# An alternative approach of stem cell delivery to myocardium: combined usage of antegrade coronary arterial infusion and retrograde venous obstruction

*Miyokard dokusuna kök hücre nakline alternatif bir yaklaşım: Antegrad koroner arteryel infüzyon ve retrograd venöz obstrüksiyonun birlikte kullanımı*

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## Introduction

Four main routes of stem cell delivery methods have been reported in cardiac stem cell therapy studies: antegrade intracoronary infusion, direct endocardial injection, retrograde coronary sinus infusion and transepicardial injection (1-4). We present an alternative technique involving antegrade stem cell infusion, with the simultaneous obstruction of related coronary vein.

## Case Report

A 54- year-old man admitted to our institute with a functional capacity of class II (NYHA) and chest pain for the last three months. Patient had history of successful primary direct stent implantation to proximal left anterior descending artery (LAD) due to an acute anterior myocardial infarction three years ago. The electrocardiogram showed chronic QS patterns at V1-V3 leads and the echocardiogram revealed mid- and apical anterior akinesia and septal hypokinesia with an ejection fraction (EF) of %30. Tetrophosmin SPECT showed an anterior and anterior septal scar. Coronary angiography revealed patent stent in LAD. We decided to perform stem cell therapy aiming to enhance left ventricular function and perfusion. Therefore, 80 ml of bone marrow was aspirated under local anesthesia from posterior iliac crest of the patient. We used the same technique for isolation of bone marrow-derived mononuclear cells (BMCs) as previously described by Strauer et al. (1). Isolated number of the BMCs was $4.4x10^8$ with a 98.4% viability tested by Tryphan Blue. After arrival of the BMC suspension to cardiac catheterization laboratory, first, a fiberoptic pressure-temperature sensor tipped guidewire (Intracoronary pressure wire sensor 4, Radi Medical Systems, Uppsala, Sweden) was introduced through a 6F guiding catheter and placed distal to the stented segment of the LAD. Proximal aortic and distal coronary pressures were recorded and by using papaverine, baseline thermodilution derived coronary flow reserve (CFR) was calculated as the resting mean transit time divided by the hyperemic mean transit time (5). The mean transit time at rest and during hyperemia were recorded after rapid injection of 3 ml of room-temperature saline through the guiding catheter as previously described (6). Index of microvascular resistance (IMR) was defined as simultaneously measured distal hyperemic mean coronary pressure divided by the inverse of the thermodilution derived hyperemic mean transit time (7). Thereafter we inserted a second guide wire in LAD and the over-the-wire balloon catheter (Occam International, Eindhoven, Netherlands) was inserted in the stented segment. Consequently, the coronary sinus was catheterized through femoral vein and a 4.0x20 mm balloon was placed in great cardiac vein. Both balloons were inflated thus the LAD artery and great cardiac vein were occluded for one minutes in 3-4 atmospheres in attempt to produce stagnation of coronary flow (Fig 1). Then we infused 10 cc of BMC suspension directly in to the infarcted region through the LAD artery via the central

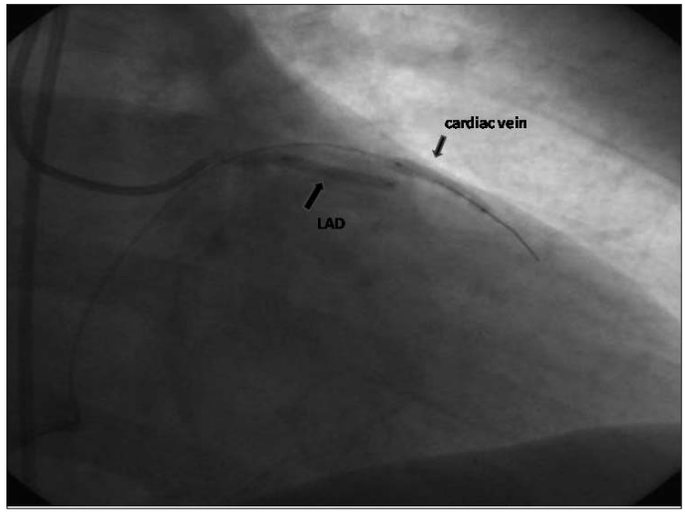


**Figure 1. Baseline coronary angiography; patency in LAD. 3.0x20mm over-the-wire balloon locating in the stented segment of mid LAD and 4.0x20mm balloon positioned in the major cardiac vein. Both balloons were inflated thus the LAD artery and great cardiac vein were occluded for three minutes under low atmosphere pressures in attempt to produce stagnation of coronary flow**

LAD – left anterior descending artery

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lumen of the inflated balloon catheter. The inflation time was prolonged for 30 seconds for coronary balloon and 2 minutes for venous balloon after the infusion completed to allow maximum contact time with the microcirculation. After six-month, the patient was asymptomatic, with exercise test showing a 15% improvement in exercise capacity without evidence of ischemia accompanied by a functional capacity of class I (NYHA). We revealed an increase in EF (30% to 38%) by echocardiography. SPECT (Bull's Eye technique) demonstrated a significant decrease in initial infarct size (from 56% to 41%) and a moderate decrease in left ventricular diastolic and systolic volumes (167 to 155ml; 106 to 91ml) was obtained (Fig. 2). The control angiography showed patent LAD with improvement in left ventricular ejection fraction. Furthermore we observed a significant increase in CFR (1.5 to 2.6) and decrease in IMR (45.5 to 11.2) which are known to be probable evidences of neovascularization (Fig. 3A-3B).

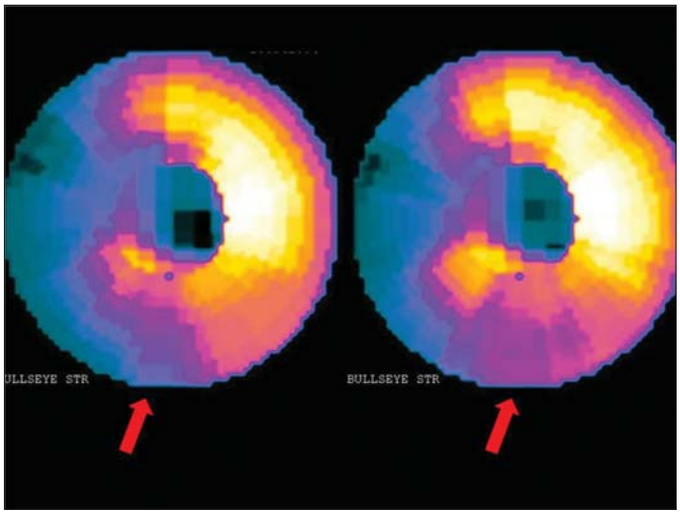


**Figure 2. Quantitative tetrophosmine scintigraphy (Bull's Eye technique) of initial and after procedure infarct size**

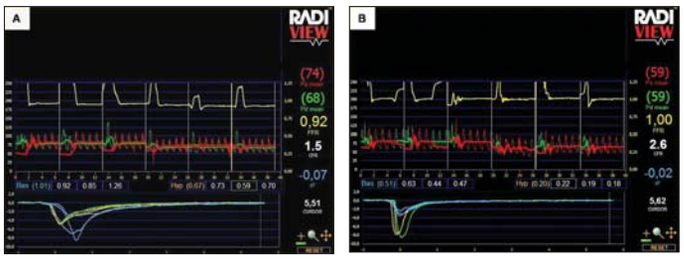


**Figure 3. A significant increase in coronary flow reserve (1.5 to 2.6) (A) and decrease in index of microvascular resistance (45.5 to 11.2) (B) are observed in pressure wire measurements**

## Discussion

Previous studies suggested that, intracoronary BMC transplantation beneficially affects on neovascularization, left ventricular remodeling, and contractility in coronary artery disease (8, 9). The appropriate route of cell administration to the damaged organ is a crucial requirement for the success of organ repair. Reaching high cell concentrations within the target area and preventing homing of transplanted cells into other organs are also critical. Therefore, targeted and regional administration and transplantation of cells should be preferred. In the current case, we used an alternative approach for cellular cardiomyoplasty, which is a ctually a combination of two established techniques, and demonstrated an improvement in left ventricular contractility and myocardial perfusion supported by intracoronary hemodynamic measurements. We think that distribution of stem cells into other organs may be decreased and homing of stem cells in the targeted area can be achieved by this technique.

## Conclusion

Aiming more effective cellular implantation to myocardium, this alternative technique seems to be feasible and safe in our case.

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