Results: The BMCs group presented a significant increase in EF at sixth months (26.75±4.85 vs. 37.82±6.97%, p=0.001) and 12 months post-transplant (26.75±4.85 vs. 37.27±7.51%, p=0.002). There was a significant improvement in functional capacity (NYHA) in the transplanted group at 6 and 12 months (p<0.001). There were no significant changes concerning left ventricular volumes, heart rate variability and exercise stress testing. We observed no improvement of these variables in the control group. There were no complications related to the BMCs transplant.

Conclusions: Intracoronary infusion of autologous BMCs, in addition to standard therapy, was associated with significant improvement of left ventricular function at 12 months in patients with HF. We observed no complications relative to the procedure.

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FIVE YEARS MORTALITY REVIEW ON 15 CONSECUTIVE PATIENTS WITH END-STAGE CARDIOMYOPATHY AND INTRACORONARY MESENCHYMAL STROMAL CELLS INFUSION

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Background: Symptomatic end-stage dilated cardiomyopathy with reduced function is associated with a high mortality estimated at 25 to 50 percent per year. Mesenchymal stromal cell (MSC) have the potential to improve cardiomyopathy through resolution of scar tissues, cardiomyogenesis and/or angiogenesis. We have previously reported improvement in echocardiographic parameters at 12 months after intracoronary injection for patients with no-options ischemic cardiomyopathy. Now we present the 5-year follow-up results of 15 patients with end-stage cardiomyopathy of ischemic (n=9) and non-ischemic (n=6) aetiology.

Methods: Fifteen patients with symptomatic heart failure and echocardiographic findings of left ventricular end-diastolic diameter (LVIDD) of 55 mm of more and left ventricular ejection fraction (LVEF) of 35% or less were recruited. All patients were deemed by at least two cardiologists to have no other options including revascularization or cardiac resynchronization therapy. MSC was obtained from bone marrow of the patients and expanded *ex vivo* according to published protocol. About 2×10^6 MSC/kg body weight were injected through the lumen of an over-the-wire balloon during catheterization. Echocardiographic parameters including LVIDD, LVEF and interventricular septal wall thickness in diastole (IVSD) were obtained at baseline, 6 months, and 6 monthly thereafter.

Results: There were no immediate complications and no deaths in the first 12 months. At the end of 5 years, 4 patients with (2 ischemic, 2 non-ischemic) had died of (1 myocardial infarction, 3 progressive heart failure). One patient with non-ischemic cardiomyopathy required a permanent pacemaker for complete heart block. All 11 survivors improved symptomatically indicated by New York Heart Association (NYHA) classification. Mean LVIDD, LVEF and IVSD also improved.

Conclusions: MSC intracoronary infusion for patients with end-stage dilated cardiomyopathy appears to be associated with symptomatic and echocardiographic improvement, and lower mortality when compared to epidemiological data. These results need to be validated in larger randomized trials.

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BONE MARROW MONONUCLEAR CELL SEPARATION YIELD IN MYOCARDIUM INFARCTION, CORONARY DISEASE AND TYPE 2 DIABETES AND DILATED CARDIOMYOPATHY PATIENT GROUPS

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Bone marrow derived mononuclear cells (BM-MNC) are widely used in various clinical trials. Preliminary data show that these cells can benefit and improve some of the clinical outcomes e.g. elevated LV EF in acute myocardium infarction (AMI) patients and stabilized glycose levels for type 2 diabetes (T2D) patients (ongoing clinical trials).

The aim of this side study was to compare the yield of BM-MNCs and CD34+ cells between three patient groups: AMI, T2D and dilated cardiomyopathy (DC) patients. The multifactor analysis will be made focusing on different risk factors and their influence on cell yield within two groups (AMI and T2D).

BM-MNC were separated using Ficoll-Pague density gradient centrifugation. Initial average volume of bone marrow aspirate for AMI and T2D patients was 44 ml. Average bone marrow aspirate volume for DC was 27 ml. Average age of AMI and T2D patients is 52-58 and for DC patients is 9 years. There were no significant differences in BM-MNC and CD34+ cell numbers between AMI (n=53) and T2D (n=8) patients whereas BM-MNC and CD34+ cell counts are almost two times more ir young DC patients (n=6). For comparison MNC count per ml initial volume in AMI patients was 0.93 million cells/ml, in T2D patients it was 0.87 million cells/ml and in DC patients - 1.73 million cells/ml.

However, more patients included in clinical trials could improve statistical analysis. The work on cell number correlation with clinical outcome is under the process.

Also multi-centre randomized trials have to determine the efficacy of stem cell therapy in all three group patients.

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CARDIAC STROMAL CELLS INHIBIT PROLIFERATION OF TUMOR CELLS

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Stromal cells are in important component of the stem cell niche and control proliferation and differentiation of stem cells. Bone marrow (BM) stromal cells (MSC) have been extensively studied and shown to control differentiation of hematopoietic stem cells (HSCs) in part through secreted growth factors. Recent studies have demonstrated the presence of stromal cells in cardiac tissue however, the role of cardiac stromal cells (CStrC) is unclear. In this study we have compared human CStrCs to human BM-MSCs and demonstrate that CStrCs have a similar morphology and surface marker expression as BM-MSCs. To further characterize the CStrCs we performed micro array analysis of human CStrCs compared to human BM-MSCs. The CStrCs expressed a distinct cytokine and cytokine receptor profile compared to BM-MSC. In addition, a number of micro RNAs were expressed at very high levels in CStrCs compared to BM-MSC. Cardiac- associated microRNAs, including miR-1, miR-133a, and miR-206 were expressed at higher levels in CStrCs compared to BM-MSC. These data demonstrate that cardiac derived stromal cells have a similar phenotype to BM-MSC but have a distinct gene expression profile.

Given the lack of tumor development in cardiac tissue we hypothesized that CStrCs would fail to support tumor cell growth which has been described for BM-MSCs. Therefore, we cultured human tumor cell lines on CStrCs and compared the tumor cell proliferation to BM-MSCs. CStrCs inhibited the proliferation of all cell lines tested while BM-MSCs supported the proliferation of tumor cells. Further we tested media conditioned by CStrCs and demonstrated similar inhibition of proliferation. Previous studies have implicated miR-206 in inhibition of proliferation of tumor cells and given the high levels of expression of miR-206 in CStrCs we hypothesize that miR-206 is a key player in the inhibitory effects of CStrCs and this effect is mediated via secreted molecules.

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NOREPINEPHRINE DIRECTLY INFLUENCES CIRCULATING HEMATOPOIETIC PROGENITOR CELL FUNCTIONALITY IN VITRO: A POSSIBLE HINT FOR AN EXERCISE-INDUCED STRESS MODEL

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Background: The influence of exercise on the hematopoietic system is very complex. A previous study proofed that exhausting ergometry can increase circulating hematopoietic stem and progenitor cell (CPC) number in the periphery but at the same time decreases their colony forming capacity. The exact mechanism of this inhibitory effect of exercise on CPC