The impact of stepwise stent deployment on the angiographic and clinical outcome of coronary angioplasty in the setting of an acute myocardial infarction

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ABSTRACT

الأهداف: تحديد كيفية التغلب على انعدام تدفق الدم أثناء عملية قسطرة الشريان التاجي بعد الإصابة بالاحتشاء الأمامي الحاد للعضلة القلبية، بالإضافة إلى عمل مقارنة بين نفخ المعلاق الداعم بالطريقة التدريجية، أو نفخ المعلاق الداعم بالطريقة التقليدية وذلك اعتماداً على نسبة التحسن في دوران الدم بالأوعية الدموية والنتائج الملموسة في كلي الطريقتين.

الطريقة: أُجريت هذه الدراسة المتعددة المراكز والعشوائية في قسم القلب بمستشفى فالياسر، زنجان، إمام ريزا، وفي مستشفى شهيد مداني لأمراض القلب، تبريز، إيران، وقد استمرت الدراسة خلال الفترة من مارس 2007م إلى ديسمبر 2009م. شملت الدراسة 403 مريضاً مصاباً بالاحتشاء الأمامي الحاد للعضلة القلبية والذين تم علاجهم بعقار الستربتوكيناز بعد ظهور المشكلة بأقل من 6 ساعات. لقد تم تقسيم المرضى عشوائياً إلى مجموعتين وهما: المجموعة 1 التي أُجريت لها عملية قسطرة الشريان التاجي بالطريقة التدريجية لنفخ المعلاق الداعم (العدد=202)، والمجموعة 2 التي أُجريت لها نفس العملية ولكن باستخدام الطريقة التقليدية لنفخ المعلاق الداعم (العدد=201). ولقد وصل معدل عمر المرضى المشاركين في الدراسة إلى 57.7 ± 10.7 عاماً.

النتائج: أشارت نتائج الدراسة بأن قياس تروية الشرايين لعضلة القلب 0/1 والتي كانت تشير إلى انعدام تدفق الدم قد كانت عالية في المجموعة 2 (p=0.0001)، ولقد وصل عدد الوفيات في المستشفى في المجموعة 2 إلى 15 وفاة (7.5%)، فيما كان عدد الوفيات في المجموعة 1 4 وفيات (2%) (p=0.01). وكان قياس تروية الشرايين لعضلة القلب أعلى بكثير في المجموعة 1 (2.32 ± 0.18) مقارنة بالمجموعة 2 (1.66 ± 0.24) (p=0.0001). وأظهرت النتائج بأن إجراء قسطرة الشرايين بالطريقة التقليدية قد كان مؤشراً مستقلاً لانعدام التدفق وذلك في تحليل الانحدار اللوجستي المتعدد المستويات (نسبة الخطر 1.43، 95% مؤشر الأمان الإحصائي 1.15-1.73، p=0.01).

خاتمة: أثبتت الدراسة مدى فعالية الطريقة التدريجية في نفخ المعلاق الداعم حيث أنها أدت إلى تحسين تروية الأوعية الدموية لعضلة القلب، كما أنها قد قللت من نسبة الوفيات بين المرضى المصابين بالاحتشاء الأمامي الحاد للعضلة القلبية والذين خضعوا لعملية قسطرة الشريان التاجي.

Objectives: To detect a reduction in the incidence of no-reflow, and a possible improvement in angiographic and clinical outcome after stepwise stenting in comparison with conventional method in the percutaneous coronary intervention (PCI) of patients with anterior ST elevation myocardial infarction.

Methods: Between March 2007 and December 2009, patients with anterior acute myocardial infarction (AMI) treated with streptokinase less than 6 hours from presentation who underwent early PCI were enrolled in this multicenter randomized clinical trial. The study was carried out in the Cardiology Departments of Valiasr Hospital of Zanjan, Imam Reza, and Shahid Madani Heart Hospitals, Tabriz, Iran.

Results: Four hundred and three patients were enrolled in this study. Patients were randomly divided into 2 groups: Group I (n=202) with stepwise stent deployment (SSD), and Group II (n=201) with routine conventional stent deployment (CSD). The patients' mean age was 57.7 ± 10.7 years. After PCI, thrombolysis in myocardial infarction myocardial perfusion grade (TMPG) 0/1, suggestive of no-reflow was significantly higher in the CSD group (p=0.0001). In the hospital, death occurred in 15 patients (7.5%) from the CSD group, while 4 (2%) from the SSD group (p=0.01). The TMPG was also significantly higher in the SSD group (average 2.32 ± 0.18) compared with the CSD group, (average 1.66 ± 0.24) (p=0.0001). The conventional stenting technique was an independent predictor of no-reflow in multivariate logistic regression analysis (hazard ratio - 1.43; 95% confidence interval: 1.15-1.73; p=0.01).

Conclusion: The SSD was associated with improved angiographic reperfusion indices and reduced mortality in early PCI for AMI.

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No-reflow phenomenon remains a serious complication of percutaneous coronary intervention (PCI) in the setting of acute coronary syndromes, and still occurs in a large number of patients with a patent epicardial infarct-related artery.[1] The incidence of no-reflow appears to be the highest in the subgroups of patients undergoing PCI for acute myocardial infarction.[2] A series of consistent data has clearly indicated that no-reflow has a robust negative impact on outcome, negating the potential benefit of primary PCI.[3-6] Therefore, prevention and treatment of no-reflow probably have a significant impact on the outcome of patients with ST segment elevation myocardial infarction (STEMI) undergoing PCI.[7] The mechanism underlying microvascular dysfunction after the restoration of epicardial blood flow is likely multifactorial.[8] Massive embolization of atherothrombotic debris,[9] free radical-induced endothelial dysfunction, increased myocardial cell calcium level and interstitial edema,[10] or a combination of these factors[8] have all been proposed. Also, fibrin formation, red-cell, platelet and neutrophil aggregation contribute to microvascular occlusion and increased resistance in the microvasculature.[8] Although several strategies have been utilized in the treatment of clinical no-reflow phenomenon, none of them is an established therapy in the reduction of clinical end points.[11-13] Considering the role of massive embolization of athero-thrombotic materials as one of the major mechanisms of no-reflow phenomenon,[9] we hypothesized that by applying stepwise coronary stent implantation versus conventional technique, the distal microcirculation would have enough time to absorb distal thrombotic and atherosclerotic debris, and therefore, it can reduce the likelihood of an abrupt, violent, and diffuse distal flow reduction, and prevent slow/no-reflow phenomenon.

This multicenter randomized study was designed to detect a reduction in the incidence of no-reflow, and a possible improvement in angiographic and clinical outcome after stepwise stenting in comparison with conventional method in the PCI of patients with anterior STEMI. The primary end point was the occurrence of no-reflow phenomenon (thrombolysis in myocardial infarction myocardial perfusion grade [TMPG 0/1]). Secondary end points were other angiographic (TIMI flow grade [TFG], corrected TIMI frame count [CTFG], TMPG) and clinical (in-hospital heart failure and major adverse cardiac events [MACE] including death of cardiac etiology, recurrent myocardial infarction, and the need for repeat revascularization of the target lesion [TLR]) endpoints.

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Methods. The study protocol was approved by the Local Ethics Committee at each participating institution and complies with the provisions of the Declaration of Helsinki. Written informed consent was obtained from all patients. Standard qualitative and quantitative definitions were used for the angiographic analysis.

Four hundred and three patients with acute anterior STEMI treated with streptokinase less than 6 hours from presentation, and who underwent early PCI for a significant thrombotic lesion with TFG 2/3 suitable for direct stenting were enrolled in this multicenter randomized clinical trial. The study was carried out in the Cardiology Departments of Valiasr Hospital of Zanjan, Imam Reza, and Shahid Madani Heart Hospitals of Tabriz University of Medical Sciences, Tabriz, Iran, between March 2007 and December 2009. Patients were randomly divided into 2 groups: Group I (n=202) with stepwise stent deployment (SSD) and Group II (n=201) with routine conventional stent deployment (CSD).

All 3 high-volume interventional centers used exactly the same database and definitions for procedural analysis and clinical events. We included patients with STEMI under 6 hours from presentation who received thrombolysis with streptokinase with ST segment resolution >50%; significant (>60% diameter stenosis) lesion with definite thrombus in the infarct-related artery (thrombolysis in myocardial infarction [TIMI] thrombus grade 2-4), and TIMI 2 or 3 flow that permit direct stenting. The exclusion criteria were: MI on stent thrombosis, left main coronary artery lesion, highly calcified lesion, vein graft lesion, total occlusion (TIMI 0, even if the infarct-related artery was identified after the guide wire being passed through the thrombus), cardiogenic shock, rescue PCI after failed thrombolysis, and unable to provide informed written consent.

Randomization and interventional procedure. Eligible patients that met the inclusion and exclusion criteria for stenting with informed written consent were randomly assigned (with a ratio of 1:1) to undergo SSD, or CSD according to a computer-generated random series of numbers at the time of coronary angiography. We used simple randomization in Excel software method separately in 3 different hospitals; 203 in Madani Hospital and 100 cases in each of Valiasr and Imam Reza hospitals.

Reference vessel diameter (RVD), target lesion length, percentage of diameter stenosis, and pre- and post- procedural minimal lumen diameter (MLD) were determined using quantitative coronary angiography

(QCA) system by an independent observer not involved in the procedure. The frames analyzed were end-diastolic frames that demonstrated the stenosis in its most severe form in a non-foreshortened projection. Angiographic TFG of the dilated artery was estimated before the procedure, and on the last control injection after completion of stent implantation, according to the 4 grades of flow. Also, thrombus burden grade was defined according to Gibson et al.[14] The PCI procedure was conducted according to the standard techniques. Only infarct related artery (IRA) stenting was performed. The choice of stent delivery balloon and stent design was made by the operator during the procedure based on a visual assessment of the reference diameter of the vessel (balloon/artery ratio=1). The procedure was performed similarly in both groups, except for the method of balloon inflation. In the CSD group, angioplasty procedure was performed according to standard methods, and on the first attempt the balloon was inflated up to the maximum determined inflation pressure depending on the reference vessel diameter. Maximum inflation pressure of approximately 14 atmospheres (atm) was maintained for 30 seconds followed by rapid deflation. In the group with SSD method, at first step, the stent balloon was inflated up to 6 atm, then 4 times stepwise re-inflations were performed with 2 atm increments for 30 seconds duration. These inflations were separated with balloon deflation and a 90-second reflow intervals. This 90-second reflow period between inflations was given in order to provide an opportunity for distal coronary microcirculation to absorb embolized atherothrombotic debris (**Figure 1**).

Post-procedural assessments. Coronary angiograms were reviewed off-line by 2 independent expert interventional cardiologists who were blinded to the stent inflation method. All images were acquired at 25 frames per second, and correction was made to assess the number of frames according to a 30 frames per second speed. The TFG were assessed visually, as described above. For the evaluation of myocardial perfusion grade for left anterior descending coronary artery (LAD), a right anterior oblique/cranial projection was used. This angiographic run was acquired during breath hold to avoid artifacts due to diaphragmatic motion. The TMPG was classified as previously reported by Gibson et al.[15] The TIMI frame count (TFC) was also used to measure the coronary flow. These frame counts were corrected for the longer length of the LAD by dividing the TFC of LAD by 1.7 to arrive at the corrected TIMI frame count (CTFC). Then, these CTFCs were corrected to frame rate of 30 frames. Procedural success was defined as the presence of less than 20% residual stenosis after stenting with TMPG 2 or 3. The no-reflow phenomenon was defined as a TIMI myocardial perfusion grade 0/1. Clinical success was defined as angiographic success without major in-hospital complication (death, MI, stent occlusion and target lesion revascularization). Evaluation of secondary end points was also blinded.

Data analysis was carried out using the Statistical Package for Social Sciences version 16 (SPSS Inc., Chicago, IL, USA). The results of the quantitative variables were presented as the mean ± standard deviation (SD), and the results of qualitative variables as percentages. To compare quantitative and qualitative variables between groups, t-test, and chi-square test

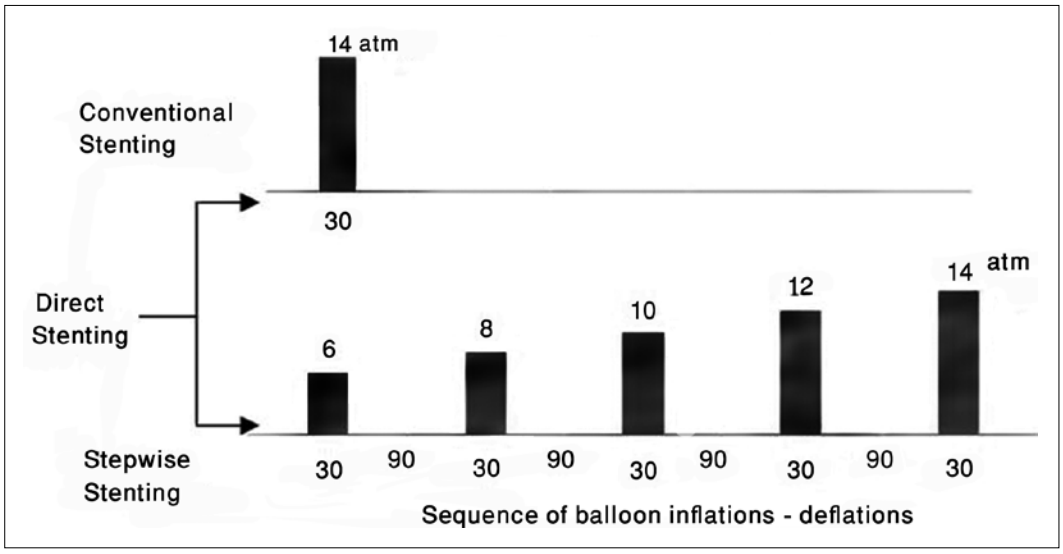

Figure 1 - Schematic representation of balloon inflation techniques in groups with conventional and stepwise stent deployment.

were used. The significance of differences between the medians was determined by a non-parametric method (Mann-Whitney U and Wilcoxon's signed rank test). Multivariate logistic regression analysis was performed to determine the independent correlates of no-reflow. *P*-value <0.05 was considered significant.

Results. Two groups of patients with CSD and SSD balloon inflation were similar considering their basic clinical, and angiographic characteristics (**Table 1**). The mean heart rate and blood pressure at hospital admission, and time from onset of chest pain to PCI were comparable between the 2 groups. More than 90% of cases had a modified American College of Cardiology/American Heart Association lesion types B2 or C, and 80.5% of them had a TIMI thrombus grade 3 or 4.

There was no significant difference between pre-intervention TFG of the 2 different groups (p=0.541), but post-PCI, the difference between TFGs of the 2 groups was significant (2.44 ± 0.05 versus 2.04 ± 0.06 in SSD and CSD groups, p=0.047) (**Table 2**). The analysis showed a significant difference between baseline and final TFGs of the 2 groups with different methods of stent inflation (p=0.0001). There was no significant difference between pre-PCI corrected TIMI frame count of the 2 groups (28 frames versus 26 frames, p=0.35), but post-PCI mean CTFC was significantly lower in the SSD inflation group 14.2 ± 6.6 frames versus 19.5 ± 8.4 frames, p=0.0001). The TMPG could be assessed in 97.6% of patients. The myocardial perfusion grade was significantly better in the SSD inflation group (average of 2.32 ± 0.18) than in the CSD group (average of 1.66 ± 0.24) (p=0.0001). After the angioplasty procedure, TMPG 0/1 suggestive of no-reflow was present in 39.7% of patients with TFG 2 or 3 in the CSD group compared to 14.7% of those with TFG 2 or 3 in the SSD group (p=0.0001) (**Table 2**). All heart failure episodes occurred in patients with TMPG zero or one (patients with no-reflow).

There were 6 (3%) intra-procedural deaths in the CSD group compared with 1 (0.5%) in the SSD group. In-hospital mortality due to cardiogenic shock was 4.5% (9 patients) in the CSD group compared with 1.5% (3 patients) in the SSD group one (total in-hospital death was 7.5% versus 2%, p=0.01) (**Table 3**). Glycoprotein IIb/IIIa receptor inhibitor (Integrilin) was used in 24.4% of the cases in the CSD group versus 8.6% in SSD inflation group (p=0.03), including all cases with no-reflow state. The intra aortic balloon pump was used in 15.9% in the CSD group, and 7.8% in the SSD group (p=0.03). Stepwise inflation did not

Table 1 - Baseline demographic, clinical, and angiographic characteristics of groups.

Variables	Conventional group (n=201)	Stepwise group (n=202)	*P*-value
Age (mean ± SD)	56.9 ± 10.3	58.6 ± 11.2	NS
Male (%)	144 (71.6)	149 (73.8)	NS
Body mass index (kg/m^2), mean ± SD	26.2 ± 2.8	25.6 ± 2.2	NS
Diabetes (%)	40 (19.9)	42 (20.8)	NS
Pre-infarction angina (%)	86 (42.8)	80 (39.6)	NS
Heart rate on admission (bpm), mean ± SD	85.8 ± 16.3	84.9 ± 15.6	NS
Systolic blood pressure on admission (mean ± SD)	111.6 ± 19.8	109.7 ± 17.7	NS
Time from symptom onset to SK (hour), mean ± SD	4.30 ± 2.36	4.04 ± 2.47	NS
Time from symptom onset to PCI (hour), mean ± SD	19.07 ± 3.45	18.25 ± 3.15	NS
Multivessel disease (%)	79 (39.3)	79 (36.6)	NS
Renal failure (GFR<60) (%)	18 (8.9)	21 (10.4)	NS
Killip class III (%)	33 (16.3)	32 (15.8)	NS
Lesion length (mm), mean ± SD	15.8 ± 7.9	14.9 ± 8.1	NS
Reference vessel diameter (mean ± SD)	3.15 ± 0.42	3.05 ± 0.36	NS
MLD (mm) (pre-PCI) (mean ± SD)	0.78 ± 0.28	0.76 ± 0.24	NS
Diameter stenosis (pre-PCI) (mean ± SD)	81.2 ± 8.2	82.4 ± 8.1	NS
Thrombus score 3 or 4 (%)	162 (80.6)	165 (81.7)	NS
Type B2 or C lesion (%)	182 (90.5)	186 (92.1)	NS
Mean level of Troponin I (ng/ml) (mean ± SD)	10.4 ± 10.2	10.8 ± 8.66	NS
Mean level of CK-MB (mean ± SD)	184.92 ± 157.72	188.64 ± 166.94	NS

SK - streptokinase, PCI - percutaneous coronary intervention, GFR - glomerular filtration rate, MLD - minimal luminal diameter, CK-MB - creatine kinase, NS - non significant

Table 2 - Post-procedural angiographic data in 2 groups of patients.

Variables	Conventional group (n=201)	Stepwise group (n=202)	*P*-value
MLD (mm) (post-procedure)	3.2 ± 0.6	3.1 ± 0.65	NS
Diameter stenosis (post-procedure) %	8.6 ± 5	7.3 ± 4	NS
Post-procedural proximal reference diameter (mm)	3.3 ± 0.62	3.2 ± 0.58	NS
Maximal inflation pressure (atm)	15.52 ± 3.25	16.05 ± 3.45	NS
Number of stents per lesion	1.2 ± 0.22	1.2 ± 0.20	NS
Total stent length (mm)	22.3 ± 11.1	21.6 ± 10.3	NS
Post-dilatation(%)	29.6	31.0	NS
TFG	2.04 ± 0.05	2.44 ± 0.05	0.047
CTFC	15.5 ± 8.4	11.2 ± 5.8	0.0001
TMPG	1.79 ± 0.28	2.44 ± 0.18	0.0001
TMPG 0/1 (no-reflow) in patients with TFG 2 or 3	35.7	14.7	0.0001

MLD - minimal luminal diameter, TIMI - thrombolysis in myocardial infarction, TFG - TIMI flow grade, CTFC - corrected TIMI frame count, TMPG - thrombolysis in myocardial infarction myocardial perfusion grade

Table 3 - In-hospital adverse events in the conventional and stepwise groups.

Variable	Conventional group (n=201)	Stepwise group (n=202)	*P*-value
Cardiac death (%)	15 (7.5)	4 (2.0)	0.01
Recurrent infarction (%)	6 (3.0)	4 (2.0)	0.39
Emergency CABGs (%)	0	0	1.0
IABP (%)	32 (15.9)	16 (7.9)	0.03
GPIs (%)	49 (24.4)	17 (8.4)	0.02
Stent thrombosis (%)	2 (1.0)	1 (0.5)	0.30
Heart failure (%)	34 (16.9)	17 (8.4)	0.07
Major bleeding (%)	12 (5.9)	13 (6.4)	0.65
Death/ReMI/TLR (%)	23 (11.4)	8 (4.0)	0.004

ReMI - recurrent myocardial infarction, TLR - target lesion revascularization, IABP - intra aortic balloon pump, GPIs - glycoprotein IIb/IIIa receptor inhibitor, CABG - coronary artery bypass grafting

Table 4 - Independent correlates of no-reflow in multivariate logistic regression analysis.

Variables	Hazard ratio	95% confidence interval	*P*-value
Lesion length >12mm	3.1	1.89-10.6	0.0001
Age >65 years	1.04	1.01-1.06	0.0001
Male gender	1.58	1.05-2.13	0.02
Conventional stent inflation	1.43	1.15-1.73	0.01

cause proximal or distal edge dissection of stent. There was no emergency coronary artery bypass graft surgery in either group. Univariate analysis showed that low LVEF, age >65, multi-vessel disease, male gender, lesion length, need for intra-aortic balloon pump, Integrilin administration, and CSD inflation were predictors of no-reflow. Independent correlates of impaired myocardial perfusion and no-reflow by multivariate logistic regression analysis are shown in **Table 4**.

Discussion. As an adjunct to thrombolysis, PCI might relieve residual stenosis and reduce reocclusion.[5] Data from Combined Abciximab REteplase Stent Study in acute myocardial infarction (CARESS in AMI) trial pointed out that high risk patients presenting with evolving STEMI who undergo thrombolytic therapy, should be transferred for PCI early after thrombolysis, regardless of the success of the thrombolytic therapy.[16] Also, the new European Society for Cardiology guidelines on STEMI recommend angiography after fibrinolytic therapy between 3 and 24 hours after the initial treatment.[17] Also, recent American College of Cardiology/American Heart Association guidelines follow this advice, with a similar IIa recommendation, but without a specific time window.[18] This study showed a better myocardial tissue perfusion and less in-hospital morbidity/mortality by early PCI after thrombolysis with new SSD technique compared with CSD stenting in patients with anterior wall AMI and TFG 2 or 3. Among clinical and angiographic variables, advanced age, lesion length, male gender, and conventional balloon inflation technique were independent predictors of no-reflow in this group of patients. More than one-third of the patients with TFG 2/3 in our conventional stent inflation group (compared with <15% in patients with TFG 2 or 3 in the SSD group) had TMPG 0/1 indicating no-reflow state. Since, the 2 groups were matched in their basic pre-PCI clinical and angiographic characteristics, the difference in post-procedural clinical and angiographic outcomes would be attributed to the

method of stent inflation. Optimal myocardial tissue perfusion is not always achieved in patients with a patent infarct-related artery, in spite of TFG 3 after PCI.[1-7,15] In our study, 40% of patients with TFG 2/3 in CSD group had TMPG 0/1. Despite excluding the patients with total occlusion of infarct-related artery and performing early (not primary PCI), the incidence of no-reflow in our study population was rather high. Henriques et al[4] showed that in patients with TIMI 3 flow after primary PCI, myocardial blush grade 0/1 occurred only in 11% of patients. The fact that we included only patients with anterior infarction, may explain at least partly the higher ratio of no-reflow in our study. In the study of Henriques et al,[4] patients with reduced blush grade had higher frequency of anterior myocardial infarction.[4] Also, it has been shown that more delay to PCI and higher extent of ischemia are associated with more prevalence of no-reflow. Lower rate of GpIIb/IIIa Inhibitor administration (mean 16%), and the type of thrombolytic we had used (streptokinase) may be the 2 other contributory factors.[4,7]

Compared with those in the CSD balloon inflation group, patients in the SSD inflation group had significantly better CTFC and TMPG (p=0.01), but this difference for TFG had borderline statistical significance (p=0.05). This may be related to the intrinsic limitations of TFG classification in the assessment of coronary blood flow. Substantial observer variability has been noted with TFG. Furthermore, although TFG classically compares flow in the infarct-related artery to flow in the normal nonculprit artery, flow in the non-infarcted -related artery in patients with STEMI is not truly normal compared with the flow in patients without STEMI.[14] Some studies addressed the technical considerations for the prevention of no-reflow. Isaaz et al,[19] recommended postponing stent implantation during primary PCI in patients with high thrombus burden or a long target lesion if adequate antegrade flow is achieved by initial predilatation, and they proposed treatment with low-dose thrombolysis or gpIIb/IIIa antagonists, and postponing stent implantation in this group of patients. Kirma et al,[20] have observed that when they have achieved TIMI 3 flow in the infarct-related artery after predilatation, the same patient developed no-reflow following stenting. However, plain old balloon angioplasty in this setting is associated with high rate of re-occlusion, and it has been shown that among AMI patients undergoing primary angioplasty, coronary stent implantation in addition to benefits in terms of TVR, reduces mortality in high-risk patients.[21] In our study, CSD technique was associated with pretty high incidence of no-reflow compared with the SSD method. This higher rate of no-reflow in CSD group most likely results from abrupt, and massive distal embolization of microparticulated atherothrombotic material, and plugging in capillary bed followed by inflammation, activation of neurohormonal reflexes and vasoconstriction. Gibson et al[22] showed that a negative residual stenosis (RS <0%) following rescue/adjunctive PCI after fibrinolytic therapy for STEMI, was independently associated with impaired myocardial tissue perfusion. In our study, balloon/artery ratio was ≤1 in 2 groups, but early clinical and angiographic results were better in the SSD group than in the CSD group. Theoretically, it might be postulated that stepwise balloon inflation gives some opportunity to microvascular system to evacuate embolized particles, and preclude their accumulation and reduce subsequent inflammatory response and mechanical obstruction. Some investigators suggested the utility of gradual balloon inflation during PCI for less arterial wall trauma and injury. However, this method did not lead to a significant reduction in restenosis or clinical adverse events during follow-up.[23]

More recently, Leibowitz et al,[24] have showed the combination of gradual computerized balloon inflation and subsequent stent deployment was especially effective in reducing TLR as compared with standard manual inflation. They used a computerized device (CAPSID) for gradual and very slow balloon inflation. But these studies were not conducted in patients with STEMI, in which no-reflow phenomenon is a major problem. The present study without the need for computerized devices such as CAPSID showed that SSD (not gradual) technique results in more optimal perfusion at the myocardial tissue level compared with conventional stenting. It seems that the combination of SSD inflation technique probably along with upstream adjunctive glycoprotein IIb/IIIa antagonists especially intra-coronary administration of abciximab[25,26] may be the most effective method for the prevention of no-reflow in the setting of PCI for STEMI, and it should be tested in a large randomized trial.

In our study, independent predictors of impaired myocardial tissue perfusion after PCI were age, lesion length, male gender, and conventional technique. There is a simple clinical and angiographic model for predicting no-reflow during primary PCI. In particular, advanced age, delayed reperfusion, low TFG, long target lesion, the presence of high thrombus burden on baseline angiography, reference lumen diameter of the IRA ≥4.0 mm[27] have been associated with the development of no-reflow. However, in this study, male gender was also an independent predictor of no-reflow after PCI in patients with anterior wall MI. Female gender has been repeatedly shown to influence the outcome of treatment of coronary stenosis with PCI. Women experience greater complications and early

mortality after revascularization.[28] However, in this study, male gender was consistently associated with the development of no-reflow after PCI in patients with STEMI. It is well-established that the presence of no-reflow during PCI has been associated with poor short- and long- term outcomes.[3-7,29] In our study, the SSD group had significantly lower rate of no-reflow state, and 3.7 times lower in hospital mortality compared with CSD group and multivariate logistic regression analysis confirmed the role of this technique as an independent predictor of this outcome. Our stepwise method of stent deployment not only reduced the incidence of no-reflow phenomenon and post-PCI mortality and complications, but also was very safe and it was not associated with any complication including proximal or distal edge-dissection. Furthermore, it has no additional cost as compared with other previously suggested therapies such as GpIIb/IIIa antagonists, and manual catheter aspiration and CAPSID. Therefore, it might be an attractive option in treating highly thrombotic lesions in the setting of acute MI. Nevertheless, larger studies with long-term follow-up, especially in the setting of primary PCI, are needed to determine how this early beneficial effect of SSD on myocardial perfusion may be translated in long-term improvement in cardiovascular morbidity and mortality in patients with AMI.

No intravascular ultrasound scan evaluation was used in this study to evaluate plaque content and thrombus burden, and to compare the influence of the 2 strategies of stent implantation on the arterial wall. The sample size was relatively small, and the small number of events observed limits the statistical power of this analysis in detecting a difference in event rates among the treatment groups. Moreover, we did not evaluate microvascular no-reflow using nuclear scintigraphy or myocardial contrast echocardiography. Also, the effect of these techniques on patients with totally occluded infarct related artery is uncertain, because these patients were excluded from the study.

In conclusion, among this highly selected patients with acute anterior STEMI treated with streptokinase less than 6 hours from presentation, and a thrombotic LAD lesion with TFG 2 or 3 and ST resolution >50% who underwent early PCI, stepwise stent inflation compared with routine stent inflation method, had a better clinical and angiographic outcome. Larger studies especially in the setting of primary PCI are needed to confirm this hypothesis.

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