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RACE/ETHNICITY: IS IT AN OUTCOME PREDICTOR IN PATIENTS WITH HEART FAILURE?

by

DIGANT V BHATT

M.B.B.S., GEORGIA STATE UNIVERSITY, 2006

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RACE/ETHNICITY: IS IT AN OUTCOME PREDICTOR IN PATIENTS WITH HEART FAILURE?

by

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Reference: References available on request

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Abstract

Objective:

The aim of this study was to determine the role of race as a significant risk factor for prediction of outcomes in heart failure (HF).

Methods:

The data was collected on demographics, detailed history of HF, family history, vital signs, medication and laboratory profile for 585 patients from Heart failure Treatment Center of Emory University after year of 2000. Outcome of HF was defined as combination of death, placement of left ventricular assisted devise, heart transplant or emergency transplant. The independent relationship between race and outcomes of HF was evaluated by univariate and multivariate logistic regression analyses. The survival analysis was done by Cox regression modeling.

Results:

Among 585 HF patients, 58.1% were whites and 41.9% were blacks and 28.2% HF patients had positive outcomes. Although Whites tended to have a more positive outcome (34.6%) than blacks (28.9%), the difference was not statistically significant. Factors predicting the outcome in whites were male gender (OR 5.02), history of hypertension (OR 2.3), ventricular arrhythmias (OR 2.4), placement of AICD(OR 0.09), low EF% (OR 0.95), high NYHA class (OR 3.25), use of beta blockers (OR 0.12), aldosterone blockers (OR 2.19), furosemide (2.18); while in blacks they were age in years (OR 0.96), history of PTCA (OR 7.04), dislipidemia (OR 3.90), depression (OR 0.01), placement of AICD (OR 0.14), low EF% (OR 0.92), systolic blood pressure (OR 0.96),

high NYHA class (OR 4.01), use of beta blockers (OR 0.14), torsemide (OR 2.86), and digoxin (OR 4.91) etc. Blacks had higher survival than whites ($p < 0.001$).

Conclusion:

There is no significant difference in combined outcome (death, transplant, emergency transplant, and Left Ventricular Assisted Devise placement) of HF between whites and blacks. There are differences regarding the risk factors, which are more prominent in each race. Further exploration is required to evaluate the race as significant risk factor for predicting the outcome in HF.

Chapter I Introduction

Definition of Heart Failure:

Heart Failure (HF) is a condition in which heart is unable to pump sufficient blood for metabolizing tissues or can do so only from an abnormally elevated filling pressure (Kasper et el). From the point of hemodynamics, HF is defined as a pathophysiologic condition in which impaired cardiac performance is the cause for inability of the heart to increase cardiac output, at normal filling pressure to meet the metabolic demands of the body (Zevitz M. 2008). HF is considered as a syndrome with a variety of cardiac and systemic abnormalities.

Annually more than 350, 000 people die because of sudden cardiac death and the major risk factor for this is heart failure with left ventricular systolic dysfunction (Thom, Haase et al. 2006) (Hernandez, Fonarow et al. 2007). HF affects 4.7 million people in United States and 550,000 new cases are added every year (East, Peterson et al. 2004). It is a leading cause of mortality, morbidity and hospitalization in individuals with age of 65 years and older (Ruo, Capra et al. 2004). Furthermore, as the age advances the risk of HF will increase and the most growing population is geriatric population in the United States, so in upcoming years the number of patients with heart failure will be substantially increased (Ruo, Capra et al. 2004). All these explain why HF remains a significant public health concern and why the prediction of incident of HF and the prediction of HF outcomes are important fields of investigation.

There are lots of causes and risk factors for development of HF. Risk factors can also be associated with development or progression of HF and some of them are

associated with both. Age and gender are consistently related to risk of development of HF; male gender and older age increases the risk significantly (McKee, Castelli et al. 1971). In the United States, the major leading cause of systolic HF is coronary artery disease (Tsao and Gibson 2004). The other major cause for HF is hypertension and it increases the risk of development of HF by two to three times (Chen, Vaccarino et al. 1999). Without coronary artery disease the lifetime risk for development of HF in patients with hypertension is 1 in 9 men and 1 in 6 women (Lloyd-Jones, Larson et al. 2002). In addition, patient with metabolic syndrome which consists of diabetes, hypertension, hyperlipidemia and obesity are at increased risk for development of HF. Diabetes alone is an important risk factor as it is also associated with ischemic heart disease and subsequent HF. Other independent risk factors are obesity, smoking, valvular heart disease, renal insufficiency, sedentary life style, left bundle branch block and family history of cardiomyopathy. (Tsao and Gibson 2004)

There is always a question that whether race plays a role for variation in risk factor, etiology and outcome of heart failure. This is because studies have indicated that blacks were more likely to have noniscemic etiology and whites were more like to have ischemic etiology for HF (Thomas L. K. et al 2005). In addition, treatment for heart failure differs in these two races e.g. blacks are more likely to be on Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARBs) because of more prevalence of hypertension in blacks and less likely to be on beta blockers because of low ischemic etiology for heart failure (Deswal, Petersen et al. 2006). Apart from that, Blacks are at high risk of having significant co-morbidities like obesity, hypertension, diabetes, renal disease, more severely reduced ejection fraction, which can

put them for worse outcome of heart failure (Thomas L. K. et al 2005). Studies have shown that Blacks have higher rates of hospitalization than Whites and also some studies have suggested that race is not an independent predictor of mortality in CHF (Carroll, Mulla et al. 2007). It has been suggested that African American patients with HF may have lower prevalence of Atrial Fibrillation than Caucasian (Vaccarino, Gahbauer et al. 2002). Some studies have found higher risk of mortality in African American compared to Whites even after adjustment of other predictors of mortality, randomized treatment assignment, baseline imbalances between races and indicators of socioeconomic status (Mitchell E. J et al. 2005). According to some studies on renal transplant, in Blacks the most common etiologies for development of end stage renal disease are diabetes mellitus and hypertension. Many factors have been implicated for this finding including excess salt intake, genetic variation in drug response and socioeconomic factors which limits the access to health care (Flattery and Baker 2004). Also studies have suggested that Blacks are less likely to be referred to renal transplant by their dialysis center (Wolfe 2003). According to surveys Blacks are less likely to be referred for kidney transplant than Whites (King, K. 2000).

Because of aforementioned reasons, the exploration of the role of race as a significant risk factor for prediction of outcomes in HF is still important, so the aim of this study is to determine this relation.

The questions which will be addressed are:

1). Is there any difference in outcomes of HF between Whites and Blacks?

2). Do the predictors of outcome vary between Whites and Blacks?

Chapter II Literature Review

Mechanism of Heart Failure:

The inciting event in development of HF is the inadequate adjustment of cardiac muscles to increased wall stress to maintain adequate cardiac output following injury to myocardium. Most important things for this adaptation are: 1) Frank-Starling Mechanism – increase in preload helps to maintain cardiac performance 2) Hypertrophy of cardiac myocytes with or without cardiac chamber dilatation; 3) Neurohumoral system activation, particularly norepinephrin release by cardiac adrenergic nerve endings, and the activation of rennin-angiotensin-aldosteron system (RAAS) help to maintain arterial pressure and perfusion to vital organs (Zevitz M., emedicine 2006).

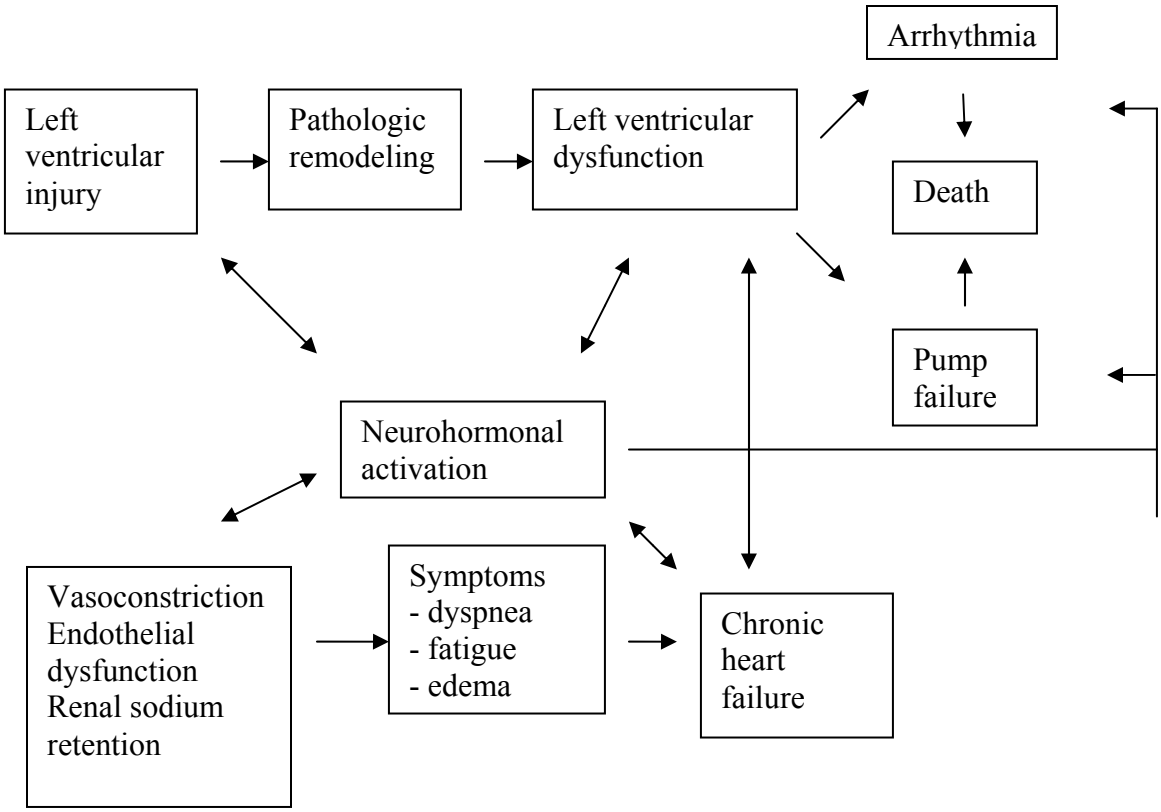

Figure 2.1. Pathophysiology for development of HF (Tsao and Gibson 2004)

Symptoms treatment and Outcome of Heart Failure:

The cardinal symptom of Heart Failure is Breathlessness. With increase in severity it manifests as exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, dyspnea at rest and acute pulmonary edema. Apart form this, patient also experiences fatigue and weakness because of poor perfusion of skeletal muscles. Because of poor perfusion of brain patient might complain of confusion, memory impairment anxiety, and headaches (Zevitz M., emedicine 2006).

Treatment for heart failure includes both nonpharmacologic and pharmacologic modalities. Nonpharmacologic measures are very important for successful management of heart failure. The first attempt is to further decrease the risk of recurrent cardiovascular injury with the control of hypertension, hyperlipidemia, diabetes, smoking cessation, weight reduction for obese patient, and participation in a well organized exercise program should be encouraged. Patients with HF are at risk for infection which can cause worsening of heart failure. Therefore, pneumococcus, influenza and hepatitis vaccinations are recommended in these patients (Tsao and Gibson 2004).

Various kinds of medications are available to treat congestive heart failure. Most of the patients receive multiple drugs for heart failure. Drugs for heart failure includes Angiotensin-converting enzyme inhibitors e.g. enalapril, lisinopril – they are the mainstay drug for heart failure which decreases the mortality. Other drug decreases mortality in heart failure patients is beta-blocker which also lowers the blood pressure and decreases the heart rate (Norgard and Stark 2008). Other drugs used in treatment of heart failure are diuretics, spironolactone, digoxin, nersitide. Diuretics have some mortality benefits according to some clinical trials (Pitt, Zannad et al. 1999). Apart from

heart failure medications, patients also receive nitrates for chest pain, calcium channel blocker to lower blood pressure and improve circulation, antiarrhythmics to prevent abnormal electric rhythm of the heart, and blood thinners to help prevent blood clots. In case of severe heart failure treatment by surgery and medical devise therapy are necessary. They are heart valve repair or replacement, coronary bypass surgery, heart transplant, ventricular assisted devise placement, cardiac pacemakers, and defibrillators. (Mayo clinic 2008).

Different studies have taken different measures as outcome of HF. Some studies have taken the outcome as death, rehospitalization, in hospital complication rates including myocardial infarction, admission to coronary care unit or intensive care unit (ICU), renal failure, hypotension, shock and the need for mechanical ventilation (Bhatia, Tu et al. 2006). Study by Smith et al. has taken clinical outcomes of heart failure as death, decline in functional status and readmission to hospital due to cardiac reasons (Smith, Masoudi et al. 2003). Myers et al. study has taken his end point for heart failure as cardiac related mortality. In his study two other end points also has been studied and they are cardiac transplantation and left ventricular assisted devise placement (Myers, Arena et al. 2008).

The studies on heart failure and outcome suggest that, more often, Black patients have hypertension, diabetes, renal insufficiency, more symptomatic heart failure by New York Heart Association (NYHA) HF classification. Also Blacks have low ischemic etiology for heart failure and less previous percutaneous coronary intervention or coronary artery bypass grafting. Where as Whites have more myocardial infarction as

etiology for heart failure and multi vessels coronary artery disease (Thomas, East et al. 2005).

Study suggests that Black patients with mild to moderate left ventricular dysfunction are at high risk for progression to severe heart failure and death from any cause than White patients with similar type of left ventricular dysfunction (Dries, Exner et al. 1999). Studies also suggest that the higher mortality in Black patients than in White patients have been due to differences in severity and cause of heart failure, more prevalence of coexisting conditions in Blacks, socioeconomic and cultural factors, and access to high quality medical care (1990; Alexander, Grumbach et al. 1995). Some of the studies suggest higher mortality in Blacks with heart failure. However, recent statewide study on hospital discharge data on congestive heart failure patient suggests lower case fatality rate in Blacks than their counter part (Philbin and DiSalvo 1998).

A recent study on heart failure prognosis by race and etiology has taken the outcome of heart failure as death or rehospitalization or both. In this study there is no significant difference in unadjusted and adjusted mortality rates in whites and blacks at the end of 1 and 5 years. In this study mortality rates are also examined by ischemic and nonischemic etiology which shows that at the end of 5 years, mortality rate is different in nonischemic left ventricular systolic dysfunction e.g. Blacks have higher mortality rate compare to Whites. Also this study has suggested several variables predictive of decrease survival in patients with left ventricular systolic dysfunction including renal insufficiency, diabetes, history of connective tissue disease, valvular disease, and peripheral vascular disease. Also in this study there are two other predictors for

rehospitalization and they are renal disease and ischemic etiology of heart failure (Thomas, East et al. 2005).

A study by Mathew et al. suggest that Blacks have higher risk for rehospitalization than Whites but the reason for this finding is not clear. They suggested that cardiomegaly and diabetes have quantitatively different effect in both the races. This study also suggest that difference in morbidity of HF in Blacks and Whites are more likely due to difference in other co-morbid conditions such as diabetes, hypertension etc., socioeconomic factors such as attitudes, access to health care; difference in lifestyle and psychological factors like depression, stress; and not due to biological differences.

Renal impairment is a critical risk factor for outcome measure in HF patients because renal impairment increases the risk for death and rehospitalization (Smith, Vaccarino et al. 2003). A study on race and renal impairment in HF suggests that Whites with impaired renal function have greater risk for death than Blacks with renal impairment (Smith, Shlipak et al. 2005). According to Carson et al. HF is associated with poor prognosis in Blacks than in Whites. This study was aimed to determine the racial difference in response to treatment for HF. This study suggested that combination of hydralazine and isosobide dinitrate combination is associated with reduction in mortality in Black patients with HF. The ACE inhibitors are not much effective in these patients because of less active rennin-angiotensin system in Blacks (Carson, Ziesche et al. 1999).

Chapter III Methodology

Study Design:

As described earlier in the introduction, this study was conducted with the aim to describe the racial differences in the outcomes and the predictors of outcomes in patients with HF. This is a retrospective cohort study design.

Data Collection and Variable definition:

All patients seen by Heart Failure Treatment Center of Emory University after year of 2000 are included in this study. Inclusion criteria for this study were 1) age ≥18, 2) patients should have systolic HF, 3) ejection fraction ≤ 45 documented within 6, months of evaluation, 4) Patients should be on optimal therapy for HF e.g. on beta blocker, ACE inhibitors, aldosterone receptor blocker, diuretics, 5) New York Heart Association class II-IV

Based on these criteria, data was collected for 606 patients. Out of these, 18 patients were excluded from the study because of non-white, non-black race. All data was collected from the hospital and the HF clinic electronic databases. Data regarding patient's age, sex, race, etiology for HF, history of myocardial infarction, coronary artery bypass, angioplasty, atrial arrhythmias, ventricular arrhythmias, placement of cardiac devices like biventricular pacemakerr, defibrillator or both, other co- morbidities like diabetes, hypertension, dyslipidemia, chronic lung diseases, sleep apnea, thyroid disorder, depression, cerebrovascular accident, malignancy, history of smoking and alcohol consumption was collected. Also, data was recorded for family history of premature ischemic heart disease and idiopathic dilated cardiomyopathy. Index date was determined as the first available date after year of 2000 where the patients were stable, on optimal

medical treatment and most of the laboratory tests were available (Deswal, Petersen et al. 2006). On the evaluation date, data was collected on height, weight, ejection fraction, NYHA class, heart rate, systolic blood pressure, diastolic blood pressure, and patient's medications. The categories of collected medications were ACE inhibitors, Angiotensin Receptor Blockers (ARB), beta blockers, statins, ezetimibe, allopurinol, aldosterone blocker,diuretics (bumetanide, furosemide, torsemide, metolazone, hydrochlorthiazide), digoxin, aspirin, clopidogrel, oral nitrates, calcium channel blockers, antiarrhythmics, non-steroidal anti-inflammatory agents, warfarin, antidepressants, antianxiety agents, and antidiabetic medications. In addition data on patient's laboratory tests such as White Blood Cell count, Red Blood Cell count, hemoglobin, hematocrit, Red Cell Distribution Width (RDW), platelet, mean platelet volume, lymphocyte percentage, blood metabolic profile, cardiac enzymes, serum lipid profile, and thyroid stimulating hormone.

Study outcome was defined as a combination of death, placement of left ventricular assisted device, emergency heart transplant and transplant, while survival period was defined as the time period between the patient's index date and the patient's last follow up visit. Left Ventricular assisted devise is a mechanical devise that is implanted surgically. It helps to maintain the ability of the heart to pump blood. It is used in people waiting for heart transplantation, so it is also known as "bridge to transplant. For analysis purposes, the etiology of HF was defined as either ischemic or non-ischemic cause. Non-ischemic causes are characterized the following conditions: idiopathic dilated cardiomyopathy, hypertensive cardiomyopathy, cardiomyopathy because of valvular heart disease, post partum cardiomyopathy, cardiomyopathy due to chemotherapy, and myocarditis. According to New York Heart Association, symptoms of HF was

categorized into four classes: Class I patients with no limitation of activities; they suffer no symptoms from ordinary activities, Class II patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion, Class III patients with marked limitation of activity; they are comfortable only at rest, Class IV patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest (2009). Recent smoking was defined as smoking during the last two years but not currently smoking and former smoking was defined as quitting smoking two years before the index date. Former alcohol consuming was defined as quitting alcohol consumption two years before the index date. As chronic lung diseases was consider Chronic Obstructive Lung Disease, asthma, and restrictive lung disease e.g. pulmonary fibrosis, sarcoidosis.

Statistical Analysis:

The demographics, clinical characteristics, treatment, and laboratory values of patients with HF were compared in Whites and Blacks and in patient subgroups with positive outcome and no outcome. In addition both combined outcome and each component of the outcome were compared in Whites and Blacks. Chi-square test was used for dichotomous variables and student's t-test was used for continuous variable (Bhatia, Tu et al. 2006). In this study missing laboratory values were imputed using mean values of the cohort study for that parameter (Deswal, Petersen et al. 2006).

Univariate logistic regression analysis was performed to identify which variables were associated with the outcome of HF in each group e.g. Blacks and Whites. This was done individually in Whites and Blacks without doing comparison in between these groups. This analysis was done using all the variables mentioned above.

Finally, multivariate logistic regression analysis was performed to determine which variables affect the outcome in Whites and Blacks. It was performed by using backward analysis method. Risk adjustment was done by controlling simultaneously for covariates used in univariate analysis. The aim of this analysis was to find all the factors which affect the outcome of HF in Whites and Blacks. Some of the variables were eliminated from the analysis because in one group their values were less than 5 and so cannot perform logistic regression and they were weight, height, diastolic blood pressure, history of thyroid disease, atrial arrhythmias; in the drugs they were ezetimibe, bumetanode, clopidogrel, oral nitrates, NSAIDS, anti-anxiety, Sulfonylurea, Biguanide, Thiazolidinedine; in the laboratory variables some of them were uric acid, Beta natriuretic peptide, total cholesterol, triglycerides, low density lipoprotein (LDL), high density lipoprotein (HDL)etc. In both univariate and multivariate analyses, first variable was taken as reference value e.g. female in gender, no smoking in smoking, no history of sleep apnea in History of sleep apnea etc.

Cox regression analysis was performed to evaluate the survival in White and Black patients with HF. Survival curve was also constructed.

The statistical analysis was done with Statistical Package for Social Science (SPSS) for windows version 16.

Chapter IV Results

Data of 585 patients were analyzed. Out of these, 340 patients were Whites and 245 patients were African Americans. The study outcome was observed in 165 patients with HF. Clinical characteristics, which were statistically significant between Whites and Black, described in Table 1. Whites have higher proportion of male, lower proportion of former smokers, more ischemic etiology for HF, history of myocardial infarction, history of PTCA and CABG, dyslipidemia, and EF% compared to blacks. However, blacks were younger, more female population, more current smokers, high proportion of non-ischemic cause for heart failure, hypertension, history of CVA, and family history of dilated cardiomyopathy, high heart rate, systolic BP, and low EF% compared to whites. Appendix 1 shows all the other findings of the clinical variables which also include the findings of table 1.

In Table 2 are shown the medication and laboratory characteristics; those are statistically significant for white and black patients with HF; all the values are shown in Appendix 2. Whites were using more ACE inhibitors, statins, antidepressants, and antianxiety medications; while blacks were using more aldosterone blockers. Whites had higher level of hemoglobin, serum potassium, and triglyceride and blacks had high level of platelets, mean platelet volume, serum sodium, uric acid, and HDL.

Table 1. Clinical Characteristics of Heart Failure in Whites and Blacks.

Variable	*Whites*	*Blacks*	*P-value*
Gender			**<0.001**
Male	75.9%	56.7%	
Female	24.1%	43.3%	
Smoking			**<0.05**
Never Smoke	44.9%	51.0%	
Smoker	18.9%	23.8%	
Former Smoker	36.1%	25.2%	
Primary Cause of HF			**<0.001**
Ischemic	52.1%	22.3%	
Non-Ischemic	47.9%	77.7%	
History of Myocardial Infarction			**<0.001**
Yes	46.2%	20.3%	
No	53.8%	79.7%	
History of CABG			**<0.001**
Yes	31.0%	9.6%	
No	69.0%	90.4%	
History of PTCA			**<0.001**
Yes	21.9%	9.6%	
No	78.1%	90.4%	
Hypertension			**<0.001**
Yes	52.5%	75.7%	
No	47.5%	24.3%	
Dislipidemia			**0.001**
Yes	54.8%	39.6%	
No	45.2%	60.4%	
History of CVA			**<0.05**
No	87.2%	80.4%	
Yes	12.8%	19.6%	
F/H of Dilated Cardiomyopathy			**<0.05**
No	75.5%	70.0%	
Yes	5.0%	12.2%	
No Mention	19.4%	17.3%	
Age	55.68±11.39	49.22±13.21	**<0.001**
Height (Inches)	69.83±3.58	66.93±3.95	**<0.001**
Heart Rate at visit	74.59±12.85	79.89±15.85	**<0.001**
Systolic BP	113.32±19.12	119.06±19.32	**<0.001**
EF%	**21.50±11.17**	**17.89±9.4**	**<0.001**

Table 2. Drugs and Laboratory profiles in Whites and Blacks

Variable	*Whites*	*Blacks*	*P-value*
ACE-I	75.0%	66.1%	**<0.05**
Statin	54.7%	34.0%	**<0.001**
Aldosteron Blocker	38.6%	50.6%	**<0.01**
Antidepressant	36.0%	18.6%	**<0.05**
Antianxiety	20.0%	4.7%	**<0.05**
Hgb	13.64±2.66	12.97±1.80	**0.001**
Platelet(×10E3)	228.97±71.98	251.49±87.08	**0.001**
Mean Platelet Volume	8.72±1.06	9.26±1.09	**0.01**
Lymphocyte%	23.40±7.8	26.45±9.02	**<0.001**
Na+	137.24±3.22	137.99±3.1	**<0.01**
K+	4.15±0.54	3.95±0.49	**<0.001**
Uric Acid	8.3±0.88	8.5±1.1	**<0.05**
BNP	649.51±845.86	981.37±1171.99	**<0.05**
Triglyceride	168.49±138.24	114.79±132.50	**<0.001**
HDL	38.67±12.27	44.65±13.67	**0.099**

In Table 3 are shown the clinical characteristics in patients with outcome and those without outcome. In this table only statistically significant variables are described and all the clinical characteristics are described in Appendix 3. Patients with adverse outcome of HF had more males, high never consumers of alcohol and former consumers of alcohol, high proportion of ischemic cause for HF, never users of CPAP, hypothyroidism, depression, atrial tachycardia, ventricular arrhythmias, high heart rate, NYHA class, and low EF%. Patients with better outcome of HF had more females, high current consumers of alcohol, high proportion of non ischemic cause for HF, history of sleep apnea, use of CPAP, no thyroid disorders, no depression, family history of dilated cardiomyopathy, paroxysmal atrial fibrillation/flutter, paroxysmal supraventricular tachycardia, use of AICD, high systolic BP, and EF%.

Table 3. Clinical Characteristics by Outcome of Heart Failure.

Variable	***Outcome Positive***	***Outcome negative***	***P-value***
Gender			**<0.05**
Male	75.2%	65.6%	
Female	24.8%	34.4%	
Alcohol Consumption			**<0.05**
No Drinker	65.2%	55.6%	
Drinker	20.0%	32.8%	
Former Smoker	14.8%	11.6%	
Primary Cause of Heart Failure			**<0.05**
Ischemic	46.0%	37.2%	
Non-Ischemic	54.0%	62.8%	
History of Sleep Apnea			**<0.001**
No	75.8%	80.9%	
Yes	14.3%	18.0%	
No Mention	9.9%	1.2%	
History of CPAP			**<0.001**
No	82.4%	87.9%	
Yes	6.9%	10.9%	
No Mention	10.7%	1.2%	
Thyroid Disorder			**<0.01**
No Disorder	78.2%	82.5%	
Hyperthyroidism	17.3%	17.5%	
Hypothyroidism	4.5%	0%	
Depression			**<0.01**
No	66.2%	78.5%	
Yes	27.5%	20.3%	
No Mention	6.2%	6.2%	
F/H of Dilated Cardiomyopathy			**<0.05**
No	76.6%	64.9%	
Yes	8.9%	9.4%	
No Mention	14.67%	25.7%	
Atrial Arrhythmias			**<0.01**
No Atrial Arrhythmias	59.9%	48.6%	
Paroxysmal Atril Fibrillation/Flutter	14.8%	17.8%	
Chronic Atrial Fibrillation/Flutter	19.1%	19.7%	
Atrial Tachycardia	3.1%	1.2%	
Paroxysmal Supraventricular Tachycardia	0%	5.8%	
No Mention	3.1%	6.9%	

Ventricular Arrhythmias			**<0.05**
No	43.2%	50.2%	
Yes	53.1%	41.0%	
No Mention	3.7%	8.8%	
AICD			**<0.01**
No	78.3%	66.5%	
Yes	21.7%	33.5%	
Heart Rate at visit	79.74±15.61	76.22±13.13	**<0.05**
Systolic BP	110.92±19.68	116.25±18.67	**<0.01**
NYHA at Visit	2.80±0.72	2.37±0.63	**<0.001**
EF%	**17.05±8.87**	**19.77±9.03**	**<0.01**

Table 4 shows the medication and laboratory profile of patients regarding the outcome subgroups. In this table, only statistically significant variables are described and all the variables are described in appendix 4. Patients with adverse outcome of HF were using less beta blockers, more aldosterone blockers, torsemide, digoxin, antiarrhythmics; while the patients with better outcome were using more beta blocker and thiazolidinediones. Adverse outcome of HF patients had high serum BUN, and creatinine patients with better outcome of HF had high platelet count, lymphocyte%, high serum sodium, BNP and triglyceride.

Table 4. Drugs and Laboratory Profile for Outcome of Heart Failure Patients.

Variable	***Outcome Positive***	***Outcome negative***	***P-value***
Beta-Blocker	76.4%	95.1%	**<0.001**
Aldosteron Blocker	51.5%	41.3%	**<0.05**
Torsemide	34.5%	17.5%	**<0.001**
Digoxin	66.7%	44.5%	**<0.001**
Antiarrhythmics	38.8%	27.3%	**<0.01**
Thiazolidinedione	0%	10.3%	**<0.05**
Platelet(×10E3)	229.22±71.84	244.42±85.01	**<0.05**
Lymphocyte%	21.85±8.15	25.40±7.44	**<0.001**
Na+	136.5±3.21	138.03±3.1	**<0.001**
BUN	25.80±13.87	21.38±16.81	**<0.01**
Creatinine	1.58±1.38	1.30±0.72	**<0.05**
Uric Acid	8.4±1.69	8.4±0.43	
BNP	1.32±1331.61	6.5±843.57	**<0.001**
Triglyceride	**123.25±73.45**	**155.29±158.65**	**<0.05**

Table 5 presents the differences in combined outcome and each component of the outcome between Whites and Blacks. According to this table, 34.6% of Whites and 28.9% of Blacks had positive outcome, but this difference is not statistically significant. A percentage of 18.3% of Whites had died while a 22.9% of Blacks had died. Although Blacks had more death than Whites, this difference is not statistically significant. Moreover, a percentage of 0.9% of Whites and a percentage of 0.4% of Blacks had placement of left ventricular assisted devise and this is not statistically significant, while a percentage of 12.6% of Whites and a percentage of 6.5% of Blacks had received heart transplant which is statistically significant. A 3.3% of Whites and a 2.8% of Blacks had received emergency heart transplant as a treatment of HF, which is not statistically significant.

Table 5. Outcome of Heart Failure by Race

Variables	White	Black	P-value
Outcome	34.6%	28.9%	0.16
Death	18.3%	22.9%	0.17
VAD	0.9%	0.4%	0.49
Transplant	12.6%	6.5%	<0.05
Emergency Transplant	3.3%	2.8%	0.70

Table 6 shows the relationship of individual variables and outcome in Whites and Blacks. Factors decreasing the risk for adverse outcome and statistically significant were male (OR0.44), former smokers (OR 0.45), former consumers of alcohol (OR 0.38), history of CPAP use (OR 0.12), aldosterone blockers (OR 0.53), torsemide (OR 0.46), digoxin (OR 0.53), antiarrhythmics (OR 0.48), lymphocyte% (OR 0.89), and serum sodium (OR 0.87); while factors increasing adverse outcome and statistically significant were history of ventricular arrhythmias (OR 1.34), high NYHA class (OR 2.48), use of beta blockers (OR 6.28), and high serum BUN (OR 1.02). Factors decreasing the risk of adverse outcome and statistically significant were age (OR 0.96), use of CPAP (OR 0.08), high EF% (OR 0.91), high systolic BP (OR 0.97), use of beta blockers (OR 5.46), torsemide (OR 0.31), digoxin (OR 0.23), and serum sodium (OR 0.85). Factors increasing adverse outcome and statistically significant were history of hypertension (OR 3.16), ventricular arrhythmias (OR 3.47), NYHA class (OR 2.81), use of beta blockers (OR 5.46), furosemide (OR 2.19), and serum uric acid (OR 1.57).

Table 6. Relationship of Individual Variables and Outcome of HF by White and Black.

Variable	*Whites*		*Blacks*	
	OR	*CI*	*OR*	*CI*
Age (Yr)	1.006	0.98-1.02	**0.965**	**0.943-0.987**
Gender				
Male	0.44	0.230-0.844	**0.937**	**0.522-1.68**
Smoking				
Smoker	0.721	0.40-1.28	**0.955**	**0.460-1.98**
Former Smoker	0.455	0.22-0.93	**1.03**	**0.446-2.40**
Alcohol				
Drinker	1.02	0.46-2.28	**0.764**	**0.30-1.89**
Former Drinker	0.38	0.15-0.97	**0.605**	**0.22-1.64**
Primary Cause of HF				
Ischemic	1.34	0.56-3.17	**0.62**	**0.25-1.53**
Idiopathic	0.82	0.33-2.05	**0.48**	**0.22-1.03**
History of Myocardial Infarction	0.781	0.47-1.27	**0.98**	**0.47-2.04**
History of CABG	1.40	0.81-2.40	**0.82**	**0.31-2.16**
History of PTCA	1.09	0.60-1.98	**0.63**	**0.24-1.64**
Hypertension	0.69	0.41-1.16	**3.16**	**1.59-6.26**
Diabetes	0.85	0.49-1.46	**1.25**	**0.67-2.33**
Dislipidemia	0.92	0.55-1.56	**0.69**	**0.37-1.30**
History of Sleep Apnea				
Yes	0.11	0.02-1.54	**0.10**	**0.01-1.93**
No Mention	0.11	0.02-0.61	**0.007**	**0.00-0.68**
History of CPAP				
Yes	0.12	0.02-0.56	**0.08**	**0.01-0.74**
No Mention	0.09	0.01-0.54	**0.04**	**0.00-0.49**
History of Depression				
Yes	0.19	0.03-1.01	**0.11**	**0.01-1.04**
No mention	0.25	0.04-1.35	**0.26**	**0.02-2.69**
History of CVA	1.61	0.69-3.74	**0.40**	**0.18-1.87**
History of Malignancy	0.33	0.14-1.76	**1.39**	**0.46-4.15**
Family h/o premature				
ICM	1.82	0.92-3.59	**1.44**	**0.63-3.32**
Yes	2.69	0.19-6.17	**1.50**	**0.53-4.17**
No Mention in the history				
Family History of DCM				
Yes	2.36	0.19-4.70	**1.75**	**0.75-4.08**
No Mention	2.71	0.80-9.13	**1.21**	**0.37-3.91**
Atrial Arrhythmias				
Paroxysmal atrial	2.57	0.66-9.99	**3.04**	**0.62-14.82**

Fibrillation				
Chronic Atrial	2.31	0.54-9.90	**1.31**	**0.22-7.54**
Fibrillation	1.71	0.41-7.07	**3.09**	**0.55-17.16**
Atrial Tachycardia	4.50	0.49-41.24	**9.00**	**0.52-155.24**
History of Ventricular Arrhythmia				
Yes	1.34	0.39-4.57	**3.47**	**0.73-16.48**
No mention	2.37	0.70-8.00	**4.04**	**0.84-19.43**
Device	1.62	0.94-2.77	**1.26**	**0.69-2.29**
AICD	1.54	0.87-2.72	**2.23**	**0.12-4.44**
BivPaceAICD	1.39	0.83-2.30	**0.95**	**0.51-1.76**
BivPace	0.35	0.06-1.92	**0.50**	**0.03-6.43**
Height(In)	0.99	0.85-1.16	**1.49**	**1.00-2.23**
Weight (LB)	0.99	0.98-1.00	**1.00**	**0.98-1.02**
EF%	0.98	0.95-1.00	**0.91**	**0.86-0.95**
Heart Rate	1.01	0.99-1.03	**1.03**	**1.00-1.05**
Systolic BP	0.99	0.98-1.01	**0.97**	**0.95-0.98**
Diastolic BP	1.01	0.95-1.06	**0.93**	**0.84-1.02**
NYHA class	2.48	1.66-3.71	**2.81**	**1.74-4.53**
ACE Inhibitors	0.92	0.52-1.63	**1.51**	**0.82-2.75**
ARB	1.11	0.59-2.08	**0.73**	**0.38-1.42**
Beta-Blocker	6.28	2.88-13.69	**5.46**	**2.06-14.43**
Statin	0.90	0.55-1.46	**1.57**	**0.82-2.98**
Allopurinol	0.72	0.30-1.68	**0.69**	**0.19-2.46**
Aldosterone Blocker	0.53	0.32-0.87	**0.81**	**0.45-1.45**
Furosemdie	0.91	0.55-1.49	**2.19**	**1.21-3.97**
Torsemide	0.46	0.25-0.82	**0.31**	**0.16-0.59**
Metolazone	0.62	0.24-1.68	**0.37**	**0.12-1.12**
Hydrochlorothiazide	0.43	0.14-1.33	**3.81**	**0.47-30.73**
Digoxin	0.53	0.32-0.88	**0.23**	**0.12-0.46**
Aspirin	0.46	0.14-1.54	**0.37**	**0.06-2.14**
Calcium Channel Antagonist	0.21	0.09-1.49	**2.14**	**0.78-5.90**
Antiarrhythmics	0.48	0.28-0.79	**0.86**	**0.45-1.63**
Warfarin	0.75	0.23-2.42	**1.68**	**0.32-8.75**
Antidepressant	1.52	0.46-4.97	**1.10**	**0.06-20.01**
Insulin	3.00	0.45-19.92	**0.50**	**0.03-6.43**
Other drugs	2.12	0.49-9.07	**0.58**	**0.09-3.50**
WBC (10E3)	1.06	0.96-1.17	**0.98**	**0.85-1.12**
RBC (10E6)	0.48	0.13-1.68	**0.52**	**0.16-1.70**
RDW	1.06	0.83-1.37	**1.11**	**0.588-2.12**
HgB	1.01	0.90-1.13	**0.98**	**0.84-1.15**
Hct	0.96	0.92-1.00	**1.02**	**0.97-1.08**

PLT (10E3)	0.99	0.99-1.00	**0.99**	**0.99-1.00**
Mean Platelet volume	1.22	0.69-2.14	**1.64**	**0.59-4.54**
Lymphocyte	0.89	0.85-0.93	**0.98**	**0.95-1.02**
Na	0.87	0.80-0.94	**0.85**	**0.77-0.94**
K	0.81	0.52-1.27	**0.98**	**0.54-1.77**
CO2	1.22	0.95-1.57	**0.90**	**0.68-1.19**
Glucose	1.00	0.99-1.00	**0.99**	**0.98-1.00**
BUN	1.02	1.00-1.04	**1.01**	**0.99-1.02**
Creatinine	1.38	0.97-1.96	**1.37**	**0.99-1.88**
Protein total	0.80	0.28-2.28	**1.44**	**0.26-7.97**
Albumin	0.28	0.03-2.34	**0.91**	**0.70-11.81**
Uric Acid	0.56	0.38-1.81	**1.57**	**1.07-2.29**
Total Cholesterol	1.001	0.99-1.008	**0.99**	**0.98-1.001**
Triglyceride	0.99	0.99-1.00	**0.99**	**0.99-1.002**
HDL	0.99	0.92-1.07	**0.68**	**0.39-1.18**
LDL	1.00	0.98-1.02	**0.99**	**0.96-1.01**
TSH	1.11	0.93-1.33	**0.97**	**0.92-1.03**
BNP	**1.00**	**1.00-1.001**	**1.00**	**1.00-1.001**

Yellow highlight indicates the statistical significance.

Table 7 represents the multivariate logistic regression analysis of all the variables with HF outcome in White and Black patients. Factors significantly predict the outcome in Whites were males (OR 5.02), history of hypertension (OR 2.30), history of sleep apnea (OR 1.85), ventricular arrhythmia (OR 2.40), AICD (OR 0.09), EF% (0.95), NYHA class (3.25), use of beta blockers (OR 0.12), aldosterone blockers (OR 2.19), furosemide (OR 2.18), lymphocyte% (OR 0.70), serum BUN (OR 0.94). For Blacks they were age in years (OR 0.96), history of PTCA (OR 7.04), dyslipidemia (OR 3.90), depression (0.01), AICD (0.14), EF% (OR 0.92), systolic BP (OR 0.96), NYHA class (4.01), use of beta blockers (OR 0.14), torsemide (OR 2.86), digoxin (OR 4.91), WBC (OR 0.03), hemoglobin (0.00), hematocrit (OR 1.87), and lymphocyte% (OR 0.47).

Table 7. Relationship of individual variables with HF Outcome in Whites and Blacks in a multivariate model.

Variable	*Whites*		*Blacks*	
	OR	*CI*	*OR*	*CI*
Age (Yr)		-	0.96	0.92-1.00
Gender				-
Male	5.02	1.71-14.68		
History of PTCA		-	7.04	1.16-42.61
Hypertension	2.30	1.08-4.90		
Dislipidemia		-	3.90	1.21-12.55
History of Sleep Apnea				-
Yes	1.85	0.68-5.01		
No Mention	26.66	1.64-43.46		
History of CPAP		-		-
Yes				
No Mention				
History of Depression		-		
Yes			0.01	0.00-0.37
No mention			0.03	0.00-0.92
History of Ventricular Arrhythmia				-
Yes	2.40	1.06-5.45		
No mention	0.37	0.06-2.29		
AICD	0.09	0.03-0.28	0.14	0.04-0.49
EF%	0.95	0.91-0.99	0.92	0.86-1.00
Systolic BP		-	0.96	0.94-0.99
NYHA class	3.25	1.78-5.95	4.01	1.72-9.32
Beta-Blocker	0.12	0.05-0.28	0.14	0.04-0.43
Aldosterone Blocker	2.19	1.22-3.38		-
Furosemdie	2.18	1.03-4.58		-
Torsemide		-	2.86	1.42-5.74
Digoxin			4.91	2.37-10.15
WBC (10E3)		-	0.03	0.00-1.72
HgB		-	0.00	0.0-13.48
Hct		-	1.87	0.43-8.33
Lymphocyte	0.70	0.52-1.94	0.47	0.21-1.05
BUN	0.94	0.86-1.02		-

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Figure 4.1 represents the survival analysis by Cox regression model. As you can see

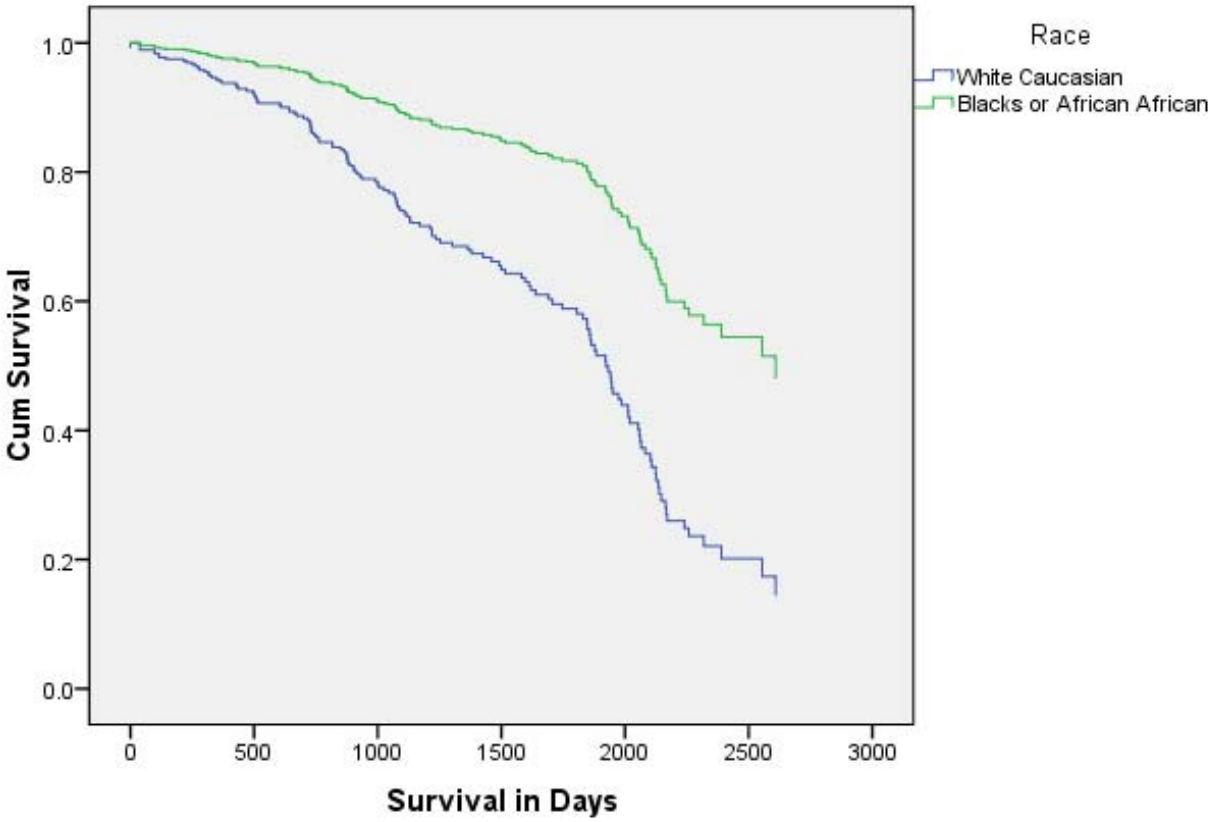

Figure 4.1 Survival analysis for HF patients in whites and blacks (P<0.001)

In this figure, Blacks have higher survival than Whites at the end of 2500 days. Also, the curve is steep for Whites than Blacks. The difference is statistically significant as the p-value is <0.001.

Chapter V Discussion

This is a retrospective cohort study examining the differences in the outcome of HF and predictors of HF outcome in Whites and Blacks. This study suggests that there is no significant difference in the combined outcome of HF even when each component of the outcomes was checked. However, an exception was observed regarding heart transplant as there was a statistically significant difference in transplant between Whites and Blacks. Generalizing this finding about the outcome might be tricky as the power is 0.42 which is not strong enough for something like this. There are studies describes the difference of renal transplant in between Whites and Blacks (Flattery and Baker 2004). One of these studies has shown that Blacks are less likely to be referred for the renal transplantation by their dialysis center and this could be due to poor antigen matching, unfavorable socioeconomic factors and immunological differences. Furthermore, Black patients are less likely to find living identical donors than Whites. The socioeconomic disadvantage is best represented by outcome based on insurance provider. Those who have private insurance are tend to survive more (Flattery and Baker 2004). This study could explain the difference in the transplant and HF outcome in Whites and Blacks. There is also a study suggests that after heart transplantation Blacks have higher overall rejection and hospitalization rates. (Pamboukian, Costanzo et al. 2003)

From the univariate analysis the factors which are important for predicting the outcomes in Whites are male gender, former smoker, former alcohol users, history of sleep apnea, history of CPAP users, high NYHA class, use of beta blocker, aldosterone blockers, torsemide, digoxin, and antiarrhythmics, high percentage lymphocyte count, high serum sodium, high serum BUN, and low serum uric acid levels. However the

predicted factors in Blacks are age, history of hypertension, sleep apnea, and CPAP use, AICD placement, height, EF%, systolic blood pressure, and NYHA class, use of beta blockers, furosemide, torsemide, digoxin, sodium and uric acid and there are some differences compared to Whites. Thus, from this analysis we can say that some of the variables are different between the Black and White races regarding prediction of outcome.

This study suggested that Blacks who develop HF are younger compared to Whites and they also receive heart transplant at younger age than Whites (Pamboukian, Costanzo et al. 2003; Flattery and Baker 2004). Furthermore, blacks tend to have more hypertension and diabetes than Whites and according to United States renal data system (1999) African Americans have highest rate of hypertension, so hypertension is an important risk predictor for Blacks. In Whites, male gender has worst outcome which might be due to predominant male population in this dataset. Also, in Whites, have left smoking and alcohol consumption has low risk for positive outcome. Alcohol consumption is associated with direct myocardial toxicity and risk for hypertension development. So former alcohol consumption is associated with more adverse outcome.(Marmot, Elliott et al. 1994) Smoking is associated with oxidative stress, endothelial dysfunction and insulin resistant which can lead to worst outcome. However, patients with history of past smoking seem to have lower risk for adverse outcome (Gvozdjakova, Kucharska et al. 1992). There is a study demonstrating that sleep apnea leads to adverse hemodynamic, autonomic and inflammatory consequences in both Whites and Blacks patients with ischemic cardiomyopathy, but not in non ischemic cardiomyopathy and leads to worse outcome in patients with HF (Yumino, Wang et al.

2009). It has been postulated that AICD reduces mortality in patients with HF due to reduced left ventricular function. Also several studies suggest that Blacks have lower rate of AICD placement than Whites, so according to these studies AICD reduces the adverse outcome in Blacks (Bardy, Lee et al. 2005; Hernandez, Fonarow et al. 2007). This study was conducted on patients with systolic HF with very low ejection fraction. Higher ejection fraction leads to better cardiac output and better perfusion of sensitive organs like kidney, brain etc, so it decrease mortality significantly. According to studies ejection fraction interacts with mean arterial pressure for predicting mortality, so it is an independent risk factor of survival in patients with HF (Adamopoulos, Zannad et al. 2007). In both Whites and Blacks, NYHA classification is a risk factor for prediction of outcome. NYHA classification is given for assessing the severity of HF and functionality of patient with HF. As the classification advances from class II to class IV, the functional status of the patients decreases, patient becomes bedridden, outcome will be worst in these patients (Hurst, Morris et al. 1999). Studies also suggest that systolic blood pressure is a risk predictor for outcome of HF. High systolic blood pressure, but within normal range increases the survival of patients with HF irrespective of etiology for HF (Lee, Chen et al. 2006; Adamopoulos, Zannad et al. 2007). However, in this study, systolic blood pressure is a significant risk predictor in Blacks but not in Whites.

It has been postulated that use of beta blocker in HF decreases the mortality in HF patients. However, according to the univariate analsysis of this study, beta blocker increases the risk of positive outcome in both Whites and Blacks. Although, use of carvedilol has been prove effective in both the races in decreasing the mortality.(Yancy, Fowler et al. 2001) This effect can be due to unadjustment of beta blocker use with other

variables and discussed in more detail later in this chapter. In Blacks use of furosemide increases the risk for adverse HF outcome and this might be due to relative hypovolemia in Black population. Apart from that Aldosterone blocker is more effective in Whites than Blacks because Blacks have relatively low level of renin-angiotensin-aldosterone system level and that is the reason that aldosterone blockers are not much effective in Blacks than in Whites. Also, ACE inhibitors are less effective in Blacks and this is due to above mentioned reason plus ACE gene polymorphisms in Whites and Blacks. (Bloem, Manatunga et al. 1996) Studies have suggested that digoxin has favorable effect in decreasing hospitalization and mortality from HF. (1997; Mathew, Wittes et al. 2005)

According to multivariate model, in Whites important predictors are male gender, hypertension, history of ventricular arrhythmias, AICD, EF%, NYHA class, beta blocker, Aldosterone blocker, furosemide, and lymphocyte when adjusted for other co-variates used in univariate analysis. For Blacks important factors are age, history of PTCA, dyslipidemia, history of depression, AICD, EF%, systolic blood pressure, NYHA class, beta-blocker, torsemide, and digoxin when adjusted for other co-variates.

According to univariate analysis AICD was decreasing the adverse outcome only in Blacks, but when adjustment for other variables was performed the same finding was observed in Whites as well. High ejection fraction is associated with decrease risk for adverse outcome in both races and high NYHA class is associated with worst outcome in both races. As mentioned above, carvedilol decreases the mortality in both Whites and Blacks and in this study when adjustment for other variables was performed use of beta-blockers proves to increase survival in both races. In Whites use of furosemide is associated with increases adverse outcomes and it seems to an insignificant risk factor in

Blacks. It has been suggested that furosemide has adverse renal effect at high optimal doses and apart from that it can prolong the hospitalization (Peacock, Costanzo et al. 2008). Also aggressive use of diuretics in the treatment of HF results in electrolyte and volume depletion, arrhythmias, hypotension and worsening renal function.(Goebel and Van Bakel 2008) Apart from that torsemide increases the mortality in Blacks for above mentioned reasons. According to DIG trial, digoxin proved to increase survival in patients with HF; however, there was a racial difference in this medication effects. An increased risk of adverse outcomes was observed in Blacks, when use of digoxin was adjusted for other variables, but not in Whites. These differences of medication effects could explained by the different genetic response to medications in Blacks and Whites (Bloem, Manatunga et al. 1996; Small, Wagoner et al. 2002).

In this study history of PTCA is important risk factor for Blacks but not for Whites. Study have been reported about the PTCA and high mortality in African American. According this study, at 5 year follow up, African American have worst clinical outcome who have undergone PTCA compared to Whites (Pradhan et al. 2008). Several studies have shown that depression is an independent risk factor for both ischemic heart disease and HF. This is because tricyclic antidepressant used for treatment of depression also have class IA antiarrythmic properties and found to increase the mortality in these patients (1989; Carney, Freedland et al. 1997). In this study, depression is an important risk factor for Blacks, but not for Whites when depression was adjusted for other variables. In Blacks, obesity and dyslipidemia are major problems and they are important risk factors for adverse outcomes.

This study shows that Blacks have higher survival rate than Whites. There are several studies reporting on survival rates in Black and White patients with HF. Data of these studies are controversial as Blacks seems to have similar, higher or lower mortality rates compared to Whites (Dries, Exner et al. 1999; Rathore, Foody et al. 2003). According to study by Dries et al., this difference is due to differences in the severity, causes and management of HF, the prevalence of coexisting conditions, and socio economic factors. According to study by Rathore et al. Blacks have lower mortality risk than Whites. The study was conducted retrospectively on Medicare beneficiary hospitalized patients. However, in this study Blacks had higher hospitalization rate, but lower mortality rate compared to Whites.

There are several limitations in this study among one was, a retrospective study, so it was difficult to find the missing data values in this dataset. Furthermore, the power is low and because of that the finding of this study cannot be generalized to general population. Although the findings were adjusted for potential confounders, the possibility that these findings could be explained by interaction of other variables that was not taken into account cannot be excluded.

Recommendations:

As explained above there may be genetic polymorphism in Whites and Blacks and that might be the reason for different treatment response in these two races, so large study required to explore this finding. Large datasets are available for other cardiac diseases such as myocardial infarction, hypertension and there are studies reported on the variation in the etiology, pathophysiology and treatment responses in Whites and Blacks.

Health care resources should be more easily accessible as HF is a condition which can be deteriorated very fast. Apart from that, proper counseling should be available for all the patients without any racial discrimination.

Heart transplant is a major procedure, very expensive, and every year very few transplants occur. Also donor organs are very limited as there are few living donors for heart transplant. Thus, it would be wise more detailed data to be collected regarding heart transplant, in order for physicians to better understand possible racial differences in this outcome and also if race is a prognostic factor for post transplant survival.

In conclusion, there is no significant difference in the combined outcome (death, transplant, emergency transplant, and LVAD) of HF between Whites and Blacks. There are differences regarding the risk factors which are more prominent in each race, however, some of them are common between the two races. Further studies on larger population are required to establish race as a significant risk factor for predicting the outcome in HF.

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Appendices

Appendix A. Clinical Characteristics of Heart Failure in Whites and Blacks.

Variable	*Whites*	*Blacks*	*P-value*
Gender			**<0.001**
Male	75.9%	56.7%	
Female	24.1%	43.3%	
Smoking			**<0.05**
Never Smoke	44.9%	51.0%	
Smoker	18.9%	23.8%	
Former Smoker	36.1%	25.2%	
Alcohol Consumption			**0.621**
No Drinker	64.3%	60.6%	
Drinker	23.4%	27.3%	
Former Drinker	12.2%	12.1%	
Primary Cause of HF			**<0.001**
Ischemic	52.1%	22.3%	
Idiopathic	47.9%	77.7%	
History of Myocardial Infarction			**<0.001**
Yes	46.2%	20.3%	
No	53.8%	79.7%	
History of CABG			**<0.001**
Yes	31.0%	9.6%	
No	69.0%	90.4%	
History of PTCA			**<0.001**
Yes	21.9%	9.6%	
No	78.1%	90.4%	
Hypertension			**<0.001**
Yes	52.5%	75.7%	
No	47.5%	24.3%	
Diabetes			**0.385**
Yes	35.1%	38.9%	
No	64.9%	61.1%	
Dislipidemia			**0.001**
Yes	54.8%	39.6%	
No	45.2%	60.4%	
History of Chronic Lung Disease			**0.879**
No	76.4%	77.8%	
Yes	22.2%%	21.2%	
No Mention	1.4%	1.0%	
History of Sleep Apnea			**0.451**
No	78.5%	80.9%	
Yes	16.2%	16.2%	
No Mention	5.3%	2.9%	

History of CPAP			**0.346**
No	83.6%	88.3%	
Yes	10.7%	8.2%	
No Mention	5.7%	3.6%	
Thyroid Disorder			**0.898**
No Disorder	80.4%	81.9%	
Hyperthyroidism	18.2%	16.6%	
Hypothyroidism	1.4%	1.5%	
Depression			
No	70.6%	79.8%	**0.073**
Yes	26.0%	17.7%	
No Mention	3.5%	2.5%	
History of CVA			**<0.05**
No	87.2%	80.4%	
Yes	12.8%	19.6%	
Cancer			**0.598**
No	89.3%	90.8%	
Yes	10.7%	9.2%	
F/H of Idiopathic Cardiomyopathy			**0.493**
No	60.0%	65.3%	
Yes	20.0%	16.8%	
No Mention	20.0%	17.9%	
F/H of Dilated Cardiomyopathy			**<0.05**
No	75.5%	70.0%	
Yes	5.0%	12.2%	
No Mention	19.4%	17.3%	
Atrial Arrhythmias			**0.698**
No Atrial Arrhythmias	52.9%	56.4%	
Paroxysmal Atril	16.6%	17.8%	
Fibrillation/Fluter	20.4%	14.4%	
Chronic Atrial	1.7%	2.0%	
Fibrillation/Flutter	3.1%	3.5%	
Atrial Tachycardia			
Paroxysmal Supraventricular Tachycardia	5.2%	5.9%	
Ventricular Arrhythmias			**0.312**
No	50.7%	54.1%	
Yes	44.1%	38.3%	
No Mention	5.2%	7.7%	
Device			**0.153**
No	31.5%	37.1%	
Yes	68.5%	62.9%	
AICD			**0.517**
No	72.0%	69.5%	
Yes	28.0%	30.5%	

BivPace/Device			**0.173**
No	65.0%	70.4%	
Yes	35.0%	29.6%	
Biv Pace			**0.607**
No	79.6%	83.3%	
Yes	20.4%	16.7%	
Outcome			**0.169**
Yes	34.6%	28.9%	
No	65.4%	71.1%	
Age	55.68±11.39	49.22±13.21	**<0.001**
Height (Inches)	69.83±3.58	66.93±3.95	**<0.001**
Weight (LB)	208.13±47.67	195.38±41.62	**0.133**
Heart Rate at visit	74.59±12.85	79.89±15.85	**<0.001**
Systolic BP	113.32±19.12	119.06±19.32	**<0.001**
Diastolic BP	72.06±11.40	74.81±10.08	**0.172**
NYHA at Visit	2.43±0.74	2.46±0.70	**0.598**
EF%	**21.50±11.17**	**17.89±9.4**	**<0.001**

Appendix B. Drugs and Laboratory profiles in Whites and Blacks

Variable	*Whites*	*Blacks*	*P-value*
ACE-I	75.0%	66.1%	**<0.05**
ARB	19.5%	24.7%	**0.136**
Beta-Blocker	88.8%	89.8%	**0.708**
Statin	54.7%	34.0%	**<0.001**
Ezetimibe	3.0%	0%	**0.251**
Allopurinol	9.4%	6.1%	**0.146**
Aldosteron Blocker	38.6%	50.6%	**<0.01**
Furosemide	60.6%	65.3%	**0.245**
Bumetanode	0.9%	2.0%	**0.236**
Torsemide	19.8%	26.1%	**0.069**
Metolazone	5.6%	6.5%	**0.642**
Hydrochlorothiazide	4.4%	4.5%	**0.970**
Digoxin	49.7%	54.3%	**0.275**
Aspirin	59.0%	51.2%	**0.386**
Clopidogril	8.1%	4.7%	**0.463**
Oral Nitrates	12.0%	14.0%	**0.747**
Calcium-Channel Antagonist	13.0%	12.8%	**0.926**
Antiarrhythmics	33.1%	26.9%	**0.109**
NSAID	5.0%	7.0%	**0.637**
Warfarin	56.4%	58.1%	**0.850**
Antidepressant	36.0%	18.6%	**<0.05**
Antianxiety	20.0%	4.7%	**<0.05**
Insulin	10.0%	9.35%	**0.898**
Sulfonylurea	13.0%	11.6%	**0.821**
Biguanide	7.0%	4.7%	**0.596**
Thiazolinidiones	7.0%	2.3%	**0.265**
Other Drugs	67.7%	66.7%	**0.907**
WBC(×10E3)	10.03±40.56	7.05±2.28	**0.255**
RBC(×10E6)	4.38±0.53	4.48±0.71	**0.406**
RDW%	14.63±2.2	17.69±15.63	**0.085**
Hgb	13.64±2.66	12.97±1.80	**0.001**
Hct%	39.19±6.1	38.82±5.97	**0.484**
Platelet(×10E3)	228.97±71.98	251.49±87.08	**0.001**
Mean Platelet Volume	8.72±1.06	9.26±1.09	**0.01**
Lymphocyte%	23.40±7.8	26.45±9.02	**<0.001**
Na+	137.24±3.22	137.99±3.1	**<0.01**
K+	4.15±0.54	3.95±0.49	**<0.001**
CO2	27.77±6.1	27.38±2.7	**0.697**
Glucose	119.34±50.55	112.84±39.53	**0.096**
BUN	22.02±12.14	22.97±19.27	**0.470**
Creatinine	1.29±0.71	1.45±1.18	**0.50**
Protein Total	7.10±0.64	7.33±0.73	**0.176**

Albumin	3.7±0.40	3.68±0.46	**0.661**
Uric Acid	8.3±0.88	8.5±1.1	**0.017**
CPK	113.56±96.75	181.0±154.86	**0.202**
CK-MB	4.71±8.38	2.38±0.744	**0.128**
Troponin-I	1.2±3.65	0.15±0.32	**0.378**
BNP	649.51±845.86	981.37±1171.99	**0.046**
Total cholesterol	158.60±37.82	161.88±43.14	**0.361**
Triglyceride	168.49±138.24	114.79±132.50	**<0.001**
HDL	38.67±12.27	44.65±13.67	**0.099**
LDL	88.94±39.33	103.28±51.18	**0.238**
TSH	**3.43±1.05**	**4.73±1.69**	**0.381**

Table C. Clinical Characteristics by Outcome of Heart Failure.

Variable	***Outcome Positive***	***Outcome negative***	***P-value***
Gender			**<0.05**
Male	75.2%	65.6%	
Female	24.8%	34.4%	
Race			**0.169**
White	60.6%	54.2%	
Black	39.4%	45.8%	
Smoking			**0.208**
Never Smoker	41.8%	43.8%	
Smoker	19.6%	25.2%	
Former Smoker	38.6%	31.0%	
Alcohol Consumption			**<0.05**
No Drinker	65.2%	55.6%	
Drinker	20.0%	32.8%	
Former Drinker	14.8%	11.6%	
Primary Cause of Heart Failure			**<0.05**
Ischemic	46.0%	37.2%	
Idiopathic	54.0%	62.8%	
History of Myocardial Infarction			**0.251**
Yes	39.6%	34.4%	
No	60.4%	65.6%	
History of CABG			**0.588**
Yes	21.6%	23.8%	
No	78.4%	76.2%	
History of PTCA			**0.635**
Yes	18.5%	16.8%	
No	81.5%	83.2%	
Hypertension			**0.210**
Yes	59.7%	65.7%	
No	40.3%	34.3%	
Diabetes			**0.937**
Yes	38.2%	38.6%	
No	61.8%	61.4%	
Dislipidemia			**0.283**
Yes	52.5%	47.1%	
No	47.5%	52.9%	
History of Chronic Lung Disease			**0.129**
No	70.2%	78.8%	
Yes	28.6%	20.0%	
No Mention	1.2%	1.2%	
History of Sleep Apnea			**<0.001**

No	75.8%	80.9%	
Yes	14.3%	18.0%	
No Mention	9.9%	1.2%	
History of CPAP			**<0.001**
No	82.4%	87.9%	
Yes	6.9%	10.9%	
No Mention	10.7%	1.2%	
Thyroid Disorder			**<0.01**
No Disorder	78.2%	82.5%	
Hyperthyroidism	17.3%	17.5%	
Hypothyroidism	4.5%	0%	
Depression			**<0.01**
No	66.2%	78.5%	
Yes	27.5%	20.3%	
No Mention	6.2%	6.2%	
History of CVA			**0.459**
No	83.8%	86.4%	
Yes	16.2%	13.6%	
Cancer			**0.064**
No	85.0%	91.0%	
Yes	15.0%	9.0%	
F/H of Idiopathic			**0.055**
Cardiomyopathy	60.4%	57.5%	
No	23.3%	17.0%	
Yes	16.4%	25.5%	
No Mention			
F/H of Dilated Cardiomyopathy			**<0.05**
No	76.6%	64.9%	
Yes	8.9%	9.4%	
No Mention	14.67%	25.7%	
Atrial Arrhythmias			**<0.01**
No Atrial Arrhythmias	59.9%	48.6%	
Paroxysmal Atril	14.8%	17.8%	
Fibrillation/Flutter	19.1%	19.7%	
Chronic Atrial	3.1%	1.2%	
Fibrillation/Flutter	0%	5.8%	
Atrial Tachycardia			
Paroxysmal Supraventricular	3.1%	6.9%	
Tachycardia			
No Mention			
Ventricular Arrhythmias			**<0.05**
No	43.2%	50.2%	
Yes	53.1%	41.0%	
No Mention	3.7%	8.8%	
Device			**0.09**

No	35.2%	27.8%	
Yes	64.8%	72.2%	
AICD			**<0.01**
No	78.3%	66.5%	
Yes	21.7%	33.5%	
BivPace/Device			**0.433**
No	66.0%	62.5%	
Yes	34.0%	37.5%	
Biv Pace			**0.162**
No	76.7%	89.7%	
Yes	23.3%	10.3%	
Age	51.52±14.27	53.18±11.45	**0.159**
Height (Inches)	69.98±3.8	68.52±4.37	**0.143**
Weight (LB)	198.95±38.79	201.62±51.42	**0.802**
Heart Rate at visit	79.74±15.61	76.22±13.13	**<0.05**
Systolic BP	110.92±19.68	116.25±18.67	**<0.01**
Diastolic BP	70.41±12.43	72.21±9.2	**0.206**
NYHA at Visit	2.80±0.72	2.37±0.63	**<0.001**
EF%	**17.05±8.87**	**19.77±9.03**	**<0.01**

Outcomes = Death or Emergency Transplant or Transplant or LVAD

Table D. Drugs and Laboratory Profile for Outcome of Heart Failure.

Variable	*Outcome Positive*	*Outcome negative*	*P-value*
ACE-I	69.7%	72.2%	**0.557**
ARB	21.8%	20.7%	**0.782**
Beta-Blocker	76.4%	95.1%	**<0.001**
Statin	43.9%	45.0%	**0.818**
Ezetimibe	2.3%	3.4%	**0.763**
Allopurinol	8.5%	6.0%	**0.3**
Aldosteron Blocker	51.5%	41.3%	**<0.05**
Furosemide	57.6%	64.2%	**0.149**
Bumetanode	0.6%	1.4%	**0.415**
Torsemide	34.5%	17.5%	**<0.001**
Metolazone	9.1%	4.9%	**0.065**
Hydrochlorothiazide	4.8%	4.8%	**0.778**
Digoxin	66.7%	44.5%	**<0.001**
Aspirin	61.4%	39.3%	**0.067**
Clopidogril	7.0%	3.4%	**0.521**
Oral Nitrates	15.9%	6.9%	**0.252**
Calcium-Channel Antagonist	9.5%	9.5%	**0.093**
Antiarrhythmics	38.8%	27.3%	**<0.01**
NSAID	4.5%	0%	**0.244**
Warfarin	56.8%	55.2%	**0.89**
Antidepressant	27.3%	31.0%	**0.728**
Antianxiety	13.6%	10.3%	**0.676**
Insulin	9.1%	13.8%	**0.529**
Sulfonylurea	9.1%	10.3%	**0.859**
Biguanide	2.3%	13.8%	**0.057**
Thiazolidinedione	0%	10.3%	**<0.05**
Other Drugs	70.5%	75.0%	**0.675**
WBC(×10E3)	7.67±2.73	7.42±2.18	**0.363**
RBC(×10E6)	4.22±0.67	4.49±0.51	**0.256**
RDW%	15.3±2.4	14.9±2.3	**0.684**
Hgb	13.33±2.48	13.27±1.77	**0.165**
Hct%	38.79±6.36	39.17±5.58	**0.262**
Platelet(×10E3)	229.22±71.84	244.42±85.01	**<0.05**
Mean Platelet Volume	9.00±0.99	8.74±1.26	**0.540**
Lymphocyte%	21.85±8.15	25.40±7.44	**<0.001**
Na+	136.5±3.21	138.03±3.1	**<0.001**
K+	4.05±0.522	4.07±0.54	**0.597**
CO2	27.23±2.52	26.70±2.98	**0.419**
Glucose	114.71±40.75	117.12±47.05	**0.265**
BUN	25.80±13.87	21.38±16.81	**<0.01**
Creatinine	1.58±1.38	1.30±0.72	**<0.05**

Protein Total	7.06±0.85	7.12±0.48	**0.154**
Albumin	3.58±0.46	3.71±0.34	**0.181**
Uric Acid	8.4±1.69	8.4±0.43	
CPK	107.67±49.34	90.50±53.03	**0.971**
CK-MB	2.67±2.29	3.00±1.41	**0.438**
Troponin-I	0.06±0.1	0.03	**0.725**
BNP	1.32±1331.61	6.5±843.57	**<0.001**
Total cholesterol	157.00±44.61	161.04±38.45	**0.318**
Triglyceride	123.25±73.45	155.29±158.65	**<0.05**
HDL	37.30±10.95	41.73±15.32	**0.116**
LDL	98.15±48.69	97.47±45.85	**0.517**
TSH	**4.07±1.17**	**3.77±1.41**	**0.88**