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CORRESPONDENCE

Letters to the Editor

Endothelial Progenitor Cells in Coronary Artery Disease

We have been prompted to write by the small study of Güven et al. (1) showing increased endothelial progenitor cell (EPC) colonies in patients with coronary artery disease (CAD). In contrast, a wide literature demonstrates that the extent of the EPC pool is an indicator of cardiovascular health, as EPCs negatively correlate with severity of both peripheral and coronary atherosclerosis (2,3).

The investigators attribute their paradoxical results to the longer culture method they used to distinguish between true EPCs and circulating angiogenic cells (CACs) in comparison with previous studies. Even if we consider that earlier studies evaluated CACs rather than true EPCs, the findings by Güven et al. (1) are contrasting, because they report higher CACs in patients with CAD. The researchers hypothesize that significantly ischemic CAD triggers the mobilization of EPCs/CACs from bone marrow. However, patients with actual myocardial ischemia, for whom increase in EPCs/CACs have been previously demonstrated, were excluded from the study, and only patients with stable CAD were enrolled. Moreover, whereas EPC colonies directly correlated with maximum stenosis, they did not correlate with the number of diseased vessels, which should be more informative on the extent of myocardial ischemia.

We suggest that the use of intravascular ultrasound may provide further information on coronary atherosclerosis and help explain the paradoxical results when CAD is assessed angiographically. Finally, should the data by Güven et al. (1) really reflect a previously unknown regulation of EPCs in CAD, we would like to offer a counter explanation: the increase in circulating cells with high angiogenic potential dependent on CAD severity may be causally related to plaque angiogenesis and growth (4) the Janus face of EPCs in cardiovascular diseases.

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REFERENCES

1. Güven H, Shepherd RM, Bach RG, Capoccia BJ, Link DC. The number of endothelial progenitor cell colonies in the blood is increased in patients with angiographically significant coronary artery disease. J Am Coll Cardiol 2006;48:1579–87.
2. Fadini GP, Coracina A, Baesso I, et al. Peripheral blood CD34+KDR+ endothelial progenitor cells are determinants of subclinical atherosclerosis in a middle-aged general population. Stroke 2006;37:2277–82.
3. Kunz GA, Liang G, Cuculoski F, et al. Circulating endothelial progenitor cells predict coronary artery disease severity. Am Heart J 2006;152:190–5.
4. George J, Afek A, Abashidze A, et al. Transfer of endothelial progenitor and bone marrow cells influences atherosclerotic plaque size and composition in apolipoprotein E knockout mice. Arterioscler Thromb Vasc Biol 2005;25:2636–41.

Reply

We would like to thank Dr. Fadini and colleagues for their comments regarding our study (1) recently published in *JACC*. Dr. Fadini et al. point out that our data, which shows that the numbers of endothelial progenitor cells (EPCs) and circulating angiogenic cells (CACs) in the blood of patients referred for cardiac catheterization are increased in those patients with angiographically significant coronary artery disease (CAD), differs from the results of some previously published studies. We agree. But as discussed in our study and highlighted by Drs. Leor and Marber in an accompanying editorial in *JACC* (2), it is critical when comparing different studies that the type of circulating angiogenic cells be precisely defined. Indeed, a recent study by Yoder et al. (3) suggested that culture techniques commonly used to quantify EPCs actually measure myeloid progenitor cells (3). In our study, we used rigorous histological and flow cytometry techniques to quantify EPCs and CACs (not simply a longer culture method, as suggested by Dr. Fadini et al.). Furthermore, whereas we compared these cell numbers to angiographically defined CAD among patients across a wide spectrum of disease severity, many previous studies identified atherosclerotic disease or its absence noninvasively, which may seriously limit sensitivity and specificity. We agree that a more precise definition of atherosclerosis by, for example, use of intravascular ultrasound, may add to our understanding of the relationship between the different EPC subsets and CAD.

From our observations, we speculated that significant myocardial ischemia may be a proximal determinant of EPC number in the peripheral blood. Dr. Fadini et al. question this, but in support of their opinion they wrongly state that patients with actual myocardial ischemia were excluded from our study. Although patients with acute myocardial infarction and unstable angina were excluded from our investigation, the majority of our patients with significant CAD were symptomatic (and anginal symptoms likely underestimate the frequency of true myocardial ischemia). Importantly, we observed the highest numbers of circulating EPCs and CACs in patients selected clinically to require revascularization. Of relevance, previous studies have shown an increase in circulating EPCs in patients with unstable angina (4) or acutely in response to exercise-induced ischemia (5), observations that appear consistent with the hypothesis that ischemia may be an important factor for the number of circulating EPCs.