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Determinants of Mortality Among Seniors Acutely Readmitted for Heart Failure: Racial and Socioeconomic Disparities

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An abstract of

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Abstract

Determinants of Mortality Among Seniors Acutely Readmitted for Heart Failure: Racial and Socioeconomic Disparities

By

Tuoyo O. Mene-Afejuku

Background: Heart failure (HF) is common and characterized by a high rate of mortality. Seniors (people 65 years and older) make up a significant proportion of the total HF population but are not well represented in many clinical trials. We aim to assess predictors of mortality among seniors acutely re-hospitalized for decompensated HF.

Methods: A single-site prospective study of seniors with HF readmitted within 30 days of discharge for HF over a six-month period (January 1, 2020, to June 10, 2020). Following the review of electronic medical records, demographic, and laboratory parameters at the time of hospitalization were extracted. Cox proportional hazards regression was used to assess predictors of mortality. Statistical significance was defined as a p-value of < 0.05 and a confidence interval of 95%.

Results: Our study included 452 patients. The age range of the cohort was 65 to 101 years (mean 78.73 ± 8.48 years). Of this, 206(46%) were males, 28% were 85 years or older. The median follow-up time was 84 days, and the observed short-term mortality was 22%. After univariate analysis, the hazards for death among seniors with HF significantly decreased by 5% for each unit increase in serum sodium. Following multivariate analysis, nonblacks who were not discharged home after the index hospitalization had lower hazards of death than blacks not discharged home at the index admission (adjusted hazards ratio (aHR) 0.32, 95% confidence interval (CI) 0.16, 0.67). Patients with the lowest tertile range for systolic blood pressure (SBP) had twice the hazard for death compared to patients with the highest tertile for SBP. Patients with access to primary care provider (PCP) had 5 times the hazards of death compared to patients without access to a PCP.

Conclusion: Seniors who are acutely re-hospitalized for decompensated HF have a very high short term mortality rate. Hyponatremia and low systolic blood pressure are independent predictors of mortality. Black seniors who were not discharged home after their index hospitalization for HF had higher hazards for all-cause mortality compared to nonblacks.

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1.1 Literature Review

Heart failure (HF) is a devastating condition characterized by a high rate of mortality and morbidity (Tomasoni et al, 2019). About 6.2 million individuals are grappling with the burden of HF in the United States (U.S) (Benjamin et al, 2019). Of this over 6 million individuals affected with HF, a higher proportion is made up of people older than 65 years because of increased life expectancy in the U.S (Heidenreich et al 2011; Benjamin et al, 2018). Seniors do not just account for the greater proportion of individuals affected by HF but also have a worse outcome compared to younger individuals with HF (Yokokawa et al, 2017). Seniors are not well represented in many clinical trials, bringing to fore the need to carry out research specific to this age group to improve applicability and increase potential benefits of current guidelines (Screever et al, 2017).

Several factors have been attributed to the high mortality rates associated with HF, some of which are but not limited to the following; racial disparity, lack of health insurance, as well as lack of access to primary care physicians (Lee et al, 2019; Miles et al ,2019; Ponce et al,2018). Not much has been reported on the impact of these disparities among seniors acutely re-hospitalized due to HF. This study aims to assess these disparities as predictors of mortality among seniors readmitted due to decompensated HF.

The cost of care for HF in the U.S is very high and is expected to rise from $20.9 billion in 2012 to about $53.1 billion by 2030 (Ziaeian & Fonarow, 2016). The cause of this enormous cost burden is multifactorial and may be related but not limited to the following; length of hospital stays, diagnostic procedures, hospital readmissions and loss of man hours (Konstam, 2012).

The high morbidity and mortality from HF as well as its attendant high cost of care has been a major concern for health systems in the U.S. As a result, initiatives to expand efforts that control the risk factors for hospital readmissions, mortality and cost reduction are of utmost importance to public health experts nationally. In fact, 30-day readmission is a big factor in US hospitals as the present policy imposes penalties for readmission within 30-days (Abdul-Aziz et al, 2017). These penalties were put in place to incentivize strategies geared towards decreasing preventable rehospitalizations for HF (Dharmarajan & Krumholz, 2014).

There is gender difference with regards to the lifetime risk of HF which is 15% and 11% for women and men respectively without a history of myocardial infarction at age 40 (Louis et al, 2003; Hoang-Kim et al, 2020). As a result, gender differences should be considered when assessing patients for risk of death or readmission.

Even though 30-day readmission is important 7-day readmission is also important and some researchers have implied that this may be reflective of the quality of care the patient received (Eastwood et al, 2017). Eastwood et al identified frailty (commoner in seniors) as one of the factors that predict readmission within 7 days of discharge for HF. The quality of care in turn is dependent on sociodemographic and other clinical factors as care by a specialist was associated with 7-readmission (adjusted odds ratio [aOR], 2.10; 95% CI, 1.32-3.42) while a lower likelihood of readmission was associated with instructions for follow-up with a family physician within 1 week of discharge (aOR, 0.56; 95% CI, 0.36-0.88) (Eastwood et al, 2017).

In the light of the above, we aim to address socioeconomic and racial disparities as they affect seniors with HF in terms of early readmission and mortality in addition to other potential prognostic indices.

1.2 Definitions of heart failure

HF is defined as an abnormality of cardiac function or structure leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at the expense of increased filling pressures) (Kasper et al, 2005 ; McMurray et al, 2012).

HF may also be defined as a clinical syndrome characterized by a constellation of symptoms (dyspnea, orthopnea, lower limb swelling) and signs (elevated jugular venous pressure, pulmonary congestion) usually caused by a functional and/or structural cardiac abnormality resulting in reduced cardiac output and/or elevated intracardiac pressures (Ponikowski et al, 2016 ; Kurmani & Squire, 2017).

HF could be acute when there is a rapid onset of symptoms and signs due to abnormal cardiac function usually necessitating emergent treatment and or hospital admission and may occur with or without pre-existing heart disease (Gheorghiade et al, 2005; Kurmani & Squire, 2017). Acute HF may present in one of the following distinct clinical conditions; acute decompensated HF (ADHF), hypertensive acute HF, pulmonary edema, cardiogenic shock, and high output failure and unclassified (Nieminen et al, 2005; Kurmani & Squire, 2017).

On the other hand, chronic HF is said to occur when patients have a diagnosis of HF for a period spanning greater than 3 months (Witte et al, 2006). If the symptoms and signs of HF have remained unchanged for at least a month despite treatment, such patients are described as having stable HF. ADHF is said to occur if a patient with chronic stable HF deteriorates, acutely (Nieminen et al, 2005; Witte et al , 2006; Kurmani & Squire, 2017).

Congestive HF is characterized by evidence of congestion (i.e. sodium and water retention) and may occur in patients with acute or chronic HF (The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure, 2012).

1.3 Epidemiology of heart failure

HF is invariably a disease of the elderly and the incidence and prevalence increases with age (Dharmarajan & Rich; 2017). More than 50% of patients hospitalized due HF are older than 75 years (Chen et al, 2013). In general, the prevalence of HF doubles for each decade of life and is <1% for people less than 40 years, and >10% for individuals more than 80 years (Mozaffarian et al, 2016). HF is also the most common reason for hospitalization among seniors (Dharmarajan & Rich, 2017). HF accounts for more than 1 million hospitalizations per year in the U.S and a 25% readmission rate at 1 month (Yancy et al, 2013).

Men and women have equal lifetime (1 in 5) risks of developing HF by age 40 (Lloyd-Jones et al, 2002; Bozkurt & Khalaf, 2017). However, women at older age are stated to have higher risk of HF than men (Goldberg, 2005). The mortality and morbidity secondary to HF is still very high despite advances in medical and device therapy (Dharmarajan & Rich, 2017).

1.4 Diagnosis and classification of heart failure

The Framingham's criteria as well as the European Society of Cardiology (ESC) criteria are one few fairly objective methods of making a diagnosis of HF. The diagnosis of HF based on the ESC criteria is based on symptoms of HF at rest or with exercise with evidence of cardiac dysfunction detected on echocardiography. Alternatively, natriuretic peptide levels can serve as a rule out test for HF and may sometimes preclude the need for an echocardiogram emergently to make a diagnosis. However, if the diagnosis of HF is inconclusive, response to guideline directed medical therapy (GDMT) for HF can help confirm the diagnosis of HF (The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology).

The Framingham criteria is an older criterion which requires the presence of at least one major and two minor criteria, or two major criteria to make a diagnosis of HF (Kasper et al, 2008). The major criteria include paroxysmal nocturnal dyspnea, distended neck veins, rales, cardiomegaly, acute pulmonary edema, S3 gallop, increased venous pressure (>16 cmH2O) and positive hepatojugular reflux (Kasper et al, 2008). On the other hand, the minor criteria include the following; extremity edema, nocturnal cough, dyspnea on exertion, hepatomegaly, pleural effusion, decrease in vital capacity by one-third of normal and tachycardia (greater than 120) (Kasper et al, 2008). While weight loss of more than 4.5kg over 5 days of treatment can either be a major or minor criterion (Kasper et al, 2008).

The American College of Cardiology classification of HF is as follows; class A- high risk with no symptoms, class B- Structural heart disease with no symptoms, class C- Structural heart

disease with present or previous symptoms and class D- Refractory symptoms requiring special interventions (inotropic support, vasodilators, revascularization and cardiac resynchronization etc) (Kasper et al, 2008).

Left ventricular ejection fraction (LVEF) is one of the favored modes of classifying HF (Fonarow , 2017). Many clinical trials have established important differences with respect to demographics, etiology, comorbidities, prognoses, and response to therapy among patients with HF are based on LVEF (Hsu et al, 2017; Fonarow, 2017). In this light, HF may be classified into three main groups namely; heart failure with reduced ejection fraction (HFrEF) when LVEF is <40% (characterized by impaired myocardial contraction) , HF with preserved ejection fraction (HFpEF) when LVEF is >50% (impairment in cardiac muscle relaxation) and HF with borderline ejection fraction (HFbEF) (Fonarow, 2017).

1.5 Predictors of mortality among patients with heart failure

There are several established markers of a poor outcome among patients with HF. Some of these indices for poor prognosis are as follows; low LVEF, hyponatremia, renal dysfunction (elevated urea or creatinine, or low glomerular filtration rate), NYHA class (III and IV), the underlying etiology, prolonged QTc, advanced age, male gender, increased brain natriuretic peptide (BNP) and reduced 6-minute walk distance, abnormal exercise response as well as reduced heart rate variability (Chen et al,2012; McCallum et al, 2020; Ingle et al, 2007).

These prognostic factors may have some interplay with age, gender, race as well as socio-economic status. One of such relationships is described by Miles et al, 2019 were they noted that

Hispanic patients who were not hyponatremic and admitted for HF, had an independent decreased risk of death compared to other racial groups. These findings hypothesized to be probably secondary to the difference in the activity of the renin-angiotensin-aldosterone system (RAAS) among various racial/ethnic groups (Miles et al, 2019).

The role of race, gender and socio-economic status with respect to prognosis have not been fully explored among patients acutely re-hospitalized following discharge for HF related acute decompensation (Foraker et al, 2011). An interesting study in Japan reported that the clinical significance in terms of adverse outcomes of acutely readmitted patients for HF was lower in Japan when compared to that in reported in western countries and that male gender was an important predictor and not clinical indices (Ishihara et al, 2020).

Foraker, et al in 2011, low socio-economic status and high burden of comorbidity was associated at baseline, with an elevated risk of death (1.36, 1.02–1.80), and rehospitalization or death (1.36, 1.08–1.70) compared to with high socio-economic status and high burden of comorbidity after controlling for race/ study community, gender, age at HF diagnosis, body mass index, hypertension, educational attainment, alcohol use and smoking. Patients with HF who were Medicaid recipients with a low level of comorbidity had an increased risk of rehospitalization or death (1.21, 1.07–1.37), and a higher rate of repeat hospitalizations compared to non-Medicaid recipients (Foraker et al, 2011).

There are also limited studies with regards to disparity in quality of care along racial and socio-economic divides which in turn may portend a poor prognosis (Casale et al, 2013)

Casale, et al in 2013, reported that among patients with advanced HF, African American ethnicity (odds ratio [OR] 0.56, 95% CI,.46-68, P < .0001) and poverty, comparing the poorest quintile to other quintiles (OR 0.86, 95% CI, .76-98, P < .02), were associated with less cardiac resynchronization therapy (CRT) after adjusting for older age, male gender, prior myocardial infarction or bypass surgery and intraventricular conduction delay.

1.6 Cost of medications and financial considerations

HF is a chronic condition which can managed to a large extent by daily use of medications. Seniors, however, represent a unique group who are no more in the unemployment class and therefore mostly dependent on proceeds from astute investments (very small proportion) or dependence on some of government issue insurance coverage. In the light of this, Saver and colleagues, in 2004, reported that seniors with lower income, lower assets, higher out of pocket medication cost and poor health status were independent predictors of difficulty with affording medications.

Race was also noted to play a role with respect to ability of seniors to able to afford GDMT (Chaudhry et al, 2011). In this study, black patients were more likely compared to white patients to report that there were not able to take prescription medication because of prohibitively high cost of medications after unadjusted analyses (OR 2.22, 95% CI 1.66-2.97).

Another worrying fact is that some of the more recent lifesaving medications for HF are very expensive and put more strain on the limited financial capacity among seniors who represent a vulnerable group who sadly represent a higher proportion of individuals with severe HF (Bogner

et al, 2010; Park et al, 2019). Out of pocket medications costs are to a large extent dependent on the presence of prescription benefits as part of an individual's medical coverage (Saver et al, 2004).

Also, it stands to reason that since outcomes are contingent on adherence to GDMT as mentioned above, policies to focus to excellent medical insurance coverage especially for seniors should be considered (Kripalani et al, 2015).

1.7 Health Literacy and heart failure

The management of HF is complex and requires a high degree of participation by the patient and care givers (Riegel et al,2009; Moser et al, 2015). Health literacy has been noted by several studies to be influential in improving outcomes among patients with chronic disease conditions such as HF (Riegel et al, 2009; Moser et al, 2015; Sterling et al, 2018). Low health literacy may be associated with some other factors and may affect outcomes. Health literacy may be of higher significance among seniors because of the significantly higher prevalence of cognitive dysfunction which may obliterate some of the effects of literacy in this population (Cannon et al, 2017; Mene-Afejuku et al, 2019).

Older age, male gender, low literacy, and unemployment were noted to be more likely to have low health literacy (Moser et al, 2015). In turn, Moser et al in 2015 revealed that patients with inadequate or marginal health literacy were almost two times more likely ($p < 0.001$) to die compared to those with adequate health literacy after unadjusted Cox regression.

Medication adherence is affected by low health literacy and may confer poor outcome among patients with HF (Oscalices et al, 2019).

Health literacy appears to be related to non-modifiable factors such as race and gender that may act independently or in concert to affect outcomes of seniors with ADHF. Chaudhry et al in 2011 explored this connection in great detail. They found that black patients were more likely to have a lower socio-economic status, to be uninsured or on Medicaid, compared to whites. Blacks were also more likely than whites to have poor health literacy (odds ratio [OR] 2.98, 95% CI, 2.18-4.08) (Chaudhry et al, 2011). They also found that a higher proportion blacks reported limited access to specialist's care compared to whites (OR 1.65, 95% CI 1.20-2.26) (Chaudhry et al, 2011).

Another group of researchers found out that low health literacy correlated with increasing age even after controlling for race, gender, educational attainment and immigration status (Cordasco et al, 2009). Health literacy may therefore be a composite and surrogate marker of demographic indices among seniors acutely readmitted for HF and should probably be assessed in all patients with HF.

1.8 Survival paradox of black seniors

In general, blacks have a lower life expectancy compared to that of other races (Pollard et al, 2013). Several studies have attributed that this may be multifactorial and as result, predictors such as education, income levels among others may account for much of this racial disparity in life expectancy but not all (Pollard et al, 2013). In line with this, Geruso attempted to assess the extent to which ancillary factors contribute to this racial difference in life expectancy (Geruso , 2012). After some intricate analysis, they reported that demographic attributes and

socioeconomic differences account for 80% (males) and 70% (females) of the disparity in life expectancy between whites and blacks (Geruso , 2012).

However, this disparity does not appear to hold throughout life as this appears to hold only up to age of about 80 to 85 years, following which blacks tend to outlive their white counterparts (racial crossover) (Yao & Robert, 2011; Geruso, 2012). The mechanism for this racial crossover phenomenon is poorly understood but some researchers have suggested that it may be due to selective longevity such that very old nonwhites who survive to the age of 80 years and above probably have some instinctive survival attributes (Yao & Robert, 2011; Lynch, 2003). Interaction between age and race has therefore been advocated when analysis of mortality among seniors is being contemplated because of this phenomenon (Yao, 2011; Lynch et al, 2003; Corti et al, 1999).

It would be useful to explore the issue of racial crossover further, as the understanding the attributes that confer the longevity among older black seniors may be have an extended applicability and usefulness among younger blacks burden with chronic disease conditions such as HF.

1.9 Selected landmark heart failure trials.

It is a paradox that even though HF is commoner among seniors and is also more consequential in this group, there are inadequate clinic trials to study HF in this unique group of patients (Yokokawa et al, 2017; Screever et al, 2017). This may be due to the fact that seniors are sicker, have more severe disease and also multiple comorbidities one or more of which may be in the exclusion criteria of most of these clinical trials. All the same, more clinical trials among seniors

is advocated for better understanding and implantation of lifesaving policies and therapies that would benefit this unique population.

Here we discuss a few landmark trials among patients with HF.

The Assessment of Treatment with Lisinopril and Survival (ATLAS study) suggest that higher doses of angiotensin converting enzyme inhibitors (ACEIs) are required to provide morbidity and mortality benefit (MacFadyen et al, 1999). Other studies that proved modulators of RAAS system confer mortality benefit include the Studies of Left Ventricular Dysfunction (SOLVD, enalapril 1994), the Co-operative North Scandinavian Enalapril Survival Study (CONSENSUS), Survival and Ventricular Enlargement (SAVE) as well as the Trandolapril Cardiac Evaluation (TRACE) trials (Mann, 2012). Titrating medications to these high doses may be limited among seniors because of several side effects that limit maximization of therapy in this age group. Also, some patients have other classical side effects of ACEIs irrespective of age leading to use of angiotensin II receptor blockers ARBs which were also found to have mortality benefit (Mann, 2012).

In this light, Candesartan and ARB, was shown to significantly reduce all-cause mortality, cardiovascular death, and/or hospital admission in the Candesartan Heart Failure: Assessment of Reduction in Mortality and Morbidity trial (CHARM) (Young, 2004). Importantly, candesartan reduced all-cause mortality, irrespective of background ACEI or beta blocker therapy. Similar findings were shown with valsartan in the Valsartan Heart Failure Trial (Val-HeFT) (Cohn & Tognoni, 2001). Losartan has been also been shown to reduce morbidity and mortality in the Evaluation of Losartan in the Elderly study, ELITE-II (Pitt et al, 1997).

Interestingly, a retrospective analysis, of the Vasodilator in Heart Failure Trial I (V-HeFT I) suggested that the overall mortality and HF hospitalization were significantly reduced in black patients who receive combination therapy with hydralazine and isosorbide, whereas whites had no treatment effect when compared with placebo (Yancy, 2005). In contrast, in V-HeFT II, only white patients showed a significant mortality reduction from ACEI therapy (enalapril) when compared with hydralazine and isosorbide therapy, whereas black patients had no apparent treatment benefit from ACEIs (Yancy,2005). To address the role of hydralazine plus isosorbide treatment in blacks, the African American Heart Failure Trial (A-HeFT) compared the adjunctive use of isosorbide dinitrate and hydralazine to a standard HF regimen of ACEIs, beta blockers, and diuretics among blacks with NYHA Class III or IV HF (Taylor et al, 2004). The primary endpoint was death from any cause, a first hospitalization for HF, and change in the quality of life. The study was terminated early because there was a significant 43% reduction in the rate of death from any cause and a significant 33% relative reduction in the rate of first hospitalization for HF (Taylor et al, 2004).

Three beta blockers have been shown to be effective in improving outcomes among patients with HF (bisoprolol and sustained-release metoprolol succinate (Metoprol CR/XL) (Merit-HF Study Group, 1999). and carvedilol (Eichhorn & Bristow, 2001; Parker et al, 2001).

The use of beta blockers among seniors appears to be a problem because of the attendant side of effects such as hypotension, bradycardia, weakness, dizziness among others (Wikstrand et al, 2014). Nebivolol was hypothesized to be more favorable among seniors because of its additional vasodilatory property (Shibata, 2002). The SENIORS Study (Study of the Effects of Nebivolol

Intervention on Outcomes and Rehospitalization in Seniors with Heart Failure) was carried out to assess the effect of nebivolol on mortality and morbidity among seniors with HF, irrespective of the LVEF (Shibata et al, 2002). In this study nebivolol did not appear to significantly reduce mortality compared to placebo for the secondary end point of all-cause mortality (15.8% vs 18.1%; (hazard ratio (HR) 0.88, 95% CI 0.71–1.08; *P*=0.21). However, it appeared to be useful when the endpoint was death or cardiovascular hospitalization 31.1% vs 35.3% in the placebo group; HR 0.86, 95% CI 0.74– 0.99; P 0.039] (Shibata et al, 2002).

This study underscores the importance of carrying out studies specific to high-risk groups such as seniors rather than extrapolating results from that done in younger and healthier cohorts. More studies focused on seniors with HF is therefore advocated as they findings may be more applicable and useful to this unique population.

2.0 Study objectives.

2.1 Problem Statement:

Racial and socio-economic disparities exist in healthcare delivery and may be independent predictors of mortality among elderly patients acutely readmitted for HF.

The findings from this study may help in improving HF management by highlighting areas that may require further research to improve the overall outcome of patients with HF at Bridgeport hospital, Connecticut.

2.2 Purpose Statement:

The purpose of this study is to determine the predictive value of race and socio-economic status for mortality among seniors readmitted for HF at Bridgeport hospital, Connecticut.

To assess the predictive value of other factors apart from race and socio-economic factors as predictors of mortality patient among seniors acutely readmitted for HF.

2.3 Approach:

I hypothesize that seniors from minority groups with low socio-economic status would have greater hazards of dying if acutely readmitted for HF compared to seniors from well represented groups with good socio-economic status. Electronic medical records of seniors readmitted for decompensated HF from January 2020 to June 2020 was reviewed. It is important to emphasize, that there are not many studies on seniors and more so, seniors who are acutely hospitalized for HF within 30 days after discharge for HF. They, therefore, further represent a unique cohort that has not been extensively studied. The inclusion and exclusion criteria for this study is outlined below.

Inclusion Criteria:

1. Patients 65 years and above readmitted for decompensated HF.

Exclusion criteria:

1. Patients younger than 65 years of age
2. Patients without race or ethnicity documented in the electronic medical record

The demographic and clinical parameters of the study population was be recorded. Survival times were defined as the date of readmission for HF till death or date of censorship which was 30th June 2020. The number of patients who died was be recorded.

2.4 Data description

The data was obtained following a single-site prospective study of patients with HF readmitted within 30 days of discharge for HF at Bridgeport hospital over a six-month period (January 1, 2020 to June 10 2020). The patients were split into two groups based on survival status at the end of the study period (dead or alive). Race was split into two groups namely black and nonblack. Insurance and primary care provider status were used as surrogate indicators for socio-economic status. Insurance status was split into those with Medicare and non-Medicare health insurance. Age was split into two namely those 85 years and above (extremely elderly group) and those between 65 years and 84 years (Screever, 2017). Systolic blood pressure (SBP) was split into three tertiles. The least tertile was SBP of 121 mmHg or less, second tertile was SBP between 122 mmHg and 136 mmHg. The last tertile was SBP greater than 137 mm Hg. The Other relevant data were documented. The disposition or discharge status of the prior hospitalization was split into home or not home. The discharge status "not home" was defined as those who were discharged to one of the following: skilled nursing facility, long term acute care hospitals or rehabilitation centers. Patients with a disposition status of hospice were excluded.

2.5 Statistics

Continuous variables were expressed as means ± standard deviation. The categorical variables were expressed as frequencies and percentages. The difference between means of two variables was done with the student t-test with the assumption that near normality was attained (large sample size). The pooled or non-pooled t-test was carried depending on how close the standard deviations of the two means were. The Chi square test was done to assess for differences between two categorical variables and the Fishers exact test applied as needed.

Candidate predictor variables for mortality were selected using forward selection, backward elimination, stepwise selection, and best subset selection methods. Race was forced into the Cox proportional hazards regression model as it is the primary exposure variable for this study. Effect modifiers were sort for, and stratified estimates were presented if interaction was present. The final Cox proportional hazards regression model was made up of race, age, serum sodium, disposition status of previous admission, systolic blood pressure and primary care provider status. The proportional hazard assumptions were assessed using the log-log plots, graphical versus expected plots, as well as Schoenfeld and Martingale residuals. All the variables in the final multivariate model met the proportional hazards assumption except age and a stratified Cox proportional hazards regression was therefore employed stratifying for age.

Crude and adjusted survival curves were plotted for relevant variables. The level of significance was set at a p-value of less than 0.05 with a confidence interval of 95%.

3.0 Results

The study was made up of 452 seniors with a mean age of 78.73 years and age range of 65 years to 101 years. About 28% of the study population was 85 years or older. There were 206 males and 246 females. The median follow-up time in this study was 84 days. At the end of the study 101(22%) of the patients died.

As shown in table 1, non-Blacks were significantly older than blacks ($p = 0.0002$). SBP was also significantly higher among blacks compared to non-Blacks ($p=0.037$). There was no gender ($p= 0.29$) or Medicare status ($p=0.41$) difference between blacks and non-blacks as shown in table 1. Non-blacks had significantly higher blood urea nitrogen compared to blacks (22.82 ± 9.99 vs 17.16 ± 9.21; $p <0.0001$).

There was no racial difference with respect to the health insurance status ($p=0.41$).

There was interaction between index hospital discharge disposition and race as a result, stratified estimates are presented. As shown in table 2, among seniors with HF who were not discharged home in their index hospitalization, nonblacks had a hazard rate for mortality that was 0.32 that of the hazard rate of mortality among blacks controlling for SBP, serum sodium, age, and PCP status. This is also depicted graphically in figures 1 and 2 for the two strata of age (age greater than 85 and age between 65 and 84 years). Race on its own without controlling for the variables stated above among seniors with HF who were not discharged home in their index hospitalization, was a significant predictor of mortality as shown in figure 3. Among patients who were discharged home at their index hospitalization for HF, race was not a predictor of mortality after univariate and multivariate analysis as shown in table 2.

Table 1: Baseline characteristics of study participants.

	Total, N=452	Black, N = 68	Non-Black, N = 384	p-value
Age(years)	78.73 ± 8.48	75.26 ± 6.81	79.35 ± 8.61	0.0002**
LOS1 (days)	8.29 ± 9.96	9.38 ± 17.76	8.10 ± 7.84	0.56
readmission(days)	10.95 ± 8.69	11.09 ± 8.33	10.92 ± 8.76	0.89
SBP (mmHg)	130.32 ± 19.50	134.9 ± 19.64	129.5 ± 19.39	0.037**
DBP (mmHg)	69.14 ± 10.39	71.31 ± 12.43	68.76 ± 9.95	0.06
Pulse (beats/min)	76.66 ± 14.25	74.51 ± 12.86	77.04 ± 14.47	0.18
BUN (mg/dl)	21.97 ± 10.07	17.16 ± 9.21	22.82 ± 9.99	<0.0001**
Sodium (mmol/L)	137.88 ± 4.16	137.8 ± 4.77	137.9 ± 4.05	0.77
Gender				
Male, n(%)	206(45.58)	27 (39.71)	179 (46.61)	0.29
Female, n(%)	246 (54.42)	41 (60.29)	205 (53.39)	
Dead, n(%)	101 (22.35)	17 (25)	84 (21.88)	0.57
Alive, n(%)	351 (77.65)	51 (75)	300 (78.12)	
PCP, Yes, n(%)	412 (91.15)	56 (82.35)	356 (92.71)	0.0056**
PCP, No, n(%)	40 (8.85)	12 (17.65)	28 (7.29)	
Index disposition				
Home, n(%)	254 (56.19)	53 (77.94)	201 (52.34)	<0.0001**
Not home, n(%)	198 (43.81)	15 (22.06)	183 (47.66)	
Medicare, n(%)	439(97.12)	65 (95.59)	374 (97.40)	0.41
Medicaid, n(%)	13(2.88)	3(4.41)	10 (2.60)	

LOS1= index length of hospital stay, SBP= Systolic blood pressure, DBP= diastolic blood pressure; BUN= blood urea nitrogen, PCP= primary care provider, **= Statistically significant.

For each unit increase in serum sodium, the hazards for death among seniors with HF decreases by 5% following univariate analysis. Sodium was no longer a predictor of mortality among seniors acutely re-hospitalized for HF after multivariate analysis as shown in table 2.

Lower SBP tertiles (SBP1 and SBP2) have significantly higher hazards of death (2.34 and 2 respectively) compared to higher SBP tertiles (SBP3) adjusting for other variables as shown in table 2. Crude estimates of SBP also reveal SBP as a predictor of mortality among seniors as shown in table 2 and depicted graphically in figure 4.

Patients with HF who had access to a PCP had about 5 times the hazard rate for death compared to the hazard rate for death among seniors with HF who do not have access to a PCP controlling for age, race, serum sodium, SBP and index hospital discharge disposition status as shown in table 2.

Table 2: Stratified Cox Proportional Hazard regression of predictors of mortality among seniors (stratified for age).

Parameter	Univariate Hazard ratio	Crude 95% confidence interval	Adjusted Hazard ratio	Adjusted 95% confidence interval
Nonblack vs black discharged home	1.37	0.61, 3.06	0.97	0.43, 2.19
Nonblack vs black discharged other than home	0.35	0.18, 0.69	0.32	0.16, 0.67**
PCP (yes vs no)	5.28	1.30, 21.41	4.94	1.21, 20.18**
Sodium	0.95	0.91,0.99	0.96	0.92, 1.00
SBP1 VS SBP3	2.46	1.47, 4.12	2.34	1.38, 3.95**
SBP2 VS SBP3	2.03	1.18,3.50	2.00	1.15, 3.47**

SBP= Systolic blood pressure, PCP= primary care provider, DC= discharge, SBP1= systolic blood pressure less than 121 mmHg; SBP2= systolic blood pressure between 122 and 136 mmHg, SBP3= systolic blood pressure greater than 137mmHg, **= Statistically significant.

Figure 1

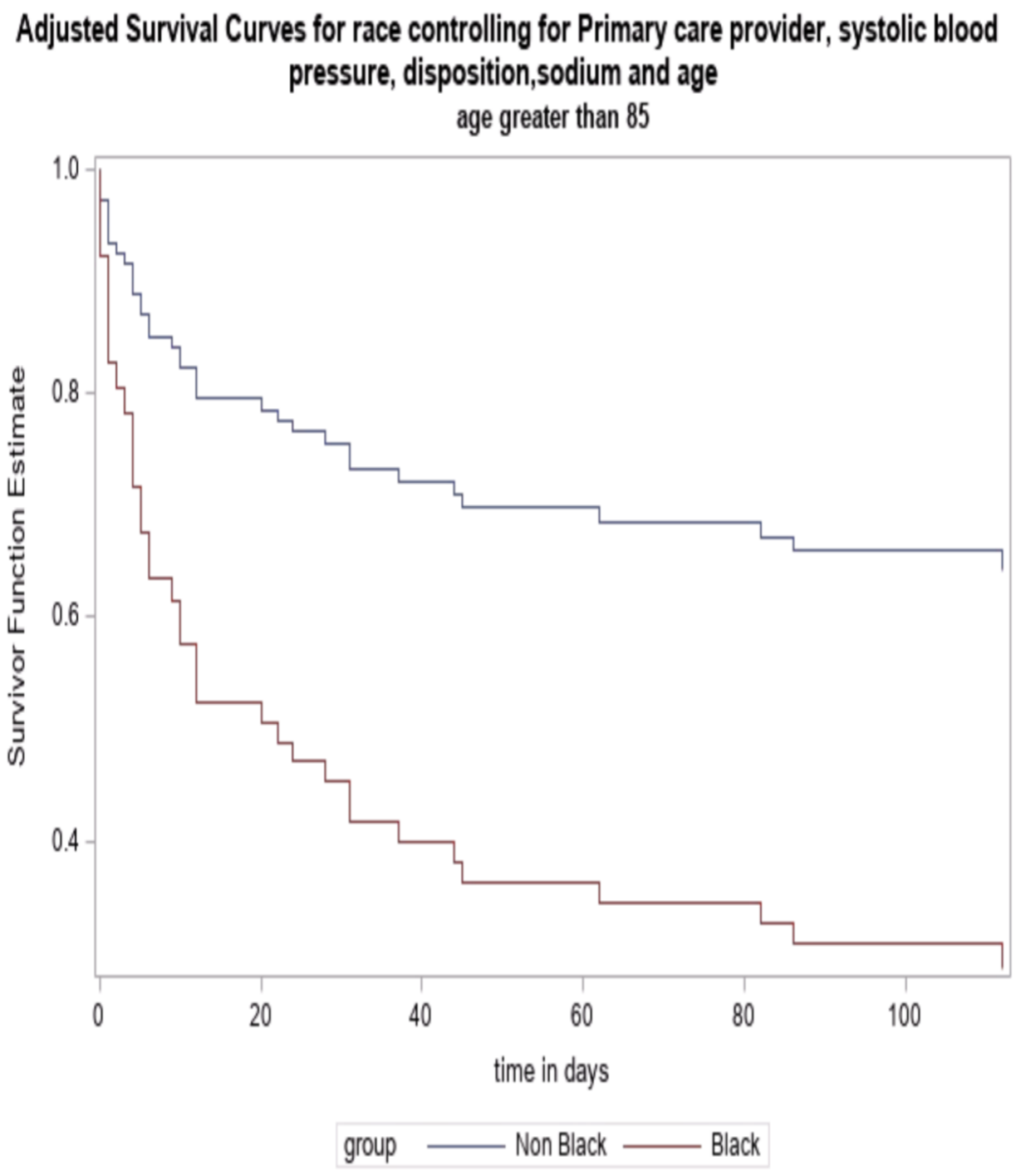

Adjusted Survival Curves for race controlling for Primary care provider, systolic blood pressure, disposition,sodium and age
age greater than 85
Survivor Function Estimate
1.0
0.8
0.6
0.4
0
20
40
60
80
100
time in days
group
Non Black
Black

Figure 2

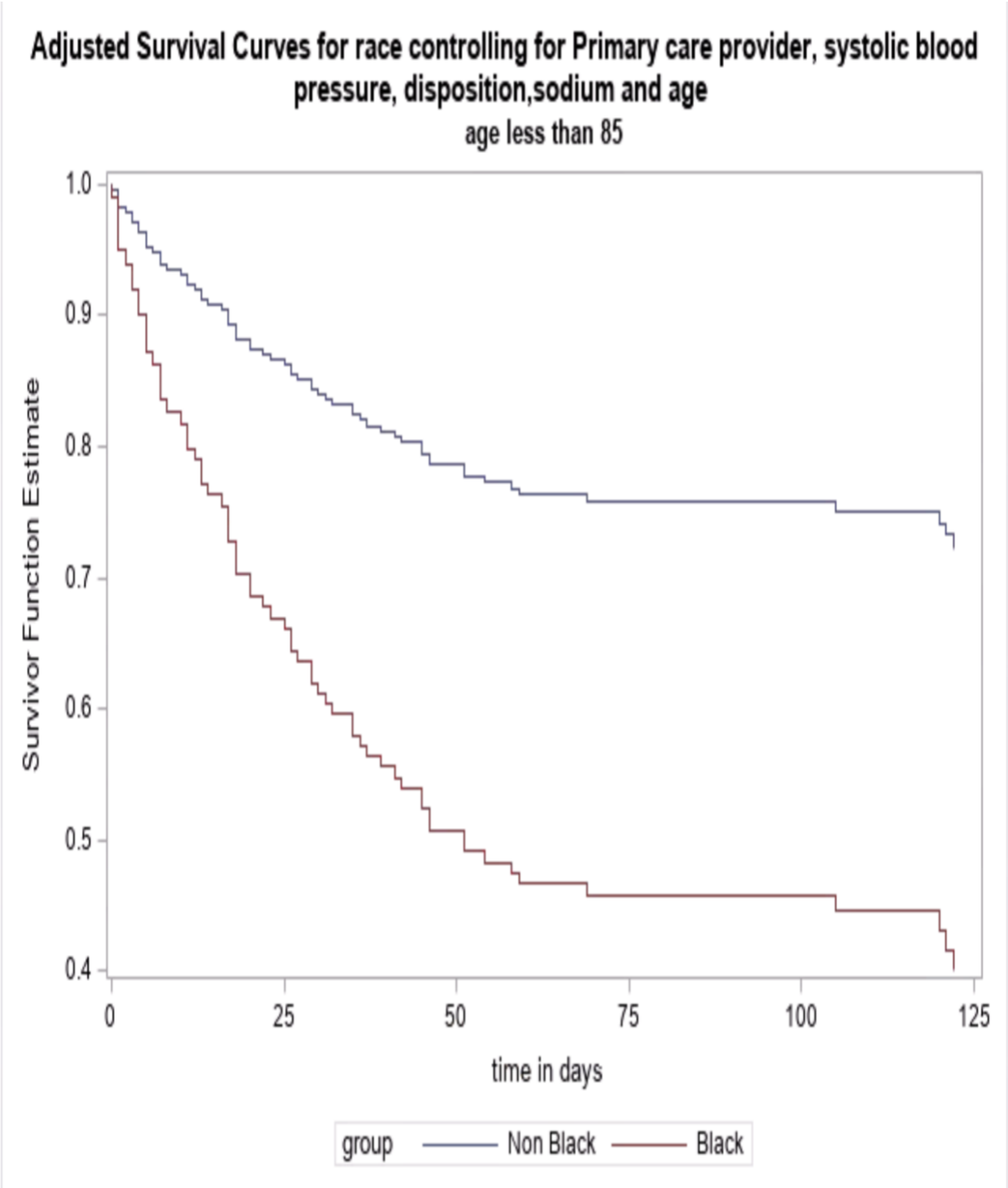

Adjusted Survival Curves for race controlling for Primary care provider, systolic blood pressure, disposition,sodium and age
age less than 85
Survivor Function Estimate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0
25
50
75
100
125
time in days
group
Non Black
Black

Figure 3: Survival plot of race as a predictor of mortality among patients with heart failure discharged elsewhere other the home in the index hospitalization

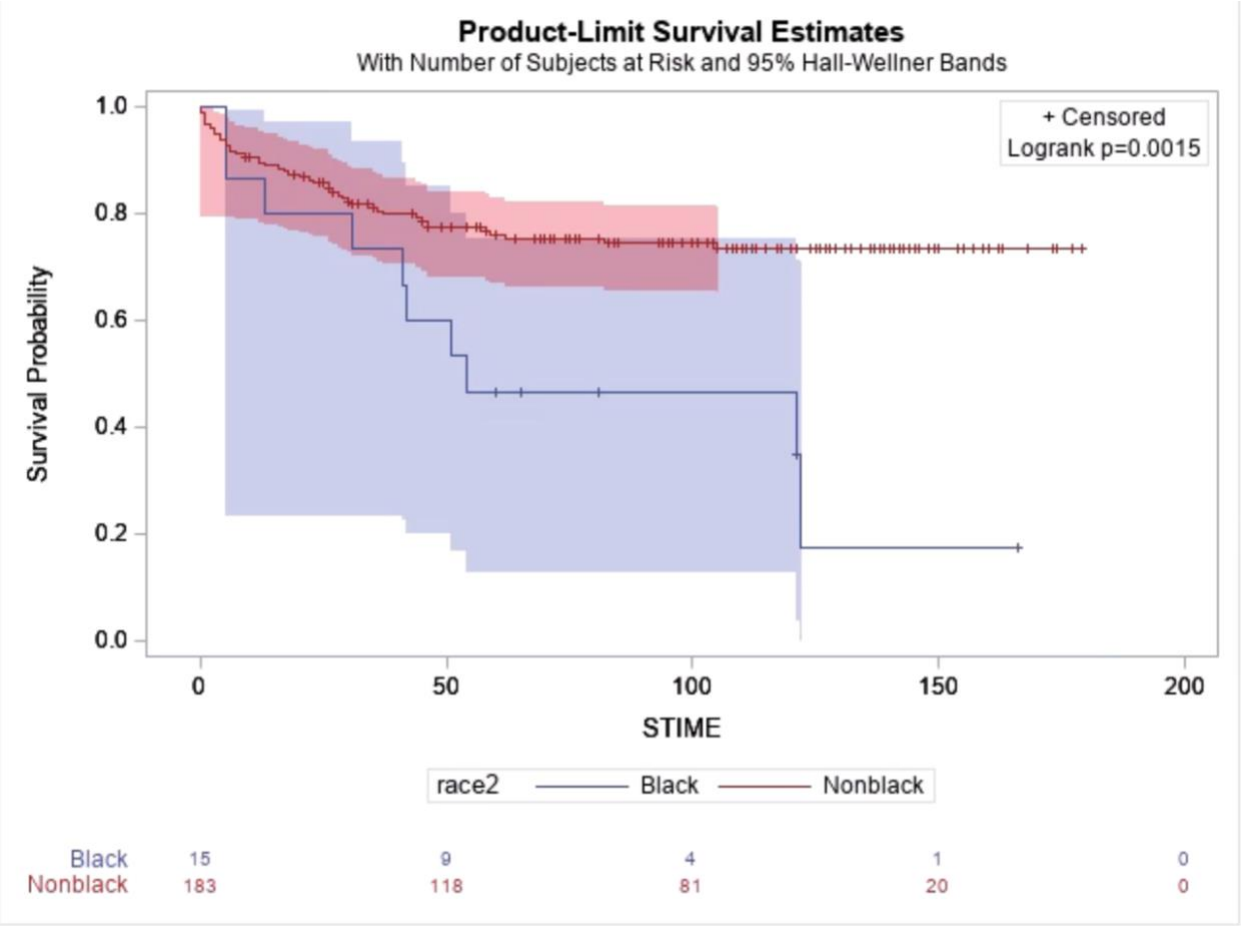
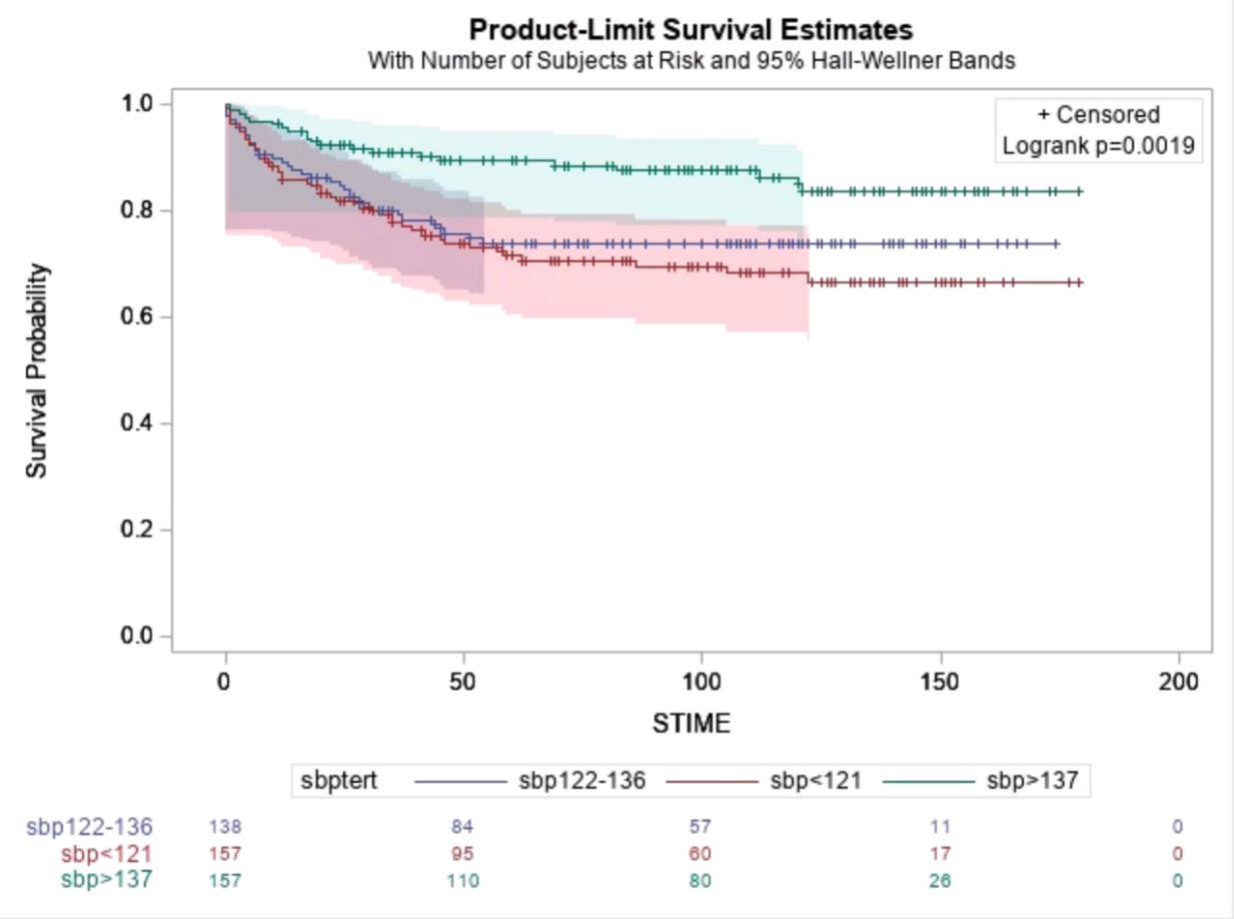


Figure 4: Survival plot of systolic blood pressure as a predictor of mortality among patients with heart failure



4. 0 Discussion.

This study is made of 452 seniors acutely re-hospitalized for HF and therefore, represent a high-risk cohort at baseline for being seniors as well as being acutely admitted for HF. This line of thinking is corroborated by the fact that the mortality rate in this study after a median follow up time of 84 days is 22% among acutely re-hospitalized seniors with HF. This would be considered very high when compared to findings by other researchers of lower rates and longer follow up periods for instance 13% in one year (Buddeke et al, 2020; Groenewegen et al,2020).

In this study, nonblacks were almost 5 times the number of blacks. It is unclear if this occurred by chance or if this is a representation of black seniors who were able to survive with their burden of HF beyond the age of 65 years. Without regard to this differential in numbers, nonblacks were significantly older than blacks and also appeared to have significantly worse renal function than blacks (higher blood urea nitrogen). This finding may be attributed to the fact that nonblacks being older might have more comorbidities, longer duration of HF and probably more severe disease.

There were no significant gender differences by race and there was also no difference with respect to insurance status by race. This may be due to the fact that most of the cohort had access to quality health insurance as shown in table 1.

Even though there was a disproportionately lower number of blacks in this study, they appeared to have higher hazards for death compared to nonblacks after controlling for other factors. This is in keeping with reports from other studies (Pollard & Scommegna,, 2013). In this study, this racial disparity appeared to be present only among patients whose index discharge from the

hospital was anywhere other than home. This may imply that the difference in outcomes in race may also be partly dependent of the severity of HF. It is unclear why there was a marked difference in outcomes based on race for patients who were not discharged home at their prior hospitalization for HF. This difference might have driven by gulf in quality of the skilled nursing facilities or rehabilitation centers because these in turn accept certain profile of patients (quality and type of insurance among other factors). In addition, the differential in social support of blacks versus nonblacks may be another important reason for why blacks had worse outcomes than nonblacks when they are discharged to these skilled nursing facilities. Other reasons for racial disparity in outcomes such as education, income levels among others have been posited as possible contributors (Pollard & Scommegna, 2013). The survival paradox among black seniors as described above was not demonstrated in this study probably because there was only a small proportion of black seniors in the 80-to-85-year age group to elicit this paradox (28% of the total cohort). A focused study in this direction may be useful in assessing and understanding the survival attributes of this unique cohort and see if it can be extrapolated in younger seniors to generate better outcomes among black seniors with HF. The surrogate indices for economic status in this study, were PCP and insurance status.

PCP status was not an effect modifier of race as a predictor death among seniors acutely readmitted for HF in this study. Paradoxically, patients who had a PCP had about 5 times the hazard rate for mortality compared the hazard rate of patients without a PCP controlling for race, SBP, sodium, age and index disposition status. This may imply severe HF as patients who are very symptomatic may most likely have PCPs they follow up with regularly for management of

their care as opposed to patients with HF with less symptoms who may get by without much follow up.

Hyponatremia was predictive of mortality after univariate analysis and narrowly missed out on statistical significance after multivariate analysis which is like that reported by other researchers (Jao & Chiong, 2010). Research has shown that even mild hyponatremia among patients acutely hospitalized for HF, is independently associated with poor outcomes and conversely, slight improvement in serum sodium levels may have meaningful prognostic implications (Gheorghiade et al,2007; Rossi et al, 2007). Understanding of the mechanism of hyponatremia in HF and how to control may be useful in improving outcomes among patients with HF (Jao & Chiong, 2010).

Systolic blood pressure (SBP) has varying significance in terms of outcomes among patients with HF (Elgendy et al, 2020). SBP may be low irrespective of the LVEF and may also be low due to other factors such as inherent severity of HF or side effects of GDMT (Böhm et al, 2016). In this study, as shown in table 2 and figure, seniors with HF who had the lowest tertile range for HF had the highest hazards for death. This is in consonance with results of other researchers, with one of them indicating SBP has a j-shaped relationship with outcomes among patients with HF (Elgendy et al, 2020, Gheorghiade et al,2013; Ambrosy et al, 2014). Most of the work appears to agree that SBP less than 120 mmHg confers poor prognosis (Elgendy et al, 2020, Gheorghiade et al,2013; Ambrosy et al, 2014). Optimal SBP however, appears to be in a range of 120-140mmHg according to the findings of some other researchers, (Elgendy et al, 2020). However, in this study, patients in the second SBP tertile range (122-136 mmHg) still had higher

hazards of death compared to patients with SBP greater than 136mmHg and other parameters may need to be considered in the holistic approach to seniors with HF. This varying SBP ranges and associated implications may simply imply that adverse outcomes increase as the SBP becomes lower. A meta-analysis of six studies by Zhang et al revealed that the lowest SBP on admission significantly increased the hazard of all-cause mortality (hazard ratio of 2.22) when compared with the reference higher SBP category. Heart rate may also be considered in conjunction with SBP as was done in some other studies, but heart rate was not predictive of mortality as an independent variable as was not considered in the multivariate analysis (Elgendy et al, 2020).

The mechanisms by which a low SBP exerts its deleterious effects among patients with HF are myriad. One mechanism is symptomatic hypotension limiting the attainment of optimal doses of GDMT and therefore resulting indirectly to increased mortality because patients are not able to have lifesaving benefits of these proven medications (Wikstrand et al,2014; Ambrosy et al, 2013).

Low SBP may also limit the ability to adequately titrate HF medications to optimal doses and may even not be tolerable in seniors thereby limiting mortality benefits in this group.

Low SBP may also be an inherent characteristic of severe HF as greater mortality from low SBP has been noted to be more associated systolic dysfunction (LVEF less than 0.45) and NYHA classes II and III symptoms (Lee et al, 2006).

Another plausible mechanism of death among patients with very low SBP is the associated maladaptive activation of catecholamines, neurohormones and counterregulatory systems which

contribute to progressively worsening cardiac dysfunction and heightened risk of arrhythmias (Lee et al, 2006).

There is still some confusion on the extent of contribution to low SBP between severe HF and GDMT but is apparently clear is that low SBP constitutes harm and blood pressure should be tightly regulated to obtain the best outcomes.

4.1 Conclusion

Seniors who are acutely re-hospitalized for decompensated HF represent a high-risk cohort and have a very high short term mortality rate. Hyponatremia and low systolic blood pressure are independent predictors of mortality. Black seniors who were not discharged home after their index hospitalization for HF have higher hazards for all-cause mortality.

4.2 Limitations

The follow up period was short. A longer follow up period might have uncovered the predictive value of some factors that were not found to be significant in this study.

The effect of therapy on outcomes could not be assessed. There are other important explanatory variables which might further provided more understanding into some of the significant differences noted in this study which were not available for review. Some of these explanatory variables are; etiology of heart failure, heart failure medications, echocardiographic parameters as well as presence of heart failure medications such as atrial fibrillation.

4.3 Line of future research

Assess the survival paradox among black seniors aged 85 years and above to have greater insight into possible attributes that conferred longevity despite co-existent HF.

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