THE ROLE OF CLIENT CHARACTERISTICS, SYSTEM CHARACTERISTICS, AND INTERVENTIONS IN ISCHEMIC STROKE OUTCOMES

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BY

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To the Dean of Graduate Studies and Research:

I am submitting herewith a dissertation written by Mary Clark Robinson entitled "The Role of Client Characteristics, System Characteristics, and Interventions in Ischemic Stroke Outcomes." I have examined this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy with a major in Nursing.

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ABSTRACT

THE ROLE OF CLIENT CHARACTERISTICS, SYSTEM CHARACTERISTICS, AND INTERVENTIONS IN ISCHEMIC STROKE OUTCOMES

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The purpose of this study was to utilize an administrative database to examine differences in system characteristics, client characteristics, and interventions as they influence identified stroke outcomes. Additionally, the study investigated differences that might exist in clinical evaluation and treatment between men and women presenting with ischemic stroke that might indicate a gender bias. The Quality Health Outcomes Model was used as the conceptual framework for this study. MANCOVA, chi-square, multiple regression, and logistic regression were used to test the research questions on a sample of 867 patients, aged 23-100 years, from a large administrative Stroke Database.

MANOVA results indicated significant differences between males and females for total costs (p = .033) and mean admission age (p = .000). The chi-square analysis

demonstrated a significant difference for the following: neurology consultation and gender ($p = .005$); Carotid Doppler Study ($p = .003$) and endarterectomy ($p = .007$) interventions and gender; mortality ($p = .009$) and discharge disposition ($p = .000$) and gender. Males received both procedures at a higher percentage than females. Females had a higher mortality.

The total cost multiple regression model indicated that nursing cost ($p = .007$), endarterectomy ($p = .000$), APR severity "4" ($p = .000$), first care unit medical surgical ($p = .000$), attending physician specialty ($p = .016$), and neurologists consulting ($p = .025$) were all significant predictors. The model successfully predicted 86.5% of the variance for total cost. The LOS multiple regression model indicated that nursing cost ($p = .000$), first care unit medical surgical ($p = .000$), coumadin ($p = .000$), APR severity "4" ($p = .000$), APR risk of mortality "4" ($p = .000$), APR severity "3" ($p = .008$), first care unit ICU ($p = .001$), Caucasian ($p = .001$), APR risk of mortality "1" ($p = .007$), and endarterectomy ($p = .020$) were all significant predictors of LOS. This model successfully predicted 76.8% of the variance for LOS.

The logistic regression model demonstrated that the significant predictors of mortality included: Carotid Doppler Study, LOS, APR mortality, nursing costs, aspirin,

coumadin, and ED patient. Goodness-of-fit tests reveal that the model is a good fit for the data. The results indicate that there appear to be gender issues related to age of stroke onset and access to some interventions and treatments that are common in stroke management. Complex interactions between patients and within genders exist which need further investigation.

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CHAPTER I

INTRODUCTION

Stroke is the third leading cause of death in the United States. When stroke does not kill, it can be very costly and debilitating to those who live beyond the initial stroke event. In looking at the treatment and care of stroke patients, there is considerable variability in patterns of care, costs, and outcomes after stroke (Matcher & Samsa, 2000). Generalist physicians care for some patients, while others are cared for by specialist physicians. Treatment patterns and preventive efforts are different as well. Additionally, it is not clear what relationship client characteristics such as age, race, and gender play in the outcome of stroke.

Little attention has been given to stroke as a potential woman's health issue. Health care investigators and providers have spent years talking about the gender issues surrounding the care and treatment of heart disease, but little is known about any issues that may be present related to stroke. Stroke is a primarily a problem for the older American. Large scale, sociodemographic changes such as the aging of the population combined with the increasing technological developments have altered the populations served by the hospital, specifically the stroke population. In light of these changes, it becomes very important that the approach to the management of this problem be investigated and understood. It has been well documented that women tend to outlive men; therefore, issues for the old and very old tend to have gender ramifications (Barker & Mullooly, 1997).

Several treatment and care initiatives have been shown to decrease mortality and morbidity related to stroke. Matcher and Samsa (2000) reported that patients who are cared for by neurologists have better outcomes. Additionally, they reported that certain treatment options, such as carotid endarterectomies and warfarin administration reduce the risk of stroke. There is gap in information about the effectiveness of these treatments in the presence of ischemic stroke diagnosis.

Stroke is widely feared, and it is costly. As the nation looks at increased use of health care resources, focus must be placed on those preventable conditions that create excessive resource depletion. The drain that stroke places on limited national financial resources places a new priority on controlling the variables that may have an impact on stroke outcomes. Current databases that house large stores of information must be used to shed light on current treatment practices as ways are sought to improve stroke prevention and acute stroke treatment. It is imperative that we improve our ability to compare and contrast patient information through advances in technology as we critically examine utilization and outcomes of health care services. Administrative databases are becoming obvious sources of important information that will help evaluate how care is provided across patient groups, physicians, treatments, and institutions.

Problem of Study

The purpose of this study was to utilize an administrative database to examine differences in system characteristics, client characteristics, and interventions as they influence identified stroke outcomes. A critical examination of current actions and treatments among large groups of patients will give guidance toward health care practices that work. In addition, it is important to research any differences that exist in clinical evaluation and treatment between men and women presenting with ischemic stroke that may indicate a gender bias. It is well documented that women are less likely to undergo intensive evaluation and invasive treatment for cardiac diseases when compared to men with similar symptoms. The cited reasons for these differences with relation to cardiac disease include the older age of women at onset of heart disease, smaller body size, coexisting diseases, and suboptimal or delayed care (Bergelson & Tammaso, 1995). These same issues may exist with women experiencing stroke. While great interest in stroke treatment has been demonstrated, there is a lack of research investigating the possible gender bias that may occur in the care and management of the stroke population. Gender differences in cerebrovascular disease have not been well studied either. Large administrative databases have not been used to glean information about client, treatment and care variables that may influence stroke outcomes.

As the knowledge about stroke and the treatments has become more complex, it becomes difficult to sort out those variables that are specifically making a difference. There are more factors complicating the traditional approaches to stroke management. Additional studies are needed to test the efficacy of specific interventions as well as to test the equity of services, treatments, and resources available between different groups. It is well known that various treatments are effective at reducing risk. It is well known that stroke teams improve patient outcomes. The Brain Attack Coalition has gone so far as to strongly recommend the use of acute stroke teams; however, there is little detail as to what aspects of the work of this team lead to improved outcomes. Understanding the variables associated with ischemic stroke outcomes may help in earlier treatment, improved care, and more desirable long-term outcomes for both male and female patients who experience ischemic stroke. It is important to identify what is working well in terms of care and treatment. The care and treatment of the population of women who present with ischemic stroke has not been well characterized. Research of involving administrative data may provide new insights or more accurate data from which to make patient care decisions.

Rationale for the Study

Stroke is the third leading cause of death and disability in the United States. While death is a tragic outcome of this neurovascular insult, the physical and emotional devastation suffered by the survivors of stroke make it one of the most dreaded words and events in modern society. In an effort to understand the complexity of this disease, it is important to discuss the incidence and cost, the national response, risk factors, treatment approaches to stroke management and outcomes.

The incidence and cost of stroke is staggering. In America, an estimated 700,000 to 750,000 strokes occur each year at an annual cost of $71.4 billion (Williams, Jiang, Matcher, & Samsa, 1999). Annually, 500,000 new strokes occur and 100,000 individuals suffer recurrent stroke. As the population ages, these numbers may increase. In 1998, stroke killed 158,448 people, accounting for 1 out of every 12 deaths in the United States. The age-adjusted death rate is 25.1 deaths per 100,000 population (Center for Disease Control [CDC], 1998). The majority of strokes (80%) are ischemic in nature and are potentially preventable and responsive to treatment if recognized (Johnston et al., 2000). Of those who have a stroke, approximately 22% of men and 25% of women will die within the year from the stroke. Additionally stroke often strikes the vulnerable, being reported more commonly in women, African Americans, and Hispanics (CDC, 1998; Morgenstern, Steffan-Batey, Smith, & Moye, 2001). Stroke is a significant problem in the United States; and despite advances in treatment, diagnosis, and prevention, it continues to be a very common disorder mandating the attention of the healthcare community as well as the general public.

As a nation, the U.S. must place greater emphasis on improving the devastating effects of stroke through further understanding of the disease, improved uses and advances in treatment, and increased research and education. Since stroke takes such a large human and financial toll on its victims, it is clear that stroke prevention, care, and management deserve attention. It is unclear why advances in the area of stroke care have not been fully embraced. To this end, two nationally recognized agencies have taken the lead in promoting a national response to this issue. The Agency for Healthcare Research and Quality (AHRQ) and the American Heart Association (AHA) have made stroke management and care an important initiative that requires national attention. The goal of this directive is to improve outcomes for people at risk and for those experiencing stroke. The American Heart Association has shown its commitment to reducing death and disability due to stroke through the activities of the Stroke Council, the International Stroke Conference and the development of the American Stroke Association. The AHA has been a dynamic leader in the great strides in the early detection and treatment of heart disease. With the same attention, stroke outcomes may also be improved and mortality decreased (Fletcher, 2001). One of the major goals of the AHRQ-sponsored Patient Outcomes Research Team (PORT) studying stroke is to identify practice variations in the way physicians and health care providers diagnose, treat, and manage stroke (Matcher & Samsa, 2000).

Risk factors are recognized as variables that influence the incidence of cerebrovascular disease and stroke. Several studies (Bronner, Kanter, & Manson, 1995; Feinburg, 1996) have shown that identification and treatment of risk factors can reduce the occurrence of stroke. Certain risk factors have been identified as significant predictors of stroke, and these include age, hypertension, antihypertensive treatment, alcohol intake, previous stroke, and atrial fibrillation (Simons, McCallum, Friedlander, & Simons, 1998). Previous stroke is a common indicator of increased risk for death or poor functional outcomes. Hart (2001) points out that atrial fibrillation is reported as a strong, prevalent, and independent risk factor for stroke. If an individual has atrial fibrillation and is not treated with anticoagulants, the risk for stroke due to cardioembolic causes increases dramatically. Strokes associated with atrial fibrillation are reported to be more severe, more disabling, and have a higher mortality. Other risk factors include: smoking, diabetes, excessive alcohol intake, family history of stroke, and heart disease.

Risk factors, as with heart disease, can be addressed as those that are modifiable and non-modifiable. Gender and race are two non-modifiable factors that are often discussed in the stroke literature as well. Some studies have shown that men seem to be at higher risk of stroke (Brown, Whisnant, Sicks, O'Fallan, & Wiebers, 1996; Stegmayr et al., 1997). As women age, the stroke rate increases as well. At age 85, women have a higher incidence of stroke (Holroyd-Leduc, Kapral, Austin, & Tu, 2000). As with cardiovascular disease, the incidence of stroke is lower in younger women up to a point. As women age, the incidence and risk apparently increase. The management and treatment of stroke have only been minimally evaluated with respect to potential differences in treatment that may be present between men and women. Stroke appears in some ways to be very much like cardiovascular disease in that it affects men and women equally over time with differences based on gender occurring later in life. This evolution of gender-related crises in later years makes stroke initiatives vulnerable to the "equality of care" issues that cardiac care has experienced over the years. The ischemic stroke population is an ideal population for the investigation of gender differences in care.

Race is an another non-modifiable risk factor that seems to influence the incidence of stroke. Morgenstern et al. (2001) reported that stroke incidence in Hispanic populations is higher than in non-Hispanic whites. Other researchers have reported being a member of the African-American race as a significant predictor of stroke (Gillum, 1988; Lackland, Egan, & Jones, 1999; Wein, Smith, & Morgenstern, 1999). Blacks are known to have higher rates of hypertension and thus hypertension-related complications, such as stroke. Studies have addressed the race/ethnic differences in stroke but are primarily descriptive in nature. Stroke risks have only been minimally addressed in the African-American and Hispanic races. There are many risk factors that must be considered in the efforts to decrease the incidence and mortality associated with stroke. While risk identification is important, the management of these risks becomes paramount in the battle against stroke.

Treatment approaches to stroke management vary from risk factor reduction to interventional strategies. The most crucial actions to reduce risk factors include management of hypertension, use of aspirin in moderate or high-risk patients, and anticoagulation in patients with atrial fibrillation (Kalra, Perez, & Melbourne, 1998). Many researchers concur that carotid endarterectomies are the treatment of choice for prevention of stroke in patients who have blocked carotid arteries and are symptomatic; however, it is not clear that this philosophy has been widely embraced (Goldstein et al., 2001). Other treatment variables that are mentioned as effective in the treatment and management of stroke include: diagnostic studies (Carotid Doppler Studies, CT, MRI), physician type, Tissue Plasminogen Activator (TPA) use, and the type of care that is given to the stroke patient upon presentation to the hospital (Goldstein et al., 2001). Many authorities, such as the Brain Attack Coalition (BAC), have made recommendations for the establishment of stroke centers/acute stroke teams (Alberts et al., 2000). The team includes a physician and another health care professional (nurse, physician's assistant, and nurse practitioner) who are available 24 hours a day. One member of the team would have experience and expertise in diagnosing and treating patients with cerebrovascular disease. Alberts et al. (1998) recommended that this team be involved with the patient as soon as possible in the acute care setting. The use of stroke teams and stroke units is reported to be associated with better patient outcomes.

Great variability has been associated with outcomes related to stroke, and attempts have been made to identify factors related to actual outcomes and predicators of outcomes. Many people may not be gaining access to beneficial treatment options and therapy simply because there is no established relationship to outcomes. Typically, outcome studies reported in the literature related to stroke focus on morbidity/mortality, length of stay, functional outcomes, and use of rehabilitation therapy (Baptista, van Melle, & Bogousslavsky, 1999; Chen, Tang, Chen, Chung, & Wong, 2000; Hackett, Duncan, Anderson, Broad, & Bonita, 2000; Hoenig, Sloane, Horner, Zolkewitz, & Reker, 2001; Rubin, Firlik, Levy, Pindzola, & Yonas, 2000). Stroke management and treatment has become more complex over the years. Increasing choices present a challenge to caregivers as they are forced to make difficult decisions.

Based on the high incidence and prevalence of stroke among the nation's most vulnerable populations, researchers are obligated to search for specific factors that may influence stroke incidence, risk and outcomes. Despite advances in care and great interest in stroke, additional study is needed to develop a more complete understanding of this very complex problem.

Conceptual Framework

The Quality Health Outcomes Model

The Quality Health Outcomes Model is the conceptual framework for this study. This model is based on Donabedian's (1966, 1982) classical framework, which identified three major dimensions of health care evaluation: structure, process, and outcomes. These dimensions were identified as approaches to evaluate the attributes that constitute or define quality. Donabedian's model is considered to be a linear model supporting the thought that structure and process precede or affect outcomes. P. Mitchell, Ferketich, and Jennings (1998) through their work with the American Academy of Nurse Expert Panel on Quality Health Care expanded on this model by postulating that dynamic relationships exist and act reciprocally upon each other. These authors included the multiple contextual factors that influence health care delivery and outcomes.

"Interventions affect and are affected by both system and client characteristics in producing desired outcomes…and no single intervention acts directly through either system or client alone" (P. Mitchell et al., 1998, p. 44). Unlike the traditional linear model that Donabedian's work suggests, the Quality Health Outcomes Model has no single direct connection that links interventions and outcomes. This model is dynamic in that it demonstrates the reciprocal relationships among system characteristics, intervention, client characteristics and outcomes. An illustration of this model is depicted in Figure 1.

P. Mitchell et al. (1998) broadly characterize system characteristics as traditional structure and process elements in as far as they pertain to the level of analysis. Specific examples include a hospital or provider network acting as an organized system or agency. "The size, ownership, skills mix, client demographics and technology would be among the system characteristics that would interact with interventions to affect health outcomes" (P. Mitchell et al., 1998, p. 45).

Interventions consist of clinical processes that are direct and indirect actions and related activities by which they are delivered. Examples include nursing interventions and care, self-care, and work group interactions (P. Mitchell et al., 1998).

Client characteristics refer to the qualities and identifiers of the clients to whom the interventions are directed. Client characteristics are defined as those variations in clients that might affect outcomes such as client health, demographics, and disease risk factors.

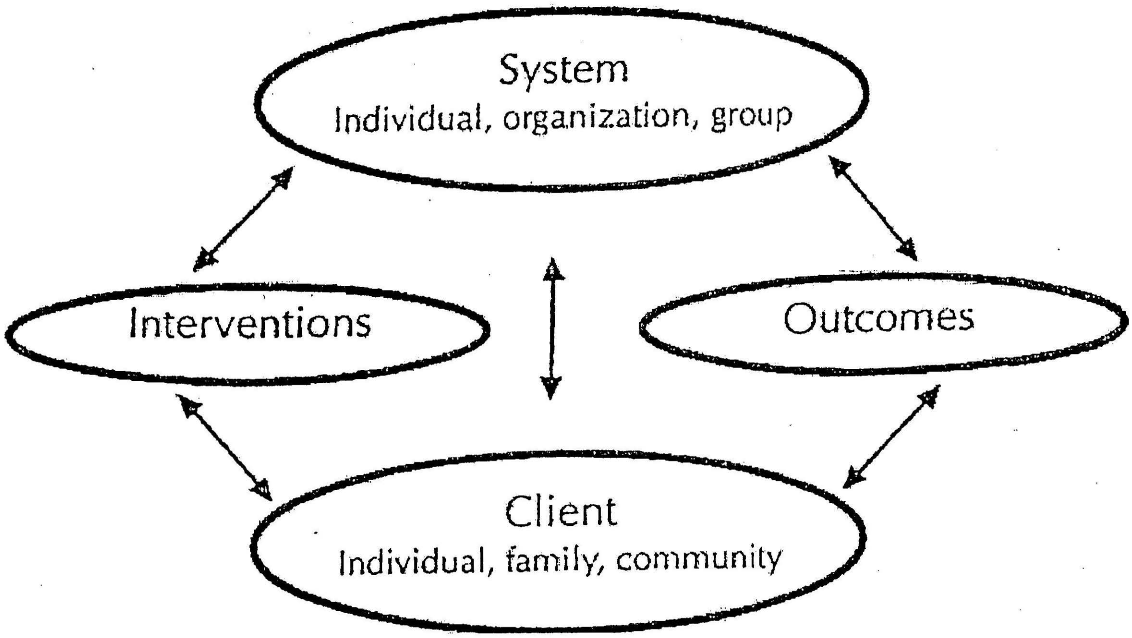

Figure 1. Quality health outcomes model.

From "Quality health out comes model," by P. Mitchell, S. Ferketich, & B. Jennings, 1998, Image Journal of Nursing Scholarship, 30(1), 43-46. Reprinted with permission, see Appendix A.

Outcome measures "should be results of care structures and processes that integrate functional, social, psychological, physical, and physiologic aspects of people's experience in health and illness" (P. Mitchell et al., 1998, p. 46). P. Mitchell et al. proposed that these outcome measures be operationalized into five categories: achievement of appropriate self-care, demonstration of health-promoting behaviors, health-related quality of life, perception of being well-cared for, and symptom management. Further, they strongly suggest that living, dying, clinical health status, and health care costs should not be ignored. Additionally, P. Mitchell et al. suggested that little work has been done to evaluate the effect of organizational factors on the above outcomes.

The dynamic and recursive nature of this model is supported by the solid two sided arrows that connect the four main components of the model. These indicators not only act upon, but the indicators reciprocally affect, the various components (P. Mitchell et al., 1998). Essentially, this model demonstrates a completely interactive and reciprocal relationship between all of the components (interventions, client characteristics, system characteristics, outcomes) of the model.

The Quality Health Outcomes Model is intended to reflect the true dynamic nature of patient care and interaction among the system, interventions, the client and outcomes. This further expansion of Donabedian's model offers a theoretical explanation of the many variations among patients that are observed and reported in patient care and healthcare research. "The outcomes of care that tell us something about its quality comprise an almost limitless set of phenomena that correspond to aspects of physical, physiological, psychological, and social health" (Donabedian, 1982, p. 4).

The interrelationships of the concepts in the Quality Health Outcomes Model allow the researcher to identify the potential relationships of the variables of interest. System characteristics are represented by the attending physician specialty, emergency department stay, first unit of care and neurologist consult variables. Client characteristics are represented by the severity of illness, age, race, risk of mortality, and gender variables. Interventions are identified as pharmacy/medication (aspirin, coumadin, activase), nursing costs, surgical intervention (endarterectomy), and radiologic intervention (Carotid Doppler Study) variables. Outcomes are indicated by length of stay, mortality, discharge disposition, total cost, and inpatient readmission variables. An illustration is depicted in Figure 2. This comprehensive dynamic model will be used to guide the analysis of a large database to further clarify gender differences and predictors of stroke in an adult population.

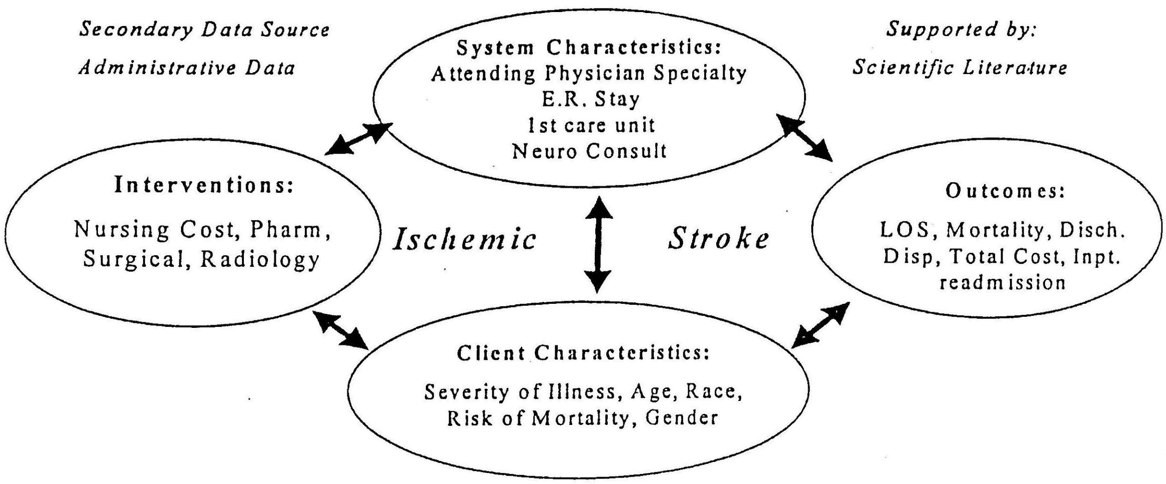

Figure 2. Ischemic Stroke Quality Health Outcomes Model.

Assumptions

The assumptions of this research study were:

1. Outcomes are a direct result of a practitioner's interventions on a specific individual (P. Mitchell et al., 1998).

2. Interventions affect and are affected by both system and client characteristics in producing desired outcomes (P. Mitchell et al., 1998).

3. No single intervention acts directly through either the system or client alone (P. Mitchell et al., 1998).

4. The effect of an intervention is mediated by client and system characteristics (P. Mitchell et al., 1998).

5. Teams of nursing or interdisciplinary providers interact with a patient and often family or other significant groups (P. Mitchell et al., 1998).

6. Outcomes can be measured and evaluated to determine patterns of care (Donabedian, 1982).

Research Questions

The following research questions were investigated:

1. Is there a difference in the interventions (nursing cost), client characteristics (age), and outcomes (total cost, length of stay) among men and women with ischemic stroke who were admitted to a large community hospital over a 2-year period?

2. Are the specific system characteristics (neurological consultation, emergency department stay, first care unit, attending physician specialty), interventions (coumadin, aspirin, and activase/TPA, Carotid Doppler Study, endarterectomy), and outcomes (mortality, 30-day readmission, and discharge disposition) independent of gender?

3. What are the primary predictors (system characteristics, interventions, client characteristics) of ischemic stroke outcomes in a large community hospital over a 2-year period?

Definitions

The following key terms are defined:

1. Ischemic stroke is a stroke that results from low cerebral flow, usually because of occlusion of a blood vessel. The occlusion can be either thrombotic or embolic in nature (Thelan, Urden, Lough, & Stacy, 1998). Ischemic stroke is operationalized by designation on the Stroke Database with ICD-9 codes: 433-Precerebral Occlusion, 434-Cerebral Artery Occlusion, and 436-Cerebral Vascular Accident.

2. System characteristics are defined as traditional structure and process elements in as far as they pertain to the level of analysis. Specific examples include a hospital or provider network, the size, ownership, skills mix, client demographics and technology (P. Mitchell et al., 1998). This concept is operationalized as the following: attending physician specialty, Emergency Department stay, first care unit, and neurology consultation as designated in the Stroke Database.

3. Interventions consist of clinical processes that are direct or indirect actions and the related activities by which they are delivered (P. Mitchell et al., 1998). Interventions are operationalized as the following: nursing costs, pharmacy/medication interventions (coumadin, aspirin,

and activase/TPA), surgical interventions, and radiology interventions in the Stroke Database.

4. Client characteristics refer to the qualities and identifiers to whom the interventions are directed. These are defined as those variations in clients that might affect outcomes such as client health, demographics and disease risk factors (P. Mitchell et al., 1998). This is operationalized as the following: age, race, All Patient Refined-Diagnosis Related Groups (APR-DRG) severity of illness, APR-DRG risk of mortality, and gender as designated in the Stroke Database.

5. Outcomes are the results of care structures and processes that integrate functional, social, psychological, physical, and physiologic aspects of people's experience in health and illness. Examples include: appropriate self-care, demonstration of health-promoting behaviors, health-related quality of life, perception of being well-cared for, symptom management, living, dying, clinical health status, and health care costs (P. Mitchell et al.,1998). This concept was operationalized as the following: length of stay (LOS), mortality, discharge disposition, total costs, and inpatient readmission within 30 days as designated in the Stroke Database .

Limitations of the Study

The limitations of this study were anticipated and recognized:

1. The generalizability of this study is limited by the fact that the study consisted of only one sample group of an entire population of ischemic stroke patients in the United States and is reflective of only those individuals being treated in a large community hospital in the North Texas area.

2. The use of a nonprobability, convenience sample from one setting restricted the internal validity of the study.

3. There was a lack of standardization within the individuals sampled which could inflate error variance and decrease the chance of obtaining information which reflects true differences (Cook & Campbell, 1979).

4. An established database was used as the source of data and internal consistency of coding and data entry may be threatened by the number of different individuals involved in coding and data entry.

Summary

The morbidity of stroke is reflected by the impact and effects that subsequent disabilities have on the lives of patients and their families. The effect on their personal, physical, psychological, emotional, and social well-being can be grave. The economic losses and decreases in general quality of life can be devastating. Further, the impact on the health care system and the cost of treating this condition over the lifetime of patients who are affected is astounding.

Opportunities exist for understanding what works among the great variety of approaches used for stroke management. Effective stroke management and promotion of improved outcomes requires due diligence in examining current care practices. Research is needed to explain variations and differences that occur in the care of ischemic stroke. Critical review may provide support for different approaches to patient care, specifically the primary predictors of stroke outcomes in men and women.

CHAPTER II

REVIEW OF LITERATURE

The purpose of this study was to utilize an administrative database to examine differences in system characteristics, client characteristics, and interventions as they influence identified stroke outcomes. This study also investigated differences that exist in clinical evaluation and treatment between men and women presenting with ischemic stroke that may indicate a gender bias. This chapter examines the research literature about ischemic stroke on three fronts. The first section includes client and system characteristics including epidemiology and economics, etiology and risk factors, age considerations, gender issues, cultural and ethnic considerations, and the severity of illness/mortality factors. The second section includes ischemic stroke interventions including surgical, radiological, and pharmacological factors. The third section focuses on the outcomes, aspect of ischemic stroke care with attention to cost, readmission, and mortality research.

Ischemic Stroke--Client/System Characteristics

Stroke is the third leading cause of death and disability in the United States. A stroke occurs when there is a disruption of blood flow to any area of the brain. This disruption can be caused by either an obstruction of blood flow to the brain (ischemic) or rupture (hemorrhage) of a vessel that supplies blood to the brain (Bratina et al., 1997). Ischemic stroke is defined as a stroke that results from low cerebral flow, usually because of occlusion of a blood vessel. The occlusions can be either thrombotic or embolic in nature (Thelan et al., 1998). In an effort to understand the complexity of stroke, it is important to review the epidemiology and economics, etiology, gender issues, cultural differences, and prevention.

Epidemiology and Economics

The incidence and cost of stroke is staggering. In America, an estimated 700,000 to 750,000 strokes occur each year at an annual cost of $71.4 billion dollars (Williams et al., 1999). Annually, 500,000 new strokes occur and 100,000 individuals suffer recurrent stroke. Stroke patients account for more than one-half of all hospitalizations that are classified as neurological (Bratina et al., 1997). As the population ages, these numbers will increase. In 1998 stroke killed 158,448 people, which accounted for one out of every

12 deaths in the United States. The age-adjusted death rate is 25.1 deaths per 100,000 population (CDC, 1998). The majority of strokes (80%) are ischemic in nature and are potentially preventable and responsive to treatment if recognized (Johnston et al., 2000). Of those who have a stroke, approximately 22% of men and 25% of women will die within the year from the stroke. Over the past several years stroke as a disease has begun to receive the attention that other more visible diseases, such as heart disease have received. Bratina et al. (1997) stated that the further investigation and research related to stroke has led to the understanding that stroke is a medical emergency and should be treated as such. The care options and the prevalence of stroke have made acceptance of this reality difficult among health care providers.

Etiology/Risk Factors

Studies of stroke incidence, etiology, and risk factors have been reported by numerous authors. According to Simons et al. (1998), age, hypertension, antihypertensive treatment, previous stroke, and the presence of atrial fibrillation are significant predictors of stroke. In this study, the authors evaluated the independent contributions of risk factors to stroke and stroke outcomes using the Cox proportional hazards model. The sample consisted of 2,805 men and women who lived in Australia. Forty-four percent of the subjects in this study were males with a mean age of 69. Point estimates and relative risk (RR) of stroke were calculated from the regression coefficients. Age and previous stroke were found to be the most powerful variables for relative risk at the 95% confidence interval ($p < .001$). The presence of atrial fibrillation, hypertension, and antihypertensive medications were predictive of relative risk and statistically significant ($p < .05$). Interestingly, this study did not demonstrate any significant prediction with prior coronary heart disease (CHD), diabetes, total cholesterol and triglycerides, current cigarette smoking, and alcohol intake, while other studies have indicated these as risk factors.

In a stroke risk management study, Kalra et al. (1998), identified hypertension, atrial fibrillation, previous stroke or Transient Ischemic Attack (TIA), smoking, diabetes mellitus, ischemic heart disease, and peripheral vascular disease as pertinent risk factors for stroke due to the reported evidence that shows aggressive management of these factors is associated with reduced stroke incidence. This observational study looked at the frequency of known risk factors before the incident of stroke in the study population, as well as the management of these risk factors prior to the stroke. The sample for this study had a mean age of 76. Sixty percent of the sample consisted of women. The study took place over a 2-year period from 1994-1996. The risk factors of primary interest to the researchers in this study were hypertension, atrial fibrillation, and past history of TIA or stroke were of primary interest to the researchers because of their potential for intervention to control for risk. Subjects were evaluated for the presence of these risk factors prior to an acute stroke event as evidenced in previous hospital and general practice records. Of the 1,345 subjects, 87% were diagnosed with ischemic stroke and 61% of these were women. Pre-stroke hypertension was reported in 43% of subjects. Atrial fibrillation was reported in 18% and past history of stroke or TIA in 26% of subjects. Symptomatic vascular disease was evidenced in 58% of patients.

Elkind and Sacco (1998) presented risk factors as modifiable and nonmodifiable in nature. Nonmodifiable risk factors were identified as age, gender, race, ethnicity, and heredity. Modifiable risk factors for stroke were identified as hypertension, atrial fibrillation, other cardiac diseases, hyperlipidemia, diabetes, cigarette smoking, physical inactivity, carotid stenosis, and TIA. These are all identified as treatable conditions that if untreated could predispose an individual to stroke.

A population-based model for the analysis of risk factors was developed and investigated by Whisnant, Wiebers, O'Fallon, Sicks, and Frye (1996). Utilizing a multiple logistic-regression model, these authors created an estimation of odds ratios regarding ischemic stroke in relation to multiple risk factors. Age, date of stroke, TIAs, hypertension, current smoking, atrial fibrillation, ischemic heart disease, mitral valve disease, and diabetes mellitus were identified as risk factors predictive of stroke. Unlike Simons et al. (1998), these researchers did not identify antihypertensive treatment as a risk factor for increased stroke incidence in their model.

Petty et al. (1999) expanded the work of Whisnant et al. (1996) to determine age and sex specific incidence rates and risk factor associations for ischemic stroke subtypes. The sample included 454 subjects who experienced a first time ischemic stroke between 1985 and 1989. In this study, the researchers first divided the sample into stroke infarct subtypes including: cardioembolic, large-vessel cervical, or intercranial atherosclerosis with stenosis > 50%, lacuna, other unusual causes, and uncertain cause. The distribution of risk factors among subjects in the five subtypes was evaluated with the chi-square or Fisher exact test. Among risk factors investigated, there was no difference in prior ischemic attack and hypertension among subtypes of ischemic stroke ($p > .05$). The variables age and male gender were significant predictors of all types of stroke ($p < .001$). Men were found to have a 4 times higher incidence of stroke due to stenosis of the large cervicocephalic vessels. Additionally, it was found that diabetes and smoking were significant risk factors among patients with first ischemic stroke ($p < .05$).

Many studies have investigated the role that single risk factors play in the development of stroke as opposed to the Petty et al. (1999) who looked at groups of risk factors. These studies provide reliable information about the role that the following risk factors have played in the development of stroke: cigarette smoking, blood pressure, and alcohol consumption.

The comprehensive Framingham Heart Study involved 4,255 men and women in a 26-year longitudinal analysis of stroke incidence. Wolf, D'Agostino, Kannel, Bonita, and Belanger (1988) reported that smoking was significantly related to stroke even after age and hypertension were factored into the analysis. These authors determined that smoking contributed as an independent risk factor for stroke and, in fact, that risk increased as the total number of cigarettes increased. In a study specific to women, Kawatchi, Colditz, and Stampfer (1993), using the Nurses' Health Study cohort, identified that smoking was a risk factor for ischemic and hemorrhagic stroke for middle-aged women. The overall age adjusted relative risk (RR) among current smokers when compared to those who never smoked was 2.58 (95% CI, 2.08 to 3.19). Additionally, the finding of the study indicated that stroke risk would decrease if smoking cessation occurred with the greatest benefit occurring 2 to 4 years after the smoking stopped.

Hata et al. (2000) investigated the relationship between office blood pressure (BP) variability and the risk of brain infarction in elderly patients receiving antihypertensive therapy. These researchers found that increased variability in office BPs was associated with a higher risk of brain infarction after adjustment for the BP level and other confounding factors. These findings could further explain the opposite findings in the literature related to the role of antihypertensive medications as a risk factor for stroke. Perhaps the variability in the blood pressure is the predictor and not the treatment per se.

Several studies have shown that moderate alcohol consumption has a protective effect for cardiac mortality and myocardial infarction (Maclure, 1993; Rimm, 1996). The information regarding the effect of alcohol on ischemic stroke is mixed. Some authors report that no beneficial effects are seen, while others have found that moderate alcohol consumption is beneficial. The effect seems to vary depending on population differences, specifically race and ethnicity. In an effort to further understand the risk relationship between alcohol and stroke, Sacco et al. (1999) conducted a population-based case-control study between July 1993 and June 1997. The study focused on determining stroke incidence, risk factors, and prognosis in a multiethnic and urban population. Alcohol use was assessed through structured in-person interviews using questions adapted from the National Cancer Institute food frequency questionnaire. Multivariate conditional logistic regression was used to calculate the odds ratios (OR) and 95% confidence intervals (CI) for alcohol consumption and the incidence of stroke. There were 688 participants in this study with a mean age of 70. Women made up 55.8% of the sample, 19.5% were non-Hispanic white, 28.4% were non-Hispanic black, 50.7% were Hispanic, and 1.4% were other. The findings indicated the moderate alcohol intake (< 2 drinks/day) was protective for stroke. Those subjects who drank up to two drinks per day had a statistically significant reduced risk for ischemic stroke compared to those who were not current drinkers (OR .51, 95% CI, 0.39 0.67).

Age Considerations

The effects of aging on the body, specifically the cardiovascular and cerebrovascular system, contribute to the increased risk of stroke. The addition of risk factors to the cumulative effects of aging make stroke a disease of the older individual. For each decade after 55 years of age, the risk of stroke doubles (Brown et al., 1996). The effect of this nonmodifiable risk factor is a fact that cannot be ignored when looking at client characteristics and ischemic stroke. Multiple studies have evaluated the relationship between age and stroke. Curb et al. (1996) evaluated the 6-year incidence of stroke among men aged 45 to 81 years of age in a Japanese-American population. The men were evaluated three times over the period of 6 years. The incidence of stroke and hypertension increased significantly with age ($p < .01$).

While most studies validate that stroke is a disease of the older population, one study found that ischemic stroke under the age of 45 was not a rare occurrence. Bogousslavsky and Pierre (1992) utilized the Lausanne Stroke Registry to evaluate the causes of stroke in young adults. The study showed that more than 10% of the subjects in the stroke registry were under the age of 45. The researchers found that the frequency of strokes was not the same for this younger population, but that the causes did not really differ from those of older stroke individuals with the exception of atherosclerosis. Cardiac embolism, arterial dissection, and migraines were the most commonly identified causes with limited cases caused by atherosclerosis.

In a study focused on age and stroke, Sheth, Nair, Muller, and Yusaf (1999) evaluated seasonal variations in mortality from acute myocardial infarction and stroke by age. The Canadian Mortality Database was used to access data on subjects for two time periods: 1980 to 1982 and 1990 to 1992. The four seasons were analyzed by month using chi-square and relative risk rations for statistical analysis. It was found that stoke mortality was highest in January (RR = 1.113) and lowest in September (RR = 0.914). There was no seasonal variation detected for those in the database who were less than 65 years old. There was higher seasonal mortality for the winter season that increased with age: 11.6% mortality for ages 65 to 74, 15.2% mortality for ages 75 to 84, and 19.3% mortality for > 85 years of age ($p < 0.005$ for trend). Therefore, the elderly demonstrated a greater winter increase in stroke mortality than those younger subjects in the database.

In a study designed to identify the predictors of stroke that are associated with age, Noto et al. (2001) studied the 1,351 subjects (622 males and 729 females) in a rural Sicilian town. The town was selected due to the higher incidence rates of stroke in the Mediterranean compared to northern Europe. These subjects also were ideal because of their relative homogeneous ethnic background and low mean cholesterol levels. Through multivariate analysis, the researchers demonstrated that there was an independent association between stroke and age, diabetes, leukocyte count, hypertension, and previous neurological symptom (PNS). There were differences demonstrated between the < 65 years age group and the > 65 years age group in relation to predictors of stroke. Diabetes, high body mass index (BMI), and high uric acid levels were associated with stroke in those individuals < 65 years of age. Hypertension, diabetes, high waist-hip ratio, PNS, leukocyte count, and hematocrit above the 95th percentile were associated with stroke in those individuals > 65 years of age. Thus, as the study pointed out, risk factors associated with stroke may vary depending upon the age of the individual, and, consequently, different strategies for risk reduction may be necessary.

The connection between age, stroke risk, and mortality is strongly supported in the literature. Research by Barker and Mullooly (1997) found that there was no difference in stroke incidence over the years; however, stoke mortality had declined over the years. A retrospective analysis of HMO data in a metropolitan community using three periods of time (1967-1971, 1974-1978, and 1981-1985) was conducted for persons greater than or equal to 65 years of age. The researchers found that the 1-month case fatality rate decreased from 33% in 1967 through 1971 to 18% in the 1981 through 1985 cohort (p = .01). The severity of stroke decreased as evidenced by the declining coma rate for 27% to 12% (p = .067) in the same time cohort comparison. The authors concluded that stroke has become a less disabling and lethal disease over the past 30 years. However, age continues to play a pivotal role in the incidence of stroke. There is no doubt that age is an important consideration in the care and treatment of stroke patients.

Gender Issues

The concept of gender inequality in health care or differences in health care related to gender is not a new idea. Since the early 1990s, great emphasis has been placed on the investigation of differences related to cardiac care. The knowledge provided by many studies about cardiac care demonstrated that differences in health care do exist related to gender. They may exist for a variety of reasons. As one investigates the questions surrounding gender and health care it is important to determine if differences exist as a function of the prevalence and severity of a particular disease, patient preferences, supply factors, clinical judgement or any combination thereof. As previously stated, there are many articles that support the fact that cardiac disease is a disease that has gender issues.

Bergelson and Tommaso (1995) have stated that women undergo evaluation and treatment for cardiac diseases less frequently than men with similar symptoms. The purpose of this study was to use a retrospective chart review to determine what differences exist in clinical evaluation and treatment between men and women presenting with coronary heart disease. The database review focused on the coronary care unit, the stress test lab, the cardiac catheterization lab, and the cardiac surgical service. The authors found that stress tests were performed more often on men than on women (63% vs. 37%). More men than women underwent coronary arteriography (67% vs. 33%). Interventional coronary procedures and coronary bypass surgery were skewed towards men as well (70% vs. 30%) and (76% vs. 24%), respectively. In comparing the incidence of diagnostic procedures and interventions, the authors found that women were less likely to have cardiac catheterization. However, once the catheterization was done, women were as likely as men to receive an interventional coronary procedure.

Yarzebski et al. (1996) investigated gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction. The findings suggested that the use of thrombolytic therapy was increasing over time for both men (13.9% in 1986, 31.6% in 1991) and women (3.2% in 1986, 19.0% in 1991). Findings additionally suggested that there was a greater relative increase observed in the women's group over time.

In a more recent similar study, Mahon et al. (2000) compared the clinical features, management, and outcome in men and women from a consecutive, unselected series of patients with acute myocardial infarction (AMI) who were admitted to a university cardiac center over a 3-year period. Women were older and were noted to have a higher hospital mortality even after adjusting for age (OR 1.48, 95% CI 1.07 to 2.04). Women were also less likely to receive thrombolysis (OR .48, 95% CI 0.27 to 0.86). This study conducted several years later demonstrated that gender issues continue to exist in cardiac care of women.

Like cardiac disease, the prevalence and severity of stroke between genders has been investigated to some degree. There is a great deal of information in the literature about gender as a stroke risk factor; however, the findings conflict each other. Men have been identified in the literature as high-risk or stoke-prone individuals. However, the literature is mixed in relation to a woman's risk for stroke. Brown et al. (1996) stated that stroke is more prevalent in men than in women. In the Dubbo Study of the Elderly, Simons et al. (1998) researched the predictors of ischemic stroke. They found that female sex created a 48% lower risk of ischemic stroke. The study population consisted of 1,235 men and 1,570 women who were residents of the town of Dubbo in Australia. Persons born before 1930 were eligible and participation rate was 73%.

The Rochester Epidemiology Project was another large-scale study that attempted to shed light on the gender differences related to ischemic stroke. The data for this study were extracted from medical records in Rochester from 1960 to 1984. A multiple regression model was used to estimate the odds ratio of ischemic stroke for multiple risk factors. While gender was not looked at as a specific risk factor, the findings indicated that the effect of TIA on stroke incidence and its relationship to gender was significant. The odds ratio was almost twice as large in women as it was in men and for both sexes the odds ratio decreases as the subject ages (Whisnant et al., 1996). In a similar study Petty et al. (1999) used residents of Rochester again during the period of 1985 to 1989. All patient information from residents with a first ischemic stroke was accessed from the Rochester Epidemiology project medical records. This study was more comprehensive than the initial study in efforts to evaluate gender differences related to subtypes of ischemic stroke. The sample included 454 patients with first stroke who were 96% white and 51% female. Only one stroke subtype demonstrated significant difference in terms of sex-related incidence. Age-adjusted incidence rates of ischemic stroke due to large-vessel cervical or intracranial atherosclerosis with stenosis were nearly 4 times greater for men (47.3 per 100,000, $p < .0001$) than for women (11.9 per 100,000). The authors inferred that there might be a biological difference between men and women and alluded to the fact that this helps to explain the differences in endarterectomy rates between men and women. Endarterectomy rates are reported to be 30% to 60% higher for men (Petty et al., 1999).

Among gender issues in stroke care and stroke risk management, particularly in the area of carotid studies, one study investigated the assumption that treatment guidelines may not apply equally to men and women. Di Tullio, Sacco, Savoia, Sciacca, and Homma (2000) evaluated whether the prevalence of different degrees of aortic plaque thickness differed in men and women with ischemic stroke. Plaque thickness was determined by transesophageal echocardiography conducted on 152 patients (76 men and 76 women) who had experienced ischemic stroke and 152 control subjects. Aortic plaques > 4 mm were found significantly more frequently in men than in women (31.5% vs. 20.3%, $p = .025$) and were associated with ischemic stroke in both sexes (men-adjusted OR 6.0,CI 2.1 to 16.8; women-adjusted OR 3.2, CI 1.2 to 8.8). In addition the researchers found that plaques from 3 to 3.9 mm in size had a significant relationship to stroke in women (adjusted OR 4.8, CI 1.7 to 15.0). This relationship was not found with men and no significant relationship was suggested for either sex with plaque size smaller than 3 mm. The findings suggested that smaller aortic plaques are significantly associated with stroke in women. Therefore, the conclusions of this study suggested that the guidelines for performing carotid endarterectomy may need to be adjusted downward for women.

Randomized controlled trials have indicated that carotid endartectomy can decrease the risk of stroke in symptomatic patients. Ramani et al. (2000) explored this further in studying the differences in treatment between men and women. A logistic regression model was used to estimate relative risk of use of carotid endarterectomy for women while controlling for age and comorbidity. The sample consisted of Medicare enrollees aged 65 to 84, who were hospitalized with stroke in 1992. This group was further divided into a subgroup of those patients who had carotid artery disease and who would then be likely candidates for endarterectomy. A total of 1,009 women and 990 men were included in the subgroup sample. The results showed that women were less likely than men to have a carotid endarterectomy procedure before and after adjusting for age and comorbidities. The incidence of receiving endarterectomy was 23% lower for women in the carotid disease subgroup. The overall age-adjusted female to male relative risk for undergoing carotid endarterectomy in the carotid disease subgroup was .77 (95% CI, 0.72-0.82).

In a study designed to evaluate the sex differences and similarities in the management and outcome of stroke patients, Holroyd-Leduc et al. (2000) investigated 44,832 patients who were admitted to Ontario hospitals between 1993 and 1995. The sample was 49.7% men and 50.3% women. The study involved investigation of a large administrative database focusing on sex differences in comorbidities, the use of rehabilitation services, the use of antiplatelet therapy and anticoagulants, discharge destination, and mortality. A history of heart disease and diabetes mellitus was more prevalent in male stroke patients than female stroke patients (18.1% vs. 15.3%, respectively; $p < .001$; and 20.1% vs. 18.7%, respectively; $p < .001$). Female patients were more likely to have hypertension (33.8% vs. 30.0%; $p < .001$) and atrial fibrillation (12.9% vs. 10.2%; $p < .001$). Male stroke survivors greater than 85 years of age were more likely than women to receive aspirin and ticlopidine (36.0% vs. 30.7%, respectively; $p < .001$, and 9.2% vs. 6.8%, respectively; $p < .001$). There was no sex difference in the use of rehabilitation services, warfarin use, and postdischarge aspirin and ticlopidine use in stroke survivors between 65 to 84 years of age. Men were more likely to be discharged to home than women (50.6% vs. 40.9%).

In another large prospective study conducted in Denmark, lifestyle factors and risk of cerebrovascular disease in women was investigated. Lindenstrom, Boysen, and Nyboe (1993) conducted this study beginning in 1976. Women in the study were offered two cardiovascular examinations 5 years apart. The subjects were 35 or older and had no previous stroke or TIA when the study began. An analysis of risk factors was completed at the first examination. A total of 265 cases of stroke and TIA occurred in the sample population over the 5-year period. Cigarette smoking was reported to have significant influence on risk of cerebrovascular disease (95% CI, 1.02 to 1.94) as well as lack of physical activity were reported as significant (95% CI, 1.01 to 2.08). There was no significant influence from cigarette smoking, body mass index, or alcohol consumption.

Many studies have reported varying types of relationships between hormone therapy and the risk of stroke. Since the introduction of contraceptives in the early 1960s, there has been great concern about he safety of hormone use and hormone replacement. Like heart disease, the risk of stroke related to hormone therapy has been widely investigated. An epidemiological case-control study was conducted by Pettiti, Sidney, Quesenberry, and Bernstein

(1998) in an effort to investigate the relative risk of stroke in relation to duration of use of postmenopausal hormones in a population with relatively high hormone use. The sample included women, aged 45 to 74 years, who were cared for in 10 medical centers of the Kaiser Permanente System from the period of November 1991 through November 1994. The study involved both case review and interview for data collection and analysis was restricted to postmenopausal women. Conditional logistic regression was used for the main statistical analysis. After identifying factors that would contribute to elimination for the sample, the final sample for analysis was 349 case/control sets. After adjusting for confounding variables, the authors reported the odds risk for ischemic stroke in current hormone users compared with never hormone users was 1.03 (95% CI, 0.65 to 1.65). The post-menopausal hormone use was not associated with the increase in risk of ischemic stroke.

In a similar study, Gillum, Mamidipudi, and Johnston (2000), conducted a meta-analysis of literature to determine if oral contraceptive use was associated with increased risk of stroke. Sixteen studies were analyzed using random effects modeling. A total of 804 studies were found to have been published in the 40-year period from 1960 to 1999. After reviewing these studies for exclusion and inclusion criteria, 16 studies met all of the inclusion criteria. The overall summary risk estimate for ischemic stroke among oral contraceptive users compared with those not using contraceptives was 2.75 (95% CI, 2.24-3.38, $p < .001$). Interestingly, these authors noted that as they plotted the relative risk of the studies of interest over time, the relative risk decreased over time. This finding was presumed to be related to the administration of lower dose estrogens for oral contraceptive use over time. Smaller estrogen dosages were associated with less elevated risk of stroke ($p = .01$). In conclusion, the authors suggested that while there is an increased risk of ischemic stroke with oral contraceptives, these risks are outweighed by the health benefits of oral contraceptive use.

In assessment of hormone therapy and risk of stroke among postmenopausal women with heart disease, Simon et al. (2001) investigated the relationship between postmenopausal hormone therapy to risk of stroke and TIA. The Heart and Estrogen-Progestin Replacement Study enrolled 2,763 postmenopausal women with congestive heart disease (CHD). The subjects were randomly assigned to receive conjugated estrogen plus progestin or placebo, and the effect of this intervention was evaluated against recurrent CHD events. A secondary data analysis related to stroke incidence and death was conducted on data collected on these subjects over a period of 4 years. Hormone therapy was not significantly associated with risk of nonfatal stroke, relative hazard (RH) was 1.18 (95% CI 0.83 to 1.66), nor was hormone therapy associated with fatal stroke (RH 1.61, 95% CI 0.73 to 3.55). If stroke is a cause of morbidity and mortality in women, these findings have implications for the care and treatment over their lifetimes and the efforts to decrease stroke. Based on the work of these authors, it is logical to conclude that hormone use is not a significant risk factor for the development of ischemic stroke.

This issue of hormone replacement therapy was further investigated through the Cardiovascular Health Study. Utilizing a population-based prospective study, Luoto et al. (2000) studied the relationship between the use of estrogen replacement therapy and cerebral magnetic resonance imaging (MRI) abnormalities in older women. The variables of interest included: presence of global brain atrophy, white matter changes, small infarct-like lesions, cognitive mental function as measured by the Mini-Mental State Exam (MMSE), and estrogen replacement use. The goal of the study was to determine if women who took estrogen hormone replacements had less brain atrophy, less MRI infarcts, and less white matter changes as compared to non-estrogen users. The Cardiovascular Health Study involved 5,888 men and women who represented four counties randomly sampled in the United States. As part of this study, participants were offered cranial MRI scanning over a 2-year period. Approximately 2,133 women had the MRI completed and changes reflecting the variables of interest were collected from these MRIs. Medication use was assessed by an inventory of prescriptions and past use information was obtained via self-report. Statistical analysis between estrogen replacement therapy and the variables of interest included both analysis of covariance (ANCOVA) for continuous variables and logistic regression for categorical variables. Approximately 15% of the women who underwent the MRI were current estrogen users and 23% were past estrogen users. The findings suggest that the prevalence of MRI infarctions was not any different among current or past estrogen replacement therapy users and nonusers (current users--28.6%, past users--29.9%, and nonusers--29.9%; $p = .70$). As far as the evaluation of cognitive function, the researchers found that women who had been past users of estrogen had the highest MMSE scores (adjusted score, 89.9; 95% CI, 89.0-90.7). Current users of estrogen had the next highest scores (adjusted score, 89.2; 95% CI, 88.3-90.2) and nonusers the lowest (adjusted score, 87.8, 95% CI, 87.3-88.3).

Engstrom et al. (2001) conducted a study related to gender addressing stroke incidence in an urban population in Sweden. The Stroke Register in Malmo, Sweden was used to access data on 3,540 patients who suffered an initial stroke between 1989 and 1998. The researchers sought to investigate the incidence of stroke related to prevalence of cardiovascular risk factors and socioeconomic circumstances. A cardiovascular risk score was computed related to the presence of hypertension, diabetes, smoking history, and overweight status. A composite score was derived for each subject reflecting his or her socioeconomic circumstance. The findings indicated that socioeconomic scores correlated significantly with area specific stroke rates among men (r = 0.62, p = .008) and women (r = 0.67, p = .004). The authors also concluded that the cardiovascular risk score was significantly associated with the incidence of stroke for each area studied (men, r = 0.53, p < .05; women, r = 0.76, p < .001). This finding gives support to the idea that cardiovascular disease and cerebrovascular disease are strongly interrelated.

In the following study, physical activity was evaluated as to the effects that it might have on the prevention of stroke. It is well known that physical activity decreases the risk of coronary artery disease; however, there is limited research addressing the role that physical activity might play in the prevention of stroke. To that end, Hu et al. (2000) set out to investigate this possible relationship. Utilizing the Nurses Health Study, a total of 72,488 women were included as subjects. Questionnaires regarding medical history and health practices were filled out by the participants in 1980, 1982, 1986, 1988, and 1992. The findings indicated an inverse relationship between total physical activity level and total strokes. To evaluate the long-term effects of physical activity, they examined the cumulative averages of physical activity level in relation to incident stroke from 1980 to 1994 (695 stroke cases with 1,168,015 person-years of follow-up). Multivariate RRs across categories of average hours spent on moderate/ vigorous physical activity (< 1 hour, 1-1.9 hours, 2-3.9 hours, 4-6.9 hours, and > 7 hours) were 1.0, 0.83, 0.90, 0.79, and 0,60, respectively ($p = .01$) (Hu et al., 2000). The inverse relationship between physical activity and stroke was observed primarily with ischemic strokes.

In a related study, Rexrode et al. (1997) also related weight and body mass as risk factors for stroke in women. The authors used a prospective cohort study of women participating in the Nurses' Health Study. A group of 116,759 women aged 30 to 55 were selected as the participants for this study which began in 1976. Inclusion criteria required that the women be free of coronary artery disease, stroke, and cancer at the beginning of the study. The subjects were followed for 16 years and the stroke subset had 866 strokes of which 403 were ischemic in nature. Using a multivariate analysis the researchers determined that even after adjusting for other risk factors such as age, smoking, and menopausal status, women who had an increased Body Mass Index (BMI) (> 27 km/m2) had a significantly increased risk of ischemic stroke (RR-1.75, 95% CI, 1.17-2.59; $p < .001$). A direct relationship was noted between total weight gain and total stroke risk ($p < .001$).

Gender differences related to aspirin use and risk of stroke have been evaluated in another study that involved many of the authors of the Rexrode et al. (1997) study. Iso et al. (1999), using the Nurses' Health Study again, accessed 79,319 women in 1980. A questionnaire was mailed to all participants age 34 to 59, who were free of diagnosed cardiovascular disease, cancer, and rheumatoid arthritis. The questionnaire solicited information about aspirin use and was sent again in 1982, 1984, and 1988. At the time of return of each questionnaire, women who reported a nonfatal stroke were asked for permission to review their medical records. Statistical analysis was conducted based on this incidence of stroke that occurred within the population of interest during the 14 years of follow-up from the date of initial questionnaire in 1980. Logistic regression was used to determine relative risk of stroke related to aspirin use. Five hundred and three cases of stroke were documented, and of those, 295 were ischemic strokes. The findings indicated that there was no clear relationship between aspirin use and risk of total stroke. The investigators did find that women who took one to six aspirins per week had a lower risk of large-artery occlusive infarction compared with women who took no aspirin at all. After adjusting for other cardiovascular risk factors and selected nutrients, the multivariate relative risk was 0.50 (95% CI, 0.29-0.85, $p < .01$). Additionally, the findings indicated that women who took 15 or more aspirin per week had a higher risk of subarachnoid hemorrhage with multivariate risk of 2.02 (95% CI, 1.04-3.91, $p = .02$). Aspirin use was not associated with risk of any other type of stroke.

Race/Ethnicity Issues

As the 21st century begins, more than 25% of the population in the United States is composed of ethnic minorities (United States Bureau of the Census, 1999). An understanding of the race/cultural differences in stroke will help to provide appropriate prevention and treatment strategies. The variables of race and ethnicity have been positively and significantly correlated in the literature with stroke. Wityk et al. (1996) set out to investigate the influence of race, sex, and other risk factors on the location of atherosclerotic occlusive lesions in cerebral vessels. This study was based on previous angiographic studies of patients with stroke or TIA which indicated that intracranial disease was more common in blacks and extracranial disease was more common in whites (Caplan, Gorelick, & Hier, 1986). A total of 274 ischemic stroke or TIA patients admitted to a community hospital over a 2-year period served as the sample for this study. The mean age was 66.7 years. Races were distributed as follows: 32% black women, 28% black men, 22% white men, and 17% white women. Demographics, risk factors, tests performed, and results of neurological evaluations were collected. Carotid ultrasound and magnetic resonance angiography (MRA) were performed on all subjects in order to determine the presence of extracranial and/or intracranial lesions. Statistical analysis included comparison of diagnostic tests between racial groups using independent t-tests for continuous variables and X^2 or two-tailed Fisher's exact tests for categorical variables. Following this, multivariate analysis was conducted on risk factors that were significantly different between races. Variables were entered into a stepwise fashion into a multivariate logistic regression model to determine potential predicators of extracranial or intracranial lesions. There was no statistically significant difference between sexes among vascular tests used for the evaluation of intracranial or extracranial vessels. Whites were more likely than blacks to have extracranial carotid artery lesions (33% vs. 15%, $p = .001$). However, the total proportion of patients with intracranial lesions was very similar (24% vs. 22%). Men were found to be more likely to have intracranial lesions than women (29% vs. 14%, $p = .03$). In terms of predication, white race was the only predictor identified for extracranial carotid artery lesions (OR, 2.85; 95% CI, 2.05 to 3.97). In addition, male sex was found to be an independent predictor of the presence of intracranial lesions (OR, 2.42; 95% CI, 1.60 to 3.66), but race was not a predictor of the presence of intracranial lesions.

Overall incidence rates of stroke among various races are limited. Sacco et al. (1998) endeavored to determine and compare stroke incidence rates among whites, blacks, and Hispanics living in the same urban community over a 3-year period from 1993 to 1996. Surveillance was conducted on all admissions, discharges, and computed tomography logs at the only hospital in the region of interest. The study concluded that the average annual age-adjusted stroke incidence rate for age 20 or older, per 100,000 population, was 223 for blacks, 196 for Hispanics, and 93 for whites. Blacks had a 2.4 times increase in stroke risk compared to whites and Hispanics who had a two-fold increase. The authors concluded that part of the high stroke mortality for blacks may be related to racial and ethnic differences in stroke incidence.

In a unique study related to stroke incidence, Kissela et al. (2001) focused their study on first-ever black ischemic stroke patients. The purpose of the study was to examine the volume of stroke seen on imaging scans (CT and MRI) for first-ever stroke patients. The researchers hypothesized that if the true volume of ischemic stroke was smaller than is currently accepted, and associated with milder symptoms, then some stroke patients may not be receiving all options for treatment due to the decreased recognition of the stroke event. This study compared the volume and location of infarcts in the black population studied and compared these findings to current available literature regarding acceptable stroke volumes. A total of 150 patient records met the inclusion criteria for the study and were included in the sample. The volume of cerebral infarction among blacks in this study was smaller than volumes reported in acute stroke therapy trials. The median volume was 2.5 cm^3 and mean volume was 20.1 cm^3 compared to other stroke therapy trials which reported median volumes between 10.5 to 55 cm^3. Additionally, the authors concluded that most strokes in the black population are smaller with milder symptoms. These findings may give reason to think about current directions for treatment specifically in the area of TPA. Blacks may not be getting full access to treatment due to their presentation not matching with the nationally accepted standards that govern treatments such as Tissue Plasminogen Activase (TPA).

Other studies have evaluated cultural and race issues in stroke as they relate to geographical areas. Higher mortality rates have been reported in the southeastern region of the United States for over 50 years with South Carolina leading in deaths related to stroke. Blacks are known to have more cerebrovascular deaths than do whites living in the southeast area of the United States (Perry & Roccella, 1998). In an effort to further investigate these differences, Lackland et al. (1999) set out to determine the effects of birthplace (nativity) on stroke mortality in South Carolina. Proportional mortality rates (PMRs) were calculated for stroke deaths during the period of 1980 to 1996. The PMR was calculated according to birthplace and stratified by age, race, gender, and educational status. Most of the subjects in the sample of South Carolina residents were born in the state (68.5%) and another 16.9% were from other states in the southeast. The percentage of deaths related to stroke was highest for those subjects born in South Carolina (9.0%) and lowest for those born outside the southeast (6.7%). There was no difference between races in the percentage of death pattern listed above. The effects of nativity appear to be similar for blacks and whites.

Stroke in America is considered more deadly for blacks than it is for non-Hispanic whites. There is however, limited information about the incidence of stroke among Hispanic Americans. Morgenstern, Spears, Goff, Grotta, and Nichaman (1997) utilized Texas vital statistics records for a 5-year period from 1988 to 1992 to investigate the differences among non-Hispanic whites, African Americans, and Hispanics. The researchers used any death coded as ICD-9 430 to 438, which represented cerebrovascular disease, in the 4-year time frame as subjects for this study. Stroke deaths within this group were 76% non-Hispanic whites, 12% blacks, and 12% Hispanics. Blacks had a threefold increase in stroke mortality between the ages of 45 to 59 compared to non-Hispanic whites at these same ages. Hispanics had a significantly higher rate of stroke mortality at younger ages (RR, 1.73) compared to non-Hispanic whites but then were significantly lower at older ages as compared to the other two groups.

In an extension of interest in the racial/ethnic issues related to stroke care, another group of researchers (Morgenstern et al., 2001), investigated the barriers to acute stroke therapy and prevention among Mexican Americans. Morgenstern et al. attempted to identify specific targets that could be used to improve acute stroke treatment and stroke prevention among the Mexican American population. A phone survey of 719 subjects was utilized to identify present risk factors and knowledge about stroke, 357 were Mexican Americans and 362 were non-Hispanic whites. The Mexican Americans were significantly younger, less well educated, and had a lower income than the whites (p = .001). Mexican Americans had a significantly higher prevalence of diabetes (p = .001), were less knowledgeable about stroke therapy (p =.029), and were less likely to be willing to call 911 for stroke symptoms (p = .01). Mexican Americans were less confident than whites in their ability to prevent stroke (p < .001). These findings demonstrated that there are significant differences among races, and that these differences might influence successful stroke recognition, treatment, and prevention.

The early research done by Sacco, Hauser, and Mohr (1991) demonstrated the same race and stroke incidence patterns that have been mentioned previously. These researchers accessed discharge data for 1,034 patients who were over the age of 39 and hospitalized for stroke between 1983 and 1986. Age-adjusted stroke incidence rates per 100,000 were highest for blacks (567), 352 for whites, and lowest for Hispanics at 306. Whites were reported to have more ischemic cardiac disease. Black and Hispanics had a higher prevalence of hypertension and diabetes.

The National Longitudinal Mortality Study (Anderson, Sorlie, Andrews, Backlund, & Burke, 1994) revealed information that is particularly relevant when presenting the research regarding race/ethnicity and stroke. Anderson et al. extracted data from the National Longitudinal Mortality Study to determine the incidence and burden of stroke on the Hispanic white population. Stroke deaths among the sample included: 1,844 among 239,734 non-Hispanic whites, 46 among 12,527 Hispanic whites, and 234 deaths among 23,468 black subjects. Black men and women had a higher hazard ratio of stroke mortality by > 4.0 at age 45 compared to non-Hispanic whites. However, this hazard ratio equalized at < 1.0 by age 85. Hispanic men and women had a low hazard ratio at < 1.0 at age 45, which was similar to non-Hispanic whites. Hispanics had a significantly lower mortality risk at < 1.0 at age 85 as compared to non-Hispanic whites. The researchers concluded that mortality risk for blacks occurred at a much younger age than for non-Hispanic whites or Hispanics. The incidence of stroke mortality in Hispanics and non-Hispanic whites is similar at young ages, but significantly lower at older ages.

Severity of Illness/Mortality Index

Severity of illness is defined as "the extent of physiologic decompensation or organ system loss of function" (Brough & Gay, 1998, p. 1). Risk of mortality refers to "the likelihood of dying" (Brough & Gay, 1998, p. 1). With respect to ischemic stroke, severity of illness is a major consideration in determining the complexity or care needs regarding this or any other medical population. Case mix complexity is a term that incorporates several attributes including severity of illness, risk of mortality, prognosis, treatment difficulty, and need for intervention. The evolution of the Diagnosis Related Group (DRG) is the classification system that is widely accepted as a way to relate the types if patients that the hospital treats with its case mix. The premise of this system is that the case mix of any group of patients or those seen in a hospital, determine costs. The case mix demand that is behind each DRG represents the resource intensity demands that patients place on an institution.

The first operational set of DRGs was developed at Yale University in the early 1970s. The original DRGs were formed by physician panels who divided all principal diagnoses into 23 mutually exclusive principal diagnosis categories referred to as Major Diagnostic Categories (MDCs). Once the MDCs were defined, each MDC was evaluated to determine if there were any additional patient characteristics, which would have a consistent effect on the consumption of hospital resources. The groups were then divided into medical and surgical groups. Once these groups were formed the next step involved the evaluation of each group to determine if complications, comorbidities or the patient's age would consistently affect the consumption of hospital resources. A physician panel would convene and discuss each group in an effort to determine if complications and comorbidities would significantly effect the use of resources. Finally, the discharge status was also used as a variable for determining the definition of the DRG. The process of forming the DRGs in the 1970s involved a combination of statistical results from test data which included clinical judgement as well (Brough & Gay, 1998).

In 1987, the legislature of New York state passed legislation requiring that a DRG-based prospective payment system be developed for all non-Medicare patients. In addition, the DRG system in place focused heavily on resource intensity and was not effective in providing severity of illness or risk of mortality information. The All Patient DRG (AP-DRGs) was created to help answer this concern. The original DRG system was not effective in addressing neonates and people with Human Immunodeficiency Virus (HIV) infections. These deficiencies were to be addressed by the AP-DRG system. The database of 722,626 discharges from 85 New York hospitals was used in the initial development of the AP-DRGs. Cost-to-charge ratios and length of stay data were used in the development of the AP-DRG as well.

The All Patient Refined-Diagnosis Related Group (APR-DRG) expanded the basic AP-DRG structure by adding four subclasses to each DRG. The subclasses were designed to address differences in severity of illness and risk of mortality. "Severity of illness relates to the extent of physiologic decompensation or organ system loss of function experienced by the patient while risk of mortality relates to the likelihood of dying" (Brough & Gay, 1998, p. 17). Essentially, subclasses within severity of illness and risk of mortality were created to reflect patient differences within a given DRGs. The four subclasses for both severity of illness and risk of mortality are numbered in sequential order from 1 to 4. The numbers 1 to 4 indicate the following: minor, moderate, major, or extreme for either severity of illness or risk of mortality. These values represent categories and not scores. Therefore, severity categories cannot be compared across DRGs. However, Brough and Gay reported that the APR-DRG severity of illness and risk of mortality subclasses could be used to compute an expected value for a measurement of interest such as mortality. The underlying theory behind the APR-DRG is that the severity of illness and risk of mortality subclasses are highly dependent on the patient's complete clinical picture including underlying problems. Thus, a high severity of illness would indicate multiple serious diseases.

The process of development of the APR-DRG involved a recursive approach to formulating clinical hypotheses and then testing those hypotheses with clinical data (Brough & Gay, 1998). Separate clinical models were developed for each of the entire group of 355 APR-DRGs. The clinical models were tested with historical data to ensure that patients with high severity of illness would incur greater costs and patients with high risk of mortality would die more frequently. The researchers reported that when discrepancies were discovered between the clinical expectations and the data results, the researchers deferred to the clinical expectations. The data used for the analysis included a random, nationwide database that included 5.7 million discharges. The data were derived from 657 hospitals, in 35 states, which included all types of payers.

The APR-DRG is a widely accepted set of severity of illness and risk of mortality adjusted patient groups. The APR-DRG classification is the most current iteration of a model that began in the early 1970s. The further development of the APR-DRG gives healthcare providers the opportunity to understand the patients that are being cared for within a particular disease process.

Ischemic Stroke--Interventions

Surgical Treatment

The appropriate management of ischemic stroke in the early period of stroke evolution or occurrence is of great interest to the scientific community. Surgical interventions have been investigated as a means of promoting improved neurological function and stroke outcomes. Carotid endarterectomy has been the mainstay for surgical treatment of emerging stroke-related symptoms.

Since the early 1950s carotid endarterectomies have been performed on patients suspected of having blockage or stenosis of the carotid arteries. However, over the years there has been a great deal of debate in the medical community regarding the effectiveness of this surgical intervention. In the last several years, researchers have set out to investigate, through randomized studies, the effectiveness and indications for this surgery. There are two major concerns related to the carotid endarterectomy, and these include the presence or lack of symptoms in patients with carotid stenosis. Physicians have struggled to understand the risks associated with asymptomatic carotid disease and the risks of the carotid endarterectomy surgery.

In the randomized Asymptomatic Carotid Atherosclerosis Study (ACAS) conducted between 1987 and 1993, 39 sites were used to access 1,662 patients from 42,000 who were screened for inclusion in the study. In order to be included in this study, the participant ages had to be between 40 and 79 years. Seventy percent of patients were asymptomatic in distribution of both carotid arteries, while 25% had a prior recent hemispheric event in the contralateral carotid circulation (Executive Committee for the Asymptomatic Carotid Atherosclerosis Study, 1995). Patients were assigned randomly to the surgical or medical arm of this study. All patients who were assigned to the surgical arm were given preoperative cerebral arteriography. Arteriography was not part of the medical arm, however, many patients (37.5%) in the medical arm had arteriography before they were randomized. In determining treatment options, a significant stenosis noted on radiographic study was defined as a 60% reduction in the diameter of the carotid arteries. Evaluation in the surgical arm participants identified that 8% of patients had less than a 60% blockage of the carotid arteries. The surgical arm yielded a total of 825 patients and the medical arm had 834 patients. All patients in the study were placed on aspirin 325 mg as a risk factor reduction strategy. This longitudinal study involved follow-up evaluations at 1 month, 3 months, 6 months thereafter for 2 years, and annually until the completion of the fifth year interval. Other end points included stroke occurrence or death. The study outcomes indicated that surgery reduced absolute risk by 5.9% and relative risk reduction by 53% at 5 years ($\underline{p}$ = .004, 95% CI). In men, carotid endarterectomy (CEA) reduced the 5-year event rate by 66%, compared with only a 17% reduction in women. The relative risk reduction for major disabling stroke or perioperative death and major stroke was 43%, which was not statistically significant (6% for the medical arm vs. 3.4% for the surgical arm, $\underline{p}$ = .12).

It appears that when surgery was used, the benefits associated with that surgery were generally realized within the first year after surgery; relative risk reduction was 60% for those participants less than 67 and 43% for those greater than 67. Both the medical and surgical intervention proved to be less effective for women than men. Men demonstrated an absolute risk reduction from 12.1% to 4.1% (relative risk reduction of 66%). Women demonstrated an absolute risk reduction of 1.4% and relative reduction of 17%. One major finding of the ACAS study was the fact that described surgical benefit was achieved whether subjects were in the medical or surgical arm of the study. One major consideration in looking at this study is to realize that the investigators combined stenosis rates from 60% to 99%

together in the analysis of this study. The investigators did not set up the study to break down event rates by deciles of carotid stenosis. This happening may have diluted the presence of statistically significant areas of carotid stenosis.

Many physicians have believed that a carotid stenosis of greater than 80% is suggestive of surgery to correct this problem. The European Carotid Surgery Trialist (ECST) Collaborative Group investigated the issue of when to perform carotid endarterectomy. The European Carotid Surgery Trialists Collaborative Group (1995) accessed data from 2,295 patients over a 3-year period with a goal of determining stroke risk among patients with asymptomatic internal carotid artery stenosis. The researchers found a very low level of risk at 3 years. The overall Kaplan-Meier estimate of stroke risk was only 2.1% at 3 years. The findings also indicated that stroke risk was very low (< 2%) for any blockage of the carotid arteries less than 80%. Stroke risk for stenosis in the 80% to 89% interval was 9.8% and 14.4% for carotid artery stenosis in patients with 90% to 99% asymptomatic stenosis.

In a more recent study, Inzitari et al. (2000) evaluated the causes and incidence of stroke in patients with asymptomatic carotid artery stenosis in an effort to shed light on the use of carotid endarterectomy in these patients. The sample included 1,820 patients with unilateral symptomatic carotid-artery stenosis and asymptomatic contralateral stenosis from 1988 to 1997. For patients with less than 60% stenosis, the risk of first stroke was 8%. In the patients with a higher degree of stenosis (60% to 99%), the risk of first stroke was 16.2%. The stroke risk of the asymptomatic occluded artery was annualized at 1.9%. These findings were consistent with other studies supporting the idea that risk of stroke increased with severity of carotid artery stenosis.

Other studies have investigated the role of carotid endarterectomy among symptomatic patients with carotid artery stenosis. Warlow (1993) in his work with the European Carotid Surgery Trial (ECST) focused on the benefit of carotid endarterectomy for symptomatic carotid artery stenosis patients. The sample included 455 surgical patients and 323 medical patients who were followed over a period of 2.7 years. Carotid artery stenosis was determined through the use of minimal residual lumen compared with the estimated normal lumen at the level of greatest stenosis. The study focused strictly on outcomes, participating surgeons had no quality controls placed on them, and there was no uniform medical therapy required. Among patients who were symptomatic with 70% to 99% stenosis, surgical patients had decreased risk of outcome events compared to medical patients. Risk of stroke and perioperative death was 10.3% in the surgical patients and 16.8% in those patients who did not have treatment. Surgical patients had a 12.3% risk of death due to carotid endarterectomy or stroke from any cause during follow-up compared to 21.9% risk among nonsurgical patients. There was no benefit indicated for carotid endarterectomy for patients with 0% to 29% stenosis. In a more recent study the ECST found that after randomizing 1,590 symptomatic patients with 30% to 69% stenosis, there was no benefit identified for treatment with carotid endarterectomy (European Carotid Trialists' Collaborative Group, 1996).

Additional research has supported the effectiveness of carotid endarterectomy for patients who are symptomatic with severe (70% to 99%) internal carotid artery stenosis. Investigators participating in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) analyzed data from 50 centers in Canada and the United States focusing on surgeons who had documented carotid endarterectomy stroke morbidity and mortality rates of 6% for 50 consecutive cases over a period of 2 years (North American Symptomatic Carotid Endarterectomy Trial Collaborators, 1991). Patients were eligible to participate if they were less than 79 years, and had experienced cerebral or retinal transient ischemia, or a non-disabling stroke in the previous 120 days. The NASCET investigators reported a final sample of 328 patients with 70% to 99% blockage who underwent carotid endarterectomy. The surgical group 30-day stroke morbidity and mortality rate was 5.8%. The 2-year risk for ipsilateral stroke was 26% for patients treated medically and only 9% for surgical patients. Additionally, the incidence of major or fatal ipsilateral stroke was only 2.5% for the surgical group and 13.1% for the medical group. The consensus of the investigators was that surgical intervention among patients with severe symptomatic carotid artery stenosis was very beneficial.

In a landmark study, the Carotid Endarterectomy and Prevention of Cerebral Ischemia in Symptomatic Carotid Stenosis study, the role of carotid endarterectomy was investigated with attention to its potential neuroprotective outcomes. Mayberg et al. (1991) looked at the relationship of carotid endarterectomy to protection against subsequent cerebral ischemia in men with ischemic cerebral hemispheric symptoms and > 50% ipsilateral internal carotid artery diameter stenosis as indicated by arteriography. Veterans Affairs (VA) hospitals with low stroke morbidity and mortality (< 6%) were selected as recruitment centers for subjects. Two groups were formed. One group (92 patients) received carotid endarterectomy plus medical management and the other (101 patients) received medical management only.

Mayberg et al. found that for patients with > 70% diameter stenosis, the stroke rate was 7.9% for the surgical group. The stroke rate for the medical group with the same degree of stenosis was 25.6%. These findings are consistent with the NASCET and ECST study findings mentioned above.

While carotid endarterectomy has been demonstrated to be effective for treating symptomatic and some asymptomatic patients, there is some discussion that female gender may be a risk factor for stoke and death after carotid endarterectomy. There are only a few studies that address the surgical outcomes of carotid endarterectomy with regard to sex. In a large study involving 520 women and 778 men, Akbari et al. (2000) reviewed carotid endarterectomy procedures that were performed in one institution between 1990 and 1998. The study showed that cardiac risk factors varied significantly between men and women, with women more likely to have diabetes (42% vs. 36%) and hypertension (77% vs. 66%) ($p < .05$). Women were less likely to be symptomatic upon presentation (men, 44% vs. women, 51%, $p = .022$). The overall postoperative stroke rate was 1.5% (1.7% in men and 1.2% in women, p = not significant). Operative mortality was not significant either. The total operative mortality was .3% (.4% for men and .2% for women). Although the literature suggests that there could be gender differences with respect to outcomes associated with carotid endarterectomy, this study did not identify differences in outcomes.

In light of the findings suggested by the ACAS study with regard to better stroke event reduction between men and women, Rockman et al. (2001) set out to study carotid endarterectomy in female patients. The purpose of the study was to determine if perioperative results differed between women and men. A sample of 991 women and 1,485 men was obtained from a computerized database of surgeries performed at New York University Medical Center between 1982 and 1997. Contrary to the study above, the women in this sample had lower incidence of diabetes than did male patients. There were no significant differences in perioperative stroke rates between men and women overall (2.3% vs. 2.4%, $p = .92$). There were no significant differences even when looking at symptomatic (2.5% vs. 3.0%, $p = .52$) and asymptomatic (2.0% vs. 1.2%, $p = .55$) cases. Therefore, at this time there does not appear to be a great difference in stroke risk between men and women in the surgical intervention arena of stroke management.

Radiological Treatment

In today's healthcare environment many radiological or diagnostic imaging procedures can be used in the care and treatment of the ischemic stroke patient. The availability of multiple types of radiological tests and procedures make the decision-making regarding appropriate selection and use a challenge. This review focuses on the research related to the approaches for the radiological management of the patient with acute stroke.

Radiological procedures can be critical in the determination of appropriate management strategies for the treatment of stroke. The objective of radiological studies in the evaluation of acute stroke focuses on the need to determine if there is, in fact, a stroke and whether the cause is ischemic or hemorrhagic in nature.

Computed Tomography (CT) is a critical test that is used in the early evaluation of patients with stroke. CT scan can detect infarction of the brain; however, the time that the CT is done in relation to the occurrence of the stroke affects what can be seen. Bryan et al. (1981) compared the use of CT and MRI in the diagnosis of acute cerebral infarction. These researchers found that detection of stroke by CT depends on the time between the stroke occurrence and the actual CT examination. The ability of the CT to detect stroke is also to a lesser amount dependent upon the character of the infarct and the location of the infarct. CTs do not detect large cortical surface infarcts before the 3-hour mark from onset, but almost 60% can be detected at 24 hours. The ability of the CT to detect changes related to the infarct improves over time such that 100% can be detected by CT at 7 days post-infarct.

Two studies looked at the ability of the CT to detect stroke and infarction due to involvement of the middle cerebral artery. von Kummer et al. (1994) focused their study on subtle changes that may appear in a CT scan related to ischemic stroke. The findings of these researchers indicated that the most common early sign of cerebral infarction was what is known as "obscuration" of the lentiform nucleus, and the loss of the "insular ribbon." These changes are thought to reflect early ischemic changes, which cause edema. In a study conducted by Truwit, Barkovich, Gean-Marton, Hibri, and Norman (1990), these authors reported that, like the study above, CT changes such as the loss of normal white-gray matter in the lateral margins of the insula (insular ribbon) were early signs of stroke. In addition, the research indicated that these early CT-detected anatomic changes reflected infarcts of the middle cerebral artery (MCA).

In the a landmark time honored study, the Cerebral Embolism Study Group (1984) evaluated the effects of immediate anticoagulation on embolic stroke and brain hemorrhage and management options. Within this study much was learned about CT detection of infarction. The study found that in instances where there were massive infarcts in the MCA or infarcts involving the posterior-inferior cerebellar artery distribution, early CT scans performed within the first 2 hours from onset would detect large infarcts. Early CT findings, such as changes in the cortical sulci and effacement of the body of the lateral ventricle that were associated with a consistent clinical picture of stroke, were indicative of massive infarction. The authors concluded that in the presence of these changes, heparin was contraindicated due to the risk of hemorrhage associated with large embolic cerebral infarction.

Another area of interest in the field of CT is the concern about the use of contrast with CT. There appears to be controversy over the use of intravenous contrast for CT evaluation. Wing, Norman, Pollock, and Newton (1976) found in their investigation of IV contrast and CT scan with stroke that use at 2 to 3 weeks after stroke can be valuable. Physiologic changes can make the identification of cerebral infarction difficult at the 2 to 3 week time frames. The study demonstrated that contrast could enhance documentation of infarction as much as 60% to 65% for patients at this point in their stroke evolution. In a study of contrast use versus no contrast in CTs among patients with acute ischemic stroke, Kendall and Pullicino (1980) found no evidence that supported the use of contrast for CTs in acute stroke patients. In addition the authors expressed concern that the contrast might contribute to additional problems for the patients given contrast related to cerebral toxicity in patients with compromised blood-brain barriers.

More recently, investigators have looked at the effectiveness of magnetic resonance imaging (MRI) in the documentation of early ischemic infarction identification. MRI is reported to have a higher success rate than CT in the early documentation of infarction and is very effective in its ability to document the hemorrhagic component that may be present with stroke. In a study conducted by Mohr et al. (1995), a comparison of MRI to CT in acute stroke resulted in the finding that use of a high field strength (1.0 to 1.5) magnet was superior to the CT in early detection of acute infarction. These researchers found that echoplanar MR diffusion and perfusion MR may document changes within minutes of the stroke occurrence. With a conventional high-field MRI, about 15% of patients will demonstrate diagnostic changes in the MRI signal within 8 hours and 90% will demonstrate changes on MRI at 24 hours. These findings applied to both small deep lacunes in the anterior and posterior circulation and cortical surface infarcts. The MRI was found to be 90% more effective in the detection of cerebral ischemic infarction within the first 24 hours of stroke onset.

The MRI is reported to be more effective in documenting hemorrhagic infarction and shows the early signs of post-infarct brain edema. Dul and Drayer (1994) reported that the MRI may detect areas of hemorrhagic infarction within the brain earlier than CT. The MRI can be used to detect the presence of various stages of chemical transformation of the hemoglobin molecule. The predictable sequence of the hemoglobin transformation gives specific signal changes that the MRI can detect. These authors believe that the MRI has an advantage over CT in the ability to date intracerebral hemorrhage events accurately. Additionally, the MRI can detect associated lesions that may have caused the cerebral bleed.

The findings of Horowitz, Zito, Donnarumma, Patel, and Alvir (1991) contrast what the authors above espoused about MRI. This study investigated the CT findings that were present within the first 5 hours post-cerebral infarction. The CT was found to be very effective in discriminating between hemorrhagic and ischemic stroke and determined that CT was the most important initial diagnostic study. The CT also was able to differentiate nonvascular lesions in the effort to rule out other problems in the face of stroke-like symptoms. These researchers found that the CT was effective in detecting intracerebral hemorrhage at the 100% level. The CT was able to detect edema, hydrocephalus, and hypodensity in 50% to 60% of cases studied. As indicated above, these authors reported that the CT might not identify an ischemic lesion in the first few hours following a stroke. The CT was considered superior to the MRI due to its availability in all hospitals and the speed with which the CT can be done.

Pharmacological Treatment

Some types of pharmacological treatment can reduce the occurrence and outcome of ischemic stroke. Treatment options for ischemic stroke in the form of tissue plasminogen activator (TPA) are effective for the small amount of patients who are eligible. However, the prevention of stroke through risk reduction pharmacological therapies offers great promise for the control of ischemic stroke.

Atrial fibrillation is a common arrhythmia and is considered a major risk factor for ischemic stroke. Many studies have established and supported the role of anticoagulation as a means of preventing ischemic stroke. Among the occurrence of ischemic stroke, atrial fibrillation is responsible for 50% of thromboembolic strokes. Benjamin, Wolf, and D'Agostino (1998) found that stroke risk from atrial fibrillation was age related, from 1.5% risk at 50 to 59 years of age to 23.5% for subjects who were 80 to 89 years of age. With the clotting risk associated with atrial fibrillation well documented, numerous studies have looked at the efficacy of warfarin (coumadin) and aspirin in the setting of atrial fibrillation and stroke prevention.

The following placebo-controlled trials investigated the effectiveness of coumadin as a preventive agent for thromboembolic stroke. Peterson, Boysen, Godtfredsen, Andersen, and Andersen (1989) conducted the Copenhagen Atrial Fibrillation Aspirin and Anticoagulation (AFASAK) trial. The trial involved 1,007 outpatients who had been diagnosed with chronic non-rheumatic atrial fibrillation. Subjects were randomized into three groups; 335 received warfarin openly, in the double blind arm 336 received aspirin 75 mg once a day, and 336 received the placebo. The participants were followed over period of 2 years from 1985 to 1988. End points of the study were death or thromboembolic complication. The researchers found that the incidence of thromboembolic complications and vascular mortality were significantly lower in the warfarin group than in the aspirin and placebo groups ($p < .05$).

The Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF) was conducted by the Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators (1990). This study was designed as an unblinded, randomized, controlled trial of long-term, low-dose warfarin therapy in patients with nonrheumatic atrial fibrillation. The control group did not receive warfarin, but might have been given aspirin as part of their treatment. Among the two groups, 212 subjects were in the warfarin group and 208 were in the control group. Subjects were followed on average about 2 years. Incidence of stroke was higher in the control group at 13 stroke events compared to 2 stroke events in the warfarin group. This difference between groups accounted for an 86% reduction in risk of stroke (warfarin: control incidence ratio = 0.14; 95% confidence interval, 0.40 to 0.49; p = .0022). The researchers also found that the death rate was also lower among the warfarin subjects, incidence ratio of .38 (95% CI, .17 to .82; p = .005). The authors concluded that long-term warfarin treatment in patients with nonrheumatic atrial fibrillation was effective in preventing stroke.

The Canadian Atrial Fibrillation Anticoagulation (CAFA) Study evaluated the effectiveness of warfarin treatment with atrial fibrillation and added the component of assessing inherent risk of hemorrhage associated with warfarin treatment. A total of 378 patients with chronic atrial fibrillation were involved in this study; 187 were randomized to warfarin treatment and 191 to placebo. The findings of this study were very similar to the previous studies. The annual rates of the primary outcome event cluster were 3.5% in the warfarin-treatment group and 5.2% in the placebo group with a relative risk reduction of 37%

(95% CI, p = 0.17). The annual rates of intracranial and major bleeding in patients receiving placebo or warfarin were .5% and 2.5%, respectively. While there is some increased risk of serious hemorrhage on warfarin, the investigators believed that the benefit of stroke risk reduction outweighed the bleeding risk.

Ezekowitz et al. (1992) conducted another study focused on the effectiveness of warfarin in subjects with nonrheumatic atrial fibrillation. This study was different from previous studies in that the subjects were all men. This study was a randomized, double-blind study in which subjects were either given warfarin (260 patients) or placebo (265 patients). The primary end point of the study was cerebral infarction or cerebral hemorrhage and death. Over a period of 1.8 years follow-up the risk reduction with warfarin therapy was .79 (95% CI, 0.52 to 0.90, p = .001). This study also supports the use of warfarin as a preventive treatment for thromboembolic stroke among nonrheumatic atrial fibrillation patients.

In 1994, a panel of the American Heart Association Stroke Council recommended that thrombolytic drugs should not be used for acute ischemic stroke. Within 2 years multiple studies testing the use of intravenous thrombolytic drugs were conducted and completed leading the council in a totally different direction. Based on the findings of these major studies, the American Heart Association Stroke Council reversed their earlier recommendation and recommended thrombolytic drugs in clinical practice for selected patients experiencing acute ischemic stroke (Adams et al., 1996).

del Zoppo et al. (1996) conducted the Prolyse in Acute Cerebral Thromboembolism Trial (PROACT). This double-blind, randomized controlled trial evaluated the rate of recanalization, safety, and efficacy of recombinant prourokinase (r-proUK). Subjects were selected from those individuals who presented within 6 hours of stroke that was secondary to the occlusion of the middle cerebral artery. Patients were randomized to the 6 mg. intra-arterial r-proUK arm of the study or were given placebo. Of those studied, 58% were found to have a recanulated middle cerebral artery following treatment with r-proUK compared with 14% among the placebo group (p = .017). In addition there was no difference between groups on the incidence of brain hemorrhage, r-proUk (15%) incidence and placebo (14%) incidence.

Following the effectiveness of thrombolytic therapy among cardiac patients, several studies were designed to investigate the use of pro-urokinase, recombinant tissue plasminogen activator (rt-PA) and alteplase, the biosynthetic form of tissue plasminogen activator (TPA) in an ischemic stroke population. Two major studies were conducted simultaneously in America and Europe. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group (1995) conducted a randomized, placebo-controlled, double blind trial that had two parts. Part 1 enrolled 291 patients at eight centers in the United States. This study compared the performance of rt-PA and the placebo as evidenced by improvements in the NIH stroke scale. When the stroke scale was measured at 24 hours after treatment, there were no differences between groups. After 3 months the patient's outcomes as indicated by the Barthel Index and modified Rankin Scale, the NIH Stroke Scale and the Glascow Coma scale had improved by at least 30% when the treatment with Alteplase was initiated within 3 hours onset of signs and symptoms ($p < .01$).

In Part II of the same study, 333 patients were enrolled at the same hospitals, and the study was conducted again in an effort to confirm the findings of Part I. The Part II trial showed that those patients who received rt-PA were at least 30% more likely to have minimal or no disability at 3 months compared to those patients who had received the placebo.

Hacke, Kaste, and Fieshci (1996) conducted a multicenter, randomized, double-blind, placebo-controlled trial with rt-PA called the European Cooperative Acute

Stroke Study (ECASS). This study randomized 620 patients between the rt-PA and placebo groups. The rt-PA was administered at a dosage of 1.1 mg/kg within 6 hours from onset of stroke signs and symptoms. The outcome measure of interest was the Barthel Index and the modified Rankin Scale. Patients treated with rt-PA had a significantly greater ($p < .001$) in functional and neurological outcomes compared to patients receiving placebo. These patients also had better neurological recovery ($p = .03$) at 90 days as evidenced by Scandinavian Stroke Scale scores. The only significantly negative outcome of this study was the occurrence of larger parenchymal hemorrhages compared to the placebo group ($p < .001$). Based on the positive results of the above studies, in 1996, the Food and Drug Administration approved rt-PA for the treatment of ischemic stroke within 3 hours of symptom onset.

Physician Specialty/Care Units

Ischemic stroke patients have their medical needs managed by a variety of types of physicians. There is a growing question in this country about who is the best physician to manage any patient's variety of medical needs that may come up over a course of a lifetime. The growing cost of medical care has also driven investigations into the issues of generalist versus specialist types of care. In an era of cost containment, studies sprang up to address the neurologists and the other physicians' roles and outcomes in stroke management.

As early as 1996, studies were conducted to focus on the value that neurologists provide in terms of cost and outcome. J. Mitchell et al. (1996) examined the claims data of 20% (38,612) of all Medicare patients hospitalized in 1991 with one of two stroke diagnoses (ICD 9 code 434 or 436). The random sample reflected Medicare patients who were 65 and older admitted to hospitals around the United States. The attending physician was identified as that physician who was billing for routine hospital visits during the first 7 days of the hospital stay. Neurologists were compared to internists, family practice physicians (FPs), and all other specialists grouped together. In 24.7% of the cases examined, both a neurologist and a primary care physician were both billing. In these cases a combination category was created. Physician specialty was then compared to cost and outcomes. Costs were determined from claims associated with the hospitalization (acute care, rehabilitation, and long-stay hospitals) and the post-acute-care period, which included up to 90 days after admission.

Outcomes included mortality and discharge destination. Mortality rates were calculated for the 90-day time period after the initial hospitalization. One in every nine

Medicare patients had a neurologist as attending physician, which was an 11.3% occurrence. Another one-fourth of patients had both a neurologist and primary care physician. The findings indicated that stroke patients who were treated by neurologists had better outcomes than those treated by other specialists. Ninety-day mortality rates were significantly lower than those who had other attending physicians; 31% lower than internists and 36% lower than FPs. Another major finding related to cost was the fact that neurologists were significantly more expensive than other physicians. Neurologists were 34% more expensive than FPs and 22% more expensive than internists and other specialists. Interestingly, those patients who had the combination of neurologist and primary care physician had the highest cost of all the groups, averaging 5% more than the neurologist only group. The difference in cost was attributed to the utilization of hospital services. Stroke patients treated by neurologists had longer lengths of stay and had more diagnostic tests ordered. Stroke patients treated by neurologists were more likely to be discharged to rehabilitation facilities or to home versus skilled nursing facilities or nursing homes. In conclusion, the researchers identified that neurology specialists might be more skilled and knowledgeable in the care and treatment of stroke, thus influencing outcomes.

In a similar study, Horner, Matcher, Divine, and Feussner (1995) investigated the relationships between physician specialty and outcomes of ischemic stroke patients. The subjects consisted of 146 patients experiencing their first stroke, hospitalized at a private, university, or Veterans Affairs hospital. Patient demographics, disease severity, risk factors for stroke, diagnostic tests, pharmacological management, mortality, and physical and functional impairment data were collected. The researchers found that patients who were admitted to neurology services at the various hospitals had a lower likelihood of having either a completed stroke and were less likely to die within 1 and 6 months following the initial stroke.

Gillum and Johnston (2000) utilized an administrative database from the University Health System Consortium to study the outcomes of ischemic stroke when a neurologist is the attending physician. This database contained information from 84 academic health centers. The researchers abstracted discharge information for all ischemic stroke patients admitted through the emergency room from 1997-1999. Through statistical analysis, the investigators evaluated attending physician specialty as a predictor of in-hospital mortality. A total of 28,571 ischemic stroke patients made up the sample. Of this sample, 58% were admitted to a neurologist's care. Patients admitted to a neurologist's (4.7%) care had a significantly lower risk of in-hospital mortality compared to those admitted to non-neurologists (9.4, $p < .001$). In contrast though, the researchers found that risk of death was not lower at hospitals admitting a larger portion of ischemic stroke cases to neurologists ($p = .54$) as might be expected if admission to a neurologist care led to improved outcomes.

While the question regarding the efficacy of physician management and medical management are very important, an equally important issue in the management of ischemic stroke patients lies in the concern about where these patients should be treated. Unit placement within the hospital and care of the ischemic stroke patient varies greatly around the country. Some research has been conducted that investigates the issues surrounding the care unit and the ability of a hospital to provide the necessary infrastructure to support stroke care.

Briggs, Felberg, Malkoff, Bratina, and Grotta (2001) evaluated the in-hospital placement of patients with mild and moderate acute strokes with regard to the placement of these patients on a general ward or intensive care unit. A total of 138 patients at two side-by-side hospitals were reviewed and compared with the following outcome measures: complication rates, discharge Rankin scale, hospital discharge placement, length of stay, and costs. The patients admitted to the university hospital represented 43% mild and moderate strokes that were admitted to the ICU. The community hospital admitted 18% of mild and moderate stroke patients to an ICU, indicating a significant difference in the placement of ischemic stroke patients between hospitals ($p < .004$). While there were significant differences in placement of the mild and moderate stroke patients, there were no significant differences in outcomes of these patients. Further analysis indicated that mild stroke patients who were admitted to an ICU versus a general ward indicated better outcomes when patients were placed on the ward. This study was conducted in two hospitals who do not have a stroke unit, and the indication is that in this type of environment it is more conducive to admit mild and moderate stroke patients to the medical ward as there appears to be no cost or outcome benefit to placing them in the ICU.

The concept of stroke patient placement has been presented in many research studies focusing on the effectiveness of "stroke units". Stegmayr et al. (1999) looked closely at the whether the stroke care units result in superior care. This study was a multicenter observational study of procedures and outcomes in acute stroke patients who were admitted to stroke units, or general medical or neurological wards. These researchers found that among patients who had lived independently prior to admission, and who were fully conscious upon admission, then admitted to a stroke unit, had a lower case fatality than those who were cared for on a general ward (RR for death, .87; 95% CI, 0,79 to 0.96). Many of the patients who were cared for in the stroke unit were also discharged to their homes (RR, 0.91; 95% CI, 0.85 to 0.98). The authors reported no difference in outcomes between the stroke unit and general ward if the patient had impaired consciousness on admission to the hospital.

In an effort to develop recommendations for development and opening of primary stroke centers, Alberts et al. (2000) reviewed an enormous amount of literature published from 1966 to March 2000. The researchers sought evidence for supporting care recommendations for patients with acute stroke that included care unit selection. It was found that many of the randomized clinical trials suggested that stroke centers would improve clinical outcomes. Among the elements that would make up the stroke center would be the use of stroke unit or units. The researchers concluded that stroke patients who received their care on stroke units had a 17% reduction in death, a 7% increase in ability to live at home following discharge, and 8% reduction in length of stay. These researchers further suggested that stroke units may not have to be distinct areas or units but, more importantly, the hospital should be staffed by employees and personnel knowledgeable in caring for patients with cerebrovascular disease.

The effects of the department care (medicine vs. neurology) on the outcomes of elderly stroke patients were studied by Kaste, Palomaki, and Sarna (1995). A total of 243 elderly stroke patients were the subjects of this randomized trial. Patients were randomized to receive care in the Department of Medicine or the Department of Neurology at a large university teaching hospital. The length of hospital stay was noted to be significantly different among those patients younger than 75 years of age ($p = .02$) who were managed by the department of neurology. The functional outcome was better for those randomized to the neurological ward as evidenced by Barthel Index and Rankin grades at 1 year ($p = .02$ and $p = .03$, respectively). While the study suggests that outcomes are clearly better when patients are managed on neurological wards, there is no discussion as to the specifics of that management that make a difference in these outcomes.

Ischemic Stroke--Outcomes

Costs

Considering the cost of healthcare, it is important to be knowledgeable about the predictors of cost with any given disease process. Knowledge about cost additionally provides a mechanism to assist care providers in making decisions about care with relation to old therapies and new therapies. Stroke is a major cause of disability and death. Preventive interventions and treatments have been offered to those who are at risk and those who have suffered stroke. However, these interventions must be demonstrated to provide value. To this end, research studies have been conducted which have analyzed outcomes related to ischemic stroke care with relation to cost, readmissions, and mortality.

As the third leading cause of death and disability, stroke contributes a great deal of cost to the healthcare budget. The aggregate cost of stroke in the United States is more than $40 billion per year, with cost per case estimated at $50,000 (Manzella & Galante, 2000). The evaluation of healthcare costs as an outcome is limited regarding the research related to ischemic stroke. While many studies address the cost-effectiveness of stroke initiatives, few investigate predictors of acute hospital costs particularly in the United States.

Diringer et al. (1999) sought to determine predictors of acute hospital costs in patients with ischemic stroke. This prospective study focused on ischemic stroke patients admitted to an academic medical center. A total of 191 patients was selected for the study having demographic and clinical data collected on them as they were admitted to the hospital. A step-wise multiple regression was conducted with the following variables: insurance status, premorbid modified Rankin scale, stroke location, stroke severity (NIH Stroke Scale), and presence of comorbidities. Cost was determined by converting hospital charge data to cost by application of department-specific cost-to-charge ratios. The median cost per discharge was $4,408 with a range of $1,199 to $59,799. Of these costs, it was determined that 50% were for room charges, 19% for stroke evaluation, 21% for medical management, and 7% for acute rehabilitation therapies. Length of stay accounted for the majority of the variance in cost at 43%. Other predictors of cost included the stroke severity, heparin treatment, atrial fibrillation, male sex, ischemic cardiac disease, and premorbid functional status.

In a study conducted in Denmark, Jorgensen, Nakayama, Raaschou, and Olsen (1997) analyzed social and medical factors that influenced length of hospital stay as evidence of cost. The authors used the Copenhagen Stroke Study data to determine the direct cost of stroke in the community-based population of the Stroke Study. There were 1,197 acute stroke patients included in the study. The care for these subjects was provided on a dedicated stroke unit. Using a multiple linear regression model, the influence of social and medical factors was analyzed with relation to length of hospital stay. Stroke severity was significantly correlated with length of hospital stay ($p < .0001$). Single marital status was also significantly correlated with length of hospital stay ($p = .02$). Age, sex, diabetes, hypertension, ischemic heart disease, atrial fibrillation, previous stroke, smoking, daily alcohol consumption, and type of stroke had no independent effect on length of hospital stay. The authors concluded that cost could only be decreased by reducing initial stroke severity.

In a more recent study, Caro, Huybrechts, and Kelley (2001) used patient characteristics as variables for predicting treatment costs after acute ischemic stroke. This multinational trial involved 1,341 ischemic stroke patients. Data were collected on a variety of neurological, functional, and cost parameters and analyzed by means of multiple linear regression. The focus of this analysis was to obtain a model to predict costs. Major predictors of cost were stroke subtype, neurological impairment, congestive heart failure, and country. The strongest predictor of cost was the Barthel Index. The researchers reported a good model fit (model $\underline{F} = 84$, 3 $\underline{df}$, $\underline{p} < .0001$). Consistent with the findings reported in the above study, these results indicate that reducing stroke severity would have the strongest impact on decreasing stroke costs.

As research indicates, reducing stroke severity appears to be a potentially significant approach to improving patient outcomes and decreasing costs. To this end, one study evaluated the role of thrombolysis in reducing acute stroke costs. As a new treatment option for ischemic stroke patients, the impact of this intervention on cost must surely be considered. It is well known that treatment with rt-PA improves outcomes at 3 months. Wein, Hickenbottom, and Alexandrov (1998) took this finding a step further by evaluating the impact of rt-PA on costs. When the National Institute of Neurological Disease and Stroke study results were examined using a Markov model, savings of $4 to $5 million per 1,000 patients treated were projected. These savings are projected at 1996 values. The model savings were predicated on decreased length of stay, decreased inpatient rehabilitation and nursing home costs, and increases in the number of patients discharged directly to home. In conclusion, the authors stated that increased rt-PA use would positively impact the cost outcomes associated with ischemic stroke.

Readmissions

The appropriate identification and treatment of individuals who present with ischemic stroke is strongly related to the outcomes these individuals experience. One indirect indication of quality of care and outcomes is the readmission occurrence that any given patient might experience. As evidence of this expectation, Medicare will not pay claims for patients readmitted to the hospital within 30 days of a hospital admission. No research has addressed the readmissions that occur among stroke populations. Stroke recurrence has been evaluated to some degree, but research involving readmission as an outcome of interest related to adequacy of medical management of ischemic stroke patients could not be located.

Mortality

Unlike readmission outcomes, several clinical trials have been conducted that evaluate a variety of variables that impact ischemic stroke mortality. Henon et al. (1995) conducted a study that evaluated which variables, of those easily discernable during the first 24 hours after stroke, would predict 8-day mortality rate and 3-month clinical outcome as measured by the Glasgow Outcome Scale. A stepwise logistic regression analysis was used to determine the predictive ability of the following: age, sex, body mass index, atrial fibrillation, previous stroke, existence of headache, Orgogozo score, level of consciousness, swallowing disturbances, hemianopia, pulse rate, mean blood pressure, hematocrit, glycemia, and computed tomographic scan data as they relate to the above mentioned outcomes. The only predictor identified for the 8-day mortality rate was the level of consciousness on admission ($p = .0001$). Death outcome at 3 months and low Glascow Outcome Scales were dependent on severity of clinical deficits ($p = .0001$), previous stroke ($p = .0018$), and age ($p = .0237$). The researchers concluded that these variables be taken into consideration as further research is designed to assess the impact of interventions on stroke outcomes. Few interventions will alter clinical deficits, previous stroke, or age; thus, randomization should include an equal distribution of these characteristics within study populations.

Over a decade ago, Bamford, Dennis, Sandercock, Burn, and Warlow (1990) conducted a prospective analysis of 675 consecutive patients with first-ever stroke. Subjects were analyzed within the first 30 days after stroke with either computed tomography (CT) and/or necropsy examinations for stroke pathology and the incidence of mortality. The case fatality rate (CFR) for the total sample was 19%. Cerebral infarction was associated with a 10% CFR, and subarachnoid hemorrhage with a 45% CFR. The CFR for patients who had been functionally dependent was higher than in those patients who had been functionally independent (33% vs. 17%, respectively). Age was significantly correlated with increasing CFR (chi-square for trend = 4.0, $p < .05$).

The effects of the department care (medicine vs. neurology) on the outcomes for elderly stroke patients were studied by Kaste, Palomaki, and Sarna (1995). A total of 243 elderly stroke patients were the subjects of this randomized trial assessing mortality, length of hospital stay, ability to live at home on discharge, Barthel Index, and Rankin grades at 1 year. Patients were randomized to receive care in the Department of Medicine or the Department of Neurology at a large university teaching hospital. The length of hospital stay was noted to be significantly different among those patients younger than 75 years of age ($p = .02$) who were managed by the department of neurology. There were no differences in mortality between patients treated by the department of medicine or neurology. The 1-year mortality rate was 21% for both services. Functional status was significantly influenced by department of neurology management ($p = .02$).

In a more recent study, Baptista et al. (1999) set out to study in-hospital mortality after first-ever stroke and to determine predictors of mortality. Subjects included

3,362 consecutive patients, both ischemic and hemorrhagic stroke, from the Lausanne Stroke Registry. Overall mortality was reported at 4.8%. Hemorrhagic stroke proved to be more fatal than ischemic stroke at 14.4% and 17.5%, respectively. Interestingly, age was not a significant predictor of stroke mortality. Consistent with other studies, these researchers found level of consciousness on admission as a significant predictor of mortality for ischemic stroke. In addition, using multivariate analysis, limb weakness, left ventricular hypertrophy, past history of cardiac arrhythmia, and previous TIA also were good predictors of ischemic stroke mortality. A variety of studies has been conducted to evaluate predictors of stroke mortality. The significance of these studies lies in the use of this information in the design of future research studies.

Summary

The relationship between system characteristics, client characteristics, and interventions as they influence stroke outcomes is very complex. The literature suggests that differences may exist in the clinical evaluation and treatment between men and women presenting with ischemic stroke. Therapies for acute stroke have changed, and with that there is increased expectation for better recovery and positive outcomes. The literature suggests that much of the challenge to improve outcomes lies in the preventive aspects of care that may alter the client characteristics that influence outcomes. Age is one of the major factors that negatively influences the outcomes associated with ischemic stroke. Multiple studies have demonstrated that uncontrolled hypertension, cigarette smoking, alcohol consumption, and hormone therapy are risk factors that contribute in various ways to ischemic stroke occurrence. The importance of gender in predicting outcomes after stroke is less clear. Some studies have shown that male sex is associated with a poorer outcome, while other studies have shown no difference. Estrogen plays a preventive role for some cases of stroke occurrence and has been attributed as a risk factor in others.

It appears to be well understood that there are differences in occurrences and outcomes among various races and ethnic groups. In spite of the ethnic differences, little has been identified regarding differences in outcomes among these groups. Outcome research is difficult to accomplish due to the complexity of measuring outcomes. As expertise increases the likelihood of more data in the area of ethnicity outcomes is expected.

The literature suggests that interventions to treat atrial fibrillation as an identifiable direct cause of ischemic stroke must be in place to influence positive outcomes. Patients who suffer ischemic stroke as a result of atrial fibrillation are more likely to suffer more disability and higher mortality. The examination of the literature indicates that this population is undertreated or inappropriately managed.

The literature also suggests that surgical, radiological, and pharmacological treatments offer promise for the ischemic stroke population. CT and MRI may best be used to predict outcome in the acute phase of stroke. Carotid endarterectomy is controversial with regard to efficacy in the prevention of stroke for all patients with stenosis of the coronary arteries. Thrombolytics and antiplatelet medications offer a new approach to the management and control of brain injury in the presence of ischemic stroke. An examination of the literature suggests that preventive medications may not be being used to their full potential among appropriate candidates. In addition, knowledge about the predictive nature of their use in relation to outcomes is in the infant stages of development.

Finally, ischemic stroke is a pervasive disease that has many factors that appear to influence outcomes. Many variables have been identified as having some predictive ability with respect to cost and mortality outcomes. The challenge rests in the ability to understand how the combination of these client characteristics, systems characteristics and interventions interact and influence ischemic stroke outcomes. The ability to understand differences in care that may exist as well as the variables that predict outcomes will create further understanding of ischemic stroke and, ultimately, influence the way that care is provided.

CHAPTER III

PROCEDURE FOR COLLECTION AND TREATMENT OF DATA

This study was a descriptive, comparative, retrospective design which examined the predictors of outcomes related to ischemic stroke patients. Retrospective designs are used when the researcher observes the presentation of some phenomenon and tries to retrospectively identify its causes or antecedents (Polit & Hungler, 1991). Comparative studies utilize a group of subjects whose presentation of a dependent variable is used to evaluate the presentation of that variable in another group of primary interest (Polit & Hungler, 1991). This design was selected to explore predictive relationships between antecedent and outcome variables. This study was a descriptive study in which variables were explored without deliberate manipulation or control. The purpose of this study was to determine if differences exist in system characteristics, client characteristics, and interventions as they influence stroke outcomes to determine differences with a particular interest in gender implications.

Setting

The setting for this study was a non-profit acute care community hospital in an urban location in the southern part of the U.S. This hospital was classified as +500 beds and provides a variety of services that support neurology, cardiac, orthopedic, trauma, and women and infant's service lines. The community served by this hospital consisted of people from a variety of ethnic backgrounds with the following breakdown: white (60%), African-American (20%), Hispanic (19%), and Asian (1%). The service area for the hospital is derived from 20 surrounding counties that are both urban and rural. Over 2 million people live in the immediate service area.

Population and Sample

The population for this study was the group from which the sample was drawn and to which inferences are made following the analysis of the data (Tabachnick & Fidell, 1989). The target population for this study consisted of ischemic stroke patients who received their inpatient stroke care and treatment from services and physicians using the target hospital from January 1999 through December 2000.

The sample for this study was acquired from the Stroke Database of the hospital. The sample consisted of all ischemic stroke patients as designated by ICD-9 codes:

433--Precerebral Occlusion, 434--Cerebral Artery Occlusion, and 436--Cerebral Vascular Accident. This large administrative database was established to track multiple variables of interest within the stroke population seen at the target hospital facility. The database had information on over 90 variables reflective of patients with ischemic stroke ICD-9 codes admitted to the hospital over the period from 1997 to 2000. The sample was reflective of the entirety of stroke patients seen at this facility over a period of 2 years and consisted of approximately 2,200 patients. Those subjects available in the Stroke Database dictated the number of subjects for the designated 2-year period. The sample selected from the larger database consisted of those patients who had an ischemic stroke ICD-9 code (433, 434, 436) and who were categorized as inpatients. Individuals were excluded from the database if there was missing data in the selected variables of interest. The years 1999 and 2000 were selected because these were the first two complete years where the APR-DRG data were complete. The APR-DRG designations were not added to the coding process until the middle of 1998. The database did not have complete data for the 1998 year at the time of this research.

Protection of Human Subjects

Permission to conduct this research study was obtained from the Institutional Review Board for Human Protection of the Medical Center of interest (see Appendix B), and from the Human Subjects Review Committee at Texas Woman's University (see Appendix B). Because unique identifiers having been assigned by the Stroke Database manager, identities of patients composing the database were not discernable for individual patients. Patient's information was traceable to a specific patient's medical record only through the database administrator. As a result, there was limited risk to human subjects. Access to additional patient information, if needed, was to occur through request to the database administrator using the unique patient identifier. However, no additional access to data was needed. In an effort to protect the subjects and the content of this database, all data were secured in locked files and on a computer accessible only to the researcher. All data were reported as aggregates to protect individual patient information. Written permission to access the data from the database was obtained from the target hospital.

Instrument

This study used the Stroke Database, which was a large, comprehensive database begun in 1997 and contained information from medical, pharmacy, and financial records. Comprehensive data were tracked on approximately 90 variables of interest related to the care and treatment of stroke patients. All inpatients receiving stroke care at the hospital beginning in 1997 were included in this database. Variable types fell under the following major content areas: demographic information, cost information, interventions, drugs, diagnosis, Diagnosis Related Groups (DRGs), type of physicians, discharge, and resource utilization. The collective data composing the Stroke Database were derived from data housed in a variety of other databases. For example, the cost data reported in this database were extracted from the patient billing and cost system. Demographic/client characteristics were extracted from the medical record. Drug information was derived from the hospital pharmacy database and records. The Quality Department was responsible for the oversight of the collection and treatment of data. One database administrator had oversight for the integrity of the data with input from the Quality Department employees.

Data were gathered based on the outcomes and variables of interest that were identified and operationalized. Following the identification of the outcomes and variables of interest the best data source was identified by the researcher based on information from the scientific literature and theory. To promote systematic data collection a secondary source was selected and the variables/data were selected for extraction. Additional data regarding the use of aspirin, coumadin, and TPA were pulled from the pharmacy system and added to the current larger Stroke Database. The selected data were then processed using relational data that were merged into Access by patient account numbers. After the data were merged into one database, the database administrator exported the data (over 90 variables) to the analytic tool (SPSS, 1999). The data were gathered electronically based on filters identified by the researcher. Validation and analysis then occurred. Analysis occurred through the statistical processes including multivariate analysis of covariance (MANCOVA), chi-square, multiple regression, and logistic regression. Reports of the findings were then generated. An illustration of the process is depicted in Figure 3. Appendix C demonstrates an example of data and variables that were available within the Stroke Database.

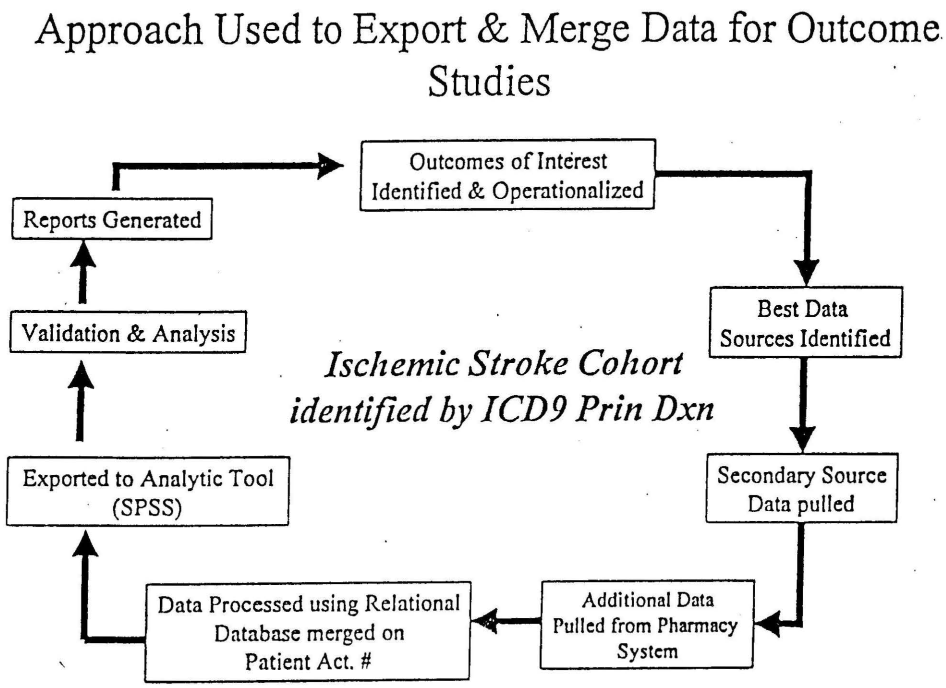

Figure 3. Data Mining Model for secondary data analysis.

Data Collection

Data were extracted from the Stroke Database. The data reflected information extracted from medical records, pharmacy records, and financial data related to each patient. Pharmacists and pharmacy technicians input the pharmacy specific data into the pharmacy system. Accounting personnel were responsible for data entered into the financial management system. Medical record data were entered by professional coders according to a standardized language and entry template, which ensured reliability and accuracy of data. The coders had multiple levels of training and education that were required prior to functioning in their role. All data input into these three systems was done by employees of the hospital.

The Stroke Database was a compilation of stroke specific data that were derived from each of these three databases. Data selected from these three databases were combined in the Stroke Database to reflect the areas of common interest surrounding stroke care that had been identified by physicians, nurses, and quality management personnel. Two physicians and a clinical nurse specialist had responsibility and oversight for the data selection process and two data analysts were responsible for importing data into the database. Data were selected and extracted from the database by the database administrator. After the identified variables had been selected from the database, they were analyzed in SPSS using MANCOVA, multiple regression, and logistic regression as dictated by the research questions. The variables of interest included: total cost, Carotid Doppler Studies, aspirin use, coumadin use, activase/TPA use, surgical cost--endarterectomy, nursing cost, discharge disposition, race, gender, Emergency Department (ED) stay, first care unit, length of stay (LOS), attending physician specialty, neurologist consult, total cost, inpatient readmission within 30 days, APR-DRG risk of mortality, APR-DRG severity of illness, and mortality.

Treatment of Data

The researcher compiled data from the Stoke Database of the hospital of interest. Data selected from two consecutive calendar years, January 1999 through December 2000, were used as the source of data for this study. There were 867 ischemic stroke patients in the sample.

Exploratory data analysis was used to evaluate the data for distribution, homogeneity, and normality. Race, gender, mortality, principle diagnosis, attending physician type, 30-day mortality, longest level of care unit, and type of stroke diagnosis were nominal level data and were analyzed using frequencies and percentages. Age was ratio level data and was analyzed using means and standard deviations. The demographic data were summarized using frequency distributions and percentages to assist the researcher in describing the sample. Descriptive statistics were used to assist the investigator in describing and researching the data. The normality of the data was explored using the Kolmogorov-Smirnov statistic with a Lilliofors significance level prior to statistical manipulation of the data (SPSS, 1999).

Research Question One

The first research question for this study was: Is there a difference in the interventions (nursing cost), client characteristics (age), and outcomes (total cost, length of stay) among men and women with ischemic stroke who were admitted to a large community hospital over a 2-year period?

Statistical Packages for the Social Sciences (SPSS, 1999) was used to compute the exploratory as well as the statistical analysis suggested by this question. A multivariate analysis of covariance (MANCOVA) was performed to determine if there was an overall significant difference between the genders. A MANCOVA will decrease the error associated with multiple variables of interest as well as perform separate univariate tests to determine which variables show significant differences. This was an appropriate test to use because it will evaluate the differences among men and women when there are two or more levels of an independent variable and covariate (Tabachnick & Fidell, 1989). MANCOVA was used to determine if there was a significant difference between men and women with the following variables: age, length of stay, nursing cost, and total costs. A filtering program was used to look at subgroups based on APR-DRG Mortality Risk and APR-DRG Severity of Illness in an effort to further characterize the degree of difference among groups within gender.

Research Question Two

The second research question was: Are the specific system characteristics (neurological consultation, emergency department stay, first care unit, attending physician specialty), interventions (coumadin, aspirin, and activase/TPA, Carotid Doppler Study, endarterectomy), and outcomes (mortality, 30-day readmission, and discharge disposition) independent of gender?

Chi-square was used to describe frequencies for categorical data. Chi-square is appropriate for statistical analysis when variables are measured at the nominal or categorical level. It is useful with groups and compares the actual numbers in each group with the expected number in each group (Munro, 1997). A chi-square test was used to determine the independence between the dichotomous variables (Porter & Hamm, 1986). The chi-square was used to determine whether mortality is independent of gender. In addition, each dichotomous variable listed above was independently compared to gender with the chi-square statistical test. While a significant difference cannot be determined between the genders with dichotomous variables, the chi-square test allows for one to determine dependence or independence (Porter & Hamm, 1986).

Research Question Three

The third research question was: What are the primary predictors (system characteristics, interventions, client characteristics) of ischemic stroke outcomes in a large community hospital over a 2-year period?

Multiple regression and logistic regression were used to answer this study question. Initially, multiple regression was used to determine predictors for continuous outcome variables (length of stay and total costs). Multiple regression was used to define variables that are the best predictors for each of the continuous outcome variables. Multiple regression is a technique used to answer research questions focused on being able to predict one continuous variable by using two or more continuous variables (Tabachnick & Fidell, 1989). Multicollinearity was evaluated via correlations prior to data analysis through multiple regression and logistic regression.

Logistic regression was utilized to determine predictors for outcome variables that were dichotomous in nature (LOS and 30-day readmission). Logistic regression is a technique that has been used to answer research questions about relative risks or odds of whether an event will or will not occur, based on known explanatory variables (SPSS, 1999). This technique was appropriate for use with this question because it requires that the dependent variable be binary or dichotomous with the independent variables remaining either continuous or categorical. The dependent variables in this study that were dichotomous in nature were mortality and readmission within 30-days. In logistic regression, the independent variables may be at any level of measurement from nominal to ratio. Logistic regression is particularly useful for outcome research because it allows for the dependent variable to be dichotomous (Munro, 1997).

Additionally, the results in logistic regression include odd ratios, which provide more information from which to interpret the data. The odds ratio is useful because it helps to identify how much more likely or unlikely it is for an outcome to be present in any given condition (Munro, 1997). Additionally, multiple regression and logistic regression were used to find the best-fitting model for the predictor variables. Multiple and logistic regression analyze the relationship between multiple independent variables and a single independent variable, yielding information about the predictive ability of a given model. While normal distribution of the data was a concern in the multiple regression data analysis, the sample size was quite large and, thus, this concern was allayed by the central limit theorem. For large samples, it is expected that normality will make little difference on the analysis due to the central limit theorem (Porter & Hamm, 1986).

Summary

This chapter has presented a description of the (a) methods and design, (b) setting for data collection, (c) population and sample description, (d) instrumentation, (e) data collection, and (f) treatment of the data. As a descriptive, comparative, retrospective study, the goal of this research was to provide insight into the predictive relationships between antecedent and outcome variables with an emphasis on gender differences that may or may not exist. Descriptive and inferential statistical analyses were used to determine if there was any predictive relationship between the variables of interest.

CHAPTER IV

ANALYSIS OF DATA

The purpose of this research was to utilize an administrative database to examine differences in system characteristics, client characteristics, and interventions as they influence identified stroke outcomes. Additionally, the study explored differences that exist in clinical evaluation and treatment between men and women presenting with ischemic stroke. Specifically, it was theorized that there was a difference in system characteristics, interventions, client characteristics, and outcomes about men and women with ischemic stroke who were admitted to a large hospital over a 2-year period. It was further hypothesized that there would be differences in system characteristics, interventions, and outcomes independent of gender. Finally, the study explored whether attending medicine specialty, ED patient status, first level of care, neurology consult, nursing costs, coumadin, aspirin and TPA therapy, endarterectomy, Carotid Doppler Studies, APR mortality, APR severity, age, race, and gender were associated with outcomes and whether these variables would predict outcomes.

This chapter describes the findings of a multiple analysis of variance (MANCOVA), chi-square, multiple regression, and logistic regression analysis of the data. The sample of this large administrative database will be described first. An account of data exploration will be presented, followed by an examination of the data based on the four statistical tests listed above, including a close look at the goodness-of-fit of the model as it describes the sample studied. Finally, descriptive data will be presented regarding the variables that may influence the outcomes associated with ischemic stroke and the gender implications.

Description of the Sample

The Stroke Database sample consisted of over 1,200 patients classified as stroke patients. The final sample consisted of 867 patients who were classified with ischemic stroke ICD-9 codes over the period from January 1999 through December of 2000. Data collection for the Stroke Database occurred in an ongoing basis as patients were discharged from the hospital. A total of 867 subjects were identified from the Stroke Database. Of this sample, 372 were men and 490 were women with 5 missing information as to gender. The average age of all subjects was 70.53 (SD = 13.34). The women who were included in the sample ranged from 25 to 100 years of age with a mean age of 72.48 (SD = 13.10). The men who were included in the sample ranged from 23 to 98 years of age with a mean age of 68.0 (SD = 13.27).

Many races were represented in the sample; however, the sample was predominantly Caucasian at 72.3%. African Americans were the next largest group represented in the sample at 19%. Hispanics represented 7.7% of the sample. Asians were represented in a very small percentage at 0.6%; and 0.5 % of the sample had unknown ethnic origins.

The severity of illness was distributed across the sample as follows: 48 women and 43 men were classified as having APR severity "1", 254 women and 297 men were classified as having APR severity "2", 130 women and 76 men were classified as having APR severity "3", and 56 women and 43 men were classified as having APR severity "4". Internal Medicine Specialists, as primary physicians, were the predominant care providers at 90%. Only 1% of the sample had neurologists consulting on their cases. Most of the patients (87.2%) entered the hospital facility through the ED and were primarily admitted to medical surgical units as the first care unit (67.5%).

In terms of pharmacologic interventions, only 2.7% received activase (TPA), 52.5% received aspirin therapy, and 24.8% received coumadin therapy. Carotid Doppler Study, as a radiologic intervention, was used in 69.6% of the sample. Endarterectomy procedures were performed on 1.6% of the sample. Thirty-day readmission occurred for 5.7% of the sample. Overall mortality was 7.5%. Summary statistics for the demographics information are presented in Table 1. Other demographic information such as level of education, income, and marital status was not available in the Stroke Database.

Table 1

<u>Demographic Data for Ischemic Stroke Patients in 1999 to 2000 Stroke Database</u>

Data	Total Number (N = 867)	Percentage
Gender:		
Female	490	56.8
Male	372	43.2
Missing data	5	.6
Age in Years:		
< 18	0	0.0
19-45	49	5.7
45-59	124	14.3
60-74	306	35.3
> = 75	388	44.8
Missing data	0	0.0
Race:		
Caucasian	623	72.5
African American	164	19.0
Hispanic/Latin	66	7.7
Asian/Pacific Islander	5	.6
Unknown	4	.5

Table 1 (continued)

Data	Total Number (N = 867)	Percentage
APR Severity:		
<u>APR severity "1"</u>		
Female	48	9.8
Male	43	11.7
<u>APR severity "2"</u>		
Female	254	52
Male	207	56
<u>APR severity "3"</u>		
Female	130	26.6
Male	76	20.6
<u>APR severity "4"</u>		
Female	56	11.5
Male	43	11.7
Attending Physician:		
Internal Medicine	781	90
General Surgery	23	2.6
Otolaryngology	1	.1
Family Practice	40	4.6
Neurosurgery	2	.2
Cardiology	21	2.4
Activase/TPA:		
Activase charge	23	2.7
No charge	844	97.3
Aspirin:		
Aspirin charge	455	52.5
No charge	412	47.5

Table 1 (continued)

Data	Total Number (N = 867)	Percentage
Coumadin:		
Coumadin charge	215	24.8
No charge	652	75.2
Readmission:		
None	805	94.3
Readmission within 30 days	49	5.7
Missing data	13	--
Mortality:		
Lived	802	92.5
Expired	65	7.5

Findings

All analyses were performed using the Statistical Package for Social Sciences, Version 9.0 (SPSS, 1999). Initial data exploration was conducted to determine if there was a difference in severity of illness between men and women. A chi-square analysis of APR severity by gender was conducted. In comparison of the four levels of severity indicated by the APR severity variable, the computed chi-square was not significant (X^2 4.492, $df = 3$, $p = .213$) indicating no difference between men and women regarding the severity of their conditions across APR severity upon admission. The cross tabulation chart for the severity of illness by gender is found in Table 2. Data analysis proceeded without further need to filter or control for differences between male and female groups.

Table 2

Cross-tabulation of Relationship between Gender and APR Severity of Illness

	Female 1	Male 2	Total
APR severity "1"			
Count	48	43	91
Expected count	51.8	39.2	91.0
% within gender	9.8%	11.7%	10.6%
Total %	5.6%	5.0%	10.6%
APR severity "2"			
Count	254	207	461
Expected count	262.5	198.5	461.0
% within gender	52.0%	56.1%	53.8%
Total %	29.6%	24.2%	53.8%
APR severity "3"			
Count	130	76	206
Expected count	117.3	88.7	206.0
% within gender	26.6%	20.6%	24.0%
Total %	15.2%	8.9%	24.0%
APR severity "4"			
Count	56	43	99
Expected count	56.4	42.6	99.0
% within gender	11.5%	11.7%	11.6%
Total %	6.5%	5.0%	11.6%
Total			
Count	488	369	857
Expected count	488.0	369.0	857.0
% within gender	100.0%	100.0%	100.0%
Total %	56.9%	43.1%	100.0%

Research Question One

Research question one stated: Is there a difference in the interventions (nursing cost), client characteristics (age), and outcomes (total cost, length of stay) among men and women with ischemic stroke who were admitted to a large community hospital over a 2-year period? MANCOVA was used to determine differences between gender for the following continuous variables: nursing cost, age, length of stay, and total cost as representations of interventions, client characteristics, and outcomes as indicated by the conceptual framework. As a point of interest, all variables were analyzed for normality with Kolmogorov-Smironov test of normality (see Table 3). The results indicated that none of the variables were distributed normally; however, this finding would not affect the MANCOVA, as this is not an assumption for this statistical test.

While the sample for this study is identified as a large sample size in which the central limit theorem applies, analysis of the assumptions for MANCOVA was conducted to more fully understand the type and quality of the data. In an effort to evaluate data for compliance with the assumptions for MANCOVA, the following statistical analysis was conducted: The Box's Test of Equality of Covariance Matrices and the Levene's Test of Equality. To determine if errors were distributed normally, the Levene's

Table 3

Tests of Normality

	Kolmogorov-Smirnov Statistic	df	Sig.
Admission age	.101	828	.000
LOS hrs.	.145	828	.000
Total cost	.193	828	.000
Nursing department standard total cost	.177	828	.000

Test of Equality was used. The Levene's Test of Equality (see Table 4) was met for total cost (p = .793). Admission age did not pass this assumption (p = .048).

Table 4

Levene's Test of Equality of Error Variances

	F	df 1	df 2	Sig.
Admission age	3.935	1	855	.048
Total cost	.069	1	955	.793

Further analysis was necessary to determine if there was equal error variance across groups. While some error is unavoidable, the next best thing is to ensure that it is equally distributed across all measurements and to control for variance if at all possible. Smaller error variance provides a more powerful test of mean differences among groups (Tabachnick & Fidell, 1989). The Box's Test of Equality of Covariance Matrices demonstrated that observed covariance matrices of the dependent variable are equal across groups ($\underline{F}$ = .089, $\underline{df}$ = 3, $\underline{p}$ = .966). This test is used to test the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups. Residual error variances demonstrates that errors are independent of each other and distributed normally which is evident by the residual matrices. Not all of the groups had normal distributions. However, the central limit theorem applies due to the sample size, and therefore this assumption should have little effect on the results. For large samples it is expected that normality will make very little differences on the analysis due to the central limit theorem (Porter & Hamm, 1986).

A bivariate correlation was conducted on the four variables of interest; nursing cost, age, total cost, and length of stay (LOS). The Spearman's Rho calculation (see Table 5) demonstrated that nursing cost and total cost are strongly correlated at .857 and LOS and total cost are strongly correlated at .840. Additionally, LOS and nursing cost were strongly correlated at .822. Age and total cost were not correlated. Likewise, there was no correlation noted between LOS and admission age. The Spearman's Rho calculation did identify several correlation issues between the variables of interest. Therefore, to avoid multi-collinearity issues, the researcher determined that total cost and age would be utilized for the MANCOVA. The Wilks' Lambda demonstrated an overall statistically significant difference between genders (F = 8.198, df = 3, p = .000). Furthermore, the analysis of variance demonstrated statistically significant differences between males and females for mean total costs and mean admission age (p = .033, p = .000, respectively). LOS did not demonstrate significant differences between gender. There was a statistically significant difference in total cost and age between men and women. There was no difference in LOS between men and women.

Table 5

Spearman's Rho Correlation Matrix for Predictor and Outcome Variables for Ischemic Stroke

	Admission Age	LOS Hours	Total Cost	Nursing Cost
Admission age	1.000	.06	-.045	-.024
LOS hours	--	1.000	.840	.822
Total cost	--	--	1.000	.857
Nursing cost	--	--	--	1.000

Research Question Two

Research question two stated: Are the specific system characteristics (neurological consultation, emergency department stay, first care unit, attending physician specialty), interventions (coumadin, aspirin, activase [TPA], Carotid Doppler Study, endarterectomy), and outcomes (mortality, 30-day readmission, and discharge disposition) independent of gender? This research question was analyzed with cross-tabulations and chi-square analysis. The cross-tabulations are useful for examining the association between variables. Chi-square calculates the expected frequency for each cell and compares it to the actually observed frequencies (Porter & Hamm, 1986).

The cross-tabulations and chi-square reported in Table 6 show the relationships between system characteristics and gender. Neurology consultation demonstrated statistical significance between genders. The chi-square value is 7.729 ($p = .005$). Significantly more men than women had neurology consultations. Statistical significance was further supported by the Fisher's exact test which showed significance ($p = .007$). This test is an alternative to Pearson's chi-square for the 2 x 2 table. It assumes that the marginal counts remain fixed at the observed values and calculates exact probabilities of obtaining the observed results if the two variables are independent (Munro, 1997).

The Fischer's exact test is considered to be more appropriate than the Pearson's chi-square. Attending physician specialty was determined to be statistically significant as well. However, these findings should be accepted with caution as four cells (33.3%) had an expected frequency less than 5. This breaches one of the basic assumptions for chi-square analysis which states that if there are more than two cells, no more than 20% of the cells can have expected frequencies smaller than 5 (Porter & Hamm, 1986). Emergency Department patient status and first care unit did not demonstrate statistical significance.

Table 6

System Characteristics Relationships to Gender as Defined by Chi-square Analysis

Variable	Gender	Chi-square	*df*	Sig.
Neurology Consult	Male *n* = 8 Female *n* = 1	7.729	1	.005
ED Patient	Male *n* = 318 Female *n* = 435	2.361	1	.124
First Care Unit:		1.856(a)	3	.603
ICU	Male *n* = 38 Female *n* = 46			
Step-down Unit	Male *n* = 89 Female *n* = 100			
Medical-Surgical Unit	Male *n* = 243 Female *n* = 340			

Table 6 (continued)

Variable	Gender	Chi-square	df	Sig.
Other Care Unit	Male n = 3 Female n = 4			
Attending Physician Specialty:		15.495(b)	5	.008
Internal Medicine	Male n = 323 Female n = 453			
General Surgery	Male n = 15 Female n = 8			
Otolaryngology	Male n = 0 Female n = 1			
Family Practice	Male n = 18 Female n = 22			
Neurosurgery	Male n = 1 Female n = 1			
Cardiology	Male n = 16 Female n = 5			

(a) Two cells (25%) had expected counts < 5; minimum expected count is 3.03.
(b) Four cells (33.3%) had expected counts < 5; minimum expected count is 0.43.

The cross-tabulations and chi-square reported in Table 7 show the relationships between interventions and gender. None of the pharmacologic interventions (coumadin, aspirin, or activase) were significantly different related to gender. It was, however, interesting to note the very small number of subjects receiving activase in this sample. Carotid Doppler Study and endarterectomy were statistically different with relation to gender (p = .003, p = .007, respectively) with males receiving both procedures at a higher percentage than females.

Table 7

Interventions Relationship to Gender as Defined by Chi-square Analysis

Variable	Gender	Chi-square	df	Sig.
Coumadin	Male n = 100 Female n = 113	.724	1	.395
Aspirin	Male n = 205 Female n = 248	.267	1	.605
Activase (TPA)	Male n = 10 Female n = 13	.001	1	.980
Carotid Doppler Study	Male n = 279 Female n = 321	8.624	1	.003
Endarterectomy	Male n = 11 Female n = 3	7.247	1	.007

The cross-tabulations and chi-square reported in Table 8 show the relationships between mortality and gender. Mortality was found to be statistically different between males and females ($p = .009$), with females demonstrating higher mortality than males. Discharge disposition was statistically significant between groups at $p = .000$. However, this finding must be taken with caution as six cells (33%) had an expected frequency less than 5. Thirty-day readmission was not significant. In summary, of the variables of interest neurology consult, attending physician specialty, Carotid Doppler Study, endarterectomy, mortality, and discharge disposition were all significantly different between genders.

Table 8

Outcomes Relationship to Gender as Defined by Chi-square Analysis

Variable	Gender	Chi-square	*df*	Sig.
Mortality	Male *n* = 18 Female *n* = 47	6.908	1	.009
30-day readmission	Male *n* = 26 Female *n* = 22	4.568(a)	3	.206
Discharge disposition		29.626(b)	8	.000
Home	Male *n* = 166 Female *n* = 155			
Short-term hospital Unit	Male *n* = 4 Female *n* = 5			
Skilled nursing unit	Male *n* = 44 Female *n* = 95			
Other type facility	Male *n* = 100 Female *n* = 131			
Home health	Male *n* = 37 Female *n* = 47			
AMA	Male *n* = 2 Female *n* = 0			
Expired surgery	Male *n* = 18 Female *n* = 47			
Hospice-medical facility	Male *n* = 2 Female *n* = 9			

Table 8 (continued)

Variable	Gender	Chi-square	*df*	Sig.
Home hospice	Male *n* = 0 Female *n* = 1			.

(a) Two cells (25%) had expected counts < 5; minimum expected count is 0.43.
(b) Six cells (33%) had expected counts < 5; minimum expected count is 0.43.

Research Question Three

Research question three stated: What are the primary predictors (system characteristics, interventions, and client characteristics) of ischemic stroke outcomes in a large community hospital over a 2-year period? Due to the combination of continuous and dichotomous variables in the stroke outcomes variable set, both multiple regression and logistic regression statistical testing were selected to test research question three. Multiple regression requires that outcome variables are continuous in nature (Porter & Hamm, 1986).

A scatterplot showed linearity between total costs and other predictor variables and LOS and other continuous predictor variables (see Appendix C). In addition, all variables were evaluated for multi-collinearity. There were no correlations among the independent variables. In further evaluating the data, another assumption in multiple regression requires that the residuals be distributed normally. In this data set, this assumption was not met. The central limit theorem assumes that even when error is not normally distributed, when sample size is large, the sampling distribution of the beta coefficient will still be normal. Therefore, violations of this assumption usually have little or no impact on substantive conclusions for large samples. However, when the sample size is small, tests of residual normality are important (Chass, 2001). The final assumption that must be considered when using multiple regression is that the errors are independent of each other. A scatterplot of the residuals was observed to determine if any patterns existed. No patterns were noted and, thus, the assumptions of independence of error were met.

A stepwise multiple regression for total cost was performed and found these significant variables: nursing cost, endarterectomy, APR severity "4", first care unit medical surgical, and attending physician specialty. Stepwise multiple regression was utilized to assess predictors for total cost. The significant predictors were nursing cost (p = .007), endarterectomy (p = .000), APR severity "4" (p = .000), first care unit medical surgical (p = .000), attending physician specialty--cardiology (p = .016), and neurologists consulting (p = .025). All Beta coefficients for these variables contributed to increased total cost. This model successfully predicted 86.5% of the variance for total cost.

A second stepwise multiple regression was done to determine predictors for LOS. The significant predictors were nursing cost (p = .000), first care unit medical surgical (p = .000), coumadin (p = .000), APR severity "4" (p = .000), APR risk of mortality "4" (p = .000), APR severity "3" (p = .008), first care unit ICU (p = .001), Caucasian (p = .001), APR risk of mortality "1" (p = .007), and endarterectomy (p = .020). The Beta coefficients for nursing cost, first care unit medical surgical, coumadin, APR severity "4", APR severity "3", and endarterectomy indicated a contribution to increased LOS. Conversely, the following variables contributed to decreased LOS: APR risk of mortality "4", first care unit ICU, Caucasian, and APR risk of mortality "1". This model successfully predicted 76.8% of the variance for LOS.

Logistic regression is a nonparametric multivariate technique for estimating the probability of an event based on a set of identified predictor variables. Logistic regression is the statistical test of choice for two of the outcome variables of interest in this question due to the dichotomous nature of these variables (mortality, 30-day readmission). Unlike multiple regression, which requires that the outcome variable be continuous in nature, logistic regression assumes nothing about the distribution of the predictor variables, and requires that the outcome variable be dichotomous (Tabachnick & Fidell, 1996). Logistic regression estimates parameters by utilizing the maximum likelihood method and finds the best combination of predictors to maximize the likelihood of obtaining the observed outcome frequencies (Tabachnick & Fidell, 1996).

To test research question three, whether mortality is predicted by a model which contains the following variables: total cost, endarterectomy, neurologists consulting, nursing costs, activase charge, aspirin charge, coumadin charge, Carotid Doppler Study, emergency department stay, race, gender, age, first care unit, attending physician specialty, APR mortality, and APR severity, the enter method of logistic regression analysis was used. As presented in Table 9, the significant predictors of mortality included Carotid Doppler Study, LOS, APR mortality, nursing costs, aspirin, coumadin, and ED patient. Therefore, due to the absence of some of the variables as significant, it appears that the model only partially supports the occurrence of mortality in the ischemic stroke population sampled in this study.

Table 9

Logistic Regression Identified Predictors of Mortality

Variable	β	S.E.	df	Sig.	R	Lower 95% CI	Upper 95% CI
Carotid Doppler	- .9120	.3772	1	.0156	-.0947	.1918	.8415
LOS hours	- .0171	.0045	1	.0001	-.1724	.9744	.9916
Endarterectomy	-4.2911	20.5161	1	.8343	.0000	.0000	3.979
Total cost	- .0002	.0001	1	.2737	.0000	.9995	1.0001
Race ID			4	.3333	.0000	.0004	1.0339
Race ID (1)	-3.9091	2.0115	1	.0520	-.0643	.0004	1.0339
Race ID (3)	-4.5666	2.1439	1	.0332	-.0769	.0002	.6945
Race ID (4)	-9.0643	41.5190	1	.8272	.0000	.0000	2.538E+31
Gender(1)	.6476	.3781	1	.0868	.0466	.9107	4.0099
First level of care	--	--	3	.5461	.0000	--	--
First level of care ICU	5.5350	34.5667	1	.8730	.0000	.0000	6.702E+31
First level of care step down	6.4793	34.5667	1	.8513	.0000	.0000	1.726E+62
First level of care med/surg	6.2141	34.5633	1	.8573	.0000	.0000	1.315E+32
Attending physician spec.	--	--	4	.5056	.0000	--	--

Table 9 (continued)

Variable	β	S.E.	df	Sig.	R	Lower 95% CI	Upper 95% CI
Attending medicine attending	.3199	1.1866	1	.7875	.0000	.1345	14.0934
Family practice attending	-6.7622	18.1486	1	.7094	.0000	.0000	3.246E+12
General surgery attending	- .4453	1.4752	1	.7627	.0000	.0356	11.5420
Cardiology attending	2.8862	2.0853	1	.1663	.0000	.3009	1067.6903
Neurology consult	1.8138	1.2497	1	.1467	.0158	.5297	71.0276
APR severity	--	--	3	.6288	.0000	--	--
APR severity "1"	-1.1978	1.0871	1	.2705	.0000	.0358	2.54119
APR severity "2"	- .7988	.7400	1	.2804	.0000	.1055	1.9186
APR severity "3"	- .2891	.6714	1	.6667	.0000	.2009	2.7920
APR mortality	--	--	3	.0437	.0702	--	--
APR mortality "1"	-2.4846	.8788	1	.0047	-.1182	.0149	.4666
APR mortality "2"	-1.9031	.7727	1	.0138	-.0973	.0328	.6779
APR mortality "3"	-1.5745	.7698	1	.0408	-.0713	.0458	.9363
Nurse total	.0008	.0004	1	.0194	.0898	1.0001	1.0015
Activase	.9150	1.2132	1	.4507	.0000	.2316	26.9173
Aspirin	-1.6611	.4274	1	.0001	-.1748	.0822	.4389
Coumadin	-1.1896	.5244	1	.0233	-.0856	.1089	.8505
ED patient	-1.2921	.4530	1	.0043	-.1196	.1130	.6675

Table 9 (continued)

Variable	β	S.E.	df	Sig.	R	Lower 95% CI	Upper 95% CI
Age	.0075	.0557	1	.6299	.0000	.9771	1.0390
Constant	- .2813	34.6961	1	.9935	--	--	--

Partial correlations of each predictor variable with the outcome variable are depicted by the R statistic. Holding all variables equal, it is clear that as Carotid Doppler Studies, LOS hours, aspirin use, coumadin use, and emergency department stay decrease, the likelihood of dying increases. Additionally, in reverse, as APR mortality and nursing cost increase the likelihood of mortality increases.

Assessing the goodness-of-fit of the model is important to determine how well the model fits the sample data as well as the population (SPSS, 1999). Several ways were utilized to assess model fit. Table 10 depicts the classification table for mortality and presents the observed and predicted group memberships when cases with a predicted probability of 0.5 or greater are classified as expiring. It is evident that while 751 of the cases were correctly predicted to live, 8 of the cases were incorrectly predicted to live. Likewise, 42 subjects were incorrectly predicted to be expired and 18 were correctly predicted to expire. The logistic regression model appears to correctly predict the chances of living at a higher rate (98.95%) than it is to predict the likelihood of expiring (30%); thus, the overall prediction rate of the model was high at 93.89%.

Table 10

Predicted and Observed Classification Table for Mortality (Expired) vs. Lived

Observed	Predicted Lived	Predicted Expired	Percent Correct
Lived	751	9	98.95%
Expired	42	18	30.00%
		Overall	93.89%

The goodness-of-fit also was determined by examining the model with the constant only and comparing this model to a model with the constant and all of the predictor variables. Comparisons of both models result in the goodness-of-fit statistic (SPSS, 1999). This statistic is used to compare the observed probabilities to those predicted by the model. The model containing the predictor variables is significantly different (p = .0000), indicating that at least one variable in the logistic regression model is related to mortality (SPSS, 1999).

Model fit was also assessed by examining model discrimination and model calibration (SPSS, 1999). Model calibration is a test that examines how closely the observed and predicted probabilities match and is determined by conducting the Hosmer and Lemeshow Goodness-of-Fit chi-square test. The Logistic Regression Mortality Model predicts well at .7392, $p > .05$.

Research question three was further tested by exploring the likelihood that 30-day readmission is predicted by a model which contains the following variables: total costs, endarterectomy, neurology consult, nursing cost, activase charge, aspirin charge, coumadin charge, Carotid Doppler Study, ED stay, race, gender, age, first care unit, attending physician specialty, APR mortality, and APR severity. The entire method of logistic regression was used to analyze data. Only endarterectomy ($p = .0166$, OR 4.9889, 95% CI 1.3398 - 18.5775) met significance. No other variables were identified as contributing to the model. As mentioned, it is important to determine how well the model fits the sample data as well as the population. The sample for the readmission was very small and might yield more predictive value if a larger sample was obtained.

The classification table for 30-day readmission was used to assess model fit. This classification table presents the observed and predicted group membership when cases with a predicted probability of 0.5 or greater are classified as having a readmission within 30 days. There were 761 patients who were predicted to have no 30-day readmission, zero were predicted to be readmitted. Likewise, 44 were predicted to not have a readmission within 30 days and they were actually readmitted. The inconsistency of this finding indicates that the model does not do an adequate job of predicting 30-day readmission.

CHAPTER V

SUMMARY OF THE STUDY

This chapter presents a synopsis of the study and a discussion of the findings in relation to current literature on this topic and the related variables of interest. Conclusions based on the findings are discussed and implications for nursing practice and ischemic stroke patient care are presented. Recommendations for further studies based on the process and outcome of this research are made.

An administrative database was used to examine the differences in system characteristics, client characteristics, and interventions as they influenced stroke outcomes including mortality, total cost, length of stay, and 30-day readmission. In addition, potential gender differences in clinical evaluation and treatment were evaluated. The final sample for the study consisted of 867 patients who were classified with ischemic stroke by ICD-9 codes over a period from January 1999 through December of 2000.

The following data were collected from the Stroke Database: age, gender, race, APR severity of illness, APR risk of mortality, attending physician specialty, Emergency Department (ED) stay, first care unit, neurology consultation, total nursing cost, coumadin charge, aspirin charge, activase/TPA charge, Carotid Doppler Study, endarterectomy, length of stay (LOS), discharge disposition, total cost, and 30-day inpatient readmission. Following identification of the variables and receiving the data of interest from the database administrator, the data were prepped, analyzed, and extracted from the Stroke Database. Demographic data were summarized into frequency distributions and percentages in order to describe the sample. Tests of normality were conducted with each research question as indicated by the assumptions of each statistical test. The following statistical tests were utilized to analyze the data specific to each research question: multivariate analysis of covariance (MANCOVA) was used for question one, chi-square was used for question two, and multiple regression and logistic regression were used for research question three.

An examination of the Health Outcomes Model, designed to explain the relationships between client characteristics, system characteristics, interventions, and outcomes (Mitchell et al., 1998) was used as the conceptual framework for this study. From this conceptual framework, the Ischemic Stroke Quality Health Outcomes Model emerged as a basis for this study. The model stipulates that system characteristics, interventions, and client characteristics influence health outcomes. A logistic regression analysis computed an equation containing the variables that indicated the best model for prediction of mortality and LOS as indicators of outcome. It was found that of the variables of interest, Carotid Doppler Studies, aspirin, coumadin, emergency department stay, LOS, APR mortality, and nursing cost were predictors of mortality. In addition, the goodness-of-fit examination supported this model as adequate for predicting mortality.

Discussion of Findings

Research Question 1

The MANCOVA analysis demonstrated statistically significant differences between males and females for total costs and mean admission age while controlling for APR severity as a covariate. The correlation matrix of the variables of interest between groups; nursing costs, LOS, age and total cost demonstrated multicollinearity between nursing cost, LOS, and total cost. This finding is consistent with the work of Diringer et al. (1999), who reported that 50% of cost was due to room charge/nursing care, and LOS accounted for 43% of the variance in cost. Therefore, nursing cost and LOS were removed from the

MANCOVA as it was determined these variables were reflected in the total cost variable. Data analysis continued with total cost, age, and gender.

There was no demonstrated difference between genders with regard to LOS. The ANOVA demonstrated that age and total cost were the variables that contributed to the overall difference between males and females. The mean cost for males was $6,541.35 and the mean cost for females was $5,825.12. Diringer et al. (1999) reported a mean cost of stroke care per discharge at $4,408.00. The mean admission age for females (m = 72, SD 13.10) was higher than males (m = 68, SD 13.27), respectively. The total cost difference supports the idea that women may receive less care and interventions, if total cost is a measure of care and interventions.

It is widely known that differences exist between men and women with respect to evaluation and treatment of coronary heart disease (Bergelson & Tommaso, 1995). While studies have focused on the prevalence and severity of stroke between genders, none specifically investigated gender differences in total cost as a variable; nevertheless, many (Mitchell et al., 1996; Ramani et al., 2000) have studied treatments as a reflection of total cost. Ramani et al. reported that women are less likely than men to have a carotid endarterectomy both before and after stroke. An empirical generalization might be made that endarterectomy use between genders contributes to total cost differences in genders. Endarterectomy as a specific variable is evaluated in research question two.

There was a statistically significant difference in age among male and female ischemic stroke patients. This finding supports the Whisnant et al. (1996) study that found the odds of stroke were higher for older women. The women in this study were older with a mean age of 72 (SD = 13.10) compared to a mean age of 68 (SD = 13.27) for men.

Research Question 2

A number of variables were statistically tested for independence from gender. Each variable of interest will be discussed in the following paragraphs as it relates to the results of the chi-square analysis findings.

A difference was found between neurology consultation and gender. Males had more neurology consultations than females. While there are no studies that have identified differences between access to neurology consults and gender, many studies have indicated that stroke care managed by a neurologist contributes to improved outcomes (Gillum & Johnston, 2000; Horner et al., 1995; Mitchell et al., 1996). Of further concern is the limited amount of neurology consults for the stroke population as a whole in this population. Only 9 patients were identified as having a neurology consult out of the population of 863. This small number may indicate an under-utilization of neurologists or a problem with accuracy of data in this administrative database.

In investigation of ED stay and gender differences, the findings suggested that there was no difference. While many studies have researched placement of the ischemic stroke patient in the hospital with regard to ICU care versus medical surgical care, none have evaluated for any differences in ED visit. Both males and females with ischemic stroke appear to have equal exposure to ED stays associated with their stroke.

No statically significant difference was found between genders and first care unit or physician specialty. The majority of patients, both male and female, went to med-surg first followed by the next grouping of patients who went to the ICU area first. Stroke placement has been evaluated with regard to "stroke units" and patient outcomes (Alberts et al., 2000; Stegmayr et al., 1999). The general consensus is that patients experience better outcomes on stroke units. The fact that both genders experienced placement on medical surgical and ICU areas would indicate an opportunity in the area of "stroke unit" establishment. The findings did indicate that both males and females who are admitted with ischemic stroke primarily have internal medicine physicians as their primary physicians. Efforts to evaluate and improve stroke care should be focused on this physician group as they care for 89% of this population.

In terms of pharmacologic management, an analysis was made of aspirin, coumadin, and activase/TPA use with regard to gender. No statistical significant difference was found between these medications and male and female gender. Since pharmacologic management can be seen as an indicator of the aggressiveness of stroke management, this finding indicates that there was no gender difference in the aggressiveness of stroke treatment, at least as far as these specific medications are concerned. Additionally, the numbers for activase use are very low. It might be very helpful to evaluate all patients who receive activase for appropriateness and for compliance with protocol. The low numbers would indicate that this scenario is a low frequency occurrence in the ED, and that those who manage these patients may be less comfortable with the administration of the medication and associated protocols. These findings also suggest that activase use might be under-utilized in this population. Patients who may be candidates for activase may not be receiving the medication. Ischemic stroke chart audits should focus on identifying missed opportunities for activase administration as this drug is an effective option for improving stroke outcomes in some patients (Adams et al., 1996).

A statistically significant difference was found between Carotid Doppler Studies and gender. While there has been no research with relation to the use of Carotid Doppler Studies involving gender, many studies have addressed the importance of the Carotid Doppler Study in ischemic stroke management. Several studies have revealed that there is an important relationship between Carotid Doppler Study findings, treatments, and outcomes (Executive Committee for the Asymptomatic Carotid Atherosclerosis Study [ACAS], 1995; European Carotid Surgery Trialists [ECST] Collaborative Group, 1995). Logically, this research assumes that the statistically significant difference in Carotid Doppler Study use in women would potentially limit women's access to the same treatments and outcomes that men experience. Physicians may need additional information about the effectiveness of Carotid Doppler Studies in both men and women with neurologic symptoms.

A statistically significant difference was demonstrated between endarterectomy and gender. While only a small percentage (1.6%) of the total sample of ischemic stroke patients received endarterectomy, males experienced more endarterectomies than females. This finding supports Akbari et al.'s (2000) findings that women were less likely to present as symptomatic and received fewer endarterectomies. The Executive Committee ACAS Study (1995) and the ECST (Warlow, 1993) study reported stroke risk reduction in both men and women with endarterectomy. There is some evidence that surgical outcomes after endarterectomy are different between men and women, but recent studies have not found this to be true (Akbari et al., 2000; Rockman et al., 2001). Studies are needed to investigate why women are not receiving endarterectomy as a treatment option. Women are older when they experience stroke but the question focuses on the differentiation of surgical need, surgical options, and tolerance.

A statistically significant difference was found between mortality and gender. Females died at a significantly higher level than males with ischemic stroke. No studies were identified that evaluated the relationship between gender and stroke mortality while many studies look at overall mortality in the stroke population. Women were older when they experienced stroke; but based on the finding that women received significantly fewer diagnostic and treatment options, such as Carotid Doppler Studies and endarterectomy, further study seems to be indicated into why women are more likely to die from stroke. One question that stems from these findings is related to protective factors from ischemic stroke that women might have prior to menopause. This protective factor plays a role in coronary disease in women and needs to be investigated for its role in ischemic stroke. Attention to presenting factors, treatment options, comorbidities, and medical management is necessary to attempt to understand these differences in mortality noted in this study.

No statistically significant difference was found between either 30-day readmission or gender or discharge disposition and gender. Only 28 patients out of the entire sample experienced a readmission within 30 days of dismissal from the hospital, and there was no difference between genders. The total readmission rate at 30 days was 5.6% which would indicate that the patients were well managed after leaving the hospital. Discharge dispositions varied between gender. Slightly more men went home than women, and more women went to skilled nursing facilities; however, these differences were not statistically significant. This finding supports Holroyd-Leduc et al.'s (2000) findings that there was no sex difference in rehabilitation services and placement. It is entirely possible that women do not have as many options for care after hospitalization because they are generally the care providers in their homes. It is unknown if the subjects in this study returned to their own homes or a family member's home. This information would give useful data on implications for care of ischemic stroke patients following hospitalization.

Research Question Three

Total cost was predicted by the following six variables: nursing cost, endarterectomy, APR severity "4", first care unit medical surgical, attending physician specialty--cardiology, and neurologists consulting. Carotid Doppler Study, ethnicity, first level of care--ICU, first level of care--step down unit, APR mortality, aspirin, coumadin, activase, ED patient, and age did not contribute significantly to total cost in this study.

The predicted relationship between nursing cost and total cost was expected due to the nature of the nursing cost variable. It is a reflection of the room cost of which nursing care is included and is generally a large part of a hospital bill. Diringer et al. (1999) reported that 50% of cost was due to room charge/nursing care, and LOS accounted for 43% of the variance in cost. It is also not surprising that endarterectomy entered into the equation as predictive of total cost. Surgical procedures add additional expense to the total cost of the hospital stay that other stroke patients would not have experienced.

The fact that APR severity "4" entered into the equation gives validity to the APR severity tool which assigns a value 1-4 to patients based on their severity of illness. The sickest patients with APR severity "4" contributed significantly to total cost. With respect for stroke, severity of illness is a major consideration in determining the complexity of care needs regarding this population. The findings of this study support the theory behind the APR-DRG severity of illness subclass which states that subclasses are highly dependent on the patient's complete clinical picture including underlying problems (Brough & Gay, 1998).

The identified relationship between first care unit--medical surgical, and total cost cannot be explained by evidence from other empirical studies. One would expect that care would be more expensive in the ICU and that first care unit ICU would be predictive of total cost. It is perplexing that the medical surgical care is more closely related to total cost. Care appears to be more expensive if the ICU is bypassed in this population. Perhaps medical surgical units get patients who have less chance of recovery and a longer length of stay than those who go to the ICU environment. A comparison of ischemic stroke patients who go to ICU versus those who go to medical surgical areas needs to be conducted to determine factors that might be contributing to increased cost associated with the medical surgical first care unit stay. Briggs et al. (2001) identified that in-hospital placement of patients with mild to moderate stroke varies greatly between community and university hospitals. The university hospital studied admitted more mild and moderate stroke patients to the ICU. Additionally, this study found that while there were significant differences in placement of the patients, there were no significant differences in outcomes of these patients.

Although attending physician specialty entered the model as predictive of cost, the relationship was found to be a negative relationship. Total cost decreased when a cardiologist was the attending physician. No empirical evidence could explain this relationship. Further investigation may be warranted to understand this phenomenon.

The predictive relationship between neurologist consulting and total cost was expected. Previous research has shown that while neurologist involvement in the care of the patient improves outcomes, it also increases cost. Neurologists were reported to be 34% more expensive than internists and other specialists (Mitchell et al., 1996). It is important to remember that the majority of patients in this data set did not have a neurology consult. In fact, the majority of ischemic stroke patients were cared for by internal medicine specialists. A comparison of care that is provided by both specialists would be of interest to determine if care patterns were similar between neurologists and internal medicine specialist. Many internal medicine specialists manage ischemic stroke patients. While it is well known that outcomes are better for patients managed by neurologists (Gillum & Johnston, 2000), the internal medicine specialists may need specific information regarding the benefits that a neurologist could provide before referral patterns will change.

An additional multiple regression analysis with LOS as the dependent variable was conducted to evaluate the model of interest. The following variables were found to be predictive of LOS in ischemic stroke patients: nursing cost, endarterectomy, coumadin, APR severity "4", APR risk of mortality "4", first care unit medical surgical, APR severity "3", first care unit ICU, Caucasian ethnicity, APR risk of mortality "1", attending physician specialty--cardiology, and neurologists consulting. The following variables: Carotid Doppler Study, first level of care--step down unit, aspirin, activase, and age did not contribute to LOS in this study.

As mentioned in the discussion of the MANCOVA, LOS and total cost were strongly correlated. Based on this knowledge, it came as no surprise that many of the predictor variables listed above for LOS were the same predictor variables as were identified for total cost. The additional variables, beyond those identified as predictors of cost, that contributed to the model with LOS as an outcome included APR risk of mortality "4", APR risk of mortality "1", coumadin, APR severity of illness "3", first care unit ICU, and Caucasian. Of these variables APR risk of mortality "4", first care unit ICU, Caucasian, and APR risk of mortality "1" were all negatively associated with LOS. This finding indicates that the more critical patients did, indeed, have shorter length of stay since they were the most at risk to die. This critical nature was indicated by a higher APR risk for mortality score and being admitted to ICU at the time of admission to the hospital. Those who were at the less severe end of the APR mortality scale (level 1) were also less likely to stay in the hospital a longer time since their condition was not as serious on admission. Being Caucasian also was associated with a shorter stay, which may support other findings indicating that Caucasians are more likely to seek health care sooner before critical symptoms arise (J. Mitchell et al., 1996).

The statistically significant relationship found between coumadin and increased LOS was expected. The nature of coumadin therapy including dosing and therapeutic level monitoring would logically increase LOS. No studies identified the relationship found in this study. The statistically significant relationship found between APR severity "3" and LOS is not surprising in light of its reported ability to indicate complexity of care needed by any given patient. Increased complexity equates to increased needs and results in increased LOS. The statistically significant difference found between APR severity of illness "3" and LOS is consistent with the ability of the APR subclasses to recognize differences in patient complexity. If a patient has an APR severity of illness "1", then it would be expected that he or she was not as sick and, thus, would have a decreased LOS.

A significant negative relationship was found between first care unit ICU and LOS. Those who experienced the longest stays tended to be admitted to some unit other than ICU. This finding is perplexing and cannot be explained by the current studies involving ischemic stroke management. The statistically significant relationship found between Caucasian race and LOS is not all together unexpected. Again, there was a negative relationship between Caucasian status and LOS. This study found that being Caucasian decreased the LOS. One study demonstrated that African-Americans living in the south are known to have more deaths attributable to stroke (Perry & Roccella, 1998). Nevertheless, Lackland et al. (1999) found that there was no difference between race and the percentage of strokes and deaths based on nativity. Hispanic Americans were identified at increased risk for stroke mortality at a younger age, but overall incidence is not known (Morgenstern et al., 1997).

The logistic regression analysis of the model using mortality as the dependent variable resulted in statistically significant findings that explained mortality in a population of ischemic stroke patients. A significant negative relationship was found between Carotid Doppler Studies, LOS, aspirin use, coumadin use, and emergency department stay and mortality or likelihood of dying. A significant positive relationship was found between APR mortality, nursing cost, and mortality. The Carotid Doppler Study is useful in identifying risk of stroke. Adequate diagnosis and treatment results in improved outcomes and thus decreased mortality. Aspirin and coumadin are accepted strategies for stroke risk reduction (Benjamin et al., 1998), and therefore were expected to stay in the model.

The study found a statistically significant relationship between APR mortality all levels 1-4 as predictive of mortality. This result is consistent with the mortality index as APR mortality "3" and "4" were stronger predictors of mortality than APR mortality "1" and "2". There is a stronger expectation that a patient might die with an APR mortality of "3" and "4" than with APR mortality "1" and "2". AP-DRGs were created to deal with Medicare and prospective payment issues. The focus of the initial work on this AP-DRG system was primarily related to resource utilization and ultimately payment for services. The AP-DRG system was found to be incomplete in describing the needs and issues surrounding reimbursement for care provided to patients in the hospital setting. The APR-DRG was created to expand the original structure and taxonomy to include severity of illness and mortality risk issues. Severity of illness and mortality subclasses were created to address the extent of physiologic decompensation or organ system loss of function experienced by the patient and the likelihood of dying (Brough & Gay, 1998).

Therefore, the APR-DRG provided a mechanism to indicate whether or not a patient had minor, moderate, major, or extreme severity of illness and a subclass with the same identifiers for risk of mortality. These values represent categories and not scores. These subclasses have only been in use since 1998 and need validation as to their accuracy and usefulness in providing a picture of a patient's category of risk. Therefore, it is somewhat curious that none of the APR severity of illness variables contributed to the mortality model while they did in the total cost analysis. This finding is not consistent with the design of the subclasses and their application in patient identification. Brough and Gay (1998) reported that the APR-DRG severity of illness and risk of mortality subclasses could be used to compute an expected value for a measurement of interest such as mortality. Specific analysis of this reported ability to compute an expected value may not hold true in this population that includes a statistically significant higher proportion of women experiencing death compared to the men in this sample.

The positive relationship between nursing cost and mortality is expected. The finding is interesting and needs more complete investigation to conceptualize those things that constitute nursing costs and the specific relationship of those variables to mortality. Interestingly, total cost was not a significant predictor of mortality. This finding is odd due to the strong correlations that were identified previously between total cost and nursing cost in the MANCOVA statistical analysis. The fact that the room costs are factored into the nursing cost might cause one to postulate that patients who die stay in the hospital longer, but do not have the interventions or treatments that add to other total costs compared to the ischemic stroke population as a whole. The sickest patients may die quickly, but there must be a percentage who linger and thus experience higher nursing cost, yet are not candidates for typical stroke interventions or treatments. The final explanation is still elusive.

The logistic regression analysis of Carotid Doppler Study, endarterectomy, ethnicity, gender, first level of care, attending physician specialty, neurology consultation, APR severity of illness, APR mortality, nursing cost, activase, aspirin, coumadin, ED patient stay, age, and the 30-day readmission occurrence indicated that there was no significant relationship between these variables and 30-day readmission. The variables did not explain the model with 30-day readmission as the dependent variable. It is likely that the small number of individuals experiencing a readmission within 30 days of dismissal was inadequate to test the model. A larger sample may offer a different result and may need to be considered before this model is completely rejected.

A model was developed and research was conducted focusing on the best data sources available to measure the variables of interest as they reflect client characteristics, system characteristics, and interventions that contribute to the outcomes conceptualized in this study as total cost, LOS, and mortality. The findings of this study indicated that the model fit, including the variables listed above, was strong for the models involving total cost, LOS, and mortality (see Figure 4, Ischemic Stroke Health Outcomes Model). Outcomes of interest were identified and operationalized, and the best data sources were identified based on available research. The model is, however, incomplete because many of the variables identified did not explain total cost, LOS, mortality, and 30-day readmission.

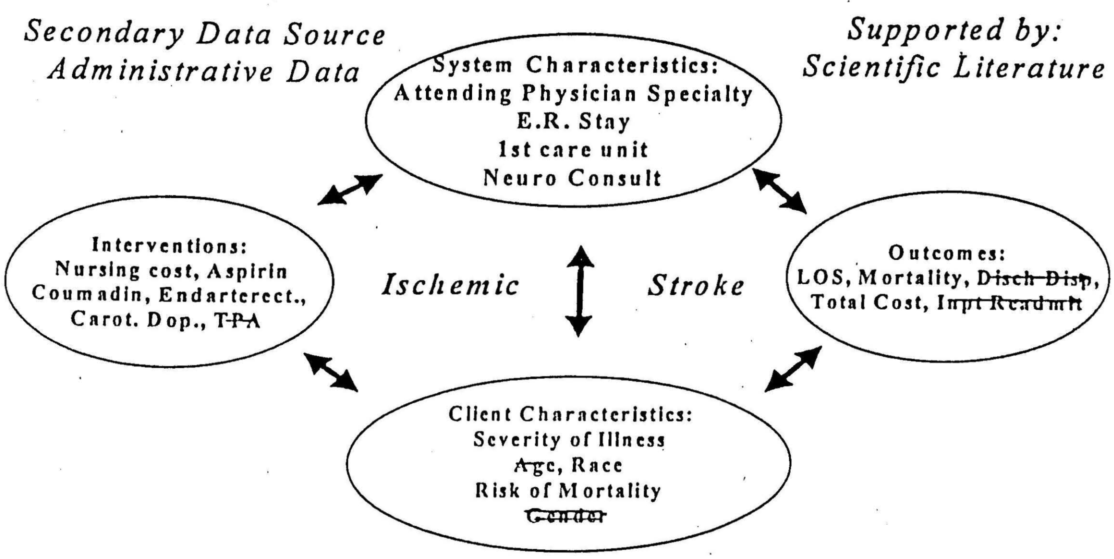

Figure 4. Ischemic Stroke Quality Health Outcomes Model.

Of the client characteristics (severity of illness, age, ethnicity, risk of mortality, and gender) identified in the framework, severity of illness, ethnicity, and risk of mortality variables explained a large percentage of the outcomes of interest in the model. The system characteristics identified in the model were predictive of outcomes as well. All of the system characteristics (attending physician specialty, ED stay, first care unit, and neurologist consultation) identified in the framework contributed to mortality and total cost outcomes identified in the model. The interventions (nursing cost, coumadin, aspirin, endarterectomy, and Carotid Doppler Study) identified in the Ischemic Stroke Outcomes Model Framework prior to this research explained LOS, mortality, and total cost outcomes. As indicated in Figure 4, those system characteristics, client characteristics, and interventions that were not effective in predicting LOS, mortality, and total cost outcomes have been marked through. Additionally, the outcome identified as inpatient readmission could not be adequately modeled in this research with the variables of interest. Discharge disposition was not evaluated.

Conclusions and Implications

Based upon the findings of this study, it can be concluded that:

1. There are differences between men and women admitted with ischemic stroke in relation to total cost and age. Women appear to be older than men when they have stroke and have less total cost associated with their hospital admissions. This finding is similar to the early results of studies investigating cardiac disease and women. Further investigation into the later onset of stroke in women as identified in this study is of concern and may affect stroke diagnosis, management, and care.

2. Neurology consultation is very low in the population studied. Males had more consultations than women and access to potentially better care. In addition internal medicine specialists care for the bulk of this population and drive treatments and outcomes in this ischemic stroke population. Efforts to care for the ischemic stroke population or improve care would need to involve internists in order to have any chance of being effective.

3. The ischemic stroke population uses the ED equally between genders as the first point of care.

4. Men and women appear to have equal opportunity to be admitted to ICU or to a medical surgical unit. In addition, there does not seem to be a difference between genders based on the specialty area of the primary physician.

5. There was no difference in pharmacologic treatment involving coumadin, aspirin, and activase between males and females. Activase/TPA use was very limited in the ischemic stroke population studied even though it is strongly recommended as a treatment to reduce adverse outcomes of stroke.

6. Men receive more Carotid Doppler Studies and endarterectomies than women do.

7. Females have higher stroke mortality than males.

8. Nursing cost, endarterectomy, APR severity, first care unit medical surgical, attending physician specialty--

cardiology, and neurologists consultation explain 86.5% total cost. Having a cardiologist as attending physician was related to decreased total cost.

9. Nursing cost, coumadin, APR severity 3 and 4, APR risk of mortality 1 and 4, first care unit medical surgical, first care unit ICU, Caucasian, and endarterectomy explained 76.8% of LOS variance. APR risk of mortality 1 and 4, first care unit ICU, and being Caucasian explained a decreased length of stay.

10. Carotid Doppler Study, LOS, APR mortality, nursing cost, aspirin, coumadin, and ED patient were related to mortality. As the incidence of these variables decreases there is an associated increase in mortality.

11. Inpatient readmission within 30 days of dismissal could not be predicted by the Ischemic Stroke Health Outcomes Model.

The findings of this study reveal information about the interrelationship between system characteristics, client characteristics, and interventions as they impact ischemic stroke patient outcomes. There appear to be gender issues related to age of stroke onset and access to some interventions and treatments that are common in stroke management. Complex interactions between patients and also within genders exist which need further investigation.

The findings of this study are generalizable only to ischemic stroke patients admitted with ICD-9 codes inclusive of ischemic stroke coding. In addition the data were mined from an administrative database. The data are only as good as the data extractors and the data entry personnel. Validity of the findings is strongly contingent on the reliability of the coders and data entry personnel. The use of the administrative data set was extremely helpful in providing large amounts of data that were useful for the analysis of the conceptual framework proposed in this research and for the evaluation of ischemic stroke and gender specific issues. Current hospital databases provide rich sources of information, which can provide guidance to future nursing practice.

Recommendations for Further Study

The findings of this study support the use of administrative databases as repositories of important information that is relevant for the evaluation of patients and patient care. There is, however, limited expertise for identifying research questions and variables that need investigation. While the Data Mining Model for Secondary Data Analysis was used as a research guide, it was not tested in this study. The model needs to be tested and the following questions answered:

1. Is the Data Mining Model for Secondary Data Analysis, used in this study, an effective model to guide the exercise of research with administrative data sets?

2. Does it articulate the approach to the research process appropriately?

The findings of the study did not support the variable called 30-day readmission as an outcome that could be explained by the model. Is the model more robust if this variable is removed? Further study is needed to understand factors that may influence LOS.

The chi-square indicated dependence between gender and mortality. In an effort to further understand mortality and specifically the increased incidence in women, it might be helpful to limit the sample to women only. What are the primary predictors of mortality in an ischemic stroke population of women in a large community hospital? It might be helpful conduct a chart audit of the women in the sample who died to ascertain other factors that might explain mortality in this population. Do women present with the same early symptoms of stroke? Is medical management the same for men and women experiencing ischemic stroke? Are women given the same treatment options as men in all areas of the country? This study needs replication beyond this sample and population to shed further light on this subject.

A larger study of the issues related to decreased Carotid Doppler Studies and endarterectomy may be appropriate. Are the women presenting with the same criteria that would warrant a Carotid Doppler Study in men? Are the criteria for performing carotid endarterectomy based on male population studies? Are there clinical grounds for differences in care between men and women in the area of Carotid Doppler Study and endarterectomy? Do physicians have up-to-date knowledge about interpretation of Carotid Doppler Study findings as they relate to men and women as well as guidelines for surgical intervention in the male and female population. What is a woman's tolerance to endarterectomy and is it higher risk for women?

There is an indication that activase may be under-utilized in this population. A study focusing in ischemic stroke chart audits with identification of potential candidates who were not given activase may be warranted. In addition, focused study on those patients who have activase is warranted due to the low frequency of current administration. The protocol for treatment and management of the ischemic stroke patient receiving activase should be monitored closely for compliance as this appears to be a high-risk, low-frequency competency for physician and nursing staff members.

Given the fact that administrative data were used for this study, validation of these data as accurate for the population of interest would give support to the use of this type of data. Does the administrative database accurately reflect the chart data? A study should be designed so that a researcher could evaluate a number of identified charts as they relate to the data reported on a given patient in the database.

The widespread use of the APR severity of illness and risk of mortality as a subclass identifier for patient populations should be further tested within patient populations. Is the tool accurate for demonstrating patient severity of illness and risk of mortality? An investigative descriptive study involving chart audits of the women who died designed to evaluate those patients' status on arrival with careful attention to factors that might have contributed to their deaths could shed light on the mortality issues as well as the accuracy of the APR-DRG mortality subclass. Why are women with ischemic stroke dying at higher rates than men with ischemic stroke? Why does APR severity of illness not explain mortality in the ischemic stroke population?

Finally, further cost analysis should be conducted in further studies. Nursing interventions play a major part in the total cost of patient care. What are the specifics of the nursing care and interventions that contribute to that cost? A comparison study of those ischemic stroke patients who go to the ICU versus those patients who go to medical surgical areas should be conducted to determine factors that might be contributing to increased cost associated with the medical surgical first care unit. Information about these aspects of nursing care could result in a better understanding of the specifics of nursing care that impact patient outcomes. Post-hospitalization options for men and women need further investigation. Do subjects return to their own homes or do go to family members' homes to receive care? Do women have the same options for post-hospitalization care, as they are generally the primary caregivers in a family unit?

Summary

This study was undertaken for the purpose of exploring the predictors of ischemic stroke in a large hospital-based population. Of interest was the relevance of gender to the diagnostic and treatment modalities used. It appears that women are older at onset and more at risk of dying from stroke than men. In addition, the data confirm that women receive fewer diagnostic tests and treatment modalities than the men in the study do. Clearly, further study of gender bias in the treatment of ischemic stroke and investigation into female stroke mortality is warranted.

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APPENDIX A

Permission to Reprint Quality Health Outcomes Model

October 14, 2001

JNS Publication Office
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550 West North
Indianapolis, IN 46202

Dear Sir or Madam:

My name is Mary Clark Robinson. I am a graduate student at Texas Woman's University and am currently writing my dissertation. I am writing you to request permission to place a copy of Figure 2 in Mitchell, Ferketich, and Jennings article published in the first quarter of 1998. I am using the Quality Health Outcomes Model as the conceptual framework and would request that I be able to copy the Quality Health Outcomes Model figure to illustrate the model in my dissertation. The figure will only be used for the purpose of my dissertation work. I have already requested and received permission from Pamela Mitchell as the primary author and have attached the email documenting her consent. Thank you for you help with this issue. I look forward to hearing back from you.

Sincerely,

Mary C Robinson

Mary C. Robinson
2033 Huntington Lane
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APPENDIX B

Permission to Conduct Study

TO: Mary Robinson, RN, PhDc
Director of Clinical Education
701 5th Avenue
Fort Worth, Texas 76104

FROM: Kenneth Hancock, MD
Institutional Review Board Chairman

DATE: 14 September 2001

RE: Expedited Approval of Protocol
IRB #HMFW-2001-05
The Role of Client Characteristics, System Characteristics and Interventions in Ischemic Stroke Outcomes

The Institutional Review Board determined that this research was eligible for expedited review in accordance with 45 CFR 46.110 and 21 CFR 56.110. The Board approved the protocol dated 14 September 2001. IRB approval of this research lasts until September 2002. If the research continues beyond twelve months, you must apply for updated approval of the protocol and one month before the date of expiration noted above. The Board waived the use of consent form in accordance with 45 CFR 46.116(d).

It is the understanding of the IRB that this study is limited to medical records research.

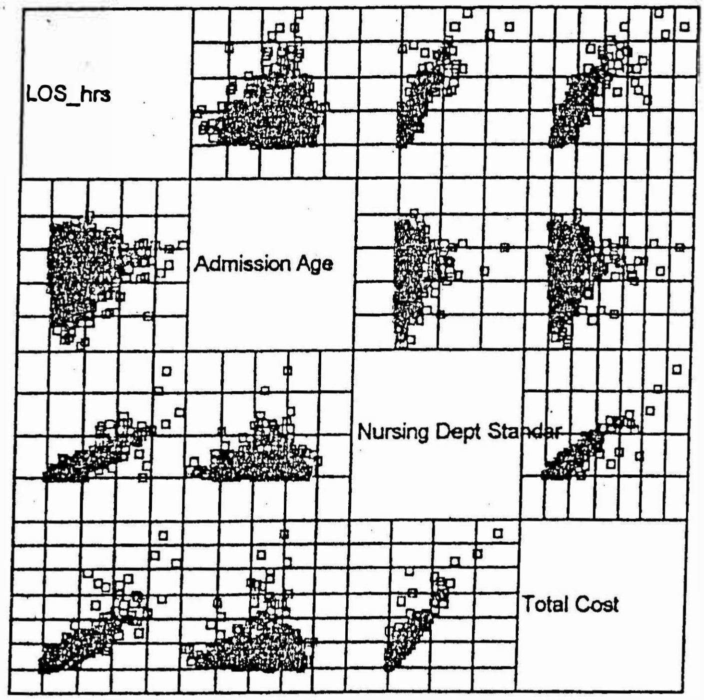
The investigator agrees to comply with the (a) ethical principles in the Belmont Report, (b) regulations in 45 CFR 46, (c) the Hospital's Assurance on file with the DHHS, and the principles of Good Clinical Practice as defined by the International Committee on Harmonisation."

If you have any questions related to this approval or the IRB, you may telephone Kelle Rudolph, IRB Administrator, at 817.820.4909.

KH/kr

APPENDIX C

Linearity Scatterplot for LOS, Admission Age, Nursing Cost, and Total Cost



Linearity Scatterplot for LOS, Admission Age, Nursing Cost, and Total Cost