Recognition of Atypical Myocardial Infarctions in the Older Adult Presenting to the Emergency Department

By

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A Dissertation

Presented to
Oregon Health & Science University
School of Nursing
In partial fulfillment
Of the requirements for the degree of
Doctor of Philosophy

April 25, 2007

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ACKNOWLEDGEMENTS

I would like to thank Linda Felver, my dissertation chair, for her solid belief that my subject was of interest, and that my abilities would be sustainable to complete this project, and especially for her encouragement and support. I would like to thank George Knafl for his well-defined statistical support and clarity of thinking. To Renee Hoeksel, thank you for your impromptu talks, clarity to my direction in this process, and your tireless support.

I would like to acknowledge the leadership of the emergency departments, present and past, and my clinical practice support colleagues for their strong support, their listening ears, and for being the 'cheering section'. A special thanks to Dr. Rose for her review of the results chapter and insightful, timely suggestions.

Finally, I would like to give a special thanks to Lin and her family, Ken and Kelly, for their love, undying support, encouragement, special meals, and constant faith in my abilities.

ABSTRACT

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Reducing the risk of delayed treatment to patients in the emergency department is a constant challenge. Recognizing atypical presentations of myocardial infarctions is a clinical challenge in the emergency department. Without the presence of chest pain, the staff is not cued to suspect a myocardial infarction, consequently delaying the onset of diagnostic interventions. To increase the care efficiency for patients with atypical symptoms of myocardial infarction, this study aimed to establish a pattern of presentation signs and symptoms, sample characteristics, risk factors and previous medical events to determine whether or not these patients have had a myocardial infarction.

The present study demonstrated that 38.6% (CI of 35-42%) of patients diagnosed with a myocardial infarction presented to the emergency department with atypical signs and symptoms that would be considered "unrecognized". Previous studies have found between 24-40% subjects had "unrecognized" myocardial infarctions.

The sample consisted of 316 subjects (171-54% with myocardial infarction) taken from the census of two hospital emergency departments, one urban setting and one community setting. The inclusion criteria were subjects who presented to the emergency department with dizziness or shortness of breath or were diagnosed with a myocardial infarction. The study was a retrospective descriptive chart review between April 2004 and August 2006.

The variable that showed strongest evidence to suspect an atypical presentation of myocardial infarction was pain in other areas of the body, not in the chest ($p = 0.0001$). Other variables which would provide prompts to suspect a myocardial infarction were dizziness ($p = 0.0001$), previous stroke ($p = 0.006$), being senior [> 65 years] ($p = 0.019$), and being white ($p = 0.016$). Presenting to the emergency department with pain in other areas ($p = 0.001$) was associated with delays in diagnosing a myocardial infarction and achieving a timely percutaneous coronary intervention.

Factors which may limit generalizability were a small sample size, comparative to the previous longitudinal research, and sampling from two hospitals within the same region.

A growing national focus calls for development of strategies to standardize care. These data would provide the basis for a practice guideline for the emergency department staff to increase their ability to detect and expedite treatment for patients with atypical symptoms of myocardial infarction.

This study utilized variable selections which were similar to other studies, however, the dependent variables and inclusion criteria varied between the studies. Presentation of pain in other areas was not a study variable in previous research. Most previous research utilized myocardial infarction patients and studied chest pain or not. The present study expanded the science by focusing on predicting myocardial infarction in patients who present to the emergency department with dizziness and shortness of breath. The clinical significance rests in the identification of this high-risk patient group of atypical presentation of myocardial infarction. The findings of this study will provide vital information targeting a large population of people at risk for myocardial infarction.

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Chapter 1

Introduction

Early in our professional medical or nursing training, we are taught to recognize classic signs and symptoms indicative of various disease states. These heuristics aid us by narrowing the list of causative problems to ones most likely to have caused those signs or symptoms. This mode of thinking is especially important in the emergency departments, where rapid diagnosis is crucial to afford a better outcome for the patient. Recognition of certain signs and symptoms creates a high index of suspicion from which to formulate an action plan for care. For example, an older adult is brought to the emergency department by her family with a sudden onset of shortness of breath and a history of renal failure. The index of suspicion for this patient would be pulmonary edema. A brief assessment of lung sounds correlates with this differential diagnosis. Interventions of oxygen administration, a chest radiograph, electrocardiogram, lab work and administration of a diuretic are accomplished within 5 minutes of presentation. With treatment, the patient has a decrease in her shortness of breath and stabilization of her condition within 15-20 minutes; the treatment has effectively decreased the cellular effects caused by the hypoxia.

Initial evaluation of patients in the emergency department depends on the subjective information given by the patient or others: family, friends, pre-hospital staff to emergency department personnel. Information given by others, however, may be distorted because the verbal descriptions they give are altered to fit their perception of the problem and may not be the actual words given by the patient. Even if the healthcare providers attempt to portray the patient's actual words, they are really providing a

synthesis of what is conveyed to formulate a clearer diagnostic picture (Peterson, E.D. & Alexander, K.P., 1998). In other words, what we hear would be more closely aligned to our index of suspicion. The hallmark symptom of a myocardial infarction is substernal chest pain, which may be associated with radiation of pain to the left arm or neck, shortness of breath and diaphoresis. Patients may describe this 'pain' by different descriptors generally relating to the quality of the pain (Zerwic, J.J., 1998). They may describe this chest pain as pressure, burning, squeezing, discomfort, 'an elephant on their chest', etc. To the emergency health care providers, these descriptors all relate to the term 'chest pain'. Differentiation of the quality and quantity of pain is important, but should not delay the initiation of diagnostic testing; it is used as an adjunct to the complete examination. The management of patients suspected to have had a myocardial infarction requires rapid assessment within the emergency department in less than 10 minutes of arrival (Custer, B.G., 2002, Graff, L. 2000).

For the past three years, emergency services of a four-hospital system have been actively working on a process to decrease time to diagnosis of myocardial infarction patients. A collaborative practice guideline was introduced. This guideline created a process so all patients who came to the emergency department with complaints of any form of chest pain were immediately taken to a room and an electrocardiogram performed. There is no time delay to consider other causes for the pain; subjectivity of the triage and primary staff is removed. The 'door time' to completion of the electrocardiogram has decreased for patients presenting with myocardial infarction and chest pain from an average of 20-25 minutes to 6.4 minutes (unpublished data, Nordblom, 2005). Reviewing the quality data on the subset of MI patients presenting

without chest pain shows the average time to electrocardiogram to be at an average of 20-30 minutes. This increase in time to completion of electrocardiogram delays the diagnosis and therefore the treatment needed, increasing the likelihood of further myocardial muscle damage.

In order to reduce the time to the electrocardiogram for patients who have had a myocardial infarction but do not have chest pain as a presentation identifier, the next logical step is to evaluate for a pattern of signs and symptoms in these patients. Is there a pattern or set of signs and symptoms in the older adult that would raise an index of suspicion? The latest study by Brieger and associates (2004) evaluated 20,881 patients admitted to the hospital with acute coronary syndrome (ACS). In this population of ACS patients (both non-ST elevation and ST elevation myocardial infarctions), 1,763 (8.4%) presented with atypical symptoms. The dominant presentation symptoms were dyspnea, diaphoresis, nausea or vomiting and syncope. Patients without chest pain were significantly older, most likely to be women and have a history of hypertension, diabetes or heart failure. Frequently atypical symptoms were not recognized as being caused by ischemia (23.8%) and were given an incorrect diagnosis. A specified trend in signs and symptoms for atypical presentations would be beneficial to alert the practitioner to order an immediate ECG to rule out ACS.

Purpose of the Study

Although chest pain is widely considered the key symptom in the diagnosis of myocardial infarction, not all patients with MI present with chest pain. Relative to myocardial infarction patients with atypical symptoms, very little consistent information is available regarding associated signs and symptoms and other risk factors in study

populations. Most recent studies look at a combination of signs and symptoms as well as risk factors. Appreciation of the crucial role of risk factors is one of the most significant advances in the understanding of coronary artery disease as well as predictive value for myocardial infarction. To avoid delays in diagnosis and therefore treatment, it is important to educate the emergency healthcare personnel to the myriad of presentations of myocardial infarctions in people without chest pain to heighten their suspicion. This study proposes to examine some of these sign and symptoms and associated risk factors to enhance the emergency health care providers' abilities to detect myocardial infarction in older adult patients who do not have chest pain.

Many studies have discussed the patient's perceptions of their illness and relate those to a delay in treatment (Ryan & Zerwic, 2003). Impaired symptom perception may contribute to lack of recognition. This study does not include a focus on why or when the patient decides to come to the emergency department. The focus is to determine if a pattern of signs and symptoms and risk factors is more prevalent in myocardial infarction patients without chest pain so the staff are aware to obtain the electrocardiogram sooner so that diagnosis of the myocardial infarction is made and treatment initiated.

Significance to Nursing

This study involves the emergency department healthcare providers' ability to use recognition of clinical presentations to influence and initiate testing and treatment for potential myocardial infarction in patients who do not have chest pain. In addition, the study will include coronary risk factor evaluation to determine if this subset of information can increase the likelihood of improved identification. The purpose of this study is to determine if there is a prevalent set of signs, symptoms, and risk factors that

would raise the index of suspicion for the patient who does not have classic signs or symptoms of myocardial infarction.

A possibility that symptom recognition differs between patients has practical implications. The clinical significance rests in the identification of this high-risk patient group of atypical presentation of myocardial infarction. This atypical symptomatology may relate to delay in diagnosis or inappropriate diagnosis and thusly delay treatment and increase the possibility of poor outcomes. The findings of this study will provide vital information to create a practice guideline so that when a patient presents with those signs and symptoms an electrocardiogram is immediately obtained. The decrease in time to diagnosis will allow treatment to be started sooner and likely will improve the outcome for the patients. Another potential benefit of these findings would be to capture the population of myocardial infarction patients that may have been missed because of the atypical signs and symptoms. This study has enormous coronary health implications targeting a large population of patients at risk for myocardial infarction.

Chapter 2

Review of Literature

Each year, approximately 1.5 million adults in the United States are diagnosed with an acute myocardial infarction (ACC/AHA, 1999). Rapid restoration of normal flow to the occluded vessel associated with the infarct is the most important factor in limiting myocardial necrosis. "Cardiovascular disease remains the chief cause of death within the United States and Western Europe, and atherosclerosis, the principal cause of myocardial and cerebral infarctions, accounts for the majority of these deaths" (Ross, 1986).

Historical Overview of Coronary Artery Disease.

Coronary artery disease has for many years been associated with myocardial infarction. A landmark article by Herrick (1912) reviewed the then current theory that sclerosis produced anemic necrosis and fibrosis of the myocardium. Most believed this phenomenon caused immediate death. Herrick challenged the thought that coronary arteries were terminal-end arteries. He showed in his experiments an anatomic anastomosis between coronary vessels. He cited case after case of totally occluded arteries in which patients lived for various amounts of time after their occlusions. "The clinical manifestations of coronary obstruction will evidently vary depending on the size, location and number of vessels included" (Herrick, 1912). Herrick pointed out the wisdom of creating a taxonomy consisting of subsets of coronary disease in which the characteristics of each subset are carefully defined so that therapy could be provided.

Ross in 1986 described the most recent advances in the understanding of cellular composition of lesions in atherosclerosis. The response to injury hypothesis proposes that injury to the endothelium of the coronary artery is initiating the event of atherogenesis. In

his investigations, Ross described the importance of monocyte interactions as an early role in the forming of the fatty streak. Both early and advanced lesions of atherosclerosis consist of smooth muscle cells and macrophages. The macrophages represent a form of inflammatory response. Ross observed that low-density lipoproteins (LDL) exposed to macrophages are oxidized and toxic to the fibroblasts, which is a source of endothelial injury and explains the changes in the fatty streak. The macrophages in the fatty streak advance to lesions containing a fibrous cap of smooth muscle that contains proliferated smooth muscle and macrophages. This may represent a defensive mechanism or progress to a pathologic response. All four principal cells (endothelial, smooth muscle, platelets, and monocyte/macrophages) either contain or can synthesize and release chemoattractants and growth factors. At least two of these pathways may lead to the formation of intimal smooth muscle proliferated lesions. The first pathway demonstrated in hypercholesterolemia involves the monocyte and platelet interaction that stimulates fibrous plaque formation by growth factor release. The second pathway involves the direct stimulation of the endothelium that may release growth factors that can induce smooth muscle migration and proliferation. Ross felt that this pathway might be important for patients with hypertension or diabetes or those who smoked cigarettes. There was a strong emphasis on the importance that hypercholesterolemia played in lesion formation, yet direct information relating to risk factors was missing.

In another article in 1999, Ross further described and concluded that although hypercholesterolemia is important in approximately 50% of patients with coronary artery disease, other factors need to be taken into consideration. "Atherosclerosis is clearly an inflammatory disease that does not simply result from an accumulation of lipids. Lesions

of atherosclerosis represent a series of highly specific cellular and molecular responses that can best be described, in aggregate, as an inflammatory response" (Ross, 1999). Each characteristic lesion of atherosclerosis represents a different stage of chronic inflammatory response in the artery. He described many factors that induce and promote inflammation or atherogenesis:

- Elevated and oxidized LDL
- Free radicals from cigarette smoking
- Hypertension
- Genetic alterations
- Elevated homocysteine
- Infectious microorganisms
- Combination of the above.

Endothelial dysfunction that results from injury leads to compensatory responses that alter the normal homeostatic properties of the endothelium. Injury causes an increased adhesiveness of the endothelium with respect to leukocytes and platelets as well as altering endothelial permeability. Injury also induces the endothelium to have procoagulant effects to form vasoactive molecules, cytokines and growth factors. If the inflammatory response does not neutralize or remove the offending agent, it can continue indefinitely. In doing so, the inflammatory response stimulates migration and proliferation of smooth muscle. If this continues unabated, the arterial walls thicken. The continued inflammation results in increased numbers of macrophages and lymphocytes that multiply in the lesion. Activation of these cells leads to release of hydrolytic enzymes, cytokines, chemokines and growth factors, which causes further damages and

leads to necrosis. These cycles, accumulation of mononuclear cells, migration and proliferation of smooth muscle and formation of fibrous tissue, lead to further enlargement and restructuring of the lesion which then becomes covered with a fibrous cap that overlies a core of lipid and necrotic tissue. At some point, the artery can no longer compensate by dilation and the lesion intrudes into the lumen of the artery and blocks blood flow.

Risk Factors for Atherosclerosis.

Cardiovascular disease is common in the general population, affecting the majority of adults past the age of sixty years. The lifetime risk of coronary heart disease was illustrated in the Framingham Heart Study. This study showed a 50% risk for a coronary event over a ten-year period.

Many of the important risk factors for cardiovascular disease are modifiable by specific preventative measures. In the INTERHEART study (Yusuf et. al., 2004), a database from fifty-two countries, nine potentially modifiable risk factors accounted for over 90% of the populations' attributable risk for the first myocardial infarction. These included smoking, dyslipidemia, hypertension, diabetes, abdominal obesity, psychosocial factors, low daily consumption of fruits and vegetables, regular alcohol consumption, and lack of regular physical exercise.

Cardiac risk factors profoundly affect many of the healthy functions of the endothelium. Most large study cohorts (Framingham and MRFIT) support the importance of individual risk factors (hyperlipidemia, hypertension, diabetes, smoking) association with atherosclerosis. Other cardiovascular risk factors that promote coronary disease are age and sex (Yusuf et al., 2004).

Among the many risk factor associations, the best-established coronary risk factors are hyperlipidemia, hypertension, cigarette smoking, diabetes, and obesity. A critically important feature of these risk factors is that each has demonstrated an impact on coronary heart disease (Greenland et al., 2003).

Normal function of vascular endothelium.

The vascular endothelium is an active dynamic tissue that performs a wide array of homeostatic functions within normal vessels. Vascular endothelium is a single-layer of endothelial cells located between the blood vessel lumen and smooth muscle cells of the vessel wall. This monolayer of endothelial cells is able to transduce blood-borne signals, sense mechanical forces within the lumen, and regulate vascular tone. Endothelium produces vasodilators (*e.g.* nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factor [EDHF]) and vasoconstrictors (*e.g.* endothelin-1, angiotensin II, thromboxane A_2) and reactive oxygen species (ROS). Endothelial dysfunction may lead to disturbances in blood flow, contribute to the pathogenesis of myocardial ischemia, and is a central feature in the evolution of atherosclerosis (Braunwald, 2001; Endemann & Schiffrin, 2004).

The normal endothelium is pivotal in the maintenance of vascular homeostasis through the balance of vasodilator and vasoconstrictive substances. One of the most important endothelial-derived vasodilators, nitric oxide, acts as a vasodilator, relaxes smooth muscle in the arteries and veins, inhibits growth and migration of smooth muscle cells, inhibits platelet aggregation and interferes with the vascular inflammatory response by decreasing the adhesive interactions between the endothelium and circulatory leukocytes, thus interfering with the atherosclerotic process. Endothelial dysfunction

generally results from decreased nitric oxide bioavailability, which also implies a loss of vascular protection (Endemann & Schiffrin, 2004; Gonzalez et al., 2003; Hsueh et al., 2004; Taylor, 2001).

In contrast, vasoconstrictors, such as angiotensin II, promote vascular damage. Angiotensin II, which is pro-inflammatory, stimulates monocyte migration, enhances monocyte adhesion to the endothelial surface, and promotes movement of monocytes into the vessel wall. Angiotensin II also stimulates platelet aggregation and thrombosis, promotes migration and growth of smooth muscle cells, and stimulates endothelin-1 expression. Endothelin-1 promotes growth and migration of smooth muscle cells, increases vascular permeability, stimulates angiogenesis and stimulates production of interleukin-6 and other inflammatory cytokines (Hsueh et al., 2004). Angiotensin II has been implicated in the pathophysiology of hypertension.

Hyperlipidemia.

The serum total cholesterol concentration is a clear risk factor of coronary disease with the risk increasing progressively with higher values. The concentrations of lipid fractions, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are also important (Yusuf et al., 2004).

Hyperlipidemia is the major cause of injury to the endothelium and underlying smooth muscle (Ross, 1999). Lipid abnormalities play a critical role in the development of atherosclerosis. Circulating LDL rapidly accumulates in the cholesterol-rich macrophages, called foam cells, of atherosclerotic plaque. Macrophage uptake of LDL may initially be an adaptive response, however, cholesterol accumulation leads to mitochondrial dysfunction and necrosis, with resultant release of cellular proteases,

inflammatory cytokines and prothrombotic molecules (Tabas, 2002). Macrophages that have been activated by oxidized LDL, release a variety of inflammatory substances (*e g.* C-reactive protein, fibrinogen, and serum amyloid-A), cytokines (*e g.* Interleukin-1β, interleukin-6 and tumor necrosis factor α-1).

LDL initiates a series of events that occur early during plaque formation. These events lead to upregulation of genes that code for and induce angiotensin-converting enzyme activity, local production of angiotensin II, and expression of endothelial cell surface adhesion molecules, as well as enzymes that promote oxidative stress. The LDL activates the foam cells and is chemotactic for other monocytes. This helps to expand the inflammatory response by stimulating the replication of monocyte-derived macrophages and entry of new monocytes into the lesion (Gonzalez et al., 2003; Vink et al., 2000).

HDL, in contrast to LDL, has antiatherogenic properties that include reverse cholesterol transport, maintenance of endothelial function, protection against thrombosis, and maintenance of low blood viscosity (Vink et al., 2000).

Hypertension.

Many of the same factors that are associated with hypertension are also associated with endothelial dysfunction. There is no single or specific cause for most hypertension. Since persistent hypertension develops in response to increased cardiac output or rise in peripheral resistance, defects may be present in one or more multiple factors. Regardless of how hypertension begins, the eventual increased peripheral resistance interplays to cause endothelial dysfunction.

It is estimated that control of hypertension to below 140/90 mmHg could, in men and women, prevent 19 and 31 percent of coronary heart disease events, respectively,

whereas optimal control to below 130/80 mmHg could prevent 37 and 56 percent of coronary heart disease events, respectively (Wong et al., 2003). In coronary vessels, hypertension causes or aggravates other conditions that diminish vessel caliber.

Concentrations of angiotension II, a potent vasoconstrictor, have a tendency to be elevated in patients with hypertension. Angiotesin II is contributory to atherogenesis by stimulating growth of smooth muscle. "It also increases smooth muscle lipoxygenase activity, which can increase inflammation and the oxidation of LDL" (Ross, 1999). Hypertension causes a reduced vasodilating response to various stimuli of nitric oxide (NO) release. Impaired NO-mediated vasodilation may promote abnormal vascular remodeling.

Diabetes.

"Diabetes Mellitus is not just a metabolic disorder-it is as much a vascular disease because most patients who have diabetes die of cardiovascular disease" (Deedwania, 2004). Although precise mechanisms by which diabetes produce endothelial dysfunction and increased risk of vascular disease remain to be clarified, there are many frequently observed metabolic, hormonal, and hemostatic abnormalities in patients with diabetes that can contribute to endothelial dysfunction. At least four mechanisms might be responsible for the vascular damage in diabetes: hyperglycemia, hyperinsulinemia, dyslipidemia, and prothrombotic state. Potential cellular mechanisms that are related to endothelial dysfunction in diabetes are decreased synthesis and responsiveness of nitric oxide, increased protein kinase C, increased advanced glycation end products, decreased prostacyclin formation and release, increased formation and release of endothelin-1, increased lipid oxidation, increased cytokine and growth factor production, hypertension,

increased oxidative stress (ROS), and acceleration of the atherosclerotic process (Deedwania, 2004; Taylor, 2001). There is compelling evidence for endothelial dysfunction in diabetic patients (Taylor, 2001). This dysfunction is manifest as blunting of the biological effect of nitric oxide and increased production of angiotensin II and endothelin-1. These agents cause increases in blood pressure and cardiac remodeling. Reactive oxygen species (ROS), overproduced in diabetes, serve as molecules that mediate many of the cellular reactions (Taylor, 2001).

Increasing evidence suggests that the progression of insulin resistance parallels progression of endothelial dysfunction to atherosclerosis (Hsueh et al., 2004).

Cigarette smoking.

Although the relationship between coronary disease and smoking appears clear, the mechanism by which it occurs is incompletely understood. Multiple factors may be involved since smoking has a variety of effects that may contribute to atherogenesis (Ambrose & Barua, 2004). Smoking is associated with:

- An adverse effect on serum lipids (elevated LDL and reduced HDL) and with insulin resistance. In addition, free radicals in cigarette smoke damage lipids, resulting in the formation of proatherogenic oxidized particles, specifically oxidized LDL cholesterol (Newby et al., 1999).
- Activation of the sympathetic nervous system, producing vasoconstriction (Newby et al., 1999).
- Damage to the vascular wall, possibly leading to impaired prostacyclin production and enhanced platelet-vessel wall interactions (Stefanadis et al., 1997).

- Impaired endothelium-dependent vasodilation and potentiation of the endothelial dysfunction induced by hyperlipidemia. The effect on endothelial function results from oxidative stress with enhanced oxidation of LDL and reduced generation of nitric oxide (Baura et al., 2001).

Cigarette smoking may produce endothelial damage and impair flow-mediated, endothelium-dependent peripheral arterial vasodilation (Neunteufl et al., 2002), an effect that is partially reversible after smoking cessation. The cardiac risks associated with cigarette smoking diminish relatively soon after smoking cessation and continue to fall with increasing length of time since quitting.

Obesity.

Obesity is associated with a number of risk factors for atherosclerosis and cardiovascular disease. These include hypertension, insulin resistance, low HDL, and an increase in thromboxane-dependent platelet activation (Davi et al., 2002).

Inflammation.

Recent studies have suggested that inflammation may contribute to endothelial dysfunction in coronary artery disease. A study on Syndrome X (effort angina, positive exercise test and normal coronary angiography) by Lanza published in 2004 reported abnormalities in coronary microvascular function. The endothelial dysfunction was characterized by the decreased release of the vasodilator nitric oxide and an increased release of vasoconstrictive factors that play a role in the pathogenesis of Syndrome X. He also found increased levels of C-reactive protein and Interleukin-1. These levels in the Syndrome X group were not as high as those in the coronary artery disease group yet significantly higher than the control group.

Ross stated there is a correlation between atherosclerosis and presence of Herpes virus and Chlamydia pneumonia. He found no direct evidence that these infections caused the lesion, but it was possible that the infection, combined with other factors were responsible for the genesis of lesions in some patients.

There is compelling evidence that elevated levels of inflammatory mediators, cell adhesion molecules and acute phase reactants correlate with increased vascular risk. Oxidized lipoproteins, components of the renin-angiotension system, high serum glucose and obesity serve as potential triggers for inflammation of atherogenesis. Several infectious agents have been implicated in the pathogenesis of atherosclerosis: Cytomegalovirus, Heliobacter pylori and Chlamydia pneumonia (Gelfand & Cannon, 2004).

In order to reduce morbidity and mortality of the 12 million patients in the United States with coronary artery disease, aggressive secondary prevention measures and control of risk factors have been strongly recommended by multiple national guidelines (AMA, 2002; ACC/AHA, 1999). Despite the strong evidence supporting those recommendations, achievement of target goals has been suboptimal (Ho et al., 2004).

Pathophysiology of Coronary Artery Disease

Coronary artery disease, myocardial ischemia, and myocardial infarction form a pathophysiologic continuum that impairs the pumping ability of the heart by depriving the heart muscle of oxygen and nutrients. The earliest lesions of the continuum are those of coronary artery disease, virtually any vascular disorder that narrows or occludes the coronary arteries. Coronary artery disease can diminish the myocardial blood supply until deprivation impairs myocardial metabolism enough to cause ischemia, a local state in

which the cells are temporarily deprived of oxygen supply. They remain alive but are unable to function normally. Persistent ischemia or the complete occlusion of a coronary artery causes infarction, or death, of the deprived myocardial tissue.

Atherosclerosis in the coronary arteries is termed coronary artery disease. As previously described, atherosclerosis is characterized by endothelial dysfunction, inflammation, and the formation of lipid-filled plaques that collect in the inner surface of the coronary arteries. Eventually, the plaque becomes fibrous as connective tissue forms, producing a narrowed, rigid vessel. The increased resistance in the rigid vessel causes reduced blood flow and myocardial ischemia that can produce signs and symptoms of angina. As the disease progresses, the weak fibrous plaque can rupture or ulcerate, which leads to a thrombosis or embolus.

Myocardial ischemia is characterized by an imbalance between myocardial oxygen supply and demand. In some instances, this imbalance is caused by a reduction in blood flow and oxygen supply that increases vascular resistance, platelet aggregation and thrombus formation, In other instances, the presence of chronic coronary obstruction, exercise or tachycardia leads to an increase in coronary blood flow that is insufficient to meet the rise in myocardial oxygen demand (Ganz & Ganz, 2001).

The term myocardial infarction reflects necrosis of the cardiac myocytes caused by prolonged ischemia. The ischemia is resultant of an imbalance between oxygen supply and demand. The coronary arteries normally supply blood flow sufficient to meet demands of the myocardium as it labors under varying workloads. Oxygen extraction from these vessels occurs with maximal efficiency. If efficient exchange does not meet myocardial oxygen needs, healthy coronary arteries are able to dilate to increase the flow

of oxygenated blood to the myocardium. A variety of pathologic mechanisms can interfere with blood flow through the coronary arteries giving rise to myocardial ischemia. Narrowing of a major coronary artery by more than 50% impairs blood flow sufficiently to hamper cellular metabolism under conditions of increased demand (Almeda, et al, 2004).

Overt symptoms of coronary artery disease, including angina, ST segment depression or myocardial infarction typically begin after the artery is 60% occluded (Braunwald et al., 2001; Cheng, 2001). The atherosclerotic lesion interferes with blood flow, decreases vessel elasticity and increases the tendency to form clots, thrombi and emboli. Over 90% of major myocardial infarctions are associated with clot formation where a plaque has ruptured (Braunwald et al., 2001). Myocardial infarctions are discussed in the next section.

Autopsy studies have demonstrated that approximately 70% of persons between 70 and 80 years of age have coronary atherosclerosis. Individuals may be unaware of having coronary artery disease until the advanced age of 75-80 years, when they sustain their first myocardial infarction. At least 40 to 50% of persons over the age of 65 years demonstrate coronary artery disease clinically. Despite the high prevalence of coronary artery disease in the older adult, clinical manifestations of the disease are often unrecognized (Tresch & Jamali (1998).

Pathophysiology of Myocardial Infarction

Myocardial infarction is the term used to describe irreversible cellular loss and myocardial necrosis that result from an abrupt decrease or total cessation of coronary blood flow to a specific area of the myocardium. Atherosclerosis is responsible for most

myocardial infarctions because it causes luminal narrowing and reduced blood flow, resulting in decreased oxygen delivery to the myocardium.

The underlying pathophysiological mechanism of myocardial infarction is rupture of the fibrous cap of an atherosclerotic plaque. Plaque rupture activates platelets, endothelial and clotting factors, leading to rapid formation of a thrombus that occludes the coronary artery lumen, resulting in myocardial necrosis (Mauri & O'Gara, 2004).

Factors that can affect plaque rupture include (Cheng, 2001):

- Mechanical injury – Blood flow, which influences the plaque to produce vessel wall stress and mechanical injury, is the key external force affecting plaque stability. A weak point in the cap of a fibrous plaque is vulnerable to shear forces, particularly at its insertion point into the vessel. Where the cap thins, it is often abound with lipid-packed macrophages, and is more susceptible to rupture.
- Inflammation – Inflammatory cells in the atherosclerotic plaque play an important role in the plaque stability. Macrophages secrete matrix metalloproteinases that have activity against the collagen component of the plaque and may weaken the fibrous cap. Macrophage-derived foam cells have been found to activate matrix metalloproteinases by elaborating reactive oxygen species.
- Infection – Associations between infectious agents and atherosclerosis have been implicated: Cytomegalovirus, Herpes virus and Chlamydia pneumonia. The exact pathophysiology

> continues to be studied. For an infectious agent to infect human endothelial and smooth-muscle cells and alter their functions in atherosclerosis, the organism must be able to survive and replicate intracellularly. It is postulated that these infectious agents exist in a persistent latent state and reactivate from time to time altering natural history and progression of coronary artery disease. Effects have been found on smooth-muscle proliferation, lipid metabolism (allows LDL to be more easily oxidized), production of pro-inflammatory cytokines), blood coagulation and induction of leukocyte adhesion (induce expression of endothelium-leukocyte adhesion molecules).

Thrombus formation is considered an integral factor in myocardial ischemia. The thrombus can occlude more than 50% of the coronary artery lumen. The vessel occlusion leads to myocardial ischemia, hypoxia, acidosis and infarction of the cardiac myocytes. The consequences of the occlusion are dependent on the extent of the thrombolytic process, the characteristics of the preexisting plaque and availability of collateral circulation (Auferhide & Brady, 2002).

Myocardial ischemia develops if coronary blood flow or oxygen content of coronary blood is not sufficient to meet metabolic demands of the myocardial cells. With treatment modalities, myocardial ischemia can be reversed. The cardiac cells remain viable for many minutes. If blood flow is restored, cellular repair begins. If the coronary arteries cannot compensate for the lack of oxygen, myocardial necrosis and myocardial infarction occurs.

Imbalances between blood supply and myocardial oxygen demand can result from a number of conditions. Oxygen supply is decreased by:

- Hemodynamic factors, such as increased resistance in coronary vessels by coronary artery thrombosis, plaque fissure or hemorrhage, coronary artery spasm, hypotension or decreased volume;
- Cardiac factors such as increases in heart rate, decreases in diastolic filling time or valvular incompetence;
- Hematological factors, such as oxygen content of the blood; or
- Systemic disorders that reduce blood flow or availability of oxygen (shock).

Increased resistance in coronary vessels usually causes myocardial ischemia, but because the myocardium has little tolerance for hypoxia, it is particularly vulnerable.

Demand for oxygen is increased by:

- Systolic hypertension;
- Increased ventricular volume (ventricular dilation);
- Myocardial hypertrophy;
- Tachycardia resulting from exercise, stress or anemia; or
- Conditions that heighten myocardial contractility.

Ischemia occurs if demand exceeds supply. Any factor that increases demand or decreases supply places individuals at risk for an episode of myocardial ischemia. Ischemia can be identified electrocardiographically with presence of ST-T depression. The pain of ischemia (angina), and/or necrosis (myocardial infarction), most typically is located substernally, but may present or radiate to the epigastrium, arm, wrist, shoulder,

jaw or back. The pain may also be associated with dyspnea, diaphoresis, nausea, vomiting, or light-headedness/syncope.

Diagnostic Criteria for Myocardial Infarction

Myocardial infarction as defined by the World Health Organization is a combination of two or three characteristics:

- Typical 'classic' symptoms of chest pain,
- A rise in cardiac biochemical markers,
- A typical electrocardiogram (ECG) pattern involving development of Q waves. (Gillum, et al., 1984).

Most myocardial infarctions are presumed to be associated with a classic description of substernal chest pain (Canto, et al., 2000). However, some patients who present to the emergency department and are diagnosed as having a myocardial infarction do not have chest pain. The lack of chest pain symptoms does not imply absence of severe or potentially lethal coronary stenosis (Reeves, 1985). There is a group of other symptoms that may be the primary presenting complaint in the emergency department. These signs or symptoms include pain in other locations, nausea/vomiting, dizziness/syncope and/or dyspnea. The growing awareness of this subgroup of patients not fitting the defined criteria for myocardial infarction predicated a need to evaluate and modify the criteria. The availability of comparable data from studies conducted throughout the 1960's into the 1990's provided a basis for the change in criteria. The WHO further delineated myocardial infarction into two groups (Non-ST elevated myocardial infarction [NSTEMI] and ST elevated myocardial infarction [STEMI]) as related or not related to ST segment elevation on the basis of the presence or absence of at least 1 millimeter of

ST segment elevation in two or more contiguous leads on the initial electrocardiogram (ACC/AHA, 1999).

Myocardial infarction can be defined from a number of different perspectives related to clinical, biochemical, electrocardiographic and pathologic characteristics. The Joint European Society of Cardiology/American College of Cardiology Committee produced the most comprehensive criteria of myocardial infarction in 2000. The participants on this committee were selected for their expertise in cardiology and their knowledge of the scientific evidence. This group defined myocardial infarction as an elevation of typical biochemical markers of myocardial necrosis with at least one of the following:

- Ischemic symptoms
- Development of Q waves on the ECG
- ST segment elevation or depression on the ECG
- Pathologic findings of an acute myocardial infarction.

Although there has been considerable research defining the diagnostic criteria for myocardial infarction, each study describes a different set of clinical signs or symptoms and uses differing definitions. Many of these terms and definitions can be used interchangeably. As diagnostics and clinical expertise advance, more is learned about myocardial infarction. The terms used are based on clinical presentation and/or diagnostic findings. Table 1 presents a list of definitions to be used in this study.

Table 1

Definitions to Describe Myocardial Infarction

Criteria for Diagnosis

1. Electrocardiogram changes indicative of infarction;
   - ST segment elevation of 1-2 mm
   - Pathologic Q waves
   - New onset left bundle branch block (LBBB)
2. Elevation of biochemical markers
   - Troponin or CK-MB
3. Typical symptoms of chest pain with or without associated symptoms.

Type	Criteria for Diagnosis	Definition
Typical Myocardial Infarction	All 3 criteria	Myocardial cell death due to prolonged ischemia
Atypical Myocardial Infarction	Criteria 1 & 2	ECG changes and elevation of biochemical markers. Pain may be located in the epigastrium, arm, jaw, shoulder, wrist or back and/or have other associated symptoms. May be "unrecognized" by staff.

		The signs and symptoms are also indicative of different disease processes; (*e.g.* esophageal reflux disease) therefore, diagnosis is delayed.
Silent Myocardial Infarction	Criteria 1 & 2	ECG changes and elevation of biochemical markers, but patient has no symptoms. This type of MI may be "unrecognized" as the MI is an incidental finding in the course of care.
Unrecognized Myocardial Infarction	Criteria 1 & 2	ECG changes and elevation of biochemical markers. Pain may be located in the epigastrium, arm, jaw, shoulder, wrist or back and/or have other associated symptoms. May be "unrecognized" by staff. The signs and symptoms are also Indicative of different disease processes; (*e.g.* esophageal reflux disease) therefore, diagnosis is delayed.

Diagnoses

Name	Definition
Chest Pain (Angina)	Ischemic pain is noted as substernal and crushing in nature. May have previously been diagnosed as angina.
Unstable Angina	Ischemic chest pain, uncontrolled by nitrate therapy without electrocardiogram changes.
Non ST Elevation Myocardial Infarction (NSTEMI)	Myocardial infarction without ST elevation. Patient has an elevation of biochemical markers and possibly some ST depression.
ST Elevation Myocardial Infarction (STEMI)	Myocardial infarction with ST elevation.

Atypical myocardial infarction.

The diagnosis of atypical myocardial infarction is based on positive electrocardiographic findings of a myocardial infarction, but the clinical pain presentation may be in the epigastric area, arm, shoulder, wrist, jaw or back, without occurring in the chest region. Many patients have no pain on presentation. Their signs or symptoms may be associated with nausea, vomiting, persistent shortness of breath, weakness, dizziness, or lightheadedness/syncope. Although many people admitted to the emergency department have symptoms as listed above, they may be 'unrecognized' by emergency department staff.

Silent myocardial infarction.

Silent myocardial infarction, by strictest definition, is a myocardial infarction in which there is clinical electrocardiographic and/or other evidence of myocardial damage (elevated cardiac enzymes), yet the patient is without signs or symptoms and is unaware of the event. Generally speaking, this finding is noticed later in the patients' treatment course, or even years later (Deedwania & Carbajal, 1991).

Unrecognized Myocardial Infarction

James B. Herrick, first used the term "unrecognized myocardial infarction" in a landmark article in 1912 (Herrick, 1983). Traditionally, silent and atypical myocardial infarctions have been discussed together as "unrecognized myocardial infarction". Unrecognized myocardial infarction is an infarction in which symptoms that occur are so non-classic that the patient and physician do not realize they are related to myocardial damage. Patients and providers will associate the symptoms with other disease entities (*e.g.,* esophagitis, or a viral syndrome). During the medical work-up for other entities, the

myocardial infarction may be diagnosed. A secondary definition involves the interpretation of signs or symptoms and the ability of the person to perceive pain (*e.g.*, autonomic neuropathy) (Sheifer, Gersh, et al. 2000).

For the purposes of this paper, this author will use the term "unrecognized myocardial infarction" to represent the population of patient's who present to the emergency department, are diagnosed with myocardial infarction by positive electrographic changes and cardiac biochemical markers, yet have no clinical presentation of chest pain. The patients clinical presentation might include pain in other locations and/or nausea, vomiting, dyspnea or dizziness/syncope.

The most comprehensive data on the frequency of unrecognized MI originates from large cohort studies. These studies have shown unrecognized MI to be between 20% and 50% of all diagnosed myocardial infarctions (Kannel et.al. 1990; Jonsdottir, et. al. 1998; Medalie & Goldbourt, 1976; Nadelmann et. al. 1990; Rosenman et. al. 1967; Sheifer et. al. 2000; Sigurdsson et. al. 1995). Unrecognized myocardial infarction seems to compromise a large percentage of the total number of infarctions and carry approximately the same prognosis as a recognized myocardial infarction (Herlitz, 2002). For providers to have appreciation for the incidence of unrecognized myocardial infarction, they must also appreciate the presenting signs and symptoms. This would enable them to obtain the appropriate tests to diagnose the myocardial infarction. Thus, a better understanding and ability to recognize atypical presentations is important.

Contributing Factors to Lack of Chest Pain in Unrecognized Myocardial Infarction

Nociceptive pain is the perception of nociceptive input described in terms of tissue damage (*e.g.* myocardial ischemia or infarction).

Unrecognized myocardial infarction differs from recognized myocardial infarction in the translation of myocardial ischemia into symptomatic pain. Why myocardial infarctions are lacking chest pain in some people and not others is still undetermined. One possibility is that the interpretation of symptoms may differ between persons exhibiting recognized and unrecognized myocardial infarction. The persons with unrecognized myocardial infarction may be less likely to conclude that their symptoms represent a significant health problem and consequently lead to a clinically unrecognized event (Deedwania & Carbajal, 1991).

Several factors may modulate the generation, conduction and processing of the afferent impulse from the cardiac pain receptors through the thalamus for interpreting the pain of myocardial ischemia/infarction. Many factors could lead to a diminished perception of the ischemic event. While it is yet to be determined whether the processes that underlie silent myocardial ischemia also lead to unrecognized myocardial infarction as defined in this study, the two conditions have an association, thus review of the proposed mechanisms for silent ischemia/infarction is relevant.

Studies of pain in angina and myocardial infarction patients.

In 1934, Libman postulated that some patients have a higher pain threshold that accounted for the differences. Instead of pain, the 'hyposensitive' patient may have what he coined substitution symptoms. These substitution symptoms were classified into two groups:

- Symptoms that may be representative of pain; e.g. pressure, burning,
- Symptoms from two clinically independent conditions present at the same time where one may cover the other.

Libman thought it necessary to study relationships of race, gender and age to sensitiveness of pain. He also thought relationships of sensitiveness to general physical and mental character of the individual was important for study (Libman, 1934).

Keele (1968) quantitated Libman's observations by describing the relationship between quantitative application of stimulus and the first complaints of pain. The tests were useful for separating patients into normal and hyposensitive groups. Of the 74 myocardial infarction patients studied (male, no age range noted), the pain pattern correlated with two factors:

1. Directly with the magnitude of necrosis as evidenced by ST segment deviation and elevation of SGOT ($t = 4.2609$; $P < 0.001$)
2. Inversely with the patients' threshold to pain ($F = 3.835$; $0.05 > P > 0.01$)

These studies highlight the importance of understanding signs and symptoms as described by patients who may be having a myocardial infarction. The response to pain stimuli as well as the sensitivity to pain are subjective and may depend on many factors.

Droste and Roskamm (1983) examined several variables in patients with asymptomatic ST segment depression and silent myocardial ischemia during exercise ECG. They compared them with patients who had typical angina with ST segment depression during exercise ECG. Despite similarities of the two groups in functional ability, angiographic data, and other risk factors, marked variability was found in various experimental pain measures. Patients with silent ischemic events had a significantly higher pain tolerance compared to those in the anginal symptomatic group. The study did not take into account differences due to social or cultural contexts concerning

acceptability of the expression of pain. They discussed three possible explanations to the differences noted.

1. Nociceptive pathways projecting from the heart may be destroyed by a substantial myocardial infarction, diffuse coronary heart disease or polyneuropathy at a more central location,
2. Patients with asymptomatic myocardial infarction may not obtain the intensity of ischemia needed to elicit angina,
3. Asymptomatic patients may exhibit a hyposensitivity to pain in general.

The central transmission of painful stimuli may vary in an individual as well. In 1965, Melzack and Wall proposed a "gate control theory of pain" in which painful stimuli are modulated at a central location. The conduction of the afferent impulse may also be affected by various "gating mechanisms". Rosen and colleagues (1994) discuss "gates" which exist between the dorsal horn of the spinal cord and in the thalamus. At these sites, multiple stimuli may converge and effectively cancel each other. Libman (1934) postulated that many patients do not perceive pain with myocardial infarction because other stimuli, such as dyspnea, saturate sensory mechanisms.

Endogenous opiode, endorphins, may vary in different patients and may contribute to the differences in the pain perception. Using a placebo control group and a group given naloxone, a specific opiode antagonist, exercise-induced angina was produced using treadmill tests (Van Rijn & Robkin, 1981). Subjects (n = 36) were found to have angina significantly earlier during testing after being given naloxone versus the control group. These data indicate that endorphins may play a role in individual variations in pain perception.

Results of the above study were reinforced by Sheps and coworkers (1987). They found post-exercise endorphin levels were significantly lower in patients with angina during exercise than those without angina but with ischemia noted on electrocardiogram. These data also suggest that endorphins may play a role in individual variations in pain perception.

Autonomic neuropathy.

The anatomic and functional integrity of cardiac nocioceptors and pain afferents is a major factor in the perception of myocardial ischemia. Inadequate receptor stimulation or frank nocioceptor dysfunction may block impulse initiation and pain perception. Autonomic neuropathy is the suggested explanation for the phenomenon. Roseman (1954) found a high incidence of painless ischemia in diabetic patients (N = 220, 163 male/57 female) with autonomic neuropathy. The presence of autonomic neuropathy leads to sensory denervation (Chiariella and Indolf, 1996). In a small study by Acharya and associates (1991), 14 diabetic patients (age 38-71, 11 male/3 female), seven whom had no chest pain, who had autonomic dysfunction and myocardial infarction, were investigated. Multiple autonomic function tests were performed. In summary, autonomic dysfunction was found to be more pronounced in the diabetic patients with the painless myocardial infarction compared with the seven patients who had anginal pain during infarction.

Frequency of Unrecognized Myocardial Infarction

Symptoms of patients with unrecognized myocardial infarction are variable. Symptoms reported or noted in retrospect include dyspnea, nausea/vomiting, abdominal pain, syncope, fatigue and palpitations (Pope et al., 2000).

In the Boston City Hospital Study (Uretsky et al., 1977), 102 consecutive patients (age - 48-82, sex - male) with myocardial infarction were studied: 25% presented without chest pain. Of these, fifteen had dyspnea, six had abdominal pain, four had extreme fatigue, one had nausea and vomiting, and one had syncope. In the most recent study by Pope (2000), women had a much higher rate of atypical symptoms on presentation. Another new finding in this study was an association that black people with unrecognized myocardial infarction had more risk factors for coronary artery disease than whites. Many providers were looking for non-cardiac reasons for the atypical presentation signs and symptoms. Even though a strong coronary history was obtained on admission to the emergency department, it did not strongly influence diagnosis.

The most comprehensive data on the frequency of unrecognized myocardial infarction originates from large cohort studies. The best known of these studies is the Framingham Study that is based on a 34-year follow-up of 5,070 study participants of all ages and both genders. Kannel and associates (1990) published the most recent analysis of myocardial infarction data. Unrecognized myocardial infarction represented 26% and 34% of all myocardial infarctions in men and women respectively. Unrecognized myocardial infarction was said to be present when routine biennial ECG demonstrated unequivocal evidence of MI during the 2-year interval when neither the patient nor the primary physician considered the symptoms to reflect an MI or there was no recollection of symptoms.

The Framingham Study data have been reinforced by many other cohort studies. The Western Collaborative Group Study (Rosenman, et al., 1967) showed a 37% rate of unrecognized myocardial infarction in men age 35-80. The Israeli Heart Attack Study

(Medalie & Goldbourt, 1976) had a 40% result of unrecognized myocardial infarction in men of all ages. The largest of the studies, the Multiple Risk Factor Intervention Trial (Grimm et al., 1987) and the Reykjavic Study for men and women (Sigurdsson, et al., 1995 & Jonsdottir et al., 1998) had unrecognized myocardial infarctions noted to be 25%, 35% and 33% respectively. Ammar et al. (2004) reviewed 14 population-based studies of unrecognized myocardial infarction and looked at the electrocardiogram criteria used in each study. They found an absence of well-defined electrocardiographic criteria between the studies. Each of the methods used has its own inherent limitations that could lead to overestimation or underestimation of the true percentage of unrecognized myocardial infarction.

For many reasons, these data may underestimate the frequency of unrecognized myocardial infarctions. Most diagnoses were based on electrocardiographic identification by Q wave presence. The identification of ischemia/infarction by the ST segment was not considered, therefore, a population of myocardial infarction patients might have been missed. Second, unrecognized myocardial infarctions resulting in cardiac death were excluded from the studies. Third, most only accepted men into their study populations. Lastly, electrocardiographic features of a myocardial infarction may have been missed because some of the features disappear on the electrocardiogram after 2-4 years. The studies used varying definitions for what was considered an unrecognized myocardial infarction.

The most recent large prospective, multinational registry of patients with acute coronary syndrome (ACS), unstable angina or non-ST elevated myocardial infarction, was the Global Registry of Acute Coronary Events (GRACE) study (Brieger et al., 2004).

This analysis stratified patients according to whether their predominant presenting symptoms included chest pain or did not. Of the 20,881 patients in the registry, 1,763 (8.4%) presented without chest pain. The atypical symptoms dominant in the non-chest pain group were syncope, nausea or vomiting, and dyspnea. These patients were more likely to be older, female, hypertensive, and diabetic.

Risk Factors Associated with Myocardial Infarction

Risk factors for myocardial infarction parallel those of atherosclerosis and include (but are not limited to) diabetes, hypertension, age, sex (female>male), truncal obesity, smoking, increased levels of low-density lipoprotein (LDL) cholesterol, decreased levels of high-density lipoprotein (HDL) cholesterol, elevated levels of homocysteine, a positive family history of atherosclerosis and increased levels of triglycerides (Hackam & Anand, 2003; Simons et al., 2002).

Risk Factors Associated with Unrecognized Myocardial Infarction

Identification of predisposing factors whether associated with age, gender, race or pre-existing diseases, is beneficial to better understand, diagnose, provide treatment, and, ultimately, prevent myocardial infarction from being unrecognized in the emergency setting. Several studies have shown a higher association with atypical symptom presentation as compared with MI patients with chest pain, but their study methods vary as well as the variables used for analysis. Table 2 addresses these studies and identifies the variables used in each.

Age.

Older patients are apt to experience more atypical symptoms of myocardial infarction that may predispose them to delays in seeking medical attention (Gurwitz et

al., 1997; Tresch, 1998). The majority of studies of unrecognized myocardial infarction included very few older patients, yet results suggest the incidence increases with age. In the Reyjkavik Study (Sigurdsson et al., 1995), the incidence of unrecognized myocardial infarction increased from 120 per 100,000 persons per year at age 40 to a high of 320 per 100,000 persons per year at the age of 65. In the Israeli Heart Attack Study (Medalie & Goldbourt, 1979), unrecognized myocardial infarction increased from 38% in ages 39-59 to 49% in those 60 years and older. The Bronx Aging Study (Nadelmann et al., 1990) admitted only persons from ages 75 - 85. The incidence of unrecognized myocardial infarction in this population was 44%. These limited studies suggest increasing age may be associated with unrecognized myocardial infarction. Whether age has an independent association or is associated with other changes of aging is uncertain at this time. Despite the high prevalence of coronary artery disease in older persons, clinical manifestations are often unrecognized or underdiagnosed in this population. Diagnostic differences between ages may reflect differences in the disease process or may be related to the superimposition of normal physiological aging changes and presence of concomitant disease that masks usual clinical manifestations (Tresch & Jamali, 1998).

Sex.

Until recently, very few studies have evaluated the association of sex to the recognition of myocardial infarction. The available data from the various studies suggest that women have a relatively higher risk for unrecognized myocardial infarction (Canto et. al, 2000 [N = 142,445]; Sheifer, Gersh, et al., 2000 [N=5,888, age ≥ 65]). The Framingham Study (Kannel, Cupples & Gagnon, 1990) showed an unrecognized myocardial infarction rate in women of 34% versus 26% in men (N = 5070, age 35-94).

Table 2

Studies Addressing Unrecognized Myocardial Infarction

Study Name, Year, Reference Factors*	Age	Sex	Diabetes	HTN	Risk
Western Collaborative Group Study, 1967, Rosenman, et al.	35-80	M	No	X	X
Israeli Heart Attack Study, 1976 Medalie & Goldbourt	40-78	M	No	X	No
Framingham Study, 1990 Kannel, et al.	35-94	M/F	X	X	X
Bronx Aging Study, 1990 Nadelmann et al.	75-85	M/F	X	X	X
Reykjavik Study, 1995 Sigurdsson et al.	49-80	M	No	X	X
Cardiovascular Health Study, 2000, Sheifer et al.	≥ 65	M/F	No	X	X

Abbreviations: M = Male; F = Female; HTN = Hypertension; No = not studied

Risk Factors: Increased cholesterol, congestive heart failure, stroke, angina, myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft.

A study in sex differences in symptom presentation by Goldberg and associates (1998) showed women with a higher percentage of atypical symptom presentation than men (n = 1360; male - 810, female - 550). The most prevalent symptoms in women were shortness of breath and nausea. The study did not differentiate unrecognized myocardial infarction from recognized myocardial infarction.

The reason for these sex differences may be multifactorial. The magnitude of the role sex plays in cardiac disease, especially women, is not well appreciated (Peterson & Alexander, 1998). Because of the compounding factors and association with atypical symptom presentation in women, delays in treatment may play a significant role (Gurwitz et al., 1997; Zerwic, 1998).

Race.

None of the large cohort studies that addressed unrecognized myocardial infarction examined race as a variable. Taylor and associates (1998) analyzed the National Registry of Myocardial Infarction 2 (NRMI 2) data set. This study found that black patients (versus whites) presented later to the hospital after onset of symptoms (median 145 vs. 122 min), were more likely to have an atypical symptom presentation (28% versus 24%, a non-diagnostic electrocardiogram (37% vs. 31%) and were less likely to receive therapy by 15%.

Another large study (N = 1855, age – 30 > 90, sex- 1101 men/754 women) by Pope and associates (2000) analyzed clinical data from a multi-center prospective trial of patients admitted to the emergency department with suggestive cardiac ischemia. This study found two variables that could be considered independent predictors for patients

who had myocardial infarctions but were not hospitalized: non-white race and normal electrocardiogram.

Klinger and associates interviewed patients seen in the emergency department (ED) and admitted to an ED chest pain center (2002). Symptoms of ischemia were found to be similar among black and white patients. The differences were found in the patients' perceptions of symptoms in regards to attribution. Black patients had a stronger tendency to attribute their symptoms to non-cardiac sources (14% vs. 9%). Whether these attributions influence diagnosis and therapeutic approaches to care are still speculative and require further study.

Hypertension.

Hypertension has a strong association with myocardial infarction due to its effects on arteries over time. Hypertension combined with coronary artery disease increases the risk of coronary artery occlusion and infarction of the myocardial tissue, whether recognized or unrecognized.

It is also suggested that hypertension is associated with alterations in pain perception (Sheifer, Gersh, et al. 2000). Several studies offer support to this association. In 1991, Deedwania and Carbajal ($N = 25$) noted an elevation of systolic blood pressure from 20-40 mm Hg of baseline frequently preceded (within 10-30 minutes) the onset of a silent ischemic event observed during routine daily activities, especially morning surges on arising. The Israeli Heart Attack Study (Medalie & Goldbourt, 1976) also showed an elevation of systolic blood pressure ($N = 9509$ men, age ≥ 40 years). This study showed an increase of systolic blood pressure greater than 160 mm Hg to be related to a higher incidence of unrecognized myocardial infarction ($F = 2.327$, $p < 0.01$). The Western

Collaborative Group Study (Rosenman et al., 1967) showed higher systolic and diastolic blood pressure in subjects with unrecognized myocardial infarction than those myocardial infarction subjects with classic pain presentation.

Although many studies have studied systolic and/or diastolic hypertension as a risk factor in unrecognized myocardial infarction, none have confirmed either to be a unique independent link. Because it contributes to atherosclerosis, hypertension remains an important clinical risk factor in the evaluation and treatment for coronary artery disease to decrease the possibility of unrecognized myocardial infarction.

Diabetes Mellitus.

Several studies over the last 60 years have suggested an association between diabetes and coronary artery disease. Many correlations, including post-mortem and angiographic studies suggest diabetic patients have more atherosclerotic disease of the coronary arteries. In 1997, the Milan Study on Atherosclerosis and Diabetes (MiSAD) Group studied prevalence of unrecognized myocardial ischemia in 925 non-insulin dependent diabetic patients (592 men/333 women), aged 40-65 years who underwent exercise electrocardiography. If abnormal, an exercise thallium scintigraphy was obtained. The prevalence of subjects with abnormal exercise response (17.1%) and subjects with abnormal response to both exercise electrocardiography and thallium scintigraphy (6.4%) is about three time higher than found in apparently healthy populations. The higher prevalence in the diabetic population did not appear to be attributable to an excess of major coronary risk factors in comparison to the general population. The findings of the Milan Study on Atherosclerosis and Diabetes (MiSAD) Group support the independent role of diabetes as a risk factor for atherosclerosis.

Evidence from the Framingham Study (Kannel et al., 1990) demonstrated that asymptomatic myocardial infarction occurred more frequently in diabetic patients (40.7% unrecognized in men $p<0.05$, 30.3% in women, not statistically significant).

While the exact mechanism has not been identified, the presence of autonomic dysfunction in diabetes has been postulated (Acharya et al., 1991). This study investigated 14 Type II diabetic patients with myocardial infarction, 7 with chest pain and 7 without chest pain (age 38-71, 11 male/3 female). The investigation showed:

- Diabetes was of a significantly longer duration in the painless MI group,
- Five of seven patients in the group without pain and none in the group with pain had evidence of peripheral neuropathy,
- autonomic dysfunction was more marked in the painless MI group.

With the risk factors previously discussed, there is supporting evidence that diabetes may be an independent predictor of unrecognized myocardial infarction. The clinical significance lies in recognition and use of this knowledge as a relatively high-risk feature in presentations of unrecognized myocardial infarction. Practitioners should use this knowledge to increase their diagnostic abilities to detect and manage unrecognized myocardial infarction.

Risk Factor Profiles.

The accuracy of diagnosis of myocardial infarction in patients in the emergency department can be maximized by a careful history and evaluation of associated risk factors. Important profile variables associated with atypical presentations of myocardial infarction were congestive heart failure, prior stroke, older age, diabetes, female and non-white race (Canto et al., 2000). Canto et al. conducted a study between 1994-1998 from

the National registry of Myocardial Infarction 2 database, which included 1674 hospitals with a total of 434,877 patients confirmed with a myocardial infarction. Patients who presented with chest pain had a higher likelihood in their risk factor profile of history of present or past cigarette smoking, increased cholesterol, prior history of angina, infarction, percutaneous coronary intervention or coronary bypass graft surgery.

Diagnosis of myocardial infarction in the emergency department

In the nursing profession, we are taught to recognize classic signs and symptoms indicated in various disease states. These heuristics aid us by narrowing the list of causative problems. Initial evaluation of patients in the emergency department is dependent on the subjective information given. This information may be distorted by the synthesis of the healthcare provider to formulate a clearer picture (Peterson & Alexander, 1998).

Many studies have discussed the myocardial infarction patients' perceptions of their signs and symptoms and related those to a delay in treatment (Ryan & Zerwic, 2003; Gurwitz, 1997; Klinger et al., 2002; Pope et al., 2000). Although delays getting to the hospital are important in the overall outcome for the patient, they will not be a focus of this dissertation. The focus will be from the time of arrival to the emergency department, to diagnostic intervention and then time to treatment modality.

The hallmark sign of myocardial infarction is substernal chest pain, which may be associated with other symptoms. The patient describes this pain by different descriptors: tightness, squeezing, crushing, burning, elephant on chest, etc. (Zerwic, 1998). To an emergency healthcare provider, these descriptors all relate to the term 'chest pain'. Atypical symptoms generally do not 'cue' the emergency healthcare practitioner to

suspect myocardial infarction on initial evaluation, therefore delaying the onset of the diagnostic intervention. In a study by DeVon and associates in 2004, documentation of symptoms related by the patients was inconsistent between the patients' report and the documentation. They interviewed 215 patients and reviewed their medical records for information about their admission symptoms. Chest pain was the most frequently reported and recorded symptom and there was good agreement between the patients' report and the medical record. Fatigue was the second most frequently reported symptoms, yet it was rarely documented in the medical record. Findings suggest that the medical record is an inadequate and inaccurate source of information about the patients' symptoms.

In a time of advancing diagnostic modalities, the diagnosis of myocardial infarction continues to be achieved by a simple, useful, easily applied, repeatable and affordable tool called an electrocardiogram (Fu et al., 2001). Time to diagnosis is dependent on the time to electrocardiogram completion and interpretation. Once myocardial infarction is diagnosed, treatment modalities can be initiated. The practitioner's ability to recognize symptoms and associated risk factors is essential to expedite ordering of the electrocardiogram, anticipating the potential diagnosis of myocardial infarction. Canto and associates (2000) observed a time interval from admission to electrocardiogram of 15.6 ($p<0.001$) minutes for patients with chest pain presentation and 31.8 ($p< 0.001$) minutes in patients with atypical presentations. Recommendation from the American Heart Association is to begin treatment within 30 minutes of arrival for thrombolytic therapy or 90 ninety minutes to angiographic

catheterization. As is identified, there is presently considerable loss of time to diagnosis and therefore treatment in patients with atypical presentations.

Management of patients suspected to have had a myocardial infarction requires rapid assessment in the emergency department in less than 10 minutes (Custer, 2002; Graff, 2000). It is important to assess the patients rapidly to enable a diagnosis to be made. The primary goal in the emergency department is to reduce delays in treatment to provide the best outcomes. Therefore, rapid diagnosis by electrocardiogram is essential. Without this vital information, therapies to limit infarction size and decrease potential untoward outcomes cannot be initiated.

Aggressive efforts have been initiated to change processes for patients presenting with chest pain to obtain the electrocardiogram within 5 to 9 minutes of arrival in the emergency department to reduce time to treatment (Graff et al., 2000). In the Graff study, chest pain was the sole complaint of 60% of patients admitted to the emergency department with myocardial infarction. Some of the other patients complained of dyspnea (10.4%), weakness/fatigue (6.2%), syncope (2.7%) and abdominal pain (2.7%). The facility used for the study developed a guideline for ordering electrocardiograms within 5 minutes for all the above presenting complaints. The mean delay for performance of the electrocardiogram decreased from 10 minutes to 6.3 minutes with use of the guideline.

In a quality study currently being performed at four local hospital emergency departments, attention to performance of electrocardiograms on patients presenting with chest pain and diagnosed with a myocardial infarction has decreased from 20 minutes average to 5-9 minutes average per facility (J. Nordblom, unpublished data). Myocardial

infarction patients with atypical presentations in these emergency departments have their electrocardiogram completed on an average of 15-30 minutes.

Summary

Although results of these various studies are fairly consistent, none support or indicate that any one of these risk factors has an independent prediction for unrecognized myocardial infarction. Being able to assess for a profile of risk factors would be important to draw attention to the need for more expedient electrocardiograms in patients with atypical signs and symptoms. Most are coronary risk factors found in all myocardial infarction patients and a unique link of these risk factors have not been shown to be associated with only unrecognized myocardial infarction.

Myocardial infarction is frequently unrecognized for reasons that have been studied in various venues and varied populations but are yet to be used as strong recommendations to change practice or process. Although many unrecognized myocardial infarctions are accompanied by symptoms considered to be atypical, without pain, and with similar risk factors and other characteristics, this population of people appears to delay getting and receiving appropriate treatment. It seems logical that clinical judgment would include recognition of these factors to assure rapid identification of myocardial infarction. More attention and education should be given to emergency staff to increase their awareness of the symptom presentation and risk factors in patients with atypical presentations as well as creation of guidelines to expedite electrocardiogram diagnosis of myocardial infarction.

Research Questions and Conceptual Framework

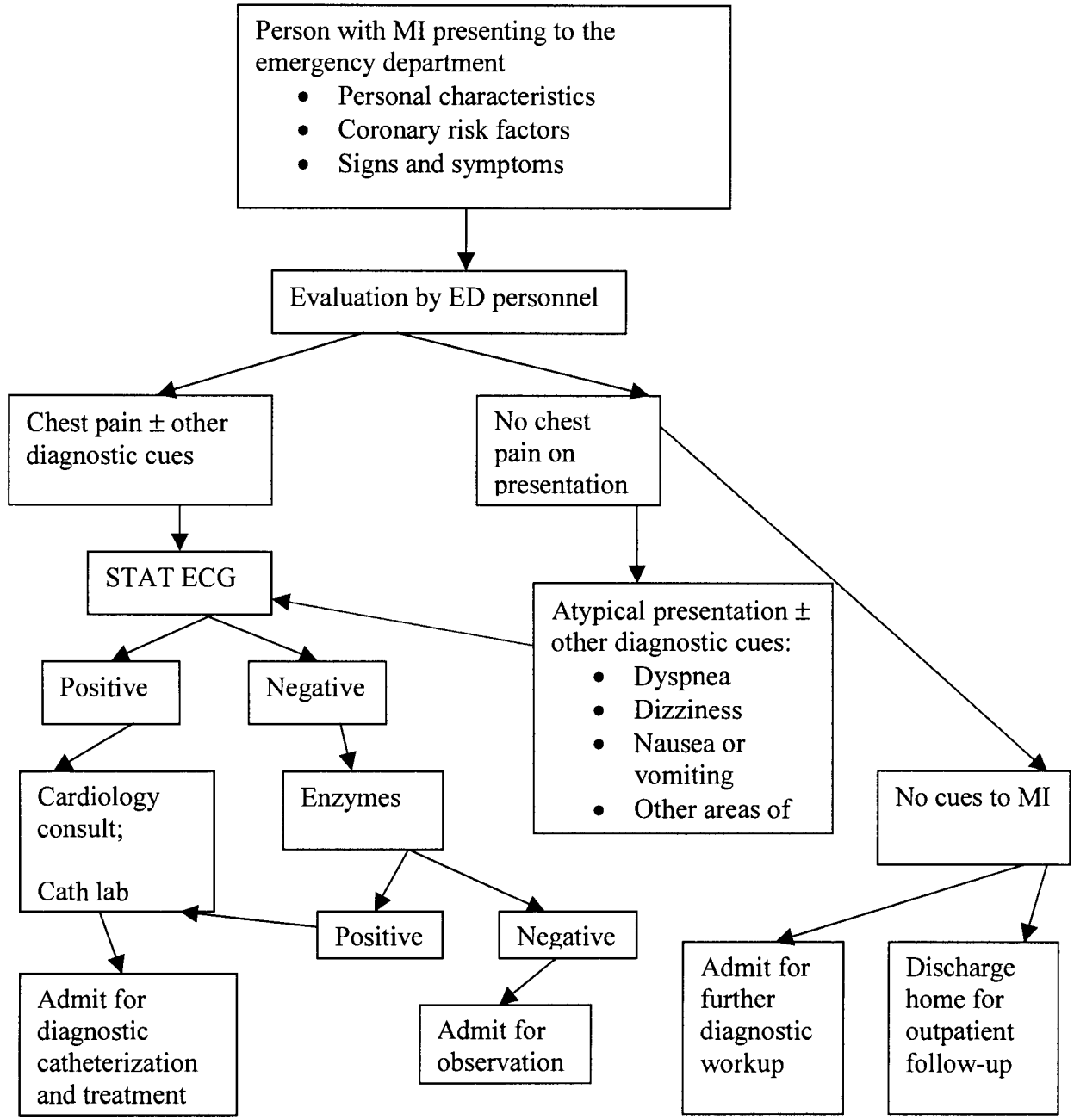
The focus of this study is patients admitted to the emergency department with atypical presentations of myocardial infarctions. The research questions are as follows:

1. What percentage of patients with myocardial infarction diagnosed in the emergency department have atypical signs or symptoms on presentation?
2. Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting with complaints of dizziness or shortness of breath is having a myocardial infarction without chest pain?
3. Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting without chest pain but with dizziness or shortness of breath is having a myocardial infarction?
4. Which signs and symptoms or risk factors, individually or in combination, predict that a patient who is diagnosed with a myocardial infarction presents to the emergency department without chest pain?
5. Which individual signs and symptoms or risk factors predict when a patient receives a diagnostic electrocardiogram within 9 minutes and receives interventional treatment within 90 minutes of arrival to the emergency department?

Having an understanding of factors associated with these atypical symptoms may help in earlier identification and treatment of patients having a myocardial infarction. The conceptual framework (Figure 1) for this study depicts progression of a patient with a myocardial infarction presenting to the emergency department, incorporating the personal characteristics, coronary risk factors and signs and symptoms on presentation that are a focus of this study.

Figure 1

Conceptual Framework
Time to Diagnosis of Myocardial Infarction



ED = emergency department
ECG = electrocardiogram
STAT = *statim*, once or immediately
MI = myocardial infarction
Cath = cardiac catheterization

Chapter 3

Research Design and Methods

Introduction

The focus of this research was to evaluate presenting signs and symptoms of patients who present to the emergency department and are diagnosed with a myocardial infarction. Classic presentation signs and symptom of chest pain are clinically easy for the emergency department personnel to recognize, yet many other myocardial infarction patients who do not have classic chest pain when presenting to the emergency department for care may have a delay in their diagnosis and treatment. Descriptive information is needed to have an accurate picture of what other factors or signs and symptoms are indicative of myocardial infarction as well as what other factors may be associated. The emergency department personnel take a patient's chief complaint and the patient's stated description of his or her signs and symptoms as important sources of information. This descriptive information is key to cue the staff to suspect certain problems. It is with research that patterns can be established from the descriptions given by patients with atypical presentation signs and symptoms to allow changes in practice.

The long-range goal of this program of study is to use descriptive data collected to create a clinical practice guideline to expedite ordering of diagnostic electrocardiograms and treatment in older adults who present to the emergency department with atypical signs and symptoms of myocardial infarction.

Study Design

This study used a retrospective descriptive research design to examine relationships between variables that have an association with myocardial infarction. Descriptive research is used to show an accurate portrayal of characteristics and the frequency with which they will occur. This design was used to investigate specific signs and symptoms, demographics, past medical history, prior medical events, and time sequencing in patients presenting to an emergency department and diagnosed with a myocardial infarction.

This design is an efficient and effective means of collecting data to examine relationships among the variables (Polit & Beck, 2004). The weakness of this design is the researcher's inability to manipulate the independent variables and the inability to assign subjects randomly into two groups. Without random assignment of subjects to comparison groups, it can never simply be assumed that the groups selected and compared in the analysis are truly equivalent or similar to each other in terms of their background characteristics. There is no all-purpose mechanism in a descriptive study to minimize the impact of potential confounding or extraneous variables. This does not mean that it is futile to reason or argue causal relationships amongst observed variables. What can be done is to control for the effects of other variables in the analysis stage. The need for such statistical control is even greater in a descriptive design; therefore, a multivariate regression was used (Strommel & Wills, 2004), but a logistic regression, since the outcome was dichotomous. With this analysis, the impact of an independent variable on the outcome variable can be demonstrated to be distinct from the effects of the other variables.

Setting

The setting for this study used two hospital emergency departments. One was a 26-bed emergency department within a 200-bed tertiary care, Joint Commission accredited hospital in a large urban metropolitan area. This emergency department, which has a 50,000 patient census per year, serves a large geriatric population and has a specialty in cardiac, endocrine and renal disease. Of this emergency department's census per year, 23% present with acute coronary syndromes (2006 Legacy Census Data).

The second facility was a 23-bed emergency department within a 75-bed Joint Commission accredited hospital in a community setting. This facility is located within a large retirement community in a rural area approximately seven miles south of the first facility. Of this emergency department's 35,000 patient census per year, nearly 20% present with acute coronary syndromes (2006 Legacy Census Data).

Personnel staffing each emergency department includes a minimum of two registered nurses trained in Advanced Cardiac Life Support, a board-certified emergency physician, an emergency technician and a unit secretary. The staff of the two hospitals have the same education and training on hire, use the same documentation forms, have the same quality improvement activities and the same clinical nurse specialist providing clinical oversight. The registered nurses are authorized to order an electrocardiogram before physician evaluation if their assessment of the presenting complaint and history indicates a potential for the patient to have a myocardial infarction. Each department has its own electrocardiogram machine. The registered nurses and emergency technicians are trained at orientation for 2 hours and maintain competencies on a yearly basis to obtain

electrocardiograms. This decreases the time that may be necessary to call and wait for a cardiopulmonary technician to arrive in the emergency department.

Sample Selection

The study sample was chosen from the population of patients who present to these two emergency departments. Eighteen percent of the patients seen in these two emergency departments are over the age of 65 years and six percent are over 85 years of age. Inclusion and exclusion criteria was used to define who is eligible to be part of the study. Inclusion and exclusion criteria, combined with the selection of clinical sites for recruitment, provided the precise, operational definition of the study population to which the research can be generalized. To optimize the ability to generalize study findings to prospective target populations, it is clearly preferable to have broad inclusion criteria and minimal exclusion criteria (Strommel & Wills, 2004). The study began including subjects at age 40 due to their high-risk life-styles and/or familial history of significant coronary artery disease. The study subjects were a convenience sample from the overall emergency population of the two settings. Subjects were taken from two hospital emergency departments with a higher census of older adults to increase the generalizability. This age range was grounded in literature over the last forty or more years.

Inclusion into the sample included patients presenting to the emergency department that have signs and symptoms who may be associated with myocardial infarction, primarily chest pain, dyspnea and dizziness. This study also included other atypical signs and symptoms in the data abstraction and statistical analyses for differentiation. Inclusion criteria were as follows:

- Age 40/100 years;

- Presented to the emergency department between April 2004 to August 2006;
- Presenting signs or symptoms, previous medical history and prior medical events are noted in the medical record. If an interpreter is used, this will be noted.

Exclusion criteria were as follows:

- Patients unable to give history of events.
- Patients with chest pain but not diagnosed with myocardial infarction;
- Patients who present to the emergency department in cardiopulmonary arrest due to myocardial infarction;
- Diagnosis of myocardial infarction made on inpatient unit after the emergency department visit (unable to determine when in the course of care the myocardial infarction occurred and this diagnosis may not be known by the emergency department staff);

Each patient who met criteria was entered into the study. It was the intent of this study to produce a facsimile of a probability sample by inclusion of every eligible subject that met criteria during April 2004 to August 2006. Each patient that presented to the emergency department with a primary chief complaint of chest pain, dyspnea or dizziness was included in the study in the order of their arrival at each facility. This information was readily available in the electronic medical record.

A power analysis to estimate the sample size was used. Power analysis builds on the concept of effect size, which expresses the strength of relationships between variables. There was no *a priori* reason for believing the relationships would be strong in

this exploratory study. A more in-depth discussion of the power analysis will be discussed in the results section (page 65).

Data Collection Procedures

The data were gathered from a retrospective chart review. Potential subjects were chosen from the electronic logs of the two facilities using the presenting complaint and admission diagnosis of myocardial infarction. The charts were pulled from the emergency department storage area for review. All privacy and compliance issues were addressed to afford protection for the subjects (Annas, 2002). The inclusion and exclusion criteria were applied by the researcher, using the Subject Screening Tool (Appendix A).

Each chart that met criteria was assigned a consecutive subject number. The subject number denoted the facility by using numbers beginning with 1 and 2. A data collection tool (Appendix B) was utilized to abstract information from the emergency department records. The information on the records was collected and documented as part of routine emergency assessment and registration processes. Data were found on the emergency department record, the emergency physician history and physical sheet (T Chart) and the electronic record. Table 3 shows the data source for each variable. Knowledge of the time of symptom onset and types of symptoms is important in order to provide appropriate treatment modalities within a specified timeframe and to afford maximal effectiveness. Yet, accuracy of this documentation is fraught with difficulties due to the patient's ability to recall this information during a crisis. It would be desirable to have an in-depth interview, but the patient's clinical course and outcomes requires expediency.

In the study done by DeVon, Ryan and Zerwic (2004) it was noted that accuracy in the medical record is diminished due to many factors, some of which are poor recall,

Table 3

Data Sources for Each Variable

Variable	Operational Definition	Data Source
Age	Present age in years at time of admission to emergency department	Subject's admission record
Sex	Male or female	Admission record
Myocardial infarction	Primary diagnosis of myocardial infarction	Medical records: emergency services encounter form
Presentation Signs or Symptoms	Chest pain, dyspnea, dizziness/syncope, nausea and/or vomiting or other areas of pain described by patient at the emergency department	Medical records: emergency services encounter form and/or emergency flow sheet.
Medical History	History of diabetes, angina, hypertension, include if being treated, or ↑ cholesterol Family history of coronary artery disease, History of asthma , history of COPD	Medical records: emergency services encounter form and/or emergency flow sheet.
Prior Events	History of previous MI, stroke, CHF, PCI or bypass grafts	Medical records: emergency services encounter form and/or emergency flow sheet.
Time Intervals	Time from ED room entry to finish of electrocardiogram, time from ED room entry to treatment of myocardial infarction	Medical records: emergency services encounter form, and/or emergency flow sheet.

anxiety, pain, high acuity or honesty of the patient. Whatever the reasons, the trade-off for having a high index of suspicion from the symptoms presented versus in-depth interviews is essential. In an emergent clinical situation, emergency department clinicians must trust and work with the information that is available now.

Study subjects have the right to expect that any data will be kept in strictest confidence and their anonymity maintained. Anonymity occurs when no one, including the researcher, can link study subjects with their data, protecting the study subjects' right to privacy. A number of steps were taken to ensure that breaches in confidentiality did not occur:

- Assignment of subject numbers, maintained in a locked file with restricted access to the researcher only;
- No identifying information on computer files;

In addition, there was a plan to destroy mapping of subject numbers to the subjects' at the earliest opportunity consistent with the research and assurance that the information was not used or disclosed to any other person (Annas, 2002).

To protect patients' information, a waiver of patient authorization for retrospective review of medical records for research purposes was requested from the Institutional Review Boards. The only variable being abstracted from the medical records that may be considered protected health information under the HIPAA law is age of patients over 89 years. A confidentiality waiver signed by the researcher and submitted to the Institutional Review Board allowed access to the records (Appendix C).

Variables

The variables are represented by the concepts of the study. The dependent variable, the variable whose variation needs to be explained, is subjects' with a myocardial infarction or not. The independent variables, whose variation might explain the variation in the dependent variable, are categorized as demographic variables, presentation signs or symptoms, medical history, prior events and time intervals. Table 1 presents the study variables with their operational definitions.

Data Coding, Entry and Verification.

Each data point for signs and symptoms was noted by its presence or absence. Some of the demographic variables were described in race categories (white, black, Hispanic, Asian and American Indian or Alaskan Native). The time variables were described in minutes. (See Table 4) After coding, data were entered into a statistical program. The data obtained in this study were analyzed on a Toshiba personal computer using SPSS (Statistical Program for the Social Sciences) Graduate Pack 15.0 for Windows (2006) statistical software package.

Statistical Analysis

Statistical analysis assists in making sense of the quantitative information: to summarize, organize, evaluate, interpret and communicate numeric information (Polit & Beck, 2004). Age was divided into categories of ≤ 65 years of age and 65 years of age. Initially, descriptive statistics were used to describe sample characteristics and synthesize data. The characteristics of the study sample were computed through use of descriptive statistics, including percentages, frequency computations, cross tabulation tables, and measures of central tendency. The use of descriptive statistics allowed summarization and

Table 4

Coding for Study Variables

Variable	Type of Data	Coding
Age	Continuous	Years
Gender	Categorical	Male = 0 Female = 1
Race	Categorical	White or Caucasian = 0 Black or African American = 1 Hispanic or Latino = 2 Asian or Oriental =3 American Indian or Alaskan Native = 4 Native Hawaiian or Pacific Islander = 5 Other = 6 Unknown = 7
Diagnosis of myocardial infarction	Categorical	Yes = 0 No = 1
Presentation Signs and Symptoms		
Chest Pain	Categorical	Yes = 0 No = 1
Dyspnea	Categorical	Yes = 0 No = 1
Dizziness/syncope/lightheadedness	Categorical	Yes = 0 No = 1
Nausea and/or vomiting	Categorical	Yes = 0 No = 1
Diaphoresis	Categorical	Yes = 0 No = 1

Other areas of pain	Categorical	Yes = 0 No = 1
	Medical History	
Diabetes	Categorical	Yes = 0 No = 1
Angina	Categorical	Yes = 0 No = 1
Hypertension	Categorical	Yes = 0 No = 1
Treatment for hypertension	Categorical	Yes = 0 No = 1
↑ Cholesterol	Categorical	Yes = 0 No = 1
Treatment for ↑ cholesterol	Categorical	Yes = 0 No = 1
History of asthma	Categorical	Yes = 0 No = 1
History of COPD	Categorical	Yes = 0 No = 1
Family history of CAD	Categorical	Yes = 0 No = 1
	Prior Events	
MI	Categorical	Yes = 0 No = 1
Stroke	Categorical	Yes = 0 No = 1
CHF	Categorical	Yes = 0 No = 1
Percutaneous Coronary Intervention (PCI)	Categorical	Yes = 0 No = 1

Bypass grafting	Categorical	Yes = 0 No = 1
Time to ECG	Continuous	Minutes
Time to Treatment	Continuous	Minutes

description of the quantitative data from the medical records review. Inferential statistics were used to make inferences about the data. Inferential statistics were used are based on Chi Square, Fisher's exact, and logistic regression.

Research Question One: What percentage of patients with myocardial infarction diagnosed in the emergency department have atypical signs or symptoms on presentation?

The percentage of patients with atypical presentations of myocardial infarction were determined by calculating the number of patients who did not present with chest pain divided by the total number of patients in the study with myocardial infarction to achieve a percentage. An associated 95% confidence interval was calculated.

Research Question Two: Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting with complaints of dizziness or shortness of breath is having a myocardial infarction without chest pain?

Research Question Three: Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting without chest pain but with dizziness or shortness of breath is having a myocardial infarction?

Research Question Four: Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting without chest pain but with dizziness or shortness of breath is having a myocardial infarction?

Research questions 2-4 made use the same analyses. Bivariate analyses of individual signs and symptoms or risk factors were conducted to determine which of those have predictive value. Chi Square analysis, a non-parametric test of significance, was used to

assess whether a relationship exists between signs and symptoms, risk factors and the outcome variables (Polit & Beck, 2004). The Chi Square test is used to decide whether differences in proportions are likely to reflect real experimental effect or only chance fluctuations. Fisher's exact test was used in place of chi-square test in cases of small expected cell counts.

Multiple regression analysis is a statistical method that is useful in forecasting (Grimm & Yarnold, 2004). It provides for understanding simultaneous effects of two or more independent variables on a dependent variable. Multiple logistic regression analysis is similar to multiple linear regression except the dependent variable is dichotomous rather than continuous. A step-wise regression is a forward selection method for empirically selecting the combination of independent variables with the most predictive power. It starts out with a constant regression relationship and adds independent variables one at a time if they meet certain statistical criteria. They may also be deleted at any step if they no longer contribute significance to the regression (Tabachnick & Fidell, 1996). Its focus is the amount of predictive power that each additional variable contributes and on the search for a small but effective set of predictive variables (Everitt et al, 2001). These predictors enter the equation in a specified order with the goal of accounting for the largest amount of variability in the dependent variable with each additional new variable added to the equation (Everitt et al, 2001). At each step, one or more new predictors are either added in forward inclusion or subtracted from in backwards elimination from those used in the previous step. The subsets used included demographics, presentation (signs and symptoms), medical history and prior events. The decision concerning which variable to add or subtract at each step was determined on the

basis of the empirical relationships among variables in the analysis. This strategy is most appropriate when the predictors are of comparable importance to the research problem but also when added in stages, *e.g.*, demographics first, signs and symptoms followed by medical history and prior events.

Typically, stepwise regression is used to develop a subset of independent variables that is useful in predicting the dependent variable and eliminates those independent variables that do not provide additional prediction beyond that of the independent variables already in the equation (Tabachnick & Fidell, 1996). Variable selection can also be conducted in a backwards fashion, beginning with the complete set of variables under consideration and systematically eliminating extraneous variables.

A regression analysis was performed to understand the effects of the independent variables on the dependent variable, myocardial infarction or not. The purpose was to determine the strength of these variables. These regression analyses were run in three different ways, using all entered, forward conditional and backward conditional procedures to obtain a more complete assessment of the impact of combinations of independent variables. Regression analysis allowed an ability to make a prediction of which variables are related. In turn, these variables will be used as the basis for a future clinical practice guideline. This would allow the practitioner the ability to create a guideline to better detect and readily diagnose myocardial infarctions in patients with atypical presentations.

An odds ratio was calculated in the logistic regression. The odds ratio is the increase (or decrease if the ratio is less than one) in the odds of being in the outcome category when the value of the predictor increases by one unit.

Research Question Five: Which individual signs and symptoms or risk factors predict when a patient receives a diagnostic electrocardiogram within 9 minutes and receives interventional treatment within 90 minutes of arrival to the emergency department?

The time variables for arrival to the emergency department to completion of the electrocardiogram and admission to the catheterization laboratory were described with descriptive statistics (mean, median) for patients with and without chest pain. The variability was described with the standard deviation.

The time variable for completion of the diagnostic electrocardiogram was categorized into ≤ nine minutes and > nine minutes. The time variable for intervention therapy was categorized into ≤ 90 minutes or > 90 minutes. Those two dichotomous outcome variables were analyzed as above in question two through four.

An estimation of sample size was computed using nQuery Advisor 5.0 (Statistical Solutions, Saugus, MA.). For two groups of patients without chest pain: those without an MI and those with an MI, to identify a risk factor for having an MI with an odds ratio of 2.0 or more, the required sample size per group ranges between 133 and 152 as the true proportion of subjects with the risk factor who also have an MI ranges between 0.4 and 0.7. To detect smaller odds ratios or an odds ratio of 2.0 with true proportions lower than 0.4 or higher than 0.7 requires larger sample sizes.

Validity.

Internal validity refers to the extent to which it is possible to make an inference that the independent variable is truly influencing the dependent variable and that the relationship between the two is not due to an extraneous variable (Polit & Beck, 2004).

Every effort was made to obtain accurate data from the retrospective chart review. Because of the design, the researcher was not able to rule out other alternative explanations to the findings and conceivably difficulty interpreting the results. These competing explanations were a threat to internal validity. Analysis of clinical data from records, especially routinely collected clinical data may have validity issues that arise from the fact that the original data collection is not researcher controlled. Validity issues that need to be considered are the completeness of the records. Clinical records may be incomplete or more importantly, the interpretation of the information from incomplete records may alter results. DeVon and associates (2004) noted differences between in-depth interviews days after the event and those done by clinicians at the time of admission to the emergency department. The proposed reasons were that the patients reported more symptoms during in-depth interviews because of the additional time taken for the interview, the increase in patient anxiety during their initial presentation and possible bias of the clinicians.

The numerous benefits of rapidly utilizing research results to change practice and improve care of patients with myocardial infarction includes trade-offs. Patients who present to the emergency department will in most circumstances have anxiety and fear, thus decreasing their cognitive abilities to accurately describe their presentation signs and symptoms at the moment and clinicians have time constraints to begin treatment. This situation is both a weakness (validity issue) and strength of this proposed study. The strength arises in its use of real clinical data obtained under normal time constraints of an emergency department. These data are what the emergency department personnel have to work with, so if they show results, it could be very useful in practice. This study of

presenting signs and symptoms in the emergency department is very important and can add to the body of knowledge of symptom presentation of myocardial infarction.

Selection bias was not an issue because the subjects are not initially divided into groups; they come from the pool of all myocardial infarction patients. The groups were divided during statistical analysis.

Content validity is an important aspect of research that uses measurement scales. The main concern with content validity is that the variables selected all reflect the conceptualization. Content validity of this type of data collection tool has been tested by Canto et al. (2000) who used all of these same variables. Content validity of the current data collection tool was based on the judgment of two nurse researchers, one with critical care experience, the other with emergency experience.

Conceivably, there are threats to external validity. Because this study draws its sample from only two facilities in one area of a state, it may not be representative of a larger population over various states (Hays, 1994).

Reliability.

Problems can occur with reliability of data recorded in the medical records. There may be omissions or errors in recording of data. In addition, medical records often include entries by multiple people of differing disciplines, either physician or nurse, therefore reflecting differing viewpoints and abstractions of the information given (Strommel & Wills, 2004).

Since this study was a retrospective medical record review, it was not possible to measure inter-rater reliability of documentation. The registered nurses and physicians have varied backgrounds in education and training in documentation during school. On

orientation to these facilities, the nurses and physicians are given education for proper documentation. Although the consistency of records may be beneficial to documentation, each registered nurse or physician has his or her own style that determines the amount of information asked of the patient and the depth and degree to the documentation of this information. Since one person performed the data collection, inter-rater reliability was not an issue at the data abstraction level. This study will be easily replicable if the same data collection tool is used.

A small sub sample of ten patient records was used to evaluate data abstraction. This researcher abstracted the data using the tool then another registered nurse used the same documentation and abstracted the data with the tool. The percentage of agreement in this abstraction was 98%. Although measurement error cannot be eliminated, the reliability and consistency of this data collection tool produced stable observations.

Protection of Human Subjects

The study utilized existing information from a retrospective records review. No additional or invasive procedures were necessary for the purpose of this study. The investigator requested an expedited review from the Institutional Review Boards of Oregon Health & Sciences University and Legacy Health Systems. All additional protections for compliance with HIPAA rules and regulations were addressed. Consent for medical records review was obtained from the institutions' Health Information Service Administration, the Institutional Review Board and the respective emergency departments.

The Belmont Report (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978) emphasizes that respect for persons, the

ethical basis of informed consent, incorporates respect for the confidentiality of autonomous persons. The investigator used subject numbers instead of names in order to maintain anonymity and confidentiality of the subjects. A separate list of medical record numbers and subject numbers was kept in a locked file cabinet in the researcher's office. It will be destroyed at the end of the study. No subject's name or identity will be used in reporting or publishing results of this study. The reports used to discuss the findings relate to all subjects of the study rather than to individuals.

Chapter 4

Results

Description of Sample

The sample size was 316 subjects. The investigator reviewed the pertinent portions of the medical record for all 316 subjects.

Sample Characteristics.

Of the 316 subjects, 171 (54.1%) were diagnosed as having a myocardial infarction in the emergency department. Characteristics for the sample are displayed in Table 5. The age of the subjects (M = 69.1, Mdn = 69.0, SD 13.5, range 43-95) is presented graphically by a histogram (Figure 2). For the purpose of this study, those ≤ 65 years of age and those > 65 years of age (senior) were used in the analysis. All 316 (100%) received an electrocardiogram in the emergency department (M = 18.2 minutes, Mdn = 10.5 minutes, SD = 25.9 minutes, range 1-242 minutes). There were eight (2.5%, range 88-242 minutes) outlier electrocardiogram times which affected the mean. The median is the more appropriate measure of central tendency. Of the 316 subjects, 148 (46.8%, M = 158.1 minutes, Mdn = 94.0 minutes, SD = 172.8 minutes) were taken for a percutaneous coronary intervention (PCI) from the emergency department. There were 25 (6.9%, range 240-936 minutes) outlier percutaneous coronary intervention times which affected the mean. Reversal of ischemic insult is possible if care and treatment are provided before these outlier times (ACC/AHA, 2000). As with the time to electrocardiogram, the median score is the more appropriate measure of central

Table 5

Sample Characteristics

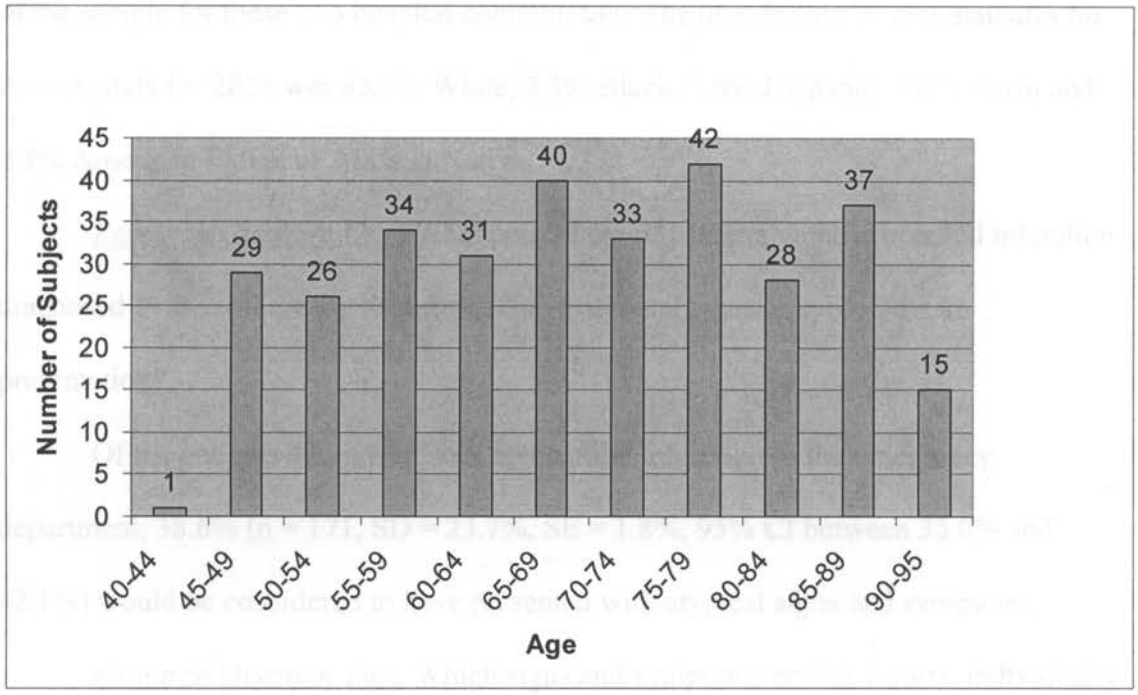
Variable	N	% of Total N (316)	N of MI (171)	% of MI
Sex				
Male	192	60.8	121	38.3
Female	124	39.2	50	15.8
Age				
≤ 65 years	121	38.3	75	23.7
> 65 years	195	61.7	96	30.4
Race				
White	282	89.2	149	47.2
Black	17	5.4	10	3.2
Hispanic	4	1.3	2	0.6
Asian	8	2.5	6	1.9
American Indian or Alaska Native	5	1.6	4	1.3
Chest Pain				
Yes	202	63.8	105	33.2
No	114	36.1	66	20.9
Shortness of breath				
Yes	184	58.2	103	32.6
No	132	41.8	68	21.5
Dizziness				
Yes	60	19.0	23	7.3
No	256	81.0	148	46.8
Nausea				
Yes	125	34.6	80	25.3
No	191	60.4	91	28.8
Vomiting				
Yes	38	12.0	24	7.6
No	278	88.0	147	46.5

Sweating				
Yes	94	29.7	69	21.8
No	222	70.3	102	32.3
Pain in other areas				
Yes	88	27.8	65	20.6
No	228	72.2	106	33.5
Diabetes				
Yes	80	25.3	41	13.0
No	236	74.7	130	41.4
Angina				
Yes	83	26.3	44	13.9
No	233	73.7	127	40.2
Hypertension				
Yes	215	68.0	112	35.4
No	101	32.0	59	18.7
Cholesterol				
Yes	159	50.3	83	26.3
No	157	49.7	88	27.8
Asthma				
Yes	24	7.6	11	3.5
No	292	92.4	160	50.6
COPD				
Yes	44	13.9	21	6.6
No	272	86.1	150	47.5
Smokes				
Yes	129	40.8	75	23.7
No	187	59.2	96	30.4
CAD				
Yes	114	36.1	21	6.6
No	202	63.9	115	36.4
Previous MI				
Yes	95	30.1	46	14.6
No	221	69.9	125	39.6

Previous Stroke				
Yes	29	9.2	15	4.7
No	287	90.8	155	49.1
CHF				
Yes	43	13.6	15	4.7
No	273	86.4	156	49.4
Previous PCI				
Yes	52	16.5	24	7.6
No	264	83.5	147	46.5
Previous CABG				
Yes	41	13.0	19	6.0
No	275	87.0	152	48.1

Figure 2

Graph of Subject Ages



tendency. The outliers for time to electrocardiogram and for time to percutaneous coronary intervention were left in the analyses. The distribution of race is representative of the sample for these two hospital communities. The distribution of race statistics for the hospitals for 2006 was 85.9% White, 3.3% Black, 3.6% Hispanic, 1.6% Asian and 0.5% American Indian or Alaskan Native.

Research Question One. What percentage of patients with myocardial infarction diagnosed in the emergency department have atypical signs or symptoms on presentation?

Of the patients diagnosed with myocardial infarction in the emergency department, 38.6% (n = 171, SD = 23.7%, SE = 1.8%, 95% CI between 35.0% and 42.1%) would be considered to have presented with atypical signs and symptoms.

Research Question Two. Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting with complaints of dizziness or shortness of breath is having a myocardial infarction without chest pain?

Research question two was initially addressed by cross tabulation tables and Pearson's chi-square values. There were 222 (70.2%) subjects presenting with complaints of dizziness or shortness of breath. The variables that were predictive (*i.e.*, at least marginally significant at $p < 0.10$) of subjects who presented with chief complaints of dizziness or shortness of breath and is having a myocardial infarction without chest pain were presented in Table 6. The most significant predictors ($p \leq 0.05$) were presentation sign or symptom of nausea ($p = 0.046$) and pain in other areas ($p = 0.047$); sample characteristics of American Indian or Alaskan Native race ($p = 0.014$) and white race ($p =$

Table 6

Chi-square for Predictors for Subjects with Chief Complaints of Dizziness and Shortness of Breath Who Were Having a Myocardial Infarction without Chest Pain (CP) (n = 222)

Predictor Variable	N (% of) MI No CP	Chi-square (degrees of freedom)[a]	*p value*
Sex		2.769	0.096
Male	37 (28.9)		
Female	18 (19.1)		
Age		1.932	*ns*
≤ 65 years	16 (19.5)		
> 65 years	39 (27.9)		
Race			
White	45 (22.7)	4.120	0.042
Black	4 (33.3)	0.499	*ns*[b]
Hispanic	1 (33.3)	0.120	*ns*[c]
Asian	1 (25.0)	0.000	*ns*[c]
American Indian or Alaska Native	4 (80.0)	8.371	0.014[c]
Nausea		3.976	0.046
Yes	16 (17.8)		
No	39 (29.5)		
Vomiting		2.159	*ns*
Yes	4 (13.8)		
No	51 (26.9)		
Sweating		0.044	*ns*
Yes	15 (23.8)		
No	40 (25.2)		
Pain in other areas		3.931	0.047
Yes	18 (35.3)		
No	37 (21.6)		

Diabetes		3.014	0.083
Yes	19 (33.3)		
No	36 (21.8)		
Angina		1.705	*ns*
Yes	10 (18.2)		
No	45 (26.9)		
Hypertension		0.135	*ns*
Yes	39 (25.5)		
No	16 (23.2)		
Cholesterol		0.730	*ns*
Yes	25 (22.3)		
No	30 (27.3)		
Asthma		0.516	*ns*
Yes	6 (31.6)		
No	49 (24.1)		
COPD		0.715	*ns*
Yes	12 (30.0)		
No	43 (23.6)		
Smoking		1.821	*ns*
Yes	19 (20.2)		
No	36 (28.1)		
CAD		1.172	*ns*
Yes	16 (20.5)		
No	39 (27.1)		
Previous MI		0.420	*ns*
Yes	18 (27.7)		
No	37 (23.6)		
Previous stroke		6.495	0.011
Yes	10 (47.6)		
No	45 (22.9)		
CHF		1.689	*ns*
Yes	12 (33.3)		
No	43 (23.1)		

Previous PCI		0.244	*ns*
Yes	7 (21.2)		
No	48 (25.9)		
Previous CABG		0.424	*ns*
Yes	6 (20.0)		
No	49 (25.5)		

ns- Not significant

[a] Degrees of freedom all equal to one.

[b] 1 cell (25%) has an expected count of less than 5, the p value the Fisher's exact test is reported.

[c] 2 cells (50%) have an expected count of less than 5, the p value the Fisher's exact test is reported.

0.042) and risk factors of previous stroke ($p = 0.011$). Relevant presentation signs and symptoms variables which show a trend ($p > 0.05$ and ≤ 0.10) were sample characteristics of being male ($p = 0.096$), and previous medical history of diabetes ($p = 0.083$). Some cells for race had expected counts of less than five. When there are small expected values, the chi-square test is unreliable; therefore, p-values for Fisher's exact test are reported instead.

The second phase of the analysis involved logistic regression. These regression analyses were run in three different ways, using all entered, forward conditional and backward conditional procedures to obtain a more complete assessment of the impact of combinations of independent variables.

Table 7 displays the logistic regression for patients presenting with complaints of dizziness or shortness of breath and having a myocardial infarction without chest pain. When the variables were all entered together, a relationship was indicated by pain in other areas ($p = 0.002$), stroke ($p = 0.017$), male ($p = 0.029$), white race ($p = 0.032$), and history of previous myocardial infarction ($p = 0.044$). Relationships indicated by forward conditional regression, Table 8, were stroke ($p = 0.005$), pain in other areas ($p = 0.0001$), and American Indian or Alaskan Native race ($p = 0.024$). Relationships indicated by backwards conditional regression, Table 9, were stroke ($p = 0.006$), pain in other areas ($p = 0.017$), white race ($p = 0.016$), being a senior ($p = 0.021$), and male ($p = 0.024$). The backwards procedure produced the most encompassing model. Odds ratios from the backwards procedure model are discussed.

Table 7

Logistic Regression with All Variables Entered for Patients Presenting with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction without Chest Pain (n = 222)

		Significance $p \leq 0.05$	Odds Ratio Step 1 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 1(a)	White	.032	.068	.006	.799
	Male	.029	.414	.188	.913
	Pain	.002	.244	.098	.608
	PMI	.044	.340	.119	.973
	Stroke	.017	.254	.082	.783

Variable(s) not significant at $p \leq 0.05$ on step 1: Nausea, Vomit, Sweat, DM, DM, Angina, HTN, Chol, Asthma, COPD, Smoke, CAD, PMI, CHF, PCI, CABG, senior, black, Hispanic, Asian, and American Indian or Alaskan Native.

Table 8

Forward Conditional Logistic Regression for Patients Presenting with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction without Chest Pain (n = 222)

		Significance $p \leq 0.05$	Odds Ratio Step 10 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 3(c)	Amer. Indian	.014	16.701	1.784	156.351
	Pain	.024	.440	.216	.895
	Stroke	.005	.259	.101	.664

Table 9

Backward Conditional Logistic Regression for Patients Presenting with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction without Chest Pain (n = 222)

		Significance $p \leq 0.05$	Odds Ratio Step 16 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 18(a)	white	.016	.309	.119	.803
	senior	.021	2.459	1.148	5.269
	Male	.024	.443	.218	.900
	Pain	.017	.404	.191	.852
	Stroke	.006	.246	.091	.664

An odds ratio is used in logistic regression as a measure of association. It is the risk of the event in this case (having a myocardial infarction without chest pain) occurring during one condition (*e.g.*, being a senior, > 65 years of age) versus the risk of it occurring if that condition does not hold (≤ 65 years of age), in analyses controlling for the impact of other independent variables in the model. Table 9 displays the odds ratio and confidence intervals for the variables of patients presenting with complaints of dizziness or shortness of breath is having a myocardial infarction without other independent variables in the model. Table 9 displays the odds ratio and confidence intervals for the chest pain using a backwards conditional logistic regression, entered in step 1 and remaining by step 18. Five variables were associated with patients presenting with complaints of dizziness or shortness of breath and having a myocardial infarction without chest pain. The odds were 2.46 larger for senior subjects than non-senior subjects, 0.44 smaller for male subjects than female subjects, 0.40 smaller for subjects with pain in other areas than those without, 0.31 smaller for white subjects than non-white subjects, and 0.25 smaller for subjects with a history of stroke than those without.

Research Question Three. Which signs and symptoms or risk factors, individually or in combination, predict that an emergency department patient presenting without chest pain but with dizziness or shortness of breath is having a myocardial infarction?

Research question three was addressed by cross tabulation tables and Pearson's chi-square values. There were 114 (36.1%) subjects presenting without chest pain but with complaints of dizziness or shortness of breath and having a myocardial infarction. The variables that were predictive (*i.e.*, at least marginally significant at $p < 0.10$) of subjects who presented without chest pain but with complaints of dizziness or shortness

Table 10

Chi-square for Predictors for Subjects Presenting without Chest Pain but with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction (n = 114)

Predictor Variable	**N (%) of No CP**	**Chi-square (degrees of freedom)[a]**	***p value***
Sex		5.518	0.029
Male	46 (66.7)		
Female	20 (49.4)		
Age		0.927	*ns*
≤ 65 years	19 (65.5)		
> 65 years	47 (55.3)		
Race			
White	55 (53.4)	8.854	0.003
Black	5 (100)	3.803	0.073[b]
Hispanic	1 (100)	0.734	*ns*[b]
Asian	1 (100)	0.734	*ns*[b]
American Indian or Alaska Native	4 (100)	3.015	*ns*[b]
Shortness of breath		0.829	*ns*
Yes	44 (61.1)		
No	22 (52.4)		
Dizziness		6.805	0.009
Yes	21 (43.8)		
No	45 (68.2)		
Nausea		4.203	0.040
Yes	18 (45.0)		
No	48 (64.9)		
Vomiting		0.773	*ns*
Yes	5 (45.5)		
No	51 (59.2)		

Sweating		2.088	*ns*
Yes	17 (70.8)		
No	49 (54.4)		
Pain in other areas		13.942	0.0001
Yes	24 (88.9)		
No	42 (48.3)		
Diabetes		1.890	*ns*
Yes	23 (67.6)		
No	43 (53.8)		
Angina		0.900	*ns*
Yes	11 (68.8)		
No	55 (56.1)		
Hypertension		0.278	*ns*
Yes	48 (56.5)		
No	18 (62.1)		
Cholesterol		0.093	*ns*
Yes	28 (59.6)		
No	38 (56.7)		
Asthma		0.830	*ns*
Yes	6 (46.2)		
No	60 (59.4)		
COPD		1.286	*ns*
Yes	12 (48.0)		
No	54 (60.7)		
Smokes		0.268	*ns*
Yes	23 (54.8)		
No	43 (59.7)		
CAD		0.074	*ns*
Yes	18 (60.0)		
No	48 (57.7)		
Previous MI		1.956	*ns*
Yes	20 (69.0)		
No	46 (54.1)		

Previous Stroke		0.975	*ns*
Yes	12 (66.7)		
No	54 (56.3)		
CHF		0.777	*ns*
Yes	12 (50.0)		
No	54 (60.0)		
Previous PCI		0.001	*ns*
Yes	7 (58.3)		
No	59 (57.8)		
CABG		0.423	*ns*
Yes	8 (66.7)		
No	58 (56.9)		

ns = Not significant

[a] Degrees of freedom all equal to one.

[b] 2 cells (50%) have an expected count of less than 5, the p value the Fisher's exact test is reported.

of breath and are having a myocardial infarction were presented in Table 10. The most significant predictors ($p \leq 0.05$) were presentation sign or symptom of pain in other areas ($p = 0.0001$) and nausea ($p = 0.040$); and sample characteristics of white race ($p = 0.003$) and male ($p = 0.03$). Relevant sample characteristics which show a trend ($p > 0.05$ and ≤ 0.10) were black race ($p = 0.07$). Some cells for race had expected counts of less than five. When there are small expected values, the chi-square test is unreliable; therefore, p-values for Fisher's exact test are reported instead.

The second phase of the analysis involved logistic regression. These regression analyses were run in three different ways, using all entered, forward conditional and backward conditional procedures to obtain a more complete assessment of the impact of combinations of independent variables. Table 11 displays the logistic regression for patients presenting without chest pain but with complaints of dizziness or shortness of breath and having a myocardial infarction. When the variables were all entered together, a relationship for subjects were indicated by pain in other areas ($p = 0.015$), and history of previous myocardial infarction ($p = 0.039$). Relationships indicated by forward conditional regression (Table 12) were pain in other areas ($p = 0.0001$), and history of previous myocardial infarction ($p = 0.020$). Relationships indicated by backwards conditional regression (Table 13) were pain in other areas ($p = 0.0001$), and history of previous myocardial infarction ($p = 0.020$).The backwards procedure produced the most encompassing model. Odds ratios from the backwards procedure model are discussed.

Table 13 displays the odds ratio and confidence intervals for the variables for patients presenting without chest pain but with dizziness or shortness of breath is having a myocardial infarction using a backwards conditional logistic regression, entered in step

Table 11

Logistic Regression with All Variables Entered for Patients Presenting without Chest Pain but with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction (n = 114)

	Significance $p \leq 0.05$	Odds Ratio Step 1 Exp(B)	95.0% C.I. for EXP(B)	
			Lower	Upper
Pain	.015	7.513	1.488	37.927
PMI	.039	5.041	1.086	23.395

Variable(s) not significant at $p \leq 0.05$ on step 1: Sex, SOB, Dizzy, Nausea, Vomit, Sweat, DM, Angina, HTN, Chol, Asthma, COPD, Smoke, CAD, Stroke, CHF, PCI, CABG, white, senior, black, Hispanic, Asian and American Indian or Alaskan Native.

Table 12

Forward Conditional Logistic Regression for Patients Presenting without Chest Pain but with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction. (n = 114)

		Significance $p \leq 0.05$	Odds Ratio Step 3 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 3(c)	Pain	.0001	10.613	2.829	39.809
	PMI	.020	3.163	1.196	8.365

Table 13

Backward Conditional Logistic Regression for Patients Presenting without Chest Pain but with Complaints of Dizziness or Shortness of Breath Who Were Having a Myocardial Infarction (n = 114)

		Significance P ≤ 0.05	Odds Ratio Step 23 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 23(a)	Pain	.0001	10.613	2.829	39.809
	PMI	.020	3.163	1.196	8.365

1 and remaining by step 23. Two variables were associated with patients presenting without chest pain but with complaints of dizziness or shortness of breath and is having a myocardial infarction. The odds were 10.61 larger for subjects with pain in other areas than not and 3.16 larger for patients with a previous myocardial infarction than those that did not.

Research Question Four. Which signs and symptoms or risk factors, individually or in combination, predict that a patient who is diagnosed with a myocardial infarction presents to the emergency department without chest pain?

There were 171 (54.1%) subjects diagnosed with a myocardial infarction. Among all of these subjects, 20.9% (SD = 23.7%, SE = 1.3%, 95% CI between 18.3% and 23.5%) did not have a classic presentation of chest pain. This is a substantial number in which the care and outcome of the subjects may have been improved with identification.

Research question four was addressed by cross tabulation tables and Pearson's chi-square values. The variables that were predictive (*i.e.*, at least marginally significant at $p < 0.10$) of subjects who had a myocardial infarction and presented without chest pain are presented in Table 14. The most significant predictors ($p \leq 0.05$) were presentation sign or symptom of dizziness ($p = 0.003$) and nausea ($p = 0.022$); sample characteristics of American Indian or Alaskan Native race ($p = 0.007$); risk factors of diabetes ($p = 0.045$); and previous medical history of previous stroke ($p = 0.004$), and angina ($p = 0.046$). Relevant presentation signs and symptoms variables which show a trend ($p > 0.05$ and ≤ 0.10) were sample characteristics of white race ($p = 0.082$), senior age ($p = 0.074$), presentation signs and symptoms of pain in other areas ($p = 0.083$), and previous medical history of a diagnosis of coronary artery disease ($p = 0.094$). Some cells for race had

Table 14

Chi-square for Predictors for Patients Diagnosed with a Myocardial Infarction without Chest Pain

Predictor Variable	N (%) of No CP	Chi-square (degrees of freedom)[a]	*p value*
Sex		2.795	*ns*
Male	46 (24.0)		
Female	20 (16.1)		
Age		3.189	0.074
≤ 65 years	19 (15.7)		
> 65 years	47 (24.1)		
Race			
White	55 (32.4)	3.032	0.082
Black	5 (20.4)	0.790	*ns*[b]
Hispanic	1 (20.8)	0.041	*ns*[c]
Asian	1 (21.1)	0.349	*ns*[c]
American Indian or Alaska Native	4 (19.9)	10.744	0.007[c]
Shortness of breath		2.443	*ns*
Yes	44 (23.9)		
No	22 (16.7)		
Dizziness		8.929	0.003
Yes	21 (35.0)		
No	45 (17.6)		
Nausea		5.265	0.022
Yes	18 (14.4)		
No	48 (25.1)		
Vomiting		1.561	*ns*
Yes	5 (13.2)		
No	61 (21.9)		

Sweating		0.635	*ns*
Yes	17 (18.1)		
No	49 (22.1)		
Pain in other areas		3.011	0.083
Yes	24 (27.3)		
No	42 (18.4)		
Diabetes		4.009	0.045
Yes	23 (28.8)		
No	43 (18.2)		
Angina		3.969	0.046
Yes	11 (13.3)		
No	55 (23.6)		
Hypertension		0.844	*ns*
Yes	48 (22.3)		
No	18 (17.8)		
Cholesterol		2.079	*ns*
Yes	28 (17.6)		
No	38 (24.2)		
Asthma		0.266	*ns*
Yes	6 (25.0)		
No	60 (20.5)		
COPD		1.262	*ns*
Yes	12 (27.3)		
No	54 (19.9)		
Smoking		1.233	*ns*
Yes	23 (17.8)		
No	43 (23.0)		
CAD		2.803	0.094
Yes	18 (15.8)		
No	48 (23.8)		
Previous MI		0.002	*ns*
Yes	20 (21.1)		
No	46 (20.8)		

Previous stroke		8.115	0.004
Yes	12 (41.4)		
No	54 (18.8)		
CHF		1.485	*ns*
Yes	12 (27.9)		
No	54 (19.8)		
Previous PCI		2.076	*ns*
Yes	7 (13.5)		
No	59 (22.3)		
Previous CABG		0.054	*ns*
Yes	8 (19.5)		
No	58 (21.1)		

ns = not significant

[a] Degrees of freedom all equal to one.

[b] 1 cell (25%) has an expected count of less than 5, the p value for the Fisher's exact test is reported.

[c] 2 cells (50%) have an expected count of less than 5, the p value for the Fisher's exact test is reported.

expected counts of less than five. When there are small expected values, the chi-square test is unreliable; therefore p-values for Fisher's exact test are reported instead.

The second phase of the analysis involved logistic regression to investigate the effects having a myocardial infarction without chest pain. These regression analyses were run in three different ways, using all entered, forward conditional and backward conditional procedures to obtain a more complete assessment of the impact of combinations of independent variables.

Table 15 displays the logistic regression for having a myocardial infarction and not having chest pain. When the variables were all entered together, a relationship for subjects with myocardial infarctions who did not present to the emergency department with chest pain was indicated by pain in other areas ($p = 0.0001$) dizziness ($p = 0.001$), male ($p = 0.013$), previous stroke ($p = 0.013$), shortness of breath ($p = 0.023$), and white race ($p = 0.029$). Relationships indicated by forward conditional logistic regression, Table 16, were pain in other areas ($p = 0.0001$), dizziness ($p = 0.0001$), shortness of breath ($p = 0.013$), senior ($p = 0.019$), male ($p = 0.019$), history of hypercholesterolemia ($p = 0.019$), American Indian or Alaskan Native race ($p = 0.025$), previous stroke ($p = 0.028$), and diabetes ($p = 0.048$). Relationships indicated by backwards conditional logistic regression, Table 17, were dizziness ($p = 0.0001$), pain in other areas ($p = 0.001$), shortness of breath ($p = 0.008$), male ($p = 0.010$), history of hypercholesterolemia ($p = 0.016$), being a senior ($p = 0.019$), previous stroke ($p = 0.028$), white race ($p = 0.041$), and diabetes ($p = 0.041$). The backwards procedure produced the most encompassing model. Odds ratios from the backwards procedure model are discussed.

Table 15

Logistic Regression with All Variables Entered for Patients Diagnosed with a Myocardial Infarction without Chest Pain

		Significance $p \leq 0.05$	Odds Ratio Step 1 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 1(a)	White	.029	.064	.005	.761
	Male	.013	.401	.195	.827
	SOB	.023	.438	.215	.890
	Dizzy	.001	.247	.109	.559
	Pain	.0001	.228	.103	.506
	Stroke	.013	.273	.098	.757

Variable(s) not significant at $p \leq 0.05$ on step 1: Nausea, Vomit, Sweat, DM, Angina, HTN, Chol, Asthma, COPD, Smoke, CAD, CHF, PCI, CABG, senior, black, Hispanic, Asian, and American Indian or Alaskan Native.

Table 16

Forward Conditional Logistic Regression for Patients Diagnosed with a Myocardial Infarction without Chest Pain

		Significance $p \leq 0.05$	Odds Ratio Step 10 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 10(j)	Senior	.019	2.320	1.147	4.694
	Amer Indian	.025	14.201	1.386	145.551
	Male	.019	.451	.231	.879
	SOB	.013	.432	.223	.838
	Dizzy	.0001	.236	.110	.507
	Pain	.0001	.285	.141	.576
	DM	.048	.491	.242	.994
	Chol	.019	2.205	1.139	4.267
	Stroke	.028	.346	.135	.889

Table 17

Backward Conditional Logistic Regression for Patients Diagnosed with a Myocardial Infarction without Chest Pain

		Significance $p \leq 0.05$	Odds Ratio Step 16 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 16(a)	White	.041	.399	.166	.962
	Senior	.019	2.309	1.149	4.641
	Male	.010	.416	.213	.812
	SOB	.008	.409	.211	.793
	Dizzy	.0001	.216	.101	.463
	Pain	.001	.298	.148	.599
	DM	.041	.484	.241	.970
	Chol	.016	2.246	1.166	4.328
	Stroke	.030	.351	.137	.902

Table 17 displays the odds ratio and confidence intervals for the variables using a backwards conditional logistic regression, entered in step 1 and remaining by step 16, for having a myocardial infarction without chest pain. Six variables were associated with having a myocardial infarction without chest pain. The odds were 2.31 larger for senior subjects than non-senior subjects, 2.25 larger for subjects with history of hypercholesterolemia than without, 1.91 larger for subjects with nausea than without, 0.48 smaller for subjects with diabetes than not, 0.41 smaller for male subjects than females, and 0.41 smaller for subjects with shortness of breath than not.

Research Question Five. Which individual signs and symptoms or risk factors predict when a patient receives a diagnostic electrocardiogram within 9 minutes and receives interventional treatment within 90 minutes of arrival to the emergency department?

Time to Electrocardiogram

Research question five was addressed first by cross tabulation tables and Pearson's Chi-Square values. There were 171 (54.1%) subjects diagnosed with a myocardial infarction (MI). Of those with a MI, 107 (62.6%) had an electrocardiogram within nine minutes.

The variables that were predictive (*i.e.*, at least marginally significant at $p < 0.10$) of subjects who had a myocardial infarction and received an electrocardiogram in greater than 9 minutes are presented in Table 18. The most significant predictors ($p \leq 0.05$) were presentation signs and symptoms of chest pain ($p = 0.0001$) and shortness of breath ($p = 0.037$); sample characteristics of white race ($p = 0.014$), risk factors of hypertension ($p = 0.019$); and previous medical history variables of previous stroke ($p = 0.007$). Relevant

Table 18

Chi-square for Predictors of Having a Myocardial Infarction and Receiving an Electrocardiogram (ECG) in Greater Than 9 Minutes From Entry in the ED

Predictor Variable	**N (%) > 9 min**	**Chi-square (degrees of freedom)[a]**	***p value***
Sex		2.22	*ns*
Male	41 (33.9)		
Female	23 (46.0)		
Age		3.74	0.53
≤ 65 years	22 (29.3)		
> 65 years	42 (43.8)		
Race			
White	61 (40.9)	6.10	0.014
Black	1 (10.0)	3.41	*ns*[b]
Hispanic	1 (50.0)	0.137	*ns*[c]
Asian	1 (16.7)	1.14	*ns*[c]
American Indian or Alaska Native	0 (0.0)	2.45	NS[c]
Chest pain		13.45	0.0001
Yes	28 (26.7)		
No	36 (54.5)		
Shortness of breath		4.34	0.037
Yes	45 (43.7)		
No	19 (27.9)		
Dizziness		0.08	*ns*
Yes	8 (34.8)		
No	56 (37.8)		
Nausea		2.45	*ns*
Yes	25 (31.3)		
No	39 (42.9)		

Vomiting		0.000	*ns*
Yes	9 (37.5)		
No	55 (37.4)		
Sweating		2.42	*ns*
Yes	21 ((30.4)		
No	43 (42.2)		
Pain in other areas		1.43	*ns*
Yes	28 (43.1)		
No	36 (34.0)		
Diabetes		1.83	*ns*
Yes	19 (46.3)		
No	45 (34.0)		
Angina		0.037	*ns*
Yes	17 (38.6)		
No	47 (37.0)		
Hypertension		5.54	0.019
Yes	49 (43.8)		
No	15 (25.4)		
Cholesterol		1.55	*ns*
Yes	35 (42.2)		
No	29 (33.0)		
Asthma		0.006	*ns*
Yes	4 (36.4)		
No	60 (37.5)		
COPD		0.301	*ns*
Yes	9 (42.9)		
No	55 (36.7)		
Smoking		0.378	*ns*
Yes	30 (40.0)		
No	34 (35.4)		
CAD		0.104	*ns*
Yes	20 (35.7)		
No	44 (38.3)		

Previous MI		1.82	*ns*
Yes	21 (45.7)		
No	43 (34.4)		
Previous stroke		7.40	0.007
Yes	11 (68.8)		
No	53 (34.2)		
CHF		3.58	0.059
Yes	9 (60.0)		
No	45 (35.3)		
Previous PCI		0.200	*ns*
Yes	8 (33.3)		
No	56 (38.1)		
Previous CABG		3.82	0.051
Yes	11 (57.9)		
No	53 (34.9)		

ns = Not significant

[a] Degrees of freedom all equal to one.

[b] 1 cell (25%) has an expected count of less than 5; the p value for the Fisher's exact test is reported.

[c] 2 cells (50%) have an expected count of less than 5; the p value for Fisher's exact test is reported.

presentation signs and symptoms variables which showed a trend ($p > 0.05$ and ≤ 0.10) were sample characteristics of black race ($p = 0.092$) and being senior ($p = 0.053$), and previous medical history of previous coronary bypass grafting ($p = 0.051$). Some cells for race had expected counts of less than five. When there are small expected values, the chi-square test is unreliable; therefore the results for Fisher's exact test are reported instead.

The second phase of the analysis involved logistic regression to investigate the effects of the multiple independent variables on the dependent variable, myocardial infarction or not. These regression analyses were run in three different ways, using all entered, forward conditional and backward conditional procedures to obtain a more complete assessment of the impact of combinations of independent variables.

Table 19 displays the logistic regression for receiving an electrocardiogram in greater than 9 minutes among subjects with a myocardial infarction. When the variables were all entered together, a relationship for subjects with myocardial infarctions who received an electrocardiogram in greater than 9 minutes was indicated by chest pain ($p = 0.004$) and white race ($p = 0.016$). Relationships indicated by forward conditional (Table 20) regression were chest pain ($p = 0.0001$), white race ($p = 0.005$), and hypertension ($p = 0.026$). Relationships indicated by backwards conditional regression (Table 21) were chest pain ($p = 0.0001$), white race ($p = 0.006$), hypertension ($p = 0.028$), dizziness ($p = 0.079$).The backwards procedure produced the most encompassing model. Odds ratios from the backwards procedure model are discussed.

Table 19

Logistic Regression with All Variables Entered for Predictors of Having a Myocardial Infarction and Receiving an Electrocardiogram in Greater Than 9 Minutes From Entry in the ED

	Significance $p \leq 0.05$	Odds Ratio Step 1 Exp(B)	95.0% C.I. for EXP(B)	
			Lower	Upper
CP	.004	4.000	1.577	10.148
white	.016	6.296	1.410	28.110

Variable(s) not significant at $p \leq 0.05$ on step 1: Sex, SOB, Dizzy, Nausea, Vomit, Sweat, DM, Angina, HTN, Chol, Asthma, COPD, Smoke, CAD, Stroke, CHF, PCI, CABG, senior, black, Hispanic, Asian and American Indian or Alaskan Native.

Table 20

Forward Conditional Logistic Regression Forward Conditional for Predictors of Having a Myocardial Infarction and Receiving an Electrocardiogram in Greater Than 9 Minutes From Entry in the ED

		Significance $p \leq 0.05$	Odds Ratio Step 3 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 3(c)	CP	.000	3.636	1.821	7.261
	HTN	.026	.433	.207	.906
	white	.005	6.594	1.762	24.679

Table 21

Backward Conditional Logistic Regression for Predictors of Having a Myocardial Infarction and Receiving an Electrocardiogram in Greater Than 9 Minutes from Entry in the ED

		Significance $p \leq 0.05$	Odds Ratio Step 23 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 23(a)	CP	.0001	4.857	2.234	10.560
	HTN	.028	.432	.204	.915
	white	.006	6.600	1.716	25.380

An odds ratio is used in logistic regression as a measure of association. Table 21 displays the odds ratio and confidence intervals for the variables using a backwards conditional logistic regression, entered in step one and remaining by step 23, for an electrocardiogram in greater than 9 minutes. Three variables were associated with having an electrocardiogram in greater than 9 minutes. The odds for a greater than minutes time to an electrocardiogram were 6.60 larger for 0.43 smaller for subjects with hypertension than not.

Time to Percutaneous Coronary Intervention

Of the 171 subjects diagnosed with a myocardial infarction, 30 (17.5%) received a percutaneous coronary intervention (PCI) in 90 minutes. The variables that were predictive (*i.e.*, at least marginally significant at $p < 0.10$) of subjects who had a myocardial infarction and white subjects than non-white subjects, 4.86 larger for subjects with chest pain than without, and received a percutaneous coronary intervention in greater than 90 minutes are presented in Table 22. The most significant predictors ($p \leq 0.05$) were presentation of pain in other areas ($p=0.003$) and chest pain ($p = 0.005$); sample characteristics of male ($p = 0.04$), being senior ($p = 0.023$); risk factors of diabetes mellitus ($p = 0.013$); and previous medical history of previous PCI ($p = 0.027$). Relevant variables which show a trend ($p > 0.05$ and ≤ 0.10) were previous medical history of asthma ($p = 0.097$). Some cells had expected counts of less than five. As before, results for Fisher's exact test are reported rather than the chi-square test.

Table 22

Chi-square for Predictors of Having a Myocardial Infarction and Receiving a Percutaneous Coronary Intervention (PCI) in Greater Than 90 Minutes from Entry in the ED

Predictor Variable	**N (%) > 90 min**	**Chi-square (degrees of freedom)[a]**	***p value***
Sex		4.23	0.040
Male	47 (45.2)		
Female	24 (64.9)		
Age		5.17	0.023
≤ 65 years	28 (40.6)		
> 65 years	43 (59.7)		
Race			
White	62 (50.4)	1.02	*ns* [c]
Black	5 (62.5)	0.500	*ns* [c]
Hispanic	2 (100)	2.06	*ns* [c]
Asian	2 (40.0)	0.222	*ns* [c]
American Indian or Alaska Native	0 (0.0)	3.11	*ns* [c]
Chest pain		7.93	0.005
Yes	40 (42.1)		
No	31 (67.4)		
Shortness of breath		0.194	*ns*
Yes	40 (48.8)		
No	31 (52.5)		
Dizziness		0.052	*ns*
Yes	9 (52.9)		
No	62 (50.0)		
Nausea		3.75	0.053
Yes	29 (42.0)		
No	42 (58.3)		

Vomiting		0.250	*ns*
Yes	10 (45.5)		
No	61 (51.3)		
Sweating		2.57	*ns*
Yes	26 (42.6)		
No	45 (56.3)		
Pain in other areas		9.06	0.003
Yes	38 (65.5)		
No	33 (39.8)		
Diabetes		6.20	0.013
Yes	20 (71.4)		
No	51 (45.1)		
Angina		1.46	*ns*
Yes	15 (41.7)		
No	56 (53.3)		
Hypertension		1.22	*ns*
Yes	47 (54.0)		
No	24 (44.4)		
Cholesterol		0.065	*ns*
Yes	35 (51.5)		
No	36 (49.3)		
Asthma		3.78	0.097[b]
Yes	8 (80.0)		
No	63 (48.1)		
COPD		2.20	*ns*
Yes	12 (66.7)		
No	59 (48.0)		
Smoking		0.006	*ns*
Yes	33 (50.0)		
No	38 (50.7)		
CAD		1.81	*ns*
Yes	29 (58.0)		
No	42 (46.2)		

Previous MI		0.021	*ns*
Yes	18 (51.4)		
No	53 (50.0)		
Previous stroke		0.001	*ns* [b]
Yes	5 (50.0)		
No	66 (50.4)		
CHF		1.02	*ns* [b]
Yes	6 (66.7)		
No	65 (49.2)		
Previous PCI		5.08	0.024
Yes	5 (26.3)		
No	66 (54.1)		
Previous CABG		0.625	*ns*
Yes	9 (60.0)		
No	62 (49.2)		

ns = Not significant

[a] Degrees of freedom all equal to one.

[b] 1 cell (25%) has an expected count of less than 5, the p value for the Fisher's exact test is reported.

[c] 2 cells (50%) have an expected count of less than 5, , the p value for the Fisher's exact test is reported.

Table 23 displays the logistic regression with all entered variables for receiving a percutaneous coronary intervention in greater than 90 minutes among subjects with a myocardial infarction. When the variables were all entered together, a relationship for subjects with myocardial infarctions who had a percutaneous coronary intervention (PCI) in greater than 90 minutes was indicated by pain other areas ($p = 0.01$), diabetes ($p = 0.024$), and male ($p = 0.047$). Relationships indicated by forward conditional regression (Table 24) were pain in other areas ($p = 0.001$), diabetes ($p = 0.004$), previous PCI ($p = 0.010$), chest pain ($p = 0.019$), and COPD ($p = 0.019$). Relationships indicated by the backwards conditional regression (Table 25) were variables of pain in other areas ($p = 0.001$), diabetes (p =, 0.002), previous PCI ($p = 0.007$), COPD ($p = 0.012$), and chest pain ($p = 0.054$). The backwards procedure produced the most encompassing model. Odds ratios from the backwards procedure model are discussed.

Table 25 displays the odds ratio and confidence intervals for the variables using a backwards conditional logistic regression, entered in step one and remaining by step 18, for percutaneous coronary intervention times in greater than 90 minutes. Four variables were associated with having percutaneous coronary intervention in greater than 90 minutes after the regression The odds for an acceptable time to a percutaneous coronary intervention were 6.01 larger for subjects having a previous percutaneous coronary intervention than those not having a previous percutaneous coronary intervention, 0.23 smaller for subjects with pain in other areas than without, 0.18 smaller for subjects with a history of COPD than those without, and 0.16 smaller for subjects with diabetes than those without diabetes.

Table 23

Logistic Regression All Variables Entered for Predictors of Having a Myocardial Infarction and Receiving a Percutaneous Coronary Intervention (PCI) in Greater Than 90 Minutes from Entry in the ED

		Significance P ≤ 0.05	Odds Ratio Step 1 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 1(a)	Male	.047	3.397	1.015	11.371
	CP	.097	2.684	.835	8.627
	Sweat	.160	2.007	.760	5.296
	Pain	.001	.183	.065	.514
	DM	.024	.190	.045	.801

Variable(s) not significant at p ≤ 0.05 on step 1: SOB, Dizzy, Nausea, Vomit, Angina, HTN, Chol, Asthma, COPD, Smoke, CAD, Stroke, CHF, PCI, CABG, white, senior, black, Hispanic, Asian and American Indian or Alaskan Native.

Table 24

Forward Conditional Logistic Regression for Predictors of having a Myocardial Infarction and Receiving a Percutaneous Coronary Intervention (PCI) Greater Than 90 Minutes from Entry in the ED

		Significance P ≤ 0.05	Odds Ratio Step 6 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 6(f)	CP	.019	2.810	1.181	6.682
	Pain	.001	.245	.107	.562
	DM	.004	.192	.062	.594
	COPD	.019	.203	.054	.769
	PCI	.010	5.188	1.492	18.034

Table 25

Backward Conditional Logistic Regression for Predictors of having a Myocardial Infarction and Receiving a Percutaneous Coronary Intervention (PCI) Greater Than 90 Minutes from Entry to the ED

		Significance $p \leq 0.05$	Odds Ratio Step 18 Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Step 18(a)	Pain	.001	.228	.096	.537
	DM	.002	.164	.051	.527
	COPD	.012	.176	.045	.687
	PCI	.006	6.007	1.683	21.439

Chapter 5

Discussion

Percentage of Myocardial Infarctions with Atypical Presentations

The present study established that between 35% and 42% of patients diagnosed with myocardial infarction in the emergency department (n = 171) would be considered to have atypical signs and symptoms on presentation. The best known of the previous studies that included data regarding atypical myocardial infarctions is the Framingham Study which was based on a 34-year follow-up of 5,070 study participants 30-62 years of age at entry and both genders (Kannel, *et.al.*, 1990). Of the 708 myocardial infarctions that evolved over the 34 years of this study, more than 25% were discovered only by the appearance of new diagnostic evidence during routine biennial electrocardiogram examinations. These subjects reported no symptoms of the myocardial infarction. Kannel and associates (1990) published that unrecognized myocardial infarction (atypical presentation) represented 26% and 34%, in men and women respectively (No p value listed). The present study showed atypical presentation of myocardial infarction to be 38% and 40% of myocardial infarction in men and women respectively ($p = 0.03$).

The percentage of atypical presentations is somewhat higher in the present study, which could be explained by the differences in inclusion criteria, designs (prospective, longitudinal or retrospective), sample size, areas of the country, and health of the population. The present study had a retrospective descriptive research design with inclusion criteria that included presentation signs and symptoms of dizziness or shortness of breath or diagnosis of myocardial infarction. In contrast, the Framingham Study (1990), Israeli Heart Attack Study (1976), Reykjavik Study (1995), and Cardiovascular

Health Study (2000) were longitudinal cohort studies in which most of the subjects were free of cardiovascular disease when entered into the study. The National Registry of Myocardial Infarction 2 (NRMI2) studies confirmed myocardial infarction patients with the main outcome variable of presentation of chest pain; 33% did not have chest pain on presentation. The present study showed 20.9% of myocardial patients did not have chest pain. The Global Registry of Acute Coronary Events (GRACE) study was a prospective observational study involving 14 countries. Subjects presenting to the hospital with suspected acute coronary syndromes (unstable angina, non-ST elevation myocardial infarctions and ST elevation myocardial infarctions) were stratified according to whether their predominant presenting symptoms included chest pain or did not (atypical). Over twenty three percent (23.8%) of these subjects were not recognized as having an acute coronary syndrome. Table 26 describes these studies. Comparison of the various studies to the present study is challenging because of the differences in design, inclusion criteria and variable selection.

Factors Predictive of Myocardial Infarction with Atypical Signs and Symptoms

Results of three of the research questions in the present study related to which presenting signs and symptoms, personal characteristics, risk factors and previous medical history might be predictive of a myocardial infarction with atypical presentations. Each of these three questions analyzed the variables, individually or in combination. There was a trend which demonstrates strength with the variables of dizziness, pain in other areas of the body (not in the chest), history of a previous stroke, being a senior (> 65 years of age), and being white. Several studies have shown a

Table 26

Comparison of Various Research Studies of "Unrecognized" Myocardial Infarction

Study Atypical MI's	Design	Description Of subjects	Inclusion Criteria	# of Subjects	# of MI	%
Framingham Kannel	Longitudinal	Healthy On entry	Diagnostic ECG	5127	708	28 M 35 F
NRMI2 Canto	Longitudinal	MI subjects	Chest pain	434,877	434,877	33
Israeli Medalie& Goldbourt	Longitudinal	Healthy on entry	Diagnostic ECG	9,509	427	39.8
Reykjavic Sigurdsson & Jonsdottir	Longitudinal	CAD	Self report Diagnostic ECG	31,000	1.014	30 M 33 F
CHS Sheifer	Longitudinal	Free of CV disease On entry	Diagnostic ECG	5,888	901	22.3
GRACE Brieger	Prospective Observational Registry	ACS	Diagnostic ECG; ↑ enzymes CAD	20,881	1,763 No chest pain	23.8
Nordblom	Retrospective	ED subjects	Dizzy; SOB; MI	316	171	38.6

statistically stronger relationship with some of the same variables of atypical symptom presentation as compared with MI patients with chest pain, but their study methods vary as well as the variables used for analysis.

The study that has variable selection most similar to the present study was done by Canto and associates (2000). The Canto Study defined the chest pain variable presence or absence of chest pain before or during admission, which may have included shortness of breath, nausea or vomiting, syncope, or cardiac arrest. However, specific signs or symptoms other than presence or absence of chest pain were not abstracted from the medical record. The Canto Study showed important profile variables associated with atypical presentations of myocardial infarction to be female, non-white race, older age, diabetes, congestive heart failure, and prior stroke (Canto et al., 2000). Subjects in the Canto study were reported as 87.6% white and 13.4% non-white. The present study showed 89.2% white and 10.8% non-white, a similar split between race categories: white, black Hispanic, Asian, and other. Canto did not specify American Indian or Native American.

Additional variables in the present study showed significance but were not significant in both statistical analyses (cross tabulations and regression). These variables were nausea, male, diabetes, and history of a previous myocardial infarction. Since the study sample was predominantly white, there may not have been enough subjects of the other races to show consistent significance. Research by Klinger and associates (2002) in the emergency department showed that symptom profiles were found to be similar among black and white patients. In the present study, the American Indian or Native Alaskan race ($n = 5$ [1.6%], $p = .0007$) demonstrated a strong significance within the non-white

races in the cross tabulations and some regression models, yet was not significant in the backward regression models. This may have been a consequence of the small number, as well as how well this sample characteristic variable worked with the other variables in pairs. It is possible that the large sample of whites influenced the non-white sample. The age range for these five subjects was 48-72 with the median age of 60; lower than the median age of 69 for the whole population. Another influence could be that 80% of the American Indian or Alaskan Native had myocardial infarctions.

Another analysis was employed separating the two facilities and running the data analysis for each question to see if there were any perceivable differences in symptom presentation between the two facilities. These analyses did not show any significant differences in the variable statistics between sites. This could signify a more homogenous group within the community.

In the published literature, risk factors for myocardial infarction parallel those of atherosclerosis and include (but are not limited to) diabetes, hypertension, age, sex (male>female), elevated cholesterol levels, and a positive family history of atherosclerosis (Hackam & Anand, 2003; Simons et al., 2002). The present study showed strength in the older age ($p = 0.05$) and with having a previous stroke ($p = 0.03$). These are also consistent with atherosclerosis and can be predictive of coronary disease not yet diagnosed. The results showed inconsistent significance in reported hypercholesterolemia, and with reported diabetes, each being significant in either the cross tabulations or the regression. There is supporting evidence in the literature that diabetes may be an independent predictor of atypical presentations of myocardial infarction (Milan Study on Atherosclerosis and Diabetes (MiSAD) Group, 1997). The

clinical significance lies in recognition and use of this knowledge as a relatively high-risk feature in assessment. Practitioners should use this knowledge to increase their diagnostic abilities to detect and manage atypical presentations of myocardial infarction.

Hypertension has been suggested to be a predictor of unrecognized myocardial infarction in some of the other studies. Hypertension did not show any significance in this study, although it is a risk factor for coronary disease. Most of the previous studies evaluated systolic blood pressures and some more recently looked at diastolic pressures. A factor which may affect the results of various studies is the focus of aggressive treatment for hypertension in the last ten years compared to 30 years ago when the longitudinal studies were started. There was no significance with a history of congestive heart failure ($p = 0.22$). The Canto Study showed an odds ratio for history of congestive heart failure to be 1.12; the present study 0.997. Again, the differences could be explained by the sample size, sample characteristics, design, and inclusion criteria. The present study showed only 6.6% of the sample had a previous history of coronary artery disease, 14.6% had a previous myocardial infarction (Canto 26.6%), and history of stroke, 4.7% (Canto-14.1%). This sample discrepancy may reflect a sample in the present study that has better cardiovascular health than the NRMI2 study sample. Differences between variables in studies may reflect differences in the disease process or may be related to the superimposition of normal physiological aging changes and presence of concomitant disease that masks usual clinical manifestations. It also suggests that there was a different approach to symptom recognition and that these studies have increased our knowledge base to improve our ability to detect atypical presentations of myocardial infarction.

Time between Emergency Department Presentation and ECG and Percutaneous Coronary Intervention

The final research questions were concerned with the time that elapsed between subject arrival in the emergency department and diagnostic electrocardiogram (ECG) and percutaneous coronary intervention (PCI). Time to diagnosis is dependent on the time to electrocardiogram completion and interpretation. Once myocardial infarction is diagnosed, treatment modalities, such as PCI, can be initiated. Management of patients suspected to have had a myocardial infarction requires rapid assessment in the emergency department in less than 10 minutes (Custer, 2002; Graff, 2000). National evidence-based practice protocols by the American Heart Association/American College of Cardiology recommend that the initial electrocardiogram be completed within 9 minutes of entry to the emergency department and that the patient receive diagnostic percutaneous coronary intervention within 90 minutes of entry. The research surrounding this recommendation has shown decreased cardiac muscle damage within these time parameters, resulting in better patient outcomes and less cardiac disability. The results in the present study showed some variation in strength of variables. There is a presumptive connectivity between these two time variables. If the ECG time is lengthy to delayed diagnosis, then the PCI time will also be lengthy under most circumstances. Of interest, the three variables which showed the greatest strength to predict an ECG time > 9 minutes in both analyses were subjects with chest pain and white race. Being senior, history of previous stroke and dizziness were significant in only one of the other analyses. In a study done by Graff (2000), the other variables for lengthy ECG times were patients who complained of dyspnea (10.4%), weakness/fatigue (6.2%), syncope (2.7%) and abdominal pain (2.7%).

The present study variables for lengthy ECG times were not comparable to this study because of the design.

Unfortunately, the time to ECG can be extended by other processes. Most emergency departments have one ECG machine. If there are many patients who need an electrocardiogram, the ones with chest pain have priority, so the others who may have atypical symptoms will be delayed. In the present study, the presentation of subjects with dizziness, being senior, and a previous history of a stroke would presently lead the staff to activate the stroke practice guideline. This guideline does include an ECG, but not until after the CT scan has been completed, some 30 minutes later. Once the CT results are obtained and the ECG is completed, the diagnosis of MI is made. The staff's ability to recognize symptoms and associated risk factors is essential to expedite ordering of the electrocardiogram, anticipating the potential diagnosis of myocardial infarction. Training and alerting the staff with other practice guidelines will alert them to do the 60-90 second ECG before CT scan. This may enhance the ability to diagnose the MI and prepare for treatment while the CT is being done.

Canto and associates (2000) observed a time interval from admission to electrocardiogram of 15.6 ($p<0.001$) minutes for patients with chest pain presentation and 31.8 ($p< 0.001$) minutes in patients with atypical presentations. In the Graff (2002) study, chest pain was the sole complaint of 60% of patients admitted to the emergency department with myocardial infarction. The present study showed that patients presenting with chest pain received a diagnostic ECG in > 9 minutes 26.7% (28 of 105) of the time while patients with no chest pain received their diagnostic ECG in > 9 minutes 54.5% (36 of 66) of the time ($p = 0.0001$). The primary goal in the emergency department is to

reduce delays in treatment to provide the best outcomes. Therefore, rapid diagnosis by electrocardiogram is essential. Without this vital information, therapies to limit infarction size and decrease potential untoward outcomes cannot be initiated.

The second part of the final research question concerned time between presentation in the emergency department to percutaneous coronary intervention (PCI). Again, the results showed some variation in strength of variables. The strongest predictors of having a lengthy PCI time were being senior, being male, and presentation of pain in other areas. The present study showed that patients presenting with chest pain received PCI in greater than 90 minutes 42.1% (40 of 95) of the time while patients with no chest pain received their PCI in greater than 90 minutes 67.4% (31 of 46) of the time, a significantly longer time interval for subjects with no chest pain ($p = 0.005$). As these data show, there is presently considerable loss of time to diagnosis and therefore treatment in patients with atypical presentation of myocardial infarction. More rapid intervention will limit infarction size and decrease potential untoward patient outcomes.

Recommendation from the American Heart Association is to begin treatment within 90 ninety minutes using angiographic heart catheterization with balloon in the heart. There is a significant amount of data being collected by the American College of Cardiology in a new study, D2B (Door-to-balloon) that has the focus on best practice initiatives. Hospitals are being registered for this study presently.

Summary and Implications

This study strongly demonstrates that 35% to 42% of patients that arrive at the emergency department and are diagnosed with a myocardial infarction have an atypical presentation without chest pain. This is a substantial number of patients that potentially

could be afforded improved care and reversal of impending poor outcomes. The accuracy of diagnosis of myocardial infarction in patients in the emergency department can be maximized by a careful history and evaluation of associated risk factors. Initial evaluation of patients in the emergency department is dependent on the subjective information given. Creating cues (practice guidelines) for the emergency staff could increase their ability to accurately identify atypical presentations.

There is substantial evidence that practice guidelines can be associated with improved patient outcomes and that "America's Best Hospitals" have these practices in place more than other institutions (Chen et. al, 1999). Strong evidence of clinically meaningful benefit is essential to the choice of data elements for guidelines. In addition, a quality measure is needed to evaluate the use and outcomes of the guideline. Most measures begin with guideline development.

The present study shows potential for development of a guideline which alerts emergency department staff to obtain a diagnostic electrocardiogram on patients presenting to the emergency department with dizziness, reported pain in other areas than the chest (e.g. epigastric, back, arms), are senior (> 65 years of age), and have a previous history of stroke. The guideline would also include an index of suspicion in patients who present with shortness of breath (regression $p = 0.008$; ECG regression $p = 0.04$). Although, the greater than 90 minute PCI times were not associated with shortness of breath, it was minimally predictive for patients with a previous history of asthma ($p = 0.10$). This would make one believe the presentation was one of shortness of breath, which may not have been recorded in the medical record from which the data were obtained.

Implications for nursing and other disciplines.

The published literature supports the idea that accuracy of diagnosis of MI patients can be maximized by a careful history and evaluation of associated risk factors (Fu, Y., Goodman, S., & Chang, W. C. (2001). The clinical challenge is in recognizing atypical presentations of myocardial infarction. Atypical symptoms generally do not 'cue' the emergency staff to suspect myocardial infarction on initial evaluation, therefore delaying the onset of the diagnostic intervention. Being able to assess for individual signs and symptoms, personal characteristics, risk factors and previous medical history per practice guideline would be important to draw attention to the need for more expedient electrocardiograms in patients with atypical signs and symptoms. Both the present study and one by Canto and associates (2000) noted important profile variables associated with atypical presentations of MI. The present study used new variables of dizziness and shortness of breath on presentation versus chest pain to predict a pattern of signs and symptoms in those with myocardial infarction that presented to the emergency department. Even though the present study was smaller than Canto's (171 MI patients versus Canto's 434,877), it shows strength variables of dizziness, pain in other areas, being senior, and history of stroke.

The results of various studies cited in this chapter have some consistency in results. None support or indicate that any one of the risk factors has an independent prediction. Given the absence of clear recommendations of variables for study, greater attention must be made in creating clinical practice guidelines which are measureable, studied, and eventually, accounted for in performance measures that can be utilized to improve patient outcomes. A growing national focus on quality in healthcare calls for

development and use of clinical practice guidelines and strategies to standardize care of patients with myocardial infarction (American College of Cardiology/American Heart Association). This strategy calls for a team of healthcare persons to investigate real world problems in real world settings. It is essential to approach assessment of patients with symptom recognition, but it is crucial to approach this assessment with a broader range of symptoms so that some patients are not missed which may result in poor outcomes. The present study provides preliminary direction for eventual development of a guideline to recognize characteristics of emergency department patients who have myocardial infarctions without chest pain. The emergency staff in these departments work in a collegial manner, physician, nurse, technician and secretary, to create the best process to assess patients who present to the emergency department with atypical symptoms of a myocardial infarction.

Limitations of the study.

Because the present study was conducted in two Oregon hospitals, the generalizability to other regions or care environments may not be possible. A key question which must be addressed is whether the robustness of this study must be considered a limitation due to the small sample size in comparison to the large cohort studies. The present study was a retrospective chart review. Generally record review provides reliable information, but completeness is always subject to lack of standards and variability of medical record documentation.

The sample size of the variables chest pain or not in the patient with myocardial infarction did not have a sample size as suggested by the power analysis. There were 105

MI patients with chest pain and 66 myocardial infarction patients without chest pain. This may be considered a limitation.

Suggestions for future research.

The research aims addressed in this dissertation provide useful insights into characteristics of emergency department patients who have a myocardial infarction without chest pain. However, these data have potential for providing further insights and future research will address these issues. Specifically, cluster analysis, will be used to identify combinations of signs and symptoms and risk factors that occur in the data.

As part of ongoing quality initiatives at the two facilities, a practice guideline will be created using the data from this study. The staff will be educated in the use of the new guideline. After a six week implementation of the guideline, time to ECG and PCI will be evaluated to see if they have decreased.

Finally, although this researcher believes that this study demonstrates the potential to improve care to the myocardial infarction patient who presents to the emergency department, the sustainability of this improvement is unproven and needs to be studied.

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Appendix A

Recognition of Atypical Myocardial Infarctions in the Older Adult

Presenting to the Emergency Department

Subject Screening Tool

Hospital identification number _____

Screening date and time _____

Inclusion criteria:

- ☐ Age 45-100 years (Subject's birthdates, age _____)
- ☐ Presented to the emergency department between October 2004 through September 2006
- ☐ Presenting signs or symptoms, previous medical history and prior medical events are noted in the medical record.

Exclusion criteria:

- ☐ Presented to the emergency department in cardiopulmonary arrest
- ☐ Diagnosis of myocardial infarction made on inpatient unit after the emergency department visit
- ☐ Patients with chest pain but are not diagnosed with myocardial infarction;
- ☐ Patient unable to give history of events

Name of person performing screening _____

Meets subject selection criteria: ☐ yes ☐ no

If entered into study, subject identification number _____

Appendix B

Recognition of Atypical Myocardial Infarctions in the Older Adult

Presenting to the Emergency Department

Data Collection Tool

Subject Number _____

Subject diagnosed with MI: ☐ Yes ☐ No

Demographic Variables	
Age –years on presentation	(Calculated from DOB and date of admission)
Sex	☐ Male ☐ Female
Race	☐ White ☐ Black ☐ Hispanic ☐ Asian ☐ American Indian ☐ Pacific Islander ☐ Other ☐ Unknown
Presentation Variables	
Chest pain	☐ Yes ☐ No
Dyspnea	☐ Yes ☐ No
Dizziness/syncope/lightheadedness	☐ Yes ☐ No
Nausea	☐ Yes ☐ No
Vomiting	☐ Yes ☐ No
Diaphoresis	☐ Yes ☐ No
Other areas of pain	☐ Yes ☐ No; area -
Medical History Variables	
History of diabetes	☐ Yes ☐ No
History of angina	☐ Yes ☐ No
History of hypertension	☐ Yes ☐ No If yes – treated with
History of ↑ cholesterol	☐ Yes ☐ No If yes – treated with
History of asthma	☐ Yes ☐ No
History of COPD	☐ Yes ☐ No
Family history of CAD	☐ Yes ☐ No
Prior Events Variables	
MI	☐ Yes ☐ No
Stroke	☐ Yes ☐ No
CHF	☐ Yes ☐ No
PCI	☐ Yes ☐ No
Previous bypass grafts	☐ Yes ☐ No
Time Interval Variables	
Time to ECG, minutes	(already abstracted in a quality report)
Time to treatment, minutes	(already abstracted in a quality report)

Appendix C

Request for Waiver of Authorization

1225 NE 2nd Ave.
Portland, OR 97232

RE: Retrospective Chart Review

Dear Mr. Bush:

This letter is written to request a waiver of patient authorization in order to facilitate the access to medical records in support of my research project "Recognition of Atypical Myocardial Infarction in the Older Adult Presenting to the Emergency Department". The purpose of this research study is to examine associated signs and symptoms and other risk factors of patients diagnosed with a myocardial infarction in the emergency department to enhance emergency healthcare providers ability to detect myocardial infarction in patient who do not present with chest pain. I would like permission to review approximately 350 charts pertaining to patients presenting to the emergency department with a primary chief complaint of chest pain, dyspnea or dizziness, as well as other minor associate symptoms of pain in other areas, nause or vomiting. A copy of my data collection sheet is attached.

In requesting this waiver of authorization I have determined that this study could not be practically done without it, that this disclosure of information poses no more than minimal risk to the privacy of the patient. The information requested is the minimum necessary required to accomplish the goals of this study.

In extracting data from the medical records, I will not be recording information that could directly identify the patient.

By signing this letter, I personally assure that the confidentiality of these medical records will be maintained. I will not be contacting the patients whose charts I am reviewing, and neither their names, nor any personal identifiers will appear in any publication resulting from this work. I will not be sharing this data with others outside of this research project. The co-signer of this letter is the chair or chief of the section or division of the medical staff most affected by this work.

Investigator
Judy Nordblom, RN, PhC

Chair Linda Felver, PhD, RN
Division/Section OH&SU SON

Appendix D

Waiver of Authorization

Legacy Clinical Research & Technology Center

LEGACY
Health System

June 23, 2006

Legacy IRB: FWA00001280

Judy Nordblom, RN, PhC
1015 NW 22nd
Portland, OR 97210

RE: **" Recognition of Atypical Myocardial Infarction in the Older Adult Presenting to the Emergency Department."**

Dear Ms. Nordblom:

This letter is written in regards to the above cited research study. Your proposal has been granted a waiver of authorization in order to allow you the opportunity to conduct a chart review as requested in your undated letter.

Your letter provides an assurance that the confidentiality of these medical records will be maintained. In order to obtain medical records please contact Hollis Brown, Manager of Health Information Services. She can be reached at (503) 413-4244.

This waiver of authorization is justified by the fact that the study could not be practically done without it, that this disclosure of information poses no more than minimal risk to the privacy of the patient, and that the information requested is the minimum necessary required to accomplish the goals of the study.

The Legacy IRB is governed by an assurance granted by the Office of Human Research Protections (Federal Wide Assurance #00001280). In addition to that assurance, the Legacy IRB is governed by FDA regulations (21CFR50) and Legacy institutional policy (LHS 100.18).

If you have any questions regarding this matter please do not hesitate to contact Casey Bush, Research Regulatory Specialist who can be reached (503) 413-2474,

Yours truly,

Alar Mirka

Alar Mirka, M.D.
Chair, Legacy IRB

Cc: Hollis Brown