COMORBIDITY FACTORS CORRELATED WITH READMISSION AFTER CORONARY ARTERY BYPASS GRAFTING (CABG) AT THE UNIVERSITY OF TENNESSEE MEDICAL CENTER KNOXVILLE, TENNESSEE

A Report of a Senior Study

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ABSTRACT

Coronary artery disease is the leading cause of death of both men and women in America. The aim of interventional treatment for Coronary Artery Disease is to increase the supply of oxygen and nutrients to the heart by bypassing the coronary arteries. The surgical procedure used to accomplish this is known as Coronary Artery Bypass Grafting or CABG. The purpose of this study was to define the risk factors (comorbidities) leading to readmission within 30 days after CABG in one Southeastern medical center by analysis of medical record data. Data was collected from 60 patients who were readmitted within 30 days after CABG and 66 randomly selected non-readmitted patients from January 1, 2006 to May 1, 2011. The one-hundred twenty nice comorbidites were analyzed using Minitab multiple-regression models. The factors deduced from the Minitab multiple regression models to significantly influence readmission were hemoglobin levels <9.97, pre-operative creatinine levels >1.03, temperature <98.24°F, angina, BUN levels >14.98, not receiving intraoperative epsilon amino caproic acid, receiving introperative blood products , LOS Admit-Surgery >0.81 days, LOS Admit-Discharge >7.55 days, mean pre-operative blood pressure >100.4mmHg, post-operative creatinine >0.97, post-operative events, and previous stent. Identification and correction of the previously mentioned comorbidities may lead to decreased readmission within 30 days after CABG, thus decreasing medical costs and increasing patient health.

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Abbreviation index

Abbreviation	Actual Word(s)
ACE	Angiotensin-converting enzyme
ARB	Angiotensin receptor blocker
ARF	acute renal failure
BMI	Body mass index
BUN	Blood urea nitrogen
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CDC	Centers for Disease Control
CHD	coronary heart disease
COPD	chronic obstructive pulmonary disease
CPB	cardiopulmonary bypass pump
CVA	Cerebrovascular accident
EKG or ECG	electrocardiogram
FFP	Fresh frozen plasma
GI	Gastrointestinal
HDL	high- density lipoproteins
HF	Heart failure
ICD	Implantable cardiac defibrillator
ICU	intensive care unit
ITA	internal thoracic artery

Abbreviation	**Actual Word(s)**
EACA	Epsilon amino caproic acid
MI	myocardial infarction
MR	Medical record
MRI	magnetic resonance imaging
LDL	low-density lipoproteins
LOS	Length of stay
PAD	Peripheral artery diseasee
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
RBC	Red blood cell
SPECT	single-photon emission computed tomography
SSC	surgical critical care
TEE	Trans esophageal echocardiography
TIA	Transient ischemic attack
TLR	toll like receptor
WBC	White blood cell

CHAPTER 1: INTRODUCTION

Statistics on Coronary Heart Disease

Coronary heart disease, also known as coronary artery disease and ischemic heart disease, is the leading cause of death of both men and women in America. Currently, 17.6 million Americans, 7.9% of the total population, have coronary heart disease making it the most common form of heart disease (CDC 2010). In 2004, 445,687 people died from coronary heart disease (Heron 2004) and this increased to 631,636 deaths attributed to coronary heart disease in 2006. In other words, coronary heart disease caused 26% of total deaths—more than one in every four—in the United States (Heron et al. 2006).

Each year in the United States alone, approximately 785,000 Americans have their first myocardial infarction, heart attack, and another 470,000 people have repeat myocardial infarctions a year. About every 25 seconds a person will suffer a coronary event and about every minute someone will die from one (American Heart Association 2010). Approximately every 34 seconds, an American will suffer a heart attack, and the estimated average number of years lost due to a heart attack is 15 (National Vital Statistics Report 2008). In 2010, heart disease cost $316.4 billion in the United States, including the cost of health care services, medications, and lost productivity (Lloyd-Jones et al 2010). Worldwide, the World Health Organization reports that 17,100,000 people died in 2004 as a result of a cardiovascular disease, 7,198,257 from ischemic heart disease (Mathers et al. 2011).

Table 1 shows the percentage of all deaths caused by heart disease in 2004 by ethnicity. Whites and African Americans have the highest mortality with 27.5% and 25.8%, respectively while American Indians or Alaska Natives have the lowest mortality with 19.8%.

Table 1: Percentage of Deaths from Heart Disease by Ethnicity in 2004 in the United States (Heart Disease Facts 2010).

Race of Ethnic Group	**% of Deaths**
Whites	27.5
African Americans	25.8
Asians or Pacific Islanders	24.6
Hispanics	22.7
American Indians or Alaska Natives	19.8

Coronary artery disease (CAD) is one manifestation of ischemic heart disease, which is the leading cause of mortality in the world. Ischemic heart disease ranges from asymptomatic rhythm problems to sudden cardiac arrest. When it occurs as obstructive coronary artery disease (CAD), the symptoms include angina pectoris, chest pain, or myocardial infarction, heart attack (King III et al. 2010). Currently, in the United States, there are approximately 16.8 million people afflicted with coronary heart disease, and there are nearly 800,000 new coronary events annually with half a million deaths (Lloyd-Jones et al. 2009).

Anatomy of the Heart and Coronary Arteries

The heart is the muscle responsible for pumping blood continuously to all parts of the body. The heart consists of four chambers, 2 atria and 2 ventricles. The right atrium receives oxygen-poor blood from the inferior and superior vena cavae. The blood travels through the tricuspid valve to the right ventricle. The right ventricle pumps the blood through the pulmonary arteries to the lungs where the deoxygenated blood becomes oxygenated as a result of gas exchange in the capillary beds of the lungs: oxygen passes from the lungs through the blood vessels to the blood while carbon dioxide is passed from the blood vessels to the lungs and is removed from the body upon exhalation. The oxygen-rich blood then enters the left atrium via the pulmonary arteries. This blood then enters the left ventricle by passing through the mitral valve. This blood is then pumped through the aortic valve where it is distributed throughout the body. Figure 1 is a diagram of the human heart.

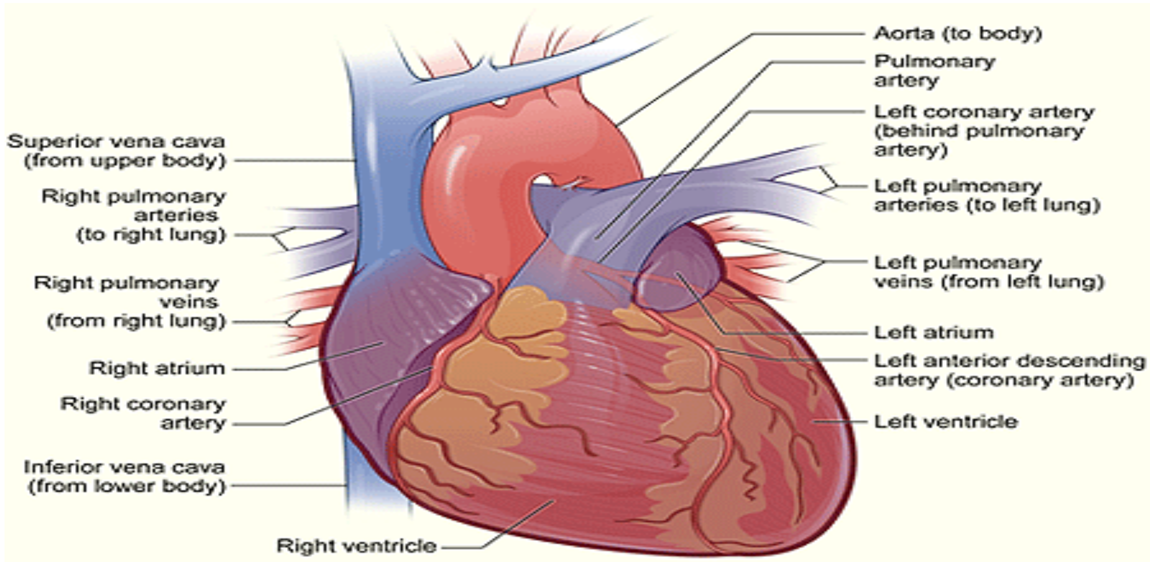

Figure 1: Diagram of the Human Heart (Courtesy of National Heart and Lung Institute 2011)

The heart muscle itself, the myocardium, receives its own supply of blood from the coronary arteries (see Figure 2). These arteries and their branches supply all parts of the heart muscle with blood. There are 4 coronary arteries: right coronary artery, left coronary artery, circumflex artery, and the left anterior descending artery. The right coronary artery supplies blood to the right atrium and the right ventricle as well and the back of the septum and the bottom of the left ventricle. The left coronary artery divides into the circumflex artery and the left anterior descending artery. The circumflex artery supplies blood to the left atrium and the back of the left ventricle while the left anterior descending artery supplies blood the front and side of the left ventricle as well as the front of the septum.

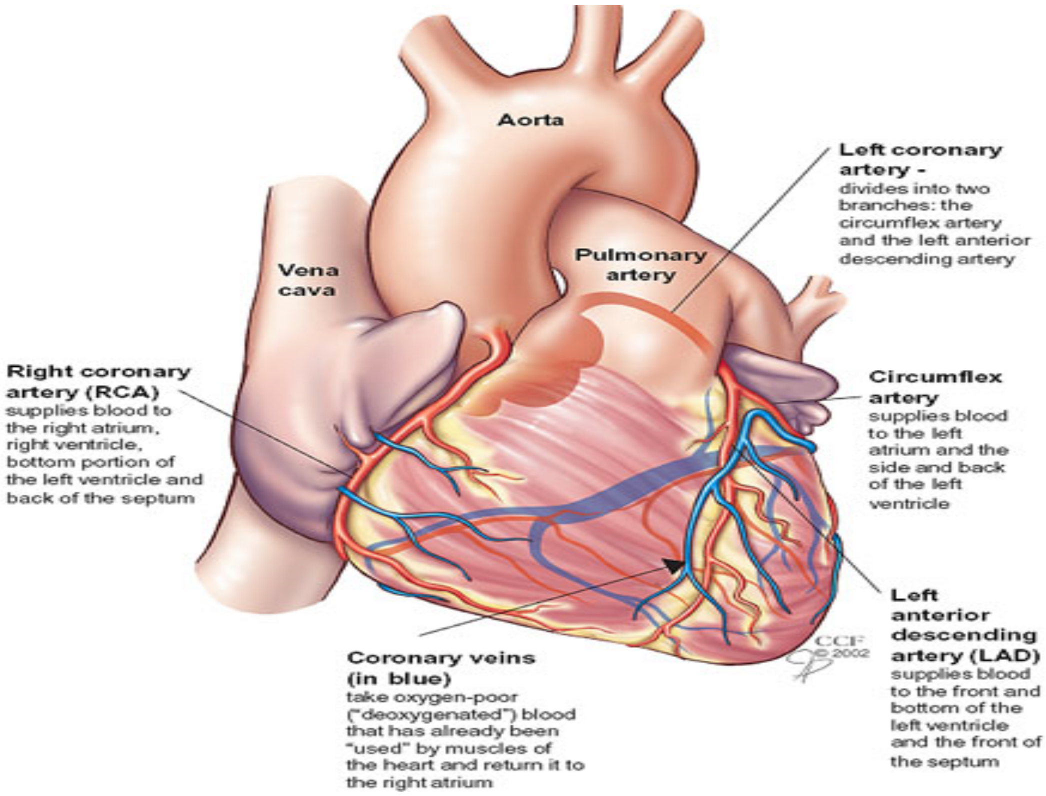

Figure 2: Diagram of the Coronary Arteries (Courtesy of the Cleveland Clinic 2011)

<u>Coronary Artery Disease</u>

Coronary artery disease is a progressive disease that is a result of atherosclerosis (Ferraris and Menter 2008). Atherosclerosis, the mechanism of plaque formation, is an inflammatory disease elicited at sites of lipoprotein accumulation and hemodynamic strain. Atherosclerosis is a multifactorial disease with the primary risk factors being smoking, diabetes, hypertension, hyperlipidemia, obesity, diabetes, low daily fruit and vegetable consumption, alcohol overconsumption, medication with cholesterol or blood pressure lowering components and sedentary lifestyle (Greenland, et al. 2003 and Yusuf, et al. 2004). Relatively recently, it was discovered that high levels of C Reactive Protein and homocystein are good indicators of atherosclerosis, as well (Schwartz et al. 2010). Thirteen genetic loci on chromosomes 1, 2, 3, 6, 9, 10, 19, and 21 have been discovered to have strong statistical evidence for association with myocardial infarction (MI) and coronary disease, indicating that coronary artery disease is a heritable trait (Musunuru and Kathiresan 2010). Furthermore, above average concentrations of lipoprotein a have a positive correlation with the risk of developing coronary artery disease (Erquo et al. 2009).

The current understanding of the atherosclerotic process is that atherosclerosis is initiated when cholesterol-containing low-density lipoproteins (LDLs) accumulate in the tunica intima of an artery (Hansson et al. 2006). Deposition of mucopolysaccharides and proliferation of endothelial cells and fibroblasts follow initial intima damage, and growth lesions, plaques, appear in the form of lipid droplets beneath the intima (Ferraris and Menton 2008). Monocytes and T cells are activated to enter the artery walls via leukocyte adhesion molecules and chemokines to initiate a local inflammatory response. Monocytes differentiate into macrophages which up regulate scavenger receptors and toll-like receptors (TLR). Scavenger receptors and TLRs are important mediators of intracellular cholesterol accumulation and innate immune activation in the atherosclerotic plaque. Furthermore, the cytokines released by Th1 cells (a subset of CD4+ Helper T cells) and macrophages are major pro-atherogenic molecules (Hansson et al. 2006).

Anti-atherosclerotic immune responses are mounted by activated B cells, plasma cells, which produce lipoprotein antibodies and produce anti-inflammatory cytokines. The presence of a plaque, which is in large part due to the inflammatory response itself, leads to further immune response to rid the plaque (Hansson et al. 2006). Activated macrophages secrete proteolytic enzymes that degrade the collagen that strengthens the plaque's fibrous cap; therefore, the plaque is weakened and prone to rupture. This ruptured plaque, thrombi, may lead to a myocardial infarction or stroke (Ferraris and Menton 2008). Rupture of the vulnerable plaque may occur spontaneously or it may be triggered by physical activity, emotional distress, drug exposure, poor sleep habits, or prolonged cold exposure (Virmani et al. 2002).

Coronary artery atherosclerosis is closely linked to lipid metabolism, and studies have shown that statin therapies, which lower lipids, have resulted in decreased mortality in coronary artery disease patients (e.g., Maycock et al. 2002). Animal studies have demonstrated that statin therapy modifies the composition of plaque's lipid core by lowering the amount of low density lipoprotein, commonly referred to as "bad cholesterol," which stabilizes the plaque and makes it more resistant to rupture (Maycock et al. 2002).

Detection and Diagnosis

A typical manifestation of coronary artery disease is angina, pectoris, which is discomfort often characterized as heaviness or tightening or the chest; however, approximately 15% of patients do not complain of angina (Ferraris and Menton 2008). A more severe indication of coronary artery disease is myocardial infarction which involves crushing heart pain, dizziness, fatigue, and vomiting (Boersma et al. 2003). Most severely, the first manifestation of coronary artery disease in some patients is sudden cardiac death resulting from a ventricular arrhythmia (Solomom et al. 2005).

At the physical examination, pertinent indicators of CAD include abnormal neck vein pulsation, weak pulse, abnormal heart sounds, and chest tenderness. If a patient is suspected to have coronary artery disease after the physical examination, appropriate laboratory studies such as a lipid profile (cholesterol, triglycerides, LDL, and HDL). An elevated cholesterol level of 10% is associated with a 20- 30% increase in heart disease. A high sensitivity C-Reactive Protein (hs-CRP) test may also be ordered which determines the amount of inflammation (Ferraris and Menton 2008).

If the laboratory studies are abnormal then diagnostic tests will become employed. The information from these tests will ultimately determine whether the patient would best benefit from medical treatment, coronary angioplasty, or coronary artery bypass grafting (Ferraris and Menton 2008).

Chest radiographs are helpful at identifying enlarged heart size (cardiomegaly), fluid in the lungs (pulmonary edema), fluid in the pleural regions between the lungs (pleural effusions), and calcifications. Electrocardiograms are employed to determine if any arrhythmias are present, which is common in patients with CAD. An exercise EKG or stress test may further determine the extent of CAD: failure to increase systolic blood pressure to more than 120 mm Hg or the appearance of ventricular arrhythmias is positive indicators of advanced CAD (Ferraris and Menton 2008 and Schwartz 2010).

Echocardiographs use reflected acoustic waves for cardiac imaging. They often reveal heart wall thinning and abnormalities which are often correlated ischemia. Dobutamine may also be injected during the Echo in incremental doses which helps to differentiate between normal and infarcted myocardium (Ferraris and Menton 2008 and Schwartz 2010).

Thallium-201 single-photon emission computed tomography (SPECT) positively detects CAD 85%- 96% of the time in patients who were unable to achieve at least 85% of their predicted exercise response and it also provides data on myocardial wall thickening and perfusion (Stein, et al. 2006).

Positron Electron Tomography (PET scan) is a technique employed to assess myocardial blood flow and viability and metabolism. The pretense of using PET scans is that when a heart is ischemic it extracts more glucose, so the radioactive glucose tracer, F-2-fluoro-2-deoxyglucose (FDG) can be used to image the heart (Ferraris and Menton 2008 and Schwartz 2010).

However, due to the radiation exposure and high cost of PET scanning, magnetic resonance imaging (MRI) is a good alternative because it has good sensitivity for viability and better imaging quality than EKG. The strengths and limitations of these diagnostic techniques are summarized in Table 2. Figure 3 is a paradigm for evaluating patients with coronary artery disease.

Table 2: Strengths and Limitations of Diagnostic Tests for Coronary Artery Disease (based on Braunwald, et al. 2001).

Detecting Coronary Artery Disease and Assessing Prognosis

Exercise Electrocardiogram (ECG)

Strengths: low cost; short duration; high sensitivity in left main coronary artery disease

Limitations: low detection rate of one-vessel disease; poor specificity in premenopausal women; must achieve ≥85% of maximum heart rate.

SPECT Imagining

Strengths: higher sensitivity and specificity than exercise ECG; can be performed in most patients; quantitative image analysis; high specificity with ^{99m}Tc

Limitations: higher cost than exercise ECG; radiation exposure; poor image quality in obese patients

Stress Echocardiography

Strengths: higher sensitivity and specificity than exercise ECG; short procedure time; identification of structural cardiac abnormalities; no radiation; relatively lower cost

Limitations: Decreased sensitivity for detection of one vessel disease; poor acoustic window in some patients; high operator dependence

Assessment of Myocardial Viability

SPECT Imagining

Strengths: higher sensitivity for predicting viability after revascularization; predictive for clinical outcomes

Limitations: reduced sensitivity relative to PET and dobutamine echocardiography; no absolute measurement of blood flow

PET Imagining

Strengths: higher sensitivity than other techniques; good specificity; simultaneous assessment of perfusion and

Limitations: Lower sensitivity than dobutamine echocardiography; high cost; limited availability

Dobutamine Echocardiography

Strengths: higher specificity than other techniques; widely available; lower cost than dobutamine MRI

Limitations: Lower sensitivity than other techniques; poor windows in 30% of patients

Dobutamine MRI

Strengths: better image quality than echocardiography; good sensitivity and specificity

Limitations: higher cost than echocardiography; limited availability; patients with pacemakers or defibrillators cannot be imaged

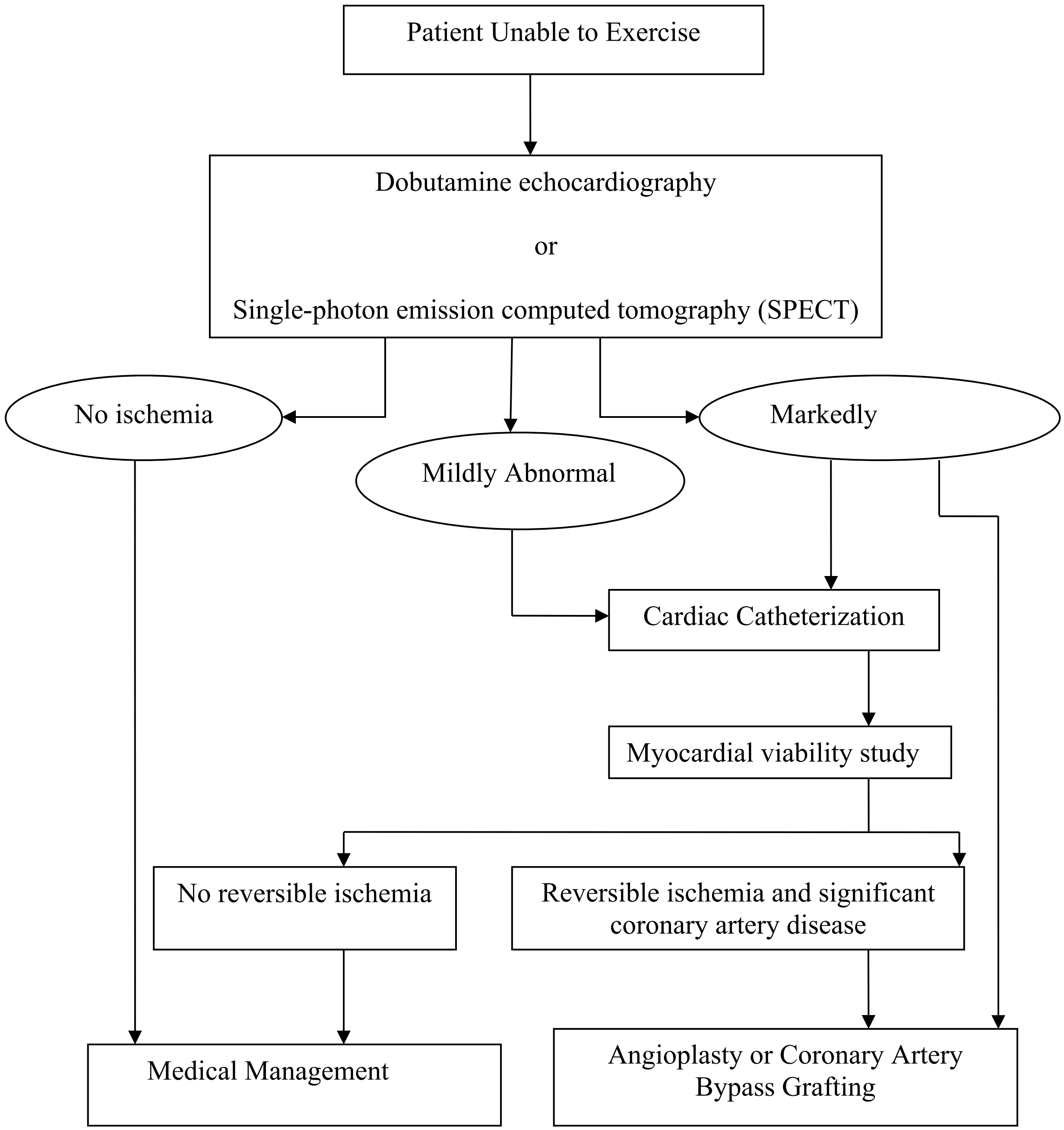

Figure 3: Paradigm for Evaluating Patients with Coronary Artery Disease (Adapted from the Division of Cardiothoracic Surgery, University of Kentucky, 2003).

Treatment

The aim of interventional treatment for Coronary Artery Disease is to increase the supply of oxygen and nutrients to the heart by bypassing the coronary arteries (Eagle, et al. 2004). The surgical procedure implemented to accomplish this is known as Coronary Artery Bypass Grafting or CABG (see Figure 4 for an outline of the procedure).

CABG may be indicated for patients with chronic or unstable angina in symptomatic patients or in asymptomatic patients with severe atherosclerosis or patients with easily provoked ischemia during stress testing (Schwartz 2010). The first coronary artery bypass grafting was performed in 1967 by Sones, Favaloro, and colleagues. Patients who respond especially well to CABG are those who have a left main coronary stenosis or multivessel disease with a proximal left anterior descending coronary artery lesion (Sabik and Lytle 2008).

CABGs are commonly performed surgeries. In 2006, there were 448,000 CABGs performed in the United States. Of these operations, 323,000 were performed on men and 125,000 on women (American Heart Association, 2010).

It has been observed that an average of 87.1% of patients will lead a relatively normal life after their operation; however, 12.9% of patients will be readmitted after his or her coronary artery bypass grafting for a number of reasons, which is the focus of the study (Hannan 2003). Research has shown that there are numerous factors which are referred to as comorbidities that may lead to unexpected readmission after CABG. Table 2 is a list of factors that have been shown to lead to readmission after coronary artery bypass grafting

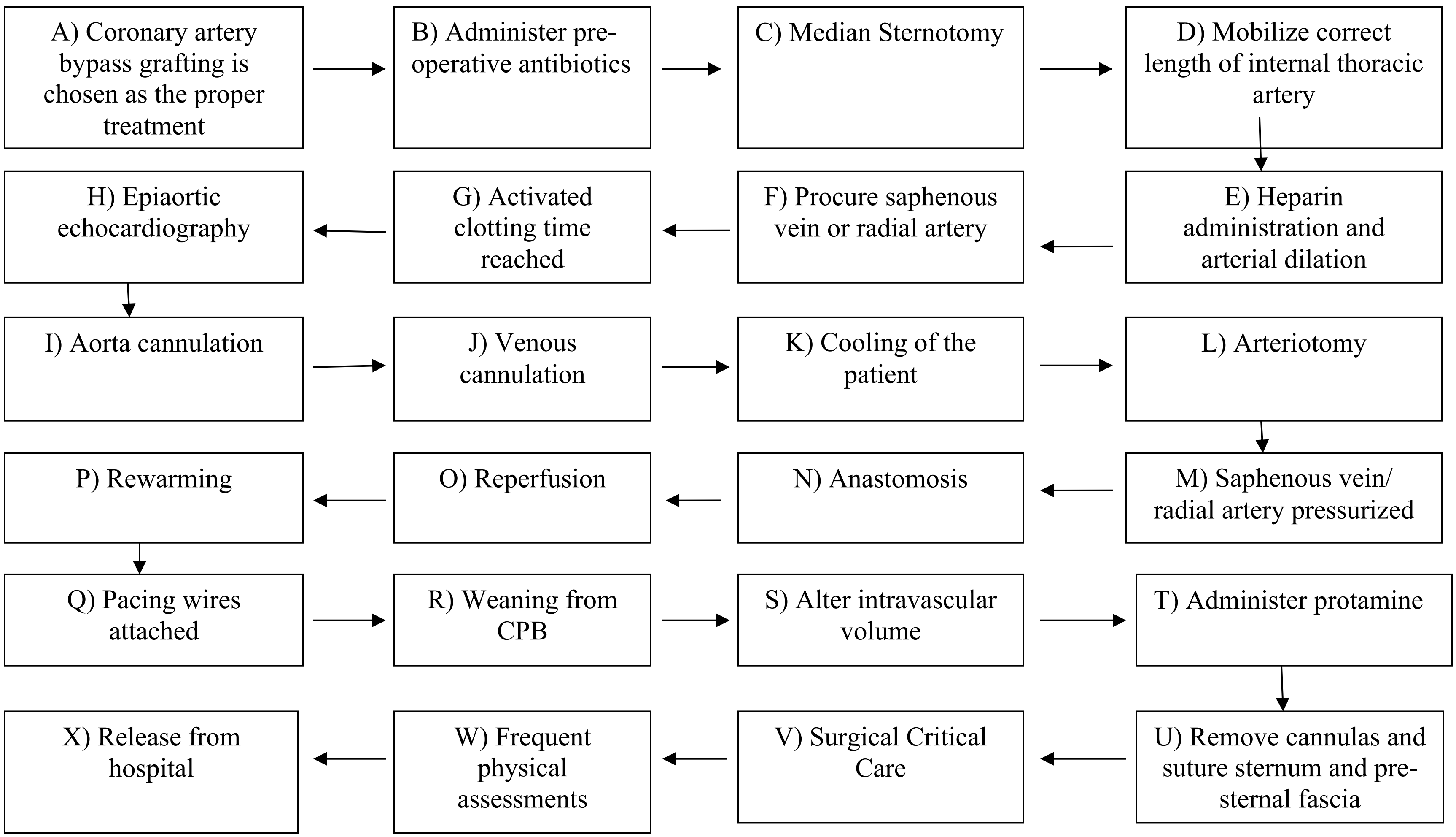

Figure 4: Flowchart of Coronary Artery Bypass Grafting (CABG)

Figure 4: Flowchart of Coronary Artery Bypass Grafting (CABG) Surgery

A) After the patient has been identified as having coronary artery disease that is non-responsive to alternative treatments, coronary artery bypass grafting is performed[1,2,3] B) Administration of pre-operative antibiotics (cefuroxime 1.5 g IV or vancomycin 1.0 g IV if patient is allergic to penicillin) at least 30 minutes before skin incision[2] C) The patient is draped, and a median sternotomy is performed by making a vertical incision from the top of the sternum to the bottom of the xyphoid process, the sternum is separated with the use of an electric saw, and the ribs are retracted to reveal the pericardium[1,2,3] D) Once the internal thoracic artery is identified, the endothoracic fascia is medially opened to the artery with care taken not to injure the vessel. Radiofrequency or electrocautery are used to mobilize the correct length of artery needed [1,2]E) The internal thoracic artery is systematically heparinized before being occluded with a clamp. The vessel is then inoculated with papaverine to induce arterial dilation and prevent vascular spasm [1] F) If the saphenous vein or radial artery are to be used, another surgical team may procure the vessel using the technique mentioned above excluding the median sternotomy [1,2,3]G) The patient is heparinized until a target activated clotting time of greater than 400 seconds is observed[1] H) Epiaortic echocardiography is employed to identify the size and exact location of calcified plaques to minimize plaque disruption and embolism[2] I) The ascending aorta is cannulated proximal to the innominate artery using double purse-string sutures. The open end of the cannula is then back flushed to remove debris and air before being attached to the arterial perfusion line of the cardiopulmonary artery bypass machine (CPB)[1] J) If a venous cannula is to be used, the cannula is introduced into the right atrium via a single purse-string suture or a dual-stage cannula is placed into the inferior vena cava and the open end is attached to the venous line of the CPB[2] K) The patient is again heparinized and then cooled to a core temperature of 30-32°C using cold cardioplegic solutions mainly consisting of potassium via cardioplegic cannula inserted in the cross-clamped aorta.[1,3] The heart is additionally cooled with a topical slush of cooled saline [2] L) The target sites of the anastomoses are selected. The ideal anastomosis site is readily accessible, free of plaque, and has at least a 1.5mm diameter.[2] Once the target site is selected, a small, sharp lance is used to puncture the vessel: this is called an arteriotomy. This arteriotomy is cut until it matches the conduit vessel size [2,3] M) If a saphenous vein is being used, the graft is pressurized with heparinized blood to test for hemodynamic stability[2] N) The ITA is beveled at an angle and sutured into the target vessel with polypropylene suture. The anastomosis is then sutured to the epicardium to prevent twisting and tension[2] O) After completion of the anastomosis, small clamps is places on each graft, and the CPB flow is slowly reduced as the aortic clamps are removed and the heart is reperfused. Once, the grafts have filled with blood, tiny punctures are made in the veins to release air. The clamps are removed and the anastomosis sites are re-examined for bleeding[1, 2] P) Systematic re-warming is initiated after the final distal anastomosis to 36.5- 37.0°C, and blood from the pleural space is suctioned into a Cell Saver for later use[2, 3] Q) After the cross-clamp is removed from the aorta, the heart normally begins to beat on its own. If normal sinus rhythm does not commence, temporary pacing wires are attached to the right atrium or ventricle and set to circa 90 beats/minute[2] R) Once the patient is re-warmed and normal sinus rhythm is re-established, the patient is carefully weaned from the CPB by slowly reducing flow rates to zero while maintaining proper volume through transfusion[2] S) It is often necessary to alter the intravascular volume and peripheral vascular resistance by infusing dobutamine, nitroglycerine, or ephinephrine[2] T) Once the patient is stable off of the CPB, protamine is administered to reverse the anticoagulation induced by heparin [2,3] U) The aortic and venous cannulas are removed and the sutures are tied in their place. Temporary pleural and mediastinal chest tubes are inserted, and once hemodynamic stability and hemostasis are achieved, the sternum is sutured back together with large-caliber stainless steel wires. The pre-sternal fascia is sutured back together in layers and then covered with steri-strips or stapled back together[2] V) The patient is then transferred to the surgical intensive care unit [1, 2, 3] W) Upon admission and frequently after admission to the intensive care unit, a physical examination and assessment of cardiac output, blood pressure, breathing sounds, pulse, body temperature, and chest tube output are performed. A portable chest radiograph may be employed to assure there is not pulmonary edema, pneumothorax, or atelectasis. And laboratory studies of blood urea nitrogen, hemocrit, and electrolytes are completed [1,2.3] X) After 3-5 days in the critical care unit and 2-3 days on a hospital floor, the patient is released from the hospital[1,2,3]

1: Schwartz 2010

2: Ferraris 2008

3: Sabik 2008

Table 3: Factors (Comorbidities) that may lead to Unexpected Readmission after Coronary Artery Bypass Grafting (CABG).

Comorbidity	Remarks	Reference
Age	The oldest patients (75 and old) had a rate twice as high as those in the youngest group (64 and younger) (34.5% vs. 18.6%). One study concluded that elderly patients have higher 30-day mortality, higher morbidity, longer length of stay in health care facilities, and an increased risk of readmission within 3 months after CABG. Increased age is a significant risk factor for being readmitted within 30 days. An important re-admittance factor after CABG is patient age.	Järvinen, Otso 2003 O'Riordan, Michael 2003 Cheng, David C.H. 2006
Aspirin use	An important re-admittance factor after CABG is duration and dosage of aspirin if taken.	Cheng, David C.H. 2006
Anesthetic agent used	The type of general anesthesia the patient is given may increase or decrease the response of the immune system while on the CPB, so whether the patient is on propofol, pentothal, isoforane, sevoforane, or morphine are important perioperative factors.	Tung, Avery 2006

Table 3: continued

Comorbidity	Remarks	Reference
Body temperature and pH during surgery	Cooling to 32-37°F at pH 7.4 while on the cardiopulmonary bypass circuit lead to better neurologic function and decreased risk or early readmission after CABG.	Muzic, David and Chaney, MA 2006
Chest tube removal	Premature chest tube removal is correlated with higher readmittance rate.	Cheng, David C.H. 2006
COPD	Being diagnosed with COPD is a significant risk factor for being readmitted within 30 days.	O'Riordan, Michael 2003
Creatinine Level	Creatinine levels greater than of 1.5 to 3.0 mg/dl had higher 30-day mortality, requirement for prolonged mechanical ventilation, stroke, and renal failure requiring dialysis at discharge than patients with lower creatinine levels.	Anderson, et al 1999
Decreased aortic clamping	Decreased aortic clamping during surgery, lead to better neurologic function and decreased risk or early readmission after CABG.	Muzic, David and Chaney, MA 2006

Table 3: continued

Comorbidity	Remarks	Reference
Diabetes Mellitus	Having diabetes is a significant risk factor for being readmitted within 30 days. Researchers have concluded that diabetes mellitus is a significant independent predictor of early readmission. There is an increased risk of organ failure and early readmission if the patient has poorly treated diabetes mellitus.	O'Riordan, Michael 2003 Sun, X et. Al. 2008 Tung, Avery 2006
Femoral/ popliteal disease	Having femoral/ popliteal disease is a significant risk factor for being readmitted within 30 days.	O'Riordan, Michael 2003
Having a heart attack soon after surgery	Having an MI within one week a significant risk factor for being readmitted within 30 days. An important re-admittance factor after CABG is post-operative MI.	O'Riordan, Michael 2003 Cheng, David C.H. 2006
Hepatic failure	Hepatic failure is a significant risk factor for being readmitted within 30 days.	O'Riordan, Michael 2003

Table 3: continued

Hospital personnel efficiency	Researchers have discovered that many hospitals have the potential for increased efficiency in the postoperative care of patients who have undergone CABG, which would decrease readmission.	Rosen, MPH et. Al. 1999
Hospital stay	Researchers concluded that length of hospital stay after CABG was higher for readmitted patients. An important re-admittance factor after CABG is time in the hospital or LOS.	Sun, X et. Al. 2008 Cheng, David C.H. 2006
Intubation period	Extubation within the first 8 postoperative hours leads to more stable hemodynamics and decreased need for vasoactive medications along with decreased cost and hospital stay and 28% decrease in being readmitted to the ICU.	Cheng, David C. H. 2008
Ischemic heart disease	There is an increased risk of organ failure and early readmission if the patient has ischemic heart disease.	Tung, Avery 2006
Left ventricular dysfunction	There is an increased risk of organ failure and early readmission if the patient has left ventricular dysfunction.	Tung, Avery 2006
Number of blood units used	Amount of blood increased the relative risk of wound complication 1.05 times per unit during CABG.	Loop, FD, et al 1990

Table 3: continued

Comorbidity	Remarks	Reference
Nursing home after surgery	Being admitted to a nursing home after surgery is a significant risk factor for being readmitted within 30 days.	O'Riordan, Michael 2003
Obesity/ Large body surface area	Obesity increased the relative risk of wound complication and early readmission 2.90 times during CABG. Increased body surface area is a significant risk factor for being readmitted within 30 days.	Loop, FD et. Al. 1990 O'Riordan, Michael 2003
Postoperative Acute Renal Failure (ARF) and/or preexisting renal dysfunction	In one study 14% of CABG patients died because of ARF, and this number was doubled if the patient required dialysis. It is important that the patient have good intraoperative cardiac output and circulation and good postoperative cardiac function, also. Dialysis a significant risk factor for being readmitted within 30 days. There is an increased risk of organ failure and early readmission if the patient has renal failure. An important re-admittance factor after CABG is renal failure.	Nunnally, Mark and Sladen, R.N. 2006 O'Riordan, Michael 2003 Tung, Avery 2006 Cheng, David C.H. 2006

Table 3: continued

Comorbidity	Remarks	Reference
Post-operative bleeding	Excessive post-operative bleeding has been associated with early readmission.	Cheng, David C.H. 2006
Sex	The major conclusion of one study was that CABG surgery is associated with lower functional gains and higher readmission rates in women than men 6 months after operation. Being a female is a significant risk factor for being readmitted.	Vaccarino, MD et. Al 2003 O'Riordan, Michael 2003
Stroke	If the patient has had a stroke prior to operation or if the patient suffers a stroke post-operatively, he or she is more likely to be readmitted after CABG.	Cheng, David C.H. 2006
Surgeon's annual CABG volume	Having a surgeon whose volume of annual CABG is less than 100 is a significant risk factor for being readmitted within 30 days.	O'Riordan, Michael 2003

Table 3: continued

Comorbidity	Remarks	Reference
Time on cardiopulmonary pump	Decreased time on the cardiopulmonary bypass circuit lead to better neurologic function and decreased risk of early readmission after CABG. There is an increased risk of organ failure and early readmission the longer the patient is on the on the cardiopulmonary bypass (CPB) circuit during surgery. The degree to which the cytokines of the immune system respond to the CPB may increase the chance of organ dysfunction and eventually failure.	Muzic, David and Chaney, MA 2006 Tung, Avery 2006
Use of TEE	An important re-admittance factor after CABG is use of TEE during surgery.	Cheng, David C.H. 2006

Regional Differences in Readmission Factors

One randomized, non-biased study conducted in 2003 by the Centers for Disease Control assessed the racial, ethnic, and socioeconomic disparities in multiple risk factors for heart disease and stroke in the Unites States (CDC 2003). Random adults throughout the United States, Guam, and The Virgin Islands were called using a random digit dialer. This analysis examined six risk factors for heart disease and stroke: high blood pressure, high cholesterol, diabetes, current smoking, physical inactivity, and obesity. The contacted people reported whether they were ever told by a doctor or other health professional that they had high blood pressure, high cholesterol, or diabetes. Current smoking was defined as having smoked at least 100 cigarettes during one's lifetime and still smoking by the date of the survey. Physical inactivity was assessed by a "no" response to the question, "During the past month, other than your regular job, did you participate in any physical activities or exercises, such as running, calisthenics, golf, gardening, or walking for exercise?" Obesity was defined as having a body mass index ≥ 30.0 kg/m^2 on the basis of self-reported height and weight (National Heart, Lung, and Blood Institute 1998).

The study showed that the contiguous states with the highest percent of people with multiple risk factors for heart disease and stroke were Kentucky (46.2%), Mississippi (45.8), Alabama (45.6%), West Virginia (44.9%), Tennessee (43.2%), and Arkansas (42.4%). The states with the lowest percentage of multiple risk factors for heart disease were Hawaii (27%), Colorado (28.9%), Utah (29%), Montana (29.9%), and New Mexico (30.1%). (Figure 5a and Appendix 1).

The map below (Figure 5b) shows that the concentrations of counties with the highest death rates due to heart disease are located throughout Appalachia, the Southern United States, and along the Mississippi River Valley. Therefore, the regions with the highest percentage of risk factors for coronary artery disease have the most deaths from coronary artery disease.

The regions of the Unites States are divided up into the Southeast, Northeast, Southwest, Midwest, and West. The average percentage of Medicare recipients who received CABG from 1994 to 1999 in the Southeast are 2.845. The average percentage of Medicare recipients who received CABG from 1994 to 1999 in the Northeast are 2.532. The average percentage of Medicare recipients who received CABG from 1994 to 1999 in the Southwest are 2.443. The average percentage of Medicare recipients who received CABG from 1994 to 1999 in the Midwest are 3.109. The average percentage of Medicare recipients who received CABG from 1994 to 1999 in the West are 2.474. Therefore, the regions with the highest average percentage of coronary artery bypass grafting in order from highest to lowest are Midwest, Southeast, Northeast, West, and Southwest (Vaughn-Sarrazin et al. 2002), (as summarized in Appendices 2 and 3, and Figure 6). Furthermore, the regions of the United States with the most risk factors for coronary artery disease and the highest death rates from coronary artery disease also perform the most coronary artery bypass graftings.

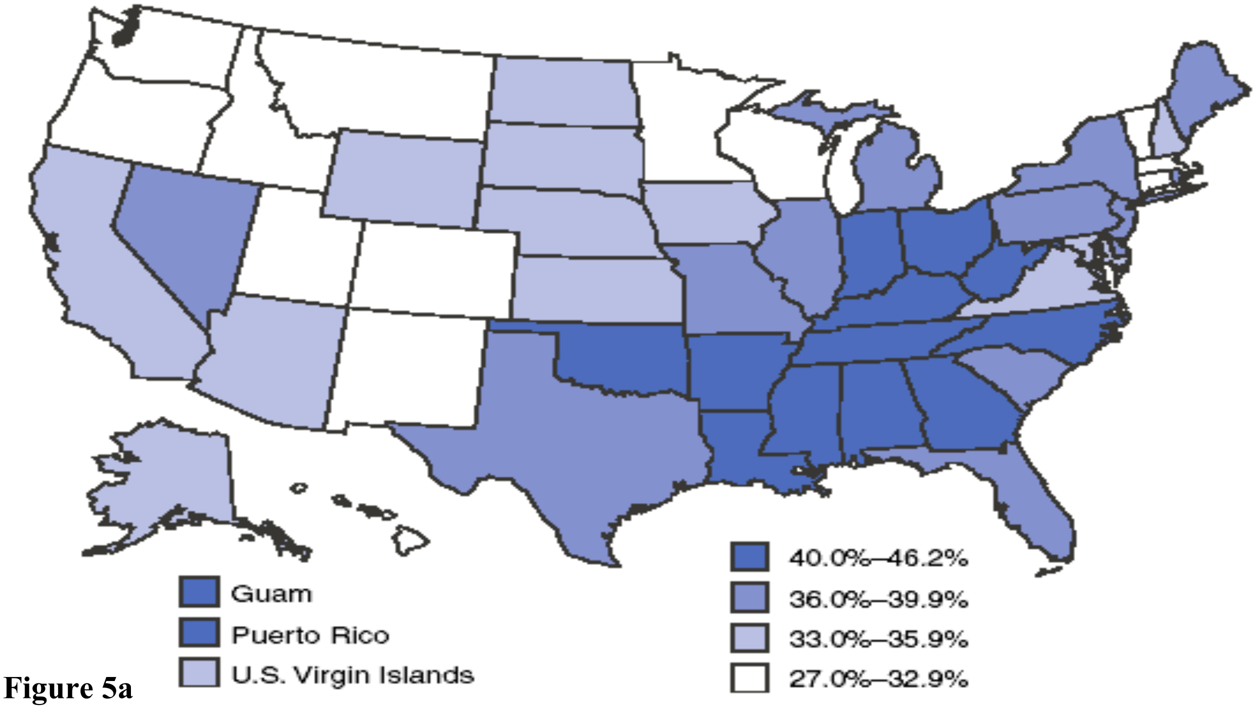

Figure 5a

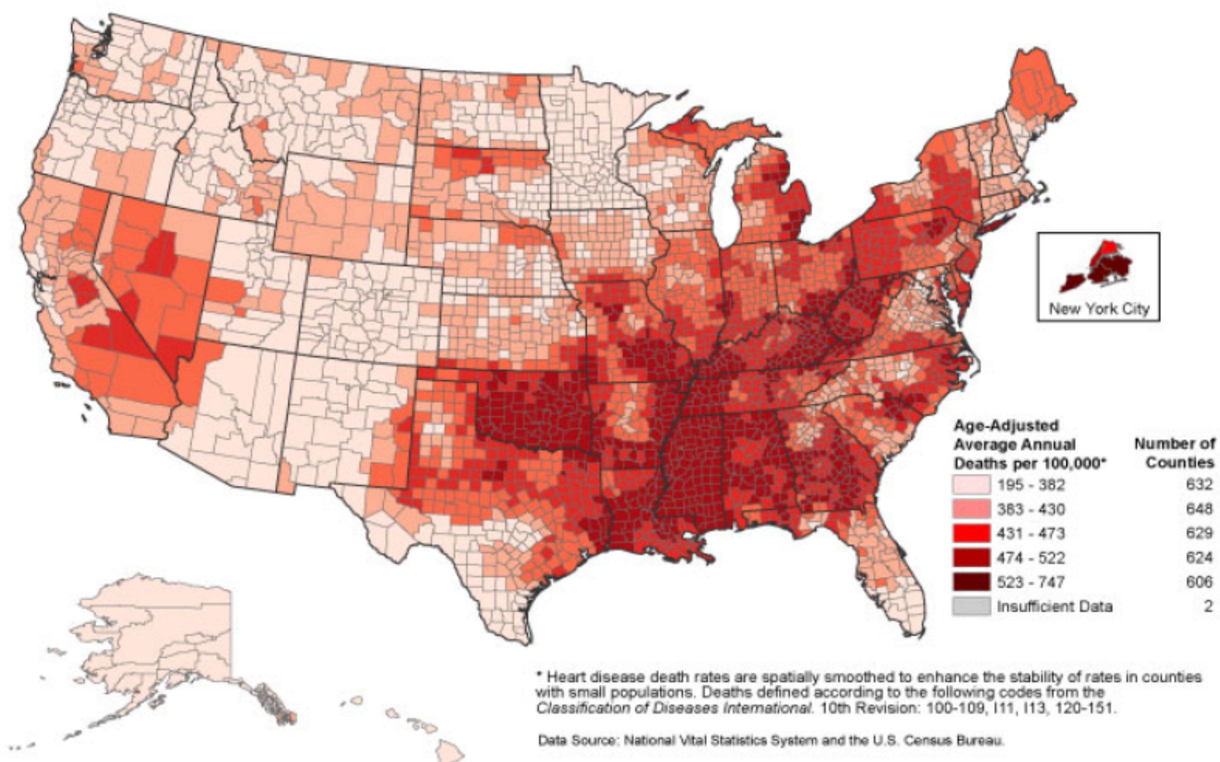

Figure 5b

Figure 5a: Prevalence of Multiple Risk Factors for Heart Disease and Stroke among Adults Aged ≥18 years, by State/Territory (CDC 2003) **Figure 5b:** Heart Disease Death Rates, 2000-2006, Adults Age 35 and Older by County (National Vital Statistics and Census Bureau)

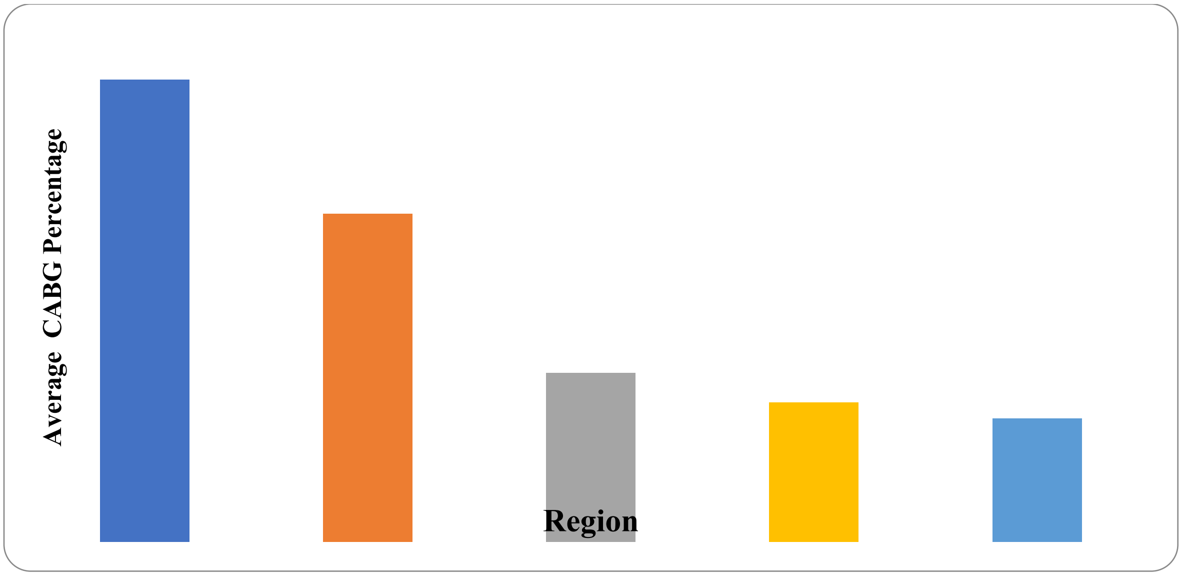

Figure 6: Average Coronary Artery Bypass Grafting of Medicare Patients from 1994-1999 in Different Regions of the United States (based on Vaughn-Sarrazin et al. 2002).

Research Question

Typically after Coronary Artery Bypass Grafting (CABG), the patient goes home after his or her stay in the hospital and lives a relatively normal life as long as he or she maintains a healthy diet, takes medicine at scheduled times, exercises regularly or according to the doctor's orders, and avoids tobacco, drugs, and excess alcohol; however, there are many factors called comorbidites that may lead to the patient being readmitted into the hospital after CABG. It is unknown what the region-specific comorbidities are; therefore, this study will define the factors leading to readmission within 30 days after CABG in one Southeastern medical center by analysis of Medical Record data.

CHAPTER 2: MATERIALS AND METHODS

Data Collection

A case-control study was designed to elucidate comorbidity factors associated with readmission after CABG procedures at a large medical center in the southeastern US. Data on the various patient comorbidities were gathered using the Society of Thoracic Surgeon's (STS) online database, ARMUS. This database was available at the University of Tennessee Medical Center (1924 Alcoa Highway, Knoxville, Tennessee 37920). Patient Medical Records are available only on University of Tennessee computers under HPF WebStation. Access to these records was obtained after (1) patient confidentiality training, (2) IRB approval from both University of Tennessee Health Center and Maryville College (see Appendices 4-8), (3) approval from University Health Systems which owns the Medical Records to view them, and (4) obtaining a private username and password to access the data. Once logged into the database, one can select for various comorbidities with specific parameters from all of the cardiac and pulmonary operations performed within the last 5 years at The University of Tennessee Medical Center. For this study, the parameters selected isolated CABG patients from January 1, 2006 to June 1, 2011 who were readmitted within 30 days.

For the "case" individuals, ARMUS generated 124 patients who had been readmitted within 30 days after isolated CABG within the selected time period. This information was verified by looking at "Operation and Procedure Notes" in the patient Medical Records (MR), after which the population that fit the parameters mentioned above was 91. Next, to verify that the patient actually was readmitted within 30 days after CABG, I searched the MR and confirmed that the patient was readmitted and recorded why the patient was readmitted. The latter information was usually available in the "History and Physical" (H&P) or the "Consultation and Consultation Note;" however, if it was not available there, it was obtained by looking at the "ER Treatment Record." After verification of readmission, there were 60 patients who fit the criteria. ARMUS generated a total patient population of 1493 who underwent CABG from January 1, 2006 to June 1, 2011, so 4.0% of the total population was readmitted within 30 days after CABG surgery.

MR for each case individual was examined to gather comorbidities that ARMUS did not generate, as well as to verify the ARMUS data. Most of the information was available by looking at the patient's "History and Physical" (H&P) or the "Consultation and Consultation Notes." In order to find the laboratory data, I went into "Lab-Final" and recorded the relevant information. Note- hematocrit, WBC count, and platelet values were recorded from the last day of the patient's inpatient stay at the hospital while albumin, bilirubin, cholesterol, glucose, triglycerides, INR, sodium, potassium, calcium, chloride, and BUN values were recorded from the lab data obtained before the patient underwent surgery.

The vital signs, blood pressure, pulse, temperature, oxygen saturation, and respiratory rate recorded are directly prior to entering the operating room, and this data was available in the "Pre-Op/ Pre-Procedure Checklist;" however, some MRs did not have the "Pre-Op/ Procedure Checklist," option, so no information was recorded. All of the comorbidity data was entered into the master Excel spreadsheet, and the selected comorbidites are shown in Table 4. ARMUS did not generate all of the operation times, so this information was found in the "OR Nurse's Notes" from "time room started" to "time ended." ARMUS generated the height of all the patients in centimeters and weight in kilograms, so equation 1 was used to calculate BMI. The normal ranges for laboratory blood products and physiological functioning are shown in Table 5. Furthermore, the New York Heart Association (NYHA) classification scale for heart failure has four classes shown in Table 6.

$$\text{BMI} = \text{Patient weight (kg)/ patient height (m)}^2 \qquad \text{Equation 1}$$

For the control population, random patients who had CABG but were not readmitted were selected and the same comorbidities were evaluated for them using the methods previously mentioned (see Table 4). So the control population was random and unbiased, random numbers were generated with the use of the “RANDBETWEEN” function on Microsoft Excel 2010. The random numbers generated were as follows in numerical order: 14, 21, 41, 71, 84, 97, 108, 142, 168, 174, 175, 178, 187, 203, 267, 297, 298, 312, 330, 332, 401, 453, 471, 509, 607, 658, 686, 704, 719, 732, 734, 767, 799, 801, 814, 815, 819, 826, 827, 892, 897, 940, 985, 996, 1040, 1043, 1059, 1061, 1065, 1066, 1074, 1111, 1128, 1169, 1186, 1203, 1205, 1208, 1252, 1290, and 1300. After these numbers were generated, the patients who were associated with that particular line on the Excel spreadsheet were selected and evaluated.

Table 4: Comorbidities Initially Sampled Using ARMUS and Viewing Medical Records

Demographic	**Pre-Operative**	**Peri-Operative**	**Post-Operative**
Age	ACE or ARB inhibitors	Aprotinin	Acute Limb Ischemia
Alcohol	Angina	Cryo units	Anticoagulation event
BMI	Angina Type	Desmopressin	Aortic dissection
Cigarette Smoker	Anticoagulants	Epsilon amino-caproic acid	Arm infection
Race	Anti-platelets	FFP units	Atrial Fibrillation
Sex	Aspirin	Intra-op blood products	Blood products
	Arrhythmia	MI	Cardiac arrest
	Arrhythmia Type	Number of bypasses	Creatinine
	Beta Blockers	Operation time	Conduit Harvest or Cannulation Site
	Blood Pressure	Surgeon	Coma
	BUN		Cryo Units
	Calcium		Deep Sternal Infection
	Cardiac PCI		Dialysis
	Cardiac Presentation at Admission		Discharge Location
	Cardiogenic Shock		FFP units
	Cerebrovascular Disease		GI event
	Cholesterol		Graft occlusion
	Chlorine		Heart block
	Chronic lung disease		Hematocrit
	Coma		ICU hours
	Congenital HF		ICU hours additional
	COPD		ICU readmit
	Coumadin		Iliac/Femoral Dissection
	Diabetes		LOS
	Dialysis		Mortality status <30days
	Drug allergies		Multi system failure
	Dyslipidemia		Paralysis
	Emergency CABG		Platelet units
	Family History of CAD		Pneumonia
	Glucose		Post-operative events

Table 4: Continued

	Heart Failure within 2 weeks		Pulmonary embolism
	Hematocrit		RBC units
	Hypertension		Readmit reason
	Illicit drug use		Reintubation
	Immunocompromised		Renal failure
	Incidence		Reoperation
	Infectious Endocarditious		Tamponade
	INR		Thoracotomy
	NYHA Classification		TIA
	Oxygen saturation		Septicemia
	Pacemaker		Stroke
	PAD		Valve disorder
	Pneumonia		Ventilator hours initial
	Potassium		Ventilator hours additional
	Previous CABG		Ventilator hours total
	Previous Cardiac Intervention		Vent prolongation
	Previous CVA		WBC count
	Previous CVD		
	Previous Heart Failure		
	Previous MI/ when		
	Previous PCI		
	Previous Stent		
	Pulse		
	Renal Failure		
	Respiratory Rate		
	Resuscitation		
	Sleep Apnea		
	Sodium		
	Steroids		
	Stroke		
	Syncope		
	Temperature		
	TIA		
	Triglycerides		
	Unresponsive Neurologic State		

Table 5: Normal Laboratory Blood and Physiological Value Ranges

Variable	Normal Range
Albumin	3.4- 4.8 g/dL
Bilirubin	0.2-1.30 g/dL
BMI (normal)	19.1-26.4
BMI (overweight)	26.4-32.3
BMI (obese)	>32.3
BUN	8-25 mg/dL
Blood Pressure	120/80 mm Hg
Calcium	8.8-10.6 mg/dL
Cholesterol	112-200 mg/dL
Chloride	112-200 mg/dL
CO2	20-29 mm Hg
Creatinine	0.7-1.5 mg/dL
Glucose	83-99 mg/dL
Hemoglobin	14-18 g/dL
Hematocrit	42-52%
INR	0.9-1.10
Oxygen Saturation	97-100%
pH	7.360-7.440
Platelets	$130\text{-}400\times10^{-3}$
Potassium	3.5-5.3meq/L
Sodium	136-147meq/L
Temperature	37°C
Triglycerides	0-150mg/dL
WBC	$4.8\text{-}10.8\times10^{-3}$

Table 6: New York Heart Association (NYHA) Classification Scale for Heart Failure (The Criteria Committee).

NYHA Class I	involves no symptoms at any level of exertion and no limitation in ordinary physical activity;
NYHA Class II	Mild symptoms and slight limitation during regular activity. Comfortable at rest.
NYHA Class III	Noticeable limitation due to symptoms, even during minimal activity. Comfortable only at rest.
NYHA Class IV	Severe limitations. Experience symptoms even while at rest (sitting in a recliner or watching TV).

Statistical Analysis

Multiple regression analysis models were built using Minitab 16 (Minitab, Inc., Station College, PA) with readmission/no readmission being dependent on eleven categories (demographics, vital signs, three groups of blood products, glucose and its influence, respiratory, surgical circumstances, medications, heart condition, and other). Five variables (±2 depending on category) were assessed in each of the 11 categories (see Table 7). To use multiple regression in Minitab 16, once all of the data had been collected in the Excel spreadsheet, it was simply copied and pasted into a Minitab document. Then "Stat" along the top row of commands was clicked followed by the "Regression" and "Binary Logistic Regression." "Readmission" was selected for the box labeled "Response in response/frequency format." The comorbidities for each category were then selected to be placed in the box labeled "Model," and if any of the categories contained text they were also selected for the box labeled "Factors (optional)" after which "OK" was clicked. Minitab then produced statistics for each category, and the P-Value was what we were interested in. If the P-Values ≤0.05, further multiple regression models were performed until only the values ≤0.05 were left.

CHAPTER 3: RESULTS

Over the period of January 1, 2006 to May 1, 60 of 1493 patients were readmitted within thirty days after isolated CABG at UT Medical Center Knoxville. Of the 129 comorbidities researched, 13 had significant P-Values ≤0.05 between the readmitted and non-readmitted groups (see Table 8). The overall P-Values for the eleven categories (Demographics, Vital Signs, Heart Condition, Blood Products A, Blood Products B, Blood Products C, Glucose and its Influence, Respiratory, Surgical Circumstances, Medications, and Other) were determined using Minitab linear regression models, and they are shown in Table 7.

The individual factors determined significant within their category were grouped into a Minitab multiple regression model, and results are shown in Table 9. The final comorbidities that had P-Values ≤0.05 were hemoglobin (-) and pre-operative body temperature (-). The means of all of the significant comorbidities for both the readmitted and non-readmitted groups were calculated and are shown in Table 10.

The factors deduced from the Minitab multiple regression models to significantly influence readmission were hemoglobin levels <9.97, pre-operative creatinine, lower temperature, higher angina rates, elevated BUN levels, absence of epsilon amino caproic acid , introperative blood products, prolonged LOS Admit to discharge, and LOS Surgery to discharge, elevated mean pre-operative blood pressure, elevated post-operative creatinine, post-operative events, and previous stent (see Figure 10).

Table 7: Categories (5±2 variables) Selected for Multiple Regression Analysis and P-Value. Bold variables were significantly correlated with readmission at the individual level within columns that had P-Values ≤0.05

Demographics	Vital Signs	Heart Condition	Blood Products A	Blood Products B	Blood Products C
Age	**Mean blood pressure**	Prior-MI	Carbon dioxide	Blood products	Calcium
BMI	**Temperature**	**Angina**	Sodium	**Intraoperative blood products**	Hematocrit
Sex	Respiratory rate	Angina Type	Potassium	Intraoperative platelets	WBC
Admit to Surgery	O_2 saturation	NYHA class	Chloride	**Intraop Epsilon amino caproic acid**	Platelets
Surgery to Discharge	Pulse	PAD	**BUN**	**Pre-operative creatinine**	Dyslipidemia
Admit to discharge		Postoperative Atrial Fibrillation		**Post-operative creatinine**	
				Last creatinine	
P<0.001	**P=0.001**	**P<0.001**	**P=0.046**	**P<0.01**	P=0.324

Table 7 (continued)

Glucose and its Influence	**Respiratory**	**Surgical Circumstances**	**Medications**	**Other**
Glucose	Cigarette smoker	Surgeon	ACE/ARB inhibitors	ICU hours
Hemoglobin	COPD	Number of bypasses	Anticoagulants	**Previous stent**
pH	Chronic lung disease	Operation Time	Aspirin	**Post-operative events**
Diabetes	Ventilator hours	Prior cardiovascular intervention	Beta Blockers	
Hypertension		Month	INR	
			Plavix	
P=0.007	P=0.259	P=0.055	P=0.068	**P=0.011**

Table 8: Individual P-Values ≤0.05 From the Categories with Overall P-Values ≤0.05

Factor	**P-Value**
Angina (+)	<0.001
BUN (+)	0.018
Epsilon amino caproic acid (No)	0.021
Hemoglobin	0.004
Introperative blood products (+)	0.049
LOS Admit to discharge (+)	<0.001
LOS Surgery to discharge (+)	0.002
Mean blood pressure (+)	0.009
Post-operative creatinine (+)	0.006
Post-operative events (+)	0.039
Pre-operative creatinine (-)	0.019
Temperature (-)	0.002
Stent (+)	0.019

Table 9: Calculated Significant P-Values from Regression Model of the Ten Individual P-Values that were ≤0.05

Factor	P-Value
Epsilon amino caproic acid (No)	0.028
Hemoglobin (-)	0.044
LOS Admit to discharge (+)	0.002
LOS Surgery to discharge (+)	0.004
Temperature (-)	0.033

Table 10: Means of Significant Comorbidities in Readmitted and Non-Readmitted Groups (±SE)

Comorbidity	Readmitted	Non-readmitted
Angina	93.3%	93.1%
Blood pressure	108.2 ±3.28SE	100.4 ±1.91SE
Blood products	36.7%	32.3%
BUN	20.6 ±1.63SE	15.0 ±0.85SE
Epsilon amino caproic acid	48.3%	81.5%
Hemoglobin	8.6 ±0.26SE	9.97 ±0.15SE
LOS Admit- Discharge	8.45 ±0.43SE	7.55 ±0.60SE
LOS Surgery-Discharge	2.07 ±0.32SE	0.81 ±0.17SE
Post-operative creatinine	1.53 ±0.22SE	0.97 ±0.12SE
Post-operative events	56.7%	33.6%
Pre-operative creatinine	1.31 ±0.22SE	1.03 ±0.14SE
Temperature	97.9°F ±0.12SE	98.2°F ±15.51SE
Stent	53.3%	27.3%

CHAPTER 4: DISCUSSION

Over a 5 and a half year period, 60 patients of 1493 total patients (4.0%) were readmitted to the University of Tennessee Medical Center Knoxville after isolated CABG procedure. This study identified 13 significant comorbidities from 11 categories that led to readmission within 30 days after CABG. The most outstanding category was "Blood Products B" with 4 of the 7 comorbidities having a significant value. This study confirms the findings in other studies that angina, length of stay, post-operative events, intraoperative blood products, blood pressure, creatinine, and hemoglobin are significantly associated with readmission after CABG, but it also identifies epsilon amino caproic acid, pre-operative temperature, and previous stent as comorbidities associated with readmission after CABG.

Factors Associated with Readmission

Angina, or angina pectoris, is defined as discomfort, tightening or pressure occurring in the chest due to lack of blood flow to the muscle. The pain may be felt in the jaw and inner-left arm and occasionally both arms (Litin 2005). The sensation is usually accompanied by a feeling of suffocation and impending death. These attacks are usually related to exertion, emotional distress, eating, and exposure to intense cold (Como 2006). A previous study reaffirmed that patients with angina/chest pain are at increased risk of being readmitted after CABG (Järvinen, Otso 2003). It is expected that a patient with positive angina symptoms would have an increased risk of readmission after CABG, because these patient's lack of blood flow and myocardial anoxia is due to atherosclerosis and which is the cause of coronary artery disease to begin with.

Hemoglobin is the iron-containing pigment of red-blood cells that carries oxygen from the lungs to the tissues (Venes 2005). A person with low hemoglobin is said to be anemic. There are several causes of anemia, but all forms lead to decreased oxygen transport throughout the body. Therefore, a low hemoglobin level, which was significantly identified in this study, implies a lower than average oxygen transportation throughout the body which has many negative implications. Anemic patients who undergo cardiac surgery have increased risks of postoperative adverse effects: patients with hemoglobin <11g/dL showed an increased incidence of all postoperative events. The extent of preexisting comorbidities also significantly affected peri-operative anemia tolerance (Kulier 2007). The presence of preoperative anemia has been independently associated with acute kidney injury after CABG, which may lead to the BUN and creatinine abnormalities found in the present study(De Santo 2009). One study determined that anemic patients had increased rates of mortality, 12.9% compared to 2.2% of non-anemic patients (Boening 2011).

Blood pressure is the force exerted by the blood against any unit area of the vessel wall, so for instance if one has a blood pressure of 70, this means that the force exerted by the blood is sufficient to push a column of mercury up to a level of 70 millimeters high against gravity (Guyton and Hall 2011). Mean blood pressure is the average of the systolic and diastolic pressures, so if one has a systole of 120 and a diastole of 80, the mean blood pressure is 100; therefore, hypertension means the heart has to work harder than normal to pump blood throughout the body (Dugdale, 2011). High blood pressure, hypertension, can cause a plethora of other health problems including myocardial infarction, stroke, heart failure, arterial aneurysm, and chronic kidney failure (Pierdomenico et al. 2009). Subsequently, it would be expected that hypertension would be an important factor in being readmitted after CABG. Interestingly, an extensive study concluded that CABG patients with arterial blood pressure ranges between 80-100 mm Hg had better postoperative outcomes than patients with arterial blood pressures between 50-60 mm Hg: the overall incidence of combined cardiac and neurologic complications was significantly lower in the high pressure group at 4.8% than in the low pressure group at 12.9% (Gold 1995). However, the arterial pressures of the readmitted group in this study were above 100 mm Hg, 108.2 ±3.28SE, while the non-readmitted group had values of 100.4 ±1.91SE, which is consistent with the previous study.

Creatinine is the measure of the decomposition product of phosphocreatinine, a source of energy for muscle contraction, metabolism. Increased quantities of creatinine are associated with advanced stages of renal disease (Venes 2005). Anderson, et al. (1999) also found that increased creatinine levels increased the probability of being readmitted within 30 days after CABG. Conversely, creatinine decreases with age as a result of decreased muscle mass (Como 2006). It was unforeseen that both decreased pre-operative creatinine and elevated post-operative creatinine would be significant factors. It is known that creatinine decreases with age due to decreased muscle mass and that increased creatinine is indicative or renal failure, but what accounts for the drastic change in creatinine levels before and after surgery is perplexing.

Patients with occult renal insufficiency and abnormal creatinine levels, especially older women with lower BMIs, have a higher risk of mortality, renal failure, prolonged hospital stay, atrial fibrillation, and prolonged ventilation than patients with normal renal function (Najafi 2009). Clearly, if a patient experiences these symptoms, they will have an increased risk of being rehospitalized, and this could explain the significance detected.

Blood urea nitrogen (BUN) is a measure of the amount of urea in the blood. Urea forms in the liver as the end product of protein metabolism, circulates in the blood, and is excreted in the urine via the kidney. The BUN is directly related to the metabolic function of the liver and excretory function of the kidney (Como 2006). If the BUN is critically elevated, it indicates renal function impairment, which has negative implications for many bodily functions such as: unregulated blood pressure; unregulated osmolarity and electrolyte concentrations; decreased ability to excrete metabolic waste products and foreign products; decreased secretion, reabsorption, metabolism of hormones, and decreased gluconeogenesis. The results of the study by Najafi, et al. (2009) are also applicable to BUN, because someone with occult renal insufficiency would also be expected to have abnormal BUN values, and as the results of the study indicate, these patients have higher risks of mortality, renal failure, prolonged hospital stay, atrial fibrillation, and prolonged ventilation than patients with normal renal function.

As shown in Table 5, the typical physiologic temperature range is 37°C, 98.6°F, and a decreased temperature, which was found to be significant in this study, can lead to decrease in overall body functions, and if the temperature gets too low death can occur. Also, pH increases with lower body temperatures leading to a decrease in respiratory rate and increased neuronal excitability. A previous study (Muzic 2006) actually found that cooling the body during surgery while on the cardiopulmonary bypass pump was beneficial and led to a decrease in readmission after 30 days, but the effects of low body temperature before surgery were not discussed.

The administration of introperative blood products is usually associated with an excessive loss of blood during surgery, so perceptibly if the patient was bleeding out during surgery it may be an indicator of other bodily problems. A previous study also by Loop et al. (1990) also found that use of intraoperative blood units increased the relative risk of wound complication 1.05 times per unit during CABG. According to the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists Clinical Guidelines (Ferraris 2007), during cardiovascular surgery, blood should be conserved only for the high-risk subset, patients who have the following: (1) advanced age, (2) low preoperative red blood cell volume (preoperative anemia or small body size), (3) preoperative antiplatelet or antithrombotic drugs, (4) reoperative or complex procedures, (5) emergency operations, and (6) noncardiac patient comorbidities.

Epsilon amino caproic acid (EACA) is an antifibrinolytic agent used in cardiac surgery to decrease postoperative bleeding (Kluger 2003). It may also be given to treat excessive blood loss due to increased fibrinolytic activity in the blood (Venes 2005). A recent study determined that EACA is as effective as the classic antifibrinoytic, aprotinin, at reducing fibrinolysis and blood loss in patients undergoing primary, isolated CABG (Greilich 2009). The absence of administration of this agent during CABG was significantly associated with readmission within 30 days in the present study, which is expected because its administration would lead to a decrease in bleeding. However, one study concluded that the use of EACA should be limited only to high-risk patients, because of the side effects such as nausea and vomiting up to fibromyalgia and organ failure, and significantly found in their study, renal insufficiency (Martin 2011).

Post-operative events including post-operative arrhythmias, bleeding, renal failure, and gastrointestinal events have previously been shown by Cheng (2006), Nunnally (2006), O'Riordan (2003), and Tung (2006) to be associated with readmission within 30 days after CABG. This is most likely due to the fact that if a patient has problems after surgery while still in the hospital that patient has an increased risk of having problems after being released from the hospital.

If a patient has already received a stent at some point in his or her life, he or she has had previous cardiac blockage which required a stent to be placed in the first place, so they may be predisposed to another cardiac event. One extensive study evaluated the effectiveness of stenting and CABG, and it was found that CABG actually had higher 8-year survival rates than stenting, 78.0% for CABG and 71.2% for stenting (Wu 2011). However, the extent of previous stent and readmission after CABG is not well elucidated.

LOS has been shown in previous studies (Sun 2008 and Cheng 2006) to be longer in patients who were readmitted with 30 days after CABG. The reason for this is most likely that the longer one stays in the hospital evidently means that the patient has problems that require him or her to stay in the hospital for an extended period of time. Also, the longer one stays in a hospital, the more exposure he or she has to bacterial and viral pathogens which further leads to sickness especially in someone who has just had surgery and whose immune system is already compromised.

Factors Not Associated with Readmission

Surprisingly, age, smoking, sex, and increased BMI were not significant comorbidities for readmission in this study. It was expected that these factors would positively affect readmission due to prior research and because the vast majority of people who smoke and/or have large BMIs are usually in worse health than the person who does not have these problems. These patients are also more susceptible to atherosclerosis which in turn can lead to further cardiac complications. There is ample research that indicates these factors are comorbidities for initially having coronary artery disease and CABG, but they do not seem to play a significant role in being readmitted after CABG. Race did not factor into this study since there are very few patients who were not Caucasian.

Remarkably, the presence of diabetes was also not identified as being significant. Diabetes is connected to many negative health conditions including hyperglycemia, increased blood pressure, peripheral arterial disease, neuropathy, and increased risk of heart disease and stroke. Diabetes is also well correlated with leading to coronary artery disease and requiring CABG in the first place, but it is not a significant comorbidity in being readmitted after surgery.

It is pleasing to report that surgical circumstances were not found to be significant, so most importantly the Surgeon performing the surgery did not influence whether or not the patient was readmitted within 30 days after CABG. However, it was unexpected that number of bypasses and operation duration did not have a higher significance since it would be logical to assume that the longer a patient is operated on and the more bypasses a patient has, the more likely there is room for error and further complications.

Conclusion and Recommendations

As a result of this study, it is recommended that the University of Tennessee Medical Center Knoxville take extra precautions with CABG patients who have decreased hemoglobin levels, pre-operative creatinine levels >1.03, temperature <98.24°F, angina, BUN levels >14.98, not received intraoperative epsilon amino caproic acid , received introperative blood products, LOS Admit-Surgery >0.81 days, LOS Admit-Discharge >7.55 days, mean pre-operative blood pressure >100.4mmHg, post-operative creatinine >0.97, post-operative events, and who have previously had a stent, to correct these problems, so they are not readmitted within thirty days after operation. It is hoped that implementing these recommendations will lower readmission rate within thirty days after coronary artery bypass grafting, thus lowering medical costs, increasing hospital bed space, and increasing overall well-being of CABG patients.

People living in the Southeastern U.S. have the highest risk factors for coronary artery disease, and 43.2% of the citizens of Tennessee have multiple risk factors for heart disease and stroke (CDC 2003). The percentage of Medicare patients who have undergone CABG in the Southeast is 2.85, but whether or not these patients were readmitted is not known (Vaughn-Sarrazin et al. 2002). Further studies need to identify what the rates of readmission are within 30 days after CABG in the different geographic regions of the United States, and whether or not the significant comorbidties associated with readmission found in the present study are also significant in other geographical regions.

APPENDIX

Appendix 1: Prevalence of Multiple Risk Factors for Heart Disease and Stroke in Adults Age 18≥ by State/ Territory (CDC 2003)

State/Territory	No. of respondents†	(%)§	(95% CI¶)
Alabama	3,240	(45.6)	(±1.9)
Alaska	2,573	(33.7)	(±2.5)
Arizona	3,102	(33.6)	(±2.4)
Arkansas	4,108	(42.4)	(±1.7)
California	4,210	(33.5)	(±1.7)
Colorado	3,954	(28.9)	(±1.5)
Connecticut	5,098	(31.4)	(±1.4)
Delaware	3,943	(39.2)	(±1.9)
District of Columbia	1,943	(36.0)	(±2.6)
Florida	4,860	(38.0)	(±2.0)
Georgia	7,434	(40.0)	(±1.5)
Hawaii	4,158	(27.0)	(±1.6)
Idaho	4,869	(32.3)	(±1.5)
Illinois	5,053	(37.9)	(±1.8)
Indiana	5,327	(41.0)	(±1.4)
Iowa	4,903	(34.5)	(±1.5)
Kansas	4,504	(34.4)	(±1.5)
Kentucky	7,445	(46.2)	(±1.7)
Louisiana	4,927	(41.6)	(±1.5)
Maine	2,325	(36.0)	(±2.1)
Maryland	4,248	(35.7)	(±1.8)
Massachusetts	7,263	(32.5)	(±1.3)
Michigan	3,490	(39.8)	(±1.8)
Minnesota	3,809	(31.9)	(±1.6)
Mississippi	4,298	(45.8)	(±1.7)
Missouri	4,150	(38.9)	(±2.0)
Montana	3,927	(29.9)	(±1.8)
Nebraska	4,823	(33.7)	(±1.5)
Nevada	2,842	(36.7)	(±2.4)
New Hampshire	4,878	(33.6)	(±1.5)
New Jersey	10,819	(36.0)	(±1.0)
New Mexico	5,298	(30.1)	(±1.4)
New York	5,318	(37.3)	(±1.5)
North Carolina	9,109	(40.4)	(±1.5)
North Dakota	2,947	(34.1)	(±1.8)
Ohio	3,685	(40.3)	(±1.9)
Oklahoma	7,457	(41.0)	(±1.3)
Oregon	3,890	(32.6)	(±1.6)
Pennsylvania	3,586	(37.9)	(±1.7)
Rhode Island	3,914	(36.5)	(±1.7)
South Carolina	5,753	(39.8)	(±1.4)
South Dakota	5,139	(34.4)	(±1.4)
Tennessee	2,539	(43.2)	(±2.1)
Texas	5,741	(39.2)	(±1.4)
Utah	3,893	(29.0)	(±1.8)
Vermont	4,156	(30.7)	(±1.5)
Virginia	5,286	(35.8)	(±1.6)
Washington	18,089	(32.9)	(±0.8)
West Virginia	3,295	(44.9)	(±1.9)
Wisconsin	3,966	(32.8)	(±1.6)
Wyoming	3,924	(35.8)	(±1.6)
Guam	766	(43.6)	(±4.0)
Puerto Rico	3,934	(42.7)	(±1.9)
U.S. Virgin Islands	1,947	(35.0)	(±2.7)
Total	**256,155**	**(37.2)**	**(±0.3)**

* Two or more of the following: high blood pressure, high cholesterol, diabetes, obesity, current smoking, or physical inactivity.
† Unweighted number of survey respondents for each state and territory.
§ Weighted percentages are age-standardized to the 2000 U.S. standard population.
¶ Confidence interval.

Appendix 2: Percentage of Medicare Patients who Underwent Coronary Artery Bypass Grafting from 1994-1999.

State	Number of Medicare Beneficiaries	Number of CABG from 1994-1999	Percentage
AL	550,163	20,282	3.69
AK	32,605	723	2.22
AZ	575,028	11,842	2.06
AR	357,492	13,769	3.85
CA	3,366,853	64,671	1.921
CO	227,021	6,747	2.97
CT	455,803	12,341	2.71
DE	95,155	2,569	2.7
FL	2,474,750	66,379	2.68
GA	733,325	22,520	3.07
HI	146,960	2,636	1.79
ID	140,873	3,856	2.74
IL	1,438,054	47,293	3.29
IN	731,674	22,850	3.13
IA	427,560	12,979	3.04
KS	347,209	10,766	3.1
KY	487,407	18,553	3.81
LA	494,756	14,919	3.02
ME	178,090	4,980	2.8
MD	560,495	14,604	2.61
MA	826,440	17,597	2.13
MI	1,192,624	38,806	3.25
MN	577,978	14,306	2.48
MS	328,066	9,812	2.99
MO	734,787	23,287	3.17
MT	117,072	3,115	2.66
NE	226,462	7,484	3.3
NV	197,533	4,485	2.27
NH	143,987	3,968	2.76
NJ	1,064,595	26,054	2.45
NM	194,640	3,685	1.89
NY	2,326,974	54,662	2.35
NC	920,847	27,951	3.04

ND	92,750	3,005	3.24
OH	1,474,607	45,922	3.11
OK	435,684	13,083	3
OR	428,343	9,291	2.17
PA	1,869,561	53,782	2.87
RI	148,878	2,988	2.01
SC	451,965	13,413	2.97
SD	106,101	3,750	3.53
TN	670,572	24,943	3.72
TX	1,933,116	54,525	2.82
UT	176,863	4,566	2.58
VT	74,236	1,824	2.46
VA	744,647	20,161	2.71
WA	633,368	13,338	2.11
WV	271,032	11,306	4.17
WI	689,230	21,089	3.06
WY	56,169	1,598	2.85

Appendix 3: Average Coronary Artery Bypass Grafting of Medicare Patients from 1994-1999 in Different Regions of the United States

Region	States	Percentage of CABG
Southeast	Alabama, Arkansas, Florida, Kentucky, Louisiana, North Carolina, Mississippi, South Carolina, Tennessee, Virginia, and West Virginia	3.69, 3.81, 2.68, 3.02, 3.04, 2.99, 2.97, 3.53, 2.71, 2.85 **Average of 2.845**
Northeast	Connecticut, Delaware, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont	2.71, 2.7, 2.8, 2.61, 2.13, 2.76, 2.45, 2.35, 2.87, 2.01, 2.46 **Average of 2.532**
Southwest	Arizona, New Mexico, Oklahoma, and Texas	2.06, 1.89, 3, 2.82 **Average of 2.443**
Midwest	Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Ohio, Nebraska, North Dakota, South Dakota, and Wisconsin	3.29, 2.74, 3.04, 3.1, 3.25, 2.48, 3.17, 3.11, 3.3, 3.24, 3.53, 3.06 **Average of 3.109**
West	California, Colorado, Idaho, Montana, Nevada, Oregon, Utah, Washington, and Wyoming	1.92, 2.97, 2.74, 2.66, 2.27, 2.17, 2.58, 2.11, 2.85 **Average of 2.474**

Maryville College

Maryville College Institutional Review Board
OHRP IRB#: IRB00007383
FWA Assurance #: FWA00015150

Principal Researcher: Jason Eli Johnson

Faculty Supervisor: Dr. Drew Crain

Division: Natural Sciences

Title: *Significant comorbidity factors that lead to unexpected readmission within 30 days after coronary artery bypass grafting*

Protocol# 020511-01

Approval Status: Approved

May 4, 2011

Dear Jason

The Maryville College Institutional Review Board (IRB) has carefully considered your proposal referenced above. The proposed procedures afford reasonable protection to the human participants involved and therefore you are granted approval for the study.

Your approval is effective May 4, 2011 and will expire one year from this date. Thereafter, continued approval is contingent upon submission of a progress report that must be reviewed and approved prior to the expiration date.

Approval is contingent upon your agreement to obtain informed consent from your participants, to abide by the protocol summarized in the approved IRB application, to obtain IRB approval or exemption from any satellite institutions involved in the project, and to keep appropriate records concerning your participants.

You are required to submit to the Maryville College IRB for review any changes in procedures involving human participants prior to the implementation of such changes.

If you have any questions concerning this approval or regulations governing human participant activities, please contact Dr. Chad Schrock, Chair of the Maryville College IRB at 865.981.8268, e-mail at chad.schrock@maryvillecollege.edu.

Sincerely,

Chad Schrock

Dr. Chad Schrock
Chair, Maryville College Institutional Review Board

502 E. Lamar Alexander Parkway, Maryville, Tennessee 37804-5907
Voice 865.981.8000 | Fax 865.981.8010 | maryvillecollege.edu

Appendix 5: Human Participants Research Proposal Form from Maryville College

MARYVILLE COLLEGE
Human Participants Research Proposal Form

Principal researcher(s): Jason Eli Johnson

Faculty sponsor (if applicable): Dr. Drew Crain

Division: Biology

Mailing address of the principal researcher: P.O. Box 2499

Title of proposed research: Significant Comorbidity Factors that Lead to Unexpected Readmission Within 30 Days after Coronary Artery Bypass Grafting

Proposed starting date: April 1, 2011

Ending date: December 15, 2011

Purpose and objectives of proposed research: (attachments as necessary)

The purpose of this retrospective study is to determine whether there are any correlations between significant comorbidities such as renal failure, postoperative length of stay, and Coumadin dosage that positively predict whether or not a patient will be unexpectedly readmitted to the hospital after coronary artery bypass grafting, also known as CABG.

Participants:

I will have access to 112 patient charts from 2008, 2009, and half of 2010 of patients who were readmitted within 30 days after coronary artery bypass surgery to the University of Tennessee Medical Center Knoxville. I will not actually come into contact with any patients.

Appendix 5 (continued)

Anonymity / Confidentiality:

In order to maintain anonymity/confidentiality, I will create a secured master list on an Excel spreadsheet that is password protected, and only I will have the password. I will link that MRN to a specific identifier: for instance, if the Medical Record Number is 0123456789 the study number would be 001, etcetera for the rest of the MRNs, so I would only need to use the study number 001, 002 etc. on the separate data collection Excel spreadsheet to perform statistical analyses. Once all of the data is collected, I will completely delete the master list of medical record numbers.

Methods and procedures:

I will have access to 50 different comorbidities, and I will statistically analyze them for correlations with being readmitted within 30 days after coronary artery bypass grafting. Once I have established the top 5-10 comorbidities, I will investigate the patient records more closely and see if there is another ideology for causation or correlation for being readmitted.

I am working under the supervision of cardiothoracic surgeon Dr. John Mack at UT Medical Center, so I completed an IRB at UT, (see attached). At UT, retrospective studies can undergo an expedited process, and since it is a retrospective study, there is a waiver for informed consent as long as I eliminate any identifying factors immediately. Also, I am an employee at UT Medical Center, so I have undergone orientation and HIPPA training.

Principal Researcher Jason E. Johnson ________ Signature **Faculty Supervisor** ________ Signature

Committee Approval ________ Signature **Date** 5-4-2014

Appendix 6: IRB approval from University of Tennessee Medical Center, Knoxville

THE UNIVERSITY of TENNESSEE UT
HEALTH SCIENCE CENTER

GRADUATE SCHOOL of MEDICINE

April 14, 2011

Institutional Review Board - FWA 2301
IORG Registration Number 0000051
1924 Alcoa Highway, U-76
Knoxville, TN 37920
Phone: 865-305-9781
865-305-9275
http://gsm.utmck.edu/irb

Jason E. Johnson
Department of Anesthesiology
University of Tennessee Medical Center
1924 Alcoa Highway
Knoxville, TN 37920

IRB ACTION: Determination that research qualifies for IRB exemption

RE: IRB #3199 Retrospective Study: Significant Co morbidity Factors Leading to Unexpected Readmission within 30 Days after CABG (January 1, 2008 through June 30, 2010)

Dear Mr. Johnson,

Thank you for allowing the IRB to review the above referenced proposed study. Based upon the information that you have provided, the IRB has determined that the research listed above qualifies for exemption from IRB review based upon 45 CFR 46.101 (b).

- Research involving the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. [45 CFR 46.101(b)(4)]

This is a formal response so that you will have in your record documentation that you sought the opinion of the IRB. So long as the project remains as described in your correspondence with the IRB, no further action is required on your part. However, if your project changes concerning any of the factors upon which this decision is based, please contact this office again for further review.

Thank you for informing this office of the above referenced project.

Sincerely,

Kimberly C. Mason, PharmD
Chair
Institutional Review Board

KCM: rl

Appendix 7: Addendum to IRB approval

Leslie, Reni M RLeslie@mc.utmck.edu to me show details Oct 20 Reply

Normally you need to submit a revision form. However, since you are not on this campus I approve the revision in the dates changing them to January 1, 2006 through May 1, 2011. Please use this email as official IRB approval. Print it and keep it in your IRB file.
Reni

Reni Leslie
Associate Director
Institutional Review Board
UT Graduate School of Medicine
FWA 2301
rleslie@utmck.edu
Phone: (865) 305-9781
FAX: (865) 305-9275
IRB Satisfaction Survey

Chad Schrock chad.schrock@maryvillecollege.edu to me show details Oct 21 Reply

That sounds fine to go ahead and complete Jason, as you are not changing protocol or source of data, only the scope.
Dr. Schrock

From: Jason Johnson [mailto:jason.johnson@my.maryvillecollege.edu]
Sent: Thursday, October 20, 2011 7:32 PM
To: Chad Schrock
Subject: Jason Johnson IRB
- Show quoted text -

Appendix 8: Certificate of Completion for Human Subject Research Training

Protecting Human Subject Research Participants — Page 1 of 1

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Jason Johnson** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 02/27/2011

Certification Number: 640730

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