American Journal of Cardiovascular Disease Research, 2015, Vol. 3, No. 1, 9-12
Available online at http://pubs.sciepub.com/ajcdr/3/1/3

DOI:10.12691/ajcdr-3-1-3

"Requiring Intravenous Nitroglycerin" Should be considered a High Risk Feature in Patients with Non-ST Elevation Myocardial Infarction and Unstable Angina

Olusegun Sheyin[1,*], Melissa Fajardo[1], Oladapo Igandan[1], Bredy Pierre-Louis[2]

[1]Department of Medicine, Harlem Hospital Center in affiliation with Columbia University Medical Center New York, NY 10037
[2]Division of Cardiology, Department of Medicine, Harlem Hospital Center in affiliation with Columbia University Medical Center New York, NY 10037
*Corresponding author: oas2120@columbia.edu

Received November 13, 2014; Revised January 20, 2015; Accepted February 12, 2015

Abstract **Introduction:** Early risk stratification of patients with unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI) is crucial to identify those at high risk for further cardiac events as they may benefit from an early invasive strategy of coronary angiography and revascularization. The TIMI score, a widely used predictive model to guide management strategy in UA and NSTEMI may not accurately stratify risk. **Case description:** A 63-year-old man, who is an active smoker with past medical history of hypertension and dyslipidemia, presented with severe sub-sternal, crushing chest pain, which began four hours prior to presentation. His EKG revealed sinus tachycardia, without ST segment deviations or Q waves. He received aspirin, three doses of sublingual nitroglycerin and metoprolol, but continued to have chest pain, thus he was commenced on intravenous nitroglycerin infusion. His chest pain went away after two hours on nitroglycerin infusion. His initial serum troponin I was 0.31 ng/mL and 3.60 ng/mL four hours after presentation. He was admitted for NSTEMI and started on clopidogrel, atorvastatin and intravenous heparin. Echocardiogram revealed inferio-septal wall a kinesis and severely reduced left ventricular systolic function. His troponin I continued to rise, peaking at 37.4 ng/mL. He was started on eptifibatide and was referred for coronary angiography and percutaneous coronary intervention, with finding of fifty percent proximal and distal left anterior descending artery (LAD) lesions. **Discussion:** With a TIMI score of 2, our patient was classified as low risk at presentation. The need for intravenous nitroglycerin infusion for continuing chest pain in the management of UA or NSTEMI may suggest a greater degree of myocardial ischemia and a higher risk for adverse cardiovascular outcomes. This case demonstrates that UA and NSTEMI patients requiring intravenous nitroglycerin initially planned for conservative therapeutic approach need continuous risk stratification which may dictate a change to the invasive management strategy.

Keywords: *high risk, myocardial infarction, non-ST elevation, nitroglycerin, unstable angina*

Cite This Article: Olusegun Sheyin, Melissa Fajardo, Oladapo Igandan, and Bredy Pierre-Louis, ""Requiring Intravenous Nitroglycerin" Should be considered a High Risk Feature in Patients with Non-ST Elevation Myocardial Infarction and Unstable Angina." *American Journal of Cardiovascular Disease Research*, vol. 3, no. 1 (2015): 9-12. doi: 10.12691/ajcdr-3-1-3.

1. Introduction

Acute coronary syndrome (ACS) is a significant cause of morbidity and mortality. Each year, an estimated 785,000 Americans have a new ACS, and 470,000 will have a recurrent attack. Approximately every 25 seconds, an American will have a coronary event, and approximately every minute, someone will die of one [1]. ACS consists of ST elevation myocardial infarction (STEMI), unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI). Patients with STEMI are reperfused emergently with primary percutaneous coronary intervention (PCI) or thrombolysis. Early risk stratification among patients with UA and NSTEMI is crucial to identify those at high risk for further cardiac events as they may benefit from a more aggressive therapeutic approach involving an early invasive strategy of coronary angiographyand revascularization [2,3,4].

A widely used predictive model to guide invasive versus conservative strategy is the TIMI risk score, which is based upon seven variables available at presentation [5]. Even after consideration that some individual factors in the TIMI risk calculator may carry more risk than others, or be more specific for ACS than others, the TIMI score may not accurately stratify risk in patients with NSTEMI or UA because some of these variables may be negative at initial presentation [6]. We report a case of a patient initially classified as low risk by TIMI score, but was later found to be indeed a high risk NSTEMI patient.

2. Case Description

A 63-year-old African American man, who is an active smoker with past medical history of uncontrolled hypertension, dyslipidemia and not compliant with medications, presented to the emergency department with severe sub-sternal, crushing chest pain, with radiation to both axillae, and which began on waking up from sleep four hours prior to presentation. The pain was constant with no known aggravating or relieving factors, and was associated with palpitations, dyspnea and diaphoresis. He had a similar episode of chest pain three years prior ago as well. At that time, he had hypertensive emergency and a stroke which left him with residual dysarthria and right-sided weakness. Coronary angiogram at that time had no significant findings and he has not had angina since then. He has been smoking two to three packs of cigarettes daily for fifty years and also smokes marijuana, but he denied cocaine or amphetamine use, or a family history of early myocardial infarction.

His sitting blood pressure on presentation was 173/115 mmHg on the right arm and 170/110 mmHg on the left arm, with a pulse rate of 98/minute and oxygen saturation of 97% on room air. His electrocardiogram (EKG) revealed sinus tachycardia at 101 beats per minute, left axis-deviation, bi-atrial enlargement, first degree atrio-ventricular block, marked left ventricular hypertrophy with repolarization abnormalities and prolonged QRS duration (132 milliseconds), without ST segment deviations or evidence of prior myocardial infarction (Figure 1).

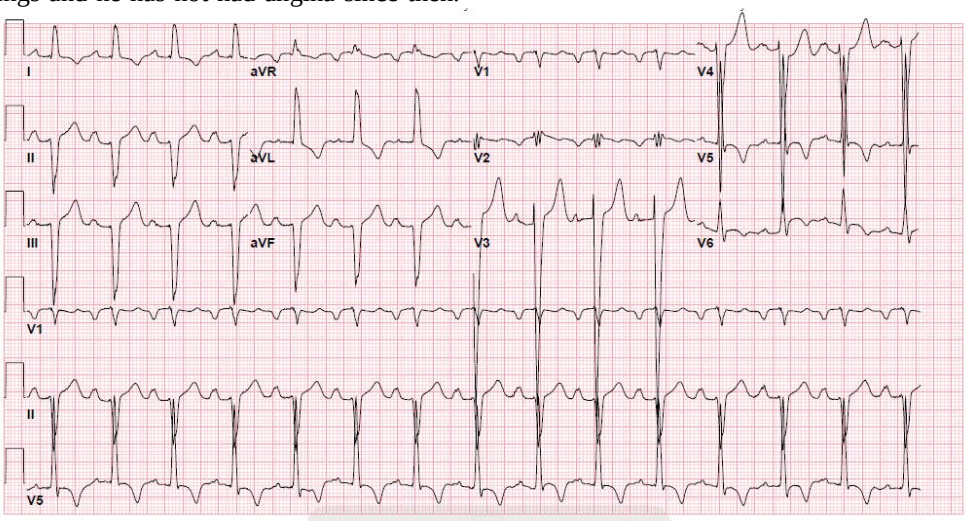

Figure 1. Electrocardiogram showing sinus tachycardia at 101 beats per minute, left axis-deviation, bi-atrial enlargement, first degree atrio-ventricular block, marked left ventricular hypertrophy with repolarization abnormalities and prolonged QRS duration

Physical examination revealed a middle aged dysarthric man in painful distress with an adynamic precordium, and without jugular venous distension, rales, wheezing or chest wall tenderness. He had a normal first heart sound, but with an accentuated aortic component of the second heart sound, and without murmurs or a third and fourth heart sounds. He had equal pulses in the limbs, without pedal edema. He received 325 mg of aspirin, three doses of sublingual nitroglycerin and 20 mg of intravenous labetalol. Metoprolo l50 mg peros every 12 hours was started, but he continued to have chest pain, thus he was commenced on intravenous nitroglycerin infusion, titrated up to 15 micrograms per minute to control his chest pain. His chest pain went away after two hours on nitroglycerin infusion.

His initial laboratory work-up revealed serum troponin I of 0.31 ng/mL, blood urea nitrogen of 30 mg/dL with serum creatinine of 2.7 mg/dL, hemoglobin of 14.1 g/dL, glycosylated hemoglobin of 6.2%, LDL cholesterol of 134 mg/dL, brain natriuretic peptide of 1520 pg/mL and toxicology screen positive for cannabinoids. His Chest X ray revealed cardiomegaly and clear lung fields. His repeat troponin, four hours after the initial labs came back at 3.60 ng/mL. He was admitted to the cardiac care unit for NSTEMI type 1, uncontrolled hypertension and acute kidney injury or chronic kidney disease. Aspirin and nitroglycerin infusion were continued, and he was started on intravenous heparin infusion at 1000 units per hour, clopidogrel 75 mg daily and 80 mg of atorvastatin daily. Echocardiogram obtained in the morning of the day after admission revealed moderate eccentric hypertrophy with inferior and septal wall akinesis, severely reduced left ventricular systolic function [left ventricular ejection fraction (LVEF) of 19.6%], moderately dilated left atrium, moderate mitral and tricuspid regurgitation and moderately elevated pulmonary artery systolic pressure. Angiotensin converting enzyme inhibitor was not given because of kidney injury

Even though he remained chest pain-free on medical management; his troponin I continued to rise, peaking at 37.4 ng/mL. He was started on the glycoprotein IIb/IIIa inhibitor eptifibatide 10 mg intravenous bolus, followed by an intravenous infusion at 120 mcg per minute. He was started on eptifibatide and he was referred for urgent coronary angiography and percutaneous coronary intervention, with finding of a fifty percent proximal left anterior descending artery (LAD) lesion, a fifty percent distal LAD lesion, a thirty percent left circumflex artery lesion and a thirty percent distal right coronary artery lesion. He was continued on aspirin, clopidogrel, atorvastatin and metoprolol. His chest pain resolved off nitroglycerin drip and his troponins trended down to 0.1 ng/mL by the third day after PCI. He was discharged and will be followed up in the cardiology and nephrology clinics.

3. Discussion

Initial management of UA and NSTEMI is the same because elevation of serum cardiac biomarkers, which give evidence for myocardial infarction, may be absent earlier on. A number of variables, including the presence and extent of ST segment depression, elevated cardiac biomarkers, evidence of hemodynamic instability, and persistent chest pain despite appropriate medical therapy; have been used to create risk scores such as TIMI, GRACE, and PURSUIT [5,7,8,9]. The TIMI risk score is based upon seven variables available at presentation; a value of one is assigned when a factor is present and zero when it is absent [5].

The seven variables are:

- Age ≥65 years;
- Presence of at least three risk factors for coronary heart disease (CHD) (hypertension, diabetes, dyslipidemia, smoking, or positive family history of early myocardial infarction [MI])
- Prior coronary stenosis of ≥50 percent
- Presence of ST segment deviation on admission electrocardiogram (ECG)
- At least two anginal episodes in prior 24 hours
- Elevated serum cardiac biomarkers
- Use of aspirin in the prior seven days

Patients are considered to be at low risk when their TIMI score is 0 to 2; intermediate risk when the score is 3 to 4; and high risk when the score is 5 to 7 [7].

The 2014 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on unstable angina and non-ST elevation MIalso recommends that patients with UA or NSTEMI with at least one of the following features are at extremely high risk for an adverse cardiovascular event in the short term and hence should have immediate angiography and revascularization:

- Hemodynamic instability or cardiogenic shock
- Severe left ventricular dysfunction or heart failure
- Recurrent or persistent rest angina despite intensive medical therapy
- New or worsening mitral regurgitation or new ventricular septal defect
- Sustained ventricular arrhythmias

These features may suggest left main disease or multivessel coronary artery disease and hence warrant urgent angiography and revascularization. Other patient groups who could benefit from an invasive strategy include patients with: advanced age (>70 years of age), prior MI, revascularization within the prior six months, ST deviation on EKG, heart failure or diabetes mellitus [2].

Our patient presented to the emergency room with chest pain and he had a TIMI score of 2 at presentation (three cardiovascular risk factors – hypertension, dyslipidemia, cigarette smoking; more than two angina episodes in the preceding twenty-four hours), which puts him at 8.3 percent risk for all-cause mortality, myocardial infarction, and severe recurrent ischemia prompting urgent revascularization at 14 days, according to the findings in the TIMI 11B and ESSENCE trials [5]. After three dosesof sublingual nitroglycerin and intravenous labetalol and then oral metoprolol to control his blood pressure, our patient continued to have chest pain. He was then commenced on intravenous nitroglycerin, and he became chest pain free at an infusion rate of 15 micrograms per minute. At this point in management, he did not have any of the aforementioned 2014 ACC/AHA guidelines very high risk criteria to warrant urgent invasive management, since his chest pain was adequately controlled on medical management. The beneficial effects of nitroglycerin including coronary artery and arteriolar dilatation, preload and afterload reduction and enhanced collateral blood flow, leads to an improvement in the symptoms of ischemia. However, myocardial ischemia may continue despite control of chest pain.

Our patient did not get any point for elevated serum cardiac biomarkers at presentation because they were negative. When repeat troponin I was obtained 6 hours later, it was elevated at 5.42 ng/mL, and even though he was no longer having chest pain, the troponin I continued to rise, peaking at 37.4 ng/mL 12 hours after presentation. Hence, even though the TIMI score was originally designed to be applied at presentation to guide management, it should be re-assessed periodically and updated with any evolution in the status of the patient. Although the initial score was low, the elevated troponin I obtained on serial testing increased his TIMI score to 3, putting him at intermediate risk for adverse outcomes. A change in management strategy from conservative to an early invasive approach was considered at this point, going by the TACTICS-TIMI 18 trial which showed that patients with high-risk TIMI scores of 5 to 7, as well as intermediate-risk TIMI scores of 3 to 4, benefited from early invasive strategy [10]. However, the decision to perform a coronary angiogram with possible revascularization was made when the patient's echocardiogram, obtained on the second day of admission, approximately 12 hours after presentation revealed severely reduced left ventricular systolic function, one of the 2014 ACC/AHA guidelinesUA and NSTEMI high risk feature.

As illustrated in this case, it is often difficult to correctly risk stratify patients presenting with UA or NSTEMI at presentation. Since intravenous nitroglycerin is considered part of medical therapy for myocardial infarction, patients whose chest pain is controlled while on nitroglycerin infusion, are not considered high risk, going by current guidelines which require recurrent angina while on optimal medical therapy. However, this case demonstrates that the management of patients with UA and NSTEMI requires continuous risk stratification. Therefore, UA and NSTEMI patients initially classified as low risk, but who require intravenous nitroglycerin should be monitored closely for prompt identification of the afore-mentioned high risk features to guide medical decision making, even in the absence of chest pain recurrence.

4. Conclusion

The need for intravenous nitroglycerin infusion for continuing chest pain in the management of UA or NSTEMI may suggest a greater degree of myocardial ischemia and a higher risk for adverse cardiovascular outcomes. UA and NSTEMI patients requiring intravenous nitroglycerin initially planned for conservative therapeutic approach need close monitoring

and continuous risk stratification. Further studies investigating the requirement for intravenous nitroglycerin as an independent risk predictor in UA and NSTEMI are needed.

References

[1] Rojer V, Go A, Lloyd-Jones D, et al. Heart Disease and Stroke Statistics--2012 Update: A Report From the American Heart Association. *Circulation.* 2012; 125: e2-e220.

[2] Amsterdam EA, Wenger NK, Brindis RG, Casey Jr DE, Ganiats TG, Holmes Jr DR, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, *Journal of the American College of Cardiology* (2014).

[3] Bertrand ME, Simoons ML, Fox KA, et al. Management of acute coronary syndromes: acute coronary syndromes without persistent ST segment elevation; recommendations of the Task Force of the European Society of Cardiology. *Eur Heart J* 2000; 21:1406.

[4] 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: 2908.

[5] Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA* 2000; 284: 835.

[6] Aragam K, Tamhane U, Kline-Rogers E, Li J, Fox K, Goodman S,Eagle K, Gurm H. Does Simplicity Compromise Accuracy in ACS Risk Prediction? A Retrospective Analysis of the TIMI and GRACE Risk Scores. *PLoS One*. 2009 Nov 23; 4 (11): e7947.

[7] Borzak S, Cannon CP, Kraft PL, et al. Effects of prior aspirin and anti-ischemic therapy on outcome of patients with unstable angina. TIMI 7 Investigators. Thrombin Inhibition in Myocardial Ischemia. *Am J Cardiol* 1998; 81:678

[8] Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, Van de Werf F, Avezum A, Goodman SG, Flather MD, Fox KAA, for the Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. *Arch Intern Med* 2003; 163: 2345-53.

[9] Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9461 patients. The PURSUIT Investigators. *Circulation*. 2000; 101: 2557-2567.

[10] Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, Di Battiste PM, Gibson CM, Braunwald E; TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)-Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies inpatients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med.* 2001 Jun 21; 344 (25): 1879-87.