Letters to the Editor
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Cell quality in the ASTAMI study

Schächinger et al. recently reported clinical improvement after treatment of acute myocardial infarction with intracoronary injection of autologous bone-marrow-derived mononuclear cells (MNCs) (the REPAIR-AMI Trial). Here, the authors discuss whether lack of improvement in global left ventricular function in our study, the ASTAMI study, could be related to impaired cell quality or insufficient cell numbers. We believe this is unlikely for the following reasons:

(i) Comparable density gradient centrifugation techniques have been used for isolation of MNCs in the REPAIR-AMI and the ASTAMI studies. The density gradient solutions used for MNC separation, Lymphoprep™ and Ficoll-Hypaque (Ficoll-Paque™), contain ficoll and sodium diatrizoate at identical concentrations.

(ii) In the ASTAMI study, MNCs were kept at 4–8°C overnight in 0.9% NaCl and 20% autologous heparin plasma, cell concentration <10⁷ cells/ml. Cold saline-plasma storage of bone marrow or peripheral blood stem cells (PBSCs) for transplantation is being used worldwide for intercontinental transportation or prior to cryopreservation. According to Schächinger et al. in their study, the difference may be explained by the mean delay between enrolment and baseline LVEF measurement (4.3 ± 1.3 days). Secondly, and more importantly, two major determinants of LVEF recovery—time-to-reflow and infarct location—are possible confounders in this study. According to Sheiban et al., LVEF recovery is usually observed after primary angioplasty if coronary flow is restored ≤4 h from symptom onset, whereas no significant improvement occurs afterwards. This time "window" may be even narrower in anterior infarctions. Indeed, we have observed no significant recovery in LVEF after primary angioplasty despite an average shorter time-to-reflow (2.5 ± 1.4 h) when only anterior myocardial infarctions were considered. In the REPAIR-AMI study, however, the authors analysed anterior and inferior infarctions together, despite the fact that these two infarct locations differ in terms of acute left ventricular impairment severity, LVEF recovery and clinical outcome after reperfusion therapy. Moreover, mean reperfusion time was >7 h, an interval usually not associated with LVEF improvement, particularly in anterior infarctions. The combination of different times to treatment and infarct locations may have a major influence on LVEF recovery.

We read with great interest the recent article by Schächinger et al. showing improved 1-year clinical outcomes in patients with acute myocardial infarction receiving intracoronary administration of bone marrow-derived progenitors cells (BMCs) after successful reperfusion therapy. The authors attribute the improved clinical outcomes in the treatment group to the recovery of global left ventricular contractile function within 4 months, as recently reported in the same patient population. However, we believe that factors other than administration of BMCs may have influenced left ventricular ejection fraction (LVEF) recovery and, hence, clinical outcomes in their study. First, we can suppose that spontaneous LVEF recovery was already occurring in both groups before BMCs or placebo administration. Indeed, baseline LVEF was 46.7 ± 10 and 47.5 ± 10% in controls and BMC-treated patients, respectively—values higher than that used as a threshold for patient inclusion in the study (<45%). This spontaneous recovery may be explained by the mean delay between enrolment and baseline LVEF measurement (4.3 ± 1.3 days). Secondly, and more importantly, two major determinants of LVEF recovery—time-to-reflow and infarct location—are possible confounders in this study. According to Sheiban et al., LVEF recovery is usually observed after primary angioplasty if coronary flow is restored ≤4 h from symptom onset, whereas no significant improvement occurs afterwards. This time "window" may be even narrower in anterior infarctions. Indeed, we have observed no significant recovery in LVEF after primary angioplasty despite an average shorter time-to-reflow (2.5 ± 1.4 h) when only anterior myocardial infarctions were considered. In the REPAIR-AMI study, however, the authors analysed anterior and inferior infarctions together, despite the fact that these two infarct locations differ in terms of acute left ventricular impairment severity, LVEF recovery and clinical outcome after reperfusion therapy. Moreover, mean reperfusion time was >7 h, an interval usually not associated with LVEF improvement, particularly in anterior infarctions. The combination of different times to treatment and infarct locations may have a major influence on LVEF recovery.

References

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Improved clinical outcome after intracoronary administration of bone marrow-derived progenitor cells in acute myocardial infarction: final 1-year results of the REPAIR-AMI trial

We read with great interest the recent article by Schächinger et al. showing improved 1-year clinical outcomes in patients with acute myocardial infarction receiving intracoronary administration of bone marrow-derived progenitors cells (BMCs) after successful reperfusion therapy. The authors attribute the improved clinical outcomes in the treatment group to the recovery of global left ventricular contractile function within 4 months, as recently reported in the same patient population. However, we believe that factors other than administration of BMCs may have influenced left ventricular ejection fraction (LVEF) recovery and, hence, clinical outcomes in their study. First, we can suppose that spontaneous LVEF recovery was already occurring in both groups before BMCs or placebo administration. Indeed, baseline LVEF was 46.7 ± 10 and 47.5 ± 10% in controls and BMC-treated patients, respectively—values higher than that used as a threshold for patient inclusion in the study (<45%). This spontaneous recovery may be explained by the mean delay between enrolment and baseline LVEF measurement (4.3 ± 1.3 days). Secondly, and more importantly, two major determinants of LVEF recovery—time-to-reflow and infarct location—are possible confounders in this study. According to Sheiban et al., LVEF recovery is usually observed after primary angioplasty if coronary flow is restored ≤4 h from symptom onset, whereas no significant improvement occurs afterwards. This time "window" may be even narrower in anterior infarctions. Indeed, we have observed no significant recovery in LVEF after primary angioplasty despite an average shorter time-to-reflow (2.5 ± 1.4 h) when only anterior myocardial infarctions were considered. In the REPAIR-AMI study, however, the authors analysed anterior and inferior infarctions together, despite the fact that these two infarct locations differ in terms of acute left ventricular impairment severity, LVEF recovery and clinical outcome after reperfusion therapy. Moreover, mean reperfusion time was >7 h, an interval usually not associated with LVEF improvement, particularly in anterior infarctions. The combination of different times to treatment and infarct locations may have a major influence on LVEF recovery.