Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol11Issue2abst021P.pdf

Blood monocyte characterization as a novel surrogate marker for atherosclerosis in at-risk asymptomatic patients

Gabriella Passacquale, Albert Ferro. King's College London, London, UK

Introduction: Predictive models of cardiovascular (CV) risk incorporating classical risk factors (e.g. the Framingham equation/JBS-2 risk charts) have greatly improved the management of atherosclerosis-related CV disease by allowing estimation of long-term CV risk and hence the nature and intensity of preventative strategies adopted in a given patient. Nevertheless, large population-based studies have shown their limitation in predicting future CV events in individuals; this is due to their poor relationship with atherosclerosis burden on an individual as compared to a population basis.

Aims: We evaluated whether assessment of circulating monocyte phenotype (previously reported to be a independent predictor for future CV events in subjects with established coronary disease) improves the accuracy of CV risk stratification in healthy patients with underlying CV risk factors, through increased accuracy in detection of silent atherosclerosis.

Methods: Patients recruited from the Hypertension and Diabetic Clinics at Guy's and St Thomas' Hospitals, London, UK, were assigned a CV risk score based on the Framingham equation and JBS-2 risk charts. Monocyte characterization was by whole blood immunofluorescence. Atherosclerosis was evaluated by carotid ultrasonography. One-way ANOVA with Dunn's correction was used for between-group comparisons; multivariate linear regression analysis was used to examine correlation between carotid intima-media thickness (IMT) and all study variables, including clinical parameters (age, blood pressure, lipid profile, high sensitivity C-reactive protein (hs-CRP), glycated haemoglobin, body mass index, estimated glomerular filtration rate (eGFR)) and level of monocytic sub-populations ("classical" $CD14^{high}CD16^{-}$, "non-classical" $CD14^{high}CD16^{+}$; and $CD14^{low}CD16^{-}$ cells).

Results: 45 patients were studied, of whom 32 underwent carotid ultrasonography. In accordance with CV risk estimation by Framingham equation they were classified into low-risk (LR, <10% over 10 years, n=22), moderate-risk (MR, 10-20% over 10 years, n=15) and high-risk (HR, >20% over 10 years, n=8) groups. Total monocyte levels and monocyte phenotype were no different between these groups, and the same was true if the patients were stratified using the JBS-2 risk charts. When data were analysed by carotid ultrasonography findings, patients with silent disease (n=10 comprising 2 patients classified at LR, 5 at MR and 3 at HR on the JBS-2 charts) displayed increased number of $CD14^{high}CD16^{+}$ cells (7.53% [3.55%-20.12%]) compared with disease-free patients (n=22; 3.95% [2.29%-7.5%]; p= 0.008). IMT strongly correlated with $CD14^{high}CD16^{+}$ monocyte count (r^2= 0.6310; p<0.0001); a linear relationship was also found with age (r^2= 0.3384; p<0.005) and eGFR (r^2= 0.2385; p=0.03), whilst no statistical correlation was found between IMT and either CV risk scores (r^2= 0.1908; p=0.06) or hs-CRP (r^2= 0.0003; p=0.9458). Among classical CV risk factors, $CD14^{high}CD16^{+}$ were directly related to age (r^2= 0.1132; p=0.03) and inversely related to diastolic blood pressure (r^2= 0.1627; p=0.01).

Conclusions: Standard CV risk calculators have little ability to predict presence of silent atherosclerosis at an individual level. Circulating $CD14^{high}CD16^{+}$ monocytes, which are increased in patients with silent carotid disease, may provide a useful adjunct for CV risk stratification.