Promotion of Collateral Growth by Granulocyte-Macrophage Colony-Stimulating Factor in Patients With Coronary Artery Disease

To the Editor:

The study by Seiler et al.2 on collateral growth stimulation in humans by granulocyte-macrophage colony-stimulating factor (GM-CSF) received a very optimistic editorial by Schaper.2 The authors should be congratulated on the study concept and the conduct of this first-time approach to assess arteriogenesis directly in humans. However, can we really draw the conclusion that there was a clear-cut effect of GM-CSF on collateral development with a short study time period of 2 weeks? I have 2 main concerns. First, looking at the data in Table 2 shows that the collateral flow index (CFI) differed considerably at baseline between both study groups; this difference of 0.21 versus 0.30 was just the same amount that was ultimately observed as increase in the treatment group (0.21 to 0.31). Surprising and completely unexplained was the fact that in the placebo group, the CFI dropped by almost that same amount, from 0.30 to 0.23. This unexplained drop of the CFI is as significant to study result as the moderate increase in the treatment group. As no balloon dilatation was done at baseline, the CFI should have remained unchanged in the placebo group. Does this change in the placebo group not simply reflect the high intrinsic variability of the applied method? No data on intraindividual variability of CFI, which would be essential in the interpretation of the study results, are given. In our experience using Doppler during balloon occlusion, we observed considerable variation of individual collateral flow measurements within 24 hours.3 Also, multiple paired t tests without corrections were used instead of a repeated ANOVA. This test would have probably shown no difference between the groups considering the individual data points (Figure 2). Only 2 patients in the treatment group showed a considerable increase, and at least 2 patients had shown a similar degree of improvement in the placebo group; however, more patients showed an unexplained decrease.

With regard to the many previous experimental attempts to promote arteriogenesis/angiogenesis in humans and the setbacks that have occurred,2 a cautious approach to the interpretation is important, but limited pilot trial is required. The interpretation of this study in the editorial that “therapeutic arteriogenesis has arrived” is premature.

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