Original Article

Risk Factors of Increased Corrected TIMI Frame Count in Angioplasty of Culprit Lesion after non-ST Elevation Acute Coronary Syndrome

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Abstract

Introduction: Non-ST elevation acute coronary syndromes (NSTE-ACS) are among the leading causes of death worldwide. The cornerstone of management strategies for NSTE-ACS is revascularization and reestablishment of coronary blood flow. However, in some patients, coronary blood flow may not be achieved despite of successful coronary intervention. However, the possible risk factors for development of abnormal coronary reflow in NSTE-ACS patients is not clearly addressed in the literature. Evaluation of risk factors relating to corrected TIMI frame count (cTFC) as an indicator of coronary artery reperfusion is the purpose of present study. **Material and Methods:** Every NSTE-ACS patients undergoing coronary interventions enrolled in present cross sectional study. Demographic data alongside of the conventional cardiac risk factors, biochemical serum markers and angiographic findings during coronary interventions were documented for each patient. T-test and Mann-Whitney test were used to evaluate the relation between mean CTFC and demographic, biochemical and angiographic findings. Linear regression was used for demonstrating the possible predictive model for CTFC in NSTE-ACS patients. **Results:** Among 210 NSTE-ACS patients, most of them were male (53.8%) and females had greater mean CTFC than males (P=0.044). Those patients who were smoker, hypertensive or diabetic had greater mean CTFC levels (P=0.017, P=0.001 and P=0.003 respectively). While those who had stent size larger than 20mm and presence of thrombosis before intervention had significantly greater CTFC (P=0.001 for both). Only blood sugar and creatinine level were correlated with mean CTFC, indicating that increase in such serum parameters will increase CTFC (P=0.001 for both). Using coronary stents larger than 20mm increased the mean CTFC for 25%. **Conclusion:** In contrast to ST segment elevation myocardial infarction, the risk factors for abnormal reperfusion following coronary interventions in NSTE-ACS is not clearly studied. The present study demonstrated that female gender, hypertension, diabetes mellitus, blood sugar level, creatinine level and stent size are related to cTFC and thrombotic lesions as a possible indicator of abnormal coronary reperfusion.

Keywords: Non-ST elevation myocardial infarction, acute coronary syndromes, percutaneous coronary intervention

Introduction

Coronary artery disease is a common cardiovascular complication which is responsible for a considerable mortality in middle income countries in contrast to low or high income ones [1]. Various modifiable or unmodifiable risk factors proposed for development of coronary artery diseases in different age groups including family history of coronary artery diseases, hypertension, dyslipidemia, diabetes mellitus and smoking [2, 3]. Fortunately, the overall coronary heart disease related death decreased by 30% from 2010 to 2020 because of improvement in controlling these risk factors especially the blood pressure and smoking [4]. Non-ST elevation myocardial infarction (NSTEMI) is a subset of acute coronary syndrome (ACS) and a well-known considerable cause of mortality and morbidity [5]. Revascularization is one of the most common therapeutic approaches for treating NSTE-ACS patients. Choosing the revascularization method depends on the patient's medical condition and personal coronary anatomy characteristics. However, even despite of appropriate management plan, the risk of developing complications following the intervention

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is a big concern [5]. It has been demonstrated that early invasive strategy for NSTE-ACS patients will provide beneficial trend on all-cause mortality [6]. While in hospital mortality of NSTE-ACS patients undergoing coronary artery bypass graft (CABG) or those who are undergoing for any procedure has been declined, however, the mortality rate for those who undergo percutaneous coronary intervention (PCI) is remained the same [7]. Regardless of the revascularization strategy, the main goal of each of these strategies is restoration of the coronary blood flow to the myocardial tissue. However, despite of restoration of artery's patency after coronary interventions, the blood flow may still remain impaired [8, 9]. This complication will increased adverse PCI outcomes including greater mortality rate [10]. Evaluation of blood flow can be done in various ways and TIMI frame count (TFC) is a readily available and inexpensive method for estimating the coronary blood flow velocity [11]. Overall, some risk factors including older age, diabetes mellitus, hypercholesterolemia and having multi-vessel disease are reported to be related to development of abnormal coronary blood perfusion following coronary interventions [12]. It has been reported that in contrast to patients with STEMI, those with NSTEMI may less commonly develop reduced coronary reflow while their short clinical outcomes may be more favorable [13]. However, some studies demonstrated that despite of the lower incidence of abnormal coronary reflow in NSTEMI patients and favorable short outcomes, these patients may develop more unfavorable long term clinical outcomes in contrast to STEMI patients [14]. These findings highlights the importance of studying blood reflow following coronary interventions in NSTE-ACS patients and the lack of enough studies regarding the development of this complication of PCI. In the present study, distribution of possible predictor factors for reduced CTFC as an indicator of coronary perfusion following coronary interventions in NSTE-ACS patients.

Material and Methods:

The present cross sectional study took place in Imam Reza and Ghaem hospitals in a one year period from Jan 2019 to February 2020 and was approved by Mashhad University of Medical Sciences Ethic committee. Those patients who had NSTE-ACS undergoing coronary interventions enrolled in the present study after filling an informed consent form. Those patients who had complicated interventions including those who had failed PCI, died or experienced cardiac arrest during their hospitalization were excluded. Demographic data alongside of the conventional cardiac risk factors including diabetes, dyslipidemia, hypertension and smoking cigarette were documented for every patients. Patient's biochemical serum markers including blood sugar, creatinine, cholesterol, low density lipoprotein, high density lipoprotein, triglyceride, hemoglobin, white blood cell and platelet counts prior to coronary intervention were also documented. The angiographic findings during PCI including presence of thrombosis, stent size and corrected TIMI frame count (CTFC) were documented for each patient. In order to calculate the CTFC, the angiographic films were taken (30 frames per second) and contrast media injection was performed. Calculation of CTFC was performed by dividing of TFC in the left anterior descending artery by 1.7 [15]. Normal CTFC Levels were considered as 21±2 for left anterori desending artery, 22±4 for circumflex artery and 20±3 for right coronary artery [16].

The study data was analyzed by SPSS software (version 16) and P values lesser than 0.05 was considered as statistically significant. T-test and Mann-Whitney test were used to evaluate the relation between mean CTFC and demographic, biochemical and angiographic findings. Linear regression was used for demonstrating the possible predictive model for CTFC in NSTE-ACS patients.

Results:

Among total number of 210 NSTE-ACS patients, 113 patients were male (53.8%) and 97 patients were female (46.2%). The patient's demographic data and their relation to CTFC is summarized in Table 1. Females had greater mean CTFC than males (P=0.044). Smoker, hypertensive and diabetic patients had greater mean CTFC levels (P=0.017, P=0.001 and P=0.003 respectively). While those who had stent size larger than 20mm and developed thrombosis during intervention had significantly greater CTFC (P=0.001 for both), however, those who had pre-dilatation or post-dilatation did not have significantly different mean CTFC levels (P=0.537 and P=0.568 respectively). Among serum biochemical markers which are summarized in table 2, only blood sugar and creatinine level were correlated with mean CTFC, indicating that increase in such serum parameters will increase CTFC (P=0.001 for both). The linear regression model for the 5 variables including age, stent size, smoking cigarettes, creatinine and development of thrombosis is demonstrated in Table 3. According to the presented model, the stent size larger than 20mm could be consider as an effective predictor for mean CTFC. Using stents larger than 20mm could increase the mean CTFC for 25%.

Discussion:

The present study demonstrated that in NSTE-ACS patients, development of thrombosis during intervention and being smoker, hypertensive or diabetic is related to greater mean CTFC levels. Moreover, using stent size larger than 20mm was an effective predictor for CTFC; increasing the mean CTFC for 25% in NSTE-ACS patients.

Poor perfusion is a common complication of PCI, complicating approximately 25% of coronary interventions [17]. Poor perfusion after coronary intervention is considered as a predictor of unfavorable clinical outcomes [18]. Establishment of the blood flow in every patient who developed myocardial infarction is the most important issue which can be usually achieved by a successful coronary interventions except those who develop poor reperfusion [19,

[20]. There are many different approaches proposed for assessment of microvascular perfusion which are useful for investigating coronary reflow including radionuclide imaging and positron emission tomography [19]. However, most of these approaches are time consuming or they are not readily available in every clinical settings [19]. TFC is an accurate and simple method for evaluation of reperfusion strategies and epicardial flow in clinical settings [20]. In contrast to those with higher CTFC, patients with lower CTFC who had TIMI 3 immediately after primary PCI has been reported to have better functional recovery and lower complications [19, 21]. Our present study demonstrated that female patients as well as smokers, hypertensive and diabetic patients have higher CTFC levels. Also, using coronary stents larger than 20mm was correlated with greater CTFC. To the best of our knowledge, in contrast to STEMI patients, possible risk factors for development of poor reperfusion is not widely studied in NSTE-ACS patients. Moreover, most of the studies on STEMI patients evaluated the no-reflow as a poor reperfusion phenomenon in patients undergoing coronary interventions. While recent meta-analysis reported that initial TIMI flow lesser than 1 and high thrombus burden are the most important risk factors for development of no-reflow phenomenon in STEMI patients, there is not enough data available for risk factors of such phenomenon in NSTE-ACS patients [18]. Kalyoncouglu et al. demonstrated that some inflammatory biomarkers including lymphocyte to monocyte ratio and monocyte to high-density lipoprotein cholesterol ratio can efficiently identify high risk NSTEMI patients undergoing PCI for development of no-reflow phenomenon [22]. Our study demonstrated that among biochemical serum markers, only low density lipoprotein, creatinine and blood sugar were correlated with CTFC level in NSTE-ACS patients. The relation between acute hyperglycemia on coronary reperfusion is not clearly understood. It has been demonstrated that admission glucose level may not be related to CTFC after PCI in those undergoing thrombectomy aspiration [23]. Similarly, the relation between serum creatinine level and development of abnormal reperfusion in NSTE-ACS patients is not clearly understood. Some studies stated that hypercoagulable state following renal impairment may be the cause of distal embolization and impaired reperfusion [24, 25]. Recent study on STEMI patients who had low glomerular filtration rate demonstrated that there is a significant relation between poor reperfusion and low initial filtration rate [24]. Among other studied risk factors, interstitial and intra-myocardial vessel fibrosis in hypertensive and diabetic individuals may be a possible cause of increased CTFC in such patients [23]. Similar to other mentioned risk factors, the importance of stenting in abnormal reperfusion of NSTE-ACS patients is not clearly addressed. It has been demonstrated that coronary stenting can lead to impairment of coronary perfusion compared with other management strategies including balloon angioplasty [26]. Kim et al. demonstrated that mean stent diameter is higher in those who develop abnormal reperfusion after STEMI [27]. However, other studies such as Mirbolouk et al. reported that in such patients, the lower stent diameter is predictor of abnormal reperfusion [28]. Further studies in both STEMI and NSTE-ACS patients are required for determination of possible risk factors for abnormal CTFC following coronary intervention.

Conclusion:

Risk factors of abnormal reperfusion following coronary intervention in NSTE-ACS patients is not widely studied. According to the present study findings, female gender, hypertension, diabetes mellitus, blood sugar level, creatinine level and stent size are related to cTFC as a possible indicator of abnormal coronary reperfusion.

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Table 1. Relation between demographic data and CTFC

variables		Number (%)	Mean CTFC (SD)	p-value
Stent size	<20	113(53.8)	7.51(3.11)	0.001*
	>20	97(46.2)	12.90(4.71)	
Thrombosis	With thrombosis	9(4.3)	15.77(5.19)	0.001**
	Without thrombosis	201(95.7)	9.74(4.58)	
Pre dilation	Yes	156(74.3)	9.90(4.71)	0.537
	no	54(25.7)	10.29(4.91)	
Post dilation	Yes	159(75.7)	9.89(4.74)	0.568
	no	51(24.3)	10.33(4.83)	
Gender	male	113(53.8)	9.46(4.63)	0.044**
	female	97(46.2)	10.63(4.58)	
Smoking status	Smoker	135(64.3)	10.72(50.5)	0.017**
	Non-smoker	75(35.7)	8.70(3.87)	
Diabetes status	diabetic	107(51)	13.13(5.48)	0.001**
	Non diabetic	103(49)	7.92(2.15)	
HTN status	hypertensive	110(52.4)	12.83(6.43)	0.003**
	normotensive	100(47.6)	8.79(2.99)	

*t-test
**Mann-Whitney

Table 2. Relation between serum biochemical markers and CTFC

Serum marker	Mean(Standard deviation)	CTFC
Blood sugar	109.07(81.92)	r=0/267 p=0/001
Creatinine	1.44(1.03)	r=0/242 P=0/001
Cholesterol	170.03(60.12)	r=0/038 P=0/588
Low density lipoprotein	136.51(51.86)	r=199 P=0/004
High density lipoprotein	41.87(5.35)	r=0/094 P=0/173
Triglyceride	180.52(64.68)	r=078 P=0/261
Hemoglobin	12.06(2.52)	r=099 P=0/154
White blood cell count	9.02(8.91)	r=0/094 P=0/174
Platelet	261.57(93.78)	r=./93 p=0/177

Table 3. Linear regression model using serum log transformation of TIMI frame count as dependent variable base on backward method

Dependent variable (log transformed TIMI frame count[a])	Independent variables	Unstandardized B	CI95% (lower bound ; upper bound)	P-VALUE	Back translate regression coefficients of log
	Thrombosis	0/178	0/074 ; 0/281	0/001	0.19
	Stent size > 20 mm	0/226	0/185 ; 0/268	<0/001	0.25

	Smoker	0/113	0/069 ; 0/156	<0/001	0.12
	Creatinine	0/018	-0/001 ; 0/038	0/07	0.018
	Age	-0/004	-0/006 ; -0/002	0/001	-0.004

[a] log transformation of TIMI frame count