The association of impaired myocardial perfusion and monocytosis with late recovery of left ventricular function following primary percutaneous coronary intervention

William J. Gibson\textsuperscript{1,2} and C. Michael Gibson\textsuperscript{1,2}\textsuperscript{*}

\textsuperscript{1}Massachusetts Institute of Technology, Boston, MA, USA and \textsuperscript{2}Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Online publish-ahead-of-print 25 September 2006

This editorial refers to ‘Significance of total and differential leucocytes count in patients with acute myocardial infarction treated with primary coronary angioplasty’\textsuperscript{T} by M. Mariani et al., on page 2511.

Mariani et al.\textsuperscript{1} add to a growing body of the literature associating elevated white blood cell counts to adverse outcomes in the setting of ST-elevation MI (STEMI). For the first time, the authors highlight the association of elevated monocytes counts particularly with late left ventricular (LV) functional recovery following primary percutaneous coronary intervention (PCI) for STEMI.

A wealth of data has accumulated relating elevated white blood cell counts to a host of adverse outcomes in the setting of acute coronary syndromes including, death, congestive heart failure, and shock.\textsuperscript{2–4} Elevations of the white blood cell count have also been associated with impairments in other surrogate/angiographic outcomes including poorer TIMI myocardial perfusion grades and slower corrected TIMI frame counts.\textsuperscript{2–4} Demographic characteristics associated with elevated white blood cell counts include prior MI, smoking, and older age.\textsuperscript{2–4}

Although the association of elevated neutrophils with impaired myocardial perfusion and adverse clinical outcomes has been reported in the past,\textsuperscript{3} the study of Mariani et al.\textsuperscript{1} highlights the importance of elevated monocytes counts and LV function. Data were drawn from 238 consecutive patients undergoing primary PCI for STEMI at one centre. Although both neutrophil and monocytes counts were related to early outcomes (impaired myocardial blush grades and poorer ST-segment resolution), it is notable that only the monocyte count was independently related to the recovery of LV function at 6 months. Lymphocytosis was not associated with clinical or angiographic outcomes. This study also adds to the body of the literature by demonstrating that the most powerful independent correlate of poorer recovery of LV function at 6 months was impaired myocardial perfusion following primary PCI.\textsuperscript{5}

The association of the monocyte, lymphocyte, and neutrophil components of the white blood cell count to clinical outcomes provides some potential insight into the pathophysiology of the inflammatory response following STEMI and its relationship to clinical outcomes. It is notable that neutrophils were associated with both the basal and peak CK, whereas monocytes were not. This difference may be explained, in part, by the early activation of neutrophils and the later arrival and longer lifespan of monocytes. It could be speculated that the early rise in the neutrophil count may reflect, at least in part, the initial infarct size. In contrast, although monocytosis was not associated with basal or peak CK, in a multivariate model, it was independently associated with LV recovery. It could be speculated that the later arrival and longer lifespan of monocytes may explain, in part, the association of this constituent of the white blood cell count with delayed recovery of LV function.

Although white blood cells are associated with poorer angiographic and clinical outcomes, it remains unclear whether the white blood cell count is simply an acausal correlate (i.e. a marker) or whether elevations of white blood cells are causally related to adverse outcomes. The hypothesis that this association represents an acausal correlation is based on the idea that elevated white blood cell counts may simply reflect larger infarct sizes at the time of patient’s arrival. Indeed, most studies do demonstrate that longer duration of symptoms, anterior MI, and basal CK-MB values (all of which are associated with larger infarct sizes) are associated with elevated white blood cell counts.\textsuperscript{2–4}

In terms of a causal association, it has been hypothesized that elevations of white blood cell constituents may be associated with greater reperfusion injury.\textsuperscript{6} Could the phagocytosis of necrotic debris following infarction also lead...
to the destruction of potentially salvageable myocardium? Reperfusion injury has also been associated with the release of oxygen free radicals that injure the endothelium and myocardium through lipid peroxidation. Other potentially toxic molecules released as part of the inflammatory milieu in the setting of acute coronary syndromes and reperfusion include phospholipases, elastases, latent metalloproteinases, cytokines, and leukotrienes. Finally, given their large size and reduced deformability, white blood cells may also be associated with mechanical plugging of the capillary network, the lumen of which is reduced in size by endothelial oedema as a result of infarction.

Do larger infarcts cause elevations of the white blood cell count, or do elevations of the white blood cell count cause larger infarcts? Perhaps the association is actually bidirectional. Despite the associations reported to date, it is notable that pharmacotherapies directed against white blood cells, such as inhibiting their activation and adhesion, have not improved clinical outcomes in human studies. This would suggest that white blood cell elevations are a marker rather than a causative agent in adverse outcomes. It is, however, also possible that the wrong route, timing, or dose of these agents was evaluated. It is also possible that the specific ligand that was targeted may not be relevant.

Although observation studies, such as the present one, demonstrate a clear association, carefully designed animal studies and/or basic science studies are needed to understand the directionality of causation, and potentially the bidirectional nature of the association if present, and the potential targets for future pharmacotherapy.

Conflict of interest: none declared.

References