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Eosinophils count and periprocedural myocardial infarction in patients undergoing percutaneous coronary interventions

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ABSTRACT

Background: Eosinophils have been involved in a wide spectrum of pro-inflammatory and pro-thrombotic conditions, with the development of cardiovascular complications in a significant proportion of hypereosinophilic patients. However, no study has so far evaluated the impact of eosinophils levels on periprocedural myocardial infarction (PMI) in patients undergoing non-urgent percutaneous coronary interventions (PCI), that was, then, aim of current study.
Methods: In a consecutive cohort of patients, myonecrosis biomarkers were dosed at intervals from 6 to 48 h after PCI. Periprocedural myonecrosis was defined as troponin I increase by 3 times the ULN or by 50% of an elevated baseline value, whereas PMI as CKMB increase by 3 times the ULN or 50% of baseline.
Results: Our population is represented by 1543 patients who were divided according to tertiles of absolute eosinophils count (AEC $\leq$ 0.1; 0.1–0.2; >0.2 $\times$ 10^3/ml). Higher AEC was related to male gender ($p = 0.002$), arterial hypertension ($p = 0.02$), diabetes ($p = 0.001$), previous coronary revascularization ($p = 0.003$ for PCI, $p = 0.03$ for CABG), treatment with ARBs, beta-blockers, diuretics and ASA ($p < 0.001$), statins ($p = 0.02$), calcium antagonists ($p = 0.05$), glycosylated hemoglobin ($p < 0001$), creatinine levels ($p = 0.001$) and platelet count ($p = 0.01$), while inversely with acute presentation ($p < 0.001$), glycemia ($p = 0.03$), HDL-cholesterol and C-reactive protein ($p = 0.02$). AEC related with multivessel coronary artery disease ($p = 0.05$), lesion length ($p = 0.01$), drug eluting stents implantation ($p = 0.001$) and use of kissing balloon technique ($p = 0.05$), while inversely to intracoronary thrombus ($p < 0.001$) and thrombectomy ($p = 0.04$).
AEC did not influence the occurrence of PMI ($p = 0.06$, adjusted OR [95% CI] = 1.06 [0.86–1.31], $p = 0.57$) or myonecrosis ($p = 0.15$, adjusted OR [95% CI] = 1.06 [0.88–1.27], $p = 0.53$). Results were confirmed at subgroup analysis in higher-risk subsets of patients.
Conclusion: In patients undergoing non-urgent PCI, eosinophils levels are not associated with the occurrence of periprocedural myocardial infarction or myonecrosis.

1. Background

Coronary artery disease (CAD) still represents the leading cause of mortality in Western countries, despite the great reduction in mortality observed in the last decades, especially in the setting of STEMI [1,2]. The improvements achieved in adjunctive pharmacological and mechanical devices [3–6] have certainly contributed to improve the results of percutaneous coronary interventions (PCI). However, suboptimal results have still been observed in high-risk patients after coronary stenting not only in STEMI [7,8] but also in the elective setting, where up to 20% of them experience a periprocedural myocardial injury or even a frank periprocedural myocardial infarction (PMI) [9], mainly consequence of procedural flow-limiting complications or microvascular thrombotic events [10,11]. Thus, large efforts have been focused in the last years on the prevention of periprocedural complications and on the

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identification of new biomarkers to improve risk stratification, with particular attention to pro-inflammatory and pro-thrombotic conditions.

Inflammation, in fact, plays a central role in CAD and among leukocytes subpopulations, eosinophils are involved in the acute pro-inflammatory response, where their pro-coagulant and cytothoxic properties can induce endothelial damage, platelet activation and then acute cardiovascular events [12–14]. In fact, an increase in eosinophils absolute count (AEC) has been reported after an acute myocardial infarction [15], and moreover, eosinophil levels have emerged as a strong predictor of mortality in patients admitted for an acute heart failure [16] and in patients with CAD undergoing percutaneous coronary revascularization, at long term follow-up [17].

However, no study has so far evaluated the role of AEC on periprocedural myocardial injury in patients undergoing PCI, that was, therefore, aim of current study.

2. Methods

We included patients undergoing coronary angioplasty at Ospedale "Maggiore della Carità" from May 2007 to January 2013 for both elective indication or acute coronary syndrome (UA/NSTEMI), the latter undergoing elective coronary angiography after pharmacological stabilization. STEMI and haemodinamically unstable patients requiring urgent angioplasty, as much as patients refusing to sign informed consent were excluded.

Diabetes mellitus, arterial hypertension and renal failure were defined according to most recent guidelines, as previously described [18]. The study was approved by our local Ethical Committee. All patients received, according to guidelines, a bolus of ADP antagonists at the time of hospitalization or before angioplasty. Patients were clinically followed up to hospital discharge.

2.1. Biochemical measurements

Blood samples were drawn at admission in patients undergoing elective (following a fasting period of 12 h) or non-emergent coronary angiography.

Glucose, creatinine, HbA1c and lipid profile were determined by standard methods. White blood cells count and formula was measured in a blood sample collected in tripotassium EDTA (7.2 mg) tubes. These blood samples were analyzed within 2 h of venipuncture by automatic blood counter (A Sysmex XE-2100). Cardiac biomarkers (Troponin I and CK MB) were measured at baseline, before coronary revascularization, and later 6, 12, 24 and 48 h after PCI as previously described [19].

2.2. Coronary angiography and PCI

Coronary angiography was routinely performed by the Judkins technique using 6-French catheters. Quantitative coronary angiography was performed by experienced interventional cardiologists by an automatic edge-detection systems (Siemens Acom Quantcor QCA, Erlangen, Germany) [20]. Coronary angioplasty was performed with standard techniques. Use of stents, type of stents and stent implantation techniques, as much as the use of directional or rotational atherectomy, IVUS, glycoprotein IIb-IIIa inhibitors, was left at the discretion of the operators.

2.3. Study endpoints

Primary study endpoint was periprocedural MI defined as CK-MB mass release $\geq$3 times the upper limit normal (ULN) or an increase by 50% of baseline if already elevated, but stable or falling, at the time of the procedure. Secondary study endpoint was periprocedural increase in troponin I $\geq 3 \times$ ULN or an increase by 50% of the pre-procedural value, if >0.04 ng/ml.

3. Statistical analysis

Statistical analysis was performed using SPSS 15.0 statistical package. Continuous data are expressed as mean ± SD and categorical data as percentage. Analysis of variance and the chi-square test (or Fisher-test) were used for continuous and categorical variables, respectively. Multiple logistic regression analysis was performed to evaluate the relationship between AEC and periprocedural myocardial necrosis or infarction, also in higher-risk subgroups, after correction for clinical and angiographic significant differences, that were entered in the model in block.

4. Results

Our population is represented by a total of 1543 patients, that were divided according to tertiles values of AEC ($\leq$0.1; 0.1–0.2; >0.2 $\times$ 10^3/ml).

As shown in Table 1, displaying main clinical and demographic characteristics, higher AEC was related to male gender ($p = 0.002$), arterial hypertension ($p = 0.02$), diabetes ($p = 0.001$), previous coronary revascularization ($p = 0.003$ for PCI, $p = 0.03$ for CABG), treatment with angiotensin receptor blockers, beta-blockers, diuretics and ASA ($p < 0.001$, respectively), statins ($p = 0.02$), calcium antagonists ($p = 0.05$), glycosylated hemoglobin ($p < 0001$), creatinine levels ($p = 0.001$) and platelet count ($p = 0.01$), while inversely with acute presentation ($p < 0.001$), glycemia ($p = 0.03$), HDL cholesterol and C reactive protein ($p = 0.02$).

Table 2 shows main angiographic and procedural characteristics according to tertiles values of AEC. AEC was related with multivessel coronary artery disease ($p = 0.05$), lesion length ($p = 0.01$), drug eluting stents implantation ($p = 0.001$) and kissing balloon technique ($p = 0.05$), while inversely to intracoronary thrombus ($p < 0.001$) and use of thrombectomy ($p = 0.04$). AEC did not significantly influence the occurrence of PMI (19.7 vs. 17.9 vs. 14.3%, $p = 0.06$; OR [95% CI] = 0.84[0.70–1.003], $p = 0.06$) or myonecrosis (61.3 vs. 64.2 vs. 65.8%; $p = 0.15$; OR [95% CI] = 1.01[0.97–1.26], $p = 0.15$), as displayed in Figs. 1 and 2, respectively.

Moreover, at multivariate analysis no role of eosinophils was confirmed for myonecrosis (adjusted OR [95% CI] = 1.06 [0.88–1.27], $p = 0.53$), while the inverse non-significant trend observed for PMI disappeared after correction for baseline differences (adjusted OR [95% CI] = 1.06[0.86–1.31], $p = 0.57$). Results were confirmed also at subgroup analysis in higher-risk subsets of patients. In fact, as shown in Fig. 3, we did not find any impact of AEC (III tertile vs. I and II tertile) on periprocedural MI according to presentation elective patients (OR [95% CI] = 0.89[0.55–1.42]; $p = 0.61$); ACS (OR [95% CI] = 0.69 [0.41–1.16], $p = 0.16$, p interaction = 0.15) and diabetic status diabetes (OR [95% CI] = 0.6 [0.35–1.01], $p = 0.06$); non diabetics (OR [95% CI] = 0.78 [0.52–1.17], $p = 0.24$, p interaction = 0.40). We furthermore found no difference in periprocedural MI according to gender (OR [95% CI] = 0.69[0.49–1.06], $p = 0.007$ for males, OR [95% CI] = 0.68 [0.33–1.4], $p = 0.30$ for females, p interaction = 0.82); age (>75 years: OR [95% CI] = 0.6 [0.33–1.01], $p = 0.10$; <75 years: OR [95% CI] = 0.74 [0.50–1.07], $p = 0.27$, p interaction = 0.73), renal function (renal failure: OR [95% CI] = 0.47 [0.26–1.04], $p = 0.07$; normal renal function: OR [95% CI] = 0.81 [0.57–1.15], $p = 0.24$, p interaction = 0.08) and use of Gp IIb-IIIa inhibitors (Gp IIb-IIIa inhibitors: OR [95% CI] = 0.87 [0.57–1.33], $p = 0.53$; no Gp IIb-IIIa inhibitors: OR [95% CI] = 0.89 [0.49–1.13], $p = 0.16$, p int = 0.69).