Hemodynamic variables and risk factors in a biracial stroke population

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ABSTRACT

Hypertension and diabetes are independent risk factors for stroke incidence and recurrence; thus management and treatment of blood pressure and hemoglobin A1c is an essential component of secondary stroke prevention. The goals of this project were to assess hemodynamic variables and related risk factors during stroke hospitalization by race and comorbid hypertension and diabetes status; examine patterns of antihypertensive and antidiabetic regimens prescribed at stroke discharge by race, age, gender, and hemodynamic variables; and compare stroke severity using The National Institutes of Health Stroke Scale (NIHSS) among stroke patients by race, age, gender, and comorbid hypertension and diabetes. Data was collected from the STEP-SC cohort, consisting of stroke patients over the age of 45 given a primary diagnosis of stroke (ICD9 430-438) at MUSC between October 2008-2009. Results showed that African Americans were significantly younger (OR=2.07; 95% CI=1.54, 2.79), had higher admission blood pressures (OR=1.52; 95% CI=1.13, 2.05), higher HbA1c (OR=2.03; 95% CI=1.37, 3.01), and a higher chance of being diagnosed with both hypertension and diabetes. Hypertension and diabetes diagnosis at discharge were significantly associated with each other. Age (OR=1.43; 95% CI=1.02, 1.99), discharge blood pressure (OR=1.57; 95% CI=1.11, 2.22), and HbA1c (OR=11.55; 95% CI=7.34, 18.19) were significantly associated with diabetes diagnosis at discharge. Blood pressure medication prescriptions at stroke discharge were related to age (OR=3.48; 95% CI=1.72, 7.03), hypertension diagnosis (OR=5.09; 95% CI=2.53, 10.26), and admission (OR=2.71; 95% CI=1.34, 5.47) and discharge blood pressures (OR=4.35; 95% CI=1.49, 12.75). Diabetes medication prescriptions were associated with diabetes diagnosis (OR=20.93; 95% CI=9.38, 46.68) and HbA1c (OR=48.25; 95% CI=15.88, 146.61). NIHSS scores were significantly associated ($p<0.05$) with age and were not related to comorbidity

status, although patients with hypertension had significantly lower scores than patients without hypertension.

INTRODUCTION

Burden of Stroke

Stroke is the leading cause of disability and the fourth leading cause of death in the United States (Ovbiagele & Nguyen-Huynh, 2011). In the United States, 7 million people--795,000 people a year--are affected by stroke (Lichtman et al., 2010; Obviagele & Nguyen-Huynh, 2011). The incidence of stroke doubles every ten years after the age of 55, and is highest in the Southeastern United States, in a region known as the “Stroke Belt” (Ovbiagele & Nguyen-Huynh, 2011). Risk factors for stroke include hypertension, diabetes, current smoking, abdominal obesity, hyperlipidemia, lack of exercise, alcohol consumption, diet, and psychosocial stress and depression (Ovbiagele & Nguyen-Huynh, 2011).

Both the incidence and mortality of stroke have been shown to differ across multiple races. Stroke is much more prevalent in African-American populations compared to Caucasian populations. Stroke rates for African-American males have been seen to be more than twice that for Caucasian males in various regions across the United States. African-American males also have higher rates of more severe strokes. The incidence of subarachnoid hemorrhage and intracerebral hemorrhage is more than twice the incidence in Caucasian males. Coma and death resulting from stroke is significantly more common in African-American populations than in Caucasian populations. African-Americans and Asian/Pacific Islanders also have significantly higher rates of mortality associated with intracerebral hemorrhage than do Caucasians, while

Hispanics have lower rates of mortality after ischemic stroke and intracerebral hemorrhage, but higher rates of mortality after subarachnoid hemorrhage (Stansbury et al., 2005).

The incidence of and recovery after stroke also varies across gender. Men and women are equally likely to suffer from a stroke, until they reach age 75. At this age, the incidence of stroke becomes higher in women than in men. Also, women do not recover from a stroke as well as men do. Women have higher mortality rates after stroke than men do, and institutional care after stroke is more likely to be needed by women than by men. (Dearborn & McCullough, 2009).

Hypertension and High Blood Pressure

The European Society of Hypertension and the European Society of Cardiology (ESH-ESC) and the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7) both define normal or optimal blood pressure as less than 120mmHg systolic blood pressure and less than 80mmHg diastolic blood pressure (Dorjgochoo et al., 2009). JNC7 also defines prehypertension as 120-139/80-89mm Hg, stage I hypertension as 140-159/90-99mmHg, and stage II hypertension as a systolic blood pressure of at least 160mmHg or a diastolic blood pressure of at least 100mmHg (Dorjgochoo et al., 2009).

Hypertension is present in over 75 million adults in the United States over the age of 20, and is one of the biggest and most prominent risk factors for stroke (Ovbiagele & Nguyen-Huynh, 2011; Pepp, Csaszar, Paulik, & Balogh, 2012). Over half of stroke patients have hypertension (Rewell et al., 2010). A linear correlation between blood pressure and mortality and morbidity due to stroke is seen in patients with blood pressures greater than 115/75mmHg

(Pepp, Csaszar, Paulik, & Balogh, 2012). Every 10mmHg increase in blood pressure increases a person's risk of having a stroke by 20-30% (Rewell et al., 2010). Also, in patients between the ages of 40 and 70, a 20mmHg increase in systolic blood pressure and 10mmHg increase in diastolic blood pressure doubles the risk of stroke (Pepp, Csaszar, Paulik, & Balogh, 2012).

Multiple pathways exist between hypertension and stroke. The high pressure within the vessels can change the functions of the endothelium and smooth muscle surrounding the vessels. The increased pressure on the endothelium can also cause an increase in the permeability of the blood-brain barrier. These alterations in the endothelium and its interactions with blood cells can result in the formation of thrombi and ischemic lesions. Also, the progression of atherosclerosis is accelerated by hypertension and leads to inhibited blood flow, further increasing blood pressure. Eventually, this weakening and thickening of the vessels can lead to either ischemic or hemorrhagic strokes (Johansson, 1999).

A variety of medications can be prescribed in order to reduce hypertension. The goal of reducing blood pressure is to decrease the patient's risk of cardiovascular morbidity and mortality (Coca et al., 2008). Diuretics and beta-adrenergic blocking agents have long been used in antihypertensive regiments. More recently, calcium antagonists and angiotensin-converting enzyme (ACE) inhibitors have been prescribed in therapy for hypertension (Pepine et al., 1998).

INVEST:

The International Verapamil-Trandolapril Study (INVEST) sought to compare the effects of treatment with calcium antagonist based strategies, using verapamil-trandolapril, versus noncalcium antagonist based strategies, using atenolol-hydrochlorothiazide, and assess the risk of adverse outcomes associated with the use of each treatment (Pepine et al., 1998). Patients were eligible to participate in this study if they were over the age of 50, had essential hypertension, as defined by JNC6, which required drug therapy, and had documented coronary artery disease (Pepine et al., 1998). The study collected data from 22,500 patients with hypertension and coronary artery disease (Nilsson, 2009). Subjects were randomly assigned to be in either the calcium antagonist-based treatment group or the noncalcium antagonist-based treatment group. The calcium antagonist group received 240 mg of verapamil SR daily, while the noncalcium antagonist group received 50 mg of atenolol daily. Dosages were adjusted and trandolapril and hydrochlorothiazide were added as needed. The results of INVEST indicated that both treatment strategies were equal in their effectiveness at blood pressure control and at preventing death, nonfatal myocardial infarction, and nonfatal stroke (Pepine et al., 1998).

ONTARGET:

The objective of the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) is to compare telmisartan, angiotensin-receptor blocker (ARB), and a combination of telmisartan and ramipril, an angiotensin-converting-enzyme (ACE) inhibitor, on their effectiveness at reducing mortality and morbidity from cardiovascular causes in patients with vascular disease or high-risk diabetes (ONTARGET Investigators, 2008). The data collected on the telmisartan treatment and the telmisartan combined with ramipril treatment was then to be compared to the effectiveness of ramipril by itself, which has already been established as an effective treatment (Fitchett, 2009). Data was collected from a total of 25,620 subjects from 40 countries. The results of the ONTARGET study showed only mild differences between the average blood pressures of the telmisartan treatment, the telmisartan and ramipril treatment, and the ramipril treatment. Also, no significant differences between the three treatments' effectiveness at reducing the incidence of cardiovascular death, non-fatal myocardial infarction, stroke, or heart failure were found, indicating that telmisartan and ramipril are equally effective. Patients treated with both telmisartan and ramipril combined, however, demonstrated a higher risk of hypotension, syncope, renal dysfunction, hyperkalemia, and renal dysfunction, leading to the conclusion that the combination of ACE inhibitors and ARBs was not beneficial (Fitchett, 2009).

PROGRESS:

The objective of the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) was to determine the effects of a perindopril-based antihypertension regimen in hypertensive and non-hypertensive patients with a history of stroke or transient ischemic attack (PROGRESS Collaborative Group, 2001). Data was collected from 6,105 subjects from Asia, Australasia, and Europe. Subjects were randomly assigned into either the active treatment group or the placebo group. Those placed in the active treatment group were treated with perindopril, an angiotensin-converting-enzyme inhibitor. Indapamide, a diuretic, was also added to this treatment at the physicians' discretion. The results of this study showed that after four years of treatment, the blood pressure of the subjects in the active treatment group was 9/4mmHg lower than that of the subjects in the placebo group. Active treatment also lowered the incidence of stroke and major vascular events in both hypertensive and non-hypertensive subjects. Subjects in the active treatment group who received a combination treatment of perindopril and indapamide saw a reduction in blood pressure by 12/5mmHg and stroke risk by 43%, while subjects who received only peridopril saw a 5/3mmHg reduction in blood pressure and no significant reduction in stroke risk. These results indicated that a combination of perindopril and indapamide should be included in antihypertension regimens (PROGRESS Collaborative Group, 2001).

PROTECT:

The Preventing Recurrence of Thromboemolic Events through Coordinated Treatment (PROTECT) Program sought to evaluate evidence-based secondary stroke prevention therapies and assess the practicability of using them to design an aggressive stroke-prevention program for hospitals to use in standard stroke care. The ultimate goal of this study was to come up with and implement eight forms of treatment, four behavioral changes and four medications (Ovbiagele et al., 2004a). The four behavioral changes included cessation of smoking, starting a diet recommended by the American Heart Association, exercise counseling, and stroke education. The four medications included antithrombotic agents, statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and diuretics. The results of the PROTECT program showed an increase in implementation for all four medication-based treatments and that patients were being educated about the four lifestyle modifications before discharge (Ovbiagele et al., 2004a). A study evaluating the adherence of the prevention measures showed a significant number of patients continued to adhere to the PROTECT therapies 90 days after being discharged from the hospital (Ovbiagele et al., 2004b).

Diabetes

The American Diabetes Association’s criteria for the diagnosis of diabetes mellitus includes a hemoglobin A1c of 6.5% or higher, a fasting plasma glucose of 126 mg/dL or higher, a 2-h plasma glucose during an oral glucose tolerance test of 200 mg/dL or higher, and a random plasma glucose of greater than 200 mg/dL in patients with classic symptoms of hyperglycemia (Malaguarnera et al., 2012). Diabetes mellitus comes in two forms: type 1 and type 2. Type 1 diabetes usually develops during childhood or adolescence, which is why it is commonly referred to as juvenile diabetes. This form of diabetes is a result of the immune system attacking and destroying the beta-cells, which produce insulin, in the pancreas, resulting in an insulin deficiency (Campbell et al., 2012). Type 2 diabetes, which is the most common form of diabetes, usually appears in adulthood and is the result of a combination of insulin deficiency and insulin resistance, which is caused by membrane receptors not functioning properly (Campbell et al., 2012; Atlantis, 2012).

Diabetes mellitus is associated with complications involving many different organs of the body, including the eyes, kidneys, nerves, heart, and blood vessels (American Diabetes Association [ADA], 2011). Hyperglycemia is often accompanied by increased urine output, increased thirst, weight loss, blurred vision, and even impairment of growth and ketoacidosis if left untreated. Retinopathy, nephropathy, peripheral neuropathy, and autonomic neuropathy are common long-term complications of diabetes, and can lead to loss of vision, renal failure, foot ulcers, amputations, gastrointestinal complications, and cardiovascular complications (ADA, 2011). Diabetes has also been shown to increase the risk of atherosclerosis and other cardiovascular diseases (ADA, 2011).

The presence of diabetes mellitus doubles a person's risk of developing many vascular diseases (Emerging Risk Factors Collaboration, 2010). Diabetes is present in 25% of stroke patients and acute hyperglycemia is present in 40% of stroke patients. Hypertension is present in 55% of diabetes patients (Rewell et al., 2010).

Studies have suggested that hyperglycemia upon admission, close to the time of the stroke, is associated with poor recovery in both diabetic and non-diabetic stroke patients (Kuwashiro et al., 2012; Hu et al., 2012). However, many say that the high glucose levels could be due to stress caused by having a stroke (Kuwashiro et al., 2012). A study by Hu and colleagues (2012) showed glucose levels at the time of admission were positively associated with mortality rates in non-diabetic patients who had ischemic strokes. The data collected on diabetic patients, however, was inconclusive (Hu et al., 2012). Another study by McFarlane, Sica, and Sowers (2005) found the presence of hyperglycemia was associated with poor recovery from stroke. A possible reason behind this association is that hyperglycemia increases lactate production in the brain, which facilitates the conversion of hypoperfused at-risk tissue into areas of infarction. The beneficial effects of early restoration of blow flow are thus reduced, leading to the inability of the patient to recover (McFarlane, Sica, & Sowers, 2005).

In 2010, the Emerging Risk Factors Collaboration conducted a collaborative meta-analysis examining diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease. The results of this study showed a moderate, non-linear relationship between fasting blood glucose concentration and risk of coronary heart disease or ischemic stroke, and no associations were found at fasting blood glucose concentrations between 3.9mmol/L and 5.6mmol/L (Emerging Risk Factors Collaboration, 2010).

There are many different types of medications used to lower blood sugar, including both oral and injectable medications. Classes of oral medications used to treat diabetes include meglitinides, sulfonylureas, dipeptidy peptidase-4 inhibitors, biguanides, thiazolidinediones, and alpha-glucosidase inhibitors. Meglitinides, such as repaglinide and nateglinide, and sulfonylureas, such as glipizide, glimepiride, and glyburide, lower glucose levels by stimulating the release of insulin. Dipeptidy peptidase-4 inhibitors, such as saxagliptin, sitagliptin, and linagliptin, work by stimulating insulin release and inhibiting glucose release from the liver. Biguanides, such as metformin, and Thiazolidinediones, such as rosiglitazone and pioglitazone, improve insulin sensitivity and inhibit the release of glucose. Alpha-glucosidase inhibitors, such as acarbose and miglitol, lower blood sugar by slowing down the breakdown and absorption of starches and sugars. Classes of injectable medications included amylin mimetics and incretin mimetics. While both amylin mimetics and incretin mimetics both stimulate the release of insulin, amylin mimetics are coupled with insulin injections while incretin mimetics are used with metformin and sulfonylurea (Mayo Clinic staff, 2012).

ACCORD:

The Action to Control Cardiovascular Risk in Diabetes study was conducted in April 2010 and studied 4,733 high-risk patients with type 2 diabetes. Subjects were divided into two groups—the intensive therapy group or the standard therapy group. The intensive therapy targeted a systolic blood pressure of less than 120 mmHg, while the standard therapy targeted a systolic blood pressure of less than 140 mmHg. After an average of 4.7 years, the mean systolic blood pressure was 119 mmHg for the intensive therapy group and 134 mmHg for the standard therapy group. While the intensive therapy group did show lower risk for pre-specified secondary endpoint stroke, this group also experienced more serious adverse events that were attributed to antihypertensive treatment (Nilsson, 2011).

UKPDS:

The UK Prospective Diabetes Study (UKPDS) examined the effects of glucose control and blood pressure control on diabetic complications. The UKPDS consisted of both a glucose control study and a blood pressure control study (King, Peacock, & Donnelly, 1999).

The goals of the glucose control study were to examine the effectiveness on intensive glycemic control, in the form of either conventional or intensive therapy, on reducing the incidence of complications associated with diabetes. The conventional therapy used in this study sought to keep fasting plasma glucose below 15mmol/L, while the goal of the intensive therapy was to keep fasting plasma glucose below 6mmol/L. Both conventional and intensive therapies implemented diet adjustments to lower fasting plasma glucose to the desired values. The results of the UKPDS glucose control study indicated a significant decrease in macrovascular and microvascular events associated with intensive glucose control. No effect, however, was found on mortality (King, Peacock, & Donnelly, 1999).

The goal of the blood pressure control study was to compare the effects of captopril, an angiotensin-converting enzyme inhibitor, and atenolol, a beta-adrenoceptor blocker, on reducing macrovascular and microvascular events. The results showed no significant difference in the effectiveness of captopril and atenolol on reducing blood pressure, macrovascular events, and microvascular events (King, Peacock, & Donnelly, 1999).

Overall, the researchers of the UKPDS study concluded that both glucose and blood pressure control resulted in a decrease in the incidence of complications associated with diabetes (King, Peacock, & Donnelly, 1999).

ADVANCE:

The Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial had both glucose control and blood pressure control branches. The glucose control portion of the study sought to implement an intense treatment to lower patients' hemoglobin A1c to below 6.5% and examine its effect on risk of microvascular and macrovascular disease. The blood pressure control portion of the study sought to examine the effects of routine administration of antihypertension therapy and assess possible added benefits when combined with other cardiovascular preventative therapies. Over 10,000 patients with type 2 diabetes participated in the ADVANCE trial and were placed in four treatment categories: intensive glucose lowering and additional routine blood pressure lowering, standard glucose therapy and routine blood pressure lowering, intensive glucose lowering and placebo, and standard glucose therapy and placebo. Gliclazide MR, a sulfonylurea, was used in intensive glucose lowering, and a perindopril/indapamide combination was used in routine blood pressure lowering.

The results of the glucose portion of the ADVANCE trial showed that the mean hemoglobin A1c in the intensive therapy group was 6.5%, while the standard therapy group had a mean hemoglobin A1c of 7.3%. Patients in the intensive control group also had a significantly lower systolic blood pressure compared to those in the standard control group, and reduced diabetic nephropathy by 20% compared to the standard control group. No increase in mortality was associated with the intensive control group, leading to the conclusion that the intensive strategies used in this study are both effective and safe (Heller, 2009).

CARDS:

The Collaborative Atorvastatin Diabetes Study (CARDS) sought to evaluate the effects of statins on the risk of cardiovascular events and stroke in patients with type 2 diabetes without cardiovascular disease. 2,838 subjects were included in this study and received either 10mg of Atorvastatin a day or a placebo. The results of the CARDS indicated a significant decrease in cardiovascular events and stroke associated with the use of statins, with a 37% decrease in cardiovascular events and a 50% decrease in the risk of stroke compared to the placebo group (Wijenaike, 2004).

IRAS:

The Insulin Resistance Atherosclerosis Study (IRAS) was a epidemiological study on the relationships between glucose levels, insulin levels, insulin resistance, factors affecting the risk of cardiovascular disease, and clinical and subclinical cardiovascular disease. The IRAS collected data on 1,625 subjects with impaired glucose tolerance, moderately elevated fasting glucose levels, or diabetes. Subjects were excluded if they had used insulin in the previous five years, so the diabetics used in this study most likely had mild forms of diabetes. The results of the IRAS indicated that a positive correlation exists between established non-insulin-dependent diabetes mellitus and fasting glucose levels and common carotid intimal medial thickness. No significant relationship, however, was found between the duration of diabetes and common carotid intimal medial thickness (Wagenknecht et al., 1997).

The National Institutes of Health Stroke Scale (NIHSS): A Measure of Stroke Severity

A variety of tests are used to measure stroke severity, including the National Institutes of Health Stroke Scale (NIHSS) and the Glasgow Coma Scale (GCS). The National Institutes of Health Stroke Scale, when it was developed in 1989, was originally composed of 15 items. This scale was later revised and shortened, and the current NIHSS consists of 13 items and takes less than 10 minutes to complete (Brott et al., 1989). The items on the NIHSS evaluate the patient's level of consciousness, vision, extra-ocular movements, facial palsy, limb strength, ataxia, sensation, speech, and language (Lyden & Hantson, 1998). The scores on the NIHSS can be used to predict both short-term and long-term outcomes and chances of recovery in stroke patients. Scores range from zero to 42, with a score of zero indicating no stroke, with the patient being completely alert and having no loss of function, and a score of 42 indicating the most severe stroke, with the patient being completely unresponsive (National Institute of Neurological Disorders and Stroke, n.d.).

Recurrent Stroke

Recurrent events, such as secondary strokes, occur in approximately 185,000 stroke survivors. These events are associated with higher mortality rates and disability levels (Lichtman et al., 2010). The American Heart Association (AHA) and the American Stroke Association (ASA) release recommendations for the prevention of recurrent stroke every few years. In these recommendations, treatments of multiple vascular risk factors are addressed, including hypertension and diabetes. For the treatment of hypertension, the AHA/ASA recommends reducing blood pressure by approximately 10/5 mmHg; lifestyle modifications, including decreasing salt intake, weight loss, regular exercise, decreased alcohol consumption, and a diet rich in fruits, vegetables, and low-fat dairy products; and the implementation of individualized drug regimens consisting of diuretics and/or angiotensin-converting enzyme inhibitors. The AHA/ASA's recommendations for the treatment of diabetes include meticulous control of glucose level and blood pressure, and aiming for the patient's hemoglobin A1c to be below 7% (Furie et al., 2010).

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) also released recommendations on treating hypertension in order to prevent recurrent stroke. The JNC 7 provides suggestions for how often hypertensive patients should be reevaluated based on their initial blood pressure. Patients with blood pressures within the normal range, <120/<80 mm Hg, should be rechecked in two years; patients with a systolic blood pressure of 120-139 mmHg or a diastolic blood pressure of 80-89 mmHg, classified as having prehypertension, should be rechecked in one year; patients with stage 1 hypertension, defined as a systolic blood pressure of 140-159 mmHg or a diastolic blood pressure of 90-99 mmHg, should be rechecked within two months; and patients with stage 2 hypertension, >160/>100 mmHg, should be rechecked within one month. The JNC 7 also suggests lifestyle modifications to prevent and manage hypertension. It is recommended that patients maintain a normal body weight, defined as a body mass index (BMI) of 18.5-24.9 kg/m^2, consume a healthy diet, rich in fruits, vegetables, and low fat dairy, decrease sodium intake to less than 100 mmol per day, exercise at least 30 minutes per day, and limit alcohol consumption to no more than 2 drinks per day for men and 1 drink per day for women. Diuretics and angiotensin-converting enzyme inhibitors are the medications recommended to prevent recurrent stroke (Joint National Committee, 2003).

Specific Aims

AIM 1: To assess hemodynamic variables and related risk factors during stroke hospitalization by race and comorbid hypertension and diabetes.

AIM 2: To examine patterns of antihypertensive and antidiabetic regimens prescribed at stroke discharge by race, age, gender, and hemodynamic variables.

AIM 3: To compare stroke severity using The National Institutes of Health Stroke Scale (NIHSS) among stroke patients by race, age, gender, and comorbid hypertension and diabetes.

METHODS

We used patients from the Stroke Education and Prevention-South Carolina (STEP-SC) project, which was an initiative of the South Carolina Aging Research Network (SCARN) that used an analytical database provided by the South Carolina Office of Research and Statistics. STEP-SC consisted of two projects, the first of which was the creation of a database that included demographic and medical information of South Carolina patients discharged from the hospital after being diagnosed as having a stroke. The second project was a survey, conducted over the telephone, of patients who had been discharged from the hospital after suffering a stroke. MUSC's Institutional Review Board (IRB) approved the STEP-SC project.

Subjects for this project were chosen from patients at the Medical University of South Carolina (MUSC) who were given a primary diagnosis of stroke between October 1, 2008 and September 30, 2009. The patients chosen were at least 45 years of age during this time period. Patients of all races, genders, and socio-economic statuses were included in this study. Data was collected from MUSC's electronic medical records, including patients' lab records, nursing records, and triage notes. The database was created using a spreadsheet in Microsoft Office Excel 2010 that will be located in a password-protected file. Values were entered into this password-protected database as they were collected. We collected subjects' hemoglobin A1c (HbA1c) levels, admission and discharge blood pressures (Adm and Dis BP), National Institute of Heath Stroke Scale (NIHSS) scores, and antihypertensive and antidiabetic medication regimen information. Hypertension (Htn) was defined as blood pressures ≥140/90 mmHg. Diabetes (DM) was defined as HbA1c levels ≥6.5%.

Patient demographics, hemodynamic values, comorbidity status, and antihypertensive and antidiabetic medication regimens prescribed at stroke discharge were compared by age (≥65 years vs. <65 years), race (African American vs. Caucasian), and gender (male vs. female). NIHSS scores were also compared by comorbidity status. Comorbidity status was divided into four categories. These categories were: neither hypertension nor diabetes, hypertension only, diabetes only, and both hypertension and diabetes. Statistical analyses were conducted using SAS Software Version 9.3 (SAS Institute, Cary, North Carolina). Pearson's chi-square tests, t-tests, and Analysis of Variance (ANOVA) were used. Statistical significance was defined as a two-sided P value of less than 0.05.

RESULTS

Baseline Characteristics

The total cohort consisted of 784 subjects, with the average age being 65.9 ± 11.6 years. The cohort was 65.05% Caucasian (CA), 34.95% African American (AA), 53.32% female, and 46.68% male. Hypertension diagnoses were given to 55.23% of patients at discharge, and diabetes diagnoses were given to 23.6% of patients at discharge. Patient characteristics, including age, sex, hypertension and diabetes diagnosis, and comorbidity status, were compared by race (Table 1). A significantly smaller ($p<0.05$) proportion of African American patients than

Caucasian patients were older the age of 65 (AA 41.61% vs. CA 59.61%; OR=2.07; 95% CI=1.54, 2.79). A larger proportion of Caucasian patients were male compared to that seen in African American patients (CA 47.84% vs. AA 44.53%). However, this difference was not shown to be significant. There was no significant difference by race in the proportion of patients diagnosed with hypertension at discharge (OR=0.91; 95% CI=0.68, 1.22). There was a significant effect ($p<0.05$) in diabetes diagnoses at discharge by race, with African American patients having a significantly higher prevalence of diabetes compared to Caucasian patients (AA 31.39% vs. CA 19.41%; OR=1.89; 95% CI=1.36, 2.66). African American patients also had higher admission blood pressures (OR=1.52; 95% CI=1.13, 2.05) and HbA1c levels (OR=2.03; 95% CI=1.37, 3.01). There was no association between race and discharge blood pressure.

Significant differences ($p<0.05$) were also seen when comorbidity status was compared by race. Although the proportions of Caucasian and African American patients with neither hypertension nor diabetes were similar (CA 37.45% vs. AA 35.4%), a higher proportion of the Caucasian patients (43.14%) had only hypertension than the African American patients (33.21%). However, the African American patients were shown to have higher rates of patients with diabetes only (AA 10.95% vs. CA 6.47%), as well as higher rates of patients with both hypertension and diabetes (AA 20.44% vs. CA 12.94%).

Hypertension Diagnosis

Patient characteristics were also compared by hypertension diagnoses (Table 2). Hypertension diagnosis at discharge was not associated with age or gender. A significant proportion (65.95%) of patients diagnosed with diabetes at discharge were also diagnosed with hypertension at discharge (OR=1.79; 95% CI= 1.27, 2.53). Neither hypertensive blood pressure at admission nor hypertensive blood pressure at discharge showed significant differences by hypertension diagnosis. Finally, there was no significant difference between hypertension diagnosis and HbA1c levels (HbA1c <6.5% :25.22% vs. HbA1c >6.5%:29.33%).

Diabetes Diagnosis

More significant differences were found when patient characteristics were compared by diabetes diagnosis (Table 3). A significantly higher proportion of patients with diagnosed diabetes were ≥ 65 years of age (DM 60% vs. No DM 51.25%; OR=1.43; 95% CI=1.02, 1.99). Gender was not associated with diagnosed diabetes at discharge. Diabetes diagnosis was significantly associated with diagnosis of hypertension at stroke discharge (OR=1.79; 95% CI=1.27, 2.53). Admission blood pressure was now found to be significantly associated with diabetes diagnoses at discharge. However, patients with discharge blood pressures 140/90 mm Hg or higher were significantly ($p<0.05$) more likely to be diagnosed with diabetes at stroke discharge compared to patients with discharge blood pressures less than 140/90 mmHg (OR=1.57; 95% CI=1.11, 2.22). A significant difference ($p<0.05$) was also found when patients' HbA1c levels were examined, with significantly higher proportions being seen among patients diagnosed with diabetes at discharge (HbA1c >6.5%: 63.89% vs. HbA1c<6.5%: 13.28%; OR=11.55; 95% CI=7.34, 18.19).

Antihypertension Medication Regimens

Table 4 shows the proportion of patients prescribed antihypertensive medication regimens at discharge as examined by race, sex, age, hypertension diagnosis at discharge, and admission and discharge blood pressure. Of the Caucasian patients, 78.36% were prescribed blood pressure medications at discharge, which did not differ significantly from the 81.13% of African American patients were given blood pressure medications at discharge. When examined by sex, males (85.11%) and females (74.62%) that were prescribed blood pressure medication at discharge were not significantly different. A significant effect ($p<0.05$) by age was found, with 88.6% of patients 65 years and older being prescribed blood pressure medication at discharge (OR=3.48; 95% CI=1.72, 7.03). Although a significantly larger ($p<0.05$) proportion of patients given a hypertension diagnosis were given antihypertensive medications at discharge (89.36%) than patients not diagnosed with hypertension, 62.92% of patients not diagnosed with hypertension were still prescribed blood pressure medications at discharge (OR=5.09; 95% CI=2.53, 10.26). The rate with which antihypertensive therapy was prescribed at discharge was also significantly higher ($p<0.05$) among patients presenting with hypertensive blood pressures at admission (OR=2.71; 95% CI=1.34, 5.47), as well as at discharge (OR=4.35; 95% CI=1.49, 12.75)

Antidiabetes Medication Regimens

Table 5 presents the proportions of patients prescribed antidiabetic medication regimen post stroke discharge compared by race, sex, age, diabetes diagnosis, and HbA1c level. Although a higher proportion of the African American patients were prescribed antidiabetic medication than Caucasian patients (30.19% vs. 18.13%), the difference was not significant. There were also no significant sex or age differences in the proportions of patients prescribed antidiabetic medications at discharge. Of the patients diagnosed with diabetes at discharge, 67.39% were prescribed antidiabetic medication. This proportion was significantly larger ($p<0.05$) than the 8.99% seen in patients who were not diagnosed with diabetes (OR=20.93; 95% CI=9.38, 46.68). Among the patients with a HbA1c level greater than 6.5%, 84.85% were prescribed antidiabetic medication regimens, which was significantly more ($p<0.05$) than the 10.4% seen in patients with HbA1c levels less than 6.5% (OR=48.25; 95% CI=15.88, 146.61).

Stroke Severity

The average NIHSS score of the total cohort (n=334) was 7.05. The NIHSS score of the African American patients was slightly higher than that seen in the Caucasian patients (7.72 vs. 6.63), but with a difference of only 1.09 points, it was not statistically significant (Figure 1). Patients 65 years old and over had higher NIHSS scores than those between the ages of 45 and 64 (≥65 years: 7.91 vs. 45-64 years: 5.98) (Figure 2). This difference was found to be statistically significant ($p<0.05$). The average NIHSS score of female patients was 7.51, and males had an average NIHSS score of 6.59 (Figure 3). The difference between the NIHSS scores of females and males was not statistically significant.

Figure 4 shows that there is no relationship between comorbidity status and NIHSS score. Stroke severity was not significantly higher or lower in patients with both hypertension and diabetes than in patients with neither condition. Scores were also lower in patients with diabetes only compared to those not diagnosed with diabetes, but not significantly so (DM 6.10 vs. No DM 7.40). However, the average NIHSS scores were significantly lower ($p<0.05$) in patients with only hypertension compared to patients not diagnosed with hypertension (Htn 6.15 vs. No Htn 8.19).

DISCUSSION

When stroke patients' baseline characteristics were compared by race, it was shown that African American stroke patients were two times more likely than Caucasian stroke patients to be between the ages of 45 and 65. This result suggests that African Americans are having strokes at significantly younger ages than Caucasians. African American stroke patients also appeared to be more likely to be female than Caucasian patients, although statistical analysis revealed the difference was not significant. Race did not appear to play a role in the occurrence of hypertension in stroke. However, results did show that African American patients were two times more likely to have comorbid diabetes than Caucasian patients, suggesting that race may play a role in the prevalence of diabetes in stroke. Race also appeared to influence the comorbidities present in stroke patients, with African American patients being more likely to have both hypertension and diabetes, and less likely to have only one comorbidity. Caucasian stroke patients were more likely to have only hypertension than were African American stroke patients. African American patients were also 50% more likely to have hypertensive blood pressures at admission and over two times more likely to have diabetic HbA1c levels. No association was found between race and discharge blood pressure.

Neither age nor sex appeared to be involved in the prevalence of hypertension diagnoses at stroke discharge. However, results did show that patients with comorbid hypertension were almost twice as likely to also have comorbid diabetes compared to patients not diagnosed with hypertension. These results suggest that the prevalence of comorbid diabetes does affect the prevalence of comorbid hypertension. On the other hand, The prevalence of results showed that just as many patients with blood pressures less than 140/90 mmHg on admission were diagnosed with hypertension as were patients who had blood pressures greater than 140/90 mmHg on admission. The same result was found when blood pressure at discharge was examined, suggesting that the presence of hypertensive blood pressures, at admission or discharge, plays no role in the likelihood of hypertension contributing to the patient's stroke. A patients' having a diabetic HbA1c level (>6.5%) also appeared to have no effect on the prevalence of comorbid hypertension, as patients with HbA1c levels greater than 6.5% were not found to be significantly more likely to be diagnosed with hypertension at discharge than patients without diabetic HbA1c levels.

comorbid diabetes appeared to be effected by more variables than was comorbid hypertension. Patients over the age of 65 were almost twice as likely to be diagnosed with comorbid diabetes, suggesting that age contributes to the prevalence of diabetes in stroke patients. Sex, however, did not appear to affect diabetes diagnosis at discharge, meaning males were just as likely as females to have diabetes contribute to their strokes. Just as the presence of comorbid diabetes increased the likelihood of the patient having comorbid hypertension, the presence of comorbid hypertension increases the likelihood of the patient being diagnosed with comorbid diabetes. Patients with hypertension were almost two times more likely to also be diagnosed with diabetes than patients without hypertension. Admission blood pressure did not appear to play a role in diabetes diagnosis. However, discharge blood pressure did appear to contribute to diabetes diagnosis at discharge, as patients with blood pressures greater than 140/90 mmHg at discharge were 1.57 times more likely to receive a diagnosis of diabetes. HbA1c levels also appeared to contribute to diabetes diagnosis at discharge, with patients with HbA1c levels higher than 6.5% being almost twelve times more likely to be diagnosed with comorbid diabetes than patients with HbA1c levels less than 6.5%.

Although treating hypertension and diabetes is important in primary and secondary stroke prevention, it has been shown that many patients with hypertension were not being prescribed antihypertensive medication regimens at stroke discharge. Therefore, we set out to assess the patterns with which antihypertensive medication regimens (as well as antidiabetic medication regimens) are prescribed after stroke. The likelihood of a patient being prescribed antihypertensive medications at discharge did not appear to be affected by race or gender. Age, however, did appear to contribute to blood pressure medication prescriptions, with patients over the age of 65 being almost 3.5 times more likely to be prescribed medications to control blood pressure than patients between the ages of 45 and 65. This result suggests that older stroke patients are more likely to be put on antihypertensive medications than younger stroke patients.

The presence of comorbid hypertension did, as would be expected, significantly contribute to the likelihood of the patient being prescribed antihypertensive medications. However, a large proportion (almost 63%) of patients not diagnosed with hypertension also received antihypertensive medications, suggesting that stroke patients are likely to be prescribed blood pressure medications at stroke discharge, whether or not they actually have been diagnosed with hypertension. Finally, blood pressure also contributed to the likelihood of antihypertensive medications being prescribed, as patients with blood pressures greater than 140/90 mmHg at admission being almost three times more likely and patients with blood pressure greater than 140/90 mmHg at discharge being over four times more likely to be prescribed blood pressure medications than patients without hypertensive blood pressures. The reason patients with hypertensive medications at discharge are more likely to be prescribed antihypertensive medications than those with hypertensive blood pressures at admission may be due to the high blood pressure at admission being related to the stroke. The doctors may be getting patients' blood pressures under control during their hospital stay, making antihypertensive medication regimens unnecessary.

The rates with which antidiabetic medications are prescribed was not shown to be significantly affected by race, although our results did suggest African American patients tended to be more likely to receive antihyperglycemia medications than were Caucasian patients. Age and sex were also not shown to be significant factors. As expected, being diagnosed with diabetes contributed significantly to being prescribed antidiabetic medications at discharge. Diabetic patients were almost 21 times more likely to be prescribed diabetes medications than were patients not diagnosed with diabetes. These results show that, unlike antihypertension medications, doctors are not likely to prescribed antidiabetic medications to stroke patients unless they have actually been diagnosed with diabetes. Finally, HbA1c levels significantly affected whether or not patients were prescribed diabetes medications. Patients with HbA1c levels higher than 6.5% were 48 times more likely to be prescribed antidiabetic medications than patients with HbA1c levels lower than 6.5%. These results suggest that doctors will prescribe antidiabetic medication regimens if the patient presents a diabetic HbA1c level, even if the patient has not been officially diagnosed with diabetes.

Race did not have a significant effect on stroke severity, although African American patients did have slightly higher NIHSS scores than did Caucasian patients. Age, however, did significantly contribute to stroke severity, with patients 65 years and older having more severe strokes compared to patients between the ages of 45 and 65. Although our results suggest females had slightly more severe strokes than males, statistical analysis revealed there was no significant effect by gender.

When we assessed stroke severity by comorbidity status, we originally expected strokes to be more severe among patients with more comorbidities than with patients without any comorbidities. However, statistical analysis showed no association between stroke severity and comorbidity status. The number of comorbidities a patient has does not lead to an increase in the severity of his or her stroke. Diabetes was also individually shown to not be a significant associate of stroke severity. Hypertension, however, was shown to be associated with less severe strokes. This unexpected result could be an artifact of our sample, as a large proportion of our patients were diagnosed with hypertension. Also, patients diagnosed with hypertension at discharge could have already been previously diagnosed with hypertension and were already taking antihypertensive medications prior to their stroke. These medications would have an effect on the vasculature in the brain and reduce the size of the blockages that do occur. Patients not already taking blood pressure medications would not have this advantage and, as a result, may have had more severe blockages and thus experience more severe strokes.

In the future, this project can be expanded to include more subjects. More subjects may lead to more significant results, especially in the rates with which antidiabetic medication regiments were prescribed, as we had the fewest subjects included in that group. Also, these variables can be broken down further by assessing them by socioeconomic status or weight. Looking at more races than only Caucasians and African Americans, such as including Hispanics and Asians, may also yield interesting results. Also, stroke types could be examined more closely. Patients with hemorrhagic strokes would naturally have lower blood pressures than patients presenting with ischemic strokes or transient ischemic attacks. This difference in blood pressure by stroke type could have affected our average blood pressure results. Finally, this project was mainly focused on finding the “what”—we were looking to find what patterns existed. Now that we have found significant patterns, future projects can focus on the “why”—finding out why these patterns exist and what is causing them.

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Table 1. Characteristics by Race

Characteristics	CA (n=510)	AA (n=274)	Total (n=784)
Age ≥ 65 years	59.61	41.61*	53.32
Male	47.84	44.53	46.68
HTN Diagnosis	56.08	53.65	55.23
DM Diagnosis	19.41	31.39*	23.6
Comorbidity Status		*	
Neither HTN or DM	37.45	35.4	36.73
HTN Only	43.14	33.21	39.67
DM Only	6.47	10.95	8.04
Both HTN and DM	12.94	20.44	15.56
Adm BP ≥140/90 mmHg	43.53	54.01*	47.19
Dis BP ≥ 140/90 mmHg	31.03	27.57	29.82
HbA1c >6.5%	22.01	36.41*	27.49

$^*p<0.05$

Table 1: Characteristics by Race. African American patients were significantly younger than Caucasian patients, and had significantly higher rates of diabetes diagnoses compared to Caucasian patients. Caucasians had higher rates of hypertension only, but African Americans had a higher likelihood of having both hypertension and diabetes. African Americans had significantly higher rates of high blood pressure at admission, but there were no significant difference by race in blood pressure at discharge. African American patients had significantly higher HbA1c levels.

Table 2: Characteristics by Hypertension Diagnosis at Discharge	
Characteristic	**Htn Diagnosis**
Sex	
Male (n=366)	54.64
Female (n=418)	55.74
Age	
45-64 years (n=366)	53.83
≥65 years (n=418)	56.46
DM diagnosis	*
Yes (n=185)	65.95
No (n=599)	51.92
Adm BP	
<140/90 mmHg (n=414)	55.07
≥140/90 mmHg (n=370)	55.41
Dis BP	
<140/90 mmHg (n=546)	54.40
≥140/90 mmHg (n=232)	57.33
HbA1c >6.5%	
Yes (n=141)	58.87
No (n=372)	53.76
***p<0.05**	

Table 2: Characteristics by Hypertension Diagnosis. Patients diagnosed with hypertension at discharge had a significantly higher chance of also being diagnosed with diabetes compared to patients not diagnosed with hypertension at discharge. Age, sex, BP, and HbA1c levels did not have significant effects on hypertension diagnoses.

Table 3. Characteristics by Diabetes Diagnosis	
Characteristic	**DM Diagnosis**
Sex	
Male (n=366)	23.22
Female (n=418)	23.92
Age	*
45-64 years (n=366)	20.22
≥65 years (n=418)	26.56
Htn diagnosis	*
Yes (n=433)	28.18
No (n=351)	17.95
Adm BP	
<140/90 mmHg (n=414)	22.71
≥140/90 mmHg (n=370)	24.59
Dis BP	*
<140/90 mmHg (n=546)	21.25
≥140/90 mmHg (n=232)	29.74
HbA1c >6.5%	*
Yes (n=141)	65.25
No (n=372)	13.98
***p<0.05**	

Table 3. Characteristics by Diabetes Diagnosis. Patients 65 years and older, patients diagnosed with hypertension at discharge, patients with hypertensive blood pressures at discharge, and patients with diabetic HbA1c levels all had a significantly higher chance of being diagnosed with diabetes at discharge. Sex and having a hypertensive blood pressure at admission did not have significant effects on diabetes diagnoses.

Table 4. Prescribed Blood Pressure Medications at Discharge by Race, Sex, Age, Hypertension Diagnosis, Admission and Discharge Blood Pressure

Characteristic	On BP Meds
Race	
CA (n=171)	78.36
AA (n=53)	81.13
Sex	
Male (n=94)	85.11
Female (n=130)	74.62
Age	*
45-64 years (n=110)	69.09
≥65 years (n=114)	88.6
Htn diagnosis	*
Yes (n=135)	89.63
No (n=89)	62.92
BP on Admission	*
<140/90 mmHg (n=121)	71.9
>140/90mmHg (n=103)	87.38
BP on Discharge	*
<140/90 mmHg (n=169)	74.56
>140/90 mmHg (n=55)	92.73

***p<0.05**

Table 4. Antihypertensive medication regimen prescription rates. Being older than 65 years, being diagnosed with hypertension at discharge, and having hypertensive blood pressure at admission or discharge increased a patient’s likelihood of being prescribed blood pressure medications at stroke discharge. Race and sex were not associated with blood pressure medication prescription.

Table 5. Prescribed Diabetes Medications at Discharge by Race, Sex, Age, Diabetes Diagnosis, and HbA1c levels	
Characteristic	**On DM Meds**
Race	
CA (n=171)	18.13
AA (n=53)	30.19
Sex	
Male (n=94)	23.4
Female (n=130)	19.23
Age	
45-65 years (n=110)	18.18
65+ years (n=114)	23.68
DM diagnosis	*
Yes (n=46)	67.39
No (n=178)	8.99
HbA1c > 6.5%	*
Yes (n=33)	84.85
No (n=125)	10.4
***p<0.05**	

Table 5: Antihyperglycemia medication regimen prescription rates. Patients diagnosed with diabetes at discharge and patients who had diabetic HbA1c levels had a significantly higher chance of being prescribed diabetes medications at stroke discharge. Race, sex, and age had no significant effects.

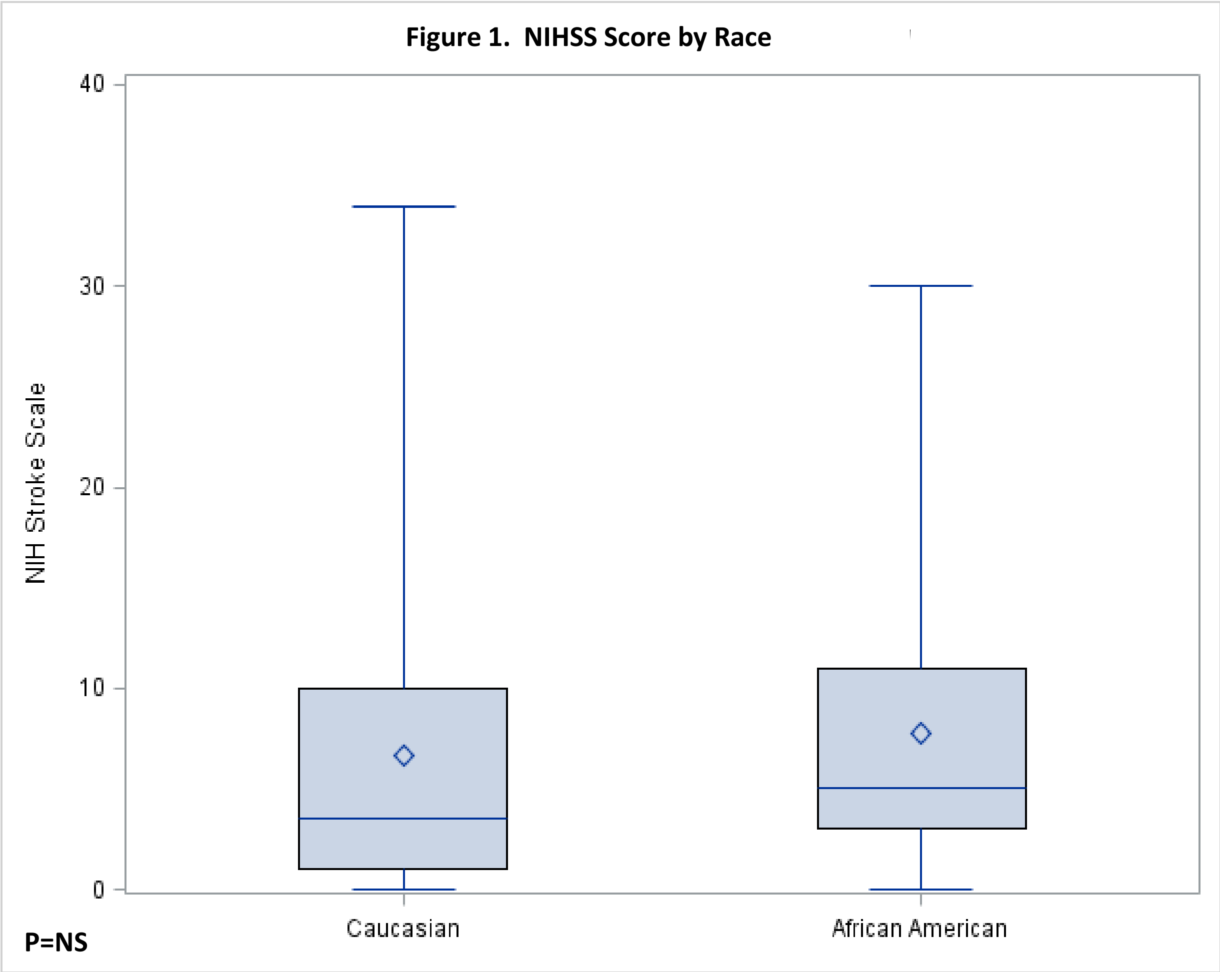

Figure 1: NIHSS score by race. Race did not have a significant effect on stroke severity.

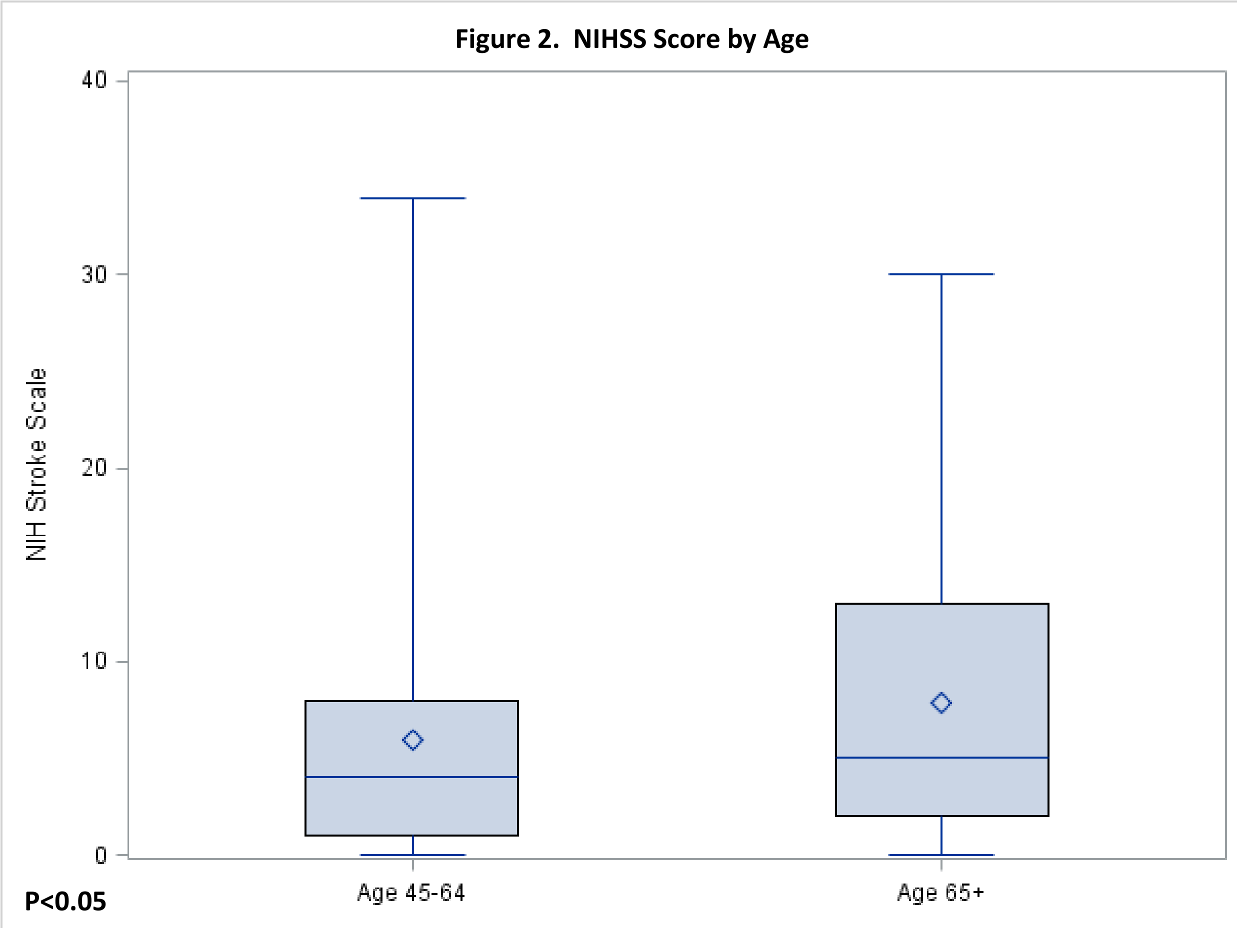

Figure 2: NIHSS score by age. Patients over the age of 65 had significantly more severe strokes than patients between the ages of 45 and 65.

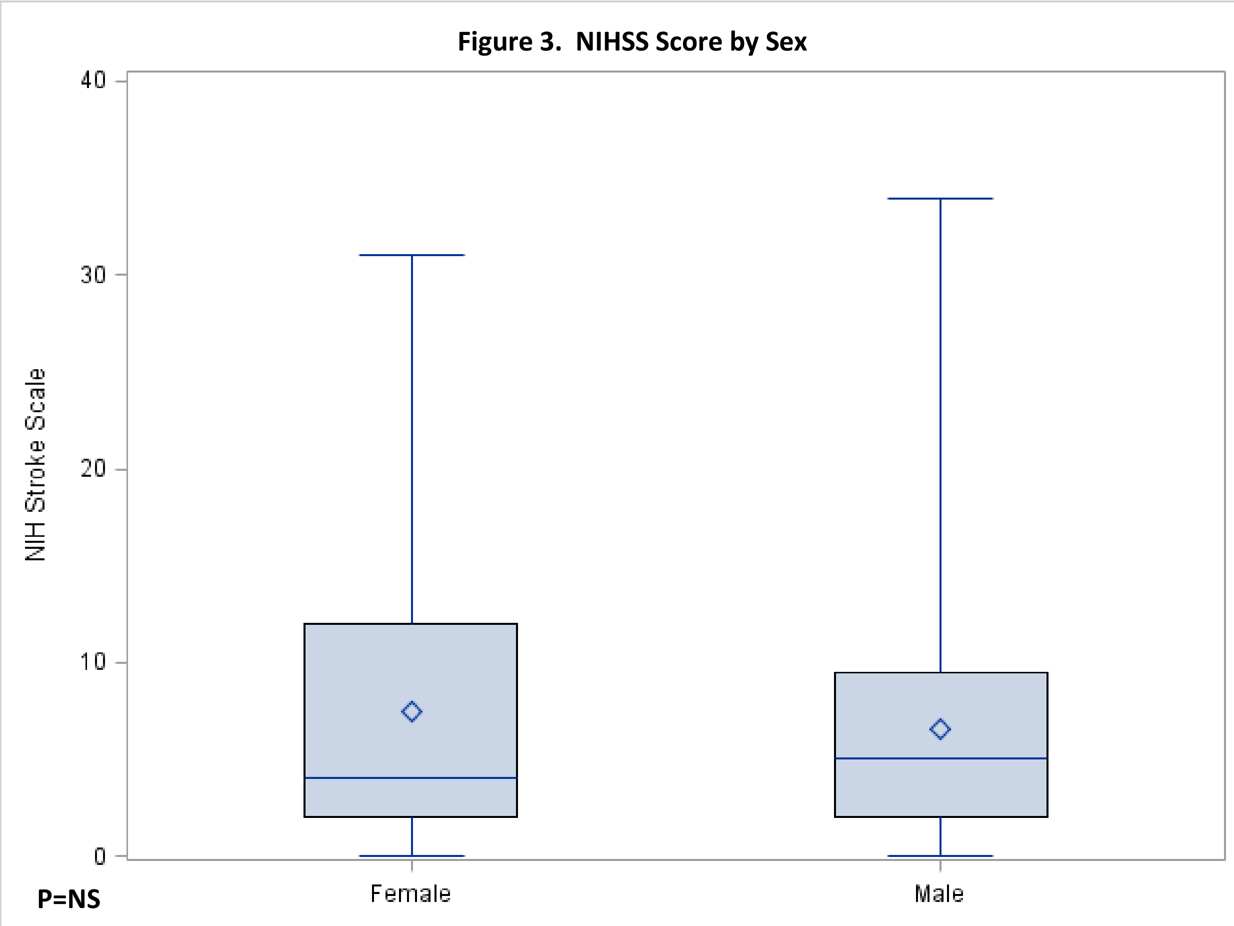

Figure 3: NIHSS score by sex. Sex did not have a significant effect on stroke severity.

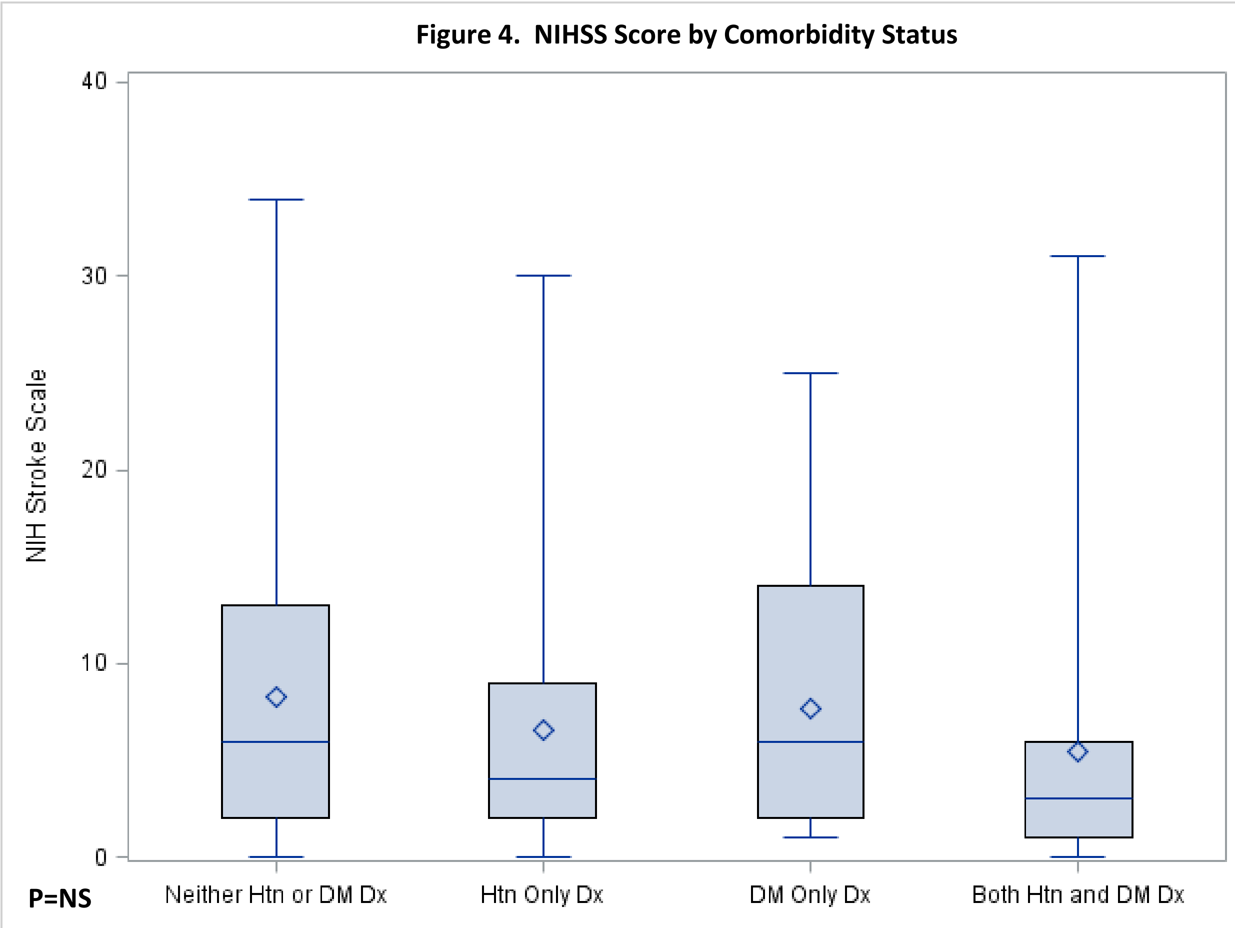

Figure 4: NIHSS score by comorbidity status. Comorbidity status was not shown to be significantly associated with stroke severity.