To the Editor:

We read with interest the article by Forcillo and colleagues on intramyocardial CD133+ autologous bone marrow stem cell application during coronary artery bypass grafting in patients with ischemic cardiomyopathy. This open-label pilot study of only 5 patients assessed safety and feasibility of the procedure. No increase in global ejection fraction was noted, but stress echocardiography and magnetic resonance imaging revealed improved regional contractility and morphology in the injected myocardium. We noticed some elements that possibly interfere with interpretation of the results.

The pilot study is a part of the IMPiantation of Autologous CD133+ sTem Cells in Patients Undergoing CABG (IMPACT-CABG) trial (NCT01033617), a randomized, double blind, placebo-controlled clinical trial. The lack of randomization and absence of placebo and/or sham in the pilot study make it virtually impossible to attribute the segmental improvement in wall motion to the stem cells. We congratulate the authors on their encouraging results, but advocate for a randomized pilot trial to make appropriate effect size calculations.

Time span from previous myocardial infarction (MI) is a critical parameter to select patients who can benefit most from intramyocardial stem cell treatment during coronary artery bypass grafting. Patients treated 7-12 weeks after MI have a higher chance of improvement than patients treated later. MI to treatment time ranges from 4 months to 4 years in this pilot study. To prevent heterogeneity and confounding results in the IMPACT-CABG trial it might be sensible to reassess the time from previous MI inclusion criterion.

Difference in cell preparations, timing of administration, baseline ejection fraction, and choice of end points all contributed to the variable efficacy outcomes in previous clinical trials. Initial beneficial results were not always reproduced in a strictly double-blind, fully randomized, placebo-controlled trial (Bypass Surgery and CD133 Marrow Cell Injection for Treatment of Ischemic Heart Failure [Cardio133]; NCT00462774). Hence, a stringent respect to guidelines on conducting a randomized, controlled clinical trial is necessary to obtain reproducible results and ensure wise utilization of resources.

Tomislav Kopjar, MD
tkopjar@gmail.com
Bojan Biocina, MD, PhD
Branka Golubic Cepulic, MD, PhD
Davor Milicic, MD, PhD

Disclosures
The authors have no conflicts of interest to disclose.

References