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Original Article

Study of the possible medical and medication explanatory factors of angiographic outcomes in patients with acute ST elevation myocardial infarction undergoing primary percutaneous intervention

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Abstract

Background: Myocardial blush grade (MBG), thrombolysis in myocardial infarction (TIMI) and corrected TIMI frame count (cTFC) are indices of successful angiographic reperfusion. This study sought to determine the predictors of angiographically successful reperfusion including demographic, clinical and angiographic factors in patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI).

Materials and Methods: A cross-sectional study of patients with a confirmed diagnosis of STEMI undergoing pPCI was designed. Eligible patients referring to a university heart center were enrolled in the study from March 2012 to December 2012. Successful epicardial reperfusion was defned as TIMI flow grade 3 or cTFC<= 28 frames and successful myocardial reperfusion as MBG 2 or 3.

Results: The study population consisted of 100 patients, including 74 males and 26 females, with mean ± standard deviation age of 58.27 ± 11.60 years. Achieving open microvasculature (MBG 2/3) was positively associated with a history of nitrate intake ($P = 0.03$) and history of calcium channel blocker (CCB) intake ($P = 0.005$). Hyperglycemia was inversely associated with achieving a final cTFC ≤ 28 frames ($r = -0.32$, $P = 0.001$).

Conclusions: Our findings suggest that patients with a history of nitrate and CCB intake had a higher likelihood of successful PCI. In addition, patients with a higher blood glucose level on admission may have a reduced rate of reperfusion success. Future studies with a larger sample size are recommended to investigate the significant relationships observed in this study.

Key Words: Corrected thrombolysis in myocardial infarction frame count, myocardial blush grade, outcome, risk factor, thrombolysis in myocardial infarction flow

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INTRODUCTION

Patients with symptoms suggestive of acute myocardial infarction (MI) are candidates for reperfusion therapy with either primary percutaneous coronary intervention (pPCI) based on the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the management of patients with ST-segment elevation myocardial infarction (STEMI)[1] or fibrinolytic therapy. Coronary reperfusion with pPCI or fibrinolytic therapy improves outcomes in patients with acute ST elevation MI.[1] pPCI is a complex and time consuming procedure for reperfusion of the myocardium, which needs frequent use of an intra-aortic balloon pump to stabilize hemodynamic derangement.[2] If pPCI performed in an expert manner, it is the preferred therapy compared to fibrinolysis because it achieves a higher rate of TIMI 3 flow (more than 90 percent) and is also associated with improved outcome and reduced rates of death and adverse events.[3]

Thrombus embolization, which happens during PCI for STEMI, may lead to microvascular obstruction and can reduce myocardial perfusion.[4] It can also enlarge infarct size and increase mortality rate.[5] Thrombolysis in myocardial infarction (TIMI) coronary antegrade flow is a parameter which is used to evaluate achievement of a successful intervention in patients with MI undergoing PCI. It is defined as TIMI 3 flow when a successful coronary intervention achieved, while an unsuccessful angiographic PCI is considered as TIMI flow scored 0 or 1. Corrected TIMI frame count (cTFC) a continuous variable index that shows reperfusion grading after PCI and reflects epicardial coronary artery flow as well as microvascular perfusion, is a useful predictor of in-hospital clinical outcome. Existing evidence suggests that faster flow (lower cTFC; cTFC ≤ 28) may reflect a better microvascular function and is associated with lower mortality rate.[6-8]

Myocardial blush grading (MBG) was assessed on visually the angiogram by the cardiologist to characterize myocardial perfusion and MBG classified in brief as follows: MBG 0/1(no/minimal myocardial blush or contrast density; grade 0 indicates no apparent tissue level perfusion), MBG 2 (moderate MBG or contrast density but less than a non-infracted related coronary artery); MBG 3 (normal MBG or contrast density). This angiographic feature has an important predictive value. It predicts strongly infarct size, survival rate and is associated with long-term mortality in patients with MI after pPCI.[4] Nevertheless, clinical studies on association between predictor factors of angiographic outcomes showed inconsistent findings. Thus, it is important to know which possible medical and medication explanatory factors could also be exploited clinically as inducers of worse outcome in patients with acute MI. As a means to get additional information in this respect and gain better insights, we evaluated the association between possible medical and medication explanatory factors and coronary flow in patients with STEMI undergoing pPCI.

MATERIALS AND METHODS

Study design

A cross-sectional study was designed and was conducted in the Tehran Heart Center a referral teaching hospital for cardiovascular disorders (CVDs) in Tehran, Iran. This study was approved by the local ethics committee. 100 STEMI patients undergoing pPCI were entered the study during the study period of March to December 2012. Patients with STEMI who were candidate for pPCI as the revascularization method of choice were included in this study.

- Chest pain lasting less than 12 h
- ST-segment elevation >1 mm in at least two contiguous leads of electrocardiogram (V1, V2, V3) or ST-segment elevation >1 mm in other leads or presence of complete left bundle branch block
- One unit increase in troponin or two units increase in creatine kinase to values greater than upper limits of their relevant normal ranges.

Exclusion criteria were previous MI, prior PCI. Furthermore, we excluded patients who underwent coronary artery bypass grafting surgery.

Explored risk factors for CVD were: Age (as men above or 45 and women above or 55 years old), current cigarette smoking, positive history of dyslipidemia, hypertension, diabetes and a family history of CVD. Regular medication taking for at least 1 month preceding pPCI was defined a positive medication history.

Procedure

All patients received aspirin 325 mg, a loading dose of 600 mg clopidogrel, an initial heparin bolus of 60 units/kg (maximum 4000 units) and atorvastatin 80 mg before procedure according to the standard clinical practice guidelines.[1] Coronary angiography was performed immediately after admission by transfemoral approach. Coronary angioplasty was undertaken on the culprit lesion by appropriate-sized balloon catheters and a bare metal or drug-eluting stent was replaced to reduce residual diameter

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stenosis to <50%. TIMI flow, cTFC[6-8] and MBG[4] were measured before and immediately after the primary coronary angioplasty objectively by one independent interventional cardiologist, who was blinded to the clinical details of the participants.

Statistical analysis

The Statistical Package for Social Sciences (SPSS, version 19.0) (IBM Company, USA) was applied for data analysis. Spearman and Kendall's rank correlations were used to determine any correlation between continuous variables (with non-normally distributed residuals) and the study outcomes. Mann-Whitney U Test was also applied to investigate any association between nominal explanatory variables with the study outcomes. $P < 0.05$ were considered as statistically significant.

RESULTS

A total of 100 STEMI patients, including 74 men and 26 women, with mean ± standard deviation age of 58.27 ± 11.60 years, undergoing primary PCI enrolled the study. Analyses were performed to assess any relationship between MBG, TIMI flow and cTFC with patient's demographic and clinical parameters [Table 1]. MBG, TIMI flow and cTFC showed significant relationships with the history of nitrate intake, history of calcium channel blocker (CCB) intake and hyperglycemia upon admission [Table 1]. It was found that achieving open microvasculature (MBG 2/3) was positively associated with a positive history of nitrate ($P = 0.034$) as well as CCB intake ($P = 0.005$). Hyperglycemia upon admission was inversely associated with achieving a final cTFC ≤ 28 ($P = 0.001$, $r = -0.32$). There were no significant association with TIMI flow Grade 3 and patient's demographic and clinical parameters.

DISCUSSION

The present study sought to investigate any relationship between possible medical and medication explanatory factors and coronary flow in patients with STEMI undergoing pPCI. The success of a PCI procedure is defined by three interrelated components: Angiographic findings, procedural events and clinical outcomes. A successful PCI produces sufficient enlargement of the lumen at the target site to improve coronary artery blood flow. A successful angioplasty is defined as a final TIMI flow Grade 3 (visually assessed by angiography). Patients with TIMI 3 flow after primary angioplasty have successful angioplasty, according to the current definition.[9,10] In compliance with many previously reported studies, our results indicate that improved myocardial perfusion or MBG is significantly better among patients with history of nitrate and CCB intake. Previous studies have showed that calcium-channel blockers can improve myocardial perfusion through their effects on myocardial microcirculation and metabolism as well as by preventing coronary spasm and improving collateral flow.[11,12] They may also increase coronary flow in coronary artery disease by selectively dilating larger arterioles.[11] A large scale experimental study demonstrated that pre-treatment with verapamil can reduce the ischemic size of subendocardial infarcts and can preserve the function of ischemic region.[12,13] Interestingly, it has been shown that calcium-channel blockers have inhibitory effects on platelet aggregation and thrombus formation,

Table 1: Medical and medication explanatory factors of study patients and their relationship with the MBG, TIMI flow and cTFC (*n*=100)

Variable (s)	Number %[α]	TIMI flow		MBG		cTFC	
		P value	*r*	*P* value	*r*	*P* value	*r*
Sex (male)	74	0.14		0.32		0.65	
Diabetes (yes)	31	0.37		0.34		0.87	
Hypertension (yes)	38	0.58		0.56		0.76	
Hyperlipidemia (yes)	28	0.30		0.90		0.65	
Positive family history (yes)	16	0.50		0.31		0.65	
Current smoking (yes)	39	0.23		0.65		0.69	
Ischemic time** (min)	242.57±171.78	0.21	−0.1	0.29	−0.10	0.65	−0.04
Fasting blood glucose**	165.27±77.33	0.84	−0.02	0.90	−0.16	0.001	−0.32
Drug history (yes)							
Beta-blocker	22	0.11		0.4		0.9	
Nitrate	10	0.14		0.03*		0.29	
Calcium channel blocker	7	0.14		0.005*		0.3	
Statin	14	0.44		0.95		0.29	

α: Numbers are as percentage (*n*=100), **P*<0.05 were considered as statistically significant, **Mean±SD, *r*: Correlation coefficient, SD: Standard deviation, TIMI: Thrombolysis in myocardial infarction, MBG: Myocardial blush grade, cTFC: Corrected TIMI frame count

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which may improve myocardial perfusion.[14,15] Demir *et al*.[16] and also Werner *et al*.[17] have reported that intracoronary verapamil has favorable effects on coronary vasospasm without no-reflow phenomenon in patients underwent pPCI for acute MI. Results of meta-analysis, i.e., Nisoldipine in Coronary artery Disease and Coronary Angioplasty Amlodipine in Restenosis Study, showed that CCBs can improve long-term clinical outcome and reduce the need for target vessel revascularization compared with placebo.[18] ENCORE I (Evaluation of Nifedipine and Cerivastatin in Recovery of Coronary Endothelial Function) study have proved that 30-60 mg/d nifedipine treatment over a 6-month period improves the coronary endothelial function.[19] In vasodilator prevention on no-reflow investigation, also pre-PCI therapy with verapamil for prevention of no-reflow phenomenon showed that there was a trend toward improved myocardial perfusion by using the TIMI myocardial perfusion grade.[20] In our study, patients with a history of nitrates intake have a better perfusion pattern. In Aoki *et al*. and Goller *et al*. studies, the acute administration of sublingual[21] or short-acting nitrates[22] could significantly decrease the ischemic perfusion severity or size of the culprit zone. Similarly, another report confirms that chronic usage of long-acting nitrates can reduce ischemic size[23] and perfusion defect size.[24,25] In addition, Zoghbi *et al*. in this study of the effects of medications on myocardial perfusion suggested that acute or chronic administration of nitrates can decrease the size and severity of exercise-induced myocardial perfusion defects.[26] Result reported by Ambrosio *et al*. shows that chronic nitrate users may have a shift from STEMI in favor of non-ST elevation myocardial infarction (NSTEMI) and have a lower release of markers of cardiac necrosis. Therefore, they suggest that nitrates protect the heart towards ischemic episodes.[27] Similarly, another study showed that previous use of nitrates was associated with a tendency to present a non-ST-segment elevation acute coronary syndrome. It may be described by the hypothesis that nitrates induce pharmacological preconditioning, reducing the size of MI.[28] We found that cTFC is directly associated with the admission blood glucose. Hyperglycemia on admission occurs in 20-50% of patients with STEMI. The relationship between risk of increased mortality and glucose was not restricted to patients with preexisting diabetes mellitus.[29] Another study on patients undergoing pPCI revealed an increase in hospital mortality and contrast-induced nephropathy in patients with hyperglycemia.[30] Kawano *et al*.[31] reported that endothelial dysfunction could be associated with hyperglycemia. Iwakura *et al*.[32] showed that the blood glucose level is one of the independent predictors of no-reflow by using contrast echocardiography method. Nurkalem *et al*. reported that Gensini scores of patients with diabetes and impaired glucose tolerance are higher compared to patients with no history of those comorbidities.[33] Shen *et al*.[34] showed that cTFC is significantly higher in patients who have the highest blood glucose level. Similarly, Nakamura *et al*.[35] have explained that cTFC could be independently correlated with glucose levels in patients with STEMI undergoing primary PCI. Furthermore, Ahmet *et al*. observed that admission glucose level is associated with less coronary blood reflow (higher cTFC) in patients with STEMI who were treated with primary PCI.[36]

The no reflow phenomenon, one of the possible factors involved in poor myocardial reperfusion, is related with a longer ischemic time.[37] A study showed no significant difference in mean ischemic time between patients with MBG 0 or 1 compared with patients with MBG 2 or 3.[38] Our result was similar to pervious work. Another study showed that Patients with total ischemic times <5 h had MBG 3 than patients with total ischemic times >5 h, therefore this study concluded that with longer ischemic time (after a 5-h) myocardial reperfusion becomes suboptimal and mortality increases.[39] Patients were included in our study had total ischemic times <5 h, so we did not found a significant association between ischemic time and successful angiographic findings. Previous studies in patients with stable angina pectoris and acute coronary syndrome (ACS) (unstable angina and NSTEMI) showed a benefit effect of statin pre-treatment before PCI, however, only a few retrospective studies have assessed statin pre-treatment in STEMI. A study has been done by Celik *et al*.[40] showed that statin pre-treatment in patients with STEMI may improve coronary blood flow after PCI, maybe through beneficial effects on microvascular function. Lev *et al*.[41] demonstrated that previous chronic statin use before primary PCI reduced the 30-day short term mortality. Beneficial effects of statin pre-treatment in PCI settings were evaluated by several prospective trials. For instance, the Atorvastatin for Reduction of MYocardial Damage during Angioplasty (ARMYDA) trial reported patients with stable angina pectoris who used 7 day atorvastatin had an 81% risk reduction for periprocedural MI after PCI.[42] In the ARMYDA-ACS trial, short-term use of atorvastatin reduced the incidence of cardiac events in patients with ACS undergoing early PCI.[43] However, our study did not show any beneficial effects of statin pre-treatment on myocardial perfusion using cTFC, MBG and TIMI flow measurements, this inconsistency may be due to fewer patients in our study had used chronic statin treatment. Though, our findings are generally in accordance with the results of previous studies, however, further studies with a larger sample size are

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recommended in order to reconfirm the relationship of the possible covariates and angiographic outcomes of PCI observed in our study.

CONCLUSION

Our findings suggest that patients with history of nitrate and CCB intake may had a higher likelihood of successful PCI. In addition, patients with a higher blood glucose level on admission may have a reduced rate of reperfusion success. Future studies with a larger sample size are recommended to investigate the significant relationships observed in this study.

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