LETTERS TO THE EDITOR

Is thrombogenesis related to residual platelet function in ischaemic heart disease?

We read with great interest the recent study by Yano et al.,1 which reported that patients after percutaneous coronary intervention exhibit increased thrombogenicity in spite of dual antiplatelet therapy. This prothrombotic state is not related to residual platelet aggregability and seems to be determined mainly by the presence of co-morbidities, such as obesity, sleep apnea, diabetes mellitus, cardiac function, and atherosclerotic burden. On the basis of these findings the authors conclude that the addition of anticoagulant therapy may possibly be beneficial to reduce the rate of treatment failure. We disagree with this treatment strategy and would like to offer the following comments.

First, the authors found a correlation between plasma biomarkers of thrombin generation, fibrinolytic activity, and endothelial dysfunction with the presence of risk factors or conditions associated with atherosclerotic disease. Thus, patients with abnormal levels of these biomarkers could have a worse prognosis, but it does not necessarily mean that reducing the level of the biomarkers will reduce the occurrence of the disease. Only the modification of the traditional or true clinical risk factors has convincingly been demonstrated to reduce disease risk.2 Indeed, the clinical usefulness of determining new biomarkers, together with the presence of traditional and emergent risk factors (e.g. the metabolic syndrome or the detection of subclinical atherosclerosis) is to improve (even slightly) the identification of the ‘high risk’ patient and to optimize treatment, if possible.

Secondly, the benefits of antiplatelet therapy are limited, and a high percentage of treated patients will suffer a new thrombotic event, giving rise to the concept of antiplatelet drug resistance. The definition of antiplatelet drug resistance is controversial, and thus far, this varies widely, depending upon laboratory methods used for the clinical definition.3 Several factors (age, other underlying co-morbidities, lifestyle variables such as smoking, and importantly compliance) have been involved in this inter-individual response heterogeneity. Also, platelet function is complex and is regulated by many stimulatory and inhibitory factors. Indeed, ADP and thromboxane, as well as collagen, thrombin, serotonin, and catecholamines, all enhance platelet function; thus targeting thromboxane and ADP alone will not eliminate the residual platelet activity, especially in the presence of potent agonists or with a decrease in the inhibition activity. Moreover, aspirin does not inhibit shear stress-induced platelet activation and adhesion which is particularly important in areas of bifurcations and stenotic vessels.4,5 In addition, Virchow’s triad of thrombogenesis includes not only abnormalities in platelets, coagulation, or fibrinolytic system, but also abnormalities in the vessel wall (endothelium) and in the blood flow, with an important interaction between inflammation and the progression of atherothrombotic disease.6

Anticoagulant treatment would focus only in a very limited area of this complex mechanism of thrombus formation. A simplistic approach of just paying attention to block individual components of this network could make clinicians forget the benefits of a more global strategy, that is the cornerstone for reducing the progression of atherosclerotic disease: for example, lifestyle changes with weight loss, exercise activity, strict control of cardiovascular risk factors, and broad use of cardiovascular prevention drugs such as statins and renin–angiotensin system blocking agents that have demonstrated a beneficial role in reducing the inflammatory and the prothrombotic state.7 Finally, the use of anticoagulant in a patient on dual antiplatelet therapy increase the risk of bleeding complications that could overload the potential benefit proposed by the authors.8

References

Francisco J. Pastor-Pérez
Department of Cardiology
Hospital Universitario Virgen de la Arrixaca
Murcia 30120
Spain
Tel: +34 968369445
Fax: +34 968369662
Email: fcpomarino@hotmail.com

Francisco Marín
Department of Cardiology
Hospital Universitario Virgen de la Arrixaca
Murcia 30120
Spain

Sergio Manzano-Fernández
Department of Cardiology
Hospital Universitario Virgen de la Arrixaca
Murcia 30120
Spain

Gregory Y.H. Lip
Haemostasis, Thrombosis and Vascular Biology Unit
University Department of Medicine
City Hospital
Birmingham
UK