

Myocardial regeneration after intracoronary injection of autologous bone marrow-derived mononuclear cells in patients with large anterior acute myocardial infarction and late reperfusion

Objective and background: Despite the use of reperfusion therapies, outcomes in patients with large ST elevation myocardial infarction (STEMI), late reperfusion and left ventricular (LV) dysfunction is poor. We investigated longterm safety and efficacy of intracoronary injections of autologous bone marrow-derived mononuclear cells (BMNCs).

Methods: 27 patients with anterior STEMI (age 59 ± 12 yrs, mean baseline LV ejection fraction (LVEF) $39 \pm 5\%$), who underwent percutaneous coronary intervention 4-24 hours after the onset of symptoms, were randomly assigned either to intracoronary BMNCs injection (n = 17, BMNCs group, out of which 14 underwent longterm follow-up), or to standard therapy (n = 10, Control group). The LVEF, the LV end-diastolic and end-systolic volumes (LVEDV, LVESV) and diastolic function (transmitral flow, pulmonary vein flow) were assessed by echocardiography at discharge, month 4 and 24. Myocardial perfusion was assessed using SPECT at baseline and month 4.

Results: At 24-month, there was no difference in rates of serious clinical events (36% vs. 50%, $p=0,54$). At Month 4 LVEF improved to similar extent in both groups (absolute change $+5,8\%$ vs. $+7,6\%$, $p=0,75$), with similar infarct size reductions ($-10,9\%$ vs. $-12,2\%$, $p=0,47$). However, at Month 24, LVEF further improved in BMNCs patients (absolute change $+12\%$ v.s $+8,5\%$, $p=0,03$). This effect resulted from a more pronounced reduction in LVESV ($-2,6\text{ml}$ vs. $-1,8\text{ml}$, $p=0,26$) and a smaller increase in LVEDV ($+16,7\text{ml}$ vs. $+17,9\text{ml}$, $p=0,27$). At month 24 we observed improvement in diastolic function in BMNCs patients in contrast to control group ($p < 0,001$). These results suggests beneficial long-term effects of BMNCs therapy on LV remodeling.

Conclusions: BMNCs injections in patients with STEMI and LV dysfunction was associated with a significant improvement of global LVEF and diastolic function during longterm follow-up compared to standard therapy. No difference was observed between the groups in adverse clinical events or restenosis.

Key Words: bone marrow-derived mononuclear cells, myocardial infarction, remodeling, left ventricular ejection fraction