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Journal

The Journal of Cardiovascular Nursing, 31(4)

ISSN

0889-4655

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Publication Date

2016-07-01

DOI

10.1097/jcn.0000000000000310

Peer reviewed



Among Unstable Angina and Non–ST-Elevation Myocardial Infarction Patients, Transient Myocardial Ischemia and Early Invasive Treatment Are Predictors of Major In-hospital Complications

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Background: Treatment for unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI) is aimed at plaque stabilization to prevent infarction. Two treatment strategies are (1) invasive (ie, cardiac catheterization laboratory <24 hours after admission) or (2) selectively invasive (ie, medications with cardiac catheterization laboratory >24 hours for recurrent symptoms). However, it is not known if the frequency of transient myocardial ischemia (TMI) or complications during hospitalization varies by treatment. **Purpose:** We aimed to (1) examine occurrence of TMI in UA/NSTEMI, (2) compare frequency of TMI by treatment pathway, and (3) determine predictors of in-hospital complications (ie, death, myocardial infarction [MI], pulmonary edema, shock, dysrhythmia with intervention). **Methods:** Hospitalized patients with coronary artery disease (ie, history of MI, percutaneous coronary intervention/stent, coronary artery bypass graft, >50% lesion via angiogram, or positive troponin) were recruited, and 12-lead electrocardiogram Holter initiated. Clinicians, blinded to Holter data, decided treatment strategy; offline analysis was done after discharge. Transient myocardial ischemia was defined as more than 1-mm ST segment \uparrow or \downarrow , in more than 1 electrocardiographic lead, more than 1 minute. **Results:** Of 291 patients, 91% were white, 66% were male, 44% had prior MI, and 59% had prior percutaneous coronary intervention/stent or coronary artery bypass graft. Treatment pathway was early in 123 (42%) and selective in 168 (58%). Forty-nine (17%) had TMI: 19 (15%) early invasive, 30 (18%) selective ($P = .637$). Acute MI after admission was higher in patients with TMI regardless of treatment strategy (early: no TMI 4% vs yes TMI 21%; $P = .020$; selective: no TMI 1% vs yes TMI 13%; $P = .0004$). Predictors of major in-hospital complication were TMI (odds ratio, 9.9; 95% confidence interval, 3.84–25.78) and early invasive treatment (odds ratio 3.5; 95% confidence interval, 1.23–10.20). **Conclusions:** In UA/NSTEMI patients treated with contemporary therapies, TMI is not uncommon. The presence of TMI and early invasive treatment are predictors of major in-hospital complications.

KEY WORDS: acute coronary syndrome therapy, electrocardiography, ST-segment monitoring, transient myocardial ischemia

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This study was supported by grant R21NR011202 (M.M.P., principal investigator) provided by the National Institutes of Health.

The authors have no conflicts of interest to disclose.

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DOI: 10.1097/JCN.0000000000000310

Acute coronary syndrome is an umbrella term used to describe 3 specific diagnoses: unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction. Of these, UA and NSTEMI represent the largest proportion of acute coronary syndrome patients (two-thirds), and both are clinically challenging to diagnose because these patients often have atypical symptoms, and nonspecific or no electrocardiographic (ECG) changes.^{1,2} While biomarkers (ie, troponin, CK-MB [creatin kinase–myocardium]) are the criterion standard for identifying myocardial infarction (MI), these biomarkers are not sensitive to transient myocardial ischemia (TMI) seen among acute coronary syndrome patients with UA and may not become positive in patients with NSTEMI for several hours after symptom onset.³ Therefore, the treatment goal in UA/NSTEMI is timely identification of myocardial ischemia or preinfarction so that treatment(s) to optimize blood flow to the myocardium can be administered immediately. Because nurses provide ongoing assessment of patients for symptoms and ECG changes associated with acute coronary syndrome, their role is pivotal in the detection of myocardial ischemia.

Currently, 2 treatment pathways are used: early invasive, which includes anti-ischemic, antithrombotic, and antiplatelet medications with coronary angiography in fewer than 24 hours after admission, or selectively invasive, which include pharmacological management as above and angiography (typically >24 hours after admission) only if a patient fails to respond to intensive medical management (eg, refractory angina, angina at rest, etc) or has objective evidence of ongoing ischemia (eg, dynamic ST-segment changes, positive biomarkers, etc).³ Data from a number of randomized clinical trials and meta-analyses show that long-term outcomes, 2 to 5 years, are better in UA/NSTEMI patients when an early invasive strategy is used versus a selectively invasive approach.^{4–13} While long-term outcomes are more favorable when an early invasive approach is used, some of these studies showed that death and MI are higher during the index hospitalization when an early invasive strategy is used, indicating increased hazard for early invasive.^{9,14–16} Another important consideration is that crossover from selectively invasive to invasive (ie, percutaneous coronary intervention/stent or coronary artery bypass graft surgery) is not uncommon.^{3,8,13,17,18} These studies show that both strategies have inherent risks/benefits; thus, current recommendations from the American College of Cardiology/American Heart Association guidelines for management of NSTEMI/UA emphasize the need to carefully risk stratify each patient when choosing the optimal treatment pathway.^{1,2} There is a need for additional diagnostic information during hospitalization that might help clinicians decide which patients are responding

well to anti-ischemia therapies and which need more aggressive management.

The 12-lead electrocardiogram is an important part of risk stratification in UA/NSTEMI because it has advantages over symptoms, which are often unreliable or nonexistent,^{19–25} or biomarkers, because ECG changes may precede the elevation of these blood tests.^{1,3} Most commonly, clinicians obtain serial resting 12-lead electrocardiograms, at 15- to 30-minute intervals, which are within guideline recommendations,³ and then apply dual lead continuous bedside ECG monitoring, ideally with ST-segment monitoring software activated,^{3,26,27} in order to expedite prompt detection of dynamic ST-segment changes indicative of ischemia. Several problems exist with these ECG approaches: (1) plaque rupture in acute coronary syndrome is dynamic, with cycles of occlusion and reperfusion; therefore, intermittent (“snap-shot”) electrocardiograms will miss acute ST-segment changes; (2) typical bedside monitors utilize only 2 to 6 ECG leads, rather than the recommended 12 leads; and (3) ST-segment monitoring software is vastly underutilized because it is plagued by a high number of false-positive alarms.^{26–32} Given the challenges clinicians face when risk stratifying UA/NSTEMI patients for early versus selectively invasive treatment, there is a need to reexamine the potential value of continuous 12-lead ECG ST-segment monitoring for detection of ischemia during the initial hospital phase. Continuous ECG information could add to our understanding of how these 2 treatment strategies evolve during the acute phase of treatment, which could ultimately be used to guide treatment for UA/NSTEMI.

The purpose of this study was 3-fold: (1) examine the occurrence of TMI, in a group of hospitalized UA/NSTEMI patients treated with contemporary therapy; (2) compare the frequency of TMI by treatment pathway, early versus selectively invasive; and (3) determine if demographic data, clinical history, treatment strategy, or TMI predict serious in-hospital complications.

Materials and Methods

The COMPARE study (R21 NR-011202; M.M.P., principal investigator), described previously,³³ was a prospective observational study designed to examine the frequency and consequences of TMI in hospitalized patients with UA/NSTEMI. In the COMPARE study, early invasive was defined as cardiac catheterization at 24 hours or less after admission, with percutaneous coronary intervention/stent or coronary artery bypass graft surgery if indicated. Selectively invasive was defined as pharmacological therapies, with cardiac catheterization at more than 24 hours after hospital admission for failed aggressive medical treatment, as indicated by recurrent symptoms, ECG changes, or positive stress test. Prior to recruitment and enrollment, approval from local institutional review boards was obtained, and all patients provided written informed consent prior to participation.

Sample/Settings

Inclusion criteria were as follows: (1) admitted for treatment of UA, NSTEMI, or suspected acute coronary syndrome and (2) English speaking. Patients were excluded if, admitted for ST-elevation myocardial infarction, they were comatose or had a major psychiatric disorder, isolation precautions, or left bundle-branch block or ventricular pacing because these conditions distort the ST-segment, making it difficult to reliably interpret the electrocardiogram for ischemia.²⁷

During the hours of 7 AM to 5 PM, Monday through Friday, any patient presenting to the hospital for symptoms suggestive of acute coronary syndrome were invited to participate. Reported in this article are only those with confirmed coronary artery disease defined by greater than 50% coronary lesion assessed by angiography, prior MI (ie, medical record or Q waves on a 12-lead electrocardiogram), positive biomarkers (ie, troponin, CK-MB), or prior diagnosis of coronary artery disease (ie, medical record, stent, coronary artery bypass graft surgery).

Data were collected at 3 private hospitals: 2 in Northern Nevada (one 380 beds and the other 720 beds) and 1 in Northern California, with 366 beds; each hospital had well-developed cardiac service lines, board-certified cardiologists, and a full range of invasive and noninvasive treatments (eg, cardiac catheterization, operating rooms, cardiac rehabilitation, etc).

Twelve-Lead Holter Electrocardiographic Data

A 12-lead ECG Holter recorder (Mortara Instruments, Milwaukee, Wisconsin) was applied to patients meeting inclusion criteria. The Holter recorder was a “black box”; hence, data were not available to clinicians for decision making, and there were no alarms generated: offline analysis (described below) was conducted after hospital discharge. To ensure high-quality ECG data, the skin on the torso was carefully prepared to remove any dirt, oils, or creams that might interfere with signal quality; chest hair was cautiously clipped if necessary; radiolucent ECG electrodes were applied in the Mason-Likar limb lead configuration so as to not interfere with radiographs; and template electrocardiograms were obtained with patients assuming supine, right-side, and left-side lying positions for use during offline analysis to identify false-positive electrocardiograms because of positional changes.^{34–36} The ECG Holter recorder remained in place until the patient was discharged. All patients were maintained on the hospital’s bedside ECG monitor (5- or 6-lead system) as per the hospital protocol. The research assistant made frequent rounds during the day to maintain accurate placement of the ECG electrodes/lead wires and reapply any that had fallen off or been taken off for procedures (eg, cardiac catheterization, echocardiogram, x-ray, etc). The research

assistant also retrieved demographic, clinical, and outcome data from the electronic health record.

ECG Ischemia Analysis

The 12-lead ECG Holter data were downloaded to a research computer and analyzed after hospital discharge using H-Scribe Analysis System (Mortara Instruments). Transient myocardial ischemia was defined as ST deviation (elevation or depression) of 100 μ V or greater in 2 or more ECG leads at 60 seconds or longer.²⁷ The H-Scribe software displays 24 hours of ECG tracings into trended data for easy inspection and semiautomatically analyzes and codes ischemic events. While the H-Scribe provides semiautomated analysis, all of the ECG data were manually overread by the principal investigator (M.M.P.), who was blinded to treatment group and clinical outcomes. In cases where there were questions about whether TMI was present/absent, 2 coinvestigators (M.G.C., T.M.K.) reviewed the ECG data, and consensus was reached.

Outcome Measures

The 6 in-hospital complications, identified from electronic health record review, are listed in Table 1.

Statistical Analysis

Data were analyzed using SPSS 22.0 (IBM Corporation 1994, 2014, Armonk, New York). Descriptive statistics were used to report demographic (ie, age, gender, and ethnicity) and clinical information including medical history (ie, prior angina, prior MI, hypertension, hyperlipidemia, diabetes, prior cardiac procedures, and coronary artery disease). In addition, descriptive statistics were used to examine the procedures performed (ie, percutaneous coronary intervention/stent, coronary artery bypass graft surgery, treadmill test, and echocardiography) and medications administered. These values are expressed as means (SD) and percentages for the entire sample and by treatment group. Categorical variables were analyzed with χ^2 analyses, with 2-sided Fisher exact test *P* values reported. Two-tailed unpaired Student *t* tests were used to compare continuous variables. *P* < .05 was adopted as the critical value to determine whether differences between the 2 groups were statistically significant.

The occurrence of each complication was examined initially by χ^2 analyses. To determine if patients with TMI compared with patients without TMI had more major in-hospital complications, a multiple logistic regression analysis was conducted. The independent predictors entered into the model were covariates known to increase adverse events in acute coronary syndrome patients including age, gender, ethnicity, history of angina, MI, percutaneous coronary intervention, coronary artery bypass graft surgery, diabetes, hypertension,

TABLE 1 List of 6 In-hospital Complications Identified From Review of the Electronic Health Record Following Hospital Discharge

1. Dysrhythmia requiring intervention with antidysrhythmic drugs, defibrillation, pacemaker
2. Hemodynamic compromise requiring intervention with drugs, intra-aortic balloon pump counterpulsation, pacemaker
3. New-onset pulmonary edema during hospitalization requiring treatment with diuretics
4. Unplanned transfer from the telemetry unit to coronary care unit because of acute complications, including unrelieved chest pain, ECG changes, acute heart failure, dysrhythmias, hemodynamic compromise, or cardiac arrest
5. Cardiovascular-related death
6. MI after hospital admission^{51,52}
 - Nonprocedural MI: CK-MB greater than upper limit of normal or >50% over previous level
 - Procedural MI: CK-MB >3 times upper limit of normal or >50% over previous post PCI/stent

Abbreviations: CK-MB, creatine kinase–myocardium; ECG, electrocardiogram; MI, myocardial infarction; PCI, percutaneous coronary intervention.

and hypercholesterolemia, as well as treatment group (early or selective) and presence of TMI detected with 12-lead ECG Holter. The multiple logistic regression analysis examined the odds afforded by each covariate for the occurrence of the dependent variable, any adverse in-hospital complication. Odds ratios and adjusted odds ratios, with 95% confidence intervals (CIs), were calculated.

Results

Of the 488 total subjects enrolled, 174 (36%) did not have confirmed coronary artery disease, and 23 (5%) had left bundle-branch block or a ventricular pacemaker, and therefore these subjects were excluded; hence, the final sample was composed of 291 patients. The mean time from hospital presentation to enrollment was 6 (SD, 5) hours, and mean monitoring time was 28 (SD, 20) hours. Of the 291 patients, 123 (42%) were treated with an early invasive strategy, and 168 (58%) with a selectively invasive strategy. Sample characteristics were typical of those with coronary artery disease with regard to age (65 [SD, 12] years) and gender (male, 66%) and did not differ by treatment strategy (Table 2). Of the mostly white sample (91%), a higher proportion of ethnic minorities were in the selectively invasive group, 12% versus 5%; $P = .04$. Patients with a history of prior angina were more likely to be treated with an early invasive approach (49% vs 24%; $P = .001$), whereas those with prior coronary artery disease (56% vs 81%; $P = .001$), MI (32% vs 53%; $P = .001$), or coronary artery bypass graft surgery (15% vs 31%; $P = .001$) were more often treated with a selectively invasive strategy. Prior percutaneous coronary intervention was equivalent by group. The only risk factor that differed by treatment group was diabetes (23% early vs 38% selective; $P = .007$). While the majority of patients were admitted to the telemetry unit (85%), a higher proportion of early invasive patients were admitted to the coronary care unit (CCU) (18% vs 7%; $P = .006$). There were no differences with regard to prescribed medication by treatment group, except for β -blocker (87% early vs

71% selective; $P = .002$). Hospital length of stay was longer in the early invasive group, 88 (SD, 92) hours versus 63 (SD, 62) hours; $P = .018$.

Frequency of Transient Myocardial Ischemia by Treatment Strategy

During 8140 hours of 12-lead ECG Holter monitoring in 291 patients, 49 (17%) had 109 total TMI events. Of the 49 patients with TMI events, 19 (15%) were treated with early invasive, and 30 (18%) with selectively invasive ($P = .637$). The mean number of TMI events was 2 (SD, 1) (range, 1–6) and was equivalent by treatment group ($P = .269$). Of the 49 patients, only 16 (33%) experienced symptoms during TMI. A higher number of patients in the early invasive group complained of symptoms (early 10/19 [53%] vs selective 6/30 [20%]; $P = 0.028$). The Figure 1 illustrates transient ischemia in a patient treated with a selectively invasive treatment strategy.

Major In-hospital Complications

Of the 291 patients, 26 (9%) experienced a major in-hospital complication. Regardless of treatment strategy, major in-hospital complications were higher in those with TMI (5% no TMI vs 31% with TMI; $P < .001$). Of the 26 patients who experienced a major in-hospital complication, a higher proportion were in the early invasive group (14% early vs 5% selective; $P = .021$). Table 3 shows comparisons of major in-hospital complications by treatment strategy and absence/presence of TMI. No patient died. Acute MI after hospital admission was higher in patients who experienced TMI regardless of treatment strategy (early: no TMI 4% vs yes TMI 21%; $P = .020$; selective: no TMI 1% vs yes TMI 13%; $P = .004$). Acute pulmonary edema occurred more often in early invasive patients with TMI (no TMI 0 patients vs 16% yes TMI; $P = .003$); however, this was not different in the selective group. Among the early invasive group, a higher proportion with TMI were transferred from telemetry to the CCU because of acute complications (no TMI 2% vs yes TMI 32%; $P = .001$). While more patients with TMI in the selectively

TABLE 2 Demographics, Clinical History, and Hospital Treatment for All Subjects and by Group

Characteristics	Study Sample	Early Invasive	Selectively Invasive	P Early vs Selectively Invasive
	(n = 291)	(n = 123 [42%])	(n = 168 [58%])	
	n (%)	n (%)	n (%)	
Demographics				
Age, mean (SD), y	65 (12)	63 (11)	66 (12)	.062
Gender				
Male	192 (66)	87 (71)	105 (63)	.169
Race				
Asian	6 (2)	0	6 (4)	.046
American Indian/Alaskan Native	5 (2)	3 (2)	2 (1)	
Black	10 (3)	3 (2)	7 (4)	
Pacific Islander	5 (2)	0	5 (3)	
White	265 (91)	117 (95)	148 (88)	
Race comparing nonwhite to white	265 (91)	117 (95)	148 (88)	.040 ^a
Cardiac history				
Prior angina	101 (35)	60 (49)	41 (24)	.001 ^b
Prior coronary artery disease	205 (70)	69 (56)	136 (81)	.001 ^b
Prior acute myocardial infarction	127 (44)	39 (32)	88 (53)	.001 ^b
Prior percutaneous coronary intervention	126 (43)	51 (42)	75 (45)	.633
Prior coronary artery bypass graft	70 (24)	18 (15)	52 (31)	.001 ^b
Risk factors				
Current smoker	65 (22)	34 (28)	31 (19)	.066
High cholesterol	209 (72)	87 (71)	122 (73)	.792
High blood pressure	212 (73)	83 (68)	129 (77)	.084
Diabetes	91 (31)	28 (23)	63 (38)	.007 ^a
Admission unit				
Cardiac telemetry	244 (85)	100 (81)	144 (86)	.336
Cardiac intensive care	34 (12)	22 (18)	12 (7)	.006 ^a
Cardiac medications				
Nitrate	171 (59)	79 (64)	92 (55)	.118
β-Blocker	227 (78)	107 (87)	120 (71)	.002 ^a
Angiotensin-converting enzyme inhibitor	135 (46)	63 (51)	72 (43)	.191
Antiplatelet	275 (95)	118 (96)	157 (94)	.441
Aspirin	272 (94)	118 (96)	154 (92)	.159
Antithrombin	209 (72)	94 (76)	115 (69)	.148
Lipid lowering	224 (77)	101 (82)	123 (73)	.091
Hospital length of stay				
Hours	75 (82)	88 (92)	63 (62)	.018 ^a

Early invasive = pharmacological therapies and cardiac catheterization at 24 hours of hospital admission or less). Selectively invasive = pharmacological therapies, with cardiac catheterization at more than 24 hours after hospital admission for failed aggressive medical treatment, as indicated by recurrent symptoms, electrocardiographic changes (hospital monitor or ordered 12-lead electrocardiogram), or positive stress test.

^a $P < .05$.

^b $P < .001$.

invasive group were transferred from telemetry to CCU, this was not statistically different (no TMI 1% vs yes TMI 7%; $P = .083$). When any major in-hospital complications were combined into 1 variable, patients with TMI, regardless of treatment strategy, had more complications (early: no TMI 8% vs yes TMI 47%; $P = .001$; selective: no TMI 2% vs yes TMI 20%; $P = .001$).

Results of the logistic regression analysis examining whether demographic, clinical history, treatment strategy, or TMI was a predictor of major in-hospital complications are shown in Table 4. Compared with patients without TMI, patients with TMI were 9.9 times more likely to experience a major in-hospital complication (95% CI, 3.84–25.78; $P = .001$), and patients treated

with an early invasive strategy were 3.5 times more likely to have a major in-hospital complication (95% CI, 1.23 to 10.20; $P = .019$).

Discussion

Among hospitalized UA/NSTEMI patients, TMI is not uncommon, occurring in 17%, and its presence is highly predictive of untoward in-hospital complications, particularly MI after admission. This study is unique in that we explore the frequency and consequences of TMI, measured with continuous 12-lead electrocardiogram, comparing groups by contemporary treatment pathway

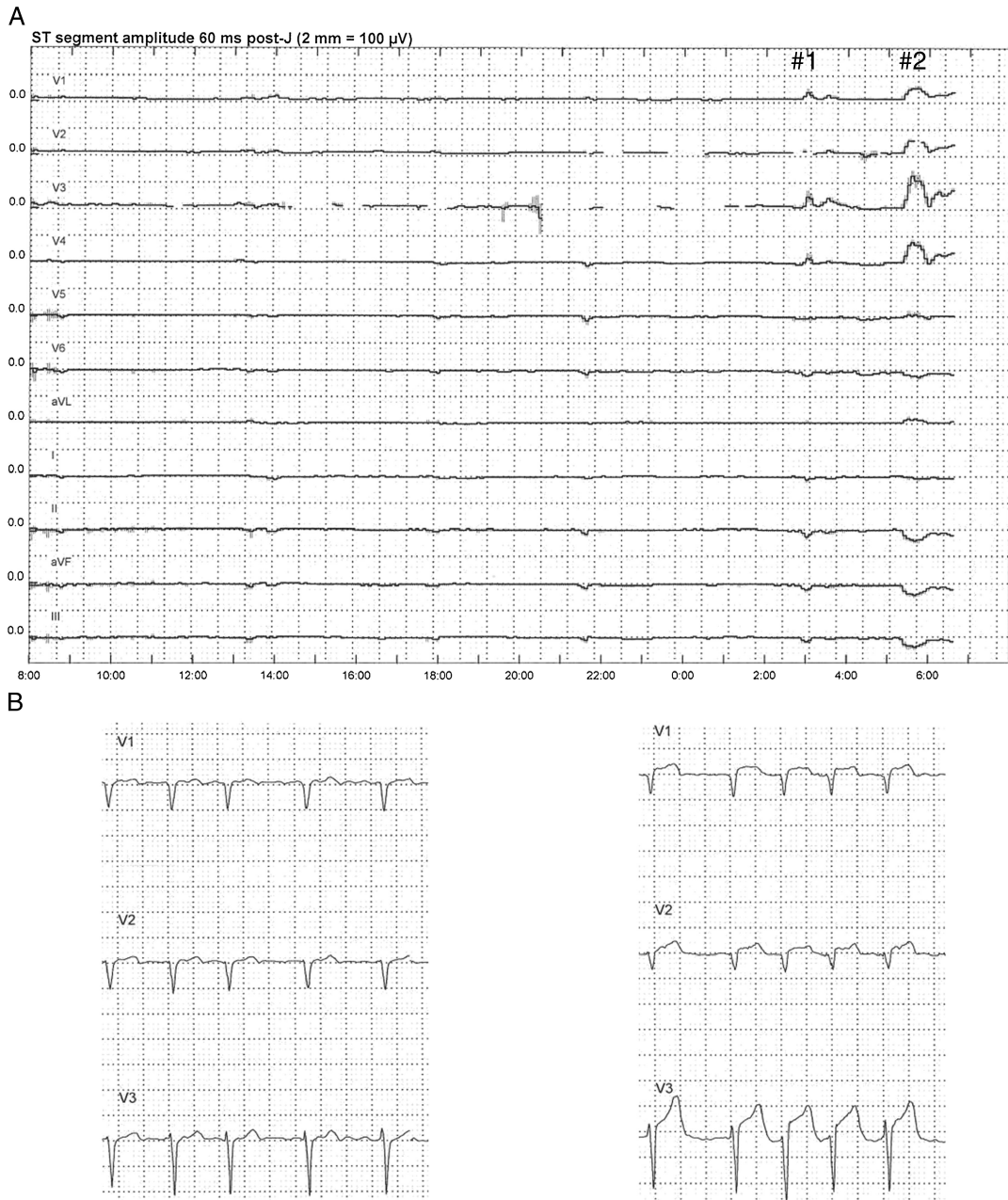


FIGURE 1. The figure (A) illustrates a patient treated with a selectively invasive strategy. A shows an ST-segment trend (y axis, electrocardiographic [ECG] leads; x axis, time). This trend was recorded in a 67-year-old man presenting to the emergency department at 3:45 AM with pain between his shoulder blades and in his right arm. His cardiac history included paroxysmal atrial fibrillation treated with metoprolol and Coumadin; the latter was discontinued for unknown reasons 1 month prior. His initial troponin I was normal, and his 12-lead ECG was unremarkable for acute ischemia. A computed tomographic scan ruled out aortic aneurysm, and he was admitted to the telemetry unit for further workup. At 3:00 AM (23 hours after admission), abrupt ST elevation is seen in leads V₁–V₄, and concomitant ST depression in leads V₆, I, II, aVF, and III. At 3:45 AM, the patient complained of back and right arm pain. The nurse gave the patient a sublingual nitroglycerin, intravenously administered morphine, and obtained a 12-lead ECG. The hospital 12-lead ECG was obtained after the ST changes resolved; hence, ischemia was not diagnosed. The patient went back to sleep. At 5:55 AM, the patient contacted the nurse complaining of 10/10 chest pain in his back and both arms. A hospital 12-lead ECG obtained by the nurse showed ST elevation in leads V₂ and V₃. The cardiologist was phoned, and the patient was taken urgently to the cardiac catheterization laboratory, where a stent was placed in the left anterior descending coronary artery. Of note, are the small ST-segment changes during the day at 1:20 PM, 6:00 PM, and 11:45 PM, likely indicating acute but brief coronary occlusion followed by reperfusion. B, left figure shows leads V₁ to V₃ (1 in the figure), obtained before transient myocardial ischemia. Right figure shows leads V₁ to V₃ (2 in the figure), obtained during transient myocardial ischemia and illustrates ST elevation indicative of complete coronary occlusion.

TABLE 3 Comparison of Major In-hospital Complications by Treatment Strategy, With Groups Divided Further by Transient Myocardial Ischemia Absent/Present (n = 291)

Complication	Early Invasive (n = 123), n (%)			Selectively Invasive (n = 168), n (%)		
	No TMI (n = 104 [85%])	Yes TMI (n = 19 [15%])	P	No TMI (n = 138 [82%])	Yes TMI (n = 30 [18%])	P
Dysrhythmia with intervention	5 (5)	1 (5)	1.000	0	0	0
Hemodynamic compromise	1 (1)	1 (5)	0.268	0	0	0
Pulmonary edema	0	3 (16)	0.003	1 (1)	0	1.000
Transfer from telemetry unit to CCU	2 (2)	6 (32)	0.001	1 (1)	2 (7)	0.083
Death	0	0	0	0	0	0
MI after having been admitted	4 (4)	4 (21)	0.020	1 (1)	4 (13)	0.004
Any major complication	8 (8)	9 (47)	0.001	3 (2)	6 (20)	0.001

Abbreviations: CCU, cardiac intensive care unit; MI, myocardial infarction; TMI, transient myocardial ischemia. Two-sided Fisher exact test is reported.

(early vs selectively invasive). At the outset of this study, we hypothesized TMI would be higher in the selectively invasive group, thinking reperfusion would not be as complete with medications alone, but found there was no difference in the rate of TMI between the groups. Our data indicate that when combined, major in-hospital complications are more common in patients with TMI, regardless of treatment pathway, but are more frequent among patients treated with an early invasive strategy as compared with those treated with a selectively invasive strategy.

Occurrence of Transient Myocardial Ischemia and Comparison by Treatment Pathway

As mentioned, we found that 17% of our sample had TMI (early 15%, selective 18%), which is similar to prior studies.^{23–25,28,30,37–42} Importantly, most of these prior studies are dated; thus, one could argue, they may not represent patients treated with present-day therapies. However, we show that this pathology is still occurring in a relatively high number of UA/NSTEMI patients despite advances in acute coronary syndrome treatment modalities.

Similar to previous reports, we found that only a third of the patients with TMI complained of chest pain or an angina equivalent.^{22,24,25,28,36,37,40,41,43} While this is not a new finding, our study underscores the problem of symptoms as a reliable indicator of myocardial ischemia. It is worth noting that a criterion for failing intensive medical management in patients treated with a selectively invasive strategy is refractory angina, or angina at rest. Given that the vast majority of patients with TMI do not experience symptoms during electrocardiography-detected ischemia, identification of failed medical therapy is very likely to be missed using symptoms alone.

Interestingly, we found that patients treated with an early invasive approach and who had TMI were more likely to experience symptoms as compared with the selectively invasive TMI group. This might suggest ischemic burden was higher in the early invasive group. In a prior study, we reported that patients were more likely to experience symptoms during TMI as the magnitude (microvolts) of ST-segment changes increased.³⁷ Our data highlight the value of continuously recorded 12-lead electrocardiograms as a way to identify transient,

TABLE 4 Multiple Logistic Regression Analysis With Any Major In-hospital Complication Used as the Dependent Variable

Variable	B	P	Odds Ratio	95% Confidence Interval
Age	0.000	.983	1.000	0.959–1.042
Gender (male = 0, female = 1)	−0.612	.278	0.542	0.179–1.638
History angina	0.097	.845	1.102	0.418–2.902
History myocardial infarction	−0.287	.632	0.750	0.232–2.427
History percutaneous coronary intervention	−0.435	.436	0.648	0.217–1.935
History coronary artery bypass graft	0.207	.733	1.231	0.374–4.052
Hypertension	0.392	.483	1.480	0.495–4.425
Hypercholesterolemia	−0.575	.267	0.563	0.204–1.553
Transient myocardial ischemia	2.297	.001 ^a	9.949	3.839–25.784
Early invasive treatment group	1.266	.019 ^a	3.547	1.233–10.204

^aP < .05.

What's New and Important

- Transient myocardial ischemia occurs in nearly 20% of UA and NSTEMI patients and is equivalent by contemporary treatment pathway (early vs selectively invasive).
- Among patients with TMI, only a third experienced symptoms. A higher number of patients in the early invasive group complained of symptoms.
- Clinically important in-hospital complications such as pulmonary edema, MI, and transfer from the telemetry unit to the CCU were associated with TMI in patients with UA or NSTEMI.

mostly silent, ischemia in NSTEMI/UA patients who represent the largest portion of patients presenting for acute coronary syndrome.

Major In-hospital Complication Rates and Predictor of Major In-hospital Complication

Major in-hospital complications were significantly higher in patients with TMI as compared with those without TMI regardless of treatment strategy group. When complications were assessed by group, patients treated with an early invasive strategy and who had TMI were more likely to have MI after admission and acute pulmonary edema and require transfer from the telemetry unit to the CCU because of acute clinical changes. Among the selectively invasive group, those with TMI were more likely to experience MI after admission, and there was only a trend for those with TMI to be transferred from the telemetry unit to the CCU because of acute clinical changes. Our findings are in agreement with others showing the relationship of electrocardiogram-detected TMI and untoward in-hospital complications.^{19,24,25,40,43} Our findings are unique in that we examine not only the influence of TMI on in-hospital outcomes, but further assess this pathology by treatment group. Our finding of higher complication rates among early invasive patients is in contrast to a meta-analysis of a large number of randomized clinical trials with large sample sizes comparing early versus selectively invasive treatment, which showed a nonsignificant trend for higher rates for non-fatal MI among patients treated with an early invasive strategy.¹¹ A possible explanation for this may be how MI after admission was defined in our study compared with the aforementioned clinical trials, dated from 1994 to 2005, which are prior to high-sensitivity troponin tests.

When controlling for known risk factors, logistic regression analysis showed 2 predictors of major in-hospital complication were early invasive treatment (odds ratio, 3.5) and TMI (odds ratio, 9.9). The latter reiterates the sensitivity of TMI to identify high-risk patients who might benefit from more aggressive anti-ischemia therapies.

Limitations

Convenience sampling did not yield all consecutive patients; thus, patients were missed. This could be important because we examined the group by treatment pathway (early vs selective). It is possible patients presenting on the weekend or at night are more likely to have selective treatment because of cardiac catheterization laboratory availability and staffing. While the mean time from hospital presentation to initiation of 12-lead ECG Holter was 6 hours, it is possible we missed TMI during the early course of hospitalization, which would underestimate the rate of TMI. This was a hospital-based study; therefore, long-term outcomes cannot be examined.

Conclusions

The data from this study support 3 conclusions: that nearly 20% of hospitalized UA/NSTEMI patients had TMI, that the frequency of TMI between treatment pathways (early vs selectively invasive) was not different, and that major in-hospital complications were significantly higher in patients with TMI and early invasive treatment. An important strength of this study was that it included UA/NSTEMI patients treated with contemporary therapies. Transient myocardial ischemia detected with continuous 12-lead electrocardiogram is a significant contributor to major in-hospital complications and should be carefully assessed for in this patient population. This finding is not necessarily novel. However, there has been marked paucity of studies on this topic in the past decade—why? Underutilization of ST-segment monitoring software for detection of TMI is multifaceted, including physician factors (lack of interest or unaware of current recommendations for ST-segment monitoring),^{31,32} nurse factors (lack of knowledge, skill, and ability),^{29,44,45} and the high number of false-positive alarms.⁴⁶ The value of assessing for dynamic, often clinically silent myocardial ischemia should not be ignored because of these issues; rather, each of these challenges should be further explored, and strategies and interventions developed to address each, for example, guidance from the American Association of Critical-Care Nurses' Alarm Management recommendations, including providing proper skin preparation for ECG electrodes, changing ECG electrodes daily, and customizing alarm parameters and levels on ECG monitors.⁴⁷ In addition, several quality assurance projects have shown that educational programs improve nurses' knowledge and use of ST-segment monitoring.^{48–50} This technology has the potential to identify high-risk patients requiring treatment adjustments. Finally, while we highlight the usefulness of ECG monitoring for detection of TMI, this software might also be useful for ruling out cardiac pathology in patients with symptoms suggestive of acute coronary syndrome, in which there is not a cardiac cause.

REFERENCES

- Khera S, Kolte D, Aronow WS, et al. Non-ST-elevation myocardial infarction in the United States: contemporary trends in incidence, utilization of the early invasive strategy, and in-hospital outcomes. *J Am Heart Assoc.* 2014;3(4):e000995.
- Mozaffarian D, Benjamin EJ, Go AS, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics—2015 update: a report from the American Heart Association. *Circulation.* 2015;131(4):e29–e322.
- Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;64(24):e139–e228.
- Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med.* 2001;344(25):1879–1887.
- Fox KA, Clayton TC, Damman P, et al. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data. *J Am Coll Cardiol.* 2010;55(22):2435–2445.
- Fox KA, Goodman SG, Klein W, et al. Management of acute coronary syndromes. Variations in practice and outcome; findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J.* 2002;23(15):1177–1189.
- Fox KA, Poole-Wilson P, Clayton TC, et al. 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. *Lancet.* 2005;366(9489):914–920.
- McCullough PA, O'Neill WW, Graham M, et al. A prospective randomized trial of triage angiography in acute coronary syndromes ineligible for thrombolytic therapy. Results of the Medicine Versus Angiography in Thrombolytic Exclusion (MATE) trial. *J Am Coll Cardiol.* 1998;32(3):596–605.
- Mehta SR, Cannon CP, Fox KA, et al. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA.* 2005;293(23):2908–2917.
- Neumann FJ, Kastrati A, Pogatsa-Murray G, et al. Evaluation of prolonged antithrombotic pretreatment (“cooling-off” strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. *JAMA.* 2003;290(12):1593–1599.
- O'Donoghue M, Boden WE, Braunwald E, et al. Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction: a meta-analysis. *JAMA.* 2008;300(1):71–80.
- Spacek R, Widimský P, Straka Z, et al. Value of first day angiography/angioplasty in evolving non-ST segment elevation myocardial infarction: an open multicenter randomized trial. *Eur Heart J.* 2002;23(3):230–238.
- Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction. Results of the TIMI IIIB Trial. Thrombolysis in Myocardial Ischemia. *Circulation.* 1994;89(4):1545–1556.
- Hoening MR, Doust JA, Aroney CN, Scott IA. Early invasive versus conservative strategies for unstable angina & non-ST-elevation myocardial infarction in the stent era. *Cochrane Database Syst Rev.* 2006;(3):CD004815.
- Charytan DM, Wallentin L, Lagerqvist B, et al. Early angiography in patients with chronic kidney disease: a collaborative systematic review. *Clin J Am Soc Nephrol.* 2009;4(6):1032–1043.
- CRUSADE Investigators. Association of intravenous morphine use and outcomes in acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. *Am Heart J.* 2005;149(6):1043–1049.
- Invasive versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS) Investigators. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med.* 2005;353(11):1095–1104.
- Desideri A, Fioretti PM, Cortigiani L, et al. Pre-discharge stress echocardiography and exercise ECG for risk stratification after uncomplicated acute myocardial infarction: results of the COSTAMI-II (cost of strategies after myocardial infarction) trial. *Heart.* 2005;91(2):146–151.
- Akkerhuis KM, Klootwijk PA, Lindeboom W, et al. Recurrent ischaemia during continuous multilead ST-segment monitoring identifies patients with acute coronary syndromes at high risk of adverse cardiac events; meta-analysis of three studies involving 995 patients. *Eur Heart J.* 2001;22(21):1997–2006.
- Drew BJ, Funk M. Practice standards for ECG monitoring in hospital settings: executive summary and guide for implementation. *Crit Care Nurs Clin North Am.* 2006;18(2):157–168, ix.
- Drew BJ, Krucoff MW. Multilead ST-segment monitoring in patients with acute coronary syndromes: a consensus statement for healthcare professionals. ST-Segment Monitoring Practice Guideline International Working Group. *Am J Crit Care.* 1999;8(6):372–386 quiz 387–388.
- Gottlieb SO, Weisfeldt ML, Ouyang P, Mellits ED, Gerstenblith G. Silent ischemia as a marker for early unfavorable outcomes in patients with unstable angina. *N Engl J Med.* 1986;314(19):1214–1219.
- Klootwijk P, Meij S, von Es GA, et al. Comparison of usefulness of computer assisted continuous 48-h 3-lead with 12-lead ECG ischaemia monitoring for detection and quantitation of ischaemia in patients with unstable angina. *Eur Heart J.* 1997;18(6):931–940.
- Pelter MM, Adams MG, Drew BJ. Association of transient myocardial ischemia with adverse in-hospital outcomes for angina patients treated in a telemetry unit or a coronary care unit. *Am J Crit Care.* 2002;11(4):318–325.
- Pelter MM, Adams MG, Drew BJ. Transient myocardial ischemia is an independent predictor of adverse in-hospital outcomes in patients with acute coronary syndromes treated in the telemetry unit. *Heart Lung.* 2003;32(2):71–78.
- Drew BJ, Califf RM, Funk M. Practice standards for electrocardiographic monitoring in hospital settings: an American Heart Association scientific statement from the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young; endorsed by the International Society of Computerized Electrocardiology and the American Association of Critical-Care Nurses. *Circulation.* 2004;110(17):2721–2746.
- Drew BJ, Califf RM, Funk M. AHA scientific statement: practice standards for electrocardiographic monitoring in hospital settings: an American Heart Association Scientific Statement from the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young; endorsed by the International Society of Computerized electrocardiology and the American Association of Critical-Care Nurses. *J Cardiovasc Nurs.* 2005;20(2):76–106.
- Drew BJ, Pelter MM, Adams MG, Wung SF, Chou TM, Wolfe CL. 12-Lead ST-segment monitoring vs single-lead maximum ST-segment monitoring for detecting ongoing ischemia in patients with unstable coronary syndromes. *Am J Crit Care.* 1998;7(5):355–363.

29. Funk M, Winkler CG, May JL. Unnecessary arrhythmia monitoring and underutilization of ischemia and QT interval monitoring in current clinical practice: baseline results of the Practical Use of the Latest Standards for Electrocardiography trial. *J Electrocardiol.* 2010;43(6):542–547.
30. Krucoff MW, Croll MA, Pope JE. Continuously updated 12-lead ST-segment recovery analysis for myocardial infarct artery patency assessment and its correlation with multiple simultaneous early angiographic observations. *Am J Cardiol.* 1993;71(2):145–151.
31. Patton JA, Funk M. Survey of use of ST-segment monitoring in patients with acute coronary syndromes. *Am J Crit Care.* 2001;10(1):23–32; quiz 33–44.
32. Sandau KE, Sendelbach S, Frederickson J, Doran K. National survey of cardiologists' standard of practice for continuous ST-segment monitoring. *Am J Crit Care.* 2010;19(2):112–123.
33. Pelter MM, Kozik TM, Loranger DL, Carey MG. A research method for detecting transient myocardial ischemia in patients with suspected acute coronary syndrome using continuous ST-segment analysis. *J Vis Exp.* 2012;(70):50124.
34. Adams MG, Drew BJ. Body position effects on the ECG: implication for ischemia monitoring. *J Electrocardiol.* 1997;30(4):285–291.
35. Drew BJ, Adams MG. Clinical consequences of ST-segment changes caused by body position mimicking transient myocardial ischemia: hazards of ST-segment monitoring? *J Electrocardiol.* 2001;34(3):261–264.
36. Drew BJ, Wung SF, Adams MG, Pelter MM. Bedside diagnosis of myocardial ischemia with ST-segment monitoring technology: measurement issues for real-time clinical decision making and trial designs. *J Electrocardiol.* 1998;30(suppl):157–165.
37. Adams MG, Pelter MM, Wung SF, Taylor CA, Drew BJ. Frequency of silent myocardial ischemia with 12-lead ST segment monitoring in the coronary care unit: are there sex-related differences? *Heart Lung.* 1999;28(2):81–86.
38. Amanullah AM, Lindvall K. Prevalence and significance of transient—predominantly asymptomatic—myocardial ischemia on Holter monitoring in unstable angina pectoris, and correlation with exercise test and thallium-201 myocardial perfusion imaging. *Am J Cardiol.* 1993;72(2):144–148.
39. Carmo P, Ferreira J, Aguiar C. Does continuous ST-segment monitoring add prognostic information to the TIMI, PURSUIT, and GRACE risk scores? *Ann Noninvasive Electrocardiol.* 2011;16(3):239–249.
40. Drew BJ, Adams MG, McEldowney DK. Frequency, duration, magnitude, and consequences of myocardial ischemia during intracoronary ultrasonography. *Am Heart J.* 1997;134(3):474–478.
41. Drew BJ, Adams MG, Pelter MM, Wung SF. ST segment monitoring with a derived 12-lead electrocardiogram is superior to routine cardiac care unit monitoring. *Am J Crit Care.* 1996;5(3):198–206.
42. Drew BJ, Pelter MM, Adams MG. Frequency, characteristics, and clinical significance of transient ST segment elevation in patients with acute coronary syndromes. *Eur Heart J.* 2002;23(12):941–947.
43. Gottlieb SO, Weisfeldt ML, Ouyang P, Mellits ED, Gerstenblith G. Silent ischemia predicts infarction and death during 2 year follow-up of unstable angina. *J Am Coll Cardiol.* 1987;10(4):756–760.
44. Pelter MM, Carey MG, Stephens KE, Anderson H, Yang W. Improving nurses' ability to identify anatomic location and leads on 12-lead electrocardiograms with ST elevation myocardial infarction. *Eur J Cardiovasc Nurs.* 2010;9(4):218–225.
45. Stephens KE, Anderson H, Carey MG, Pelter MM. Interpreting 12-lead electrocardiograms for acute ST-elevation myocardial infarction: what nurses know. *J Cardiovasc Nurs.* 2007;22(3):186–193; quiz 194–195.
46. Drew BJ, Harris P, Zègre-Hemsey JK, et al. Insights into the problem of alarm fatigue with physiologic monitor devices: a comprehensive observational study of consecutive intensive care unit patients. *PLoS One.* 2014;9(10):e110274.
47. Sendelbach S, S Jepsen. AACN Practice Alert Alarm Management, in AACN Evidence Based Practice Resources Work Group. 2013. <http://www.aacn.org/wd/practice/content/practicealerts/alarm-management-practice-alert.pcms?menu=practice>. Accessed November 4, 2015.
48. Chronister C. Improving nurses' knowledge of continuous ST-segment monitoring. *AACN Adv Crit Care.* 2014;25(2):104–113.
49. Blakeman JR, Sarsfield K, Booker KJ. Nurses' Practices and lead selection in monitoring for myocardial ischemia: an evidence-based quality improvement project. *Dimens Crit Care Nurs.* 2015;34(4):189–195.
50. Sendelbach S, Wahl S, Anthony A, Shotts P. Stop the noise: a quality improvement project to decrease electrocardiographic nuisance alarms. *Crit Care Nurse.* 2015;35(4):15–22.