Acta Cardiol Sin 2017;33:258–265
Original Article
doi: 10.6515/ACS20161103A

Percutaneous Coronary Intervention

Local Intracoronary Infusion of Glycoprotein IIb/IIIa Inhibitors via a Perfusion Catheter versus Intracoronary Guiding Catheter Injection during Primary Percutaneous Coronary Intervention: A Pilot Observational Study

Tarek Zaki,[1] Salwa Labib,[2] Maged El-Abbady,[2] Wael El-Kilany,[1] Ayman Mortada,[1] Tarek Rashid,[1] Hany Ragy,[2] Adel El-Itreby[1] and Wail Nammas[1]

Background: Glycoprotein IIb IIIa inhibitors improved short- and long-term outcome when added to primary percutaneous coronary intervention (PPCI) in patients with ST-segment-elevation myocardial infarction (STEMI). We hypothesized that intracoronary eptifibatide infusion via a perfusion catheter improves angiographic and clinical outcome of patients with STEMI undergoing PPCI, versus conventional intracoronary bolus injection.

Methods: Prospectively, we enrolled 80 patients with acute STEMI and thrombolysis in myocardial infarction (TIMI) thrombus grade $\geq$ 2. Patients were assigned to receive eptifibatide (180 μg) either via a dedicated coronary perfusion catheter (ClearWay™) during PPCI (group I), or guiding catheter (group II). Assessment of TIMI thrombus grade, TIMI flow grade, and TIMI myocardial perfusion (TMP) grade was performed both at baseline and post-procedurally. The primary 'angiographic' endpoint was final TMP grade 0/1. The primary 'clinical' endpoint was a composite of cardiac death, non-fatal re-infarction, target vessel revascularization, and recurrent ischemia at 30-day follow-up.

Results: Mean age was 52.3 $\pm$ 8.9 years (17.5% females). Clearance of visible thrombus (TIMI thrombus grade 0) at final angiogram was more frequent in group I. Additionally, both final TIMI flow grade 3 and final TMP grade 3 occurred more frequently in group I. The primary angiographic endpoint was more frequent in group II versus group I (17.5% versus 0%, respectively, p = 0.001). The primary clinical endpoint was more frequent in group II (20% versus 0%, respectively, p = 0.003).

Conclusions: In patients with STEMI, intracoronary eptifibatide infusion via a perfusion catheter during PPCI improved immediate angiographic outcome, and reduced clinical events at 30-day follow-up, versus bolus injection via the guiding catheter.

Key Words: Coronary perfusion catheter • Glycoprotein IIb IIIa inhibitors • Microvascular perfusion • Primary percutaneous coronary intervention • ST-elevation myocardial infarction

INTRODUCTION

Primary percutaneous coronary intervention (PPCI) is the standard treatment for patients with ST-segment-elevation myocardial infarction (STEMI).[1] Restoring tissue perfusion, and thereby myocardial salvage, is the single most important objective in the management of

Received: November 21, 2015 Accepted: November 3, 2016
[1]Department of Cardiology, Faculty of Medicine, Ain Shams University; [2]National Heart Institute, Cairo, Egypt.
Corresponding author: Dr. Wail Nammas, Department of Cardiology, Faculty of Medicine, Ain Shams University, Abbassia, Cairo, P.O. 11381, Egypt. Tel: +2 0122 4063718; Fax +2 02 24820416; E-mail: wnammas@med.asu.edu.eg

STEMI. Therefore, the immediate goal of reperfusion therapy has shifted from restoring normal epicardial blood flow (achievable in > 90% of the cases), to myocardial tissue perfusion, which is not restored in approximately one third of patients, even after successful PPCI.[2] Distal embolization of thrombotic material with microcirculation plugging, microvascular dysfunction, and ultimately cardiac myocyte necrosis are the main underlying causes.

Intravenous administration of glycoprotein IIb/IIIa inhibitors (GPI) improved short- and long-term outcome when added to PPCI in patients with STEMI.[3,4] Intracoronary bolus administration of eptifibatide improved glycoprotein IIb IIIa receptor occupancy and microvascular perfusion during early PCI for acute coronary syndrome, compared with intravenous bolus, possibly due to higher local drug concentrations.[5] Recently, local intracoronary infusion of GPI via a dedicated coronary perfusion catheter reduced thrombus burden and improved coronary flow in patients presenting with or developing thrombus during PCI.[6] In a small randomized trial, local intracoronary bolus abciximab via a coronary perfusion catheter, reduced thrombus burden in patients with acute coronary syndrome and evidence of culprit lesion thrombosis, compared with bolus abciximab delivered via guiding catheter injection.[7] Yet the efficacy of this novel approach as an adjunct to PPCI in patients with STEMI remains unclear. We hypothesized that local intracoronary eptifibatide infusion via a dedicated perfusion catheter would improve the immediate angiographic and clinical outcome of patients with acute STEMI undergoing PPCI, compared with conventional intracoronary bolus injection.

METHODS

Patient selection and study design

The current study was a prospective, non-randomized two-center observational study conducted during the period from July 2012 to May 2013. We enrolled 80 patients who presented with acute STEMI within six hours of the onset of chest pain. STEMI was defined by persistent ST segment elevation (≥ 2 mm in two contiguous precordial leads, or ≥ 1 mm in two limb leads), new left bundle branch block, or new Q waves in two contiguous leads; with rise of biochemical markers of myocardial necrosis (CK-MB and/or troponin) at least twice the upper reference limit. To be eligible, patients needed to have thrombolysis in myocardial infarction (TIMI) thrombus grade ≥ 2 in the infarct-related artery.[8] We excluded patients with Killip class ≥ 3, those with renal impairment (creatinine > 2 mg/dL), and those with known hypersensitivity to currently used anti-thrombotic medications. An informed written consent was obtained from each patient, and the study protocol was reviewed and approved by the Ethics Committee of each participating center as it conforms to the ethical guidelines of the 1964 Declaration of Helsinki, as revised in 2013.

Eligible patients were assigned to one of the following groups:

1) Group I: received eptifibatide via a dedicated coronary perfusion catheter (ClearWay™ RX, Atrium Medical Corporation, NH, USA) at the time of PPCI; and 2) Group II: received eptifibatide by standard intracoronary bolus injection.

The 2 groups were followed for 30 days by means of clinical visits or telephone contact.

Pharmacological interventions

Patients received oral chewable aspirin 300 mg initially at the time of admission, followed by 150 mg daily orally, indefinitely. Clopidogrel was initiated at a loading dose of 600 mg given at the time of admission, followed by 75 mg daily orally. Weight-adjusted unfractionated heparin was administered intravenously to achieve a peri-procedural activated clotting time of 200-250 seconds. Eptifibatide (Integrilin, Merck, Whitehouse Station, NJ, USA) was administered as a double bolus (180 μg) (75% of the dose after wire passage; 25% after stent deployment), either by local intracoronary infusion at the site of thrombus via the ClearWay™ catheter (group I), or by intracoronary injection through the guiding catheter (group II). In either case, eptifibatide was buffered with 2 ml of 8.4% sodium bicarbonate solution. No maintenance eptifibatide was given intravenously in either group. Additionally, all patients received intracoronary verapamil (300 μgm) (75% of the dose after wire passage; 25% after stent deployment), either via the ClearWay™ catheter (group I), or through the guiding catheter (group II). Other

anti-ischemic treatment was given according to the contemporary guidelines.

Device technique

PPCI was performed according to current international standards. In group I, the ClearWay^{TM} catheter was advanced to the site of thrombus over a 0.014-inch guidewire, and the study drug (eptifibatide and verapamil) was infused locally in the dose mentioned above. During drug delivery, the catheter balloon was inflated at 2-4 atmospheres in order to prolong contact of the drug with the thrombotic lesion. Angiographic assessment of TIMI thrombus grade, epicardial coronary TIMI flow grade, TIMI myocardial perfusion (TMP) grade, and corrected TIMI frame count was performed at baseline, immediately after the initial drug administration, and at the end of the procedure – after stent deployment and the final drug administration. Scoring of angiographic parameters was adjudicated retrospectively by experienced operators blinded to the treatment group allocation.

Study endpoints and definitions

Angiographic success was defined as successful implantation of the stent with residual stenosis < 20%, and final TIMI flow grade 3, in the absence of dissection or thrombosis. Clinical success was defined as angiographic success in the absence of in-hospital major adverse cardiac events. The primary 'angiographic' endpoint was post-procedural final TMP grade 0 or 1. The primary 'clinical' endpoint was defined as a composite of cardiac death, non-fatal re-MI, target vessel revascularization (TVR), and recurrent ischemia at 30-day follow-up. Cardiac death was defined as death from cardiovascular causes or any death without other known cause. MI was diagnosed by persistent ischemic-type chest pain with rise of biochemical markers of myocardial necrosis (CK-MB and troponin) at least twice the upper reference limit. In-hospital re-MI was diagnosed by a new rise of biochemical markers (CK-MB and troponin) at least 50% above the lowest level previously measured. TVR was defined as any repeat intervention (surgical or percutaneous) to treat a significant luminal restenosis (defined as > 50% diameter stenosis by visual estimation) within the index vessel. Recurrent ischemia was defined as recurrence of chest pain with electrocardiogram (ECG) changes of myocardial ischemia in the target vessel territory, but without a rise of biochemical markers of myocardial necrosis. ST segment resolution was assessed in ECG at baseline, 6, 12 and 24 hours. ST segment resolution was classified as complete (≥ 70% resolution of the initial ST segment elevation), or incomplete (< 70% resolution). Clinical endpoints were adjudicated by investigators blinded to the treatment group allocation.

Statistical analysis

Continuous variables were presented as mean ± SD, if they were normally distributed. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. Comparisons between the two individual groups were performed using the unpaired *t*-test or the Mann-Whitney test for continuous variables, and Pearson's χ^2 or Fisher's Exact test for categorical variables, as appropriate. All tests were two-sided and a probability value of $p < 0.05$ was considered statistically significant. Analyses were performed with SPSS version 12.0 statistical package (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline clinical characteristics and procedural data

A total of 80 patients with acute STEMI eligible for PPCI were assigned to either group I (40 patients) or group II (40 patients). Baseline characteristics and electrocardiographic data are shown in Table 1. The mean age of the whole series was 52.3 ± 8.9 years, with 17.5% females, and 42.5% diabetic. Average time to first medical contact was similar and short in the two groups ($p = 0.81$). The left anterior descending artery was the most common culprit artery in both groups. Although complete ST segment resolution was comparable between the two groups at six hours, it was more frequent in group I versus group II, at 12 and 24 hours ($p < 0.05$ for both). There were no significant differences between the two groups regarding baseline characteristics ($p > 0.05$ for all). Procedural data are summarized in Table 2. Both direct stenting and thrombectomy were used more frequently in group I, com-

Table 1. Baseline clinical characteristics and electrocardiographic data of the 2 study groups

	Group I (N = 40)	Group II (N = 40)	p
Age (years)	51.5 ± 9.4	53.1 ± 8.4	0.42
Female gender	9 (22.5)	5 (12.5)	0.24
Family history of ischemic heart disease	11 (27.5)	10 (25)	0.80
Smoking	28 (70)	26 (65)	0.63
Hypertension	14 (35)	17 (42.5)	0.49
Diabetes mellitus	16 (40)	18 (45)	0.65
Dyslipidemia	15 (37.5)	11 (27.5)	0.34
Time to first medical contact (hours)	3.6 ± 1.4	3.8 ± 1.6	0.81
Target vessel			0.58
Left anterior descending artery	18 (45)	21 (52.5)	
Diagonal branch	0 (0)	1 (2.5)	
Left circumflex artery	4 (10)	4 (10)	
Obtuse marginal branch	2 (5)	1 (2.5)	
Right coronary artery	16 (40)	13 (32.5)	
Complete ST segment resolution at 6 hrs	24 (60)	18 (45)	0.19
Complete ST segment resolution at 12 hrs	33 (82.5)	18 (45)	0.007
Complete ST segment resolution at 24 hrs	34 (85)	23 (57.5)	0.02

Continuous variables are presented as mean ± SD, whereas categorical variables are presented as frequency (percentage).

Table 2. Procedural data of the 2 study groups

	Group I (N = 40)	Group II (N = 40)	p
Direct stenting	29 (72.5)	19 (47.5)	0.02
Thrombectomy device	3 (7.5)	0 (0)	0.08
Number of stents			0.03
One stent	36 (90)	28 (70)	
Two stents	4 (10)	12 (30)	
Stent type			0.49
Bare-metal stent	38 (95)	35 (87.5)	
Drug-eluting stent	2 (5)	5 (12.5)	
Total stent length	25.4 ± 5.9	24.8 ± 4.5	0.05
Stent diameter	3.2 ± 0.4	3.1 ± 0.3	0.30

Continuous variables are presented as mean ± SD, whereas categorical variables are presented as frequency (percentage).

pared with group II. Although fewer stents were implanted in group I versus group II, the total stent length was similar between the two groups; most were bare-metal stents.

Angiographic outcome data

Although baseline TIMI thrombus grade was higher in group I versus group II, final angiogram showed the clearance of visible thrombus (TIMI thrombus grade 0) was more frequent in group I. Similarly, although baseline TIMI flow grade was better in group II versus group I, both TIMI flow grade 3 after initial GPI administration and final TIMI flow grade 3 were more frequent in group I. Likewise, although baseline TMP grade was better in group II versus group I, both TMP grade 3 after initial eptifibatide administration and final TMP grade 3 were more frequent in group I. The primary angiographic endpoint (final TMP grade 0/1) was more frequent in group II versus group I (17.5% versus 0%, respectively, p = 0.001). Furthermore, final corrected TIMI frame count was shorter in group I. Angiographic outcome data are summarized in Table 3.

Clinical outcome at 30-day follow-up

Two patients (5%) in group II developed immediate acute stent thrombosis, with final TIMI flow grade 0, and died shortly following the procedure. Both angiographic success and clinical success were more frequent in group I compared with group II (p = 0.01 for both). Similarly, the primary clinical endpoint was more frequent in group II (20% versus 0%, respectively, p = 0.003). This was mainly driven by more episodes of recurrent ischemia in group II (10% versus 0%, respectively, p = 0.04). No bleeding complications occurred in either treatment group. Clinical outcome data at 30-day follow-up are summarized in Table 4.

Table 3. Angiographic outcome data of the 2 study groups

	Group I (N = 40)	Group II (N = 40)	p
Thrombus grade at baseline			0.02
3	0 (0)	7 (17.5)	
4	4 (10)	5 (12.5)	
5	36 (90)	28 (70)	
Thrombus grade after initial GPI			0.001
0	0 (0)	3 (7.5)	
1	1 (2.5)	3 (7.5)	
2	1 (2.5)	5 (12.5)	
3	10 (25)	5 (12.5)	
4	28 (70)	16 (40)	
5	0 (0)	8 (20)	
Thrombus grade after final GPI			0.02
0	37 (92.5)	25 (62.5)	
1	3 (7.5)	7 (17.5)	
2	0 (0)	3 (7.5)	
3	0 (0)	3 (7.5)	
4	0 (0)	0 (0)	
5	0 (0)	2 (5)	
TIMI flow grade at baseline			0.001
0	39 (97.5)	25 (62.5)	
1	1 (2.5)	7 (17.5)	
2	0 (0)	4 (10)	
3	0 (0)	4 (10)	
TIMI flow grade after initial GPI			0.02
0	0 (0)	7 (17.5)	
1	22 (55)	13 (32.5)	
2	8 (20)	12 (30)	
3	10 (25)	8 (20)	
TIMI flow grade after final GPI			0.03
0	0 (0)	2 (5)	
1	0 (0)	2 (5)	
2	5 (12.5)	12 (30)	
3	35 (87.5)	24 (60)	
TMP flow grade at baseline			0.001
0	39 (97.5)	25 (62.5)	
1	1 (2.5)	7 (17.5)	
2	0 (0)	7 (17.5)	
3	0 (0)	1 (2.5)	
TMP flow grade after initial GPI			0.001
0	0 (0)	10 (25)	
1	23 (57.5)	14 (35)	
2	8 (20)	14 (35)	
3	9 (22.5)	2 (5)	
TMP flow grade after final GPI			0.04
0	0 (0)	2 (5)	
1	0 (0)	5 (12.5)	
2	10 (25)	11 (27.5)	
3	30 (75)	22 (55)	
Final corrected TIMI frame count	21.5 ± 4.0	23.8 ± 3.8	0.01

Continuous variables are presented as mean ± SD, whereas categorical variables are presented as frequency (percentage). GPI indicates glycoprotein IIb/IIIa inhibitor; TIMI, thrombolysis in myocardial infarction; TMP, TIMI myocardial perfusion.

Table 4. Clinical outcome data of the 2 study groups at 30-day follow-up

	Group I (N = 40)	Group II (N = 40)	p
Angiographic success	34 (85)	24 (60)	0.01
Clinical success	34 (85)	24 (60)	0.01
Primary angiographic endpoint	0 (0)	7 (17.5)	0.001
Cardiac death	0 (0)	2 (5)	0.15
Recurrent myocardial infarction	0 (0)	1 (2.5)	0.21
Target vessel revascularization	0 (0)	1 (2.5)	0.21
Recurrent ischemia	0 (0)	4 (10)	0.04
Primary clinical endpoint	0 (0)	8 (20)	0.003
Bleeding events	0 (0)	0 (0)	NA

Variables are presented as frequency (percentage).
NA indicates not available.

DISCUSSION

Main findings

The current study demonstrated that in patients presenting with acute STEMI who have TIMI thrombus grade ≥ 2, local intracoronary eptifibatide infusion via a dedicated perfusion catheter at the time of PPCI, reduced thrombus burden, improved the immediate angiographic outcome, and reduced major adverse cardiac events at 30-day follow-up, compared with conventional intracoronary eptifibatide bolus via guiding catheter injection. To the best of the authors' knowledge, this is the first report of local eptifibatide infusion via a perfusion catheter during PPCI for STEMI.

Glycoprotein IIb IIIa inhibitors and microvascular perfusion

GPI act as competitive inhibitors of fibrinogen for binding to platelet glycoprotein IIb IIIa receptors on the surface of activated platelets. Thus, increasing the local concentration of GPI at the site of thrombus formation would displace bound fibrinogen which serves to cross-link activated platelets to form an occlusive thrombus. Bench-top studies of coronary flow demonstrated that eptifibatide dispersed platelets more efficiently at concentrations much higher than those commonly achieved with conventional intravenous administration during PCI.[9,10] Additionally, further evidence from in vitro studies supports that higher concentration of GPI is needed to disperse older than fresh platelet thrombi.[11] The

Intracoronary Eptifibatide (ICE) trial showed that intracoronary bolus administration of eptifibatide significantly improved local 'coronary sinus' platelet glycoprotein IIb IIIa receptor occupancy and reduced cTFC, compared with intravenous bolus, during early PCI for acute coronary syndrome.[5] Moreover, in a randomized study by Thiele et al., intracoronary bolus administration of abciximab during PPCI for patients with STEMI reduced infarct size, and decreased the extent of microvascular obstruction as revealed by delayed-enhancement cardiac magnetic resonance, compared with intravenous bolus administration.[12] However, intracoronary administration of GPI via the guiding catheter would eventually lose much of the dose in side branches before reaching the site of thrombus. Local intracoronary infusion of GPI at the site of thrombus formation via a dedicated coronary perfusion catheter would achieve much higher concentration of the drug, and consequently better thrombus dispersal and improved microvascular perfusion. Unlike the ICE trial, we opted to enroll patients with a high thrombus burden (STEMI with TIMI thrombus grade $\geq$ 2 in the infarct-related artery) assuming that they have the highest risk of thrombotic microvascular occlusion; and therefore, would derive the greatest angiographic and clinical benefit. And although the ICE trial did not show a significant difference of final TIMI flow grade and TMP grade between intravenous and intracoronary administration of eptifibatide (the same with abciximab in the study by Thiele et al.), both were better with local intracoronary infusion, compared with bolus guiding catheter injection, in the current study.[5,12] This might be due to the enrollment of patients with lower thrombus burden in the ICE trial (visible thrombus in only 27.3% in the intracoronary arm, and 36.8% in the intravenous arm), who were at a lower risk of microvascular occlusion, and consequently derived less benefit.[5] In the COCTAIL (ClearwayRx System to reduce intracoronary thrombus in patients with acute coronary syndromes according to Optical Coherence Tomography after Abciximab Intracoronary Local infusion) study by Prati et al., bolus abciximab via coronary perfusion catheter reduced thrombus burden as assessed by optical coherence tomography in patients with acute coronary syndrome (38% STEMI) and culprit lesion thrombosis, compared with bolus abciximab delivered via guiding catheter injection.[7] Additionally, local abciximab delivery via coronary perfusion catheter improved the immediate angiographic outcome, and was associated with fewer procedure-related MI, and fewer major adverse cardiac events at 1-year follow-up.[7] In contrast to the current study, patients in the COCTAIL study received downstream clopidogrel loading dose – after the completion of PCI – and received maintenance intravenous infusion of GPI.[7] The results of the current study with eptifibatide support those of the COCTAIL study, improve the level of evidence for local delivery of GPI via coronary perfusion catheter, and emphasize the benefit of the novel approach in patients with STEMI undergoing PPCI. Moreover, we opted to administer intracoronary verapamil along with eptifibatide in order to further reduce no-reflow in the infarct-related artery.[13] The administration of verapamil may have further contributed to improving the final angiographic outcome in the current study.

Clinical implications

Our data supported the hypothesis that building up a higher local concentration of GPI by local infusion via a perfusion catheter not only reduced thrombus burden, and improved flow in the micro-circulation, but also reduced ischemic events at 30-day follow-up, compared with standard guiding catheter injection. However, the current study was underpowered to detect a significant difference in major adverse cardiac events, and the difference in clinical outcome should be taken as hypothesis-generating rather than conclusive. Resolution of thrombus before stent implantation in patients with STEMI undergoing PPCI allows for a better angiographic assessment of the infarct-related segment; and therefore, a better selection of the size (diameter and length) of the stent to be implanted. In this respect, direct stenting was more frequent, and fewer stents were implanted with local intracoronary infusion, compared with intracoronary bolus injection. Nevertheless, more often use of thrombectomy device with local intracoronary infusion of eptifibatide might have contributed to the better angiographic results. Moreover, giving 25% of the dose (both eptifibatide and verapamil) after stent deployment would serve to disperse residual microthrombi, and those resulting from the PCI procedure. And unlike the ICE trial, we did not give maintenance intravenous infusion of eptifibatide in either arm of the

study. This would further reduce the risk of bleeding, and reduce the amount and cost of drug used. Finally, improved microvascular perfusion as reflected by better final TMP grade and final corrected TIMI frame count was probably responsible for the better clinical outcome at 30-day follow-up. Improvement of microvascular perfusion as reflected by a better corrected TIMI frame count was associated with reduction of major adverse cardiac events, both in patients in patients with STEMI who received thrombolytic therapy and in patients with acute coronary syndrome who underwent early PCI.[14,15]

Limitations of the study

Our findings are based on a single center study with a relatively small sample size of the cohort. Multi-center studies using the same protocol and examining a larger number of patients are needed. Moreover, the current study was not randomized, and although most of the baseline characteristics were matched between the two groups, the possibility of selection bias cannot be excluded. Ultimately, further extended periods of follow-up would be more useful to delineate the long-term outcome of the index strategy.

CONCLUSIONS

In patients with acute STEMI and TIMI thrombus grade ≥ 2, local intracoronary eptifibatide infusion via a dedicated perfusion catheter at the time of PPCI was associated with reduced thrombus burden, improved immediate angiographic outcome, and 30-day clinical outcome, compared with intracoronary GPI bolus injection via the guiding catheter.

ACKNOWLEDGMENTS

None.

FUNDING

This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

CONFLICT OF INTERESTS

None declared.

REFERENCES

1. Steg PG, James SK, Atar D, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33:2569-619.
2. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Eur Heart J* 2012;33:2551-67.
3. De Luca G, Suryapranata H, Stone GW, et al. Abciximab as adjunctive therapy to reperfusion in acute ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. *JAMA* 2005;293:1759-65.
4. Zeymer U, Margenet A, Haude M, et al. Randomized comparison of eptifibatide versus abciximab in primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction: results of the EVA-AMI trial. *J Am Coll Cardiol* 2010;56:463-9.
5. Deibele AJ, Jennings LK, Tcheng JE, et al. Intracoronary eptifibatide bolus administration during percutaneous coronary revascularization for acute coronary syndromes with evaluation ofplatelet glycoprotein IIb/IIIa receptor occupancy and platelet function: the Intracoronary Eptifibatide (ICE) trial. *Circulation* 2010;121:784-91.
6. Maluenda G, Sizemore BC, Revtyak G, et al. Intracoronary glycoprotein IIb/IIIa inhibitor infusion via a perfusion coronary catheter to decrease thrombus burden: results from the ClearWay™ Multicenter Registry. *Cardiovasc Revasc Med* 2013;14:280-3.
7. Prati F, Capodanno D, Pawlowski T, et al. Local delivery versus intracoronary infusion of abciximab in patients with acute coronary syndromes. *JACC Cardiovasc Interv* 2010;3:928-34.
8. Gibson CM, de Lemos JA, Murphy SA, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. *Circulation* 2001;103:2550-4.
9. Moser M, Bertram U, Peter K, et al. Abciximab, eptifibatide, and tirofiban exhibit dose-dependent potencies to dissolve platelet aggregates. *J Cardiovasc Pharmacol* 2003;41:586-92.
10. Goto S, Tamura N, Ishida H. Ability of anti-glycoprotein IIb/IIIa agents to dissolve platelet thrombi formed on a collagen surface under blood flow conditions. *J Am Coll Cardiol* 2004;44:316-23.
11. Speich HE, Earhart AD, Hill SN, et al. Variability of platelet aggregate dispersal with GP IIb/IIIa antagonists eptifibatide and abciximab. *J Thromb Haemost* 2009;7:983-91.
12. Thiele H, Schindler K, Friedenberger J, et al. Intracoronary compared with intravenous bolus abciximab application in patients with ST-elevation myocardial infarction undergoing primary per-

cutaneous coronary intervention: the Randomized Leipzig Immediate Percutaneous Coronary Intervention Abciximab IV versus IC in ST-Elevation Myocardial Infarction Trial. *Circulation* 2008;118:49-57.

13. Fu Q, Lu W, Huang YJ, et al. Verapamil reverses myocardial noreflow after primary percutaneous coronary intervention in patients with acute myocardial infarction. *Cell Biochem Biophys* 2013;67:911-4.
14. Gibson CM, Murphy SA, Rizzo MJ, et al. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. *Circulation* 1999;99:1945-50.
15. Wöhrle J, Grebe OC, Nusser T, et al. Reduction of major adverse cardiac events with intracoronary compared with intravenous bolus application of abciximab in patients with acute myocardial infarction on unstable angina undergoing coronary angioplasty. *Circulation* 2003;107:1840-3.