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Editorial

Prediction of vascular events: Do platelet turnover parameters have a role?

Platelets play an essential role in the progression of atherosclerotic lesions, plaque activity, and consequent thrombosis. Platelet size is a marker of platelet activity because the young reticulated platelets (RPs) which are metabolically more active with increased mRNA are larger in size.[1] Thus, platelet volume is thought to be an indicator of a cardiovascular event (CVE).

With the advent of automated cell counters, platelet volume indices such as mean platelet volume (MPV) that can be measured via electrical impedance are routinely available. Although generally ignored, it is a surrogate marker of change in the level of platelet stimulation and/or rate in turnover of platelets. These indices, especially MPV, are emerging as reliable tests to predict CVEs. A very recent meta-analysis reviewed the literature describing links between MPV and cardiovascular disease (CVD).[2] MPV was found to be a good marker for risk assessment of established coronary artery disease (CAD) or risk of developing CAD. We also have found a clear association between platelet volume indices and spectrum of CAD, with MPV being highest in patients with acute myocardial infarction (MI) as compared with those with stable CAD and controls.[3] A systematic review of 13 studies calculated that patients with a CVE had an MPV about 0.69 fL higher than non-CVE individuals. Patients with a higher MPV were about 12% more likely to die than patients with a lower MPV.[4] These large platelets are associated with high-residual platelet activity after antiplatelet therapy and are surrogate indicators of unresponsiveness to therapy and further adverse events.[4,5] A high MPV is equivalent to a high-sensitivity C-reactive protein (CRP) in the prediction of long-term clinical outcomes after percutaneous coronary intervention.[6]

Diabetes is a prothrombotic state with increased fibrinogen, platelet activation factors such as beta-thromboglobulin (BTG) and platelet factor 4 (PF-4), and tendency to thrombosis. A clear link of MPV with severity of diabetes mellitus, diabetic retinopathy, and glycosylated Hb (HbA1c) has been established.[7,8] As seen in the cross-sectional study published in this issue, MPV is associated with the degree of glycemic control. In a recent cohort study, although MPV was found to be related to HbA1C values on univariate analysis, on multivariate analysis, it was not so, and independent predictors of MPV above median value (10.8 fL) were found to be age, treatment with angiotensin II receptor blockers (ARBs), and hemoglobin levels. An inverse relationship with total cholesterol was also found.[8] Thus, it may be concluded that some of the parameters of complete blood count (CBC) such as hemoglobin and MPV could be useful tools in following glycemic control of diabetics.

As already discussed, MPV is a surrogate marker of the reticulated young platelets or platelet turnover. The reticulated platelet count was an expensive and time-consuming test conducted by flow cytometry. However, now with the advent of new florescent flow cytometry–based automated hematology analyzers, this parameter is available as an immature platelet fraction (IPF%) and a calculated immature platelet count (IPC) along with the CBC at very little added cost. Thus, this parameter which reflects thrombopoiesiss and is a marker of platelet activity is now available. A comparison of MPV with the IPF in diabetes mellitus and metabolic syndrome found IPF and IPC to be the better indicators of glycemic control, and IPF was significantly higher in patients with diabetes mellitus who have CVDs.[9] IPC had been found to be the strongest independent platelet count–derived indicator of antiplatelet response to thienopyridine therapy.[10] An earlier prospective cohort study in patients with CAD found IPC to be the novel biomarker for major adverse cardiovascular event (MACEs) risk stratification in patients with CAD.[11] Time-dependent receiver-operating characteristic analysis revealed that an IPC level $\geq$7632 platelets/μl was 70.7% sensitive and 82.1% specific for MACEs. After adjustment for age, admission diagnosis, index revascularization, heart failure, smoking, hematocrit, and baseline platelet count, patients with an IPC level $\geq$7632 platelets/μl were more likely to experience a MACE (hazard ratio: 4.65; 95% confidence interval: 1.78 to 12.16; $p < 0.002$).

Thus, platelet turnover parameter such as MPV and now-available IPF, and specifically IPC, are laboratory tests that are easily obtained which can be incorporated in the routine CBC with minimal additional cost. These can be used to monitor patients at high risk of CAD/CVD and decide about appropriate primary and secondary prevention strategies. Thus, patients with CAD can be stratified in terms of risk of future MACE. It can also be used as a surrogate screening test of nonresponsiveness to antiplatelet therapy, thus initiating drug monitoring by platelets function tests and propagating change in therapy.

Conflict of interest

None.

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