Effects of EPC capture stent and CD34+ mobilization in acute myocardial infarction

Minerva Cardioangiologica
==========

Title: EFFECTS OF EPC CAPTURE STENT AND CD34+ MOBILIZATION IN ACUTE MYOCARDIAL INFARCTION
Paper code: Minerva Cardioangiol-3338
Submission Date: 2012-09-18 23:30:49
Article Type: Original Article

Files:
1): Manuscript
    Version: 2
    Description: Manuscript
    File format: application/msword

2): Tables 1
    Version: 1
    Description: Tables I-V
    File format: application/octet-stream

3): Figures 1
    Version: 1
    Description: Figure 1
    File format: image/tiff

4): Figures 2
    Version: 1
    Description: Figure 2
    File format: image/tiff

5): Figures 3
    Version: 1
    Description: dich.autori-pag2
    File format: application/pdf

EFFECTS OF EPC CAPTURE STENT AND CD34+ MOBILIZATION IN ACUTE MYOCARDIAL INFARCTION

Paolo Scacciatella[1] MD, Maurizio D'Amico[1] MD, Mauro Pennone[1] MD, Federico Conrotto[1] MD, Emanuele Meliga[2] MD, FESC, Tullio Usmiani[2] MD, Ilaria Meynet[1] MD, Monica Gunetti[3] PhD, Ivana Ferrero[3] PhD, Deborah Rustichelli[3] PhD, Franca Fagioli[3] MD, Sebastiano Marra[1] MD, FESC.

[1]Department of Cardiovascular and Thoracic Diseases, Azienda Ospedaliera Universitaria San Giovanni Battista – Turin, Italy

[2]Interventional Cardiology Unit, Mauriziano Hospital, Turin, Italy.

[3] Pediatric Onco-Haematology, Stem Cell Transplantation and Cellular Therapy Division, Regina Margherita Children's Hospital

Running Title: Primary PCI with EPC capture stent

Indexing words: percutaneous coronary intervention, stem cells, vascular healing,

Corresponding Author:

Paolo Scacciatella, MD

Corso Bramante 88, 10126 Torino Italy

Tel +39 011 6335564

Fax +39 011 6335565

paolo.scacciatella@tin.it

ABSTRACT

Objectives. PCI is the gold standard for the treatment of acute myocardial infarction (AMI), with the main limitation of in-stent restenosis for BMS and late stent thrombosis (ST) for both BMS and DES. Endothelial progenitor cells (EPC) CD34+ capture stents, promoting vascular healing, may be advantageous in preventing ST. Aim of the study is to evaluate the outcomes of AMI patients treated with EPC CD34+ capture stent and describe the mobilization kinetics of CD34+ and their clinical correlation.

Methods. 50 AMI patients underwent primary PCI with EPC CD34+ capture stent. Serial assays of CD34+ were performed by flow-cytometric analysis.

Results. Procedural success rate was 100%. At six-months follow-up cardiac death, myocardial infarction, target lesion revascularization (TLR) and target vessel revascularization (TVR) occurred respectively in 2%, 4%, 10% and 12% of patients. No case of ST was observed. The MACE-free survival was 81,2%. The mean peak value of plasmatic CD34+ was 4,69±3,76 cells/µl. A positive correlation was found between CD34+ concentration, age and infarct area. No correlation was detected between CD34+ concentration and occurrence of TVR, TLR and MACE.

Conclusions. EPC capture stent implantation seems to be safe and effective in the clinical setting of AMI, representing a possible alternative to BMS and DES. CD34+ cells plasmatic concentration seems not to correlate to coronary restenosis and atheromasic disease progression.

INTRODUCTION

The gold standard for the treatment of acute myocardial infarction (AMI) is a well-timed mechanical revascularization in an appropriate PCI-capable center [1]. Revascularization procedures seem to be effective and safe both with bare-metal stents (BMS) and drug-eluting stents (DES) [1]. The major limitations of this approach are restenosis, rising from 5,11% with DES to 11,19% with BMS [2] and stent thrombosis (ST), rising up to 2,7% for both DES and BMS [2,3]. Moreover, ST results in high morbidity and mortality rates [3].

An alternative "biological" approach could be the use of Endothelial Progenitor Cells (EPC) CD34+ capture stent. The physiological basis of this approach is the phenomenon of CD34+ spontaneous mobilization during AMI [4, 5]. Several studies demonstrated the role of EPC in the healing process after vascular endothelial injury [4]. The EPC CD34+ capture stent (Genous R stentTM, OrbusNeich, Fort Lauderdale, FL, USA) is a bioengineered stainless steel, dual-helix, modular stent coated with murine monoclonal antihuman CD34 antibodies designed to attract circulating EPC, establish a functional endothelial layer and therefore accelerate vascular healing. Early surface endothelialization could reduce the risk of ST and could positively influence restenosis [6,7]. Nevertheless, the functional role of EPC is still not well established [8]. In particular, it is not clear if EPC plasmatic concentration could influence the efficacy of this approach and even favor restenosis and the atheromasic disease progression [9,10].

The primary objective of our study was to evaluate the efficacy and safety of EPC capture stent in primary PCI, through the observation of clinical adverse events rate in a prospective cohort of ST-elevation myocardial infarction (STEMI) patients. The secondary aim of our study was to describe the spontaneous mobilization kinetics of CD34+ during

AMI and to investigate the possible relationship between EPC plasmatic concentration and target vessel revascularization or target lesion revascularization.

MATERIALS AND METHODS

In a twelve-months period of time, fifty consecutive patients who underwent primary PCI with EPC capture stent implantation in our institution were prospectively selected and analyzed. Informed written consent was obtained by all patients included in the study. Patients were eligible for inclusion if they had STEMI within 12 hours from the beginning of symptoms and a culprit lesion suitable for PCI and stent implantation. Exclusion criteria were cardiogenic shock, pregnancy and all the physiopathological conditions determining poor EPC plasmatic mobilization (age > 75 years, active malignancy, hypo-regenerative and proliferative bone marrow diseases, active infectious diseases or sepsis, autoimmune diseases, previous organ transplant, active immunosuppressive therapy). No other predefined clinical inclusion or exclusion criteria were considered.

The primary outcome was the occurrence of death, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), stent thrombosis (ST). MACE were defined as a non-hierarchical composite of cardiac death, nonfatal MI, or target vessel repeat revascularization during hospital stay and at six-months follow-up. Secondary outcome investigated measures were EPC CD34+ plasmatic concentrations in the whole population and in different predefined subgroups.

Definitions

STEMI was defined as typical chest pain lasting more than 30 minutes associated with ST-segment elevation > 1 mm in at least two contiguous leads on the ECG. [1]

Technical success was defined as successful deployment of stent(s) in the target lesion. Procedural success was defined as lesion revascularization with ≤30% residual diameter stenosis by quantitative coronary angiography, without major procedural or post-procedural adverse events (death, myocardial infarction, emergency target vessel revascularization or acute stent thrombosis). Death was classified as either cardiac or non-cardiac, according to the Academic Research Consortium (ARC) definition [11]. Deaths that could not be classified were considered cardiac. TLR was defined as any repeated percutaneous intervention of the target lesion or other complication of the target lesion. The target lesion was defined as the treated segment from 5 mm proximal to the stent to 5 mm distal to the stent. TVR was defined as any repeated PCI of any segment on the target vessel, defined as the entire major coronary vessel proximal and distal to the target lesion, including upstream and downstream branches and the target lesion itself. Myocardial infarction was defined according to the ARC definitions as elevation of cardiac enzymes three times upper the limit of normal [11]. MACE were defined as the occurrence of cardiac death (CD), non-fatal myocardial infarction (MI) or TVR during the follow-up period. Definite, probable and possible stent thrombosis (ST) were determined according to the ARC definitions [11]. Definite stent thrombosis was defined as angiographic and pathologic confirmation of acute thrombosis in patients with acute coronary syndromes, while probable stent thrombosis as any unexplained death within 30 days or as target vessel MI without angiographic confirmation of thrombosis or other identified culprit lesion. Stent thrombosis was classified as acute, sub-acute, late and very late if the event occurred within 24 hours, 30 days, <1 year or >1 year respectively, after the procedure.

Procedures, medications and follow-up

All PCIs were performed according to current guidelines. Stenting strategy, use of periprocedural glycoprotein IIb/IIIa inhibitors, route of arterial access, predilation devices, intravascular ultrasound guidance and prophylactic intra-aortic balloon pump use was at the discretion of the operator. All patients were pretreated with 250 mg aspirin and 300 mg clopidogrel loading dose; unfractioned heparin was administered in order to maintain an activated clotting time >250s during the procedure. After the procedure, all patients were prescribed lifelong aspirin 100 mg and clopidogrel 75 mg daily for 4 weeks. Patients were monitored for in-hospital events. Per protocol, all patients received atorvastatin 80 mg/od until discharge followed by drug titration in order to achieve LDL cholesterol < 80 mg/dL [12]. A follow-up visit was scheduled at 30 days and six months.

All patients underwent a complete echocardiographic study at admission, at discharge and six months later. Echocardiographic images were obtained using an HP Sonos 5500 scanner, equipped with a 2.5-3.75 MHz probe. Left ventricular (LV) end-systolic and end-diastolic volumes and ejection fraction (EF) were estimated using Simpson's modified biplane method [13,14,15]. All echocardiographic measurements were obtained by a single certified experienced operator from three different cardiac cycles and were averaged.

At the six-months follow-up, all patients underwent SPECT (single photon emission computed tomography), based on a dypiridamole stress protocol [16-19].

All repeat interventions and re-hospitalizations were prospectively collected during follow-up and entered into a dedicated database. Angiographic follow-up was not scheduled per protocol, being performed only in case of positive stress test or recurrence of symptoms.

Parameters and flow-cytometric methods

Serial assays of CD34 cell count were performed at time 0 (within the first 24 hours), 1st day, 2nd day, 3rd day, 5th day, 30th day. The determination of immunological markers that characterize endothelial precursors was assessed by flow-cytometric analysis. This analysis was performed on 100 µl of whole blood that was incubated 20 minutes at 4°C in the dark with FITC or PE antibodies. After incubation with antibodies, it was added to the cell suspension 1 ml of lyzing solution, held for 10 minutes at room temperature in the dark, in order to achieve the elimination of red blood cells that might affect the analysis. Then, cells were directly analyzed by flow-cytometric Facs Canto II (Becton, Dickinson). The flow-cytometric count was performed using ISHAGE protocol. Internal and external quality controls verified reliability and repeatability of tests carried out and of reagents and methods performances, using standard samples (internal quality control by 7-Color Setup beads, Becton, Dickinson, and external verification of quality UKNEQAS) [20].

Statistical analysis

Variables with normal distribution were analyzed using parametric tests while variables with non-normal distribution were analyzed with non-parametric tests. Continuous variables are expressed as mean ± SD. Categorical variables are expressed as counts and percentages. All statistical tests were two-tailed. All analyses were performed using SPSS version 12 statistical software (SPSS Inc., Chicago, IL, USA). A p value <0.05 was considered statistically significant.

RESULTS

Clinical and functional characteristics

Baseline clinical characteristics are shown in Table I.

Mean age was 62±11,5 years; 46 patients (92%) were male. Diabetes mellitus was present in 7 patients (14%). Hypertension was present in 34 patients (68%), 29 (58%) were active smokers, 11 (22%) were affected by obesity and 24 (48%) by dyslipidemia. Almost one-half of patients (40%) had familial history of CAD and 13 patients (26%) had prior personal history of CAD, 6 (12%) previous myocardial infarction, 2 (4%) previous PCI and 5 (10%) previous coronary artery by-pass grafting.

Functional characteristics are shown in table II.

Mean ejection fraction was 47,3±8,2% at admission and 51±8,7% at discharge. The enzymatic mean peaks were 5,8±5,2 mg/dl for Troponin T and 185,8±146,2 mg/dl for CK-MB.

Angiographic and procedural characteristics

Procedural characteristics are summarized in Table III.

Mean door to balloon time was 98,9±47,7 minutes. Overall, a total of 57 lesions were treated and the mean stent-per-patient ratio was 1,48±0,67. Technical and procedural

success was achieved in all patients (100%). The most common location of AMI was the inferior wall, with a right coronary artery lesion in 22 cases (44%). The other lesion locations were: left anterior descending artery with an anterior AMI in 20 patients (40%), circumflex artery in 6 patients (12%) and saphenous vein graft in 2 patients (4%). Mean stent length was 20,4±3,22 mm (range 15-23 mm), mean stent diameter was 3,15±0,4mm (range 2,5-3,5mm), and mean atmosphere inflation was 15,4±1,8 atm (range 10-18 atm). A thrombotic lesion was found in 33 patients (66%), and in all these cases an adjunctive thromboaspiration treatment was performed. Downstream glycoproteins IIb/IIIa infusion was performed in all cases (100%). Multivessel disease with requirement of multivessel PCI was present in 17 cases (34%).

Follow-up clinical outcomes

Follow-up outcomes are summarized in Table IV.

Mean in-hospital stay was 7,9±4,48 days (range 4-36). During the hospital stay, two patients died (4%), 1 because of refractory heart failure 10 days after the procedure and 1 for acute stroke complications, 30 days after PCI. No majors bleedings occurred. One patient had stent thrombosis which occurred in a DES deployed in a non-culprit artery during a staged procedure.

Follow-up (FU) was achieved in all patients (100%). At FU (mean: 168±39 days), the cumulative incidence of cardiac death was 2% and the incidences of MI, TLR and TVR were 4%, 10% and 12% respectively. A MACE occurred in 18% patients. No cases of subacute, late or very late stent thrombosis were detected and no patient required by-pass surgery. The Kaplan-Meyer analysis showed a MACE-free survival of 81,2% (Figure 1).

Due to the small sample population, no independent predictors of adverse events were identified at the multivariate analysis.

Mobilization kinetics of EPC CD34+

The analysis of biokinetics showed a mean EPC CD34+ plasmatic peak value of 4,69±3,76 cells/µl (range 1,44 – 19,09) and an overall mean concentration of 2,66±2,4 cells/µl. Similar mean EPC CD34+ plasmatic levels were detected respectively at time 0 (2.9±3.0 cells/µl, range 0,68 – 7,65), 24 hours (2.4±2.2 cells/µl, range 0,65 – 12,2), 48 hours (3.2±2.5 cells/µl, range 0,61 – 13,9), 72 hours (2.3±1.4 cells/µl, range 0,66 – 6,18), 5 days (3.0±1.9 cells/µl, range 0,64 – 10,6) and 1 month (2.7±3.3 cells/µl, range 0,58 – 19,09). No significant differences were demonstrated between the mean EPC CD34+ plasmatic concentrations at the different assays (Figure 2).

EPC CD34+ plasmatic mobilization kinetics in different clinical subgroups are summarized in table V. Significantly higher mean peak EPC CD34+ plasmatic levels were found in patients younger than 60 years (5,96±4,88 vs 3,61±2,14 cells/µl, $p<0.05$) and in subjects with IVA-related AMI (5,80±5,43 vs 3,89±1,68 cells/µl, $p<0,05$).

EPC mobilization was higher in non diabetic patients (4,87±4,05 vs 3,62±1,47 cells/µl), in subjects with low EF at presentation (4,82±4,31 vs 4,5±2,48 cells/µl) and in patients showing less than 3 cardiovascular risk factors (5,15±4,05 vs 4,32±3,62 cells/µl), but the differences were not statistically significant.

Furthermore, no significant differences were found in EPC plasmatic levels between patients presenting or not MACE (4,19±1,81vs 4,81±4,13 cells/µl), TVR (4,46±2,09 vs 4,72±4,01 cells/µl) and TLR (4,22±2,24 vs 4,74±3,96 cells/µl).

DISCUSSION

The main findings of this report are the following: 1) EPC capture stent use in primary intervention resulted in satisfactory clinical outcomes; 2) despite the short period of DAT and the high thrombophilic status of the patients in the acute and sub-acute phase, no sub-acute, late or very late stent thrombosis occurred; 3) no relationship was found between EPC plasmatic concentration and coronary restenosis or atheromasic disease progression.

The gold standard for the management of acute myocardial infarction is mechanical revascularization using either BMS or DES [1]. The main limitation for the use of either BMS or DES is an increased risk for stent thrombosis, with consequent high morbidity and mortality rates [3]

. Moreover, BMS efficacy is limited by the restenosis rate [2]. Data from literature report a reduced TVR rate for patients treated with DES instead of BMS (5,11% versus 11,19% respectively, $p < 0,001$); the recurrent infarction rate is as well lower (3,02% versus 3,70% respectively, $p = 0,02$), but no significant difference is described in terms of cardiac death

(2,80% versus 3,52% respectively, p = 0,21) and stent thrombosis (2,65% versus 2,76% respectively, p = 0,37) [2].

In the clinical setting of AMI, EPC mobilization from the bone marrow is stimulated and the use of EPC CD34+ capture stents, accelerating the natural healing process [20,6] could be advantageous.

Although not having data concerning the efficacy profile of those devices at very long term, data from the HEALING II study showed low MACE and low stent thrombosis rate in stable patients undergoing elective PCI [6]. EPC capture stent implantation has moreover shown to be safe in a general population of patients with acute myocardial infarction [22] as well as in series of high cardiovascular risk patients [23]. Furthermore, in small series of patients with contraindication to prolonged DAT, those devices have proven an excellent efficacy and safety profile [24,25].

Recent studies representing larger populations of patients with STEMI treated with EPC capture stents confirm the long term safety and efficacy of those devices, showing low rates of MACE of 8,1% at 30 days, 10,0% at six months and 12,2% at 1 year [26]. If compared to DES, EPC capture stents did not show a statistically significant difference in terms of MACE, TVR and repeated non-fatal AMI [27]. Our results in terms of MACE (18%) and CD (2%) are consistent with those described in series of AMI patients [26,27] and high risk not selected patients [28].

Despite the short period of DAT and the high trombophylic status of the patients in the acute and sub-acute phase, no sub-acute, late or very late stent thrombosis occurred in our population. The only thrombotic event was observed in a DES deployed in a non-culprit artery during a staged procedure. Data from other studies using EPC CD34+ capture stent in primary intervention report a stent thrombosis rate between 0,9% and

1,05% [26,27]. The ST rate with either BMS and DES rises from 2,65% to 2,76% [2]. Although considering the limitation of a small sample population in detecting thrombotic events, our findings add evidence to the efficacy of EPC capture stents in terms of stent thrombosis prevention.

There is still no consensus in literature about the role of EPC in the atherogenic process and mainly in the occurrence of in-stent restenosis after successful percutaneous revascularization. Patients who experience in-stent restenosis seem to have higher plasmatic levels of each EPC sub-population if compared to those without significant progression of coronary atherosclerosis and to normal controls [9, 29]. This finding suggests a possible role of those cells in the progression of coronary atherosclerosis, probably through an abnormal engrafting and an excessive intimal proliferation [30]. Some reports are in contrast, observing that decreased in-stent late lumen loss was associated with higher levels of circulating EPC [31,32,33]. In our population no correlation was found between EPC plasmatic concentration and adverse clinical outcomes, with particular reference to TVR and TLR. The cell mobilization after AMI seems to be more influenced by general characteristics (such as the age) and baseline pathologic conditions (type of AMI).

These discrepancies between different reports may be explained by the differences in study design and analyzed cell populations [30]. It is therefore possible that the EPC sub-population may be composed of various types of different precursor, each one with a different and not yet understood role in atherogenesis.

Limitations

The present study was designed as a prospective single centre registry, and therefore lacks randomization and intention-to-treat data. Sample size was relatively small and

events adjudication was not blinded. However, given the lack of large studies on EPC capture stent implantation in AMI and particularly of any study reporting correlations between EPC mobilization and the clinical outcome, this study, despite its inherent limitations in internal and external validities, could add an useful piece of information about the use of this novel device.

REFERENCES

[1] Wijns W ,Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal 2010; 31:2501–2555.

[2] Piscione F, Piccolo R, Cassese S et al. Effect of drug-eluting stents in patients with acute ST elevation myocardial infarction undergoing percutaneous coronary intervention: a meta-analysis of randomized trials and an adjusted indirect comparison. Eurointervention 2010; 5:853-860.

[3] Kastrati A, Dibra A, Spaulding C, Laarman GJ, Menichelli M, Valgimigli M, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. European Heart Journal (2007) 28:2706–2713.

[4] Shintani S, Murohara T, Ikeda H, Ueno T, Honma T, Katoh A, Sasaki K, et al. Mobilization of endothelial progenitor cells in patients with acute myocardial infarction. Circulation 2001;103:2776-2779.

[5] Massa M, Rosti V, Ferrario M, Campanelli R, Ramajoli I, Rosso R, et al. Increased circulating hematopoietic and endothelial progenitor cells in the early phase of acute myocardial infarction. Blood 2005;105:199-206.

[6] Aoki J, Serruys PW, van Beusekom H, Ong AT, McFadden EP, Sianos G, et al. Endothelial progenitor cell capture by stents coated with antibody against CD34: the HEALING-FIM (Healthy Endothelial Accelerated Lining Inhibits Neointimal Growth-First In Man) Registry. J Am Coll Cardiol 2005;45:1574-79.

[7] Duckers HJ, Soullié T, den Heijer P, Rensing B, de Winter RJ, Rau M, et al. Accelerated vascular repair following percutaneous coronary intervention by capture of endothelial progenitor cells promotes regression of neointimal growth at long term follow-up: final results of the Healing II trial using an endothelial progenitor cell capturing stent (Genous R stent). Eurointervention 2007;3:350-358.

[8] Co M, Tay E, Lee CH, Poh KK, Low A, Lim J, et al. Use of endothelial progenitor cell capture stent (Genous Bio.Engineered R Stent) during primary percutaneous coronary intervention in acute myocardial infarction: intermediate- to long-term clinical follow-up. Am Heart J 2008;155:128-32.

[9] Khurana R, Mayr M, Hill JM. Endothelial progenitor cells, late stent thrombosis and delayed re-endothelialisation. EuroInterv. 2007;3:518-525.

[10] Pelliccia F, Cianfrocca C, Rosano G, Mercuro G, Speciale G, Pasceri V. Role of endothelial progenitor cells in restenosis and progression of coronary atherosclerosis after percutaneous coronary interventions. A prospective study. J Am Coll Cardiol 2010;3(1):78-86

[11] Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344-51.

[12] The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. European Heart Journal (2008) 29, 2909–2945.

[13] Temporelli PL, Giannuzzi P, Nicolosi GL, Latini R, Franzosi MG, Gentile F, et al. for the GISSI-3 Echo Substudy Investigators. Doppler-derived mitral deceleration time as a strong prognostic marker of left ventricular remodeling and survival after acute myocardial infarction. Results of the GISSI-3 echo substudy. J Am Coll Cardiol 2004;43:1646–53.

[14] Savoye C, Equine O, Tricot O, Nugue O, Segrestin B, Sautière K, et al. for the REmodelage VEntriculaire study group. Myocardial infarction in modern clinical practice (from the REmodelage VEntriculaire [REVE] Study Group). Am J Cardiol 2006;98:1144–9.

[15] Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. American Society of Echocardiography Committee on Standards on Quantitation of Two-

Dimensional Echocardiograms: recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358–67.

[16] Beller GA, Zaret BL. Wintergreen Panel summaries. *J Nucl Med* 1999;6:93–155.

[17] Hachamovitch R, Berman DS, Kiat H, Cohen I, Cabico JA, Friedman J, Diamond GA. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. *Circulation* 1996;93:905–914.

[18] Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, et al. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diab Care* 2004;27:1954–1961.

[19] Abidov A, Bax JJ, Hayes SW, Cohen I, Nishina H, Yoda S, et al. Integration of automatically measured transient ischemic dilation ratio into interpretation of adenosine stress myocardial perfusion SPECT for detection of severe and extensive CAD. *J Nucl Med* 2004;45:1999 –2007.

[20] Sutherland DR, Anderson L, Keeney M, Nayar R, Chin-Yee I. The ISHAGE guidelines for CD34$^+$ cell determination by flow cytometry. International Society of Hematotherapy and Graft Engineering. J Hematother 1996; 5:213-226.

[21] Aoki J, Serruys PW, Van Beusekom K et al. Endothelial progenitor cell capture with stents covered by antibody against CD34; the HEALING-FIM (Healthy Endothelial Accelerated Lining Inhibits Neointimal Growth) registry. J Am Coll Cardiol 2005;45:1574-1579.

[22] CO M, Tay E, Lee CH et al. Use of endothelial progenitor cell capture stent (Genous Bio-Engineered R Stent) during primary percutaneous coronary intervention in acute

myocardial infarction: intermediate to long term clinical follow-up. Am Heart J 2008;155(1):128-132.

[23] Miglionico M, Patti G, D'Ambrosio A et al. Percutaneous coronary intervention utilizing a new endothelial progenitor cells antibody-coated stent: a prospective single-center registry in high-risk patients. Catheter cardiovasc interv 2008;71(5):600-604.

[24] Kutryk MJ, Fam N, Cheema A et al. Genous stent for patients that cannot be treated with dual antiplatelet therapy. EuroPCR 2008.

[25] Scacciatella P, Meliga E, D'Amico M et al. Percutaneous coronary interventions with an endothelial progenitor cell capture stent (EPC) for high risk patients with no option for drug eluting stents: long term clinical outcomes of a single centre registry. Eurointervention 2011; 6(7):826-30.

[26] Lee YP, Tay E, Lee CH et al. Endothelial progenitor cell capture stent implantation in patients with ST-segment elevation acute myocardial infarction: one year follow-up. EuroIntervention. 2010 Jan;5(6):698-702.

[27] Chong E, Keong Poh K, Liang S et al. Two-Year Clinical Registry Follow-up of Endothelial Progenitor Cell Capture Stent Versus Sirolimus-Eluting Bioabsorbable Polymer-Coated Stent Versus Bare Metal Stents in Patients Undergoing Primary Percutaneous Coronary Intervention for ST Elevation Myocardial Infarction. J Interven Cardiol 2010;23:101–108.

[28] Miglionico M, Patti G, D'Ambrosio A et al. Percutaneous coronary intervention utilizing a new endothelial progenitor cells antibody-coated stent: a prospective single-center registry in high-risk patients. Catheter Cardiovascular Intervention 2008;711:600-604.

[29] Inoue T, Sata M, Hikichi Y, et al. Mobilization of CD34-positive bone marrow-derived cells after coronary stent implantation: impact on restenosis. Circulation 2007;115:553–61.

[30] De Winter R J, Klomp M. Understanding the role of endothelial progenitor cells in cardiovascular diseases, coronary artery lesion progression and in-stent restenosis. J Am Coll Cardiol 2010;3(1):87-89

[31] Lin Y, Weisdorf DJ, Solovey A, Hebbel RP. Origins of circulating endothelial cells and endothelial outgrowth from blood. J Clin Invest 2000;105:71–7.

[32] Sieveking DP, Buckle A, Celermajer DS, Ng MK. Strikingly different angiogenic properties of endothelial progenitor cell subpopulations: insights from a novel human angiogenesis assay. J Am Coll Cardiol 2008;51:660–8.

[33] Duckers HJ, Silber S, de Winter R, et al. Circulating endothelial progenitor cells predict angiographic and intravascular ultrasound outcome following percutaneous coronary interventions in the HEALING-II trial: evaluation of an endothelial progenitor cell capturing stent. EuroIntervention 2007;3:67–75.

TABLE AND FIGURE LEGENDS:

Table 1. Baseline clinical characteristics.

IDDM: insulin dependent diabetes mellitus; NIDDM: non insulin dependent diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; AMI: acute myocardial infarction

Table 2. Functional characteristics.

Table 3. Angiographic and procedural characteristics.

LAD: left anterior descending artery; Cx: circumflex artery; RCA: right coronary artery; SVG: saphenous vein graft; PCI: percutaneous coronary intervention

Table 4. Cumulative incidence of adverse events.

MI: myocardial infarction; PCI: percutaneous coronary intervention; MACE: major adverse cardiovascular events; ST: stent thrombosis; TLR: target lesion revascularization; TVR: target vessel revascularization.

*ST occurred in a DES deployed in a non infarction-related artery during a staged procedure; MI: myocardial infarction; PCI: percutaneous coronary intervention; MACE: major adverse cardiac events; ST: stent thrombosis; FU: follow-up; TLR: target lesion revascularization; TVR: target vessel revascularization.

Table 5. Plasmatic mobilization kinetics of EPCs in different clinical subgroups.

EPC: endothelial progenitor cells; AMI: acute myocardial infarction; EF: ejection fraction.

Figure 1. MACE free survival rate.

Figure 2. Box and Whisker plot of EPC mobilization.

Table I. Baseline clinical characteristics

		N, mean±SD	%
Age (years)		62±11,5	
Gender (male)		46	92
Hypertension		34	68
Dyslipidemia		24	48
Diabetes		7	14
	IDDM	2	4
	NIDDM	5	10
Active smokers		29	58
Obesity		11	22
Familiar history		20	40
Previous PCI		2	4
Previous CABG		5	10
Previous AMI		6	12

IDDM: insulin dependent diabetes mellitus; NIDDM: non insulin dependent diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; AMI: acute myocardial infarction

Table II. Functional characteristics.

	N, mean±SD
Ejection fraction at admission (%)	47,3±8,2
Ejection fraction at discharge (%)	51±8,7
Troponin T peak (mg/dL)	5,8±5,2
CK-MB peak (mg/dL)	185,8±146,2

Table III. Angiographic and procedural characteristics.

LAD: left anterior descending artery; Cx: circumflex artery; RCA: right coronary artery; SVG: saphenous vein graft; PCI: percutaneous coronary intervention

		N, mean±SD	%
Technical success		50	100
Procedural success		50	100
Door to balloon time (min)		98,9±47,7	
Infarct Related Artery			
	LAD	20	40
	Cx	6	12
	RCA	22	44
	SVG	2	4
Evidence of thrombus		33	66
GP IIb/IIIa use		50	100
Multivessel PCI		17	34

Stents/patient (mean)	1,48±0,67
Treated lesion/patient (mean)	1,14±0,4
Stent Length (mm)	20,4±3,22
Stent diameter (mm)	3,15±0,4
Pressure (atm)	15,4±1,8

Table IV. Cumulative incidence of adverse events.

	N	%
In-hospital stay (days)	7,9±4,48	
In-hospital events		

Death	2	4
Cardiac Death	1	2
Non Cardiac Death	1	2
Re-MI	0	0
Re-PCI	1	2
Major bleedings	0	0
Minor bleedings	0	0
Stroke	1	2
MACE (hierarchical)	1	2
Definite/probable ST	1*	2
Events at FU (168±46 days)		
Death	2	4
Cardiac D	1	2
Non cardiac D	1	2
MI	2	4
TLR	5	10
TVR	6	12
Major bleedings	0	0
Minor bleedings	0	0
Stroke	1	2
MACE (hierarchical)	9	18
Definite/probable ST	1*	2

*ST occurred in a DES deployed in a non IRA during a staged procedure MI: myocardial infarction; PCI: percutaneous coronary intervention; MACE: major adverse cardiac events; ST: stent thrombosis; FU: follow-up; TLR: target lesion revascularization; TVR: target vessel revascularization.

Table V. Plasmatic mobilization kinetics of EPCs in different clinical subgroups.

		Mean EPC concentration (cells/µl)	P-value
Age	< 60 years	5,96±4,88	< 0,05
	≥ 60 years	3,61±2,14	
Risk factors	≥3	4,32±3,62	NS
	<3	5,15±4,05	
Diabetes	yes	3,62±1,47	NS
	no	4,87±4,05	
IMA	anterior	5,80±5,43	< 0,05
	non-anterior	3,89±1,68	
EF at admission	≥50%	4,5±2,48	NS
	<50%	4,82±4,31	

Figure 1. MACE free survival rate.

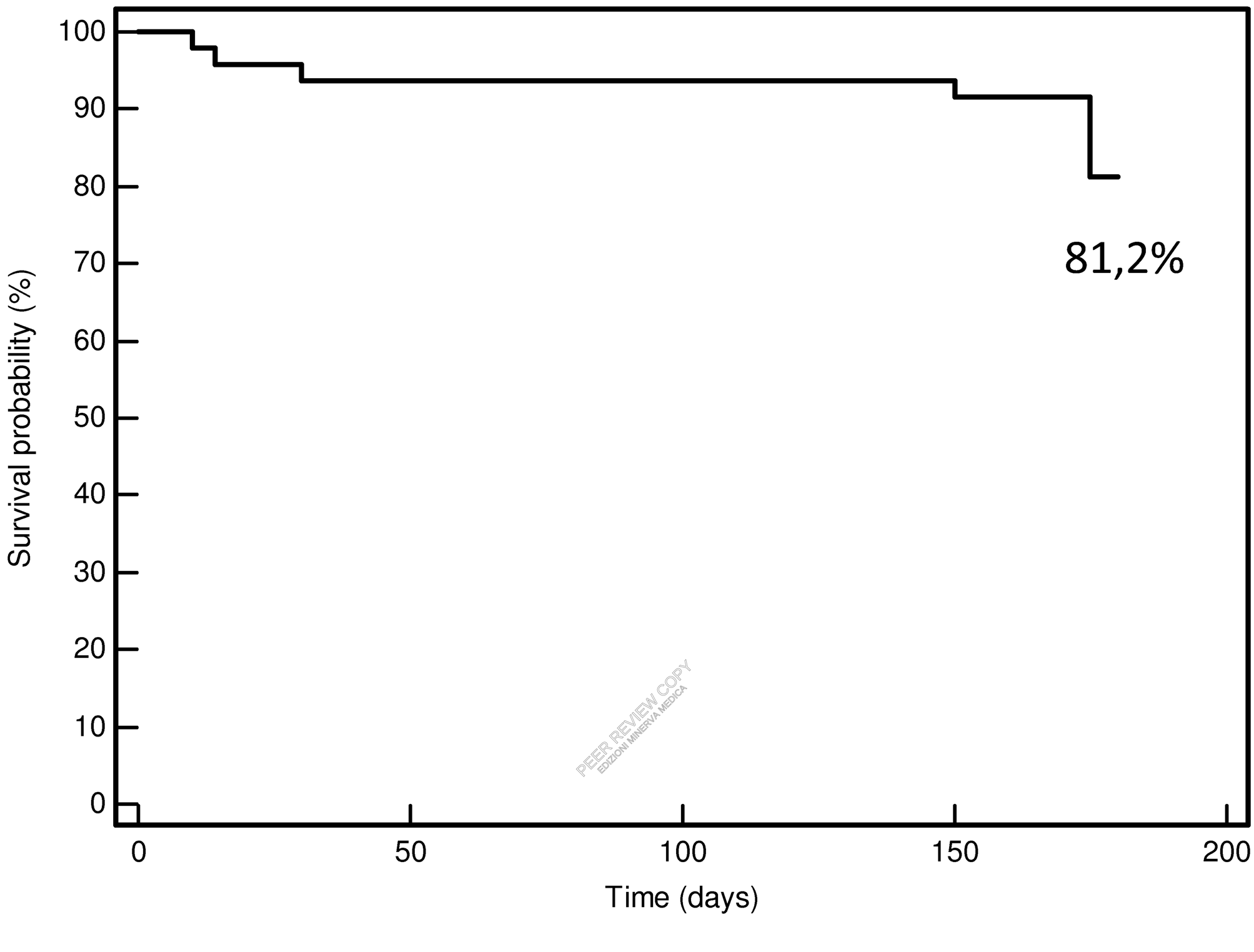

Figure 2. Box and Whisker plot of EPC mobilization.