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What are the frequency and consequences of transient myocardial ischemia in the telemetry unit setting detected with continuous 12-lead electrocardiographic monitoring?

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What are the Frequency and Consequences of Transient Myocardial Ischemia in the Telemetry Unit Setting Detected with Continuous 12-Lead Electrocardiographic Monitoring?

by

Michele M. Pelter

DISSERTATION

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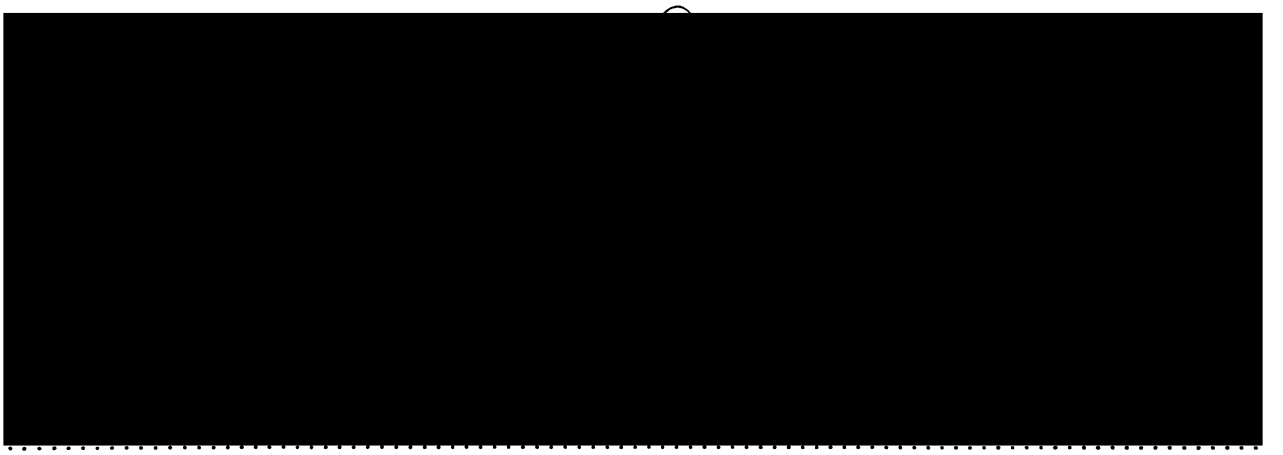

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Dedication

To my husband - Bill Pelter…

Of all the people who've encouraged me throughout my life – what distinguishes you – is your ability to *ALWAYS* make me believe that I can do it.

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P.H.

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This work would not have been possible without the encouragement, and support of a number of people in my life. First, my dear parents Harold and Sally Loranger who gave me the most valuable life tools to work with – faith, confidence, and humor. You were with me at the lowest moment – what a privilege to have you with me at the highest. My brothers – Dennis, Dan, Tom, Tim, John, and Mike – for instilling in me the tenacity required to make it in life. My sister-in laws - Carol, Val, Elizabeth, Beverly, Denise, and Tammy – for giving your ears and hearts to me. To all of my nieces and nephews – thanks for showing me what really matters in life!

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Lastly, I'd like to acknowledge the generosity of all of the wonderful patients I meet during this endeavor. You've touched and inspired me to seek ways to improve your lives.

Abstract

What are the Frequency and Consequences of Transient Myocardial Ischemia in the Telemetry Unit Setting Detected with Continuous 12-lead Electrocardiographic Monitoring?

By

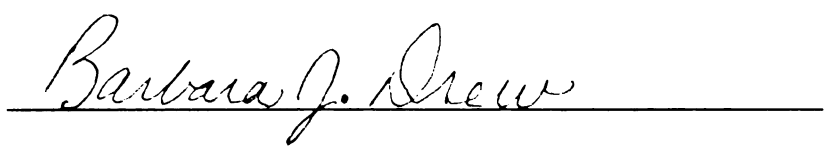
Michele M. Pelter, RN, PhD

Currently, there is little information regarding the frequency or consequences of transient myocardial ischemia in patients admitted to the telemetry unit for treatment of acute coronary syndromes (ACS). This is an important assessment given the current trend for initially admitting this group of patients to the telemetry unit, rather than the CCU. Therefore, the purpose of this study was to determine the frequency and consequences of ischemia in the telemetry unit detected with continuous 12-lead electrocardiographic (ECG) monitoring. **Methods/Results:** Continuous 12-lead ST monitoring was maintained on average 28 hours in 237 patients treated in the telemetry unit (178 [75%] initially admitted to telemetry unit; 59[25%] initially admitted to CCU then, telemetry unit). Ischemia was defined as $\geq$ 100 μV ST change, comparing a baseline ECG to the event ECG (delta ST), in $\geq$ 1 ECG lead, lasting $\geq$ 1 minute. Of the 237 patients (190 = angina; 47 = myocardial infarction [MI]), 39 (17%) had a total of 89 ischemic events, 70 events (79%) were clinically silent. Of the 89 total ischemic events, only 27 (30%) reached $\geq$ 100 μV in V1 or lead II, the two most commonly selected ECG leads for telemetry monitoring. Outcomes, comparing patients with and without ischemia are illustrated in the Table below:

	Transfer to CCU	Hospital length of stay (hours)	Adverse outcome
No TMI n = 198	2%	86 + 76	9%
Yes TMI n = 39	18%	142 + 93	41%
P value	< 0.001	< 0.001	< 0.001

TMI = transient myocardial ischemia; Adverse outcomes = shock, pulmonary edema, major arrhythmia, acute MI, death

The rate of ischemia was equivalent among a subgroup of angina patients monitored in the telemetry unit from 1997 to 2000 to a group monitored in the CCU from 1994 to 1996 (15% telemetry versus 19% CCU). **Conclusions:** Transient ischemia, which is largely silent, is not uncommon among patients with ACS treated in a telemetry unit setting. ECG-detected ischemia identified patients at increased risk for serious in-hospital complications. Therefore, ST segment monitoring may be useful for identifying patients with ischemia that may benefit from more aggressive therapies aimed at abolishing on-going ischemia.



Barbara J. Drew, RN, PhD, FAAN (Committee Chairperson)

Table of Contents

The Study Problem

Table of Contents

Literature Review and Conceptual Framework

Table of Contents

Methodology

Table of Contents

Results

Table of Contents

Discussion

Tables

Tables

Figures

Statement of the problem

Many hospitals throughout the United States, primarily in an effort to lower hospital costs, have shifted care from the coronary care unit (CCU) to the telemetry unit setting for patients diagnosed with unstable angina, uncomplicated acute myocardial infarction (MI) or following catheter-based interventions (i.e., percutaneous transluminal coronary angioplasty {PTCA}, or stent). This has resulted in a substantial increase in the acuity level of patients treated in the telemetry unit setting. A primary clinical objective is to monitor these patients for myocardial ischemia, a transient imbalance of coronary blood flow to the heart, in order to prevent or limit the extent of infarction, an irreversible state of cellular/tissue death. The most reliable way to monitor patients for transient myocardial ischemia is continuous monitoring of the electrocardiogram (ECG) for ST segment changes because ischemia is clinically silent in nearly three-quarters of patients. While it could be questioned whether clinically silent ischemia is important to identify, there is compelling evidence to show that silent ischemia identifies a subset of patients who are at increased risk for unfavorable events including MI and death. Importantly, ST segment monitoring software has not been incorporated into the vast majority of telemetry unit ECG monitoring systems. This means that ischemia, which occurs in the telemetry unit setting will most likely go unrecognized, which is unfortunate since there are several treatment options available to abolish recurrent or on-going ischemia. However, if patients are to benefit maximally from these treatment options it is imperative to accurately and immediately recognize ischemia.

With this in mind, the purpose of this investigation is to explore the significance and consequences of transient myocardial ischemia, detected using ST segment monitoring,

in patients treated in the telemetry unit setting who are most at risk for ischemia, those diagnosed with acute coronary syndromes (i.e., unstable angina, acute MI) or in patients who have had catheter-based interventions (i.e., PTCA and/or stent). Results from such an investigation may indicate that ST segment monitoring technology might be a valuable assessment tool in the telemetry unit setting that could aid clinicians to accurately and immediately identify ischemia, which is essential if patients are to benefit from currently available treatment options.

Purpose of the study

The primary aim of this clinical investigation is to determine the frequency and consequences of transient myocardial ischemia measured both in-hospital and at 90 days following discharge in patients treated in the telemetry unit setting diagnosed with acute coronary syndromes. Because of the unpredictable and mostly asymptomatic nature of transient episodes of ischemia the present study will utilize *continuous* 12-lead ECG ST segment monitoring, a non-invasive method not currently incorporated in the vast majority of telemetry unit ECG monitoring systems. Accordingly, two secondary aims of this research study are to determine if: (1) patients experience clinical symptoms (i.e., chest pain, or anginal equivalent) during ECG-detected ischemia and (2) if continuous 12-lead ECG monitoring is more sensitive than routine 1-lead telemetry unit ECG monitoring for detection of myocardial ischemia.

The Specific Hypotheses of this study are:

1. The frequency of transient myocardial ischemia, among hospitalized patients admitted for treatment of angina, will not be different comparing a group of patients treated in the coronary care unit (CCU) from November 1994 to April

1996 to a group of patients treated in the telemetry unit from September 1997 to March 2000. In addition, the rate of in-hospital complications will be higher among patients who experience ischemia, whether in the CCU or telemetry unit, compared to patients who do not experience ischemia.

2. Patients who experience transient episodes of ischemia while being treated in the telemetry unit setting will have more in-hospital complications, such as MI, arrhythmias requiring intervention, transfer to the CCU, or death compared to patients who do not experience transient myocardial ischemia.

3. A minority of patients will experience chest pain or their anginal equivalent during ECG-detected ischemia.

4. 12-lead ECG ST segment monitoring will be more sensitive than routine one-lead ECG telemetry unit monitoring for detection of transient ischemia.

5. Patients who experience in-hospital transient myocardial ischemia detected in the telemetry unit setting will have more out of hospital complications (i.e., re-hospitalization, MI, or death) measured at 90 days compared to patients who do not experience transient ischemia.

This research investigation will not only improve existing knowledge regarding the prevalence and potential consequences of ischemia, but for the first time describe an important clinical problem in a hospital environment that has not been previously studied. Ultimately, this area of study may provide valuable information regarding the use of lower levels of hospital care (i.e., telemetry versus CCU) for patients diagnosed with acute coronary syndromes, which may lead to improved monitoring, patient care, and more importantly, improved patient outcomes.

Introduction to the Problem

The Telemetry Unit: Definition and Historical Trends

Several terms have been used in the literature to describe the telemetry unit, including; progressive care unit, intermediate care unit, step down unit, and transitional care unit. However, it appears that all of these terms have been used to describe a similar concept of hospital care, which is; 1) to provide patients with more intensive care than that available on general medical wards, but not as intensive as care in the CCU, and 2) for patients who require close nursing surveillance after an initial stay in the CCU (Elisberg, 1971). It should also be pointed out that although telemetry unit care was originally designed to treat patients diagnosed with coronary conditions, telemetry unit care has been extended to patients diagnosed with non-cardiac conditions as well. However, the focus of this discussion will address the population of patients treated in the telemetry unit setting who are most at risk for ischemia, which includes patients diagnosed with acute coronary syndromes (i.e., unstable angina, following acute MI), or following catheter-based interventions such as PTCA, or stent procedures.

The term "telemetry" is used to describe the type of ECG monitoring that is utilized in this hospital setting. More specifically, "radiotelemetry" ECG monitoring is a non-invasive ECG monitoring system that does not require direct wiring from the patient to the ECG monitoring device; thus, the patient is not restricted to bedrest. This system works by attaching ECG lead wires to skin electrodes located at specific locations on a patient's chest. The ECG lead wires are connected to a battery operated very high frequency (VHF) radio transmitter device that is small enough to be worn in the pocket of the patient's gown. The ECG signal is then transmitted from the VHF radiotransmitter

device to a signal-receiving antenna, or antennas, located throughout the telemetry unit, and ultimately to a central station where it is possible to provide constant surveillance of the ECG rhythm. This ECG design allows patients the ability to ambulate throughout the unit, and thus recuperate, while still maintaining constant "on-line" ECG rhythm information. Initially, the primary goal of radiotelemetry ECG monitoring was for detection of lethal arrhythmias. However, some monitoring companies have also made available for use in their telemetry ECG systems, software that can be used for detection of myocardial ischemia, or "ST segment monitoring."

The concept of telemetry unit care was developed as a compliment, or "step-down" unit to the CCU. The initial intent of the telemetry unit was to provide acute MI patients continued and progressive care following acute recovery in the CCU. In other words, acute MI patients were initially admitted to the CCU and then transferred to the telemetry unit to recuperate until hospital discharge; hence, the term "step-down" care. Eventually, the concept of step-down care also became the standard of care for patients diagnosed with unstable angina and following catheter-based interventions, such as PTCA and/or stent. Because of the link between the CCU and the telemetry unit, for clarity, it is necessary to first discuss the development and goal(s) of the CCU.

The first CCU was developed in the United States in 1962 by Day and colleagues (1963), in the hopes of reducing the nearly 50% hospital mortality rate following acute MI, caused primarily by lethal arrhythmias (i.e., ventricular tachycardia/fibrillation) (Bainton & Peterson, 1963; Pantridge, 1966). Central to the concept of CCU care was ECG monitoring. This was because ECG technology could be utilized to detect arrhythmias, so that immediate intervention(s) could be initiated to abolish the

arrhythmia. Nurses were responsible for initiating, maintaining, and recognizing cardiac rhythm disturbances using ECG monitoring. In addition, CCU nurses were trained to initiate actions independently to abolish the arrhythmia, which included; cardiopulmonary resuscitation (CPR), pharmacological interventions, and defibrillation. According to Day, the success of CCU care was dependent upon the nurse's ability to recognize and provide immediate interventions for arrhythmias (Day, 1963).

Less than a decade after the introduction of the CCU, studies showed that CCU care had significantly reduced hospital mortality following acute MI (Grace & Yarvote, 1971; Pantridge, 1970; Resnekov, 1977). However, studies also showed that cardiac arrest, primarily from lethal arrhythmias, remained a substantial threat on the medical wards where patients were discharged to following CCU admission (Grace & Yarvote, 1971; Lown, Fakhro, Hood, & Thorn, 1967). Consequently, two primary issues were raised regarding the trajectory of care for acute MI patients; 1) the large discrepancy in nursing care and surveillance between the CCU and the general medical ward and, 2) the lack of ECG monitoring after transfer from the CCU to the general medical ward.

Gotsman and Schrire (1968) are believed to be the first to introduce the concept of telemetry unit care. They proposed that patients who had sufficiently recovered from their MI, and who no longer required intensive CCU care, should be transferred to a "progressive coronary care unit." Ideally, this unit should be in close proximity to the CCU in order to transfer patients back to the CCU should acute problems arise. This unit would require fewer nurses than the CCU, and only "minimal" nursing care would be required because patients would be in the recuperative phase of treatment. According to Gotsman and Schrire (1968), the goals of the telemetry unit should be to; 1) monitor the

ECG for arrhythmias, 2) wean the patient from "vigorous" CCU care, and 3) restore self-confidence and avoid psychological withdrawal.

Grace and Yarvote (1971) were the first to report on the implementation of an intermediate coronary care unit for acute MI patients beyond the fifth hospital day following treatment in the CCU. In their study, "intermittent" ECG monitoring obtained at four-hour intervals was utilized for arrhythmia detection. A primary recommendation offered by these researchers was that *continuous* ECG monitoring should be the standard of care for arrhythmia detection, rather than intermittent ECG monitoring. A recommendation that came about because of two patient deaths, presumably due to a lethal arrhythmia, that occurred during the four-hour interval between ECG recordings.

By the late 1970's, the concept of telemetry unit care, including continuous telemetric ECG monitoring, had been accepted as the standard of care for patients diagnosed with acute MI, or unstable angina (Frieden & Cooper, 1976; Gorfinkel, Kercher, & Lindsay, 1976; Leak & Eydt, 1978; Weinberg, 1978). The latter group are patients who present with chest pain syndromes suggestive of MI, but who do not demonstrate ECG evidence of acute MI (i.e., ST segment elevation). Hence, in this group of patients the diagnosis of MI is being "ruled out." The trajectory of care during this decade for both patient groups (MI, or unstable angina) included, a two to eight day admission in the CCU, followed by a 10 to 13 day admission in the telemetry unit setting (Frieden & Cooper, 1976; Weinberg, 1978). During this decade, the nurse to patient ratio in the telemetry unit setting was typically from 1:2 to 1:3 (Leak & Eydt, 1978).

Well into the 1980's, the trajectory of care for patients diagnosed with acute MI or unstable angina remained unchanged (i.e., CCU care followed by step-down care).

However, the length of hospital stay had been substantially reduced. For example, the average length of stay for unstable angina or acute MI patients ranged from two to four days in the CCU, followed by two to six days in the telemetry unit setting (Lipskis, Dannehl, & Silverman, 1984; Singer, Mulley, Thibault, & Barnett, 1981). During this same time period, step-down care became the standard of care for patients recovering from catheter-based procedures, such as PTCA. For example, following PTCA, patients recovered in the CCU for 24 hours, and then continued their recuperation in the telemetry unit for an additional 24 to 48 hours (Holmes et al., 1988).

By the late 1980's, managed health care organizations, primarily in an effort to lower hospital costs, forced hospitals to re-evaluate this "traditional" form of hospital care for patients diagnosed with acute coronary syndromes, and following PTCA and/or stent procedures. Three strategies were offered to address this mandate; 1) reduce admission of patients at low-risk for acute MI to the CCU, and utilize "cost-effective" alternatives, such as, telemetry unit care, 2) improve the diagnostic accuracy for acute MI in patients with chest pain syndromes suggestive of MI, (i.e., rule out MI) and 3) decrease use of the CCU by transferring patients to lower levels of care earlier in their hospital course (Lee & Goldman, 1988).

Currently, it would appear that these strategies have been embraced by hospitals throughout the United States, because many have shifted care from the CCU to the telemetry unit for the majority of patients diagnosed with unstable angina, uncomplicated MI, or following PTCA and/or stent procedures. Therefore, CCU care has been eliminated for the vast majority of these patients. In addition, the standard of care for patients diagnosed with acute MI, who are initially treated in the CCU, is early transfer

from the CCU (i.e., 24 hours or less) to the telemetry unit followed by early discharge home (i.e., 5 to 7 days). Thus, recuperation following acute MI is not only initiated earlier, but is shorter in duration, with the largest proportion of recovery taking place in the telemetry unit setting. It should be pointed out that the nurse-to-patient ratio has changed considerably as well. For example, the typical telemetry nurse to patient ratio is currently from 1:4 to 1:7 (Fiebach et al., 1990). Therefore, the nurse to patient ratio in the 1990's has more than doubled since the inception of the telemetry unit in the 1970's.

While these changes have reduced hospital costs, because fewer nurses are required to care for patients and hospital length of stay has been reduced, it is important to consider that these changes have resulted in a substantial increase in the acuity level of patients treated in the telemetry unit setting. While it cannot be assumed, one must also consider that these changes may have resulted in an increase in the prevalence of myocardial ischemia in the telemetry unit as well. For example, studies conducted in the CCU show that approximately one third of patients diagnosed with acute coronary syndromes experience episodes of myocardial ischemia (Drew, Adams, Pelter, & Wung, 1996; Gottlieb, Weisfeldt, Ouyang, Mellitis, & Gerstenblith, 1986; Klootwijk et al., 1997; Krucoff et al., 1988). Because CCU care has been replaced with telemetry unit care for many of the patients included in these studies, one should consider that the prevalence of myocardial ischemia might be maintained in these patients who are now treated in the telemetry unit setting. However, further investigation regarding the frequency and consequences, if any, of myocardial ischemia, in the telemetry unit is warranted before any conclusions can be made.

Results from such an investigation may provide evidence that additional technology for improved detection of myocardial ischemia, or ST segment monitoring, should be incorporated into the telemetry unit setting. In addition, these results may identify potential problems that may occur when lower levels of hospital care are utilized to treat patients with acute coronary syndromes. Ultimately, this area of study could lead to improved patient care in the telemetry unit setting, and more importantly, to improved patient outcomes.

Significance of Myocardial Ischemia:
Mechanisms, Patients at Risk, Clinical Manifestations, and Treatment Options

Mechanisms

Myocardial ischemia is characterized by a lack of oxygenated blood to the myocardium. An important quality of myocardial ischemia is that this condition is transient, and thus reversible, using clinical interventions (i.e., pharmacological, mechanical, or surgical). However, if ischemia is left untreated this condition will progress to an irreversible state of cellular/tissue damage, resulting in permanent myocardial damage, or infarction. Therefore, the immediate diagnosis and treatment of ischemia is essential in order to interrupt the progression of ischemia to infarction.

In general, the cause of myocardial ischemia is coronary artery disease (CAD), a disease characterized by atherosclerotic plaque formation within the coronary vessel. In patients with unstable angina, or acute MI, the coronary processes responsible for acute ischemia include vasospasm at the site of the atherosclerotic plaque, plaque fissure and/or rupture with resultant platelet stimulation, aggregation, and eventual thrombus formation, with resultant coronary occlusion (Ambrose, Winters, & Arora, 1985; DeWood et al., 1980; Mizutani et al., 1990; Terrosu, Ibba, Contini, & Franceschino, 1984). The major

difference between the disorders of unstable angina and acute MI is the severity of coronary occlusion. For example, the lumen of the coronary artery is partially occluded in the majority of patients with unstable angina, and totally occluded in the majority of patients with acute MI (DeWood et al., 1980; Mizuno et al., 1991).

Patients who are treated for CAD with transcatheter procedures, such as PTCA and/or stent are also at risk for ischemia, or abrupt reocclusion (total obstruction) of the coronary vessel treated. The mechanisms for ischemia or abrupt reocclusion following PTCA includes coronary artery spasm, localized thrombus at the intervention site, and coronary dissection (Baim & Ignatius, 1988). The mechanism of ischemia or abrupt reocclusion following stent is believed to be caused by thrombus formation at the site of the stent (Serruys et al., 1994).

Hence, patients with acute coronary syndromes (i.e., unstable angina, or acute MI), and patients who are treated with transcatheter procedures (i.e., PTCA and/or stent) are at risk for ischemia. The following section of this paper will discuss why these specific patient groups might be at risk for ischemia in the telemetry unit setting.

Patients at Risk for Myocardial Ischemia in the Telemetry Unit Setting

Unstable Angina: Since the inception of the CCU in 1962, the proportion of patients admitted to the CCU with the diagnosis of acute MI has fallen from 70% to the current figure of 30% (Brown, Macmillan, Forbath, Mel'Grando, & Scott, 1963; Gaspoz et al., 1994; Goldman et al., 1982; Killip & Kimball, 1967; MacMillan et al., 1967). While the number of acute MI patients presenting for treatment has declined, there has been an increasing number of patients presenting for treatment of unstable angina, most likely because of early and aggressive treatment options for CAD.

Traditionally, patients admitted to hospitals with angina suggestive of acute MI were itially admitted to the CCU until the diagnosis of acute MI had been ruled out. ubsequently, patients were then transferred to the telemetry unit to recuperate, or to ndergo further diagnostic tests for the presence of CAD. However, this trajectory of re has come under intense economic scrutiny. Primarily because over 50% of patients dmitted to the CCU with angina eventually "rule out" for acute MI, at an estimated conomic cost of over $3 billion dollars annually (Gaspoz et al., 1994). Hospitals have sponded by eliminating CCU care for the majority of angina patients; rather, these atients are admitted to the telemetry unit, a strategy that lowers costs because fewer urses are required to care for patients, and because hospital length of stay have been ubstantially reduced.

Monitoring for myocardial ischemia is a primary objective in patients presenting for eatment of angina. This is because studies show that angina patients who experience yocardial ischemia are more likely to develop MI, and experience major complications, uch as arrhythmias, hypotension and death compared to patients who do not experience chemia (Drew et al., 1996; Gottlieb et al., 1986; Klootwijk et al., 1997; Langer, reeman, & Armstrong, 1989; Larsson, Jonasson, Rinqvist, Fellenius, & Wallentin, 992).

Studies show that the initial 24 to 48 hours of hospitalization is the time period when atients with angina are most likely to experience ischemia (Braunwald, 1989; Klootwijk al., 1997). Under the current trajectory of hospital care, this would place the majority f angina patients in the telemetry unit setting. It is also important to consider that yocardial ischemia has been identified as the most common cause of transfer from a

"step-down" unit to the CCU for more aggressive therapy to abolish ischemia in patients diagnosed with unstable angina (Singer et al., 1981; Stewart & Voss, 1997). In this study, patients who required transfer from the "step-down" unit to the CCU were more likely to experience MI, require urgent revascularization, develop heart failure, or die.

Therefore, the initial 24 to 48 hours appears to be the most vulnerable time period for the occurrence of acute ischemia in patients with unstable angina, and patients who experience ischemia in the telemetry unit setting are at risk for major cardiac complications. This suggests that the ability to immediately detect myocardial ischemia in unstable angina patients admitted to the telemetry unit could have a profound impact on patient outcomes.

It is important to consider that, unlike the CCU, angina patients treated in the telemetry unit are not typically maintained on strict bedrest; thus, patients are free to ambulate in their room, and throughout the telemetry unit. This is an important point to consider in patients with angina, because myocardial ischemia can be induced when patients engage in routine activities of daily living (i.e., bathing, or walking to the bathroom) (Amanullah & Lindvall, 1993). This type of ischemia, named "demand-related" ischemia, occurs because the myocardium's demand for oxygen has exceeded the flow capabilities, because an atherosclerotic plaque is partially occluding the coronary vessel. Demand-related ischemia is generally self-limiting and is observed in patients diagnosed with chronic "stable" angina.

On the other hand, it is also important to consider that myocardial ischemia can occur without warning. This type of ischemia, named "supply-related" ischemia is characterized by total cessation of coronary blood flow, and is responsible for the clinical

syndrome of unstable angina. The mechanisms of myocardial ischemia in patients with unstable angina is a dynamic and unpredictable process characterized by; vasospasm at the site of the atherosclerotic plaque, plaque fissure and/or rupture with resultant platelet stimulation, aggregation, and eventual thrombus formation, with resultant coronary occlusion (Ambrose et al., 1985; Terrosu et al., 1984).

Hence, in some angina patients ischemia can be induced by activity, while in others it is unpredictable, and occurs without warning. Regardless of the mechanism of ischemia, studies show that the majority of angina patients (over 70%) are unaware of the presence of ischemia, because chest pain does not accompany the event (Gottlieb et al., 1986; Petretta et al., 1992). Thus, detection of ischemia in angina patients is complex, and clinicians cannot rely on patients to complain of chest pain to signal its presence.

Acute Myocardial Infarction: The use of thrombolysis and primary angioplasty for treatment in patients with acute MI has led to substantial reductions in both in-hospital and long-term mortality (Ochiai et al., 1997; Santoro et al., 1998; The GUSTO Investigators, 1993; The TIMI Study Group, 1985). However, studies show that recurrent ischemia, detected days following successful reperfusion, remains a substantial threat, occurring in approximately 25% of patients (Bonaduce et al., 1991; Chandra, Ouyang, Abell, & Gottlieb, 1993; Silva, Galli, & Campolo, 1993; Stone et al., 1995). Recurrent ischemia after MI prolongs hospitalization, results in further impairment of left ventricular function, and increases mortality, both in-hospital and following discharge (Betriu et al., 1998; Ellis et al., 1989; Stone et al., 1995). Therefore, detection of recurrent ischemia after MI could serve as a clinical warning to initiate therapies in order to restore perfusion to the myocardium, and ultimately improve patient outcomes.

The trajectory of care for patients who present for hospital treatment of acute MI has changed dramatically over the past decade. For example, during the 1980's, the standard of care for acute MI patients, who presented with definitive ECG changes diagnostic of MI, was CCU care for two to four days (Lee et al., 1988), followed by telemetry unit care for an additional five to ten days (Singer et al., 1981). Today, the current average length of stay for patients with definitive ECG changes indicative of acute MI, is one to three days in the CCU (Drew et al., 1996; Stewart & Voss, 1997; Walker, Wicks, Hubbard, & Thomas, 1993), followed by telemetry unit care for three to five days (Stewart & Voss, 1997). This is an important point to consider since studies show that the median time to the onset of recurrent ischemia occurs from 1.5 to seven days following acute MI (Betriu et al., 1998; Stone et al., 1995), and well over 90% of patients do not complain of chest pain during ECG-detected ischemia (Bonaduce et al., 1991; Chandra et al., 1993; Petretta et al., 1992; Silva et al., 1993). Therefore, it is likely that patients who experience recurrent ischemia following MI will be in the telemetry unit setting, and the majority will not experience the clinical symptoms. This suggests that continuous monitoring of the ECG for ST segment changes may be a valuable tool for detection of silent ischemia in patients following acute MI.

Following PTCA and/or Stent Placement: Over the last decade the number of interventional coronary procedures (i.e., PTCA and/or stent procedures) has increased. According to the American Heart Association, over 482,000 PTCA procedures and 177,000 stent procedures were performed last year (American Heart Association, 2001). Although the immediate success rate of these procedures is over 90%, the risks of abrupt reocclusion, or total occlusion of the coronary vessel, during the recovery period may

occur in as many as 7% of patients following PTCA (Krucoff et al., 1988), and in as many as 3.5% to 6% of patients following stent (Serruys et al., 1994). In addition, the risk of ischemia, or transient obstruction of the coronary vessel, detected with continuous ECG monitoring can occur in as many as 23% of patients following PTCA (Krucoff et al., 1988), and in 33% of patients following stent placement (Kathiresan et al., 1999).

Over 60% of patients who experience abrupt reocclusion following either PTCA and/or stent develop myocardial infarction, and well over half of the patients who experience myocardial ischemia have major complications, including MI, urgent bypass surgery, or death (Krucoff, Jackson, Kehoe, & Kent, 1990; Serruys et al., 1994). Therefore, it is imperative that abrupt reocclusion and ischemia are identified immediately, and treatment initiated in order to restore myocardial perfusion.

Importantly, many hospitals in the United States have shifted post PTCA/stent care from the CCU to telemetry units. For example, a survey of 70 hospitals in the United States reported that only 36% of hospitals surveyed provided post PTCA/stent care in the CCU (Juran, Smith, Rouse, DeLuca, & Rund, 1996). The majority of hospitals surveyed provide post PTCA/stent care in either the telemetry unit, recovery room, or other hospital units. Therefore, under the current health care system it is likely that the majority of patients who experience reocclusion or ischemia will be in the telemetry unit setting.

Summary

Myocardial ischemia is not uncommon in patients diagnosed with acute coronary syndromes, or following PTCA and/or stent procedures, and its presence alone identifies patients at risk for serious consequences both in and out of hospital. In the past, the

occurrence of ischemia was most likely to occur in the setting of the CCU, since this was the hospital unit where most of these patients were treated during the acute phases of their illness. However, under the current trajectory of hospital care it is important to consider that; (1) CCU care has been replaced with telemetry unit care for most unstable angina and PTCA and/or stent patients, and (2) CCU care has been substantially reduced, and telemetry unit care initiated earlier during the recovery phase following ST elevation MI. This suggests that the risk of transient myocardial ischemia has increased in the telemetry unit setting. However, further investigation is required before any conclusions can be made regarding the frequency and clinical significance of ischemia in the telemetry unit setting.

Clinical Manifestations of Myocardial Ischemia

One of the most important pathophysiological manifestations of myocardial ischemia is contractile dysfunction of the ventricular myocardium, which occurs within minutes following myocardial ischemia. Contractile dysfunction influences cardiac performance, and results in a reduction of cardiac output. If a sufficient area of the myocardium is ischemic and is left untreated, acute heart failure can occur, with devastating sequela to patients, including death.

Reimer and co-workers (Reimer, Lowe, Rasmussen, & Jennings, 1977) showed that as myocardial ischemia progresses over time, a "wavefront" of cellular death occurs. For example, within minutes following ischemia, the subendocardium, or the innermost layer of the myocardium is affected, and cellular death will occur within 20 to 40 minutes in this myocardial region if myocardial perfusion is not restored (Reimer et al., 1977; Reimer, Rasmussen, & Jennings, 1976). If ischemia is not reversed, irreversible injury

will progress from the subendocardial layer towards the subepicardial (middle and outer) layers of the myocardium; hence, a wavefront of ischemia from the innermost aspect of the myocardium to the outer myocardium occurs. Permanent coronary occlusion for longer than 24 hours will result in transmural necrosis, or death of the entire thickness of the myocardium. These observations indicate that viable myocardial tissue is salvageable for a period of hours. Thus, the goal of treatment is to restore and maintain myocardial perfusion in order to prevent irreversible tissue damage, or infarction. Numerous treatment options are currently available for the treatment of ischemia, and include pharmacological, mechanical, and surgical options. The following section of this paper will discuss the treatment options available for treatment of myocardial ischemia.

Treatment Options

There is substantial and compelling evidence that therapies aimed at abolishing on-going ischemia can substantially improve patient outcomes. For example, clinical studies that utilized thrombolytic therapy for treatment of acute MI, show that successful, and sustained reperfusion of the infarct related artery improves left ventricular function, and ultimately patient survival (Schofer et al., 1988; Simoons et al., 1986; The GUSTO Investigators, 1993; The TIMI Study Group, 1985; White et al., 1987; Wilcox et al., 1988; Yusuf et al., 1985). Moreover, studies show that the mortality rate is significantly higher in patients who do not achieve reperfusion of the infarct related artery, or reocclusion of the artery occurs following an initial period of reperfusion, compared to patients who achieve and maintain reperfusion of the infarct related artery (Krucoff et al., 1993; Ohman et al., 1989). These studies suggest that restoring and maintaining

myocardial perfusion of the infarct related artery in patients with acute MI using thrombolysis improves patient survival.

Successful reperfusion of the infarct related artery in patients with acute MI can also be achieved using primary (emergency) PTCA. There is evidence that primary PTCA may provide more complete and sustained reperfusion of the infarct related artery compared to thrombolytic therapy. For example, primary PTCA resulted in earlier patency of the infarct related artery, smaller infarct size, improved left ventricular function, and lower mortality compared to thrombolytics for treatment of acute MI (Gibbons et al., 1993; Grines et al., 1993; Lange & Hillis, 1993; O'Neill et al., 1986; Ribeiro et al., 1993; Zijlstra et al., 1993). While these investigations suggest that primary PTCA may establish more complete myocardial perfusion compared to thrombolytics, it should be emphasized that the success of primary PTCA requires the institutional capability of performing emergency PTCA procedures 24 hours a day, 7days a week. Because many hospitals are incapable of providing this type of clinical coverage, thrombolytics remain an important and successful strategy in the management of acute MI. In summary, these clinical investigations show that thrombolytic therapy or primary PTCA can be used to successfully restore myocardial perfusion, and more importantly can improve patient survival, even in patients experiencing the most severe form of ischemia.

Numerous therapies are also available for use in patients with unstable angina. Myocardial ischemia in patients with unstable angina occurs as a result of vasoconstriction, and thrombus (clot) formation at the site of an atherosclerotic plaque. Thus, anti-ischemic therapies are aimed at vasodilatation and relaxation of vascular

musculature (i.e., nitrates, beta-blockers, and calcium antagonists) and inhibiting thrombus formation (i.e., aspirin, heparin, IIB/IIIa platelet receptor inhibitors). Typically, clinicians use a combination of these therapies. Studies show that a combination of nitrates, beta-blockers and calcium antagonists, substantially reduce the number and duration of ischemic episodes, and improve short and long term patient survival (Deedwania & Carbajal, 1990; Knatterud et al., 1994; Pepine et al., 1994; Stone et al., 1990). Clinical investigations in patients with unstable angina, which compare placebo to anti-platelet therapies, show a significant reduction in the occurrence of MI, death, or urgent revascularization for refractory ischemia following administration of these agents (The CAPTURE Investigators, 1997; The EPIC Investigators, 1994; Topol et al., 1994). These investigations show that pharmacological therapies used to treat patients with unstable angina reduce the severity of ischemia, and ultimately improve patient outcomes.

Catheter-based interventions such as PTCA and/or stent are also available for treatment of ischemia in patients with unstable angina. One study reported that patients who were treated with PTCA for unstable angina showed improved left ventricular function and were less likely to experience recurrent ischemia, compared to patients who did not have treatment with PTCA (de Feyter et al., 1987). Studies also show that at long term follow-up, over three-quarters of the patients who have PTCA and/or stent remain angina free, and the long term survival is over 90% (Halon, Merdler, Shefer, Flugelman, & Lewis, 1989; Kamp et al., 1989; Pepine et al., 1994; Serruys et al., 1994). Thus, catheter-based interventions (i.e, PTCA and/or stent) for treatment of unstable angina

appear to restore and, in most patients, maintain myocardial perfusion, and improve patient survival.

One final treatment option available for patients with acute coronary syndromes is coronary artery bypass surgery. Clinical trials show that patients who have surgical revascularization experience more favorable long term outcomes compared to patients who have medical treatment, including; greater relief of angina, improved exercise performance, fewer anti-anginal medications prescribed following surgery, and decreased mortality (The VA Coronary Artery Bypass Surgery Cooperative Study Group, 1992; Varnauskas, 1985; Yusuf et al., 1994). Therefore, restoration of myocardial perfusion and improved patient survival can be achieved using surgical revascularization.

In summary, a wide variety of treatment strategies are currently available for use in patients with acute coronary syndromes. However, if patients are to appreciate the maximal benefits of these therapies, early identification of ischemia is imperative in order to preserve myocardial tissue, and normal contractile function. The final section of this paper will discuss important considerations and limitations of ischemia detection in the telemetry unit setting.

Ischemia Detection in the Telemetry Unit: Important Considerations/Limitations

Myocardial ischemia signals an interruption of myocardial blood flow, and indicates that more aggressive therapy is needed to restore and maintain myocardial perfusion. Therefore, a primary clinical objective in patients diagnosed with acute coronary syndromes or following transcatheter procedures is to monitor the perfusion status of the myocardium. Typically, chest pain has been used as a primary indicator of myocardial ischemia. However, studies show that continuous monitoring of the ECG for ST segment

changes is considerably more reliable than chest pain alone, because well over half of the patients who experience myocardial ischemia do not complain of chest pain (Drew et al., 1996; Gottlieb et al., 1986; Krucoff et al., 1993; Krucoff et al., 1985). This would suggest that ECG ST segment monitoring could substantially improve the detection rate of ischemia in patients with acute coronary syndromes who are treated in the telemetry unit setting. While ECG monitoring is a standard of patient care in the telemetry unit setting, important limitations of current telemetric ECG monitoring for ischemia detection should be discussed.

First, many of the current telemetry ECG monitoring systems are capable of monitoring only a limited number of ECG leads (i.e., one, two or three leads), rather than the accepted "gold standard" 12-lead ECG. This is an important limitation because studies show that when one or three ECG leads are used for ischemia detection, ischemia may be missed all together, or the leads selected may not reflect the area of the myocardium that is most ischemic (Drew et al., 1996; Drew, Wung, Adams, & Pelter, 1998b; Klootwijk et al., 1997). Therefore, it is possible that ischemia could be missed or the diagnosis delayed, when only a limited number of ECG leads are utilized for ischemia detection.

Second, ECG ST segment monitoring for ischemia detection requires the installation of additional ST segment software into the current telemetry ECG monitoring system. This is because ST segment software is capable detecting ST segment changes, and then generating an audible alarm that alerts clinicians to the presence of ischemia. This is important because the majority of patients do not experience chest pain during myocardial ischemia, and because ST segment changes indicative of ischemia can be

subtle, as little as one millimeter of ST segment deviation, making visualization of these changes extremely difficult. While visual detection of ischemia is possible, one study found that the "visual" rate of ischemia detection was substantially lower than the rate of ECG ischemia detection (31 visual episodes detected versus 213 ECG episodes detected) (Biagini et al., 1984). In this study, fatigue was sited by the investigators as one of the most important factors responsible for the low rate of visually detected ischemia. This finding is important since most hospitals employ only one monitor watcher to "watch," simultaneously, the ECG recordings of the patients admitted to the telemetry unit. Thus, detection of ischemia is an unrealistic expectation for even the most experienced monitor watcher because: (1) only one ECG lead is observed for each patient at the central nursing station, (2) ST segment changes are often subtle, and (3) monitor watchers may be susceptible to fatigue. Hence, detection of ECG ST segment changes indicative of ischemia using visual techniques is unreliable.

While ECG ST segment monitoring technology is currently available for use in some telemetry ECG monitoring systems, in general, hospitals have not incorporated this technology into the telemetry unit setting. One possible explanation might be that traditionally, patients with acute coronary syndromes were treated in the CCU during at least the first 24 hours of hospitalization, a time period when patients are most at risk for ischemia. However, because many hospitals have replaced CCU care with telemetry unit care for the majority of patients diagnosed with angina, uncomplicated MI, or following PTCA and/or stent, it may now be appropriate for hospitals to re-think the addition of multi-lead ST segment monitoring technology into the telemetry unit setting. However, further investigation regarding the frequency and consequences of ischemia in the

telemetry unit setting is required before any conclusions or recommendations can be made.

Summary/Conclusions

Coronary artery diseases, which include the sub-categories of acute coronary syndromes, represent the single most prevalent health problem in the United States (American Heart Association, 2001). The principal goal of therapy for patients diagnosed with acute coronary syndromes is to achieve and then maintain reperfusion to the myocardium. Myocardial ischemia signals a compromise of myocardial perfusion, and its presence alone has independent value for predicting patients that may be at significant risk for MI or death at both short- and long-term follow-up periods. Thus, the presence of myocardial ischemia could be used to guide more aggressive medical therapy. On the other hand, the absence of myocardial ischemia could validate the success of current treatment interventions, and in the hospital setting, this information could be utilized to triage patients for early discharge.

While numerous therapies are currently available for the treatment of ischemia, it is imperative that these therapies be utilized in the early stages of ischemia in order to limit the area of infarcted tissue. Because chest pain is an unreliable indicator of ischemia, other methods should be sought to improve early detection of ischemia.

Continuous monitoring of the ECG for ST segment changes indicative of ischemia is a method which is reliable, non-invasive, and relatively simple to implement. While ST segment monitoring technology is currently available, in general, this technology has not been incorporated into the telemetry unit setting where a large proportion of patients diagnosed with acute coronary syndromes are currently treated. In the past, it may have

been reasonable to assume that ST segment monitoring would not be necessary, or cost effective, in a hospital setting recognized as a "step down" unit of the CCU, since patients were considered to be in stable condition while in the telemetry unit setting. However, in the current health care system, this assumption may need to be re-evaluated, since there has been a shift of primary hospital care from the CCU to the telemetry unit, primarily in an effort to lower hospital costs. While the initial implementation of ST segment monitoring technology would incur some costs to hospital, it is possible that the overall cost of patient care might be decreased because ST segment information could provided clinicians with vital information that could be used to guide patient care. For instance, ST segment monitoring could be used to identify patients who may benefit from more aggressive therapy(s), which might prevent subsequent untoward cardiac events (i.e., MI, re-hospitalization, or death). On the other hand, ST segment monitoring could be used to identify patients who are at low risk for cardiac events, those without ST segment changes, in whom it may be safe to discharge early from the hospital.

Today, the CCU is reserved for patients who are in obvious distress. The majority of patients with unstable angina, uncomplicated MI, or following PTCA and/or stent receive primary treatment in the telemetry unit setting, rather than the CCU. In addition, acute MI patients, initially treated in the CCU, are transferred to the telemetry unit and then subsequently discharged home at an ever-increasing pace. Thus, today's telemetry unit nurse, who is responsible for the care of as many as 7 patients, must possess advanced knowledge regarding the signs and symptoms of ischemia and be prepared to diagnose, report and then provide treatment in order to halt the progression of ischemia to infarction, an irreversible state of cellular death. Because of the unpredictable and often

asymptomatic nature of myocardial ischemia, it is possible that ST segment monitoring could enhance and potentially improve patient care in the telemetry unit setting. However, this research must be investigated in order to justify the addition of this technology into the telemetry unit setting. A study describing the frequency, characteristics and consequences, if any, of ischemia would be an important initial determination. This preliminary assessment would address the significance of ischemia in the telemetry unit setting, and could provide guidance not only to nurses who work in the telemetry unit setting but also to nurse educators and hospital administrators, all of whom make decisions regarding the addition of technology in hospital units. Finally, clinicians could utilize ST segment monitoring to make decisions regarding patient care and incorporate ST segment information into triage decisions such as early discharge or more aggressive treatment options, which may result in decreasing the overall cost of care.

Clinical Syndromes of Coronary Artery Disease

Acute Coronary Syndromes

Last year in the United States nearly one million deaths occurred as a result of cardiovascular disease; of these deaths over half (487,490) occurred as a result of acute MI (American Heart Association, 2001). Nearly all acute MIs result from an acute disruption of an atherosclerotic plaque with resultant occlusive thrombus formation within a coronary vessel (DeWood et al., 1980). Although the ultimate consequence of CAD is acute MI, other important clinical syndromes are also associated with CAD and include non-ST elevation MI, and unstable angina pectoris. These disease states are now categorized under a broader category of "acute coronary syndromes." Coronary artery disease should be considered a disease process that occurs in a continuum, since patients with acute coronary syndromes can vacillate between periods of stable angina and acute coronary syndromes. For example, patients with acute MI may develop unstable angina following MI or patients with stable angina may progress to unstable angina, or acute MI. Myocardial ischemia is the pathophysiological link between these clinical syndromes, and identifies states of health or illness for patients when ischemia is absent or present, respectively (Figure 1).

ACUTE CORONARY SYNDROMES

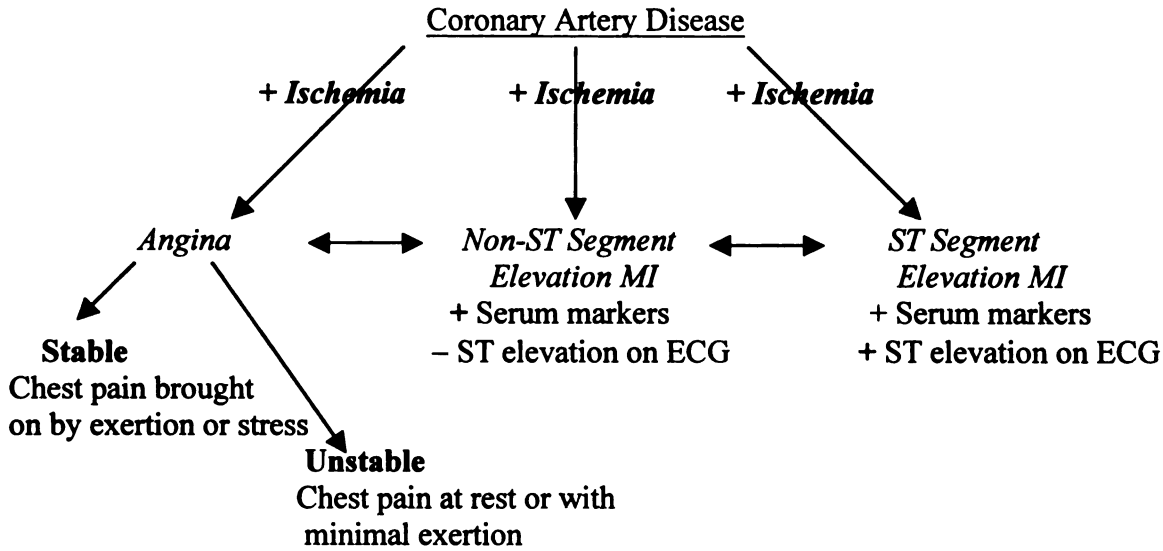


Figure 1. Illustrates the sub-categories of acute coronary syndromes and demonstrates that myocardial ischemia is the pathophysiological link between these clinical syndromes. ECG = electrocardiogram; MI = myocardial infarction

Pathophysiology of Coronary Artery Disease and Myocardial Ischemia

The pathogenesis of CAD is atherosclerosis, a complex process that begins in childhood, and may progress until the clinical manifestations of this disorder are demonstrated in middle and later adulthood (generally 45 years and beyond). Atherogenesis within a coronary artery is a complex biological process that begins with the deposition and accumulation of lipids into the vessel wall, inflammation, formation of a connective tissue matrix and the accumulation of smooth muscle cells (Fuster, Badimon, Badimon, & Chesbro, 1992; Ross, 1999). The end result of this complex process is an atherosclerotic plaque that is organized and characterized by a lipid rich center, and covered by a fibrous cap. The lumen of the coronary artery can become narrowed and blood flow compromised if the atherosclerotic plaque becomes large enough. An atherosclerotic plaque that has reduced the cross-sectional area of a coronary

artery lumen by more than 65 % to 75% will restrict coronary blood flow and can alter the normal function of the myocardium (Brown, Bolson, & Dodge, 1984; Quyyumi, 1992). An important quality of the fibrous cap, which covers the lipid core of a plaque, is that it can vary in thickness. It is this quality which makes the plaque more or less vulnerable to rupture, which may result in acute coronary syndromes. Libby (1995) describes the fibrous cap that covers the lipid rich center of a plaque as being one of two types 1) thin and "vulnerable" or 2) thick and "stable." Vulnerable, or thin capped plaques, are prone to rupture and have been found to possess irregular borders, and are xanthomatous (soft yellowish plaque) in nature (Loree, Kamm, Stringfellow, & Lee, 1992; Mizuno et al., 1991; Richardson, Davies, & Born, 1989). Whereas, stable plaques are white and smooth in appearance (Libby, 1995; Mizuno et al., 1991). An additional distinction between these two types of plaques, assessed with angiography, is that vulnerable plaques are less likely to cause narrowing of the coronary lumen, whereas, stable plaques demonstrate luminal narrowing. Although each of these two types of plaques may lead to acute coronary syndromes, it is now believed that vulnerable plaques are more likely to precipitate acute coronary events, such as acute ST elevation MI, non-ST elevation MI, and unstable angina, rather than stable plaques. There is evidence to suggest that vulnerable plaques can be stabilized with interventions such as diet, exercise, stress reduction and/or lipid lowering drugs; and important in myocardial ischemia, serves as an important marker for success during these treatment regimens.

Myocardial ischemia occurs when arterial blood flow to the myocardium can no longer supply oxygen to meet the demands of cellular respiration. At the cellular level, there is a shift of intracellular respiration from an aerobic form, which utilizes oxygen, to

an anaerobic form, which is oxygen independent. Because the heart is considered an aerobic organ that relies almost entirely on the oxidation of chemical substrates for generation of energy, any loss of oxygen rich blood will compromise its function. Anaerobic metabolism results in the accumulation of metabolic waste products (i.e., lactic acid, ammonia, and inorganic phosphate) that interfere with the contractile proteins (actin and myosin) of the myocardium and lead to wall motion abnormalities. If the area of non-functioning myocardium is sufficiently large enough to drop cardiac output and increase end-systolic and end-diastolic left ventricular volume, acute heart failure can occur causing symptoms of pulmonary congestion, with devastating sequela to patients.

Two types of myocardial ischemia have been identified in patients who have CAD: 1) "demand" -related ischemia, and (2) "supply" -related ischemia. Both types of ischemia are characterized by an imbalance between the supply and demand for oxygen. The difference between the two types of ischemia is the cause of the imbalance. In general, demand-related ischemia is induced by situations such as exercise, tachycardia or emotional stress that increase the myocardium's demand for oxygen beyond the flow capabilities in a patient with CAD. Demand-related ischemia is generally self-limiting and is observed in patients diagnosed with chronic "stable" angina.

One cause of supply related ischemia is coronary vasospasm, which can occur in individuals with normal coronary arteries. In addition, patients with CAD are also at risk for supply-related ischemia, resulting from a complex cascade of events. The coronary processes believed to be responsible for supply-related ischemia in patients with CAD include vasospasm at the site of an atherosclerotic plaque, plaque fissure and/or rupture with resultant platelet stimulation, aggregation, and eventual thrombus formation, with

resultant coronary occlusion (Ambrose et al., 1985; DeWood et al., 1980; Terrosu et al., 1984). Supply-related ischemia, which is characterized by total cessation of coronary blood flow, is responsible for the clinical syndromes of acute MI (both ST and non-ST elevation MI) and unstable angina. The major difference between the disorders of MI and angina is the severity of coronary occlusion. For example, Mizuno et al. (1991) found that a thrombus in the lumen of the coronary artery was totally occlusive in the majority of patients with acute MI, and partially occlusive in the majority of patients with unstable angina.

Manifestations of Myocardial Ischemia

The manifestations of myocardial ischemia can include chest pain, ST segment deviation on the electrocardiogram (ECG), poor uptake of nuclear imaging agents during perfusion scans, and myocardial wall motion abnormalities during echocardiography. Although serum cardiac markers are available for the determination of tissue damage in acute MI (i.e., creatine kinase or troponin I), a serum cardiac marker for detection of myocardial ischemia using a peripheral blod site is not available. It is possible to detect myocardial ischemia from a blood sample, however, the blood must be obtained from the coronary sinus, the vein that empties deoxygenated blood into the right atrium (Gilard et al., 1998). Unfortunately, this method is invasive, expensive and not without risk and is therefore, an impractical measurement method for determining myocardial ischemia in hospitalized patients. Therefore, subjective (chest pain), non-invasive (ECG or echocardiography) or minimally invasive (sestamibi or thallium scans) measures are currently the available tools used to determine if ischemia is absent or present. It should be mentioned that echo studies and sestamibi or thallium scans are "snap shot" tests and

only provide information at the moment the test is being performed. Because ischemia occurs as a transient event it is possible that ischemia would be missed during these tests and the diagnosis of ischemia would be missed. Moreover, exercise testing is used to provoke ischemia, however, patients with acute coronary syndromes are often too unstable to exercise. In clinical practice, what is important in guiding treatment decisions is whether unprovoked or spontaneous ischemia is occurring. Because ECG data can be obtained non-invasively and in a continuous manner, this method has important advantages for the assessment of transient myocardial ischemia in hospitalized patients. In addition, ECG changes, specifically ST segment changes, are often the only indication of ischemia, since 80 – 90% of all ECG-detected episodes of ischemia occur in the absence of chest pain (Drew et al., 1996; Gottlieb et al., 1986; Krucoff et al., 1990). This last point is important since in current clinical practice, assessment of chest pain serves as the primary determinant of the presence or absence of ischemia.

Because chest pain is an unreliable indicator of ischemia, newer-generation ECG monitors are equipped with special ST segment analysis software that allows for continuous "on-line" monitoring for episodes of ischemia. ST segment software is named after the portion of the ECG complex that is altered during episodes of myocardial ischemia. This software is programmed to sound an audible alarm when ST segment changes, either elevation or depression, occur. In the acute care setting, it is imperative to immediately respond to a ST segment alarm and then confirm if ischemia is present so that treatment can be initiated. The primary goal of treatment is to halt the progression of myocardial ischemia to infarction, an irreversible state of cellular death, which impairs contractile function. In the hospital setting, the bedside nurse is the clinician responsible

for the immediate assessment of ischemia since she/he provides constant surveillance of the patient and is responsible for the immediate interpretation of ST segment alarms. Thus, nurses must be knowledgeable about the pathophysiology of ischemia, the associated ECG changes that occur with ischemia, and be able to identify those patients most at risk.

Therefore, the following discussion will address cardiac physiology and then describe the ECG manifestations of myocardial ischemia. This will be followed by an in-depth review of research studies that have utilized ECG ST segment monitoring to detect myocardial ischemia in patients hospitalized for treatment of acute coronary syndromes.

Physiology of the Heart

Normal Physiology

The heart is a mechanical organ that functions to pump deoxygenated blood from the right ventricle to the lungs for re-oxygenation and oxygenated blood from the left ventricle to the rest of the body. The pumping action, or myocardial contraction, follows electrical activation, or depolarization of the myocardium. In other words, the electrical events of the myocardium precede the mechanical events. The ECG is used to measure the electrical activity of the myocardium and serves as a valuable tool to determine both normal and abnormal electrical events of the myocardium.

The origin of a cardiac cycle begins at the cellular level where there is a shift of charged particles, or ions, across the cellular membrane resulting in depolarization of the myocardium. These ions then shift back across the cellular membrane and result in repolarization of the myocardium. The process of depolarization and repolarization evokes an action potential, which represents the electrical activity of a single myocardial

cell. The action potential is composed of five phases. A graphic representation of an action potential can be obtained by introducing a microelectrode into a single myocardial muscle cell (Figure 2).

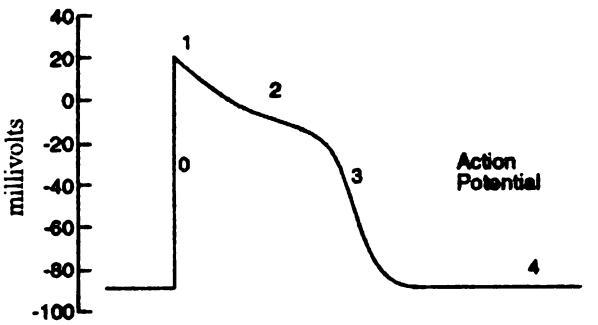


Figure 2. Illustrates the five phases of an action potential.

Phase 0: Depolarization: The abrupt upstroke portion of the action potential represents depolarization of the myocardial cell. Under normal conditions, depolarization of ventricular myocardial cells is dependent upon a stimulus, which in the normal heart comes from specialized cells called pacemaker cells. The arrival of the stimulus to the ventricular cell causes a sudden voltage change in the cellular membrane that begins to open Na^+ channels in the cell membrane. This causes the resting membrane potential to shift from –90 mV to approximately –70 mV to – 65 mV (Hanck, 1994). When the myocardial cell membrane potential reaches – 70 mV to – 65 mV the cell is said to have reached a "threshold," at which point Na^+ channels open and Na^+ rushes into the cell (Katz, 1993). Chemical forces draw Na^+ into the cell since the inside of the cell has a low concentration of Na^+ ions compared to the outside of the cell. In addition, because

the inside of the cell is negative relative to the outside, electrical forces also attract Na^+, a positively charged ion, into the cell. The inside of the cell shifts from a negative environment (-90 mV) to a positive environment where the peak voltage inside of a ventricular muscle cell is + 30 mV.

Phase 1 – Early Rapid Repolarization: During this phase there is an initial and slight repolarization of the myocardial cell, causing the action potential mV value to decrease to approximately + 20 mV to 0 mV. This slight repolarization results from the activation of K^+ channels, resulting in the outward movement of this ion (Nabauer, Beuckelmann, & Erdmann, 1993). The outward movement of K^+ is due to both chemical (intracellular calcium or Ca^{++}) and voltage activated forces, the latter being regulated by neurotransmitters (Zipes, 1997). The outward movement of K^+ ions is brief, at which point the channels close and phase 2 begins.

Phase 2 – Plateau: This phase of the action potential is called the "plateau phase," and represents the longest phase of the action potential, lasting for several hundred milliseconds. The membrane potential of the myocardial cells remains between 0 and +20 mV during the plateau phase. The plateau phase results from continued movement of Ca^{++}, specifically L-type Ca^{++} also called "long-lasting" Ca^{++}, into the cells of the atrium, His-Purkinje and ventricular muscle cells (Flockerzi & Hoffmann, 1995). The significance of L-type Ca^{++} is that it is needed to interact with troponin-C, which triggers the contractile process of the myocardium (Opie, 1997). Simultaneously, there is an outward movement of K^+ ions, which functions to balance the inward movement of Ca^{++} (Zipes, 1997).

Phase 3 - Final Rapid Repolarization: This phase is named the "rapid repolarization phase" and results from inactivation of L-type Ca^{++}, so that the inward movement of Ca^{++} decreases. Simultaneously, there is an increase in outward movement of K^+ (Lederer & Nichols, 1994). The intracellular environment becomes increasingly negative and continues to do so until the cells have returned to their resting membrane potential of – 90 mV, at which point phase 4 begins and the process repeats itself.

Phase 4 - Resting Phase: This phase of the action potential coincides with the resting or diastolic phase of the cardiac cycle. Potassium (K^+) is considered to be the major ion that determines the resting potential of the myocardial cell and is the predominant ion inside the cell, whereas sodium (Na^+) is the predominant ion outside the cell (Carmeliet, 1992; Zipes, 1997). The distribution of these ions is the result of the Na^+-K^+ pump, which functions to pump Na^+ out of the cell against its electrical and chemical gradient and simultaneously pump K^+ into the cell against its chemical gradient. For every three ions of Na^+ that the Na^+-K^+ pump moves out of the cell, two ions of K^+ are pumped into the cell.

During the resting phase, the cellular membrane is permeable to K^+; therefore, this ion is free to move in and out of the cell. In contrast, the cell membrane is impermeable to Na^+; thus, this ion remains outside of the cell. Because the outside of the cell has a low concentration of K^+ ions compared to the inside of the cell, K^+ is compelled to move down its concentration gradient, or from the inside of the cell to the outside of the cell. The movement of K^+, a positively charged ion to the outside of the cell leaves the inside of the cell progressively more negative until the forces attracting K^+ to leave the cell equal the forces attracting K^+ to remain inside of the cell and there is no net movement of

K^+ in or out of the cell. At this point the cell is said to be in a "polarized state" where the cell interior measures about – 90 millivolts (mV) with respect to the exterior of the cell.

Correlation of ECG Waveform to the Action Potential

Normal physiology

The phases of the action potential are measured by inserting a microelectrode into a single myocardial cell. This is an important technique in the laboratory setting to study cellular electrical activity, however in the clinical setting it is more important to analyze the summation of the heart's electrical activity from the body surface to diagnose cardiac rhythm and abnormalities such as myocardial ischemia. It is possible to measure the summation of the action potentials of the myocardium non-invasively using the ECG. The waveforms and intervals of the ECG complex, which include the P-wave, the QRS complex, the ST segment and the T-wave correlate with the phases of the action potential are illustrated in Figure 3.

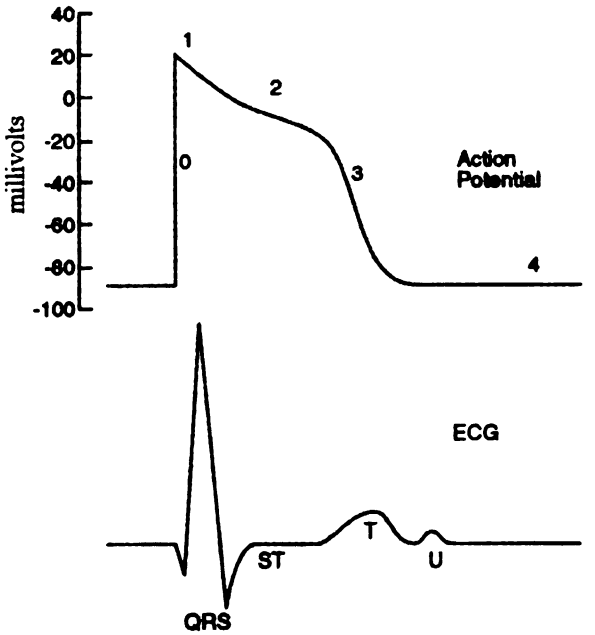


Figure 3. Illustration of how the 5 phases of the action potential correlate with the ECG waveform.

In ventricular myocardial cells, the QRS complex of the ECG waveform correlates with phase 0 of the action potential, and thus, myocardial depolarization. The ST segment correlates with phase 2 of the action potential, which is the early and slow phase of repolarization. The normal ST segment is "isoelectric," neither above nor below the baseline waveform of the PR segment, although slight up-sloping, down-sloping, or horizontal depression of the ST segment can be a normal variant (Wagner, 1994). The T-wave correlates with phase 3 of the action potential, the more rapid and terminal portion of repolarization. Thus, the QRS waveform represents depolarization and the ST segment and T-wave combined represent myocardial repolarization. Although both depolarization and repolarization may be altered during myocardial ischemia, the process of myocardial repolarization is more susceptible to ischemia than that of myocardial

depolarization (Wagner, 1994). Therefore, the waveform of the ECG complex that is predominantly affected during myocardial ischemia are the ST segment and the T-wave.

Myocardial Ischemia

Mechanisms of ECG ST Segment Changes During Ischemia

Classic work by Samson and Scher (1960) identified two mechanisms for ST segment alterations that occur during myocardial ischemia, a "diastolic" current of injury and a "systolic" current of injury. In order to determine how the ECG, specifically the ST segment, was altered during myocardial ischemia it was necessary for these researchers to measure the intracellular changes that occur during ischemia. In their study, intracellular recordings of the action potential were made using the canine model during total occlusion of the coronary artery, an experimental model that depicts acute MI, or supply-related ischemia. The first mechanism described was a "diastolic current of injury," because the alteration of the action potential occurred during electrical diastole, which corresponds to the resting membrane potential of the myocardial cell. Following the onset of ischemia there is a shift of the resting membrane potential from the normal resting membrane potential of approximately – 90 mV, to approximately – 60 mV; thus the transmembrane potential becomes less negative (Kleber, Janse, van Capele, & Durrer, 1978). This alteration corresponds to depression of the T – Q portion of the ECG complex, which produces what appears to be ST segment elevation on the ECG recording (Figure 4).

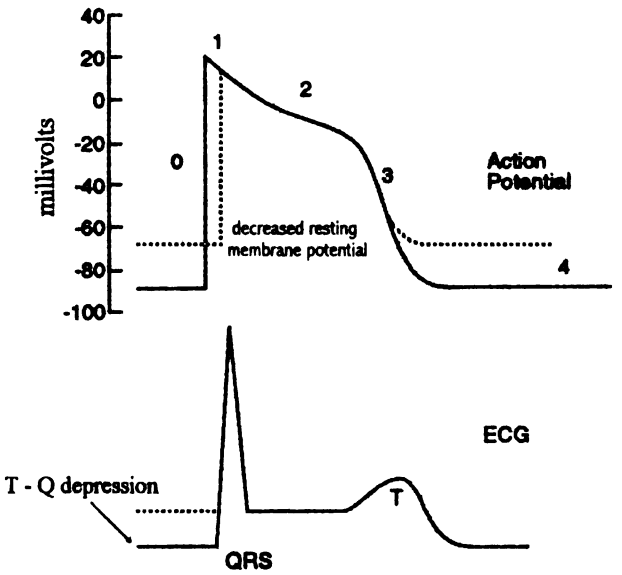


Figure 4. Illustration of the alteration of the action potential (dotted line) that occur during myocardial ischemia and how these changes alter the T- Q segment portion of the ECG complex.

T – Q depression cannot be recorded using a standard ECG machine since the "capacitor-coupled" (A – C) amplifier, which is automatically built into standard ECG machines, automatically corrects the T –Q segment to a "control" or baseline level (Vincent & Abidskov, 1977). Thus, when a standard ECG machine is used to assess for ischemia, T –Q depression may be the mechanism of the myocardial ischemia; however, this change will appear on the ECG recording as ST segment elevation.

Samson and Scher (1960) also showed that as myocardial ischemia progresses over time, within minutes a "systolic current of injury" occurred. In this case, systole refers to electrical systole, which corresponds to phases 0 through 3 of the action potential. Kleber et al. (1977) noted that after three minutes of myocardial ischemia, alterations of electrical systole resulted in a loss of both the amplitude and duration of the action

potential. These changes correspond to ST segment elevation on the electrocardiogram (Figure 5).

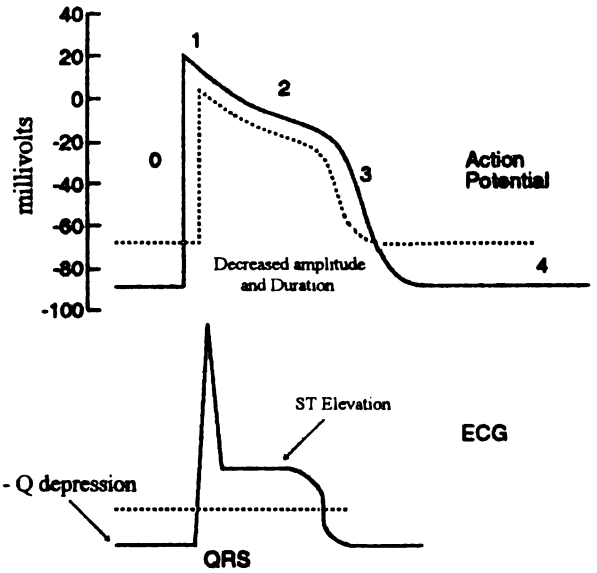


Figure 5. Illustration of the alterations of the action potential (dotted line on the upper figure) that occur during myocardial ischemia and how these changes alter the T- Q and ST segment (see lower figure) of the ECG complex.

A current of injury is directed outward from the surface of the myocardium that is ischemic. When an ECG electrode is placed over an area of injury, it will record ST segment deviation indicative of ischemia. However, one must consider the mechanism of ischemia in order to understand the direction of ST segment deviation, which could be manifested as either ST segment elevation or depression. For example, supply-related ischemia, which is characterized by total occlusion of one of the major epicardial arteries, will direct a current of injury outward from the epicardial surface of the myocardium towards the skin surface of the torso. A skin electrode placed over an area of epicardial ischemia will record a current of injury that is characterized by ST segment elevation.

On the other hand, demand-related ischemia, which is characterized by a partial obstruction of the coronary artery, affects the subendocardial surface or the inner most layer of the myocardium. Again, the current of injury will be directed outwards from the current of injury, which in this case means the current of injury will be directed toward the center of the ventricular cavity, away from the skin surface of the torso. Thus, an ECG electrode placed over an area of subendocardial injury will be characterized by ST segment depression, which is the reverse change as viewed from the skin surface of the torso.

Multilead ECG ST Segment Monitoring

When using the ECG to evaluate hospitalized patients for the presence of myocardial ischemia, it is imperative to record the maximum amount of ECG information. This is because the pathophysiological mechanisms may differ over time in individual patients with acute coronary syndromes (i.e., "fixed" coronary plaque stenosis versus plaque rupture with resultant thrombus formation and coronary occlusion), and result in distinctly different ECG patterns. This is a vital consideration in clinical practice because the latter type of ischemia requires immediate and aggressive treatment in order to avoid acute infarction. The purpose of the following section of this paper is to discuss why multilead, preferably 12-lead, ECG monitoring is necessary for ischemia detection in patients diagnosed with acute coronary syndromes.

The 12-Lead Electrocardiogram

The standard 12-lead ECG is considered to be the non-invasive gold standard for ischemia detection; it can be used to determine the type, location, extent, and in some cases, the coronary artery responsible for ischemia. In order to have a clearer

understanding of how the 12-lead ECG can be used to make these specific diagnoses, it is essential to have an understanding of how the heart is oriented in the chest, and the relationship that each of the 12 ECG leads has to the myocardium.

The standard 12 lead ECG is comprised of six *limb* leads, designated as I, II, III, aVR, aVL, and aVF. These six leads are obtained by placing a skin electrode on each of the four limbs of the body (i.e., right arm, right leg, left arm, left leg). These leads record, or "view," the myocardial activity in the frontal plane of the body. Figure 6 illustrates the orientation of the myocardium within the chest, and the relationship of each of the limb leads to the myocardium.

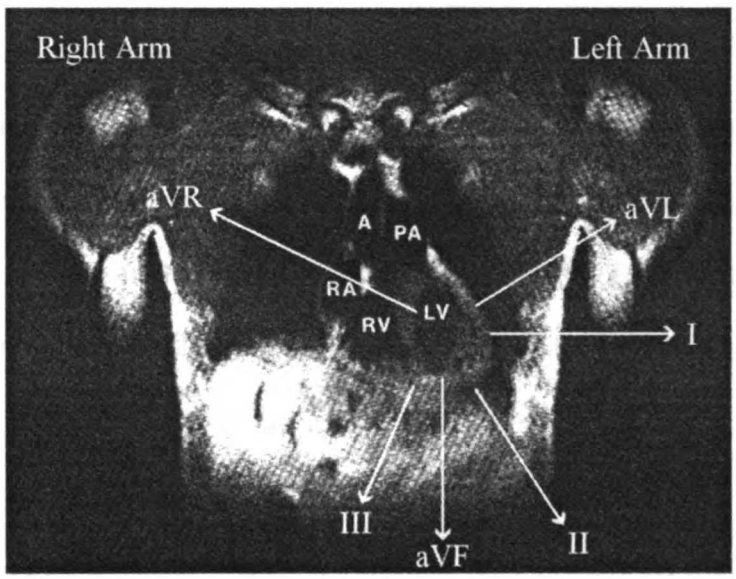


Figure 6. This magnetic resonance image of the torso from the frontal plane view illustrates the relationship between the six limb leads (i.e., I, II, III, aVR, aVL, aVF) and the structures of the myocardium. A = aorta; RA = right atrium; RV = right ventricle; PA = pulmonary artery; LV = left ventricle. The arrows indicate the "view" that each of the leads has to the myocardium.
Source: modified from: Califf, Mark & Wagner, 1988, page 4.

Leads II, III, and aVF view what has been designated the inferior portion of the myocardium, which is supplied by the right coronary artery (RCA) (Wagner & Wagner, 1988). Leads I and aVL view what has been designated the anterosuperior region of the myocardium, which is supplied by either the diagonal branch of the left anterior descending coronary artery (LAD), or a marginal branch of the left circumflex coronary artery (LCX) (Wagner & Wagner, 1988). Lastly, lead aVR views the subendocardial surface, or innermost aspect of the myocardium, which is supplied by the microvasculature of the LAD and LCX, or the terminal portion of the blood supply line (Wagner & Wagner, 1988).

The remaining six leads that comprise the 12-lead ECG are labeled as the *precordial*, or chest leads, and are designated as leads V1, V2, V3, V4, V5, and V6. The precordial leads are obtained by placing skin electrodes at specific sites along the chest wall, directly over the myocardium. These leads record, or "view," the myocardial activity in the transverse, or horizontal, plane of the body. Figure 7 illustrates the orientation of the myocardium within the chest, and the relationship of each of the precordial leads to the myocardium.

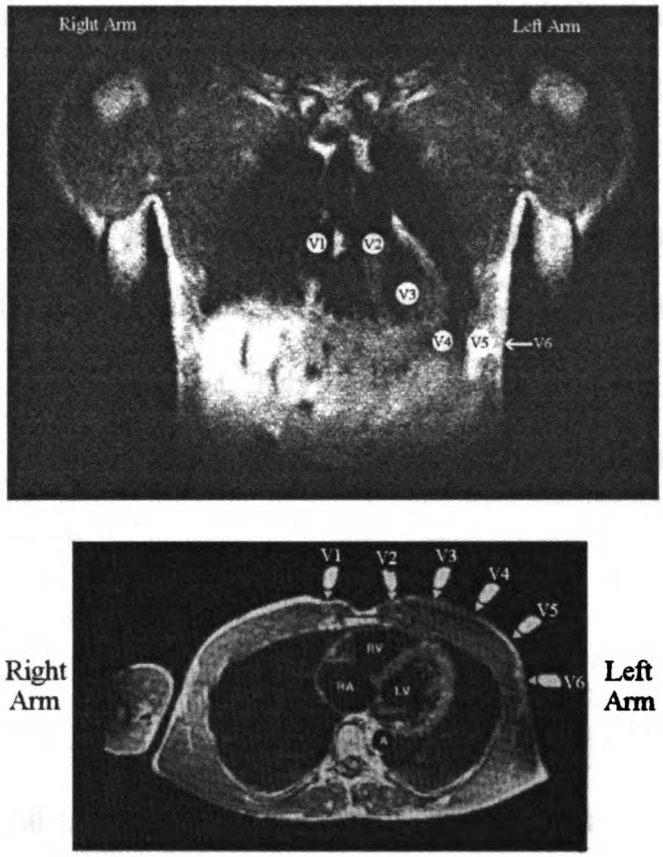


Figure 7. The top figure illustrates the location of the six precordial leads on the torso of the chest. The bottom figure is a horizontal plane view (looking up towards the head from the patient's feet), illustrating the relationship between the six precordial leads (i.e., V1, V2, V3, V4, V5, V6) and the structures of the myocardium. A = aorta; RA = right atrium; RV = right ventricle; PA = pulmonary artery; LV = left ventricle; R = right arm; L = left arm. *Source:* modified from: Califf, Mark & Wagner, 1988. Page 34.

Leads V1 through V6 view what has been designated as the anterior region of the myocardium, which is supplied primarily by the LAD (Wagner & Wagner, 1988). Of the three major coronary arteries, the LAD supplies blood to the largest area of myocardial tissue, or the left ventricle; thus, ischemia in this region of the myocardium threatens a large area of myocardial tissue. Because the precordial leads are located close together along the chest wall, in general, it is possible to view isolated portions of the LAD by

assessing two contiguous leads, or leads located side-by-side. For example, leads V1 and V2 view the proximal, or initial portion of the LAD. Leads V3 and V4 view the middle portion of the LAD. Leads V5 and V6 view the distal, or final portion of the LAD (Wagner & Wagner, 1988). Therefore, the precordial leads may be used to reflect anterior ischemia, and isolate the location of total coronary occlusion within the LAD, as might be seen in patients with acute MI. This ECG information could be used to guide anti-ischemic therapies and identify individual patients at risk for infarcting large areas of left ventricular myocardium.

ECG Manifestations of Ischemia

The typical ECG ST segment manifestation of "demand-related" ischemia, which is characterized by a partial "fixed" coronary obstruction that limits the amount of blood flow to the myocardium during periods of increased heart rate, is ST segment *depression* (Figure 8).

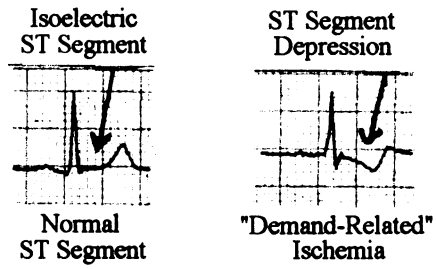


Figure 8. Illustrates the typical ECG manifestations of "demand-related" myocardial ischemia, which is characterized by ST segment depression. Source. From the "Ischemia Monitoring Laboratory" Barbara J. Drew Principal Investigator, University of California San Francisco. Reprinted with permission.

Demand related ST segment changes on the 12-lead ECG reflect ischemia of the subendocardial layer of the myocardium, or innermost aspect. Typically, the ST segment changes associated with demand-related ischemia disappear when the supply and demand for myocardial blood flow is equalized (i.e., heart rate decreases). While lead V5 often shows maximal ST deviation during demand-related ischemia, it is not uncommon for diffuse ST changes to occur in multiple ECG leads. Accordingly, it is necessary to record all 12 ECG leads in order to accurately quantify ischemic burden in patients who experience demand-related ischemia.

The typical ECG ST segment manifestation of "supply-related" ischemia, which is characterized by total coronary occlusion, is ST segment *elevation* (Figure 9).

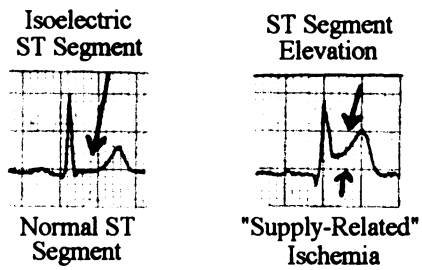


Figure 9. Illustrates the typical ECG manifestations of "supply-related" myocardial ischemia, which is characterized by ST segment elevation. The figure on the right also illustrates the development of a Q-wave, which indicates that infarction has occurred. Source. From the "Ischemia Monitoring Laboratory" Barbara J. Drew Principal Investigator, University of California San Francisco. Reprinted with permission.

The causes of supply-related ischemia include coronary vasospasm, abrupt reocclusion of the coronary vessel following PTCA, or acute atherosclerotic plaque rupture with resultant thrombus formation and coronary occlusion. The latter cause of supply-related ischemia typically occurs in patients with either acute MI or unstable angina.

In general, supply-related ECG findings reflect total coronary occlusion of one of the three major coronary arteries, which results in transmural ischemia, or ischemia of the entire thickness of the myocardium. Because the entire thickness of the myocardium is threatened as a result of this type of ischemia, it is imperative that this condition be reversed immediately in order to prevent acute heart failure.

Unlike demand-related ischemia, ST segment elevation caused by supply-related ischemia can be used to localize the area of the myocardium that is ischemic and in most cases identify the "culprit" artery responsible for ischemia. For example, ST segment elevation of leads V2 to V4 reflects ischemia of the anterior portion of the myocardium, and most often indicates occlusion of the left anterior descending (LAD) coronary artery (The GUSTO Investigators, 1993). ST segment elevation of leads III, aVF, and II reflects ischemia of the inferior portion of the myocardium, and most often indicate occlusion of the right coronary artery (RCA) (The GUSTO Investigators, 1993). Finally, occlusion of the left circumflex (LCX) coronary artery may produce inferior, lateral, or posterior ECG patterns; thus, no one ECG lead, or leads has been found to be superior for detecting ischemia (Aldrich et al., 1987; Bush, Ferguson, Angelini, & Willerson, 1990; Drew & Tisdale, 1993). However, it is possible to diagnose posterior ischemia, which is most often the result of LCX artery occlusion, using ST segment depression in leads V1, V2 and V3, since these ST segment changes reflect the reciprocal ST changes of posterior ischemia (Wagner, 1994). Therefore, the 12-lead ECG manifestations of supply related ischemia can be used to identify, differentiate, and localize myocardial ischemia.

Moreover, it is important to consider that while the ECG manifestations of supply-related ischemia result in ST elevation over the specific myocardial region that is

ischemia, it is not uncommon to also observe ST segment depression in ECG leads opposite the ischemic region, or "reciprocal" ST changes. Hence, the ECG manifestations of supply-related ischemia are not exclusive (i.e., solely ST elevation). Therefore, in the setting of supply-related ischemia, if only the reciprocal ST changes were recorded on the ECG, as is probable when fewer than 12 ECG leads are recorded, it is possible that this ischemic process would be mis-diagnosed as demand-related ischemia (ST segment depression). This mis-diagnosis could have a profound impact on patient outcomes, because demand-related ischemia is often treated less aggressively than supply-related ischemia.

It is important to consider that ischemia is rarely a "global" myocardial phenomenon, but rather affects specific locations of the myocardium, generally described as either anterior, inferior or posterior ischemia. Therefore, it is possible that ischemia could be missed if an ECG electrode were not placed over the site of the myocardium that is ischemic. This is an important consideration in clinical practice since most current bedside monitors offer only a limited number of ECG leads, which means ischemia could go unrecognized.

Literature Review of ECG ST Segment Monitoring

Over the last decade numerous research studies have been conducted using ST segment monitoring technology for detection of ischemia in hospitalized patients. Initial studies focused on determining the usefulness of ST segment technology in the detection of ischemia during the recovery period following acute MI, unstable angina, or following catheter based interventions (i.e., percutaneous transluminal angioplasty (PTCA), atherectomy, or stent). Subsequent studies have been conducted to determine the

prognostic value of ischemia detected using ST segment monitoring for identifying patients at risk for poor outcomes such as death, MI and re-hospitalization for treatment of acute coronary syndromes.

The following discussion will be a review of the literature of ST segment monitoring studies that have been conducted thus far. The review will address the frequency, implication and prognostic significance of ischemia detected using ST segment monitoring in three patient populations: 1) following catheter based interventions (i.e., PTCA, stent) 2) during hospital recovery for unstable angina and 3) during hospital recovery following acute MI. The limitations and implications for future research will be the focus of the discussion.

ST Segment Monitoring Following Catheter Based Interventions

Over the last decade there has been a steady increase in the number of catheter based interventions such as PTCA and stent procedures performed in the United States. Last year 482,000 PTCA procedures and 177,000 stent procedures were performed (American Heart Association, 2001). Although the immediate success rate of these procedures is remarkable, the risks of abrupt reocclusion and/or ischemia are important risks that may occur during the recovery period following these procedures. Successful PTCA results in intimal disruption, which has been described as a "crack," "tear," or "fracture" at the site of the atherosclerotic plaque where the PTCA procedure is performed (Waller, 1987). This creates a potentially unstable area at the intervention site, which is susceptible to coronary artery spasm, thrombus formation and coronary artery dissection (Baim & Ignatius, 1988). These conditions can lead to ischemia, which is characterized by partial obstruction of the artery. This may lead to abrupt reocclusion, which is characterized by

a total obstruction of the coronary artery. Therefore, the prime objective of assessment following PTCA is the immediate detection of myocardial ischemia, since this may signal coronary artery occlusion at the site where the PTCA procedure was performed.

Krucoff and co-workers (1988) were the first to study the use of ST segment monitoring for detection of coronary reocclusion following PTCA. These researchers obtained three-lead ECG recordings of the ST segments during catheter balloon inflation in 512 patients and then provided continuous ST segment monitoring in the coronary care unit (CCU) for 24 hours following PTCA. The authors theorized that an ECG template or "ST fingerprint," which is produced during PTCA balloon inflation when an artery is totally occluded, would be useful for evaluation of subsequent reocclusion. In other words, if a patient experienced abrupt reocclusion following PTCA, the ischemic ST pattern would mimic the "ST fingerprint" obtained during the PTCA procedure. Of the 512 patients included in the study, 43 (8%) experienced in-hospital reocclusion. The "ST fingerprint" obtained during the PTCA procedure was reproduced exactly in 26 (60%) of the patients who had reocclusion and an additional 12 (28%) had a "related" pattern, defined as at least one lead demonstrating the same changes as those observed during PTCA. Thus, the authors concluded that the "ST fingerprint" which was obtained during the PTCA procedure identified 88% of the patients who experienced reocclusion following PTCA.

This study by Krucoff et al (1988) is important since it was the first to describe the usefulness of ST segment monitoring technology following PTCA for detection of reocclusion. In addition, the concept of an "ST fingerprint" was a novel and significant contribution since it suggested that subsequent ischemia would be isolated to specific

ECG leads. This is important in clinical practice since most bedside monitors are able to monitor only one to three ECG leads, which means the nurse, who initiates and maintains bedside monitoring, must choose the single best ECG lead or leads for ischemia monitoring. If a patient's ST fingerprint ECG pattern was available to the nurse, she/he could tailor the ECG monitoring to the single most valuable ECG lead set.

However, important limitations should be addressed regarding this study. First, abrupt reocclusion was diagnosed using the ECG, rather than the accepted gold standard angiogram. Hence, one cannot conclude that patients who did not demonstrate ECG changes did not have abrupt reocclusion. Second, the "ST fingerprint" used as the template ECG for identification of abrupt reocclusion was obtained using only three ECG leads, which is far fewer than the 12-leads that constitute the accepted gold standard for ischemia and MI determination. Therefore, the patient's true ST fingerprint may not have been recorded in Krucoff's study. Third, this study did not assess the frequency of chest pain in their study sample. This is important since one could argue that chest pain would have occurred in the patients who experienced reocclusion and therefore ST segment monitoring would not have provided additional information. Finally, outcome data was not reported comparing the patients who had reocclusion to those who did not have reocclusion. This information would be valuable since it may indicate that ST segment monitoring data has predictive value and therefore ST segment technology could be utilized in clinical practice to improve patient outcomes.

Subsequent studies have been conducted in patients treated with either PTCA or stent, a small metal device that functions to retain coronary vessel lumen patency following successful PTCA, which have addressed many of the above mentioned limitations. For

example, many of these studies have included patients with varied demographics (i.e., age, gender and ethnicity) and a variety of ECG methods have been utilized including12-lead ECG analysis. Finally, several studies described not only abrupt reocclusion but also the frequency of ischemia, characterized by a transient or partial obstruction of the coronary artery (Table 1).

Table 1. ST segment monitoring studies conducted during and/or following PTCA or stent.

Investigator(s)	N	ECG method During PTCA/stent	ECG Method in CCU Following PTCA/stent
Krucoff et al., 1990	282	3 lead or 12-lead	3 lead or 12-lead
Mitzutani et al., 1990	50	12-lead	1 lead
Drew & Tisdale, 1993	18	12-lead	2-lead
Foley et al., 1993	53	2 lead	2 lead
Gurfinkel et al., 1994	57	Not Monitored	12-lead
Drew et al., 1996	250	Derived 12-lead	Derived 12-lead
Kathiresan et al., 1999	30	12-lead	12-lead

N= sample size; PTCA = percutaneous transluminal coronary angioplasty; pts. = patients
CCU = Coronary Care Unit

Abrupt reocclusion is a life threatening complication following catheter-based interventions because blood flow to the myocardium has ceased. Therefore, a primary clinical objective following catheter-based interventions is to immediately identify this serious complication in order to re-establish blood flow to the myocardium. Studies conducted in patients treated with PTCA patients show that the frequency of acute coronary reocclusion, measured using continuous ECG ST segment monitoring, ranges from 4% to 9% (Drew et al., 1996; Krucoff et al., 1990). Unfortunately, the gold standard, a repeat angiogram, was not done in all patients regardless of the signs or symptoms of abrupt reocclusion; thus, the true incidence of abrupt reocclusion cannot be determined from these studies. However, there was angiographic confirmation of abrupt

reocclusion in the group of patients who demonstrated ECG changes matching their ST fingerprint. Therefore, these studies show that continuous ECG monitoring can be used during the recovery period following PTCA to detect acute ST segment changes that may indicate that acute coronary occlusion has occurred. The study by Kathiresan et al. (1999), is the only study to exclusively assess stent patients for ischemia using ST segment monitoring. In their study, 33% of patients experienced ECG-detected ischemia, but none experienced reocclusion. However, as was the case in the PTCA studies a repeat angiogram was not performed in all of their patients. One might conclude that this finding is not surprising since the stent was developed to treat abrupt reocclusion by providing a scaffolding of the intimal flap that is created during successful PTCA (Palmaz, 1988). However, there is evidence to indicate that reocclusion remains an important threat following stent placement, which is believed to be caused by thrombus formation at the site of the stent (Gawaz, Neumann, Ott, May, & Schömig, 1996; Neumann et al., 1996). For example, studies show that acute thrombus reocclusion following stent occurs in 3.5% to 6% of patients, which was measured by angiography rather than with ST segment monitoring (Dabbs, Chambers, & Macauley, 1998; Serruys et al., 1994). Thus, abrupt reocclusion remains an important threat during the recovery phase following stent. Because studies indicate that ST segment monitoring is a valuable tool for detecting acute ST changes following PTCA, further studies should be conducted to determine if this tool would be valuable following stent placement as well.

Patients are also at risk for transient myocardial ischemia, which is characterized by a partial or transient obstruction of the coronary artery. The causes of transient ischemia could be due to atherosclerotic plaques in other coronary arteries that were not treated

with PTCA/stent, vasospasm, or partial occlusion of the coronary vessel at the intervention site in patients where complete vessel opening in not achieved. The frequency of transient ischemia, measured with ST segment monitoring, following PTCA ranges from 8% to 26% of patients (Drew & Tisdale, 1993; Krucoff et al., 1990).

A consistent finding in these studies is that over 80% of transient ischemic episodes occur in the absence of chest pain, (Drew et al., 1996, Kathiresan, 1999 #208; Foley et al., 1993; Krucoff et al., 1990). Among the patients who experience chest pain during ST changes, it is not uncommon for ST segment changes to occur several minutes prior to a complaint of chest pain (Krucoff et al., 1990). Hence, in this subgroup of patients, ST segment monitoring provides an early warning of ischemia, which could result in quicker treatment and possibly less tissue damage. Unfortunately, it is not uncommon for patients to experience non-ischemic chest pain during the recovery period following catheter-based interventions. For example, one study found that as many as 40% of stent patients and 12% of PTCA patients experience non-ischemic chest pain during the recovery period. One possible explanation thought responsible for non-ischemic chest pain is stretching of the coronary artery during PTCA or stent placement (Jermias et al., 1998; Tomai et al., 1993). In addition, non-ischemic chest pain may result from gastrointestinal (GI) discomfort because patients have been in a fasting state for the procedure, or esophageal reflex caused by eating in a supine position following the procedure. In clinical practice this creates a dilemma because clinicians utilize chest pain as the primary indicator of ischemia. Therefore, in some cases ischemia would go unrecognized and in other cases it would be misdiagnosed when there was no ECG evidence of its presence. The latter scenario could result in an unnecessary re-

catheterization procedure to determine if the coronary artery is patent, which could add risk to the patient and incur unnecessary hospital costs. These points indicate that ST segment monitoring could be utilized to more accurately diagnose ischemia in patients during the recovery period following catheter-based interventions.

Finally, several studies have reported that patients who experience ischemia or reocclusion after PTCA have significantly more in-hospital complications, such as MI, death, and need for urgent by-pass surgery compared to patients who do not have ischemia or reocclusion (Drew et al., 1996; Krucoff et al., 1990). Gurfinkel et al. (1993) showed that patients, who experienced in hospital transient myocardial ischemia following apparently successful PTCA, were more likely to have recurrent angina at a three-month follow-up period. Therefore, ischemia has predictive value for determining subsequent poor outcomes during the in-hospital recovery phase and several months following treatment.

Important Considerations/Limitations: It should be pointed out that approximately 20% of patients do not exhibit ST segment changes during PTCA/stent balloon inflation (Drew et al., 1998b; Mizutani et al., 1990). This means that an ST fingerprint is not available in these patients and clinicians cannot rely on ST segment monitoring for detection of abrupt reocclusion or transient episodes of ischemia in this subgroup of patients. The most reliable way to identify patients who do not exhibit ST changes during PTCA and/or stent balloon inflation would be to record a 12-lead ECG during the procedure. This information could then be incorporated into the post procedural care of the patient and aid clinicians during the recovery period following the procedure.

All of these studies were descriptive studies that used a prospective, comparative, within-subjects design, to describe the frequency, ECG characteristics, and consequences of myocardial ischemia and reocclusion after PTCA using ST segment monitoring. This nonexperimental study design would be considered appropriate since the goal of these studies was to explore the use of ST segment monitoring for detection of ischemia and reocclusion following PTCA (LoBiondo-Wood & Haber, 1990). While these studies have provided important foundation knowledge regarding the use of ST segment monitoring for detection of ischemia and reocclusion, future experimental studies should be conducted to determine if ST segment monitoring data could be incorporated into clinical decision making in order to improve patient outcomes. In addition, because the sample sizes in many of these studies were small, statistical tests could not always be performed to determine if the complication rate was higher for patients who had ischemia compared to patients who did not. This would be important to determine since there should be evidence that ST segment monitoring could be used to improve patient care and ultimately patient outcomes. Finally, because not all of the subjects in these studies had repeat angiography, there is no empirical evidence to determine the value of continuous ECG ST monitoring for detection of abrupt reocclusion.

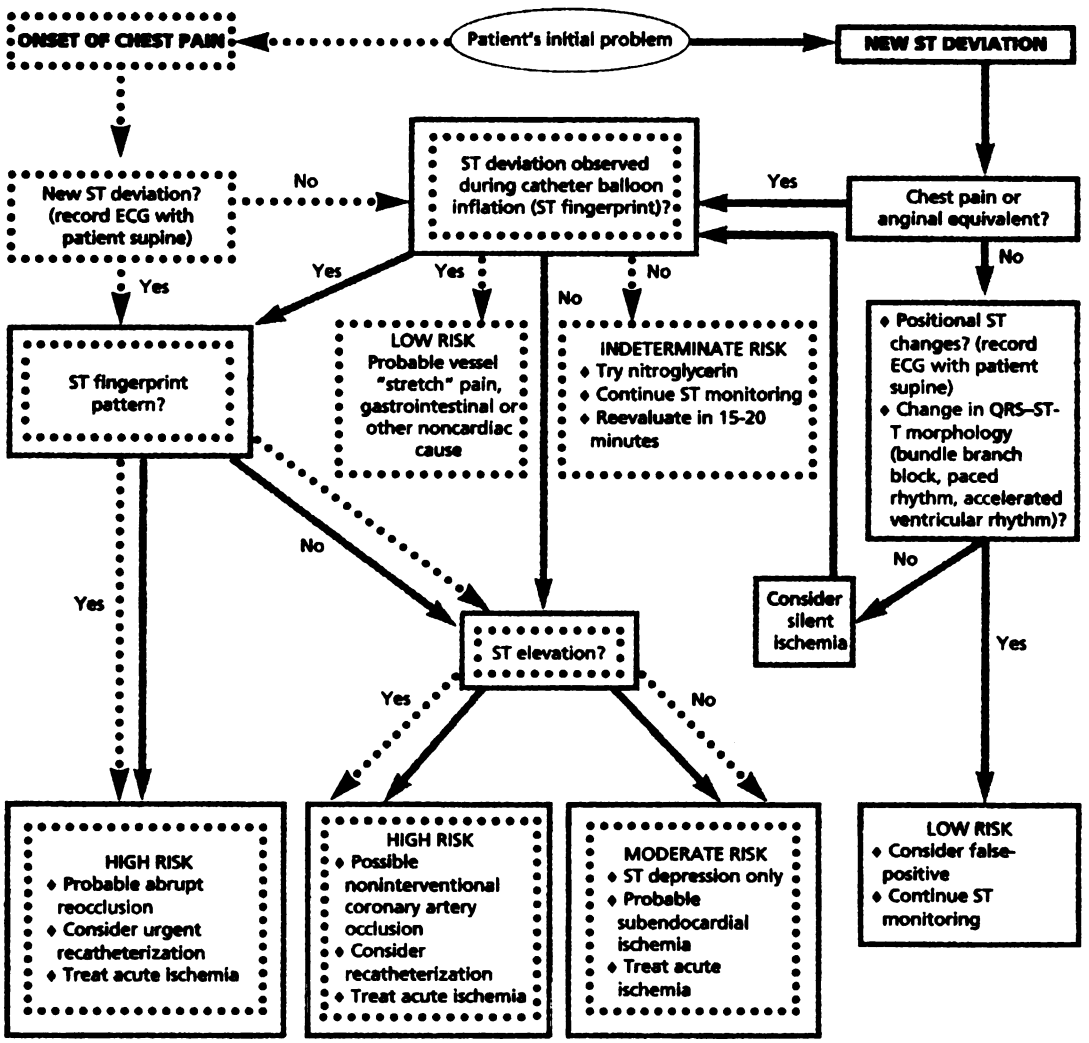
Summary/Implications of Ischemia Following Catheter-Based Interventions

The immediate success of PTCA and/or stent is over 90%, and the vast majority of patients recover from interventional procedures without any untoward consequences. However, abrupt reocclusion and transient ischemia must remain key assessment points during the recovery period following both of these procedures. Abrupt reocclusion is considered a medical emergency, since blood flow to the myocardium through the

epicardial coronary artery treated, has ceased. Acute MI will result in nearly three-quarters of the patients who experience this complication, which is preventable since immediate intervention (i.e., re-catheterization and stent placement, intracoronary thrombolytics, or emergency CABG) to reverse this complication is available. Myocardial ischemia that is not caused by abrupt reocclusion still carries significant risk for patients both in- and out- of the hospital. Therefore, immediate detection and reversal of these conditions is essential in order to restore blood to the myocardium.

The concept of a patient specific ST fingerprint could be easily incorporated into clinical practice as a guide for clinicians, especially for nurses who must decide which ECG lead(s) are most appropriate for detection of reocclusion and/or ischemia. Identification of the patients who do not exhibit a ST fingerprint ECG pattern during PTCA/stent balloon inflation is also valuable because this could alert clinicians to the subgroup of patients where ST segment monitoring has limited value for detection of abrupt reocclusion or ischemia. Accordingly, in 1999, an international panel of experts in the field of ischemia monitoring developed a practice guideline that included a strategy for optimal ST segment monitoring following catheter-based interventions(Drew, Krucoff, & For the ST-Segment Monitoring Practice Guideline International Working Group, 1999a). Figure 10 illustrates an algorithm for use in clinical practice for high-risk patients who require close monitoring following PTCA or stent.

Figure 10. Illustrates the clinical flow diagram developed by nurse scientists at the University of California, San Francisco. The algorithm is intended for high-risk patients who require close monitoring in an intensive care or immediate care unit after angioplasty or stent placement. Source: (Drew et al., 1999a) page 376.



Follow the black dotted lines (• • •) for patients whose initial problem is onset of chest pain.
Follow the solid gray lines (▬▬) for patients whose initial problem is new ST deviation.

In summary, ST segment monitoring has important advantages over chest pain alone for detection of ischemia. For example, the majority of PTCA/stent patients will not experience chest pain during ischemia; thus, ST segment changes will be the only indication of ischemia. For the subgroup of patients who do experience chest pain during ischemia, ST segment changes will often proceed the symptoms by several minutes. Lastly, ST segment monitoring could be utilized to differentiate non-ischemic chest pain syndromes, which are not uncommon during the recovery period following PTCA and/or stent.

Gaps in the literature: To date, only one study has evaluated the frequency of ischemia following stent placement (Kathiresan et al., 1999). Further assessment of this patient population is warranted since the use of this device is increasing both as an elective treatment option for patients with unstable angina and for treatment of acute MI as well. In addition, there have been no recent ST segment monitoring studies regarding the incidence of reocclusion or ischemia following either PTCA and/or stent. This might be important since the use of these procedures has expanded far beyond treatment for simple, discrete, single vessel lesions. Today, PTCA and/or stents are utilized to treat lesions in multiple coronary vessels, within saphenous vein grafts, small coronary arteries, and in older and often high-risk patients with multiple co-morbidities (i.e., renal disease, diabetes, severe hypertension). It is possible that these patients may be more vulnerable to ischemia and/or reocclusion, however, this must be evaluated further. Finally, efforts to determine whether silent reocclusion occurs should be pursued. Currently, a repeat angiogram is only performed when a patient has chest pain or ST elevation, which means we assume that patients who do not experience chest pain or

exhibit ST changes do not have reocclusion. However, the literature shows that the majority of ischemic episodes are clinically silent (Krucoff et al., 1990; Krucoff et al., 1988), and that approximately 20% of patients do not exhibit ST changes during PTCA/stent despite total occlusion of the coronary vessel (Drew et al., 1998a; Krucoff et al., 1990; Mizutani et al., 1990).

Importantly, recovery following these interventional procedures has shifted from the CCU to other less acute hospital settings i.e., telemetry, recovery or medical units, primarily in an effort to lower hospital costs. Importantly, ST segment monitoring is not available in the majority of these hospital settings; thus, nurses who work in these units must rely primarily on patient complaints of chest pain to signal ischemia, which is problematic since this is an unreliable indicator of ischemia in most patients. Among patients who experience chest pain during ischemia, the perception of pain often occurs several minutes after the onset of ischemia when myocardial damage is done. This would indicate that an assessment of the value of ST segment monitoring in hospital units, such as telemetry or recovery room units, that now provide post PTCA and/or stent recovery is indicated.

ST Segment Monitoring in Patients with Unstable Angina

The goal of treatment for patients who present to hospitals with unstable angina is to definitively diagnose the disease as cardiac in origin and to initiate treatment to abolish on-going ischemia and prevent myocardial cell death. Although chest pain is the most common presenting symptom in these patients, it is important to note that in the vast majority of patients transient episodes of ischemia occur in the absence of chest pain.

Because of this important limitation, researchers have sought improved methods for detecting ischemia.

Continuous monitoring of the ECG for ST segment changes has emerged as an important diagnostic tool that can identify myocardial ischemia in patients with unstable angina. A computerized literature search was used to identify studies that have utilized ECG ST segment monitoring in patients with unstable angina (Table 2).

Investigator(s)	n	ECG method	Ischemia Criteria	Frequency of Ischemia
Johnson et al., 1982	92	Holter 2 lead	ST ↓ or ↑ 100 μV	21/92 (23%)
Von Essen et al., 1984	10	Precordial Mapping	Q, R, or ST changes	1/10 (10%)
Gottlieb et al., 1986	70	Holter 2 lead	ST ↑ or ↓ ≥ 100 μV	37/70 (53%)
Nademanee et al., 1987	49	Holter 2 lead	ST ↑ or ↓ ≥ 100 μV	29/49 (59%)
Langer et al., 1989	135	Holter 1 lead	ST ↑ or ↓ ≥ 100 μV	89/135 (66%)
Wilcox et al., 1990	66	Holter 2 lead	ST ↑ or ↓ ≥ 100 μV	7/66 (11%)
Dellborg et al., 1992	43	Frank vectorcardiographic leads	QRS or ST vector difference	9/43 (43%)
Romeo et al., 1992	76	Holter 2 lead	ST ↓ or ↑ > 100 μV	76/76 (100%)
Larsson et al., 1992	198	Holter 2 lead	ST ↓ ≥ 100 μV	17/75 (23%)
Amanullah & Lindvall, 1993	43	Holter 2 lead	ST ↓ or ↑ > 100 μV	42/43 (98%)
Bugiardini et al., 1995	104	Holter 2 lead	ST ↓ or ↑ > 150 μV	96/104 (94%)
Drew et al., 1996	148	Derived 12-lead	ST ↑ or ↓ ≥ 100 μV	23/148 (16%)
Patel et al., 1996	212	Holter # of leads NR	ST ↓ ≥ 100 μ ST ↑ ≥ 200 μV	32/212 (15%)
Klootwijk et al., 1997	114	Standard 12-lead	ST ↓ or ↑ > 100 μV	88/114 (77%)
Klootwijk et al., 1998	332	Frank vectorcardiographic leads	ST ↑ or ↓ ≥ 100 μV	68/332 (21%)
Goodman et al., 2000	231	Holter 3 lead	ST ↑ or ↓ ≥ 100 μV	87/231 (37%)

Table 2. Summary of studies using ST segment monitoring to detect transient ischemia in hospitalized patients diagnosed with angina; MI = myocardial infarction; N = sample size; NR = not reported; μV = microvolt

As illustrated in table 2, the reported frequency of ischemia varies considerable among these studies. The wide range of values probably reflects differences in: (1) inclusion/exclusion criteria, (2) number of ECG leads used to detect ischemia (3) time from hospital admission to initiation of ST monitoring, (4) duration of monitoring (5) definition of ischemia, and (6) protocol for eliminating false positive ST changes. How each of these factors may have influenced the reported frequency rate of ischemia will be discussed in the following section of this paper.

A computerized literature search was conducted to identify ST segment monitoring studies that assessed patients with unstable angina. Interestingly, the diagnostic criteria of unstable angina differed considerably among these studies. For example, the reported frequency of ischemia was typically highest in the studies that defined unstable angina as: (1) angina at rest, (2) crescendo angina, (3) angina refractory to typically medical treatment, (4) worsening angina in patients with previous stable angina, and (4) chest pain accompanied by ST segment changes on the admitting ECG (Table 3).

Table 3. Illustrates the reported frequency of ischemia in studies that defined unstable angina as; (1) angina at rest, (2) crescendo angina, (3) angina refractory to typically medical treatment, (4) worsening angina in patients with previous stable angina, and (4) chest pain accompanied by ST segment changes on the admitting ECG.

Investigator(s)	n	Frequency of Ischemia
Gottlieb et al., 1986	70	37 (53%)
Nademanee et al., 1987	49	29 (59%)
Langer et al.,1989	135	89 (66%)
Romeo et al., 1992	76	76 (100%)
Amanullah & Lindvall, 1993	43	42 (98%)
Bugiardini et al., 1995	104	96 (94%)
Klootwijk et al., 1997	114	88 (77%)
Klootwijk et al., 1998	332	68 (21%)
Goodman et al., 2000	231	87 (37%)

These strict diagnostic criteria meet those developed by the Agency for Health Care Policy and Research (AHCPR) guidelines used to diagnose and manage unstable angina (Bruanwald, Mark, & Jones, 1994). Therefore, these studies are likely to represent the true population of unstable angina patients. In contrast, the reported frequency of ischemia was typically lower in the studies that did not identify patients using the AHCPR guidelines for diagnosing and managing unstable angina (Table 4).

Table 4. Illustrates the reported frequency of ischemia in studies that did not identify unstable angina patients using the AHCPR guidelines.

Investigator(s)	n	Frequency of Ischemia
von Essen et al., 1984	50	5 (10%)
Wilcox et al., 1990	66	7 (11%)
Dellborg et al., 1991	43	9 (43%)
Larsson et al., 1992	75	17 (23%)
Drew et al., 1996	148	23 (16%)
Patel et al., 1996	212	32 (15%)

Although the studies presented in table 4 were identified during a computerized literature search as studies that assessed unstable angina patients, the inclusion criteria did not incorporate the AHCPR guideline definitions of unstable angina. For instance, patients were not required to have both chest pain and exhibit dynamic ST segment changes on the admitting ECG in order to be included in the study. Therefore, it is likely that these latter studies may have included patients with both stable and unstable angina, and may explain why, in general, this group of studies reported a lower rate of ischemia compared to the studies that included patients who met the AHCPR diagnostic criteria for unstable angina. Therefore, before generalizing the findings from these studies it is essential to carefully evaluate the inclusion/exclusion criteria used to diagnose unstable

angina. Accordingly, for the purposes of this discussion only those studies that included patients who were likely to have unstable angina will be addressed in this section.

Despite using similar inclusion criteria, there was still a great deal of variation in the reported frequency of ischemia among these studies. For example, in the two separate studies conducted by Klootwijk et al., in one study 77% of patients experienced recurrent ischemia (Klootwijk et al., 1997), and in the other, 21% of the patients experience recurrent ischemia (Klootwijk et al., 1998). One possible explanation for the later rate of ischemia might be that these patients were enrolled in the CAPTURE study, a randomized clinical trial evaluating an intravenous anti-platelet medication (abciximab/ReoPro). Therefore, it might be possible that the reduction of recurrent ischemia in this study reflected stabilization of the atherosclerotic plaque using the study drug, which was administered to half of the subjects. However, the rate of ischemia was not statistically different between the group of patients who received the study drug compared to patients who received placebo (18% versus 23%; NS). Thus, it would appear that the study drug did not influence the rate of ischemia. One could also argue that the variations in the rate of ischemia might be related to the administration, or lack of, other cardiac medications such as, aspirin, heparin, nitrates, B-blockers, and calcium channel blockers. However, in each of these studies there was mention that all patients received medical therapy using many of the aforementioned drugs, which appropriately meets the standard of care in patients diagnosed with unstable angina (Braunwald, 1989). However, it was not always clear how the drugs were administered (i.e., orally, subcutaneously, or intravenously) or the dosage, which might be important because it may indicate that patients were not receiving the maximal benefit from these drugs. The

results, therefore, of many of these studies may not be relevant to current clinical practice.

Another possible explanation for the frequency variations among these studies might have been the number of ECG leads used to diagnose ischemia. This is an important consideration in patients with unstable angina because the mechanism of recurrent ischemia may be due to more than one mechanism (i.e., demand- or supply-related ischemia). As a result, individual patients may exhibit different ST patterns (i.e., elevation or depression) that shift among different ECG leads. This is supported by studies which show that a substantial proportion of ischemic episodes may be missed when only one or three ECG leads versus all 12-lead ECG lead are used to detect ischemia (Drew et al., 1998a; Klootwijk et al., 1997). Therefore, one might conclude that the frequency of ischemia might be lower in the studies that used only one or two ECG leads, and higher in the studies that used 12-lead ECG monitoring. Table 5 illustrates a comparison between the number of ECG leads used to detect ischemia to the reported frequency of ischemia among these studies.

Table 5. Illustrates the reported frequency of ischemia in unstable angina patients, and the number of ECG leads used to detect ischemia .

Investigator(s)	# of ECG leads used	Frequency of Ischemia
Gottlieb et al., 1986	2 leads	37 (53%)
Nademanee et al. 1987	2 leads	29 (59%)
Langer et al.,1989	1 lead	89 (66%)
Romeo et al. 1992	2 leads	76 (100%)
Amanullah & Lindvall, 1993	2 leads	42 (98%)
Bugiardini et al., 1995	2 leads	96 (94%)
Klootwijk et al., 1997	12 leads	88 (77%)
Klootwijk et al., 1998	12 leads	68/332 (21%)
Goodman et al. 2000	3 leads	87/231 (37%)

In reviewing table 5 it is not clear that the use of all 12 ECG leads improved ischemia detection compared to using only one or two ECG leads. For example, a number of studies reported that over 90% of their sample experienced ischemia despite using only two ECG leads (Amanullah & Lindvall, 1993; Bugiardini et al., 1995; Romeo et al., 1992), while Klootwijk et al., (1997) who used 12-lead ECG monitoring, reported that 21% of their sample experienced ischemia. This is perplexing because there is evidence to show that 12-lead ECG monitoring is more sensitive than one or even three lead ECG monitoring (Drew et al., 1998a; Klootwijk et al., 1997). One possible explanation for these wide variations may have been that false positive ST segment changes, which can occur in as many as 40% of patients, may not have been eliminated during the ECG analysis phase (Drew et al., 1998b). For example, the most reliable way to eliminate false-positive ST changes should include assessment of both the ST trend for abrupt ST changes, which often indicates false-positive ST segment changes, and by also printing out and assessing individual ECGs (Drew et al., 1998b; Klootwijk et al., 1997). Unfortunately, only the two studies by Klootwijk et al. (1998; 1997) addressed

eliminating false-positive ST changes. Therefore, it is possible that in many of these studies ischemia was diagnosed when there was none; hence, ischemia may have been over-reported.

One could argue that the reported frequency variations in these studies might have occurred because there was a long time delay from CCU admission to the initiation of ECG ST segment monitoring. This could be important since studies show that recurrent ischemia occurs most frequently during the first 15 to 24 hours of hospitalization (Braunwald, 1989; Klootwijk et al., 1997). Therefore, the reported rate of ischemia might be highest in studies with little or no time delay from CCU admission to initiation of ST monitoring, and lowest in the studies when there was a delay from CCU admission to initiation of ECG ST segment monitoring. In addition, it might also be important to consider the length of time that ST segment monitoring was maintained since ischemia may have been missed if the monitoring time was less than 24 hours, which may have resulted in a lower rate of ischemia. Table 6 illustrates these two points.

Table 6. Illustrates the time from CCU admission to initiation of ST segment monitoring, length of monitoring time, and the reported frequency of ischemia.

Investigator(s)	Time from CCU Admission to Initiation of ST Monitoring	Mean Monitoring Time (hours)	Frequency of Ischemia
Gottlieb et al., 1986	NR	48	53%
Nademanee et al., 1987	NR	24	59%
Langer et al., 1989	6.5 hours (mean)	24	66%
Romeo et al., 1992	$\leq$ 12 hours	48	100%
Amanullah & Lindvall, 1993	Within 24 hours	72	98%
Bugiardini et al., 1995	8 hours (mean)	24	94%
Klootwijk et al., 1997	NR	44	77%
Klootwijk et al., 1998	$\leq$ 1 hour	30	21%
Goodman et al., 2000	NR	64	37%

NR = not reported

Reviewing table 6 shows that the frequency variations cannot be entirely explained by the time from CCU admission to initiation of ECG ST segment monitoring, or the length of time that ECG ST segment monitoring was maintained. Unfortunately, the time from CCU admission to initiation of ST monitoring was not reported in a number of the studies; thus, how this factor may have influenced the reported frequency of ischemia cannot be determined. Interestingly, despite having the shortest time delay from CCU admission of start of ST monitoring Klootwijk et al (1998) reported the lowest rate of ischemia among all of the studies.

In summary, no single factor can be attributed as the cause of the frequency variations among these studies. Rather, it appears as though there are multiple factors responsible. However, it is too simplistic to just dismiss the findings from these studies and assume the researchers under- or over-reported ischemia. An important way to determine the

validity of ST changes during continuous ECG monitoring would be to determine if the prognosis differed among the patients who had ST changes compared to the patients who did not have ST changes. Unfortunately, a statistical comparison (i.e., patients with ST changes versus patients without ST changes) cannot be made in several of these studies since there is an insufficient number of subjects who did not have ST changes (Amanullah & Lindvall, 1993; Bugiardini et al., 1995; Romeo et al., 1992). Thus, among these studies there cannot be absolute certainly about whether the ST changes observed in these patients were truly ischemia. However, despite the fact that no comparison could be made between patients with and without ST changes, these studies show that the duration of ST changes, which are predominantly asymptomatic, are significantly correlated with an adverse outcome (Amanullah & Lindvall, 1993; Bugiardini et al., 1995; Romeo et al., 1992). These findings support the use of continuous ECG ST segment monitoring for identifying a subgroup of unstable angina patients at risk for adverse outcomes.

The available data comparing patients with and without ST changes show that ST changes detected with continuous ST segment monitoring are associated with an adverse in-hospital outcome (Klootwijk et al., 1998; Klootwijk et al., 1997). In addition, patients who exhibit ST changes during hospitalization for unstable angina are more likely to experience MI or death following discharge (Table 7).

Table 7. Comparison of studies that assessed long-term outcomes (i.e., MI or death) of unstable angina patients who experienced ST changes during hospitalization for unstable angina.

		Complications			
Investigators	**N**	**- Ischemia**	**+ Ischemia**	**P value**	**Odds Ratio**
Gottlieb et al., 1986; 1987					
30 day follow-up	70	4/33 (12%)	16/37 (43%)	< 0.01	5.5
2 year follow-up	70	6/33 (18%)	21/37 (57%)	<0.001	5.9
Nademanee et al., 1987					
6 month follow-up	49	1/20 (5%)	5/29 (17%)	< 0.001	3.9
Goodman et al., 2000					
1 year follow-up	231	12/144 (8%)	16/87 (18%)	<0.05	0.4

These findings indicate that there is a strong relationship between ST deviation, detected with continuous ECG monitoring, and poor patient outcomes. Therefore, continuous monitoring of the ECG for ST segment changes appears to be an important index for identifying a subgroup of patients who may benefit from more aggressive therapies to abolish recurrent ischemia. Conversely, the absence of ST segment changes during continuous ECG ST segment monitoring identifies patients at low risk who may benefit form early hospital discharge.

In summary, patients who experience myocardial ischemia, which is mostly asymptomatic, are at increased risk for major in-hospital complications. Importantly, the risk for major cardiac complications remains substantial for many months after discharge from the hospital. Therefore, it is reasonable to conclude that ST segment changes detected with ST segment monitoring are clinically important, which indicates that this data could be utilized by clinicians when deciding upon treatment options for patients diagnosed with unstable angina.

Gaps in the literature: A great deal of research has been generated in the unstable angina patient population using ST segment monitoring to detect ischemia. However, in the majority of these studies a strict inclusion criteria was used (i.e., unstable angina and ECG changes) and in nearly all of these studies the patients were treated in the setting of the CCU. Thus, the prevalence and characteristics of ischemia in other hospital settings (i.e., telemetry unit) is unknown. The telemetry unit setting is important in today's health care system because angina patients receive primary treatment in this hospital setting rather than the CCU. Thus, many of the patients included in the above literature review are now treated in the telemetry unit setting.

There is ample evidence to indicate the value of ST segment monitoring for detection of ischemia in unstable angina patients. However, there have been no studies conducted to determine if ST segment ECG data could have a significant impact in clinical practice, thus improving patient outcomes. An experimental study design to determine if ST segment monitoring ECG data could affect patient outcomes would be ideal. The major advantage of an experimental study design over observational studies is the strength of casual inference is greater, and experimental study designs are best for controlling confounding variables (Hulley, Feigal, Martin, & Cummings, 1988). Future studies should assess if ST segment ECG data alone could influence clinical decision making and thus patient outcomes.

ST Segment Monitoring Following Acute Myocardial Infarction

The use of thrombolytics or primary PTCA for the treatment of acute MI has led to significant reductions in both short and long term morbidity and mortality (Collen et al., 1984; Gibbons et al., 1993; Grines et al., 1993; The GUSTO Investigators, 1993; The

TIMI Study Group, 1985). For the majority of acute MI patients treated with thrombolytics or PTCA/stent, complete reperfusion of the infarct-related artery occurs within minutes, or at least, hours following acute treatment. However, following this initial period of successful reperfusion, recurrent ischemia may occur in approximately one third of treated patients. Patients who experience recurrent ischemia following successful reperfusion have significantly higher rates of reinfarction, congestive heart failure, and death (Barbagelata et al., 1995; Betriu et al., 1998; Stone et al., 1995). In addition, these patients have longer hospital stays and thus, incur significantly higher hospital costs (Barbagelata et al., 1995; Stone et al., 1995). Therefore, the ability to identify, detect or predict patients at risk for recurrent ischemia could have a profound impact on treatment strategies in this subgroup of patients.

Recurrent ischemia in patients treated with thrombolytics may occur because the atherosclerotic lesion responsible for the acute event remains untreated within the coronary artery, and thus, is susceptible to vasospasm, platelet formation and occlusion (Ohman et al., 1989). The mechanism responsible for recurrent ischemia in patients treated with primary PTCA is similar to patients who have elective PTCA or stent i.e., intimal flap occlusion, vasospasm or thrombus formation. In either case, recurrent ischemia and or infarction may result. The table below summarizes several studies assessing the frequency of myocardial ischemia following successful treatment for acute MI.

Table 8. Summarizes the frequency of myocardial ischemia, measured using chest pain, in several studies assessing in-hospital myocardial ischemia following acute MI.

Investigators	Definition of Ischemia	N	Sex M/F	Frequency of Ischemia
Ellis et al., 1989	Chest pain > 20 min. & ECG changes.	174	139/35	41/174 (24%)
Stone et al., 1995	Chest pain > 20 min. & either ECG changes or pulmonary edema	395	Not Reported	76/395 (19%)
Barbagelata et al., 1995	Chest pain & ECG changes	1,233	963/270	226/1,233 (18%)
Betriu et al., 1998	Chest pain, or ECG changes, or pulmonary edema	40,848	30,560/ 10,288	8,131/40,848 (20%)

N= sample size; M = male F = female

A consistent finding illustrated in Table 8 is that the reported frequency of myocardial ischemia using chest pain as the primary indicator of ischemia occurs in approximate 20% of patients following acute MI. Additional findings from these studies include, that the reported median time to recurrent ischemia following thrombolytic therapy ranges from 1.5 days (Betriu et al., 1998) to 6 days (Ellis et al., 1989). There have been reported differences in the frequency and timing of recurrent ischemia depending upon the treatment strategy used to treat MI, i.e., thrombolytics versus primary PTCA. For example, Stone et al. (1995) found that the frequency of recurrent ischemia was significantly less in patients treated with primary PTCA versus thrombolytics (10.3% versus 28%; $p < 0.0001$). This same study reported that the majority of recurrent ischemic events following thrombolytics occurred during the first 2 days after admission, however, a significant proportion of patients continued to experience ischemia from day

3 to 7. In contrast, following primary PTCA, recurrent ischemia rarely occurred after the second day.

Finally, several of these studies showed that a significant proportion of patients who have recurrent ischemia following MI are more likely to experience reinfarction or death both during and following hospitalization compared to patients who do not have recurrent ischemia (Table 9).

Table 9. Rate of reinfarction or death comparing MI patients with recurrent myocardial ischemia to MI patients without recurrent ischemia.

		Complication Rate		
Investigators	**N**	**- Ischemia**	**+ Ischemia**	**P value**
Stone et al., 1995 **In-hospital**	395	(3.1%)	(27.6%)	<0.0001
Barbagelata et al., 1995 **In-hospital**	1,232	(4%)	(12%)	< 0.0001
Betriu et al., 1998 **In-hospital**	40,848	(6.3%)	(29.1%)	< 0.0001
30 day follow-up		(3.9%)	(29.1%)	< 0.0001

N= sample size

This summary table illustrates that recurrent ischemia following acute MI is associated with major cardiac complications, during both the early and late recovery periods. An important strength in all of these studies was that all were comprised of large sample sizes, in one case over 40,000 patients; thus, there was sufficient power to detect differences between the two groups. However, it is important to consider that in all of these studies, recurrent ischemia was measured using chest pain as the primary indicator of ischemia and confirmation of the diagnosis with an ECG was obtained only after a patient complained of this symptom. This is an important consideration since chest pain

is absent in the majority of recurrent ischemic events detected using continuous ST segment monitoring (Bonaduce et al., 1991; Currie et al., 1993; Drew et al., 1996).

On the other hand, acute MI patients can experience recurrent chest pain in the absence of ECG changes. For example, Betriu et al. (1998) in a large cohort of over 40,000 patients found that 20% of their sample had recurrent chest pain following acute MI. In over 50% of these patients, ECG changes did not accompany the symptom of chest pain. One possible explanation for this finding might be a time delay from the onset of the patient's chest pain to when the 12-lead ECG was obtained to confirm the diagnosis of ischemia. For example, there is often a time delay in this process because in most hospitals the nurse must retrieve a 12-lead ECG machine, bring the machine to the patient's bedside, apply the ECG electrodes, and then record the ECG. Moreover, nurses are likely to administer nitroglycerin to the patient prior to obtaining the 12-lead ECG. Therefore, it is likely that the ST segment changes indicative of ischemia may have disappeared not only because there was a time delay from the compliant of chest pain to when the ECG was obtained, but because the nitroglycerin may have established blood flow to the myocardium.

Thus, definitive diagnosis of recurrent ischemia in patients following acute MI is complex, in some instances it may be unrecognized and in others it cannot be confirmed. Because chest pain was the primary indicator of ischemia in all of these studies a significant subgroup of patients experiencing silent ischemia may have been missed. ST segment monitoring technology, which could capture ischemia in this subgroup of patients, may improve the detection of recurrent ischemia during the recovery period following acute MI. In addition, ST segment technology might prove useful in

deciphering non-cardiac chest pain in the subgroup of patients who experience chest pain but do not have accompanying ECG changes.

In reviewing the plethora of ST segment monitoring studies conducted in the acute MI patient population, it is clear that the focus of these studies has been at two distinct hospital periods; one during the initial hours after acute MI and the second period, several days following acute MI presentation (Tables 10 and 11).

Table 10. Summary of ST segment monitoring studies conducted during the early hospital phase of acute MI treatment.

Investigators	Monitoring Duration
Krucoff et al., 1986	48 hour
Dellborg et al., 1991	15 minutes to 8 hours
Dellborg et al., 1991	24 hours
Dellborg et al., 1991	24 hours
Kwon et al., 1991	10 hours
Krucoff et al., 1993	90 minutes
Dellborg et al., 1995	12 hours
Doevendans et al., 1995	90 minutes
Langer et al., 1995	18 hours
Drew et al., 1996	46 hours
Klootwijk et al., 1996	18 hours
Santoro et al., 1998	30 minutes

Table 11. Summary of ST segment monitoring studies conducted during the late hospital phase of acute MI treatment.

Investigators	Start Monitoring Prior to Hospital DC	Monitoring Duration
Bonaduce et al., 1991	mean 17 days after MI	24 hours
Petretta et al., 1992	mean 13 days after MI	22.8 hours
Chandra et al., 1993	mean 5 days after MI	Not reported
Silva et al., 1993	24 hours after MI until CCU discharge	4 days
Currie et al., 1993	6 days after MI	23 hours
Gill et al., 1996	5 to 7 days after MI	42 hours

The primary objective of ST segment monitoring studies conducted during the early hours after MI has been to determine the utility of ST segment monitoring for prediction

of coronary vessel patency, rather than transient episodes of ischemia, following thrombolytic therapy. The methodology used in these studies included initiating ST segment monitoring prior to thrombolysis and then maintaining ST monitoring for minutes to hours following treatment. These studies indicate that patients who have successful reperfusion following thrombolytic therapy demonstrate complete and rapid ST segment recovery. On the other hand, unsuccessful reperfusion, despite the administration of thrombolytics, is characterized by persistent ST segment deviation. A significant proportion of this latter subgroup of patients experience death and reinfarction compared to patients in whom reperfusion of the infarct related artery is achieved.

Several studies have assessed the frequency and consequences of ischemia during the recuperation period measured several days following acute MI. This is an important time period of recovery because patients are engaged in activities that may increase heart rate, which may in turn lead to demand-related ischemia. If ischemia is diagnosed during this recuperation period, it might be possible to provide treatment for these patients to eliminate on-going ischemia. Table 12 summarizes the results of these studies.

Table 12. Summary of the frequency of ischemia among ST segment monitoring studies conducted during the late hospital phase (days) following acute MI.

Investigators	N	Age (mean)	Sex M/F	Frequency of Ischemia
Bonaduce et al., 1991	178	54	164/14	25/178 (14%)
Petretta et al., 1992	270	59.7	214/56	64/270 (24%)
Chandra et al., 1993	52	60	39/13	14/52 (27%)
Silva et al., 1993	453	55	396/57	35/453 (8%)
Currie et al., 1993	201	58	152/51	29/201(14%)
Gill et al., 1996	406	61	315/91	95/406 (23%)

N = sample size; M = male F = female

In reviewing these studies, it is clear that recurrent ischemia is not uncommon days after acute MI. Importantly, these studies show that patients who experience ischemia

are at significant risk of death and MI at both short-term and long-term follow-up periods. In addition, ECG changes are often the only indication of ischemia since chest pain does not occur in the majority of patients (Bonaduce et al., 1991; Currie et al., 1993). Therefore, ischemia remains a threat throughout hospitalization for acute MI, even after apparent successful reperfusion.

Several limitations should be addressed with regards to these studies. First, many of these studies excluded patients over the age of 70 years, thus, the samples were relatively young (mean age 59 years), which means these results should be applied to older MI patients with caution. In most of these studies, the treatment strategy (thrombolysis versus primary PTCA) for acute MI was not stated; thus, it cannot be determined if there are differences in the rate of ischemia when either thrombolysis or primary PTCA is used to treat MI. These studies did not determine if ischemia corresponded to activity level, which might be an important potential mechanism for ischemia during acute MI recuperation. If activity, which increases heart rate, triggers ischemia, then treatment strategies to lower heart rate can be initiated to abolish on-going ischemia prior to a patient's discharge from the hospital. Finally, in the majority of these studies, ST segment monitoring was initiated an average of 8 days following acute MI (range 5 to 17 days). The time period of hospitalization in these studies is considerably longer than the current average length of hospital stay, which is 6 days (Every et al., 1996). Therefore, these studies may not be applicable to the current standard of patient care, which is early transfer from the CCU to the telemetry unit followed by early discharge home. It is possible that the frequency of ischemia may be greater under the current health care

trajectory. However, the frequency and consequences, if any, of ischemia in this ever shortening recovery phase should be examined before any conclusion can be made.

Summary

Recurrent ischemia following successful reperfusion of the infarct related artery occurs in approximately one-third of patients during the recovery period following acute MI. In this patient group, the presence of chest pain alone predicts patients who are more likely to experience both death and reinfarction. However, studies that have utilized ST segment monitoring to detect ischemia, show that the vast majority of patients do not experience chest pain during ECG-detected ischemia. This would indicate the detection of ischemia could be improved using ST segment monitoring technology.

Gaps in the literature: To date, nearly all of the ST segment monitoring studies have assessed the use of this technology in acute MI patients who have received thrombolytic therapy; thus, ischemia following primary PTCA is largely unknown. This is an important assessment to make because this treatment option is being utilized more often as a primary treatment strategy for acute MI.

Because the focus of ST segment monitoring research has been at the extreme ends of acute MI recovery, the frequency, mechanisms and consequences of ischemia during the intermediate hospital phase (i.e., transfer from the CCU to the telemetry unit) is unknown. This might be an important time period because, in general, this is when patients engage in their first activity following acute MI. In addition, a re-assessment of ischemia during the recovery period following acute MI is indicated because the current hospital length of stay has been shortened considerably compared to the studies reviewed in this paper.

Summary/Conclusions

Myocardial ischemia represents an important pathophysiological process for patients diagnosed with acute coronary syndromes, and its presence is associated with serious consequences that include MI and death. The goal of treatment in these patients, both interventional (i.e., PTCA and/or stent) and pharmacological, is to restore and maintain coronary reperfusion. Therefore, a key assessment following treatment is monitoring the perfusion status of the myocardium. Electrocardiographic monitoring of the ST segment is an easy and non-invasive method that has been shown to be more reliable than chest pain alone for detecting episodes of ischemia.

This review presents the application of ST segment monitoring for detecting ischemia for patients with acute coronary syndromes; specifically, following PTCA and/or stent, in unstable angina patients, and in patients treated for acute MI. From these studies it has been shown that recurrent ischemia is not an uncommon problem in patients with acute coronary syndromes, with an increased incidence in patients with unstable angina compared to patients with acute MI. In addition, ischemia and reocclusion remain important consequences following interventional coronary artery procedures (i.e., PTCA and/or stent). In all of these patients, ST segment monitoring has been shown to provide not only an early warning of ischemia, but more importantly, in the vast majority of patients, ECG ST segment changes are often the only indication of ischemia.

As ST segment monitoring research progresses important considerations for future development of the science should be considered. Because the majority of ST segment monitoring studies have assessed ischemia following PTCA, the frequency, characteristics and consequences of ischemia following stent placement needs to be

addressed. Stents are utilized in angina and acute MI patient populations; thus, research regarding ischemia in each of these patient populations should be addressed.

To date, the focus of ST segment monitoring studies has primarily been descriptive; thus, the value of ST segment monitoring information as a tool used in clinical practice for decision making has not been established. This is an important area that requires further study. It is critical that this area of study address both nursing and physician decision making since each of these disciplines will be involved in the process of ischemia monitoring.

Because the vast majority of ST segment monitoring studies have been conducted in the CCU setting, the value of this technology in other hospital settings where patients with acute coronary syndromes are treated is not known. The telemetry unit setting is a hospital environment that should be included in future studies, primarily because the current standard of patient care has shifted from the CCU to the telemetry unit. For example, the telemetry unit setting, rather than the CCU, is now the primary recovery site for PTCA, stent, and unstable angina patients. In addition, acute MI patients are transferred to the telemetry unit at an ever-increasing pace, often 24 hours following acute MI. Thus, many of the patients included in the studies reviewed in this paper are now treated in the telemetry unit setting rather than the CCU. Because ST segment monitoring is not available in most telemetry units, it is likely that the majority of ischemic episodes in this hospital environment will go unrecognized, by both patients and clinicians. Therefore, it would seem appropriate to determine the value of ST segment monitoring in the telemetry unit setting.

Finally, while the focus of this paper has been a discussion of the value of ST segment monitoring for detecting ischemia, it is important to emphasize that this technology could also be used to triage patients for early discharge either home or from the CCU if ST segment changes were not noted during the monitoring period. Thus, this non-invasive technology offers important advantages to improve patient care.

Validity and Reliability of ECG Data

Measuring ST Segment Deviation Indicative of Myocardial Ischemia

Myocardial ischemia is diagnosed using the ECG by measuring the amount of ST segment deviation (i.e., elevation or depression) during ischemia. Although it is possible to measure ST segment deviation using visual techniques, there are important limitations that must be considered. First, there is a high degree of interrater variability (Blackburn, Blomqvist, & Freiman, 1968; Segall, 1960). Second, the human eye may not be able to detect subtle ischemic ST changes (Krucoff et al., 1987; Pelter, Adams, & Drew, 1997). Third, an extensive amount of time is required to measure and interpret ST segment information, which in clinical practice could lead to delays in treatment (Caralis et al., 1990). Finally, in the telemetry unit setting it is unrealistic for a monitor "watcher," who is typically solely responsible for assessing the ECG rhythm in all of the patients admitted to the unit, to observe ST segment changes using visual techniques only. Fortunately, computer-assisted ECG ST segment monitoring technology has become available in clinical practice, which may lessen or even eliminate the limitations of human measurement. For example, computer measurements are free of human bias, computerized measurement can measure ST segment deviation to a precision of 10 μV, whereas humans can only detect ST changes of 50 μV or more, and computer assisted ST

measurements are immediately available for real-time analysis, which is ideal for clinical decision making. Hence, while it is possible to visually measure ST segment deviation, computer-assisted ST segment measurements may more desirable than human measurements because they are less subject to bias, are more precise and are immediately available to clinicians.

Normally, the ST segment is isoelectric, meaning the ST segment is neither above nor below a stable reference point. Typically, the PR segment serves as the isoelectric reference point from which to measure ST segment deviation. ST segment deviation is measured by the number of microvolts (μV) the ST segment is deviated (i.e., elevated or depressed) from the PR segment measured milliseconds (msec) past the J-point (Figure 11).

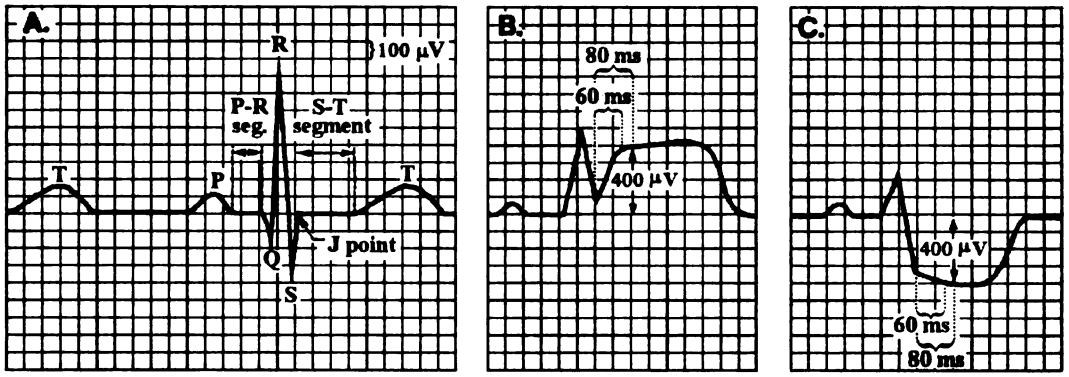


Figure 11. These three panels illustrate the measurement points used to diagnose myocardial ischemia using the ECG. (A) A normal ECG complex, with an isoelectric ST segment. Typically, the PR segment serves as the isoelectric reference point from which to measure ST segment deviation. ST segment deviation is measured from the J-point, which marks the end of QRS complex and the beginning of the ST segment, at 60 or 80 milliseconds (msec) past the J-point. When the ECG instrument is programmed with the standard amplitude settings, 100μV equals one small box (1mm) on the ECG paper as shown in panel A. The 100 μV measurement value is illustrated. (B) Illustrates ST segment elevation of 400 μV, measured 80 msec past the J-point. The 60 msec measurement point is also illustrated. (C) Illustrates ST segment depression of 400 mV, measured 80 msec past the J-point. The 60 msec measurement point is also illustrated. *Source:* modified from: (Tisdale & Drew, 1993).

The standard diagnostic criteria for ischemia diagnosis is 100 μV or more of ST segment deviation (i.e., depression or elevation), 60 to 80 msec past the J-point, lasting for greater that 60 seconds (Pepine, Singh, Gibson, & Kent, 1987). In a review of the literature surrounding this topic, it is clear that the number of milliseconds (msec) past the J-point from which to measure ST segment deviation (i.e., 60 versus 80 msec) has not been unambiguously established. For example, some investigators utilize the 60 msec measurement point (Krucoff, 1988; Larsson et al., 1992; Lundin et al., 1992; Mizutani et al., 1990) while others use the 80 msec point (Drew et al., 1996; Drew & Tisdale, 1993; Foley et al., 1993; Gottlieb et al., 1986; Langer et al., 1995; Nademanee et al., 1987; Wilcox et al., 1990). Some researchers favor the 60 msec measurement point as a more

specific diagnostic criteria for ischemia diagnosis compared to the 80 msec measurement, because the 60 msec measurement point is less likely to be measuring the upslope of the T-wave during periods of rapid heart rate (Figure 12) (Krucoff, 1988; Okin, Bergman, & Kligfield, 1991).

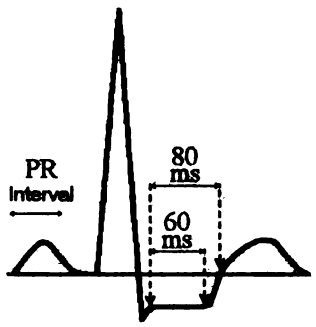


Figure 12. This figure illustrates how the J-point plus 60 millisecond (msec) measurement point may be more sensitive for detection of ischemic ST segment changes, compared to the J-point plus 80 msec measurement point. The 60 msec measurement point would be measured as an ischemic ST change (i.e., ST segment depression of greater than 100 μV). Whereas, the 80 msec measurement point would not be measured as an ischemic ST change (i.e., no ST segment change greater than 100 μV), rather the J-point plus 80 msec measurement point is "isoelectric" to the PR segment.

It is important to consider that while the 60 msec measurement point may be a more sensitive measurement point (i.e., identifies a large proportion of the patients who truly have ischemia as having ischemia), this measurement point is less specific for ischemia diagnosis. In other words, more false-positive ST changes will be detected; thus, patients who do not truly have ischemia may be diagnosed with ischemia. This could lead to over-treatment of patients who do not truly have ischemia, which may include unnecessary tests, diagnostic procedures, and pharmacological agents, all of which add risk to patients, delay hospital discharge, and increase hospital costs.

Selection of a measurement point past the J-point from which to measure ischemia (i.e., 60 msec versus 80 msec) should include consideration of the patient population being evaluated with computer-assisted ECG ST segment monitoring. For example, the 60 msec measurement point may be more appropriate if the goal is to capture the greatest proportion of patients who truly have ischemia. This would be desirable in; 1) patients with unstable angina, where the goal is to prevent acute MI, 2) in patients following PTCA and/or stent who have coronary dissection, since these patients may be at higher risk for abrupt reocclusion, or 3) in patients recovery from acute MI who have recurrent angina following successful reperfusion. On the other hand, the more specific measurement point of 80 msec may be more appropriate in patients with CAD who; 1) have slow heart rates (i.e., patients taking beta-blockers), 2) patients with uncomplicated PTCA and/or stent procedures, or 3) in patients with uncomplicated acute MI. Therefore, when deciding upon a measurement point past the J-point from which to measure myocardial ischemia, careful consideration of the patient population being evaluated is indicated.

Assessing ST Segment Changes Using "Delta ST"

A "normal" ST segment is considered to be isoelectric (i.e., the ST segment is neither above nor below the PR reference point), and ST segment deviation of 100 μV above or below the isoelectric point indicates the presence of ischemia. However, there are a number of chronic conditions, including left ventricular hypertrophy (LVH), right- or left bundle branch block, or digitalis therapy that can cause non-ischemic ST segment deviation. In other words, these patients will exhibit greater than 100 μV of ST segment

deviation (i.e., depression or elevation) at baseline, which is considered to be non-ischemic in nature (Figure 13).

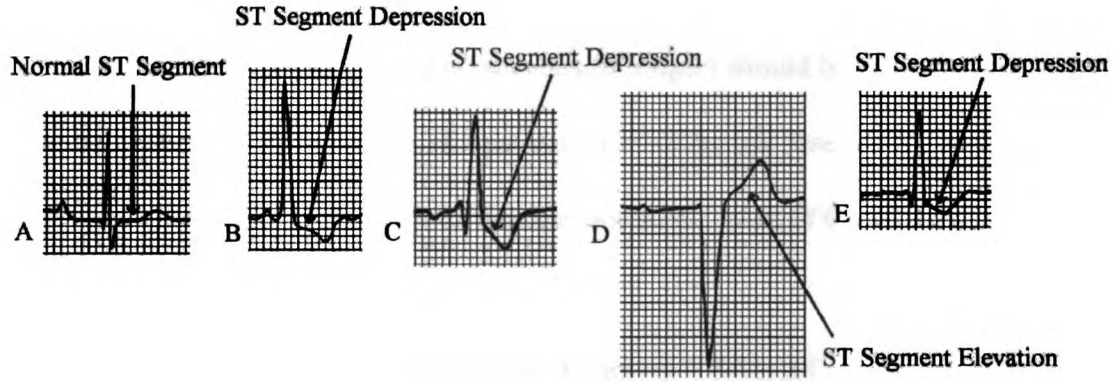


Figure 13. Illustration of various conditions that can cause non-ischemic ST segment deviation. A) Normal isoelectric ST segment, B) Left ventricular hypertrophy with ST segment "strain" pattern, C) Right bundle branch block, D) Left bundle branch block, E) Effect of digitalis therapy.

Baseline ST segment deviation is common in patients with unstable angina. For example, one study reports that as many as 63% (100/159) of patients admitted to the CCU for treatment of unstable angina or elective PTCA, who were not experiencing an acute MI, exhibited chronic non-ischemic ST segment deviation of more than 100 mV (average ST segment deviation 211 $\pm$ 142 mV) (Drew et al., 1998b). Hence, it is not uncommon for patients with unstable angina to exhibit non-ischemic ST segment deviation on the ECG.

In order to diagnose transient myocardial ischemia in patients with acute coronary syndromes, it is essential to establish each individual patient's baseline ST level at a time when the patient is not experiencing acute ischemia. In general, in patients not experiencing acute MI, the baseline ST level can be established when ST segment

monitoring is initiated. When an ST segment change occurs, the patient's baseline ST level should be subtracted from the new ST level in order to obtain an ST "change" score, or "delta" ST measurement. Any ST segment deviation that occurs from the patient's established baseline ST level that exceeds the criteria for ischemia (i.e., greater than 100 μV of ST segment deviation, lasting 60 seconds or longer) should be evaluated for myocardial ischemia. For instance, if a patient's non-ischemic baseline ST level is - 200 μV, and the ST level shifts upward to the isoelectric level of 0 μV, the delta ST value calculated would be:

$$-200\ \mu V\ (\text{baseline}) - 0\ \mu V\ (\text{new ST level}) = \mathbf{delta\ ST\ +200\ \mu V}$$

In this scenario, the patient's non-ischemic baseline level shifted from a non-ischemic ST segment depression level to an isoelectric, or normal-looking, ST segment, which exceeds the criteria for ischemia diagnosis. Hence, an ischemic event may produce a normal-looking ST segment in patients who have baseline ST segment deviation. This example, illustrates "pseudo-normalization" of the ST segment, and represents an ischemic ST change which could only be detected using the delta ST measurement calculation.

Limitations of ECG ST Segment Monitoring

Acute ST segment deviation is a reliable indicator of myocardial ischemia in patients diagnosed with acute coronary syndromes. However, both false positive and false negative ST segment changes must be considered in order to accurately diagnose transient myocardial ischemia in patients with acute coronary syndromes. For example, a number of non-ischemic conditions can cause ST segment deviation, and result in false-positive ST segment changes. In contrast, patients may have false-negative ST changes.

In other words, during ischemia the ST segment becomes normal-looking, or isoelectric, in patients who have baseline ST segment depression that is considered to be non-ischemic. Therefore, careful interpretation of ST segment changes during continuous ECG ST segment monitoring is essential in order to minimize unnecessary treatment for ischemia when none exists, versus treatment when truly indicated.

False Positive ST Segment Changes

In general, either technical or patient specific conditions cause false-positive ST changes. Therefore, the following portion of this paper will address the technical and patient specific factors that result in false-positive ST segment changes.

False-Positive ST Changes Caused by Technical Problems

Poor skin electrode contact. Because ST segment changes indicative of myocardial ischemia can be small, as little as 100 μV of ST segment deviation, it is imperative that a "clean" ECG signal is recorded. Noise, or artifact, can cause false-positive ST segment changes, and in some instances, make it technically impossible to interpret the ECG altogether (Figure 14).

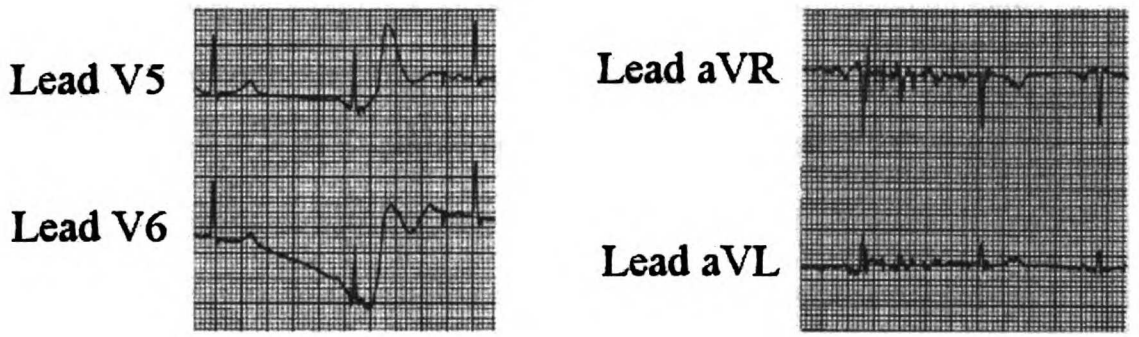


Figure 14. The panel on the left illustrates false-positive ST changes created by patients movement in leads V5 & V6. The panel on the right illustrates artifact in leads aVR and aVL caused by poor skin electrode contact. Source: (Wagner, 1994).

The most common cause of artifact is poor skin electrode contact. This can be avoided or substantially reduced by administering a careful and thorough skin preparation to the patient prior to the application of skin electrodes. This should include shaving excess hair from the body sites where electrodes are placed and cleaning the skin surface of oils, skin debris or moisture with an alcohol prep pad.

Inaccurate Lead Placement. The 12-lead ECG criteria used to diagnose the cause, location and severity of myocardial ischemia are based on ECG changes that are observed in specific leads. However, it is important to consider that these ECG criteria can only be applied when certainty exist about the exact location of the leads on a patient's body. During continuous ECG ST segment monitoring it is imperative that the ECG leads are maintained at the exact location on the chest throughout the monitoring period; moving any one electrode to a different site on the torso can alter the ST segment, causing false-positive ST changes that could be interpreted as ischemia when none exists. One way to avoid placing electrodes at a different site on the chest during monitoring is to mark the electrodes sites with indelible ink prior to initiating ECG ST segment

monitoring, so that the electrodes can be replaced to the exact location if they are removed or become detached from the patient's chest.

Patient Specific Conditions that Cause False-Positive ST Changes

Body Position changes. In the past, 12-lead ECG's obtained in hospitalized patients for the diagnosis of ischemia were recorded with patients assuming a supine position in their bed. Hence, the ECG was recorded with the patient in a stable and consistent body position. However, because 12-lead ECG monitoring for ischemia detection can now be performed continuously, with patients assuming a variety of body positions, the diagnosis of ischemia has become more difficult because body position changes are a common source of false-positive ST segment changes. One study, which maintained continuous 12-lead ST segment monitoring an average of 41 hours in the coronary care unit (CCU), showed that body position changes were the most frequent cause of false-positive ST segment changes, accounting for one-third of the false positive ST changes (Drew et al., 1998b). This same study reported that false-positive ST changes due to a change of body position were more common in women than in men (48% versus 28%; $p < .01$). Another study showed that false-positive ST segment changes due to body position changes were more likely to occur when patients assumed a left side-lying position compared to a right side-lying position (Adams & Drew, 1997). Hence, during continuous 12-lead ST segment monitoring body position changes can produce false-positive ST segment changes that could be interpreted as ischemia. Women appear to be more vulnerable to false-positive ST changes than men, and the frequency of such false-positive these ST changes increases when patients assume a left-side lying position.

Several clues and recommendations can assist clinicians in determining false-positive ST segment changes due to body position changes. First, when ST segment changes are identified, the QRS complex should also be assessed for changes. This is because the QRS complex tends to change along with ST segment changes, with the QRS complex changing amplitude, or even changing polarity [Figure 15] (Adams & Drew, 1997; Drew et al., 1998b). Additionally, the onset and off-set of QRS changes caused by positional changes are often abrupt, occurring over one to two cardiac cycles, whereas, the onset and off-set of ischemia is more gradual (Klootwijk et al., 1997). These findings can help identify ST segment changes due to altered body position(s).

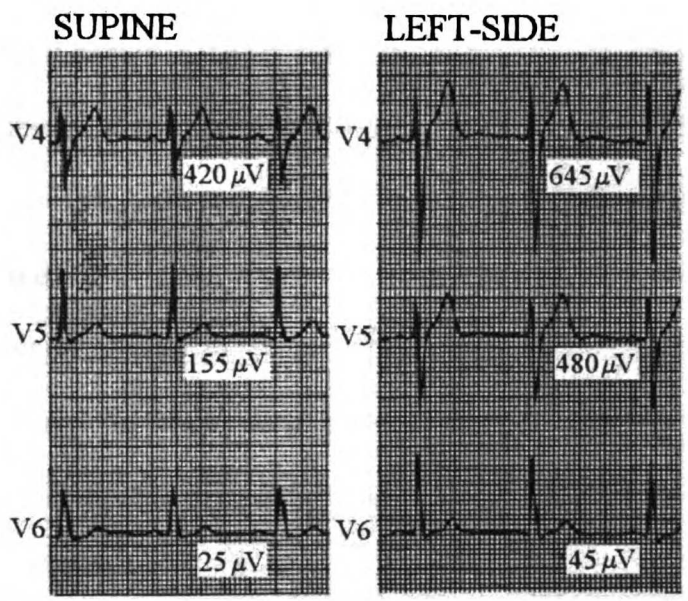


Figure 15. Illustrates both ST segment and QRS changes due to body position changes. The left panel shows computer generated μV values at the J-point plus 80 msec measurement point in leads V4 to V6 while the patient was supine (flat). The right panel shows the ST segment and QRS changes that occurred when a patient was turned to the left side lying position. Specifically, ST segment elevation occurred, as much as 325 μV in lead V5, and in this same lead the QRS complex changed from a predominantly upright complex to a predominantly downward complex. In addition, the QRS complex became taller in the left side lying position compared to the supine (flat) position in leads V1 and V6. *Source:* (Drew et al., 1998b).

Another strategy is to determine the time of day when the ST segment changes occurred, and to determine if the patient was sleeping. Positional ST segment changes are likely to occur during the night and last several hours while patients are asleep on their side. Lastly, it is recommended that prior to initiating continuous 12-lead ECG ST segment monitoring that ECGs are obtained with the patient assuming various positions. These "template" ECGs can then be used to help determine which ST segment changes occur due to body position changes.

In the aforementioned studies, the primary body positions that were accounted for were right- and left-side lying positions, which was appropriate since these studies were conducted in CCU patients who were maintained on bed-rest. However, it is important to consider that patients treated in the telemetry unit setting also assume up-right body positions since these patients are allowed to ambulate. Therefore, telemetry unit patients should also have up-right body position ECGs recorded prior to initiating ECG ST segment monitoring.

Intermittent Bundle Branch Block, Arrhythmia or Ventricular Pacing. Transient conditions, such as right or left bundle branch block (BBB), arrhythmias, or ventricular pacing causes the ST segment to become distorted, often resulting in false-positive ST segment changes (Figure 16, 17, 18).

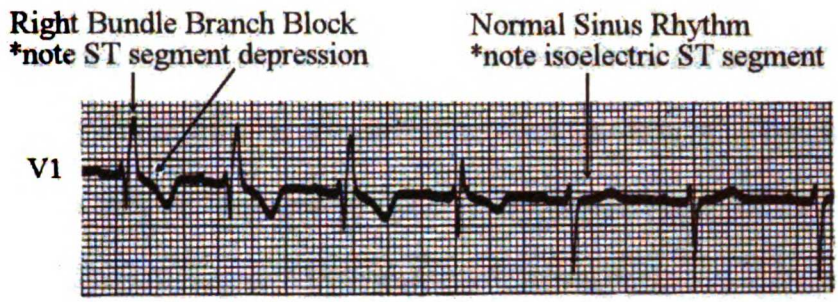


Figure 16. Illustrates how intermittent right BBB distorts the ST segment (arrows), causing false-positive ST segment changes. *Source*: edited from: (Wagner, 1994).

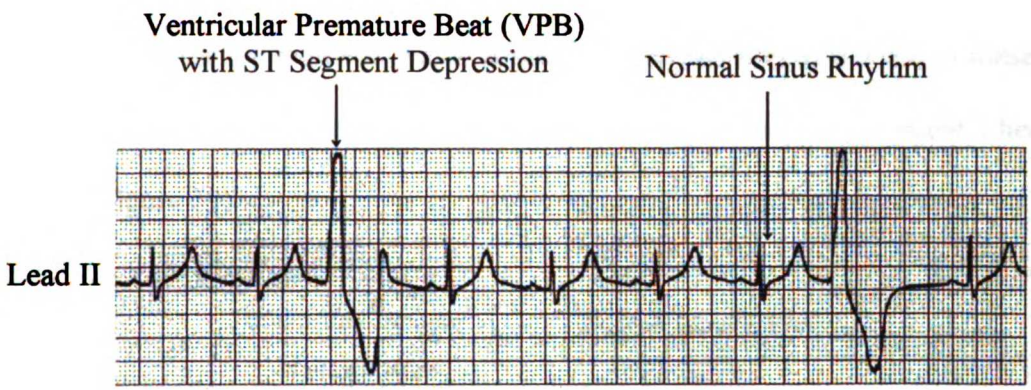


Figure 17. Illustrates how an arrhythmia, ventricular premature beats (VPB), causes intermittent ST segment changes, resulting in false-positive ST segment changes. *Source*: edited from: (Wagner, 1994).

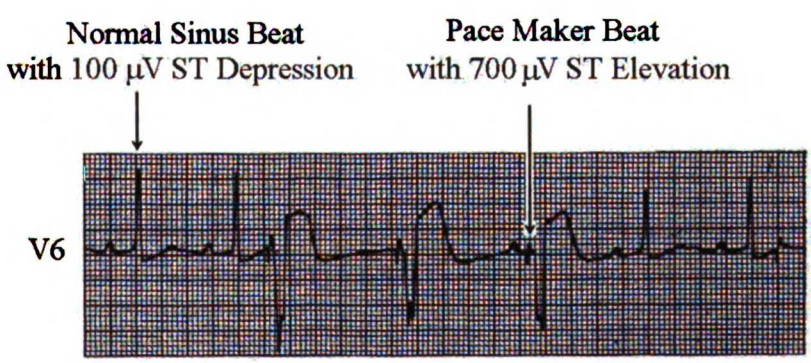


Figure 18. Illustrates normal sinus rhythm with intermittent pacemaker beats (arrow points to pacer spike). The paced beats have secondary repolarization abnormality, or ST segment deviation, causing false positive ST segment changes. *Source*: edited from: (Wagner, 1994).

It is important to consider that myocardial ischemia can be a substrate for ventricular arrhythmias, therefore, careful interpretation of the ECG for ischemic ST changes prior to the arrhythmia is necessary. If myocardial ischemia has been ruled out as the cause of the arrhythmia, then no treatment for ischemia is indicated; thus, the ST changes observed are likely to represent false-positive ST changes.

Permanent Left Bundle Branch Block, Ventricular Pacemaker, or Steeply Sloped ST Segments. Patients who have permanent left BBB, or those who require continuous ventricular pacing, are likely to experience frequent false-positive ST segment changes. This is because the ST segment, which is distorted permanently as a result of these conditions, is vulnerable to extreme measurement variations when the patient's heart rate changes (Figure 19).

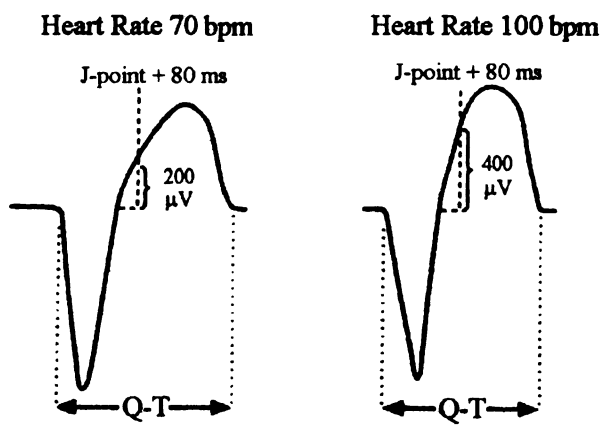


Figure 19. Illustrates false-positive ST segment changes due to heart rate changes in patients with permanent left bundle branch block (BBB). The left panel shows a QRS complex in lead V1 of a patient with left BBB, illustrating the typical secondary repolarization abnormality of the ST segment, which results in 200 μV of ST segment elevation, measured 80 msec past the J-point. The right panel shows the ST segment changes that occur when the patient's heart rate increased from 70 to 100 beats/minute, the QT interval shortened and the T-wave fused with the ST segment, changing the contour of the ST segment. As a result, the J-point plus 80 msec measurement point falls closer to the apex of the T-wave, measuring 400 μV of ST segment elevation. *Source:* (Drew et al., 1999a).

Because patients with permanent left BBB, or permanent ventricular pacemaker are susceptible to frequent false positive ST segment changes, it is recommended that ECG ST segment monitoring not be utilized in these patients (Drew et al., 1999a).

Patients with permanent right BBB, or patients with evolving ST patterns, as might be seen following acute MI, may also exhibit false-positive ST segment changes. These conditions produce a steeply sloping ST segment contour (Drew et al., 1999a). Similar to patients with left BBB, patients with steeply sloping ST segments are vulnerable to inaccurate ST segment measurement, during increased heart rates, resulting in false-positive ST segment changes (Figure 20).

One strategy that may lower the rate of false-positive ST changes in patients with steeply sloping ST segments, might be to use the J-point plus 60 msec measurement point, rather than the J-point plus 80 msec measurement point. This earlier measurement point is less susceptible to being obscured in the T-wave, compared to the 80 msec measurement point; thus, reducing the number of false positive ST segment changes. In addition, it is important to determine if the ST changes were associated with an increase in heart rate, this may indicate that the ST changes were the result of a change in the position of the measurement point within the ST segment, which would cause a false-positive ST segment changes.

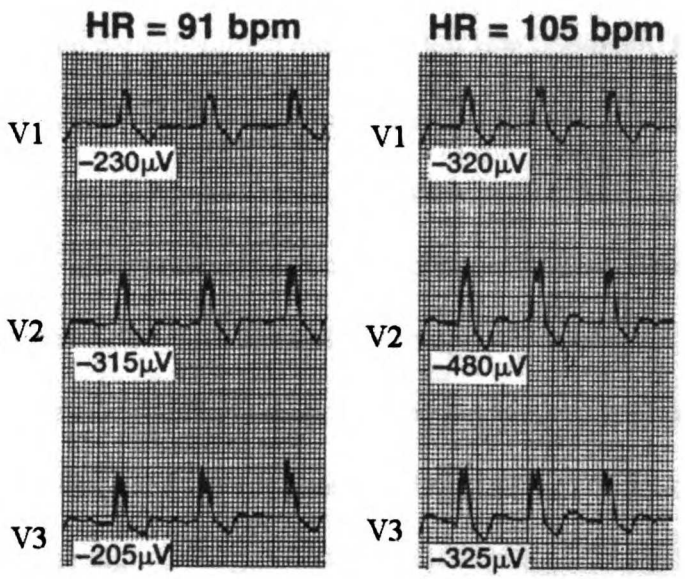


Figure 20. Illustrates false-positive ST segment changes caused by heart rate changes in a patient with permanent right bundle branch block (BBB). The left panel shows the computer generated ST segment measurements (ST depression) in leads V1 to V3, in a patient with right bundle branch block, during a heart rate of 91 beats/ minute. Although it is difficult to visualize with the human eye that more ST segment depression has occurred in the right panel, the computer generated μV measurements indicate that the ST segments have become more depressed (greater than 100 μV of ST segment depression) in both lead V2 and V3. Closer evaluation of these ST changes indicates that the changes are due to an increased heart rate (from 91 to 105 beats/minute), which caused the J-point plus 80 msec measurement point to fall closer to the apex of the T-wave. Source: (Drew et al., 1998b).

Sudden Increase in the QRS/ST Voltage. One final false-positive ST segment change described in the literature has been the occurrence of abrupt QRS/ST segment voltage changes (Figure 21).

There exists some uncertainty about the cause of these QRS and ST segment changes and whether they represent ischemia or not. For example, one hypothesis generated from observations in patients undergoing exercise testing, is that increased R-wave amplitude occurs due to acute dilatation of the left ventricle, as a result of myocardial ischemia (Brody, 1956). On the other hand, one study showed that R-wave amplitude changes

resulted from the left ventricle moving closer to the chest wall, measured with echocardiography, when patients turned onto their left side (Feldman, Borow, Neumann, Lang, & Childers, 1985). Thus, it is not clear if a sudden QRS/ST voltage change represents ischemia, or not. Because ischemia cannot be entirely ruled out in patients who exhibit these ECG changes, careful consideration of the patient's clinical findings during these episodes must be considered. For example, if the episode is accompanied by clinical findings such as shortness of breath or chest pain ischemia should be considered as the cause. On the other hand if these changes might be explained by body position changes (i.e., during the night lasting several hours), it is likely that these changes are non-ischemic. Thus, the patient's clinical scenario must be considered when interpreting these ECG findings.

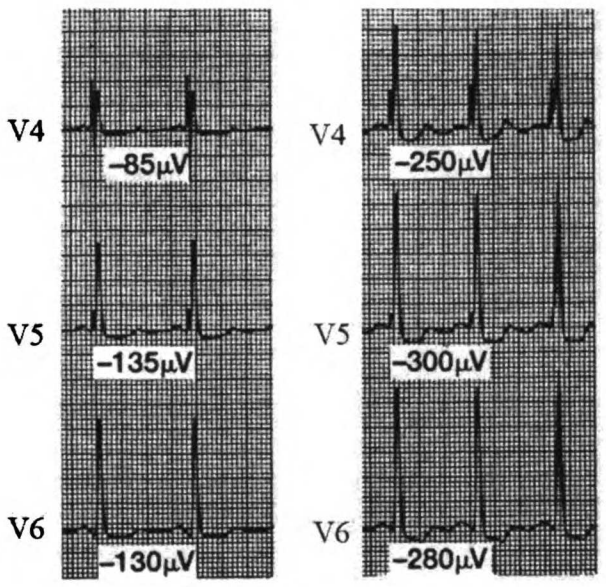


Figure 21. Illustrates what are considered to be false-positive ST segment changes that result from sudden QRS/ST voltage changes. The left panel shows the patient's baseline ECG ST segment mV values in leads V4 to V6. The right panel shows that a sudden increase in voltage of the QRS and ST segments causes ST segment changes that meet the criteria for ischemia (i.e., greater than 100 mV ST segment depression). Source: (Drew et al., 1998b).

False Negative ST Segment Changes

Transient myocardial ischemia may result in an isoelectric ST segment in patients who have baseline ST segment depression caused by either left ventricular hypertrophy (LVH), or medical therapy with digitalis. Ischemia in these patients results in "pseudo-normalization" of the ST segment, or false-negative ST segment changes, which could result in a failure to recognize ischemia (Figure 22).

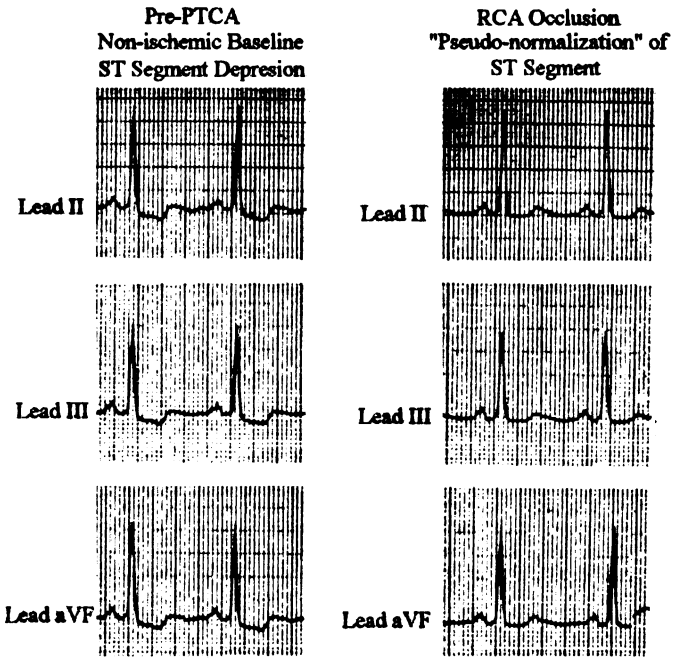


Figure 22. Illustrates pseudo-normalization of the ST segment in a patient with left ventricular hypertrophy. The left panel shows the typical non-ischemic baseline ST segment depression pattern, in the inferior leads II, III, and aVF, in a patient with left ventricular hypertrophy. The right panel shows pseudo-normalization of the ST segment during total occlusion of the right coronary artery at the time of percutaneous transluminal coronary angioplasty. Source: (Drew et al., 1998b).

In the scenario presented in Figure 22, pseudonormalization of the ST segment represents ischemia, whereas ST segment depression represents the patient's non-ischemic baseline ECG ST segment pattern. In the clinical setting, this could result in a

mis-diagnosis of ischemia because clinicians may interpret the ECG exhibiting pseudonormalization as non-ischemic, which would be a false-negative diagnosis, and the ECG with ST segment depression as ischemic, which would be a false-positive diagnosis.

The diagnosis of ischemia in these patients is complex, and can only be made by assessing the trend of the ST segments over time to determine if there is a change. For instance, if a patients non-ischemic ST level is ST segment depression and during the course of continuous ST segment monitoring there is transient pseudo-normalization of the ST segments, one must consider myocardial ischemia as a potential cause of the ST segment changes. On the other hand, if at the initiation of continuous ST segment monitoring the ST segments are isoelectric and then become depressed and remain depressed throughout the remainder of the monitoring period, one must consider that the patient was experiencing acute ischemia when ST segment monitoring was initiated. Finally, it would be helpful to determine, at the time ST segment monitoring was initiated, if the patient has been diagnosed with LVH (i.e., echocardiogram, or prior 12-lead ECG), or are taking digitalis, because pseudo-normalization in these patients may indicate ischemia.

Summary

In summary, while ST segment deviation is a reliable indicator of myocardial ischemia, there are several conditions that can produce false-positive or false-negative ST segment changes. It is possible to identify, and thus eliminate, many of these false-positive and false-negative ST segment changes in individual patients by carefully assessing the trend of the ST segments over time, and by assessing the patient's clinical situation at the time of the ST segment changes. Table 13 is a summary of false-positive

and false-negative ST segment changes that may occur during ST segment monitoring, and strategies that might be used to recognize and solve these problems.

In the present study, false positive ST changes will be minimized during the analysis of the ECG data by employing a standard protocol. For example, in order to limit false positive ST changes due to body position changes the research assistances in the parent study obtained template body position ECG's with patients assuming a supine, left, and right side lying positions. Any potential ischemic event ECG's were then compared to the template ECG's in order to ensure that the observed ST changes were not due to body position changes. In addition, all stored ECG were evaluated using a computer software program which allowed us to eliminate from the analysis any ECG's with a noisy signal, or ECG's demonstrating ST changes due to non-ischemic conditions (i.e., accelerated ventricular rhythm, intermitted ventricular pacer, or intermittent bundle branch block). This cleaned ECG data was then evaluated for ST changes (i.e., ST elevation or depression) indicative of ischemia, and computer generated μV values were used to determine if the ST changes exceeded 100 μV of ST deviation. Computer generated μV measurements are more precise than human measurements, and relevant to this analysis, eliminate human bias.

Table 13. Causes of False-Positive and False-Negative ST Segment Changes

Causes of False-Positive ST Segment Changes	**Solution**
1. Poor skin electrode contact	- Perform meticulous skin prep prior to initiating ST segment monitoring - Maintain skin electrode contact by replacing detached skin electrodes
2. Inaccurate lead placement	- Mark electrode sites with indelible ink prior to initiating ST monitoring so that electrodes will be replaced to the same location
3. Body position changes	- Obtain template ECG's with patients assuming supine, side lying (right and left) and up-right body positions, prior to initiating ST segment monitoring - Utilize template ECG's for comparing ECG likely to be due to body position changes i.e., assess QRS complex amplitude and direction
4. Intermittent bundle branch block, arrhythmia, or pacemaker	- Assess actual ECG to determine if ST changes are due to one of these intermittent conditions
5. Permanent left bundle branch block, or pacemaker	- Do not perform ST segment monitoring in these patients since frequent non-ischemic alarms will result
6. Steeply sloping ST segments	- Assess actual ECG to determine if ST segment changes are due to increased heart rate
6. Sudden QRS/ST voltage changes	- Assess patient's clinical situation since ischemia cannot be ruled out - Assess ST trend since non-ischemic QRS/ST changes occur abruptly, whereas ischemic changes are most likely to occur gradually over time
Cause of False-Negative ST Segment Changes	
1. Baseline ST segment abnormalities (e.g., left ventricular hypertrophy, digitalis therapy)	- Establish baseline ST segment pattern for each patient since it may not be isoelectric - Assess ST trend over time to determine if there is pseudo-normalization of the ST segment

Conclusions

Computer-assisted 12-lead ECG monitoring is the only non-invasive clinical test that can be maintained continuously and provide immediate information to identify, locate and estimate the severity of acute ischemia in patients with acute coronary syndromes. The value of this technology becomes even more evident, when one considers that well over three quarters of all ischemic episodes occur in the absence of classic anginal symptoms. Because of the dynamic and often unpredictable nature of myocardial ischemia in patients diagnosed with acute coronary syndromes it is necessary to monitor all 12 ECG leads. While sophisticated technology is available in clinical practice for ischemia detection, careful evaluation of ST segment changes is essential in order to avoid mis-diagnosing myocardial ischemia, which could lead to over-treatment for ischemia when none exists.

Methodology

Design/Methods

Research Design: This study was a secondary analysis utilizing an existing database of over 1,100 patients who were enrolled in a prospective clinical trial (parent study) conducted at the University of California at San Francisco (USCF). The parent study began data collection in January 1994, and ended data collection in April 2000. The primary goal of the parent study was a comparison of two 12-lead ECG monitoring methods, a standard 12-lead ECG method and an experimental 12-lead ECG method, in order to determine the value of the experimental method for detecting transient myocardial ischemia in hospitalized patients diagnosed with acute coronary syndromes. The parent study collected data in several hospital environments including the emergency department, CCU, adult cardiac catheterization laboratory and the cardiac telemetry unit. Two unique and important aspects that have not been addressed by the parent study include; (1) an independent assessment of myocardial ischemia in the cardiac telemetry unit, and (2) patient outcomes among this subgroup of patients measured both in hospital and following hospital discharge.

Description of Research Setting

Setting: The telemetry unit at UCSF, located on the tenth floor of the hospital, is comprised of 45-beds, 38 private rooms, and 7 semi-private rooms (i.e., 2 beds/room). The telemetry unit is staffed with; (1) registered nurses who provide primary patient care, (2) patient care assistants who aid the nursing staff with patient care, and (3) a monitor technician who is responsible for "watching" the ECG rhythm of all of the patients on the telemetry unit 24 hours/day at a central ECG station. The monitor technician is

responsible for reporting any ECG changes to the nursing staff. The nursing staff is then responsible for acting on this information, which may include independently initiating emergency medical procedures used to terminate lethal arrhythmias (i.e., defibrillation), notifying and organizing additional personnel needed during emergency procedures (i.e., pharmacist, additional nursing staff, respiratory therapy), communicating with the patient's physician, and then carrying out additional prescribed interventions. During the study period the nurse to patient ratio on the telemetry unit was 4:1 during a 12 hour day shift, and 5:1 during a 12 hour night shift.

Sample

Criteria for sample selection: Patients presenting to the telemetry unit for treatment of acute MI, angina (either stable or unstable), or following a catheter-based intervention, were approached as soon as possible after admission in order to determine if the patient was willing to participate in the study. Verbal assent was obtained, as approved by the Committee on Human Research (H6052-07035-08), in the patients who agreed to participate in the study. Continuous 12-lead ECG monitoring for ischemia detection was then initiated and maintained for as long as possible throughout the patient's admission to the telemetry unit.

Inclusion/Exclusion Criteria: The final analysis included only patients who had a definitive diagnosis of CAD. The diagnosis of CAD was based on; (1) documentation of prior MI using presence of Q-waves on the resting 12-lead ECG, (2) coronary angiogram demonstrating a $\geq$ 70% lesion in one or more coronary vessel(s), or (3) development of MI during hospitalization. Excluded from the analysis were patients with left bundle branch block (LBBB) or ventricular pacing rhythm, a decision based on the current ST

segment monitoring guidelines because these conditions distort the ST segment, making it difficult to reliably interpret the ECG ST segment data for ischemia (Drew et al., 1999a).

Data Collection Methods

***Collection of ECG** Data:* All patients were maintained on the routine two lead telemetry ECG monitoring system as per the protocol of the UCSF telemetry unit. While the telemetry unit ECG monitoring system is capable of monitoring two bipolar ECG leads, only one of these two leads is displayed for viewing at the central ECG monitoring station. The single ECG lead selected most often for viewing at the central ECG monitoring station was a modified chest lead (MCL_1), a unit standard adopted since this leads is the single best bipolar lead for diagnosing and distinguishing ventricular arrhythmias (Drew & Scheinman, 1991; Kindwall, Brown, & Josephson, 1988; Wellens, Bar, & Lie, 1978). The routine telemetry unit monitoring system was equipped with only arrhythmia detection software. Therefore, the parent study also initiated continuous 12-lead ECG ST segment monitoring for ischemia detection using a separate ECG device. Twelve-lead ST segment monitoring was initiated as soon as possible following a patient's admission to the telemetry unit and every attempt was made to maintain ST segment monitoring throughout the patient's entire telemetry unit admission. Because patients were ambulatory in the telemetry unit, the 12-lead ECG device was maintained on a portable wheel-based stand; thus, allowing patients the ability to ambulate throughout the unit while maintaining continuous 12-lead ECG ST segment monitoring.

In order to maintain continuous 12-lead ECG data, the parent study employed a total of four part time research nurses, and one full time project director who provided 24

hour, seven day per week clinical coverage. The research assistant responsible for clinical coverage provided in house coverage from 7am to 7pm Monday through Friday. This same research assistant was then available to the nursing staff by pager from 7pm to 7 am to assist with trouble-shooting problems over the telephone. The nursing staff received hands on instructions of how to operate the ECG device in both the clinical setting and as one component of at annual clinical review the staff was required to attend. In addition, the nursing staff had access to a trouble-shooting information sheet that was attached to the ECG device. Weekend coverage included two in-house visits, one in the morning, and one in the evening. In addition, the research assistant was available throughout the weekend by pager to assist the nursing staff to trouble shoot problems over the telephone. All of the research assistance received a one month standardized orientation program, which was administered by the project director, and included both classroom and "hands-on" clinical content. Classroom content included information about proper ECG monitoring techniques (i.e., thorough skin preparation, and proper application of ECG leads to the chest), and the research protocol (i.e., patient consent, initiating and maintaining ECG monitoring). The hands on clinical educational component took place in each of the four hospital environments where the ECG data was collected, and included exposure to a variety of patients (i.e., men, women, thin, obese, elderly, large breasted women, and men with hairy chests). Throughout the data collection period, the project director and the principal investigator ensured quality ECG data by performing random checks for correct lead placement, and assessing the quality of the ECG tracings (i.e., presence of 60 cycle interference, or lead reversal). In addition,

weekly team meetings were held throughout the study period as a forum of communication, and continuing education.

Instruments

Equipment: Continuous 12-lead ECG monitoring was obtained using the Mortara ELI 100 ST Monitor (Milwaukee, WI). The ELI 100 monitor is a portable, programmable, microprocessor-based device that acquires, analyzes and stores 12-lead ECGs at programmed intervals or when an ECG ST segment change is detected. The ELI 100 monitor was programmed with filter settings of 0.05 to 109 Hertz, as recommended by the American Heart Association for ischemia analysis (Mirvis, Berson, & Goldberg, 1989) with a standard calibration setting of 1 millivolt (mV) = 1000 microvolts (μV), and a paper speed of 25 millimeters (mm)/second, which are the standards used for clinical practice (Pepine et al., 1987). Stored ECGs from the ELI 100 monitor were then transmitted to a personal computer with additional ST analysis software installed (Mortara ST Review Station Computer, Mortara Instrument Incorporated, Milwaukee, WI) in order to perform in-depth analysis, including computerized ST segment measurements.

Procedures

Analysis of ECG ST Monitoring Data for the Presence or Absence of Ischemia:

Transient myocardial ischemia was defined as $\geq$ 100 μV ST segment deviation (elevation or depression) in $\geq$ 1 ECG lead lasting $\geq$ 60 seconds (Pepine et al., 1987). A second event in a single patient was counted only if the ST segment deviation returned to a baseline level for at least 60 seconds and then became deviated again. The process for determining the presence of ischemia using the ST Review Station (Mortara Instrument

Incorporated, Milwaukee, WI) was as follows: at the end of the monitoring period all stored ECG were evaluated, any ECG's with a noisy signal, or ECG's demonstrating ST changes due to non-ischemic conditions (i.e., accelerated ventricular rhythm, intermitted ventricular pacer, or intermittent bundle branch block) were withheld from the analysis. This "cleaned" ECG data was then evaluated for ST changes (i.e., ST elevation or depression) indicative of ischemia, and computer generated μV values were used to determine if the ST changes exceeded 100 μV of ST deviation. When a potential ischemic event was observed, three 12-lead ECG's were printed out: (1) a "baseline" 12-lead obtained prior to the ST changes, (2) "event" ECG obtained during the ST changes, and (3) a "return to baseline" ECG obtained after the event.

One possible threat to the validity of measuring ischemia during continuous ST segment monitoring is ST changes due to body position changes. False-positive ST changes due to body position changes may occur during continuous monitoring when a patient assumes a left- or right side-lying position. It is believed that the ST changes in this instance occur when the free-floating heart rotates within the chest relative to the fixed electrodes on the chest (Feldman et al., 1985). In order to limit false positive ST changes due to body position changes the research assistants in the parent study obtained "template" body position ECG's with patients assuming a supine, left, and right side lying positions. Any potential ischemic event ECG's was then compared to the template ECG's in order to ensure that the observed ST changes were not due to body position changes.

In-Hospital Complications: Retrospective analysis of medical records was done to determine in-hospital complications. In-hospital complications were defined as: (1)

myocardial infarction (MI) after hospital admission in patients admitted for angina, or "elective" PTCA/stent, as evidenced by elevation of troponin I, (2) extension of MI in patients admitted with acute MI as evidenced by new ECG ST segment changes, or re-elevation creatine kinase (CK-MB), (3) cardiovascular death, (4) arrhythmia requiring intervention (i.e., pharmacological, or defibrillation), (5) hemodynamic compromise requiring intervention, and (6) unplanned transfer from the telemetry unit to the CCU due acute complications (i.e., unrelieved chest pain, ECG changes, acute heart failure, arrhythmias, hemodynamic compromise, or cardiac arrest).

Out of Hospital Complications: The rate of out of hospital complications measured at 90-days following hospital discharge, was determined retrospectively using the UCSF computer database. Out-of hospital complications were defined as: (1) re-hospitalization for treatment of an acute coronary syndrome, (2) MI, or (3) cardiovascular death.

Ischemic ST changes in routine telemetry unit monitoring lead MCL_1 or lead II: In order to determine if MCL_1 or lead II would have detected the ischemic event, 12-lead ECG's demonstrating ST deviation indicative of ischemia were assessed to determine if the ST deviation exceeded 100 μV in lead V1 or lead II. Lead V1 was selected because this is the unipolar substitute for MCL_1 (Marriott & Fogg, 1970).

Symptomatic Myocardial Ischemia: For every ECG-detected ischemic event a retrospective analysis of medical records was done to determine if the patient experienced any symptoms during the ischemic event. Two data sources were reviewed in order to obtain this variable: 1) a detailed 24-hour diary maintained prospectively by the research assistants in the parent study who communicated frequently with patients, nurses and physicians regarding symptoms and, 2) the patient's medical chart, including nursing and

physician notes. Symptoms of ischemia were defined as any documented patient complaint of chest pain, pressure, heaviness, tightness, squeezing, or dullness in the center of the chest. In addition, any anginal equivalents such as diaphoresis, shortness of breath, nausea, jaw, neck or left arm pain was counted as an ischemic symptom. Any documented patient symptom or anginal equivalent that occurred within one half hour before or after the ischemic event was counted as a symptomatic event.

Statistical Analysis of Specific Hypotheses

Hypothesis #1: *The Frequency of transient myocardial ischemia, among hospitalized patients admitted for treatment of angina, will not be different comparing a group of patients treated in the coronary care unit (CCU) from November 1994 to April 1996 to a group of patients treated in the telemetry unit from September 1997 to March 2000. In addition, the rate of in-hospital complications will be higher among patients who experience ischemia, whether in the CCU or telemetry unit, compared to patients who do not experience ischemia.*

Descriptive statistics were used to report age, sex, ethnicity, cardiovascular risk factors, and prior cardiac interventions (i.e., CABG surgery, PTCA/stent). Chi-square tests were performed to determine if the CCU group differed from the telemetry unit group with regard to sex, ethnicity, cardiovascular risk factors, or prior cardiac interventions. A two-tailed unpaired Students t-test was used to determine if the CCU group differed from the telemetry unit group with regard to age, and the Norris prognostic indicator, which combines age, prior MI, and evidence of cardiomegaly, or pulmonary edema using chest X-ray (Norris, Caughey, Mercer, & Scott, 1974). A two-

tailed unpaired Students t-test was used to determine if the time from hospital admission to initiation of ST segment monitoring differed between the CCU and telemetry unit group. A chi-square test was applied to determine if there was a significant difference in the proportion of patients with ischemia comparing the CCU to the telemetry unit group. Logistic regression analysis was done to determine if individual variables were predictive of ischemia. Independent variables included in the logistic regression analysis included: age, Norris prognostic indicator, time from hospital admission to start of ST monitoring, total ST monitoring time, and unit the patient was monitored in (i.e., CCU or telemetry unit). The logistic regression analysis examined the odds afforded by each of the variables for the occurrence of ECG-detected ischemia, which served as the dependent variable.

To test if there was a difference in the complication rate between patients with and without ischemia a chi-square test was used. A p-value of <0.05 was employed as a critical value to determine if there was a significant difference in the rate of complications between patients with and without ECG-detected ischemia. A chi-square test was used to determine if the complication rate differed among the group of patients with ischemia, comparing the CCU group to the telemetry unit group. A p-value of <0.05 was employed as a critical value to determine if there was a significant difference in the rate of complications when comparing the CCU group with ischemia to the telemetry unit group with ischemia.

Hypothesis #2: *Patients diagnosed with acute coronary syndromes (i.e., angina, acute MI, or congestive heart failure) who experience ECG-detected myocardial*

ischemia while being treated in the telemetry unit setting will have more in-hospital complications, such as, MI, arrhythmia requiring intervention, or death compared to patients who do not experience ischemia.

Because some of the patients were admitted to the CCU prior to being admitted to the telemetry unit, only complications that occurred during the telemetry unit-monitoring period were counted. Chi-square analysis was used to determine if there was a significant difference in the rate of complications between the group with and without ischemia. A p value of < 0.05 was used to determine if the differences between the two groups was statistically significant. In order to determine if the complication rate differed among patients diagnosed with angina or MI, the groups were separated and chi-square analysis was done to determine if the complication rate differed among patients with and without ischemia. A p value of < 0.05 was adopted as the critical value to determine if the differences between the two groups was statistically significant.

Hypothesis #3: *12-lead ECG ST segment monitoring will be more sensitive for ischemia detection than the two most commonly selected electrocardiographic leads V1 alone, lead II alone, or either V1 or lead II.*

In the group of patients who had one or more ECG-detected ischemic event(s) during the monitoring period, the proportion who manifested ≥ 100 μV ST deviation in V1 was calculated. A McNemar test of proportions was used to determine if there was a difference in the sensitivity between the 12-lead ECG versus lead V1. A p-value of 0.05 was used to determine if this difference was statistically significance.

Hypothesis #4: *A minority of telemetry unit patients admitted for treatment of an acute coronary syndrome will experience chest pain or their anginal equivalent during ECG-detected ischemia.*

The proportion of ischemic events that were clinically "silent" was determined and a 95% confidence interval around this proportion was calculated. The clinical variables of age, ethnicity, and gender were examined in order to determine if those patients with clinically silent myocardial ischemia differed form the patients with symptomatic ischemia. A two-tailed independent Students t-test was used to determine if there were age differences comparing the group with silent versus symptomatic ischemia. Chi-square analysis was used to determine if there were gender or race differences between the groups with silent versus symptomatic ischemia. A p value of < 0.05 was adopted as the critical value to determine if these differences were statistically significant.

Hypothesis #5: *Patients who experience ECG-detected myocardial ischemia while being treated in the telemetry unit will have one or more out of hospital complications, measured at 90-days, compared to patients who do not experience ischemia.*

Chi-square analysis was used to determine if there was a difference in the rate of 90-day complications between the group with and without ECG-detected ischemia. A p value of < 0.05 served as the critical value to determine if the rate of 90-day complications differed between patients with and without ischemia.

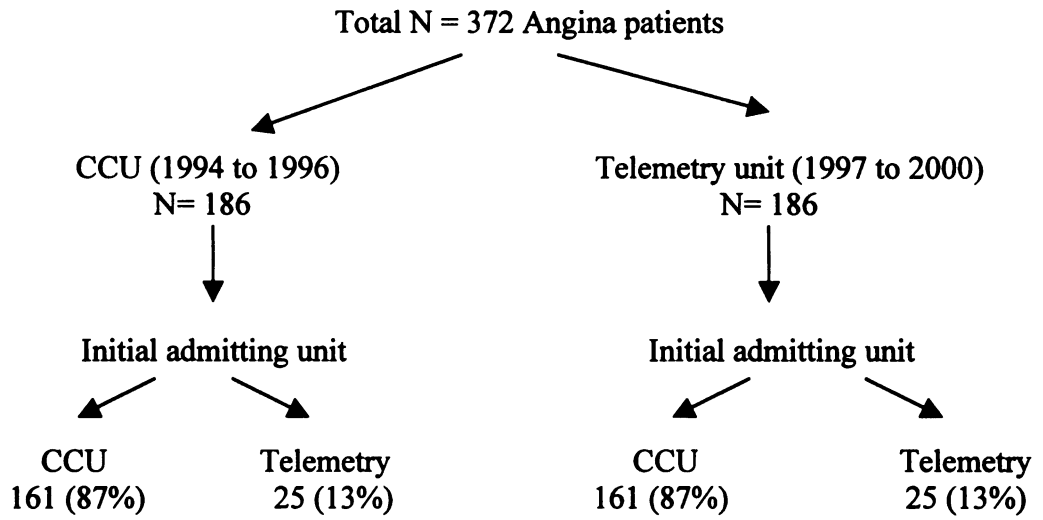
RESULTS

Hypothesis #1: *The frequency of transient myocardial ischemia, among hospitalized patients admitted for treatment of angina, will not be different comparing a group of patients treated in the coronary care unit (CCU) from November 1994 to April 1996, to a group of patients treated in the telemetry unit from September 1997 to March 2000. In addition, the rate of in-hospital complications will be higher among patients who experience ischemia, whether in the CCU or telemetry unit, compared to patients who do not experience ischemia.*

Sample/Demographics

A total of 372 patients with angina were included in this analysis. Coincidentally, 186 were monitored with continuous 12-lead ECG ST segment monitoring in the CCU from November 1994 to April 1996, and 186 were monitored with continuous 12-lead ECG ST segment monitoring in the telemetry unit from September 1997 to March 2000. Among the group monitored in the CCU from 1994 to 1996, the majority were initially admitted to the CCU, rather than the telemetry unit (161/186 [87%]). In contrast, among the group monitored in the telemetry unit from 1997 to 2000, the majority were initially admitted to the telemetry unit rather than the CCU (161/186 [87%]) (Figure 23).

Figure 23. Illustrates number of patients monitored in the CCU from 1994 to 1996, and the number of patients monitored in the telemetry unit from 1997 to 2000, and the unit patients were initially admitted to during these time periods.



The clinical characteristics of the 372 angina patients (186 CCU and 186 telemetry unit) constituting the study sample are shown in Table 14. There was no significant difference between the CCU and telemetry unit groups with regard to the clinical characteristics of sex, ethnicity, number of diseased coronary vessels, or prevalence of hypertension, hypercholesterolemia, smoking, diabetes or prior CABG surgery. However, the telemetry group was older, and a greater proportion had a history of prior PTCA compared to the CCU group ($p < 0.001$). Whereas, more of the CCU group had prior MI, and a catheter-based interventions (i.e., PTCA or stent) during hospitalization compared to the telemetry unit group ($p < 0.05$). The predominate catheter-based intervention among the CCU group was PTCA (89%), in contrast, the most common catheter-base intervention among the telemetry group was stent (89%) [$p < 0.001$]. The Norris prognostic indicator, which combines age, prior MI, and evidence of

Table 14. Clinical characteristics of the 186 CCU angina patients and 186 telemetry unit angina patients.

Variable	CCU n= 186	Telemetry Unit n= 186	P value
Sex (male)	121 (65%)	119 (64%)	0.828
Age (mean)	65 ± 12.4	68 ± 12.4	< 0.001
Ethnicity			
- Caucasian	108 (58%)	114 (62%)	
- African American	28 (15%)	20 (11%)	0.472
- Hispanic	17 (9%)	18 (10%)	
- Asian	33 (18%)	32 (17%)	
- Native American	0	2 (1%)	
# of Diseased Coronary Vessels			
- Single vessel	72 (42%)	56 (35%)	0.370
- Double vessel	42 (25%)	47 (29%)	
- Triple vessel	56 (33%)	57 (36%)	
	16 (7%) unknown (no cardiac cath. but + old MI by ECG)	26 (14%) unknown (no cardiac cath. but + old MI by ECG)	0.374
Elevated Cholesterol	105 (57%)	105 (57%)	0.423
Hypertension	126 (68%)	127 (68%)	0.616
Current Smoker	27 (14%)	33 (18%)	0.398
Diabetes	53 (28%)	57 (30%)	0.285
Prior MI	86 (46%)	67 (36%)	< 0.05
Prior CABG	35 (19%)	45 (24%)	0.207
Prior PTCA	55 (30%)	82 (44%)	< 0.05
Catheter-based intervention during hospitalization (i.e., PTCA, or stent)	120(65%)	92 (50%)	< 0.001
- PTCA	101 (84%)	10 (11%)	< 0.001
- Stent	19 (16%)	82 (89%)	
Norris Prognostic Indicator	6.0 ± 3.3	5.3 ± 2.8	< 0.05

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., age, Norris prognostic indicator); ± denotes the standard deviation. CCU = coronary care unit; MI = myocardial infarction; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal angioplasty; ECG = electrocardiogram.

Electrocardiographic ST Segment Monitoring

The variables related to continuous 12-lead ECG monitoring, and the frequency of transient myocardial ischemia comparing the CCU to the telemetry unit group is presented in Table 15. There was no significant difference between the CCU and telemetry unit group with regard to the mean time from hospital admission to the initiation of continuous 12-lead ECG ST segment monitoring when assessing the group as a whole (15 hours versus 19 hours; NS). However, when considering the group of patients who were initially admitted to CCU (n = 161) or Telemetry (n = 161), time form hospital admission to start of ST monitoring was significantly longer among the telemetry unit group (9 hours versus 19 hours; $p < 0.001$). On the other hand, when comparing the group of 25 CCU patients (1994 – 1996) who were initially admitted to the telemetry unit and then subsequently to the CCU, compared to the group of 25 telemetry unit patients (1997 – 2000) who were initially admitted to the CCU and then subsequently to the telemetry unit, the time from hospital admission to start of ST monitoring was considerably longer among the CCU group (53 hours versus 26 hours; $p < 0.001$). The CCU group was monitored with continuous 12-lead ECG monitoring on average 8 hours longer than the telemetry unit group ($p < 0.001$). Although the CCU group was hospitalized an average of 10 hours longer than the telemetry unit group this difference was not statistically significant. There was no difference in the rate of ischemia when comparing the CCU group (19%) to the telemetry unit group (15%).

Table 15. Comparison of ECG variables and the frequency of transient myocardial ischemia between the CCU and telemetry unit group.

Variable	CCU 1994 -1996 n= 186	Telemetry Unit 1997 - 2000 n= 186	P value
Time from hospital admission to start of ECG ST Monitoring (hours)	15 ± 24	19 ± 32	0.112
	Time to ST monitoring among 161 pts. initially admitted to CCU	Time to ST monitoring among 161 pts. initially admitted to Telemetry unit	
	9 ± 14	19 ± 34	< 0.001
	Time to ST monitoring among 25 pts. initially admitted to telemetry unit, then CCU	Time to ST monitoring among 25 pts. initially admitted to CCU, then to telemetry unit	
	54 ± 37	26 ± 16	< 0.001
Mean number of hours monitored with 12-lead ECG	34 ± 26	26 ± 22	<0.001
Hospital length of stay (hours)	97 ± 92	87 ± 82	0.263
Mean Number of ischemic events	3 ± 5	3 ± 2	0.374
Frequency of transient myocardial ischemia	36 (19%)	28 (15%)	0.272

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., time to ST monitoring, mean monitoring time, hospital length of stay, mean number of events) CCU = coronary care unit; pts. = patients.

Because the variables age, prior MI, prior PTCA, catheter-based intervention during hospitalization, Norris prognostic indicator score, time from hospital admission to start of ST monitoring, and total ECG ST monitoring time were statistically different when comparing the CCU group to the telemetry unit group, univariate logistic regression

analysis was performed to determine if any of these individual variables were predictive of transient myocardial ischemia. Finally, hospital unit (CCU or telemetry unit) was entered into the second step of model to determine if this variable was predictive of ischemia after accounting for the variables entered in the first step of the model. Table 16 shows the results of the logistic regression analysis. Of the clinical variables entered into the model, only ECG monitoring time was predictive of transient myocardial ischemia O.R. = 1.027 ($p < 0.01$). Thus, for every one unit increase in monitoring time (hour) a patient was 1.03 times more likely to experience transient myocardial ischemia. The remaining variables entered into the model were not predictive of transient myocardial ischemia.

Table 16. Univariate predictors of transient myocardial ischemia

Variable	P Value	Adjusted Odds Ratio	95% C.I. for the Adjusted Odds Ratio	
			Lower	Upper
Age	0.64	1.01	0.98	1.04
History of MI	0.81	0.91	0.43	1.92
History of PTCA	0.46	1.26	0.68	2.34
Catheter-based intervention during hospitalization	0.47	0.80	0.42	1.46
Time from hospital admission to start of ST monitoring	0.28	1.0	0.98	1.01
ECG Monitoring Time	.001	1.03	1.02	1.04
Norris Prognostic Indicator	0.40	1.06	0.93	1.20
Unit Monitored in (CCU or Telemetry)	0.78	0.91	0.50	1.70

ECG = electrocardiographic, CCU = coronary care unit

Clinical Outcomes CCU versus Telemetry Unit

Comparison of patients with and without transient ischemia: Adverse clinical outcomes during hospitalization comparing the CCU group, with and without ischemia, to the telemetry unit group, with and without ischemia is presented in Table 17. Regardless of the unit the patient was monitored in (CCU or telemetry) a significantly higher proportion of patients with transient myocardial ischemia experienced hypotension requiring intervention, acute MI after admission, or abrupt closure compared to patients who did not experience ischemia ($p < 0.001$). However, there was no significant difference with regard to arrhythmia requiring intervention, or pulmonary edema/congestive heart failure between patients with and without ischemia, whether the patient was monitored in the CCU or telemetry unit. A significantly higher proportion of CCU patients with ischemia died compared to patients without ischemia ($p < 0.05$). Although a higher proportion of telemetry unit patients with ischemia died (4%) compared to the group without ischemia (0.6%) this difference was not statistically significant. Among the telemetry unit group, 6/28 (21%) of the patients with ischemia were transferred from the telemetry unit to the CCU for more aggressive therapy due to acute complications compared to patients without ischemia ($p < 0.0001$). Both CCU and telemetry unit patients who experienced ischemia were hospitalized longer than patients who did not experience ischemia ($p < 0.05$).

Table 17. Clinical outcomes during hospitalization comparing the CCU group with and without transient myocardial ischemia n= 186 to the telemetry unit group with and without transient myocardial ischemia n = 186.

	CCU Patients N = 186			**Telemetry Unit Patients N = 186**		
Variable	**– Ischemia n = 151**	**+ Ischemia n = 36**	**P value**	**– Ischemia n = 158**	**+ Ischemia n = 28**	**P value**
Arrhythmia requiring intervention	6 (4%)	3 (8%)	**0.277**	3 (2%)	2 (7%)	**0.114**
Hypotension requiring intervention	1 (0.7%)	4 (11%)	**< 0.001**	1 (0.6%)	4 (14%)	**< 0.0001**
Acute pulmonary edema or congestive heart failure	5 (3%)	1 (3%)	**0.865**	1 (0.6%)	1 (4%)	**0.165**
Acute MI after admission	1 (0.7%)	11 (31%)	**< 0.0001**	7 (4%)	10 (36%)	**< 0.0001**
Abrupt closure after PTCA/stent	1 (0.7%)	3 (8%)	**< 0.001**	0	1 (4%)	**< 0.01**
Death	2 (1%)	3 (8%)	**< 0.01**	1 (0.6%)	1 (4%)	**0.165**
Transfer from Telemetry Unit to CCU for more aggressive therapy due to a complication (i.e., arrhythmia, pulmonary edema, or shock)	Not measured	Not measured		2 (1%)	6 (21%)	**< 0.0001**
Length of hospital stay (hours)	80 $\pm$ 70	165 $\pm$ 132	**<0 .001**	78 $\pm$ 76	136 $\pm$ 97	**< 0.05**
Any complication	11 (7%)	13 (36%)	**< 0.001**	10 (6%)	14 (50%)	**< 0.0001**

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., length of hospitalization; $\pm$ denotes the standard deviation. CCU = coronary care unit. MI = myocardial infarction. PTCA = percutaneous transluminal angioplasty.

Comparison of patients with transient ischemia CCU versus Telemetry unit. Table 18 shows the comparison of adverse outcomes among the 64 patients (36 CCU patients and 28 telemetry unit) who experienced ischemia. There was no significant difference in the proportion of CCU versus telemetry unit patients with regard to arrhythmia requiring intervention, hypotension requiring intervention, acute pulmonary edema/congestive heart failure, acute MI after admission, abrupt closure after PTCA/stent, or death. When combing adverse outcomes, excluding transfer from the telemetry unit to the CCU since this was not measured in the CCU group, a higher proportion of telemetry unit patients (47%) experienced an adverse clinical event compared to the CCU group (36%). This difference was, however, not statistically significant. Although the average hospital length of stay among the telemetry unit group with ischemia was an average of 29 hours shorter than the CCU group with ischemia, this difference was not statistically significant (136 hours telemetry unit group versus 165 hours CCU group; NS).

Table 18. Comparison of adverse outcomes among the 64 patients with transient myocardial ischemia, CCU (n = 36) versus telemetry unit (n = 28).

Variables	CCU + Ischemia n = 36	Telemetry + Ischemia n = 28	P value
Arrhythmia requiring intervention	3 (8%)	2 (7%)	0.860
Hypotension requiring intervention	4 (11%)	4 (14%)	0.703
Acute pulmonary edema or congestive heart failure	1 (3%)	1 (4%)	0.856
Acute MI after admission	11 (31%)	10 (36%)	0663
Abrupt closure after PTCA/stent	3 (8%)	1 (4%)	0.435
Death	3 (8%)	1 (4%)	0.435
Any complication (transfer from telemetry to CCU not included)	13 (36%)	13 (47%)	0.264
Length of hospital stay (hours)	165 $\pm$ 132	136 $\pm$ 97	0.334

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., length of hospitalization.
$\pm$ denotes the standard deviation; CCU = coronary care unit; MI = myocardial infarction; PTCA = percutaneous transluminal angioplasty

Hypothesis #2: *Patients diagnosed with acute coronary syndromes (i.e., angina, acute MI, or congestive heart failure) who experience myocardial ischemia while being treated in the telemetry unit setting will have more in-hospital complications compared to patients who do not experience ischemia.*

Sample Characteristics

Table 19 shows the clinical characteristics of the 237 acute coronary syndrome patients who were monitored in the telemetry unit with continuous 12-lead ECG ST segment monitoring. All the patients had a definitive diagnosis of CAD based on documentation of prior MI using presence of Q-waves on the resting 12-lead ECG, coronary angiogram demonstrating a $\geq$ 70% lesion in one or more vessel(s), or development of MI during hospitalization. The mean age of this ethnically diverse

sample was 68 years (range 28 – 95) and nearly 65% were men. A majority of the sample was admitted with the diagnosis of angina (79%), but patients diagnosed with acute MI (20%) and congestive heart failure (1%) were also enrolled in the study. The vast majority of the angina patients (87%), and CHF patients (75%) were initially admitted to the telemetry unit, whereas the vast majority of the acute MI patients (70%) were initially admitted to the CCU and then subsequently admitted to the telemetry unit ($p < 0.001$). Over 50% of the 237 patients had a history of CAD, hypertension, or elevated cholesterol. One third of the sample had diabetes or prior MI, and nearly 20% were current smokers. The number of diseased coronary vessels was distributed evenly among the group - single (32%), double (24%), and triple (31%). Less than one quarter of the sample (50/237) had prior CABG surgery, whereas nearly 40% (89/237) had a prior history of a catheter-based intervention (i.e., PTCA, or stent). During hospitalization 134 (57%) of the sample was treated with a catheter-based intervention, 113 (84%) patients had stent procedures.

Table 19. Sample characteristic of 237 patients with CAD monitored with continuous 12-lead ST segment monitoring in the telemetry unit setting.

Clinical Characteristics		
Age (mean)	68 ± 13	
Sex		
- men	152 (64%)	
- women	85 (36%)	
Ethnicity		
- Asian	39 (17%)	
- Black	20 (8%)	
- Caucasian	153 (65%)	
- Hispanic	21 (8%)	
- Native American	4 (2%)	
Admitting Diagnosis		
- Angina (stable or unstable)	186 (79%)	
- Acute MI	47 (20%)	
- Congestive Heart Failure	4 (1%)	
Unit Patient Initially Admitted to CCU or Telemetry?	**CCU**	**Telemetry**
- Angina n= 186 *	25 (13%)	161 (87%)
- Acute MI n = 47 *	33 (70%)	14 (30%)
- Congestive Heart Failure n = 4 *	1 (25%)	3 (75%)
Cardiac Risk Factors		
- History of CAD	152 (64%)	
- Hypertension	155 (65%)	
- Current Smoker	46 (19%)	
- Diabetes	70 (30%)	
- Hypercholesterolemia	131 (55%)	
- Prior MI	78 (33%)	
Coronary Artery Disease		
- Single vessel	76 (32%)	
- Double vessel	56 (24%)	
- Triple vessel	73 (31%)	
- Unknown # of vessels – no cardiac cath. but + for MI based on 12-lead ECG	32 (13%)	
History of Prior Cardiac Interventions		
- Prior CABG surgery	50 (21%)	
- Prior catheter-based intervention (i.e., PTCA, stent, atherectomy)	89 (38%)	
PTCA/stent during hospitalization		
- PTCA	21 (16%)	
- stent	113 (84%)	

* p value < 0.001. Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., age). ± denotes the standard deviation; CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal angioplasty

Frequency of Transient Myocardial Ischemia

The mean time from hospital admission to initiation of ST segment monitoring in the telemetry unit varied depending upon the patients admitting diagnosis. For example, time from hospital admission of start of ST monitoring was 20 hours (± 32 hours) among the group of patients admitted for treatment of angina, or CHF, and 42 hours (± 30 hours) among the patients diagnosed with acute MI ($p < 0.001$). Patients were monitored with continuous 12-lead ECG monitoring on average 28 hours (range 1 to 153 hours). During 8,306 total hours of continuous 12-lead ECG ST monitoring in 237 patients, a total of 39 patients (17%) experienced a total of 89 ischemic episodes. Among the 39 patients with one or more ischemic episode, most were patients diagnosed with angina (28 patients; 72%), and the remaining patients were diagnosed with acute MI were (11 patients; 28%). None of the four patients diagnosed with CHF experienced transient ischemia in the telemetry unit. The average number of ischemic events among the group with ischemia was 2 (range 1 to 8 ischemic episodes), and the average duration was 74 minutes (range 2 minutes to 660 minutes). An example of a patient that experienced ischemia while on the telemetry unit is shown in Figure 24.

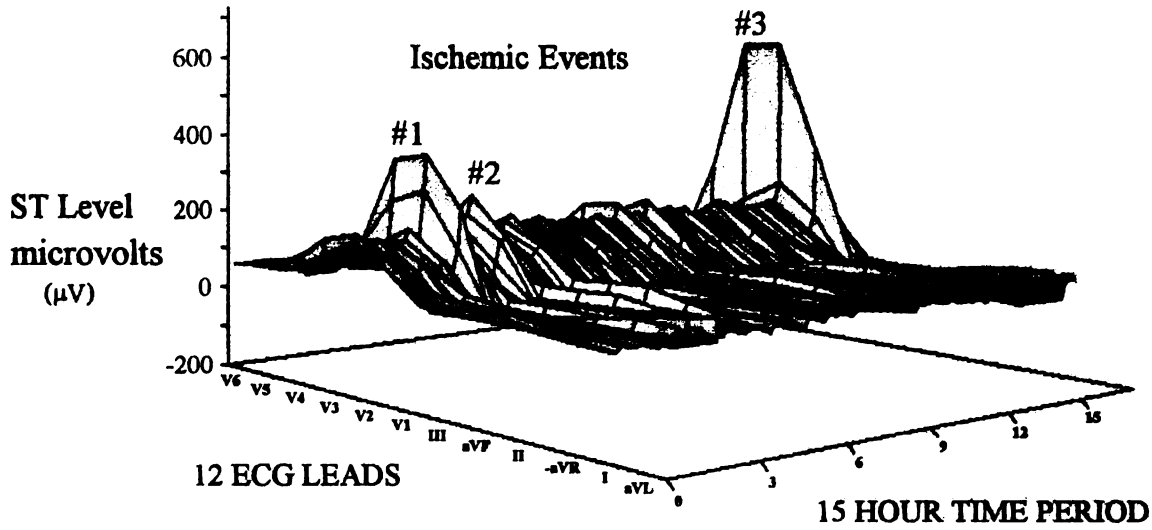


Figure 24. This 3 dimensional image illustrates ST segment deviation in microvolts (Y-axis), in 12 ECG leads (X-axis), over a 15 hour time period (Z-axis), in a 78-year-old Cantonese speaking male patient admitted to the telemetry unit with unstable angina. Illustrated are three separate ischemic events, characterized by ST segment elevation, in leads V3 to V5. It should be noted that the nurses were unaware of these ischemic events because the patient did not complain of chest pain during any of the events, and because there was no ST deviation > 100 μV in the routine telemetry unit monitoring lead V1. This patient, who was initially admitted with unstable angina and a normal troponin I level, subsequently "ruled-in" for myocardial infarction with a troponin I of 3.5 mg. The patient's angiogram later revealed a nearly 100% occluded left anterior descending coronary artery, which was treated with a stent.

A comparison of the clinical characteristics of the 237 patients constituting the study sample, comparing those with and without ischemia, is shown in Table 20. There was no difference when comparing patients with and without ischemia with regard to sex, ethnicity, or the cardiac risk factors of CAD, current smoker, diabetes, elevated cholesterol, number of diseased coronary vessels, prior PTCA, or prior MI. A higher proportion of patients with ischemia had a history of hypertension compared to patients without ischemia ($p < 0.05$). Although a higher proportion of patients with angina (72%) experienced ischemia compared to patients with acute MI (28%), there was no

statistically significant difference when comparing admitting diagnosis to the number of patients with and without ischemia. The Norris prognostic indicator, which combines age, prior MI, and evidence of cardiomegaly, or pulmonary edema using chest X-ray, was higher in the group of patients with ischemia compared to the group without ischemia ($p < 0.05$). The group of patients with ischemia were hospitalized an average of 51 hours longer than the group of patients without ischemia ($p < 0.001$).

Table 20. Sample characteristic comparing telemetry unit patients with and without ischemia N = 237.

Clinical Characteristics	– Ischemia N = 198	+ Ischemia N = 39	P value
Age (mean)	68 ± 13	70 ± 14	0.420
Sex			
- men	127 (64%)	25 (64%)	0.996
- women	71 (36%)	14 (36%)	
Ethnicity			
- Asian	33 (17%)	6 (15%)	
- African American	18 (9%)	2 (5%)	
- Caucasian	124 (62%)	29 (75%)	0.582
- Hispanic	19 (10%)	2 (5%)	
- Native American	4 (2%)	0	
Admitting Diagnosis			
- Angina (stable or unstable)	15 (79%)	28 (72%)	
- Acute MI	36 (18%)	11 (28%)	0.608
- Congestive Heart Failure	4 (1%)	0	
Cardiac Risk Factors			
- History of CAD	125 (63%)	27 (69%)	0.468
- Hypertension	123 (65%)	32 (82%)	< 0.05
- Current Smoker	38 (19%)	8 (21%)	0.515
- Diabetes	58 (29%)	12 (31%)	0.931
- Hypercholesterolemia	107 (54%)	24 (62%)	0.660
- Prior MI	61 (31%)	17 (44%)	0.121
Coronary Artery Disease			
- Single vessel	67 (34%)	9 (23%)	
- Double vessel	49 (25%)	7 (18%)	0.071
- Triple vessel	54 (27%)	19 (49%)	
- Unknown # of vessels – no cardiac cath. but + for MI based on 12-lead ECG	28 (14%)	4 (10%)	
History of Prior Cardiac Interventions			
- Prior CABG surgery	41 (21%)	9 (23%)	0.740
- Prior catheter-based intervention (i.e., PTCA, stent, atherectomy)	71 (36%)	18 (46%)	0.225
PTCA/stent during hospitalization	111 (56%)	23 (59%)	0.737
Norris Prognostic Indicator	5.1 + 2.6	6.4 + 3.8	< 0.01

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., age, and Norris prognostic indicator). ± denotes the standard deviation; CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal angioplasty

In-hospital Complication Rate Comparing Patients with and without Transient Myocardial Ischemia

The complication rate comparing the 237 patients with and without ischemia is presented in Table 21. None of the acute MI patients experienced extension of acute MI. There were no differences between patients with and without ischemia with regard to arrhythmia requiring intervention, acute pulmonary edema/CHF, or death. A significantly higher proportion of patients with ECG-detected ischemia experienced hypotension, acute MI after admission (angina patients only), abrupt closure after a catheter-based intervention, or were transferred from the telemetry unit to the CCU for more aggressive therapy due to complications compared to patients without ECG-detected ischemia ($p < 0.05$). Nearly half of the patients with ECG-detected ischemia experienced an adverse outcome, whereas, 10% of the group without ECG-detected ischemia experienced an adverse outcome ($p < 0.0001$). The group of patients with ischemia were hospitalized an average of 51 hours longer than the group of patients without ischemia ($p < 0.05$).

Table 21. Clinical outcomes during hospitalization comparing patients with and without ischemia N = 237.

Adverse Outcome	– Ischemia n = 198	+ Ischemia n = 39	P value
Arrhythmia requiring intervention	9 (5%)	4 (10%)	0.152
Hypotension requiring intervention	3 (2%)	5 (13%)	< 0.001
Acute pulmonary edema or congestive heart failure	3 (2%)	2 (5%)	0.151
Acute MI after admission *angina patients only n = 186	7 (4%)	10 (26%)	< 0.001
Extension of acute MI *acute MI patients only n = 47	0	0	
Abrupt closure after PTCA/stent	0	1 (3.6%)	< 0.05
Death	1 (1%)	1 (3%)	0.199
Transfer from Telemetry Unit to CCU for more aggressive therapy due to a complication (i.e., arrhythmia, pulmonary edema, or shock)	3 (2%)	7 (18%)	< 0.001
Any complication	18 (10%)	18 (46%)	< 0.001
Hospital Length of Stay (hours)	86 ± 76	142 ± 93	<0.001

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., hospital length of stay); ± denotes the standard deviation; MI = myocardial infarction; CCU = coronary care unit; PTCA = percutaneous transluminal angioplasty

Recognizing that several of these adverse outcomes may be considered "soft" end points, we also analyzed "hard" end points (i.e., MI or death) in order to determine if ECG-detected ischemia was associated with an adverse in-hospital outcome. Patients with ECG-detected ischemia were more likely to experience death or MI compared to patients without such events (28% versus 4%; $p < 0.001$).

Logistic regression analysis of four variables, age, sex, Norris CPI, and ECG-detected ischemia in the telemetry unit setting, revealed that the presence of ischemia was the most powerful predictor of an adverse hospital outcome ($P < 0.001$). Specifically, patients who had ECG-detected ischemia, which was clinically silent in three-quarters of

the patients, were 8.5 times more likely to experience an adverse hospital outcome (C.I. 3.71 – 19.71). Two step logistic regression analysis revealed that when considering only the hard end points of death or MI, that the presence of an ST event in the telemetry unit setting predicted MI or death independently of the other three clinical variables entered into the model (O. R. = 8.7; $p < .001$; C.I. 3.06 – 24.8).

Angina patients: Adverse clinical outcomes during hospitalization comparing the angina group with and without ischemia are presented in Table 22. There was no difference in the rate of arrhythmias requiring intervention, pulmonary edema/congestive heart failure, or death comparing patients with and without ischemia. A significantly higher proportion of patients with ischemia experienced hypotension requiring intervention, acute MI after admission, or abrupt closure after catheter-based intervention ($p < 0.05$). Among the group with ECG-detected ischemia 6 (21%) were transferred from the telemetry unit to the CCU for more aggressive treatment compared to 2 (1%) in the group of patients without ischemia ($p < 0.001$). An example of an angina patient with transient ischemia who was transferred from the telemetry unit to the CCU for more aggressive treatment is show in Figure 25. Half of the angina patients with ischemia (14/28) experienced a complication, whereas only 6% (10/158) of the angina group without ischemia experienced a complication ($p < 0.001$). The average length of hospitalization among the angina patients who experienced ECG-detected ischemia was 52 hours longer than the angina patients who did not experience ischemia ($p < 0.05$).

Table 22. Clinical outcomes during hospitalization comparing angina patients with and without ischemia N = 186.

Adverse Outcome	– Ischemia n = 158	+ Ischemia n = 28	P value
Arrhythmia requiring intervention	3 (2%)	2 (7%)	0.114
Hypotension requiring intervention	1 (0.6%)	4 (14%)	< 0.001
Acute pulmonary edema or congestive heart failure	1 (0.6%)	1 (4%)	0.165
Acute MI after admission	7 (4%)	10 (36%)	< 0.001
Abrupt closure after PTCA/stent	0	1 (4%)	< 0.05
Death	1 (0.6%)	1 (4%)	0.165
Transfer from Telemetry Unit to CCU for more aggressive therapy due to a complication (i.e., arrhythmia, pulmonary edema, or shock)	2 (1%)	6 (21%)	< 0.001
Any complication	10 (6%)	14 (50%)	< 0.001
Hospital Length of Stay (hours)	78 $\pm$ 76	136 $\pm$ 97	p < 0.005

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., hospital length of stay)
$\pm$ denotes standard deviation. CCU = coronary care unit. MI = myocardial infarction. PTCA = percutaneous transluminal angioplasty.

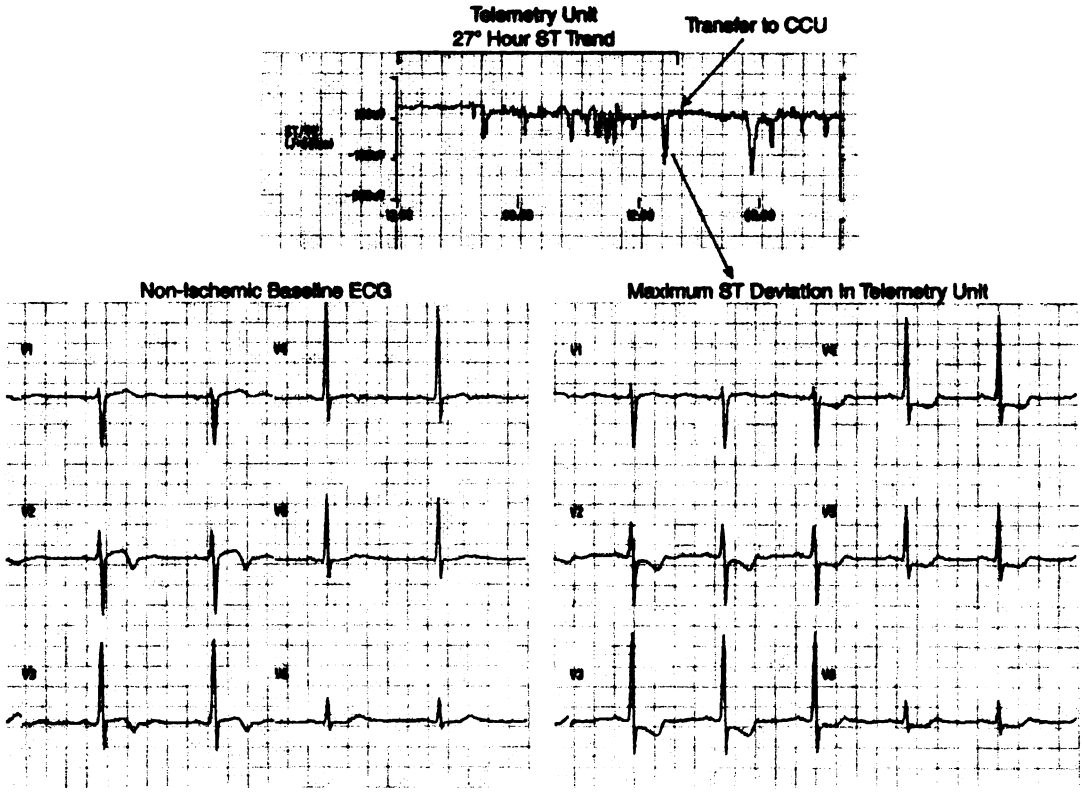


Figure 25. Illustrates an ST trend (lead V3) in a 72 year old male patient admitted to the telemetry unit for angina who was transferred from the telemetry unit to the coronary care unit (CCU) for more aggressive medical management prompted by unrelieved chest pain. Prior to transfer the patient experienced 8 separate ischemic events while in the telemetry unit setting (top panel). The first 6 ischemic events were clinically silent, however, the patient experienced chest pain during the final 2 ischemic events, which eventually prompted the physician to transfer the patient from the telemetry unit to the CCU. The panel at the bottom left of the figure shows the non-ischemic baseline ST level in the 6 precordial leads V1 through V6. The panel at the bottom right of the figure shows the maximal telemetry unit event (ST depression) in the same six precordial leads, which occurred just prior to the patient being transferred to the CCU. Following transfer from the telemetry unit to the CCU, the patient was started on aggressive medical management that included intravenous nitroglycerine, beta-blockers, and heparin. The patient was then taken urgently to the cardiac catheterization, and then subsequently to the operating room where coronary artery bypass graft surgery was performed.

Acute MI patients: The complication rate among the 47 acute MI patients with and without ischemia is presented in Table 23. There were no patient deaths or extension of acute MI in this small series of patients. There were no statistically significant differences with regard to arrhythmia or hypotension requiring intervention, acute pulmonary edema/congestive heart failure, or abrupt closure after PTCA/stent. A higher proportion of patients with ECG-detected ischemia experienced an adverse outcome compared to patients without ischemia (36% versus 22%), however, this difference was not statistically significant. Although the acute MI patients who experienced ECG-detected ischemia were hospitalized an average of 39 hours longer than the group without ischemia this difference was not statistically significant.

Table 23. Clinical outcomes during hospitalization comparing patients with acute MI with and without ischemia N = 47.

Adverse Outcome	– Ischemia N = 36	+ Ischemia N = 11	P Value
Arrhythmia requiring intervention	6 (17%)	2 (18%)	0.907
Hypotension requiring intervention	2 (6%)	1 (9%)	0.675
Acute pulmonary edema or congestive heart failure	2 (6%)	1 (9%)	0.675
Extension of Acute MI	0	0	
Death	0	0	
Transfer from Telemetry Unit to CCU for more aggressive therapy due to a complication (i.e., arrhythmia, pulmonary edema, or shock)	1 (3%)	1 (9%)	0.364
Any complication	8 (22%)	4 (36%)	0.347
Hospital length of stay (hours)	120 ± 70	159 ± 84	0.126

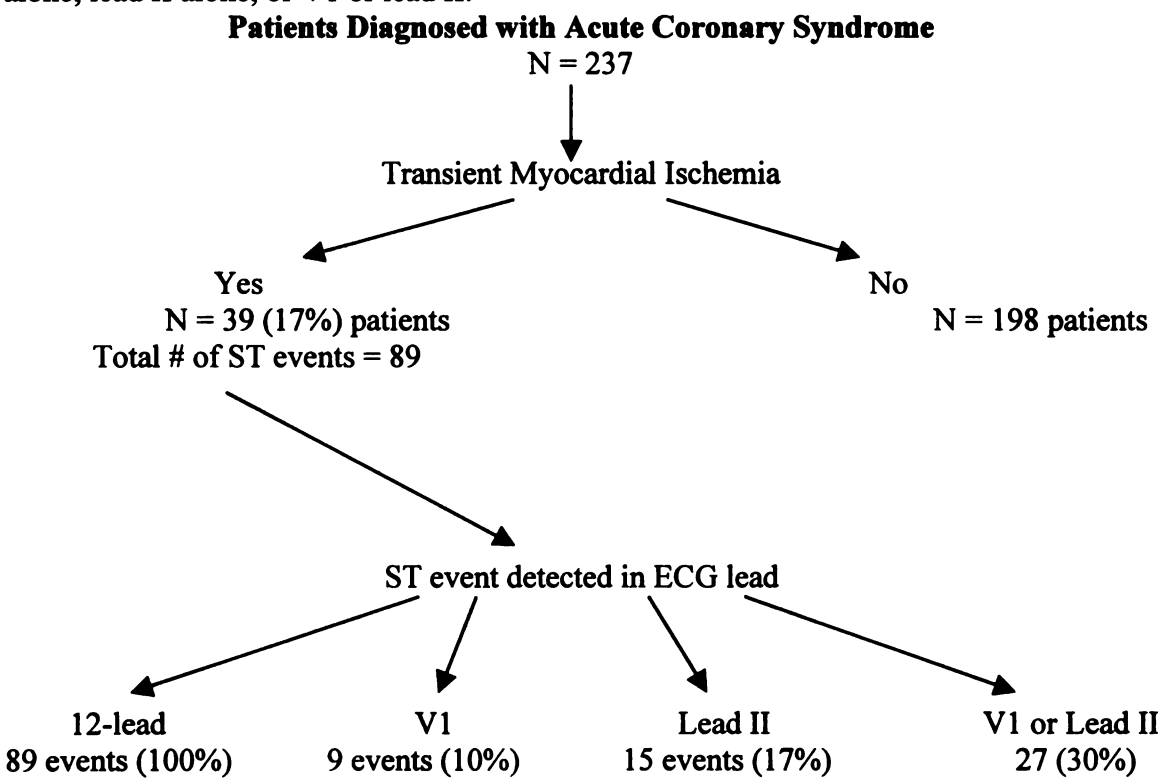
Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., hospital length of stay); ± denotes standard deviation. CCU = coronary care unit. MI = myocardial infarction. PTCA = percutaneous transluminal angioplasty.

Hypothesis #3: *12-lead ECG ST segment monitoring will be more sensitive for ischemia detection than the two most commonly selected electrocardiographic leads V1 alone, lead II alone, or either V1 or lead II.*

12-Lead versus V1 or Lead II

Of the 89 total ischemic events detected with the 12-lead ECG, only 9 (10%) exceeded 100 μV of ST deviation in lead V1 ($p < 0.0001$). Although lead II showed a slight improvement over V1, only 15 (17%) of the ischemic events detected with the 12-lead ECG would have been detected in lead II ($p < 0.0001$). Of the 89 total ischemic events, 27 (30%) events exceeded 100 μV or more of ST deviation in either V1 or lead II ($p < .0001$) [Figure 26].

Figure 26. Illustrates the sensitivity of the 12-lead ECG for ischemia detection compared to the most commonly selected leads for telemetry ECG monitoring, which are: lead V1 alone, lead II alone, or V1 or lead II.



The precordial leads V2 to V5 were more sensitive for detecting ST changes of $\geq$ 100 μV than the limb leads (Figure 25). Lead V3 was the single most sensitive lead (46%), and lead aVR was the least sensitive (8%).

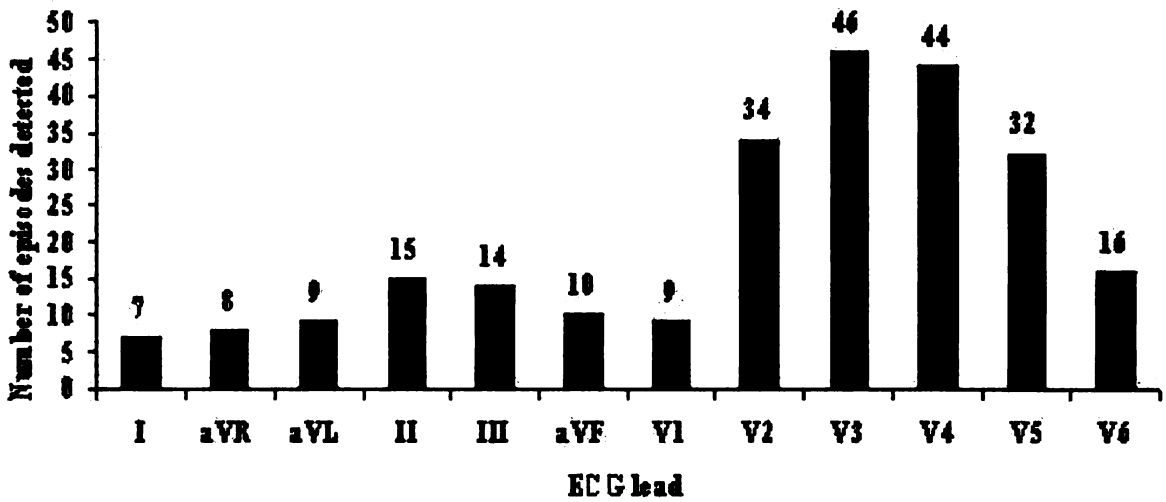


Figure 27. Illustrates the sensitivity of each of the 12 ECG lead for detection of ischemic ST changes > 100 μV.

The mean ST deviation (elevation or depression) measured in μV was 185 μV (minimum 100 μV maximum 1500 μV). Of the 89 total ischemic events, 20 (23%) were characterized as ST segment elevation, whereas, 69 events (77%) were characterized by ST segment depression. When characterizing the ischemic events by location (i.e., anterior = ST deviation in V2 to V4, or inferior = ST deviation leads II, III, and aVF), the majority occurred in the anterior zone (43 events = [48%]), and only 7 events (8%) occurred in the inferior myocardial zone. Of the remaining ischemic events, 17/89 events (19%) exhibited "global" ST changes where ST deviation occurred in both zones, and 22 events (25%) exhibited ST deviation in a zone other than the anterior or inferior myocardial zone. Maximal ST deviation (either depression or elevation) measured in μV

at 60 msec past the j-point, occurred most often in the precordial leads V2 through V5 (79/89 events [89%]), compared to the limb leads (10/89 events [11%]). Lead V4 was the single lead that most often demonstrated maximal ST deviation (31/89 events [35%]).

Hypothesis #4: *A minority of patients will experience chest pain or their anginal equivalent during ECG-detected ischemia events.*

Symptomatic Transient Myocardial Ischemia

Ten patients (26%) complained of chest pain during at least one episode of ECG-detected ischemia. Thus, ischemia was clinically silent in 74% of the patients with ECG-detected ischemia. The 95% confidence interval calculated for the sample proportion of patients with silent ischemia (0.74) was (0.60, 0.88). Thus, the population proportion of patients with silent ischemia is between 0.60 and 0.88. Of the 89 total ischemia events, 19 (22%) were accompanied by chest pain, hence, 78% of the ischemic events were clinically silent. The 95% confidence interval calculated for the sample proportion of clinically silent ischemic events (0.78) was (0.65, 0.91). Thus, the population proportion of silent ischemic events is between 0.65 and 0.91.

Table 24 shows the demographic and clinical characteristics of the 39 patients with ECG-detected ischemia, comparing the group of patients that had silent ischemia to the group of patients that had symptomatic ischemia. There were no differences when comparing the group with silent ischemia to the group with symptomatic ischemia with regard to age, gender or ethnicity. Of the 29 patients with silent ischemia, 20 (69%) were Caucasian, and 9 (31%) were non-Caucasian. Of the 10 patients who had symptomatic ischemia, 9 (90%) were Caucasian, thus, only one non-Caucasian patient experienced

chest pain during an ECG-detected ischemic event. Among the small number of diabetic patients (n = 12), 7 (58%) had silent ischemia, and 5 (42%) had symptomatic ischemia. However, this difference was not statistically significant.

Table 24. Demographic and clinical characteristics of the 39 patients with ECG-detected ischemia, comparing the group of patients who had silent ischemia to the group of patients who had symptomatic ischemia.

Variable	Silent Ischemia N = 29	Symptomatic Ischemia N = 10	P Value
Age (mean)	71 ± 14	67 ± 13	0.416
Sex			
- male	18 (62%)	7 (70%)	0.652
- female	11 (38%)	3 (30%)	
Ethnicity			
- Asian	5 (17%)	1 (10%)	
- African American	2 (7%)	0	0.557
- Caucasian	20 (69%)	9 (90%)	
- Hispanic	2 (7%)	0	
Ethnicity Sub-category			
- non-Caucasian	9 (31%)	1 (10%)	0.189
- Caucasian	20 (69%)	9 (90%)	
Diabetes	7 (58%)	5 (42%)	0.127

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., age)
± denotes standard deviation

Hypothesis #5: *Patients who experience myocardial ischemia while being treated in the telemetry unit will have more out of hospital complications measured at 90-days using the UCSF computer database compared to patients who do not experience ischemia.*

Clinical Characteristics

Two of the 237 patients died during hospitalization, and therefore were not included in the 90-day follow-up portion of the study. Ninety-day follow-up information, using the UCSF computer database, was obtained in a total of 181 (77%) of the original 235 patients who were monitored with continuous 12-lead ECG monitoring in the telemetry

unit setting, and who were discharged home. The reasons that patients were lost to follow-up included; (1) patient lives out of the state n= 15 (6%), (2) California resident, but followed at non-UCSF hospital n= 22 (9%), and (3) unknown reason n= 17 (7%). Table 25 shows clinical and demographic variables comparing the group of patients found at 90-days (n = 181) to the group of patients lost at 90-days (n = 54). When comparing the group lost at 90-days to the group included in the 90-day follow-up there were no statistically significant differences between the groups with regard to sex, race, or age. However, a higher proportion of the acute MI patients were lost at the 90-day follow-up period compared to the group who were found at the 90-day follow-up time period (42% versus 14%; $p < 0.001$). Whereas, a higher proportion of angina patients were found at the 90-day follow-up compared to the group who were lost at 90-days (85% versus 57%; $p < 0.001$).

Table 25. Comparison of clinical, demographic and presence of transient myocardial ischemia in patients lost (n = 54) and found (n= 181) at the 90-day follow-up.

Variable	Lost at 90-day Follow-up N = 54	Found at 90-day Follow-up N = 181	P value
Age (mean)	68 ± 15	69 ± 12	NS
Race			
- African American	1 (2%)	19 (11%)	
- Asian	6 (11%)	33 (18%)	
- Caucasian	42 (79%)	109 (60%)	0.130
- Hispanic	4 (7%)	17 (9%)	
- Native American	1 (2%)	3 (2%)	
Sex (males)	38 (70%)	113 (62%)	0.285
Admitting Diagnosis			
- Angina	31 (57%)	153 (85%)	< 0.001
- Acute MI	22 (41%)	25 (14%)	< 0.001
- Congestive Heart Failure	1 (2%)	3 (2%)	NS

Statistical test = χ^2 test for comparison of proportions, and two-tailed unpaired Student's t-test for continuous variables (i.e., age); ± denotes standard deviation

Of the 38 patients with ECG-detected ischemia, 27 (71%) were found at the 90-day follow-up period, and 11 (30%) were lost. Similarly, among the group without ECG-detected ischemia 154 (78%) were found at 90-day follow-up period, and 43 (22%) were lost at the 90-day follow-up period (Table 26). Chi-square analysis showed that the proportion of patients with and without ECG-detected ischemia that were found, or lost at the 90-day follow-up period was not different ($p = 0.339$).

Table 26. Compares the group of patients lost and found at the 90-day follow-up period, and the presence or absence of ECG-detected ischemia.

Status at 90-day Follow-up	NO ECG-detected Ischemia N = 197	Yes ECG-detected Ischemia N = 38	P value
Lost at 90-days	43 (22%)	11 (29%)	0.339
Found at 90-days	154 (78%)	27 (71%)	

Statistical test = χ^2 test for comparison of proportions

Clinical Outcomes at 90-Day Follow-up

Adverse clinical outcomes in the 181 patients, measured at 90-days following hospital discharge, are presented in Table 27. There was no difference when comparing patients with and without ischemia with regard to hospital re-admission for treatment of acute coronary syndrome (9% versus 11%; NS), or the frequency of MI during hospital re-admission (3% versus 4%; NS). There were 3 patient deaths, 2 were among the group without ECG-detected ischemia, and 1 was in the group with ECG-detected ischemia (1% versus 4%; NS). A higher proportion of the patients who experienced ECG-detected ischemia were re-hospitalized for treatment of acute coronary syndrome or died at 90-days compared to patients who did not experience ischemia (15% versus 10%). However, this difference was not statistically significant. A significantly higher

proportion of patients with ischemia experienced an in-hospital complication, hospital re-admission, or death during 90-days follow-up period, compared to the group of patients without ischemia ($p < 0.001$). Realizing that outcomes may be different between the group based on interventions used to restore perfusion to the myocardium we analyzed whether patients were treated with PTCA or CABG surgery during hospitalization in order to determine if the two groups (with ischemia versus without ischemia) differed. Similar proportions of patients with and with our ischemia were treated with either PTCA or CABG surgery during hospitalization.

Table 27. Clinical outcome at 90-days following hospital discharge comparing patients with and without ischemia N = 181.

Adverse Outcome	– Ischemia n = 154	+ Ischemia n = 27	P value
Hospital re-admission for treatment of acute coronary syndrome	14 (9%)	3 (11%)	0.740
Re-admitted for treatment of acute coronary syndrome and had acute MI	5 (3%)	1 (4%)	0.962
Death during 90 day follow-up period	2 (1%)	1 (4%)	0.367
Hospital readmission or death during 90-day follow-up period	15 (10%)	4 (15%)	0.427
In-hospital complication, hospital re-admission, or death during 90-day follow-up period	24 (16%)	14 (52%)	P < 0.001
PTCA or CABG during hospitalization	84 (55%)	15 (56%)	0.923

Statistical test = χ^2 test for comparison of proportions
MI = myocardial infarction; PTCA = percutaneous transluminal angioplasty; CABG = coronary artery bypass graft surgery

Angina patients: Table 28 shows adverse outcomes among the group of angina patients (n = 153). An equal proportion of patients without (9%) and with (9%) ischemia

were re-hospitalized for treatment of angina, or died at 90-days. A similar proportion of the patients with and without ECG-detected ischemia who were re-admitted during the 90-day follow-up experienced an MI during hospital re-admission (4% no ischemia versus 5% yes ischemia). There were 2 deaths, both among the group of patients without ECG-detected ischemia. A significantly higher proportion of patients with ischemia experienced an in-hospital complication, hospital re-admission, or death during 90-days follow-up period, compared to the group of patients without ischemia ($p < 0.001$).

Table 28. Clinical outcome at 90-days following hospital discharge comparing unstable angina patients with and without ischemia N = 153.

Adverse Outcome	– Ischemia n = 131	+ Ischemia n = 22	P value
Hospital re-admission for treatment of acute coronary syndrome	12 (9%)	2 (9%)	0.992
Re-admitted for treatment of acute coronary syndrome and had acute MI	5 (4%)	1 (5%)	0.994
Death during 90 day follow-up period	2 (2%)	0	0.560
Hospital readmission or death during 90-day follow-up period	13 (10%)	2 (9%)	0.903
In-hospital complication, hospital re-admission, or death during 90-day follow-up period	19 (15%)	11 (50%)	P < 0.001
PTCA or CABG during hospitalization	63 (48%)	10 (46%)	0.819

Statistical test = χ^2 test for comparison of proportions
MI = myocardial infarction; PTCA = percutaneous transluminal angioplasty; CABG = coronary artery bypass graft surgery

Acute MI patients: Table 29 shows the 90-day complication rate among the 25 acute MI patients with and without ischemia. A higher proportion of the MI patients with ischemia were re-admitted to the hospital for treatment of acute coronary syndrome, however, this difference was not statistically significant (20% with ischemia versus 10%

without ischemia; NS). None of the patients who were re-admitted to the hospital had a subsequent re-infarction. There were no patient deaths among the group without ischemia, however, one of the patients with ECG-detected ischemia died (20% with ischemia versus 0 without ischemia; $p < 0.05$). A higher proportion of patients with ischemia were either re-hospitalized or died during the 90-day follow-up period compared to patients who did not have ischemia (40% versus 20%; NS). However, in this small series of patients this difference was not statistically significant. Although a higher proportion of patients with ischemia experienced an in-hospital complication, hospital re-admission, or death during 90-days follow-up period, compared to the group of patients without ischemia this difference was not statistically different (60% versus 25%).

Table 29. Clinical outcome at 90-days following hospital discharge comparing acute MI patients with and without ischemia N = 25.

Adverse Outcome	– Ischemia n = 20	+ Ischemia n = 5	P value
Hospital re-admission for treatment of acute coronary syndrome	2 (10%)	1 (20%)	0.538
Re-admitted for treatment of acute coronary syndrome and had acute MI	0	0	NS
Death during 90 day follow-up	0	1 (20%)	< 0.05
Hospital readmission or death during 90-day follow-up period	2 (10%)	2 (40%)	0.102
In-hospital complication, hospital re-admission, or death during 90-day follow-up period	5 (25%)	3 (60%)	0.133
PTCA or CABG surgery during hospitalization	19 (95%)	5 (100%)	0.610

Statistical test = χ^2 test for comparison of proportions; MI = myocardial infarction; PTCA = percutaneous transluminal angioplasty; CABG = coronary artery bypass graft surgery

Discussion

This is the first study to describe the frequency and consequences of transient myocardial ischemia detected with 12-lead ECG ST segment monitoring in a cardiac telemetry unit. Overall, this study showed that 17% of patients admitted to the telemetry unit for treatment of an acute coronary syndrome experienced ECG-detected ischemia. A novel finding in this study was that the rate of ischemia among a subgroup of angina patients monitored in the telemetry unit from 1997 to 2000 was equivalent to the rate of ischemia among a similar group of angina patients treated in the CCU from 1994 to 1996. In this investigation, the vast majority of ischemic events would have gone unrecognized since nearly 80% of the events were clinically silent, and because the two most commonly selected telemetry unit ECG monitoring leads, V1 and lead II, only detected 30% of the ischemic events. Moreover, this study showed that patients who experience ischemia while being treated in the telemetry unit setting are at significantly higher risk for in-hospital complications compared to patients who do not experience ischemia. Over a subsequent 90-day follow-up period, deaths, or MI were rare, and hospital re-admission for treatment of an acute coronary syndrome was relatively uncommon, hence, our ability to determine if ECG-detected ischemia was predictive of an unfavorable outcome at 90-days was limited. Nevertheless, among the small group of MI patients, ECG-detected ischemia identified one patient that died within the 90-day follow-up period.

Frequency of Ischemia Among Angina Patients: comparison of a CCU group (1994 – 1996) versus Telemetry Unit Group (1997 – 2000)

Currently, there is increasing emphasis for hospitals to reduce both length and cost of hospital care. Among patients with acute coronary syndromes, cost-efficiency has been driven by two key principals; (1) reduce admission of patients at low-risk for acute MI to the CCU by utilizing "cost-effective" alternatives, such as, telemetry unit care, and (2) decrease use of the CCU by transferring patients to lower levels of care earlier in their hospital course (Lee & Goldman, 1988). The cardiac services at the University of California San Francisco (UCSF) Hospital, as with many others throughout the United States, have restructured the delivery of care to patients presenting for treatment of acute coronary syndromes in order to improve cost-efficiency. For example, at UCSF most angina patients are now initially admitted to the telemetry unit, rather than the CCU. To our knowledge, an assessment of the consequences of this shift in patient care, if any, comparing these two settings has not been reported. Prospective data from two clinical trials evaluating the usefulness of 12-lead ECG monitoring for ischemia detection; (1) the STAT Study (Drew et al., 1996), conducted in the CCU from 1994 to 1996, and (2) the STAMPEDE Study (Drew et al., 1999b) conducted in the telemetry unit from 1997 to 2000, has provided the unique opportunity to perform such an investigation. Thus, the aim of this study was to compare the frequency and consequences of transient myocardial ischemia, measured with continuous 12-lead ECG monitoring among a group of 186 angina patients monitored in the CCU from 1994 to 1996 to a group of 186 angina patients monitored in the telemetry unit from 1997 to 2000.

In this study, it was apparent that there had been a shift in the care of angina patients at our facility over the six-year study period. For example, our data showed that the

majority of the angina patients during the earlier time period (1994 to 1996) were admitted directly to the CCU, rather than the telemetry unit. In contrast, the majority of angina patients from the recent time period (1997 to 2000) were admitted directly to the telemetry unit as opposed to the CCU. However, because consecutive angina patients were not enrolled, the true number of angina who follow this course of care at UCSF cannot be determined form this investigation. Nevertheless, this study suggests that among select angina patients, the telemetry unit appears to be the initial hospital admission site for the majority, rather than the CCU. The principal finding in this study was that there was not a difference in the rate of ischemia when comparing a group of angina patients monitored in the CCU from 1994 to 1996 to a group of similar angina patients monitored in the telemetry unit from 1997 to 2000. Specifically, 19% of the CCU group and 15% of the telemetry unit group had ECG-detected ischemia. Thus, despite an obvious shift in the care of angina patients at our facility over a six-year time period, transient myocardial ischemia as detected by ST monitoring remains a common problem in the telemetry unit setting.

Because a slightly higher proportion of the CCU group had ischemia compared to the telemetry unit group one could argue that there may be a difference in the rate of ischemia, but we did not have the power to detect a difference. In the current study, the power to detect a 4% difference in the rate of ischemia between the CCU and telemetry unit group was only 19% (186 patients in each group; two-tailed significance level of 0.05). In order to achieve 80% power given the parameters in our study (i.e., two-tailed significance level of 0.05; 4% difference in the rate of ischemia) we would have needed 1,211 patients in each group. Finally, 80% power could have been achieved with the

current study parameters of, (1) 186 patients in each group, and, (2) two-tailed significance level of 0.05), if the effect size (difference in the rate of ischemia between CCU versus telemetry unit) had been 12%, rather than 4%. For instance, a statistically significant difference between the two groups would have been observed if 15% of the telemetry unit group had ischemia, and 27% of the CCU group, or vis-a-versa. While it could be questioned that this investigation was statistically underpowered, the rate of ischemia in the present study is similar to that reported in previous investigations assessing similar angina patients (Dellborg et al., 1992; Larsson et al., 1992; Patel et al., 1996; Von Essen et al., 1984; Wilcox et al., 1990). In these studies, the prevalence of transient ischemia as detected with ST monitoring is 20% (range 10% to 43%). Because the rate of ischemia in our study is in agreement with prior investigations it is likely that our study was comprised of a representative sample of angina patients. This supports the conclusion that there is not a difference in the rate of ischemia between angina patients treated in the CCU from 1994 to 1996 compared to angina patients treated in the telemetry unit from 1997 to 2000.

It was hypothesized that the recent group of angina patients initially admitted to the telemetry unit would be hospitalized for fewer hours than the CCU group, which would indicate that the current standard of care is based on a "fast track" approach. Surprisingly, in this investigation there was not a difference in hospital length of stay between the two groups, although there was a trend for the telemetry unit group to be hospitalized for fewer hours. In this study, angina patients were hospitalized on average 4 days, which is similar to that reported by Ferrero et al., (1998). This is in contrast, however, to O'Brien et al (1999) who reported that the average length of hospitalization

among angina patients in their study was 2 days. These differences most likely reflect the patients selected for study. For example, in the current investigation only patients with confirmed CAD who were diagnosed with angina (stable or unstable) were included, whereas, O'Brien et al. (1999) included patients presenting for chest pain who did not necessarily have confirmed CAD. Thus, the present study may reflect a higher risk group of angina patients who were treated more conservatively.

In the current study, hospital length of stay was considerably longer among telemetry unit patients with ECG-detected ischemia as compared to patients without ischemia. This finding is in concordance to a prior investigation conducted exclusively in the CCU (Drew et al., 1996). In the present study, there was a trend for the telemetry unit group who had ischemia to have a shorter hospital stay as compared to the CCU group who had ischemia (136 hours telemetry unit versus 165 hours CCU). Because this difference was not statistically significant no conclusions can be drawn about this finding, however, this is an interesting trend, which might suggest that a more aggressive medical approach was used in the more recent group of angina patients who were treated in the telemetry unit. However, whether this translates into an important clinical consequence for patients cannot be determined from the present study.

Although the patients included in this study were recruited from two different studies at two different time periods the data showed that the two groups were similar on the majority of the clinical variables tested. This is not surprising since the inclusion/exclusion criterion used to recruit subjects was the same among the two studies. However, in the present study the two groups differed with regards to five clinical variables. These differences may prove confounding in this study since they may

influence the rate of ischemia between the CCU and telemetry unit groups. For example, in the current study the telemetry unit group was older than the CCU group. Conversely, a higher proportion of the CCU group had prior MI, prior PTCA, or a catheter-based intervention during hospitalization, as compared to the telemetry unit group. In addition, the CCU group had a higher Norris score as compared to the telemetry unit group. Because of these differences one could argue that the CCU patients were a higher risk group compared to the telemetry unit group, which may in turn place them at higher risk for ischemia. Accordingly, logistic regression analysis was performed in order to determine if any of these variables were predictive of ischemia. In agreement with prior studies, the present study did not find that age or prior MI predicted ECG-detected ischemia (Gottlieb et al., 1986; Patel et al., 1996; Wilcox et al., 1990). This study extends these findings by showing that none of the remaining variables tested (i.e., prior PTCA, catheter-based intervention during hospitalization, and Norris score) were predictive of ischemia. Therefore, while there were clinical differences between the CCU and telemetry unit groups in our study these differences did not influence the presence of ischemia.

In the current investigation, there were differences between the two groups with regards to two variables related to ST monitoring; (1) time from hospital admission to start of ST monitoring, and (2) total ST monitoring time. Because these differences may have influenced the rate of ischemia in this study, logistic regression analysis was done to evaluate the likelihood that these variables were predictive of ischemia. The first ST monitoring variable that was compared between the two groups was time from hospital admission to start of ST monitoring. This might be an important consideration because

there are studies which show that ischemic episodes are most likely to occur within the first 24 hours of hospitalization presumably because the plaque(s) responsible for acute ischemia may not have stabilize until well after treatment for on-going ischemia has been initiated (Braunwald, 1989; Klootwijk et al., 1997). Therefore, a delay from hospital admission to start of ST monitoring could influence the detection rate of ischemia. In the current investigation, the time from hospital admission to start of ST monitoring did not differ when comparing the CCU group to the telemetry unit group (15 hours CCU; 19 hours telemetry unit). However, there were differences when the groups were separated into subgroups based upon the initial admitting site. For instance, ST monitoring was initiated sooner following hospital admission among the subgroup of CCU patients initially admitted to the CCU compared to the group of telemetry unit patients initially admitted to the telemetry unit (9 hours CCU versus 19 hours telemetry unit). Conversely, ST monitoring was initiated much later among the subgroup of CCU patients initially admitted to the telemetry unit then the CCU as compared to the telemetry unit group initially admitted to the CCU then the telemetry unit (54 hours CCU versus 26 hours telemetry unit). The data did not show that time from hospital admission to start of ST monitoring was predictive of ischemia. Although the findings in the present study did not indicate that time from hospital admission to start of ST monitoring was predictive of ischemia, it should be pointed out that the mean time from hospital admission to start of ST monitoring in our study was 17 hours. Therefore, it is likely that ischemia during these early hours after hospital admission was missed. This is not only an important limitation in the design of our study, which should be addressed in future studies, but an

important clinical limitation since timely recognition of ischemia early on in the course of hospitalization might help guide therapies that could salvage myocardial tissue.

In the current investigation, ST monitoring was maintained for a longer time period in the CCU group as compared to the telemetry unit group (34 hours CCU versus 26 hours telemetry unit). This might be an important consideration in this study since the rate of ischemia might be influenced by the number of total hours a patient was monitored. Accordingly, logistic regression analysis to determine the likelihood that this variable was an independent predictor of ischemia was undertaken. The data showed that total ST monitoring time was predictive of ischemia. Specifically, for every one-hour increase in ST monitoring time a patient was 1.03 times more likely to experience ECG-detected ischemia. This would suggest that the rate of ischemia may have been higher among the more recent angina group monitored in the telemetry unit had ST monitoring been maintained for a longer period of time. It should be pointed out that ST monitoring was not maintained throughout a patient's entire hospitalization in either study, hence, it is likely that the rate of ischemia has been under-reported in both of these studies. This is an important methodological limitation of the current study that should be addressed in future studies. Clinically, continuous ST segment monitoring throughout a patient's entire hospitalization would likely be useful since this technology could be used to identify patients who might benefit from more aggressive therapies aimed at abolishing ischemia prior to hospital discharge. Conversely, continuous ST monitoring might be a useful tool for identifying patients without ischemia who could be safely discharged home.

This report confirms previous observations regarding the importance of transient myocardial ischemia detected with ST monitoring in angina patients (Klootwijk et al., 1997; Langer et al., 1989; Patel et al., 1996). Patients who experience ECG-detected ischemia have a worse hospital course than patients who do not experience ischemia. In the current investigation, patients who experienced ECG-detected ischemia, whether in the CCU or the telemetry unit, were more likely to have hypotension requiring intervention, acute MI after admission, or abrupt closure after PTCA or stent. The present study is unique in that this it is the first to describe this association in the telemetry unit setting, which is important given the current trend to treat angina patients in the telemetry unit setting rather than the CCU. In this study, telemetry unit patients who experienced ischemia, which was largely asymptomatic, had a significantly more complicated hospital course, which was characterized by shock, acute MI after admission, or transfer from the telemetry unit to the CCU for more aggressive therapy(s) due to acute complications. This would suggest that ST segment shifts are an important prognostic marker that can identify high-risk angina patients treated in the telemetry unit patients.

In summary, the present that included patients from a relatively recent time period (1997 to 2000) showed that ischemia was not uncommon among patients admitted to the telemetry unit for treatment of angina. Moreover, in the current investigation there was a strong relationship between the presence of ischemia in angina patients treated in the telemetry unit setting and untoward hospital events, such as shock, acute MI after admission, abrupt closure after stent, or transfer from the telemetry unit to the CCU for more aggressive therapy due to acute complications. This report supports the need for

future randomized studies in order to determine if on-line ECG ST monitoring can be used in the telemetry unit setting to guide therapies and ultimately improve patient outcomes.

Prognostic Value of 12-Lead ST Monitoring in the Telemetry Unit Setting

In-Hospital

The second aim of this study was to further describe the consequences of ischemia in the telemetry unit setting and extend our analysis to include patients hospitalized in the telemetry unit setting for treatment of an acute coronary syndrome (i.e., angina, acute MI, congestive heart failure). Overall, 17% of patients treated in the telemetry unit setting experienced ECG-detected ischemia. Specifically, 15% of the angina patients experienced ischemia, and 23% of the acute MI patients experienced ischemia. This is in agreement with the prevalence rate reported in prior investigations in similar patient groups. For example, the prevalence of ischemia in patients with angina ranges from 10% to 43% (Dellborg et al., 1992; Larsson et al., 1992; Patel et al., 1996; Von Essen et al., 1984; Wilcox et al., 1990). The prevalence of ischemia among patients with acute MI ranges from 14% to 27% (Bonaduce et al., 1991; Chandra et al., 1993; Currie et al., 1993; Gill et al., 1996; Petretta et al., 1992; Silva et al., 1993). Thus, transient ischemia as detected with continuous ST segment monitoring is not uncommon among patients diagnosed with acute coronary syndromes who are treated in the telemetry unit setting.

In agreement with previous studies, the current investigation showed that in-hospital complications were significantly higher among patients who had ECG-detected ischemia as compared to patients without ECG-detected ischemia (Barbagelata et al., 1995; Betriu et al., 1998; Drew et al., 1996; Klootwijk et al., 1998; Langer et al., 1989; Stone et al.,

1990). Among the group with ischemia in the present study, 46% of the patients experienced an adverse hospital outcome. This is in concordance to that reported by Langer et al (1989) who showed that 55% of the patients with ECG-detected ischemia experienced an adverse hospital outcome. However, this is considerably higher than the rate of adverse hospital outcomes reported by other researchers, which ranges from 12% (Barbagelata et al., 1995) to 29% (Betriu et al., 1998). The higher rate of adverse outcomes in the present study may be explained by the fact that, like Langer et al (1989) the current investigation included soft end points (i.e., shock, arrhythmia requiring intervention, pulmonary edema, or urgent CABG surgery). This is in contrast to those studies with lower rates of adverse hospital outcomes that included only hard end point, that is, MI and death (Barbagelata et al., 1995; Betriu et al., 1998; Klootwijk et al., 1998; Stone et al., 1990). In the current investigation, if only death and MI were used to determine adverse hospital outcomes, 28% of the group with ischemia experienced an adverse hospital outcome, which is similar to that reported in previous studies that considered only MI and death as end points. While it could be questioned whether soft endpoints should be included, the present study highlights an important association between ECG-detected ischemia and adverse outcomes that incur significant consequences to patients that may result in longer, thus more costly, hospital admissions.

In this study, patients who had ECG-detected ischemia were 8.5 times more likely to experience an adverse hospital outcome and 8.7 times more likely to die or have an MI in the hospital, even after controlling for known high-risk clinical variables such as older age, female sex, prior MI, and evidence of heart failure.

Similar to prior studies, in the present study ischemia was associated with transfer from the telemetry unit to the CCU for more aggressive therapy due to complications among angina and MI patients (Singer et al., 1981; Stewart & Voss, 1997). The data showed that among the group who required transfer to the CCU, patients diagnosed with angina were more likely to be transferred as compared to patients diagnosed with acute MI patients, which is in agreement with that of Stewart & Voss (Stewart & Voss, 1997). In the current investigation, this might reflect a greater degree of plaque stabilization among the MI group since a higher proportion were treated with a catheter-based intervention (i.e., PTCA, or stent) compared to the angina group (85% MI versus 50% angina). In the aforementioned studies it is important to consider that chest pain was used as the only indicator of ischemia. In the present study, prior to unplanned transfer from the telemetry unit to the CCU, patients experienced ST segment changes, most of which were asymptomatic. This would imply that ST monitoring could be used to help identify patients that may benefit from anti-ischemic therapies prior to acute complications that might necessitate transfer to the CCU.

Out of Hospital

In contrast to other studies using ECG monitoring for detection of ischemia (Betriu et al., 1998; Gottlieb et al., 1986; Gottlieb, Weisfeldt, Ouyang, Mellits, & Gerstenblith, 1987; Nademanee et al., 1987), the present investigation did not demonstrate a difference in the rate of hospital re-admission, MI or death at long-term follow-up between patients with and without ischemia, although the trends we found were similar to prior studies. This may be due to the small number of patients who died, or had an MI, and because hospital re-admission for treatment of an acute coronary syndrome was relatively

uncommon. Therefore, the ability to determine if ECG-detected ischemia was predictive of an unfavorable outcome at 90-days in the current investigation was limited. Nevertheless, among the small number of MI patients we did find that ECG-detected ischemia identified one patient who died within the 90-day follow-up period.

It is not surprising that there was not find a difference in the rate of out-of hospital complications at 90-days between patients with and without ischemia because the current investigation did not have sufficient power to detect a difference. For example, based on a 15% rate of ischemia, a total sample size of 340 patients (51 patients with ischemia versus 289 without ischemia) would have been required in order to detect a significant difference between the group of patients with ischemia compared to the group without ischemia if 17% of the ischemic group experienced a poor outcome at 90-days compared to 3% of the group without ischemia. Obviously, the 181 patients included in this analysis was well below the number of patients required. In the present study, there was a trend for the group with ischemia to have a higher rate of complications at 90-days compared to the group without ischemia, therefore, it is possible that there is a difference in the rate of complications at 90-days between patients with and without ischemia. However, because there was not sufficient power to detect a difference in this study, no conclusions with regards to this variable can be made from our study.

12-Lead ECG versus Routine Telemetry Unit Leads V1 or Lead II

Previous studies in patients with angina demonstrate that 12-lead ECG monitoring is superior for ischemia detection compared to one or three lead ECG monitoring (Drew & Tisdale, 1993; Klootwijk et al., 1997; Krucoff et al., 1990). This is in agreement with the current study findings, which showed that of the 89 total ischemia events detected with

the 12-lead ECG, only 27 (30%) exceeded 100 μV of ST deviation in either of the two most commonly selected telemetry unit ECG leads, V1 or lead II (Drew, Ide, & Sparacino, 1991). Importantly, because most telemetry unit ECG monitoring systems are capable of displaying only one ECG lead at the central monitoring station it is likely that fewer than 30% of the events would have been detected. For instance, if only V1 were selected for viewing at the central monitoring station, only 10% of the ischemic events would have exceeded 100 μV ST deviation. If lead II was selected as the single lead for viewing at the central station, only 17% of the ischemic events would have exceed 100 μV ST deviation. Therefore, 12-lead ST segment monitoring significantly increases the detection rate of ischemic episodes as compared to either V1 or lead II.

In the present study, ST segment deviation occurred in all of the 12-ECG leads, however, ST changes occurred most often in the precordial leads V2 through V5, rather than the limb leads. This finding is in agreement with other investigations that have shown that the addition of the precordial leads significantly improves ischemia detection (Aldrich et al., 1987; Drew & Tisdale, 1993; Klootwijk et al., 1997; Mizutani et al., 1990). In the current investigation, the limb leads ST events were most frequently present in lead II, and among the precordial leads most ST events occurred in V3. Hence, if only two leads were available to the telemetry unit nurse, leads II and V3 would be most valuable. This is in contrast to previous studies. For example Klootwijk et al (1997), showed that leads III and V2 were the two most valuable leads for ischemia detection. While other investigators have shown that the two most valuable leads are leads III and V3 (Aldrich et al., 1987; Bush et al., 1990; Drew & Tisdale, 1993). The discrepancies reported in these studies probably reflect the dynamic physiological

mechanisms responsible for ischemia in patients with acute coronary syndromes that result in ST changes in different ECG leads. For instance, myocardial ischemia due to total coronary occlusion most often result in ST elevation, which reflects an injury pattern in the leads that lie over the ischemic myocardial zone. In contrast, ischemia may be demand-related in patients with "fixed" coronary lesions. In this case, the demand for myocardial oxygen exceeds the blood supply. The typical ECG pattern of demand-related ischemia is ST segment depression in several ECG leads with V5 most often reflecting maximal ST depression (Quyyumi, 1992). In this investigation, most ST episodes were characterized by ST depression, however, nearly 25% of the ST episodes were characterized by ST segment elevation. In addition, ST changes occurred in several myocardial zones. For example, most of the events occurred in the anterior myocardial zone (48%), the remaining events occurred in the inferior myocardial (8%), both zones (19%), or in a zone other than the anterior or inferior zone (25%). In conclusion, because patients with acute coronary syndromes are at risk for both ST elevation and ST depression events that may occur in several myocardial zones, two-lead ECG monitoring is insufficient for ischemia detection in the telemetry unit setting. The findings from this investigation, support the current recommendation which states that all 12 ECG leads are needed in order to accurately detect ischemia (Drew et al., 1999a).

Silent versus Symptomatic Ischemia

In agreement with previous studies in patients with acute coronary syndromes, the vast majority of patients in our study did not experience chest pain during ECG-detected ischemia (Drew et al., 1998a; Gottlieb et al., 1986; Klootwijk et al., 1998; Langer et al., 1992; Nademanee et al., 1987; Romeo et al., 1992). Anginal symptoms, which included

both chest pain and or an anginal equivalent, occurred in only 26% of the patients in our study who had ECG-detected ischemia. Of the 89 total ischemic events, only 19 events (22%) were accompanied by chest pain. Clinical symptoms are important because they lead patients to alert the hospital staff of potential ischemia, which often sets in motion treatment strategies aimed at abolishing on-going ischemia. Importantly, the present study shows that over three-quarters of the patients with ECG-detected ischemia were unaware of its presence because they did not complain of chest pain or an anginal equivalent during ischemia. This would imply that continuous monitoring of the ECG for ST segment changes could substantially improve the detection rate of ischemia in patients diagnosed with acute coronary syndromes.

In agreement with prior investigations, there was not find significant differences between the group of patients with silent ischemia compared to the group of patients with symptomatic ischemia with regards to age, ethnicity, sex, or diabetes (Gottlieb et al., 1987; Romeo et al., 1992). One interesting finding in the current investigation, was the disproportionate number of non-Caucasian patients who had symptomatic ischemia (10% non-white versus 90% white). Prior investigations in patients with acute MI or angina have shown that non-white patients who present to emergency departments for treatment of these disorders are more likely to report atypical symptoms, such as shortness of breath or fatigue, as compared to white patients (Clark, Adams-Campbell, Maw, Bridges, & Kline, 1990; Lee, Bahler, Chung, Alonzo, & Zeller, 2000; Pope et al., 2000). Based on these findings, one could argue that symptomatic ischemia in non-white patients was under-reported because atypical symptoms as representing ischemia were not considered. However, in the present study symptomatic ischemia was defined as any documented

patient complaint of chest pain, pressure, heaviness, tightness, squeezing, or dullness in the center of the chest. In addition, any anginal equivalents such as diaphoresis, shortness of breath, nausea, jaw, neck or left arm pain was counted as an ischemic symptom. Thus, the definition of ischemia in the present investigation included many atypical symptoms. However, fatigue was not included as an indicator of ischemia, therefore, it is possible that ischemia was not recognized among patients who had this symptom. It is important to consider that because there were multiple data collectors involved with the data collection, there may be inconsistencies with regards to what questions were asked related to symptoms. Therefore, it is possible that atypical symptoms may not have been documented. Although this was an interesting finding, the number of patients who had ischemia in our study was relatively small; therefore, it may not appropriate to generalize these findings. Because descriptions of chest pain are often a primary screening factor for patients suspected of having ischemia, future studies should be conducted in order to determine the influence that race may have on ischemia symptoms. Regardless, it should be emphasized that anginal symptoms were uncommon among all of the patients with ECG-detected ischemia. This reiterates the importance of establishing reliable, preferably non-invasive, clinical tools that can be used to detect ischemia.

Limitations/Strengths

There are several limitations in the present study that should be noted. First, this study was a secondary analysis. Therefore, the data collection methods, inclusion/exclusion criteria, and variables collected were predetermined. These predetermined factors may

be limitations or strengths, and thus, should be consider when generalizing the findings of this study.

One limitation of this study was the time delay from hospital admission to the start of ST monitoring. In the present study, among the group of patients who were initially admitted to the telemetry unit, ST monitoring was started on average 19 hours after hospital admission to the telemetry unit. Because the early hours of hospital admission, before pharmacological interventions have taken affect, are likely to be the most vulnerable time period for ischemia it is possible that we did not identify all of the patients who had ischemia since ST monitoring was initiated well after patients had been admitted. This would imply that ischemia was under-reported in the present study. This is an important limitation in the design of this study that should be addressed in future investigations. Immediate identification of ST segment changes indicative of ischemia early on in the course of hospitalization would likely be valuable information that might help guide reperfusion therapies that could prevent infarction. However, randomized controlled clinical trials must be conducted in order to determine if ST segment monitoring can be used to guide therapies that could avert MI, and ultimately improve patient outcomes.

Finally, the generalizability of these results may be somewhat limited because consecutive patients admitted to the telemetry unit were not enrolled. Most of the patients that were missed were patients presenting with chest pain rule out MI who were often admitted and discharged home from the telemetry unit in less than 24 hours. For example, among this patient groups it was not uncommon for patients to be admitted to the telemetry unit during the evening hours, go to an exercise treadmill test the following

morning, and then be discharged home in the early afternoon. Because the research assistant in the parent study was not in the hospital during the evening hours from 7 pm to 7 am, ST monitoring was not initiated until the following morning. Unfortunately, the morning hours were very often the time period when many of these patients were scheduled for a treadmill test. As a result, it was not feasible to initiate ST segment monitoring in many of these patients because they were only physically in the telemetry unit setting for a few hours prior to going to their scheduled treadmill test. Therefore, the value of ST segment monitoring in this specific patient group was not addressed in our study. This is an important patient group that should be included in future studies because it is possible that ST segment monitoring might be a valuable tool for identifying patients with ischemia. It is possible that clinicians could utilize ST segment monitoring to make decisions regarding patient care and incorporate ST segment information into triage decisions such as early discharge or more aggressive treatment options, which may result in decreasing the overall cost of care.

Although several limitations have been identified in this current investigation, it is important to identify the strengths of this study design as well. The first strength of this study was the vigorous data collection method used in the parent study to obtain the ECG data. For example, the parent study employed a total of four highly trained researcher nurses who provided 24 hour seven day/week coverage. This intense clinical coverage ensured that high quality ECG data (i.e., correct and consistent lead placement, minimal artifact) was maintained continuously during the ECG monitoring period. This is an important strength in our study that substantially increases the validity of the ECG data.

Additionally, false positive ST changes were minimized during the analysis of the ECG data by employing a standard protocol. For example, in order to limit false positive ST changes due to body position changes the research assistants in the parent study obtained template body position ECG's with patients assuming a supine, left, and right side lying positions. Any potential ischemic event ECG's were then compared to the template ECG's in order to ensure that the observed ST changes were not due to body position changes. In addition, all stored ECG were evaluated using a computer software program which allowed us to eliminate from the analysis any ECG's with a noisy signal, or ECG's demonstrating ST changes due to non-ischemic conditions (i.e., accelerated ventricular rhythm, intermitted ventricular pacer, or intermittent bundle branch block). This cleaned ECG data was then evaluated for ST changes (i.e., ST elevation or depression) indicative of ischemia, and computer generated μV values were used to determine if the ST changes exceeded 100 μV of ST deviation. Computer generated μV measurements are more precise than human measurements, and relevant to this analysis, eliminate human bias.

Future Directions

This investigation shows that continuous ECG ST segment monitoring can be used to identify clinically silent ischemia among telemetry unit patients with acute coronary syndromes. However, future investigations are needed to determine if this technology can be used in real-time to make clinical decisions. Ideally, a randomized controlled clinical trail should be conducted to determine if this technology could be used to improve patient outcomes.

Additionally, studies investigating nursing knowledge and competency regarding ischemia detection should be conducted because telemetry unit nurses will play a pivotal role in ECG monitoring since they are responsible for initiating and maintaining ECG monitoring. Results from such an investigation are likely to identify problem areas where nurse educators might focus educational efforts when instructing nurses on the use of this technology. Furthermore, nurse scientists could utilize this information to test and develop nursing interventions that might improve knowledge and application of this technology, and ultimately improve patient care.

Finally, nurses at all levels of education should continue to identify, through research, how the manufacturers of ECG-ischemia technology might improve this technology. Although continuous ECG ST segment monitoring is a reliable method for ischemia detection, there are design and engineering flaws that must be addressed by the manufacturers of this technology. For instance, current ST monitors do not have the capability to identify common false-positive ST conditions, such as body position changes, or changing ST levels due to non-ischemic conditions (i.e., steeply sloping ST segments, or sudden QRS voltage changes). Improvement of these technological limitations can only be addressed by collaborative efforts between nurse scientists, clinicians, and engineers. Research studies must not only continue to identify these technical limitations, but must also be designed to test technologies that could improve the sensitivity and specificity of ECG ST-segment monitoring.

Conclusions

Prior to this investigation, clinicians had to extrapolate the rate and potential consequences of myocardial ischemia in the telemetry unit setting among patient with

acute coronary syndromes from studies conducted exclusively in the CCU. The present study, which is a secondary analysis of a prospective clinical trial investigating the value of continuous ECG-ischemia monitoring, demonstrates that transient myocardial ischemia is not uncommon among hospitalized patients with acute coronary syndromes who are treated in the telemetry unit setting. Moreover, this study shows that telemetry unit patients with transient ST changes, which are largely asymptomatic, are at increased risk for serious in-hospital events including MI and death, compared to patients who do not experience ST changes.

With the current emphasis on cost efficiency and decreased utilization of high level hospital and nursing care (i.e., CCU), our findings support the need for a non-invasive tool in the lower cost alternative telemetry unit that can identify patients with ischemia who may benefit from the multitude of currently available non-ischemic therapies. This study provides support for the value of continuous ECG monitoring for identification of ST changes indicative of ischemia. Patients with transient ST changes represent a high-risk group who may benefit from aggressive anti-ischemic therapies. In contrast, patients without transient ST changes represent a low risk group of patients who may be suitable for early discharge. This simple, non-invasive monitoring method adds prognostic information above the commonly used variables of age, sex, and heart failure among patients with acute coronary syndromes who are treated in the telemetry unit setting.

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