

Editorial Focus

Mean platelet volume not so far from being a routine diagnostic and prognostic measurement

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Platelets as a major component of atherosclerotic process and its complication have gained an increasing importance and have become one of the major targets in cardiovascular medicine. However, there are still grey segments in the pathophysiological steps of atherosclerosis in terms of platelet function. Not long ago the concept of platelets in atherosclerosis was that of a cell type which belongs to the haemostatic process and participates in the final step of atherosclerosis, occlusion of vessel wall following plaque rupture.

Although it has been included for decades in routine complete blood counting measurements, mean platelet volume (MPV) has recently become an interesting topic in cardiovascular research. Formed via cytoplasmic fragmentation of bone-marrow derived megakaryocytes (1) platelets are enucleate cells measuring approximately 1–2 µm in length with an average life span of 8–10 days. Differences in platelet morphology and physiology are determined primarily during or before the fragmentation of their precursor cell, the megacaryocyte (2, 3). The process of megacaryocyte differentiation and platelet production is controlled by humoral factors produced in response to platelet consumption or destruction (4). Thrombopoietin stimulates platelet production up to levels 10-fold higher than baseline (5, 6) without affecting the peripheral blood red or white cell counts. In platelets, thrombopoietin enhances α-granule secretion and aggregation that is induced by thrombin in a phosphoinositide-3 kinase (PI3K)-dependent fashion (7).

Regulation of thrombopoietin production has been explained by two models. In the first, thrombopoietin production is constitutive, but its consumption, and hence the level remaining in the blood to affect megakaryopoiesis, is determined by the density of accessible c-Mpl receptors present on platelets and megakaryocytes (8). A second model argues that thrombopoietin expression is a regulated event; very low platelet levels can upregulate thrombopoietin-specific mRNA expression, at least in the bone marrow (9). On the other hand, interleukin-6 (IL-6), which is a major proinflammatory cytokine associated with coronary artery disease, can induce thrombocytosis via stimulation of hepatic thrombopoietin (10). Recently, it has been shown that the

presence of activated megakaryocytes in bone marrow in atherosclerosis correlates with increased circulating levels of IL-6 (11).

Although a positive correlation between MPV and thrombopoietin in patients with coronary artery disease has been reported (12), the clear association between MPV, thrombopoietin and platelet count needs to be elucidated in cardiovascular disease and its complications.

Muscari et al. (13) in the June issue of *Thrombosis and Haemostasis* have demonstrated that MPV is independently associated with percent body fat, blood glucose and ischemic echocardiographic (ECG) changes in elderly patients. Increased platelet size has been shown in patients with cardiovascular risk factors such as diabetes mellitus (14), obesity (15), in accordance with the report by Muscari et al. (13). Elderly patients are known to be a high-risk group in respect to cardiovascular and cerebrovascular events. Independent association of MPV and ischemic ECG changes in elderly patients indicates that these patients are more prone to cardiovascular events compared to patients with low MPV. Since MPV is a simple laboratory measurement which can be measured in almost all laboratories, it is important to identify high-risk elderly patients by means of measuring MPV. Although the study by Muscari et al. (13) is a cross-sectional observational study, and indicates independent association of MPV with ischemic ECG changes, it could be more valuable to know the clinical course of those patients in terms of thrombotic complications.

In addition to cardiovascular risk factors, atherosclerosis itself can stimulate bone marrow megakaryocytes causing circulatory platelet consumption during atherogenesis. MPV has been shown to inversely correlate with the total platelet count, which could even suggest the consumption of small platelets and a compensatory production of larger reticulated platelets (16). Regarding the least platelet numbers in patients with highest MPV tertile, it seems that platelet consumption is the major triggering factor for bone marrow stimulation in addition to associated cardiovascular risk factors in elderly patients. Either the progression of present atherosclerosis or dynamic changes at the site of lesions might play a role in the consumption of platelets.

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The question is how we should decrease MPV, and how it could be beneficial in clinical practice. Should we inhibit the stimulation of bone marrow or should we inhibit the activation of platelets in circulation? As shown by Muscari et al. (13) both cardiovascular risk factors such as high blood glucose and percent body fat, and atherosclerosis itself are independently associated with increased MPV. Therapeutic modalities should focus on both the cardiovascular risk factors and activated platelets. On the other hand it has recently been reported that elevated percen-

tage of reticulated platelets which strongly correlates with MPV is present in patients with residual platelet reactivity compared to patients without (17), suggesting that platelets are in a hyper-reactive state and that this state may contribute to resistance against the antiplatelet therapy.

In conclusion, increased MPV may be of value to detect high-risk patients for future cardiovascular events. With the support of further clinical studies, MPV can be used as a diagnostic or prognostic measurement in cardiovascular disease.

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