Transplantation of Integrin-linked kinase-overexpressing mesenchymal stem cells via coronary improves the myocardial repairing in swine model of acute myocardial infarction

Dan Mu[1], Wei Bo Chen[2], Bin Zhu[3], and Biao Xu[4]

[1]*Drum Tower Hospital, Nanjing, Jiangsu, China,* [2]*Philips Healthcare, Shanghai, China,* [3]*Radiology, Drum Tower Hospital, Nanjing, Jiangsu, China,* [4]*Cardiology, Drum Tower Hospital, Nanjing, Jiangsu, China*

Target audience: radiologist and cardiologist

Purpose: Studies have suggested that the long term benefits of mesenchymal stem cells (MSCs) therapies in acute myocardial infarction (AMI) are less than expected duo to the poor cell engraftment and survival [1]. Evidence suggests that Integrin-linked kinase (ILK) gene have myocardial repairing characters [2]. It is necessary to choose a reliable method to evaluate the myocardial protection of MSCs overexpressing ILK (ILK-MSCs).The current study aims to investigate the effects of transplanted ILK-MSCs on myocardial perfusion, myocardial fibrosis and cardiac function in the swine AMI model using cardiac MR imaging.

Methods: MSCs or ILK-MSCs（5×10^7 cells）were randomly transplanted into the ischemic myocardium via coronary artery 1 week after establishing the swine myocardial infarction model (6 swine per group) by ballon occlusion. The myocardial blood perfusion, the infarction area and the cardiac function was assessed by MR first pass perfusion, delayed enhanced examination and cine MR respectively before and 2 weeks after transplantation using MR imaging. The cardiac fibrosis and capillary density were assessed using immunohistochemistry two weeks later. The data was statistically analyzed with Independent Sample t test using SPSS17.0 software.

Results: Myocardial perfusion was significantly greater in the ILK-MSCs group than in the MSCs group (area under the perfusion curve: 44840±4807mm^2 vs. 35681±5548mm^2, $p<0.05$) and was associated with greater neovessel formation (CD31 positive cells:273.0±28.3cells/field vs. 194.2±30.7cells/field, $p<0.05$) (Fig1). The variation of infarction areas were larger in the ILK-MSCs group than in the MSCs group (the infarct size ratio: 0.96±0.11 vs. 0.76±0.09, $p<0.05$) and was associated with less myocardial fibrosis in Masson staining (the fibrosis area: 46.7±9.0% vs. 62.0±4.9%, $p<0.05$) (Fig2). There were no significant global cardiac function difference between two groups(EF:54.9±8.6 % vs. 52.7±6.1%, $p>0.05$), but transplantation of ILK-MSCs improved regional cardiac function compared with transplantation of MSCs(wall thickness ratio:60.70 ± 6.8% vs. 52.08 ± 5.6% , $p<0.05$)(Fig3).

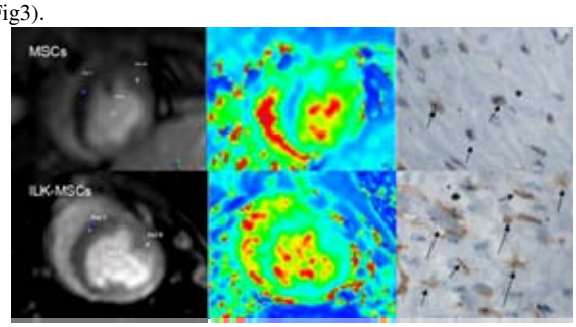

Figure1. Myocardial perfusion is greater in the ILK-MSCs group than in the MSCs group. It was associated with CD31 positive cells/field.

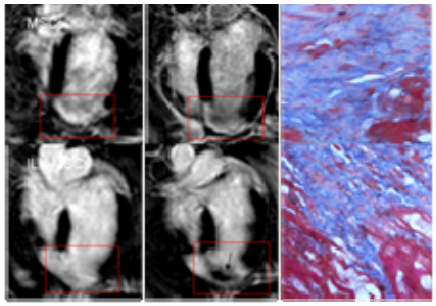

Figure 2. The variation of infarction areas are larger in the ILK-MSCs group than in the MSCs group and is associated with less myocardial fibrosis in Masson staining.

Discussion: Previous studies demonstrated that most cells died in the first 24 to 48 hrs. after transplantation to ischemic myocardium duo to regional hypoxia [3]. Genetic modification of stem cells with specific genes is proven effective in improving cell viability. Our previous study found that Integrin-linked kinase (ILK) gene can regulate cell growth, survival and proliferation [2]. With the pathological comparison, our study confirmed that the cardiac MR imaging can correctly analyze the effect of ILK-MSCs transplantation on heart function, myocardial perfusion and infarction size. The improvement of regional cardiac function after ILK-MSCs transplantation is attribute to the increased myocardial perfusion duo to greater neovessel formation and the decreased infarction area because of less interstitial fibrosis.

Conclusions: Cardiac MR imaging is a reliable one-stop method to evaluate the outcome of cell therapy in AMI. Transplantation of ILK-MSCs enhance the myocardial repairing after AMI.

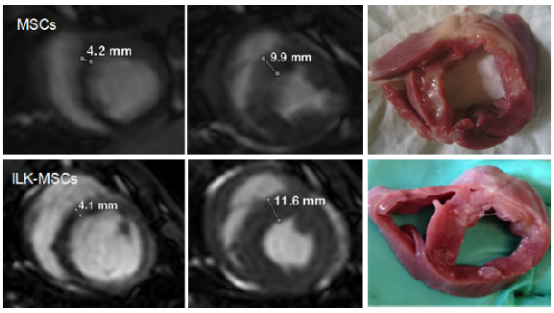

Figure 3. Transplantation of ILK-MSCs improved regional cardiac function compared with transplantation of MSCs and it is proven by anatomy.

References:

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