 20% prevalence shown for white women in the same study. Referral bias, geographic bias, small sample size, and low socioeconomic status were the most common confounding factors seen. The largest reported population studied had approximately 1000 African-American subjects, which is diminutive in comparison to the CASS study. In this study, 57% of African-American women had normal coronary arteries. Yet, in contrast, over half with coronary artery disease had three-vessel disease. These data suggest that angiographic disease prevalence appears to be inversely proportional to mortality rate. When disease is present, it is significant and prognosis is poor. This is the African-American women paradox of coronary heart disease.

CHEST PAIN

Angina as a presenting symptom of coronary disease has also been studied and found to be higher in black women compared to black and white men and white women.¹⁴⁻¹⁶ Interestingly, none of these studies correlated angiographic or functionally significant disease with symptomatology. Angina as a presenting symptom of coronary disease has also been studied and has been found to be higher in African American women compared to African American men, Caucasian men or Caucasian women.¹⁴⁻¹⁶ However, no coronary anatomy was described and, studies describing angina without the knowledge of coronary atherosclerosis raise more questions than they answer. Symptoms do not always correlate with angiographic disease as shown by Caryon and Mathews.¹⁷ Microvascular disease is a potential cause of chest pain with “normal coronary

arteries" and can occur in the setting of diabetics and hypertension. Given the significant burden in the African American population, it is conceivable that microvascular disease may play a role in the chest pain in African American women.

However, there are other possible explanations for chest pain without angiographic disease. Left ventricular hypertrophy (LVH) is another potential cause of angina-like chest pain in the setting of normal coronary arteries. The most commonly used definition of LVH is based on electrocardiographic criteria. Using these criteria, African Americans have a higher prevalence of LVH than do their white counterparts. When echocardiographic criteria are used, LVH prevalence is similar in both groups. Indeed, in patients with hypertensive LVH, chest pain frequently resolves with control of blood pressure. Current thinking suggests that resistance vessel disease in hypertensive subjects with LVH may be a cause of chest pain.

Syndrome X, as a cause of chest pain, is a diagnosis of exclusion. It is defined by chest pain, normal coronary anatomy, and perfusion defects by nuclear stress testing. Frequently, LVH is also present. Finally, endothelial dysfunction has been shown for years to be associated with chest pain both with and without coronary atherosclerosis. Until recently, treatment remained elusive, thus making this diagnosis irrelevant. In a study evaluating coronary vascular physiology in hypertensive subjects, the African-American patients with hypertension and LVH were more likely to have abnormal coronary vascular reactivity to acetylcholine than were white hypertensive patients with LVH.¹⁸

MYOCARDIAL INFARCTION

In the 1940s, coronary heart disease was not believed to occur in the African-American population.¹⁹ Since then, we have seen several studies to attest to the presence of coronary heart disease in African Americans.^{16,20-21} However, only one study has specifically documented the higher incidence of infarction and poorer prognosis in African-American women. This posthoc analysis, performed in the 1980s, specifically assesses cardiac outcomes postinfarction based on race and gender. In Tofler's analysis of the Multicenter Investigation of Limitation of Infarct Size MILIS population,² he found that the women-to-men ratio for infarct incidence was almost 1:1 in the African-American group. This is in

stark contrast to 0.3:1 ratio for the white cohort. Infarct size was greater in African-American women compared to white women. Outcome was not related to ejection fraction, which was higher in the African-American women. For the first time, the higher mortality risk in African-American women is described. Scant data have since been published addressing this higher risk.

In contrast, hospitalization rate is lower for African-American women, although there is an excess of hospital admissions for those less than 55, according to the National Hospital Discharge Survey.⁶ Johnson et al.²² compared racial differences in hospital admission and care of patients with chest pain. They found that African Americans had 31% fewer admissions than whites. Once admitted, they were less likely to be triaged to the coronary care unit.

In-hospital mortality after first myocardial infarction is higher in the African-American population and highest in the African-American women population at 48%.⁶ Community studies have shown an excess of out-of-hospital cardiac deaths.⁷ Gillum²³ analyzed the sudden cardiac death rates in U.S. African Americans. Sudden cardiac deaths, out-of-hospital or in emergency rooms, were highest in African-American women at 108 per 100,000 and lowest in Hispanic women at 35 per 100,000. White women had an intermediate rate of 74. These subjects were predominantly younger in age. And yet, delay in presentation to the emergency room can at least partially account for this. Clark et al.,²⁴ clearly described a longer prehospital delay in African Americans. In this inner city population, African Americans had a mean delay of 13 h, Hispanics had a mean delay 12 h, and whites had a mean delay of 3.3 h. The factor most strongly associated with a lower prehospital delay was belief that the symptoms represented a heart attack.

DIAGNOSIS

Noninvasive

Screening for coronary artery disease in this high-risk population has not been evaluated in the past. Exercise echocardiography has been shown to have a higher specificity than exercise electrocardiogram for the diagnosis of coronary artery disease in women and is cost-effective.^{25,26} Exercise echocardiography also provides incremental prognostic outcome information to clinical and exercise data.²⁷ Exercise thallium single-photon emission tomo-

graphic (SPECT) imaging has a significant false-positive rate. The lower energy of thallium results in a significant amount of breast attenuation in obese women. Technetium-99m SPECT imaging has shown promise because of the higher energy level in contrast to thallium and results in fewer breast attenuation artifacts.²⁷ Attenuation correction software has helped to improve accuracy in women. Although the 2-year risk of cardiac death was higher in young women vs. young men, the 2-year cost of care was significantly lower. The rate of diagnostic follow-up was significantly higher in young men.²⁸

Dobutamine echo shows promise in detecting coronary artery disease in women. No gender-based differences were detected in the sensitivity, specificity, and accuracy of dobutamine echocardiography in a recent study.²⁹ Alkeylani et al.³⁰ found that similar prognostic information could be obtained from the Tc-99m-sestamibi SPECT imaging of both African-American and white subjects. The 2-year overall survival was lower for African Americans than whites with a normal scan (96% vs. 84%). This was not found to be statistically significant. However, it suggests a possible trend that may require further research. It may also suggest that a higher clinical index of suspicion should exist when evaluating test results in African Americans.

Cardiac Catheterization

The last 10 years has seen an increase in access to care studies in African Americans. Cardiac catheterization is less likely to be performed after an abnormal noninvasive study in African Americans. A recent study looked at the use of diagnostic and therapeutic procedures based on race and gender.³¹ Women had 20% fewer catheterization procedures than men and 40% fewer revascularizations. African Americans had 30% fewer catheterizations and 60% fewer revascularizations. Of 78 disease categories, African Americans and women had more diagnostic and therapeutic procedures in only 10% of disease conditions. It is not possible to determine whether this represents underutilization in African Americans and women or referral bias. There is some evidence to support both explanations.

The referral bias is a daunting problem. In a recent study, physicians were given a history and shown videotapes of subjects of varying ethnicities and gender.¹¹ Each physician was then asked the diagnostic and treatment plan for each "patient."

With the same history, the African Americans and women were referred for cardiac catheterization less frequently than the rest of the group.

However, even with equivalent referral patterns to cardiac catheterization, there may be other, non-physician factors that decrease utilization of revascularization procedures and surgeries. In a study from Duke University, catheterization referrals were equivalent for African Americans and whites.¹⁰ However, fewer African-American patients chose revascularization over medical therapy. This difference was most significant in those with multivessel disease and in the elderly. Therefore, cultural and educational factors may present additional obstacles to utilization of catheterization procedures. Finally, Gillum³² re-examined data from the National Hospital Discharge Survey for utilization of cardiac procedures between the years of 1980 and 1993. Although the rate of coronary artery bypass surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA) rates increased in both African-American and white groups, the ratio of African Americans to whites remained the same in PTCA procedures at 0.57. This ratio increased in CABG procedures from 0.23 in the early 1980s to 0.43 in 1993. Cardiac catheterization rates increased significantly with a ratio of 0.91 African Americans to whites in 1993. This suggests that, although we have made significant inroads into utilization of cardiac catheterization procedures, there are still racial disparities in utilization of both PTCA and CABG.

INTERVENTIONAL TREATMENT OPTIONS

PTCA

The National Heart, Lung, and Blood Institute (NHLBI) PTCA registry³³ from 1977 to 1981 described the clinical characteristics of its cohort based on gender. It was shown that the women were older, had more severe angina, and a higher in-hospital mortality rate. The in-hospital mortality gap between the sexes was abolished with the next PTCA registry³⁴ from 1985 to 1986. When race and gender were analyzed, African Americans had a higher rate of multivessel disease, yet a lower rate of complete revascularization (26% vs. 44%). African-American women had a poorer long-term outcome than did white women. This did not reach statistical significance.³⁵

CABG

Coronary artery bypass graft is not utilized as much in the African-American population, even with near-equivalent access to cardiac catheterization.^{10,24} It is not clear whether incidence of inoperable disease or access to care issues are responsible for this lower rate. Long-term survival after coronary artery bypass surgery is worse in African Americans. As documented by Taylor et al.³⁶ in an analysis of the CASS registry, African Americans had a higher 16-year mortality in the surgical group. In another study,³⁷ 1- and 5-year survival was 84% and 64% in African Americans (vs. 92% and 82% in whites), respectively. Causes for this worse prognosis with CABG are uncertain, however, Taylor showed an improvement in African-American CABG risk with smoking cessation.

FUTURE RESEARCH

The Minority Health Report by the Department of Health and Human Services was a landmark in its findings of overall poorer health in the African-American population in the 80s.³ Although numerous African-American cohorts studying coronary artery disease abounded in the 1960s, today's cohorts are rare.^{16,20,21} Most notable is the National Institutes of Health (NIH) Jackson Heart Study, which is a continuation of the Atherosclerotic Risk in Communities (ARIC) study.³⁸ Also worthy of mention is the Meharry-Johns Hopkins Study.³⁹ The Jackson Heart Study seeks to develop a Framingham-type epidemiologic long-term study of coronary heart disease and coronary risk factors in the African-American population of Jackson, MS. The Meharry Study is similar to the Physicians' Health Study in design.³⁹ Physicians are followed prospectively from medical school; coronary heart disease and its risk factors are evaluated. The confounding factor of socioeconomic status is removed from the milieu, because all study patients are physicians. Unfortunately, at the time of enrollment, few women physicians existed.

Enrollment of African Americans into these studies is difficult, probably related to education, cultural bias, and general distrust stemming from observational studies such as the infamous "Syphilis Study" at Tuskegee, as well as other, less well-known studies. A problem also exists with the enrollment of women in gender-neutral studies.

Women are included less often for various reasons, such as age and reproductive status.

Within study populations specifically describing race differences, the small number of women subjects often precludes generalizations but instead alludes to certain trends guiding the researcher toward future areas of study. The NHLBI converted a Working Group on Research in Coronary Heart Disease in African Americans with identification of research areas. The NIH Women's Initiative is ongoing, and hopefully will be stratified for race within gender with an attempt at controlling for socioeconomic status.

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