To the editor:

Circulating endothelial cells in acute coronary syndromes

We read with interest Stefanec’s comments about our work on circulating endothelial cells (CECs) in acute coronary syndromes. We feel, however, that most of these comments are inaccurate.

First, Stefanec claims that we found no circulating endothelial cells in controls. We did in fact find a small number of cells in some control patients, but these cells were outside the interquartile and median range that we reported. More specifically, he indicates that we failed to demonstrate activated or apoptotic endothelial cells. Regarding cell activation, we clearly stated that a proportion of isolated cells were positive for tissue factor. If one accepts that expression of tissue factor is associated with endothelial cell activation, then it follows that a proportion of cells were activated. Furthermore, we also detected apoptotic cells, although these cells represented less than 10% of the total circulating endothelial cells isolated.

Second, Stefanec points out that our results disagree with those of Solovey et al. We feel this comment inappropriate, since nowhere in our paper do we contend that our results are directly comparable with those of Solovey; our two groups used different control subjects and different methodologies to isolate circulating endothelial cells.

Stefanec goes on to elaborate why, in his view, we have been unable to identify apoptotic endothelial cells. We agree that the TUNEL assay is not able to detect early stages of apoptosis. However, this technique has been validated for detection of apoptosis in major studies. Again, the fact that we did find a small proportion of apoptotic endothelial cells disproves Stefanec’s statement that our method is not able to identify such cells. We are also surprised that he contends that acridine orange-staining excludes apoptotic cells, since many studies have used this reagent to visualize chromatin condensation and cytoplasm blebbing accompanying apoptosis. Anyhow, we did not use this method for the purpose of identifying apoptosis in CECs. Finally, many of the references quoted by Stefanec deal with the anti-apoptotic effect of drugs administered to our patients that would act to reduce the number and apoptotic state of circulating endothelial cells. Although most of these papers refer to in vitro studies and/or animal models and have used methodologies quite different from ours, we do not contest this potential effect. Anyway, even in this hypothesis, our findings of significantly higher levels of non-apoptotic circulating endothelial cells in patients with acute coronary syndromes as compared to controls remain valid, since all patients and controls were similarly treated. In our opinion, none of the references quoted by Stefanec is in contradiction with our results or supports the hypothesis that they could be due to methodological or therapeutic artifacts.

References

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