Experimental Gerontology 62 (2015) 32–36

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Impact of age on mean platelet volume and its relationship with coronary artery disease: A single-centre cohort study

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ARTICLE INFO

Article history:
Received 11 September 2014
Received in revised form 30 December 2014
Accepted 31 December 2014
Available online 3 January 2015

Section Editor: Holly M Brown-Borg

Keywords:
Platelet
Size
Ageing
Coronary artery disease
Coronary angiography

ABSTRACT

Elderly patients represent a high risk category among subjects with atherosclerosis, due to the presence of comorbidities and suboptimal response to antiplatelet drugs. Mean platelet volume (MPV) has been indicated as a marker of platelet reactivity, with contrasting data on its role on coronary artery disease. Aim of the present study was to evaluate the impact of age on the MPV and its role on the extent of coronary artery disease (CAD).
Methods: Our population is represented by a cohort of 3750 patients undergoing coronary angiography. Elderly were defined according to age ≥ 75 years. MPV was measured at admission. Significant coronary artery disease was defined as a stenosis >50% in at least 1 coronary vessel, while severe CAD was defined as left main and/or three-vessel disease.
Results: A total of 1170 out of 3750 (31.2%) patients were ≥75 years old. Advanced age was associated with female gender ($p < 0.001$), hypertension ($p < 0.001$), renal failure ($p < 0.001$), previous myocardial infarction ($p = 0.03$) coronary artery bypass grafting ($p < 0.001$) indication to angiography ($p < 0.001$), therapy with angiotension-receptor blockers, ($p = 0.003$), nitrates, diuretics and calcium-antagonists ($p < 0.001$), serum creatinine ($p < 0.001$), fibrinogen ($p < 0.001$) and C reactive protein ($p = 0.02$), but inversely to percutaneous coronary interventions ($p = 0.02$), dyslipidemia, family history of CAD and smoking ($p < 0.001$, respectively), use of statins ($p = 0.02$) and beta blockers ($p = 0.003$), haemoglobin, total cholesterol and triglycerides ($p < 0.001$, respectively), white blood cells ($p = 0.009$) and platelet count ($p = 0.006$).
Elderly patients displayed a significantly larger platelet volume ($p < 0.001$), with a direct linear relationship between age and the MPV ($r = 0.08$, $p < 0.001$), with age being confirmed as an independent predictor of larger MPV (≥10.85 fl) at multivariate analysis (adjusted OR [95% CI] = 1.18 [1.01–1.40], $p = 0.04$).
Among the elderly, MPV value above the median (≥10.85 fl) was not associated with a higher prevalence of coronary artery disease (77.3 vs. 79.4%, $p = 0.39$, adjusted OR [95% CI] = 0.94 [0.66–1.33], $p = 0.71$), or higher prevalence of severe CAD (35.2 vs. 32.4%, $p = 0.28$, adjusted OR [95% CI] = 1.34 [0.99–1.82], $p = 0.06$).
Conclusion: Advanced age was directly associated with larger mean platelet volume that, however, did not contribute to explain the higher prevalence and extent of coronary artery disease observed in elderly patients.

1. Background

Coronary artery disease is the leading cause of mortality among developed countries (Okrainee et al., 2004). Despite the significant improvement in survival observed in the last decades in the treatment of acute myocardial infarction by the larger application of reperfusion therapies and the great improvements in mechanical devices and antithrombotic therapies (De Luca et al., 2012a; Navarese et al., 2011), the outcome is still unsatisfactory in high-risk subsets of patients (De Luca et al., 2006), such as elderly patients (De Luca et al., 2005a). In fact, these patients are still regarded as a higher risk category when experiencing cardiovascular events, due to the presence of more severe comorbidities and increased platelet reactivity, with suboptimal response to antiplatelet drugs (Gilstad et al., 2009; Silvain et al., 2012; De Luca et al., 2013a). Therefore, large interest has been focused on the identification of new risk factors and prognostic markers in order

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http://dx.doi.org/10.1016/j.exger.2014.12.019
0531-5565/

to achieve a better primary and secondary prevention (Savarese et al., 2013). Particular attention has been paid to platelets that represent a key player in atherothrombosis (Davì and Patrono, 2007).

Platelet size has been previously related to aggregation, with larger mean platelet volume (MPV) potentially representing a cheap and easy to obtain indicator of increased reactivity.

It has been reported that elevated values of MPV are associated with acute coronary and cerebrovascular events (Pizzulli et al., 1998; Bath et al., 2004) and moreover, a close relationship has been demonstrated between MPV and cardiovascular risk factors, such as diabetes mellitus, hypertension, hypercholesterolemia, and obesity (Coban et al., 2005, 2006; Nadar et al., 2004), although more recent studies did not confirm such findings.

However, ageing has recently been suggested as an independent predictor of larger platelet size (Lippi et al., 2012), and therefore, a more relevant role in coronary artery disease could be hypothesized in these patients. Therefore, the aim of our study was to evaluate the relationship between ageing, mean platelet volume and prevalence and extent of coronary artery disease among elderly patients.

2. Methods

Our population is represented by patients undergoing non-urgent coronary angiography at Azienda Ospedaliera-Universitaria, "Maggiore della Carità", Novara, Italy from March, 2007 to October, 2013. All demographic and clinical data were collected from the patients and included in a dedicated database. No exclusion criteria were applied.

Elderly patients were considered if aged ≥ 75 years. Hypertension was defined as systolic pressure > 140 mm Hg and/or diastolic pressure > 90 mm Hg or need for an antihypertensive medication. The diagnosis of diabetes was based on previous history of diabetes treated with or without drug therapies, fasting glycaemia > 126 mg/dl, random glycaemia > 200 mg/dl or HbA1c > 48 mmol/l.

Chronic renal failure was considered for history of renal failure or an admission glomerular filtrate (GFR) < 60 ml/min/1.73 m^2 as defined by the Modifying Diet in Renal Disease (MDRD) formula.

2.1. Biochemical measurements

Blood samples were drawn at admission in patients undergoing elective (following a fasting period of 12 h) or urgent coronary angiography. Glucose, creatinine, and lipid profile were determined by standard methods. As previously described (De Luca et al., 2013b), we measured MPV in a blood sample collected in tripotassium EDTA (7.2 mg) tubes. These blood samples were analysed within 2 h of venipuncture by automatic blood counter (A Sysmex XE-2100) used for whole blood analysis. The expected values for MPV in our laboratory ranged from 7.0 to 11.0 fl.

2.2. Definition of coronary artery disease

Coronary angiography (carried out by Siemens AXIOM ARTIS dTC, Erlangen, Germany) was routinely performed by the Judkins technique using 6-French right and left heart catheters. Quantitative coronary angiography was performed, by an automatic edge-detection systems (Siemens Acom Quantcor QCA, Erlangen, Germany) as previously described (De Luca et al., 2011). The measured parameters were minimal luminal diameter, reference diameter, percent diameter stenosis, and length of the lesion. Significant CAD was defined as at least 1 coronary stenosis more than 50%. Severe CAD was defined as three-vessel disease and/or left main disease. In case of patients who had previously undergone percutaneous coronary intervention, even though no restenosis was observed, the treated vessel was counted as significantly diseased. In previously bypassed patients, native arteries and grafts were taken into account in the evaluation of extension of artery disease (number of diseased vessels).

2.3. Statistical analysis

Continuous data were expressed as mean + SD and categorical data as percentage. Analysis of variance and the chi-square test were used for continuous and categorical variables, respectively. Linear regression analysis was used to evaluate the relationship between MPV and age. Multiple logistic regression analysis was performed to evaluate the relationship between age and MPV (above the median), after correction for baseline confounding factors, that were entered in the model in block. Statistical analysis was performed using the SPSS 17.0 package. Results were considered statistically significant for two-tailed p value < 0.05.

3. Results

Our population is represented by 3750 patients undergoing coronary angiography. Among them, 1170 (31.2%) were aged ≥ 75 years. The main demographic and clinical features are displayed in Table 1. Elderly patients were more frequently females, with higher prevalence of hypertension, renal failure, previous cardiovascular history and specific therapy. Ageing was directly related with serum creatinine, fibrinogen and C reactive protein, while inversely to haemoglobin, total cholesterol and triglycerides, white blood cells and platelet count.

Elderly patients displayed a significantly larger platelet volume ($p < 0.001$), with a direct linear relationship between age and the MPV ($r = 0.08$, $p < 0.001$) (Fig. 1). A larger proportion of patients with MPV above the median (≥10.85 fl) was observed among the elderly (50.2% vs 45.3%, $p = 0.006$) and age was confirmed as an independent predictor of larger MPV (≥10.85 fl) at multivariate analysis after correction for baseline differences (adjusted OR [95% CI] = 1.18 [1.01–1.40], $p = 0.04$).

Elderly patients had a slightly higher prevalence of coronary artery disease (78.3 vs. 75.6%, $p = 0.07$), but significantly more severe CAD (33.8% vs. 26.3%, $p < 0.001$), including multivessel disease, but also more complex coronary lesions, as shown in Table 2.

Among elderly, higher platelet volume (above the median value; ≥10.85 fl) was associated with renal failure ($p < 0.001$), smoking ($p = 0.04$), therapy with diuretics ($p = 0.05$) and ASA ($p < 0.001$), with creatinine levels ($p = 0.007$) and haemoglobin ($p < 0.001$), and inversely with platelet count ($p < 0.001$), as in Table 3.

However, greater MPV values were not associated with a higher prevalence of coronary artery disease among the elderly (77.3 vs. 79.4%, OR [95% CI] = 0.88 [0.66–1.17], $p = 0.38$), or to higher prevalence of severe CAD (35.2 vs. 32.4%, $p = 0.28$, OR [95% CI] = 1.15 [0.90–1.47], $p = 0.27$). These results were confirmed after correction for baseline differences for both CAD (adjusted OR [95% CI] = 0.94 [0.66–1.33], $p = 0.71$) and severe CAD (adjusted OR [95% CI] = 1.34 [0.99–1.82], $p = 0.06$). As shown in Table 4, among elderly no difference was observed in terms of angiographic features according to MPV.

4. Discussion

The present study represents the first attempt to evaluate the relationship between age, platelet volume and the extent of angiographically assessed coronary artery disease. Our major finding is that patients ≥75 years have higher MPV values, although this is not associated with increased prevalence or extent of CAD.

Platelets play a central role in coronary artery disease, and especially among elderly patients, where still a large quote of acute thrombotic events occurs despite technological and pharmacological improvements (De Luca et al., 2005b, 2008; Capozzolo et al., 2001). In fact, older patients represent a more fragile population, with higher comorbidities and risk factors. Large interests have been focused in the last years on platelet volume as a marker of platelet reactivity and prognosis (De Luca et al., 2010, 2012b, 2013b; Verdoia et al., 2013).

Previous reports underlined an increase in platelet size with ageing, thus suggesting a potential explanation for the higher thrombotic risk