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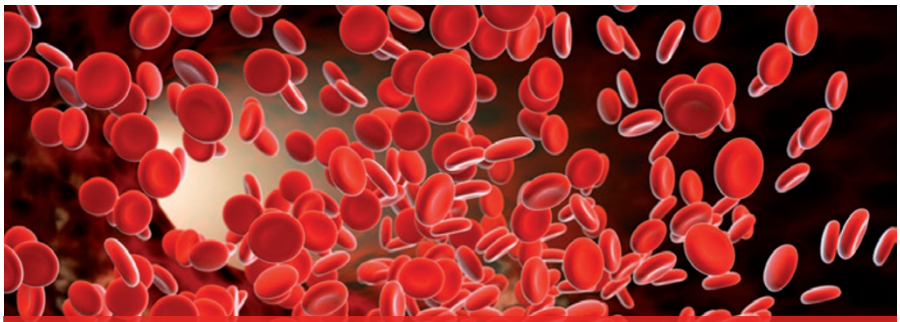

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STEM CELLS

# BMMC treatment safe but not an improvement on standard therapy

Intracoronary infusion of bone marrow-derived mononuclear cells (BMMCs) has long been hoped to improve cardiac function in patients after an acute myocardial infarction (AMI). However, the results have been mixed, and the debate surrounding mononuclear-cell treatment is still open. In a new paper from investigators conducting the HEBE trial, BMMC treatment improves left ventricular function, but is not associated with improved clinical outcomes compared with standard therapy at 5-year follow-up.

"The effect of intracoronary infusion of BMMCs after AMI in patients has been analysed in the past, with a moderate positive effect of BMMC treatment on left ventricular function at short-term follow-up," says study investigator Ronak Delewi from the University of Amsterdam in the Netherlands. "However, there [are] conflicting data regarding the long-term clinical benefit of intracoronary BMMCs."

The HEBE investigators initially enrolled 200 patients with a previous AMI and who had been treated by percutaneous coronary intervention. Participants were randomly assigned to receive either BMMCs ($n = 69$), peripheral blood mononuclear cells (PBMCs; $n = 66$), or undergo standard therapy without a placebo cell infusion ($n = 65$). The PBMC group was included to investigate whether any potential benefit was attributable to a combined effect of all cells, rather than the mononuclear progenitor cell population alone. All patients also underwent cardiac MRI at 2 years to assess cardiac function.

Patients in the BMMC group had less increase in left ventricular end-systolic function ($3.5 \pm 16.9$ ml/m$^2$) than those in the placebo group ($11.2 \pm 19.8$ ml/m$^2$; $P = 0.03$). However, at 5 years, the primary end point (a combination of death or hospitalization for heart failure) was not significantly different between the two groups (4 versus 1; $P = 0.20$), indicating that long-term BMMC use is safe and well-tolerated by patients.

No difference was seen between the PBMC and control groups for either left ventricular function or the primary end point. However, the composite end point of death or recurrent myocardial infarction occurred significantly more frequently in patients receiving PBMCs than in the placebo group (14 versus 3; $P = 0.008$). This association was not seen in those who received BMMCs (2 versus 3; $P = 0.67$).

"In this long-term follow-up study, we could not demonstrate a beneficial effect of intracoronary delivery of mononuclear cells from bone marrow or peripheral blood on regional and global systolic myocardial function at 2 years of follow-up," explains Delewi. "Nevertheless, we did observe that the increase in left ventricular end-diastolic volume was lower in the BMMC group."

"Major clinical cardiovascular adverse events were significantly more frequent in patients treated with intracoronary infusion of PBMCs," says Delewi, who adds, "our data do not support further use of local PBMC infusion in the setting of acute myocardial infarction."

*Tim Geach*

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