Endothelial Progenitor Cells, Microvascular Obstruction, and Left Ventricular Remodeling in Patients With ST Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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Endothelial progenitor cells (EPCs) are released from the bone marrow during cardiac ischemic events, potentially influencing vascular and myocardial repair. We assessed the clinical and angiographic correlates of EPC mobilization at the time of primary percutaneous coronary intervention in 78 patients with ST elevation myocardial infarction and the impact of both baseline and follow-up EPC levels on left ventricular (LV) remodeling. Blood samples were drawn from the aorta and the culprit coronary artery for cytofluorimetric EPC detection (CD34+CD45dimKDR+ cells, in percentage of cytofluorimetric counts). Area at risk was assessed by Bypass Angioplasty Revascularization Investigation myocardial jeopardy index, thrombotic burden as thrombus score and microvascular obstruction (MVO) as a combination of ST segment resolution and myocardial blush grade. Echocardiographic evaluation of LV remodeling was performed at 1-year follow-up in 54 patients, whereas peripheral EPC levels were reassessed in 40 patients. EPC levels during primary percutaneous coronary intervention were significantly higher in intracoronary than in aortic blood (0.043% vs 0.0006%, $p < 0.001$). Both intracoronary and aortic EPC were related to area at risk extent, to intracoronary thrombus score ($p < 0.001$), and inversely to MVO ($p = 0.001$). Peripheral EPC levels at 1-year follow-up were lower in patients with LV remodeling than in those without (0.001% [0.001 to 0.002] vs 0.003% [0.002 to 0.010]; $p = 0.01$) and independently predicted absence of remodeling at multivariate analysis. In conclusion, a rapid intracoronary EPC recruitment takes place in the early phases of ST elevation myocardial infarction, possibly reflecting an attempted reparative response. The extent of this mobilization seems to be correlated to the area at risk and to the amount of MVO. Persistently low levels of EPC are associated to LV remodeling. **(Am J Cardiol 2013;112:782−791)**

Endothelial progenitor cells (EPC) are bone marrow–derived cells with ability to repair the damaged endothelium, possibly participating in vascular and myocardial repair.[1] In the last decade, several studies have documented a rapid mobilization of EPC into the blood stream during an acute ischemic event,[2,3] and a continuous EPC release during the chronic phase of coronary artery disease, mirroring vascular health and impacting on long-term prognosis.[1] EPC mobilization after ST segment elevation myocardial infarction was associated with reduced left ventricular (LV) remodeling and better clinical outcome,[2,4,5] and we recently demonstrated that the extent of ischemic myocardium (and not the final infarct size) is a predictor of EPC release.[6] However, little is known on the other determinants of EPC mobilization in ST elevation myocardial infarction.[7] In particular, although it is conceivable that EPC are mobilized to help in repairing the damaged endothelium, no relation between EPC mobilization and microvascular obstruction (MVO), a feared complication of primary percutaneous coronary intervention (PCI),[8] has previously been shown. We sought to test whether EPC, assessed during primary PCI in the intracoronary and aortic blood and at 1 year in the peripheral blood, correlated with the effectiveness of reperfusion and/or predicted LV remodeling.

Methods

Seventy-eight consecutive patients with ST elevation myocardial infarction, treated with primary PCI with thrombus aspiration were prospectively enrolled from 170 primary PCIs performed in our institution during August 2009 to December 2010 (Supplementary Figure 1). All patients were admitted to our coronary care unit with chest pain, new persistent ST segment elevation, high-sensitivity cardiac Troponin T >0.0015 ng/ml, and/or new regional wall motion abnormalities.[9] Exclusion criteria for all patients were age

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See page 790 for disclosure information.

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Table 1
Clinical characteristics (n = 78)

Baseline Characteristics	All Patients	MVO		p
		No (n = 56)	Yes (n = 22)	
Men	59 (76)	43 (77)	16 (73)	0.71
Age (yrs)	63 ± 13	62 ± 12	66 ± 15	0.34
Diabetes mellitus	20 (26)	16 (29)	4 (18)	0.34
Hypertension*	55 (71)	40 (71)	15 (68)	0.77
Smoker	31 (40)	24 (43)	7 (32)	0.67
Family history of coronary artery disease	29 (37)	19 (34)	10 (45)	0.34
Hypercholesterolemia†	32 (41)	20 (36)	12 (54)	0.13
Total cholesterol (mg/dl)	178 (150–210)	172 (150–212)	192 (147–218)	0.74
LDL (mg/dl)	106 (82–134)	102 (84–131)	119 (76–140)	0.54
HDL (mg/dl)	44 (38–50)	43 (34–50)	46 (40–49)	0.31
Triglycerides (mg/dl)	125 (81–161)	142 (95–169)	86 (73–133)	0.06
Killip class				
I	50 (64)	41 (73)	9 (41)	0.05
II	17 (22)	9 (16)	8 (36)	
III	8 (10)	4 (7)	4 (18)	
IV	3 (4)	2 (4)	1 (5)	
Preinfarction angina pectoris	37 (47)	27 (48)	10 (45)	0.83
Total ischemic time (h)				
≤3	37 (47)	32 (58)	5 (23)	0.004
3–5	16 (20)	12 (21)	4 (18)	
≥6	25 (33)	12 (21)	13 (59)	
Serum creatinin (mg/dl)	1.1 (0.9–1.2)	1.1 (0.9–1.3)	1.1 (0.8–1.2)	0.43
Troponin T peak (ng/ml)	6.83 (2.58–12.30)	6.49 (2.32–9.64)	8.22 (3.39–19.92)	0.07
Troponin T at admission (ng/ml)	0.14 (0.02–1.39)	0.23 (0.02–1.42)	0.18 (0.02–1.32)	0.22
Ejection fraction (%)	50.0 (44.0–55.0)	50.0 (45.0–56.0)	50.0 (46.0–52.2)	0.68
Wall motion score index (absolute units)	1.44 (1.20–1.69)	1.50 (1.19–1.75)	1.40 (1.26–1.62)	0.95
LV remodeling	17 (47)	4 (7)	13 (59)	0.001

Data are relative number of subjects (percentage), mean ± SD, or median (interquartile range).
Chi-square or *t* test was used to compare groups.
HDL = high-density lipoprotein; LDL = low-density lipoprotein.
* Includes blood pressure >140/90 mm Hg.
† Includes total cholesterol level >200 mg/dl and/or low-density lipoprotein cholesterol level >130 mg/dl.

>80 years, infarction secondary to ischemia due to an imbalance of oxygen supply and demand, previous electrocardiographic abnormalities that could interfere with ST segment analysis and interpretation, recent or chronic infective or inflammatory diseases, malignancy, surgery or trauma in the previous month, or coronary anatomy judged unfavorable for thrombus aspiration. Patients undergoing rescue PCI were also excluded. All patients received aspirin (250 mg intravenous) and clopidogrel (600 mg or 300 mg if already on clopidogrel), plus standard heparin to maintain activated clotting time >300 seconds. Glycoprotein IIb/IIIa antagonists were administered at physicians' discretion after thrombus aspiration. Local ethical committee approved the study, and all patients signed an informed consent. All procedures were followed in accordance with the ethical standards of the responsible committees on human experimentation and with the Declaration of Helsinki.

The identification of the infarct-related artery was based on angiographic characteristics, clinical and electrocardiographic findings. Area at risk, corresponding to ischemic myocardium distal to the culprit lesion, was assessed using the Bypass Angioplasty Revascularization Investigation myocardial jeopardy index (BARI) as previously described[10] (for details, see Supplementary Materials). Angiographic collateral flow was assessed by Rentrop classification, assigning a score from 0 to 3, in which 0 indicated total absence of visually identifiable collateral vessels and 3 indicated a complete retrograde filling of the infarct-related artery.[11] Thrombus score (TS) was calculated as described elsewhere (for details, see Supplementary Materials).[12]

Thrombolysis In Myocardial Infarction flow grade and corrected Thrombolysis In Myocardial Infarction frame count (cTFC) were calculated at the end of primary PCI as previously described.[13] Myocardial blush grade (MBG) was assessed and scored as MBG 0, 1, 2, and 3 in all patients at the end of each procedure.[14] We also assessed a more reproducible angiographic measurement of microvascular perfusion, the quantitative blush evaluator (QuBE) score.[15] All patients enrolled had paired electrocardiograms recorded at baseline and at 90 minutes after primary PCI for ST resolution (ΣSTR) calculation, classified as complete (≥70%), partial (30% to 70%), or absent (<30%)[16] (for further details see Supplementary Materials). MVO was defined as a combination of ΣSTR <70% and either Thrombolysis In Myocardial Infarction flow grade <3 or Thrombolysis In Myocardial Infarction flow grade 3 with MBG <2.[16–18]

Two blood samples were sequentially obtained: one from the guiding catheter in ascending aorta before culprit coronary