The short to mid-term effect of bone marrow derived cell transfer on diastolic function after acute myocardial infarction

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Meta-analyses of numerous small- and medium-sized trials have confirmed the feasibility and short-term benefit of bone marrow-derived cells (BMC) in overall systolic function after acute myocardial infarction (AMI). However, the effects of BMC on diastolic function have not been well characterized. The short- and mid-term clinical effects of intracoronary BMC have been contradictory [1,2]. Recent studies have revealed that BMC transfer did not exhibit long-term effects on diastolic function after AMI [3,4]. To date, no systematic analysis or review has addressed early and mid-term clinical effects of BMC. Because decreased left ventricular (LV) diastolic function is a frequent complication after AMI and is associated with an increased risk for heart failure (HF), determining whether BMC therapy improves diastolic function in a time-dependent manner is important. In this study, we reviewed clinically relevant trials to explore whether autologous BMC were beneficial for LV diastolic function after AMI.

We searched the databases MEDLINE, EMBASE, the Science Citation Index and the Cochrane Central Register of Controlled Trials through Feb 8, 2011 for clinical studies using BMC therapy after AMI in randomized controlled trials (RCTs). We included RCTs with follow-up for at least 3 months and standard medical treatment, which was used as a control. There was no restriction based on publication year or language. The lack of a control group, the use of other cells as a control group, administration of cytokines, such as G-CSF, and crossover studies were excluded. Four RCTs with a total of 282 patients were eligible. All of the trials reported an intention-to-treat analysis and had patients that presented with a ST-segment elevation AMI. Standard echocardiographic and tissue Doppler echocardiography were used to acquire diastolic parameters. All of the patients accepted optimal medical treatment, including aspirin, clopidogrel, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, β-blocker and statins. The overall baseline characteristics were matched. All of the trials with BMC used intracoronary injections. Hours to percutaneous coronary intervention (PCI) and time from PCI to cell therapy were summarized (Table 1).

The ratio of mitral inflow E velocity to tissue Doppler Ea (E/Ea) is a non-invasive and reproducible estimate of the left atrial filling pressure. It exhibits a linear relationship with LV filling pressure and is recommended for the evaluation of LV diastolic function [5]. Therefore, we chose E/Ea as the primary endpoint. Other echocardiographic parameters were also measured. We grouped the studies based on the follow-up period duration. We estimate the weighted mean differences (WMD) between the BMC-treated and control patients and their associated 95% confidence intervals (CIs). Rev-Man version 4.2.2 was used for these analyses.

The pooled data showed that BMC therapy was superior to standard medical therapy for improving E/Ea ratios after a 1-year follow-up (Table 2). We detected improvement in the ratio of pulmonary vascular resistance (PVR) in the BMC group within 1 year. PVR was lower in the BMC group than in the control group. Due to limited data, we were unable to analyze group differences for PVR after 1-year follow-up. A summary of the magnitude of the changes after cell therapy (as percentages or in absolute units) is shown in Table 2 and indicated the potential clinical benefits of BMC therapy. The E/Ea ratio improved less in the control group compared to that of the BMC-treated group (absolute value: 12.3 vs. 11.81) after 1-year follow-up. PVR exhibited a decrease of 6.19% in the BMC-treated group compared to 1.31% in the control group. In our analysis, no significant changes were detected in traditional echocardiographic parameters such as the E/A-ratio, transmitral deceleration time and isovolumic relaxation time. Because these parameters have a biphasic relationship with LV diastolic properties and filling pressure, changes in these parameters should be interpreted with caution.

HF is a major cause for hospitalization. Epidemiological studies have indicated that up to 40% of these cases are related to diastolic HF. In this study, an improvement in E/Ea in the BMC group probably reflected a decrease in LV filling pressure during recovery after AMI. Decreased PVR implied a decrease in left atrial pressure and LV filling pressures after BMC therapy. Combined with the inter-group absolute change during follow-up, these results may indicate the potential clinical benefits of BMC therapy.

One limitation of the study was the small number of patients that were included in this study. Because our study was based on...
published data rather than on individual patient data, the ability to precisely identify the diastolic indices was limited.

In conclusion, our study suggests that patients from the BMC transfer group recover from a mild form of early diastolic dysfunction after AMI.

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References


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