into an ischemic area results in modulation of the local tissue immune system and altered cytokine production (4). Indeed, BMC transplantation results in local inflammatory changes that activate myofibroblasts, thus reducing infarct size (5). Thus, modulation of pro- and anti-inflammatory intramyocardial cytokine levels by transplanted cells and their crosstalk with the local tissue environment likely affect survival and differentiation of progenitor cells, as well as overall cardiac outcome.

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doi:10.1016/j.jacc.2009.07.064

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Reply

The letter by Drs. Thum and Anker touches various aspects of cardiac stem cell therapy (e.g., mortality, paracrine effects, and inflammation), all of which may be briefly addressed as follows.

Intracoronary stem cell therapy seems to represent a safe and effective regimen for treatment of heart failure after acute myocardial infarction (1,2), in an old myocardial infarction (≥8 years) with ischemic cardiomyopathy (3), and in advanced dilated cardiomyopathy (4). Our study (5) did not aim to speculate (Drs. Thum and Anker) on stem cell-induced inflammation (which has not yet been documented in the overwhelming majority of studies) and on possible paracrine effects by stem cells, but fortunately was able to analyze the different parameters of ventricular performance and potential effects on cardiac mortality in large patient groups, treated and untreated, in long-term follow-up after myocardial infarction.

When carefully reading our paper (5), the BALANCE (Clinical Benefit and Long-Term Outcome After Intracoronary Autologous Bone Marrow Cell Transplantation in Patients With Acute Myocardial Infarction) study showed that mortality, as a consequence of stem cell therapy, is significantly reduced; in a median follow-up time of 4.6 ± 2.1 years in the bone marrow cell group 1 patient died, and in 4.8 ± 2.2 years, 7 patients in the control group died ($p = 0.03$).

Mortality is dependent on both the degree of ventricular impairment and the amount of arrhythmogenicity. Dependent on the multifactorial mode of action of stem cells, systolic function (e.g., ejection fraction, stroke volume, contractility) and diastolic performance are improved; infarct size, end-systolic volume, and systolic wall stress decrease; and the arrhythmogenicity of the heart is presumably reduced. Thus, several of the main myocardial determinants of cardiac mortality are influenced in favor of reduced mortality by stem cell treatment in chronically ill cardiac patients.

Undoubtedly, further large studies are needed to analyze the action of stem cells on ventricular performance and cardiac mortality in different stages of chronic cardiac failure, especially with regard to the distinct origin of this chronic disease.

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doi:10.1016/j.jacc.2009.11.005

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Grade of Ischemia to Assess No Reflow After Reperfusion

We read with great interest the excellent review by Niccoli et al. (1) about the no-reflow phenomenon in humans. In their paper, the authors describe various techniques for the prediction of no-reflow. As far as electrocardiography is concerned, the authors only mention the QRS score as a predictor of ischemia-related injury.

The extent of terminal QRS distortion on the admission electrocardiogram, known as the grade of ischemia, is a strong predictor of failure of ST-segment resolution as well as of