Contemporary Treatment of Heart Failure: Is There Adequate Evidence to Support a Unique Strategy for African-Americans? Con Position

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Heart Failure and Hypertension in African-Americans
African-Americans have hypertension rates among the highest in the world, with greater degrees of target organ damage including heart failure, end-stage renal disease, stroke, and overall heart disease. In virtually all racial groups, there is a demonstrated rise in blood pressure with aging. African-Americans develop hypertension earlier in life and have higher rates of stage 3 hypertension than any other group in the United States [5]. Elevated blood pressure is largely attributed to potentially modifiable risk factors, including increased body mass index, inactivity, and increased sodium consumption. Hypertension, therefore, as the preeminate cause of heart failure in African-Americans, is directly related to shared environment and lifestyle habits [5] (Table 1).

Introduction
Heart failure remains a major cause of death and disability in the United States. There are over 550,000 new cases each year and prevalence continues to increase [1]. Heart failure remains the primary diagnosis for hospitalization in patients over the age of 65 years, and affects 3% of the African-American population [2]. The burden of heart failure is associated with over 285,000 deaths per year and accounts for 5% to 10% of all hospital admissions [1,2].

The etiology of systolic heart failure in most morbidity and mortality trials is coronary artery disease. However, the community-wide burden of uncontrolled hypertension is directly related to the increasing prevalence of heart failure, and for African-Americans, hypertension is the predominant etiology [1].

These factors lead to left ventricular remodeling, decreased ejection fraction, and neurohormonal activation, including the renin-angiotensin-aldosterone (RAA) and sympathetic nervous systems. Neurohormonal activation leads to peripheral vascular constriction with hemodynamic alterations, worsening of left ventricular systolic function, and further activation of the RAA and sympathetic nervous systems. The end result is myocardial toxicity and increasing morbidity and mortality [3•,4•]. In the contemporary treatment of heart failure, the use of angiotensin converting enzyme (ACE) inhibitors and β-adrenergic blockers approved by the Food and Drug Administration is compelling.

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While various unique biochemical and endocrine characteristics of black hypertensives have been suggested, a recent study in seven populations of west African descent including African, Caribbean, and US populations, utilized a highly standardized protocol to document the potential for environmental causes in various black populations [6]. This study noted lifestyle factors significantly related to high blood pressure in the populations. Most notably, increased body mass and high urinary sodium to potassium ratio were primary predictors of hypertension prevalence [6].

Dietary customs in African-Americans including cultural identity with high sodium, high fat meals, greater acceptance of the obese female, and decreased levels of exercise may be causes of higher prevalence and poorer blood pressure control [7]. Salt sensitivity increases with age along with body weight, and has been demonstrated in as many as 75% of black hypertensives. Sodium restriction, therefore, augments reduction of blood pressure, a powerful risk factor for systolic heart failure in this population [8–10].

It has been suggested that modulation of the RAA system with β-adrenergic blockers and ACE inhibitors, along with angiotensin-receptor blockers, is less effective as antihypertensive monotherapy in blacks [5]. Moreover, in blacks as well as in whites, the first pharmacologic step in the absence of conditions that prohibit their use remains diuretics. Although calcium channel blockers effectively lower pressure in blacks, there are at present no specific data documenting decreased morbidity and mortality with this class of drugs in African-Americans [5].

The Antihypertensive Lipid Lowering in Heart Attack (ALLHAT) trial will report the cardiovascular effects of antihypertensive therapy with lisinopril, amlodipine, and chlorthalidone in a large cohort of 42,448 high-risk patients, 35% of whom are African-Americans [11]. Previously, an interim ALLHAT analysis demonstrated a reduced risk of combined cardiovascular events including heart failure, which was also seen in the African-American cohort, versus doxazosin [11].

Although modulation of the RAA system may be less effective as antihypertensive monotherapy in blacks, ACE inhibitors remain attractive choices in African-Americans because of the higher rates of end-organ damage, specifically, renal disease with and without diabetes, left ventricular hypertrophy (LVH), left ventricular systolic dysfunction, and heart failure [5].

The effect of ramipril versus amlodipine on renal outcomes in hypertensive blacks with nephrosclerosis in a recent randomized controlled trial, the African-American Study Kidney Disease (AASK), demonstrates that among participants with a urinary protein to creatinine ratio of greater than 0.22 (corresponding approximately to proteinuria of more than 300 mg/d), the ramipril group had 36% (2.02 [SE, 0.74] mL/min per 1.73 m²/y) slower mean decline in glomerular filtration rate over 3 years ($P = 0.006$) and a 48% reduced risk of clinical endpoints versus the amlodipine group (95% CI, 20%–66%) [12•].

Although in the entire cohort of black patients randomized there was a nonsignificant difference in mean glomerular filtration rate, this study confirms that ACE inhibition in hypertensive blacks with evidence of nephrosclerosis retards renal disease progression [12•]. Further study awaits confirmation of the benefit of ACE inhibition in African-Americans with hypertension and heart failure. Nevertheless, a preliminary post-hoc analysis of 810 African-Americans with atherosclerotic heart disease during a 10-year follow-up showed ACE inhibitor therapy improved survival by 80%, whereas calcium channel blocker therapy increased mortality [13].

Diuretic antihypertensive therapy is equally efficacious in both African-Americans and whites, and the addition of diuretic therapy increases the efficacy of ACE inhibitors, angiotensin receptor blockers, and β-adrenergic blockers [5,7]. Presently in the evidence-based medicine, the approach to hypertension and systolic heart failure should be diuretics in uncomplicated hypertension and the addition of diuretics when needed to agents that modulate the RAA system in blacks. This approach will potentially decrease the risk of heart failure in this population specifically related to uncontrolled hypertension.

### Coronary Heart Disease in African-Americans

Coronary heart disease (CHD) remains a predominant cause of systolic heart failure in most clinical trials of morbidity and mortality. Nevertheless, hypertension appears the predominate cause of systolic heart failure in African-Americans. African-Americans have the highest rates of overall CHD mortality, and the highest out-of-hospital coronary death rates than any other ethnic group in the United States, particularly at younger ages [14]. Sudden cardiac death as the initial manifestation of CHD is considerably higher in African-Americans than whites [14].

The reason for the earlier onset and excess CHD and mortality in African-Americans has not been fully elucidated. Levels of dyslipidemia including elevated total and low-density lipoprotein cholesterol appear to be similar in the African-American population versus whites [14]. However, there is an increased clustering of risk factors in African-Americans greater than in the general population.

### Table 1. Disproportionate risk factors for heart failure in African-Americans

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
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<tbody>
<tr>
<td>High prevalence and severity of hypertension</td>
<td></td>
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<tr>
<td>High prevalence of type 2 diabetes mellitus</td>
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<tr>
<td>High prevalence end-stage renal dysfunction</td>
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<td>High incidence of morbidity and mortality with left ventricular hypertrophy</td>
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<tr>
<td>Increased cigarette use</td>
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<tr>
<td>High prevalence of coronary artery disease</td>
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