

## Quality of life in patients with coronary artery disease after intracoronary administration of bone marrow mononuclear cells

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### Abstract

A BMMC group consisted of 17 patients with severe angina pectoris when it is impossible to use mechanical revascularization. These patients underwent autologous bone marrow mononuclear stem cells intracoronary infusion between 2008 and 2010. A control group consisted of 10 patients. All patients were examined before and after the treatment. Single-photon emission computed tomography was performed to estimate myocardial perfusion. Questionnaire SF-36 was used for an estimation of the patient's quality of life. Intracoronary infusion of autologous bone marrow mononuclear stem cells has decreased such parameters as the functional class of angina pectoris, and nitroglycerine consumption, and has increased exercise time, and myocardial perfusion, while having no influence on arrhythmia. On the other hand, the functional class of angina pectoris increased, and the exercise time decreased in patients who received only medical treatment. At the end of one the year a great increase in quality of life in BMMC group can be observed. The best result it is seen in the Physical Functioning scale, and the Role-Physical scale, and the Bodily Pain scale. In the control group it is not seen considerably increasing in all scales and the scale Bodily Pain has changed in opposite direction.

**Keywords:** stem cells, mononuclear cells, angina pectoris, heart disease, coronary artery bypass surgery, angioplasty, angina treatment, exercise time, nitroglycerine consumption, questionnaire SF-36

### Introduction

Autologous bone marrow mononuclear stem cells (BMMC) have been used in clinical practice for more than nine years [13]. It has been proven proved that this therapy is effective in patients with dilated cardiomyopathy [5,12] and patients with severe heart failure [1,3,14]. However, there have been very few studies on the usage of autologous bone marrow mononuclear stem cells in patients with severe angina pectoris when it is impossible to use mechanical revascularization (percutaneous coronary intervention: PCI, or coronary artery bypass grafting: CABG), or it is refractory to conventional medical therapy [8,11,16]. This group includes patients with distal coronary atherosclerotic damage, patients who received angioplasty and stenting with only part of involvement of the coronary artery, and patients with a relapse of angina pectoris after CABG. The last group of patients is the largest because it is known that only 38-45% of venous grafts are patent after ten years of operation [10]. The number of patients who have a relapse of angina pectoris after CABG increases in proportion to the number of operations.

Patients with severe heart failure or low left ventricle ejection fraction were excluded from our clinical trial.

### Patients and Methods

The BMMC group consisted of 17 patients who underwent autologous bone marrow mononuclear stem intracoronary infusion between 2008 and 2010. A control group consisted of 10 patients. A comparative breakdown of both groups is presented below (Table 1):

It is seen that groups are comparable in sex, age, concomitant disease, and left ventricle injection fraction. There are more patients with two and thee coronary vessel diseases in the BMMC group, which explains the higher rate of angina pectoris. All of patients received optimal medical treatment, which was fixed before and was not changed during the research period. All patients were examined before and after the research period. Single-photon emission computed

Indice	BMMC group (n=17)	Control group (n=10)
Male	14 (83%)	9 (90%)
Female	3 (17%)	1 (10%)
Median age	60.2±9	62.5±7
Previous myocardial infarction	1.2±0,8	1.4±0,7
Functional class of angina pectoris (CCS)	2.9±0,4	2.3± 0,5
Exercise test (Mets)	4.6	4.6
Nitroglycerin usage (pill/week)	28	7
Arterial hypertension	12 (70%)	5 (50%)
Diabetes mellitus	2 (12%)	1(10%)
Smoking	7 (41%)	3 (30%)
Cholesterol (mmol/l)	5.5	4.6
Relapse angina pectoris after CABG	6 (35%)	4 (40%)
Distal coronary atherosclerotic damage	8 (47%)	—
Incomplete myocardial revascularization (PCI)	3 (18%)	6 (60%)
LVIDd (mm)	51.6±2	52±4
LVIDs (mm)	35.8± 2	36.5±4
LVEF (%)	57.2±4	60.3±5
One coronary vessel disease	4 (23,5%)	6 (60%)
Two coronary vessel diseases	9 (53%)	3 (30%)
Three coronary vessel diseases	4 (23.5%)	1 (10%)

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**Table 1. A comparative breakdown of the BMMC and the control groups**

tomography was performed to estimate myocardial perfusion. Questionnaire SF-36 was used for an estimation of the patient's quality of life.

## Results

During the research period one patient has died in each group, for a mortality rate of 6% in the BMMC group and 10% in the control group. The functional rate of angina pectoris (CCS) has showed an improvement in the BMMC group compared with the control group. The median of Canadian Cardiovascular Society class decreased from class 3 to 2 in the BMMC group ( $p<0.001$ ) and increased in the control group from class 2 to 3 ( $p>0.05$ ). However, control group contained more patients who received percutaneous coronary intervention. We showed that the median of exercise time rose from 4.6 to 7.0 Mets in the treatment group ( $p>0.05$ ), while there were no changes in the control group ( $p>0.05$ ). Median nitroglycerine usage fell from 28 to 7 pills of nitroglycerine per week ( $p<0.05$ ) in the treatment group and did not change in the control group over one year ( $p>0.05$ ). There were not arrhythmias in either group.

The table 2 shows versions of answers from the SF-36 questionnaire that patients gave for the question: "Compared to one year ago, how would you rate your health in general now?"

Answers	Main group (N=17)	Control group (N=10)
Much better now	7 (35 %)	1 (10%)
Somewhat better now	8 (53 %)	—
About the same	2 (12 %)	5 (50 %)
Somewhat worse now	—	4 (40 %)
Much worse now	—	—

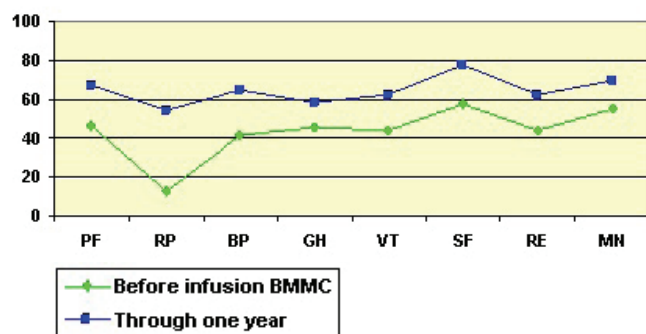
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doi:10.3205/ctt-2011-en-000097-table2*

**Table 2. Versions of answers from the SF-36 questionnaire**

It can be seen that 88% of patients from the BMMC group felt better one year after the intracoronary infusion of autologous bone marrow mononuclear stem cells. In the control group only 1 person (10%) felt better, a half the patients did not notice any changes, and 40% felt worse than a year before.

Baseline scores of the eight SF-36 scales were approximately the same in both groups before the study. At the end of one year a great increase in quality of life in the BMMC group can be observed (Fig. 1). The best result it is seen in the Physical Functioning (PF) scale, which describes exercise times of the patients, and the Role-Physical (RP) scale, which describes the influence of physical condition on our daily work.

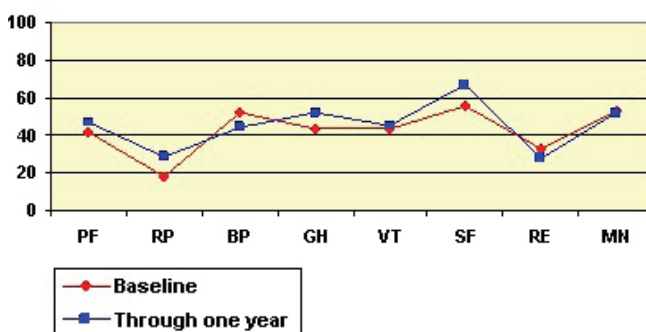
We found a strong correlation between the value of the Bodily Pain (BP) scale and the Canadian Cardiovascular Society class. (Spirman's coefficient of rank data analysis = 0.756,  $p=0.48$ ). It is seen that the Bodily Pain scale went up in the BMMC group:



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**Figure 1.** Quality of life in the BMMC group

In the control group it is not seen considerably increasing in all scales and the scale of Bodily Pain has changed in opposite direction, which correlates well with an increase of Canadian Cardiovascular Society class in the control group.



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**Figure 2.** Quality of life in the control group

A significant improvement in myocardial perfusion measured by single-photon emission computed tomography was noticed in the BMMC group; the median hypo perfusion zone decreased from 13.5 to 10.1 % ( $p>0.05$ ).

## Discussion

Intracoronary infusion of autologous bone marrow mononuclear stem cells decreases such parameters as the functional class of angina pectoris, and nitroglycerine consumption, and increases exercise time, and myocardial perfusion, while having no influence on arrhythmia. On the other hand, the functional class of angina pectoris increased, the exercise time decreased in patients who received only medical treatment.

In his article D. Kirklin [9] showed that the survival rate in patients with coronary artery disease without left ventricle dysfunction is about 75 % over 5 years, 60% over 10 years, and 45% over 15 years. That is why the most important indicator for the efficacy of stem cell treatment has become health-related quality of life (HRQL) [6,7]. HRQL estimates

components associated with disease and helps to understand the influence of disease and treatment of patient's physical and mental health. It has been established that questionnaire SF-36 has good validity and reproducibility [2,4,15]. In our research it was shown that the functional parameters of patients have good correlation with SF-36 scales. In my opinion SF-36 can be a good guide for optimal treatment, especially in new areas such as stem cells therapy, where it is difficult to estimate reliable improvements in a patient's condition.

## Conclusions

1. Intracoronary infusion of autologous bone marrow mononuclear stem cells seems to be effective in treatment of patients who are not candidates for mechanical revascularization.
2. Questionnaire SF-36 seems to be the most effective method of estimating quality of life in patients after stem cell treatment.
3. Bodily Pain scale has strong correlation dependence with the functional class of angina pectoris (CCS).

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