Old Myocardial Infarction / Remodeling 3 (IHD)

PE66

March 29 (Mon)

Booth 2 (Exhibition Hall)

16 : 00—16 : 42

PE-385

G-CSF Upregulates Myocardial Akt and Improves Function of the Hearts with Established Heart Failure due to Large Old Myocardial Infarction

[1]Yiwen Li
[1]Genzou Takemura, [1]Hideshi Okada, [1]Shusaku Miyata, [1]Rumi Maruyama, [1]Yukihiro Hayakawa, [1]Shinya Minatoguchi, [2]Takako Fujiwara, [1]Hisayoshi Fujiwara
[1]Department of Cardiology, Gifu University School of Medicine, Gifu, [2]Kyoto Women's University, Kyoto

We recently reported the beneficial effects of granulocyte-colony stimulating factor (G-CSF) that was started on the next day of acute myocardial infarction (MI) upon post-infarct ventricular remodeling and heart failure through translocation of bone marrow cells and their differentiation into cardiac myocytes. However, the effect of G-CSF is unknown on the hearts with already established heart failure due to old large MI. In the present study, we examined the potential therapeutic effects of G-CSF on post-infarct ventricular remodeling and heart failure at the chronic stage. To the mice with 12 week-old MI showing marked ventricular remodeling and established heart failure, G-CSF (10 microg/kg/day) was subcutaneous injected for 5 days/week for 4 weeks. The mice were examined 16 weeks post-infarction. The G-CSF treated group showed significantly alleviated left ventricular remodeling and dysfunction at 16 weeks post-infarction, compared with the distilled water-treated control group, according to echocardiography and hemodynamic measurement. Western blot analysis of cardiac tissues revealed a significant up-regulation of Akt in the G-CSF-treated group. In summary, G-CSF upregulated myocardial Akt and improved function of the hearts with established heart failure due to large old myocardial infarction. The present findings may imply a novel therapeutic strategy against post-infarct heart failure, which is applicable during the chronic stage of MI.

PE-386

Combination Thearpy of Antiapoptosis and Regeneration against Postinfarct Heart Failure -A Novel Therapeutic Concept-

[1]Hideshi Okada
[1]Genzou Takemura, [2]Ken-ichiro Kosai, [1]Yiwen Li, [2]Kentaro Yuge, [2]Satoshi Nagano, [2]Tomoyuki Takahashi, [2]Masayasu Esaki, [1]Shusaku Miyata, [1]Rumi Maruyama, [1]Shinya Minatoguchi, [3]Takako Fujiwara, [1]Hisayoshi Fujiwara
[1]Department of Cardiology, Gifu University School of Medicine, Gifu, [2]Department of Gene Therapy and Regenerative Medicine, Gifu University School of Medicine, Gifu, [3]Department of Food Science, Kyoto Women's University, Kyoto

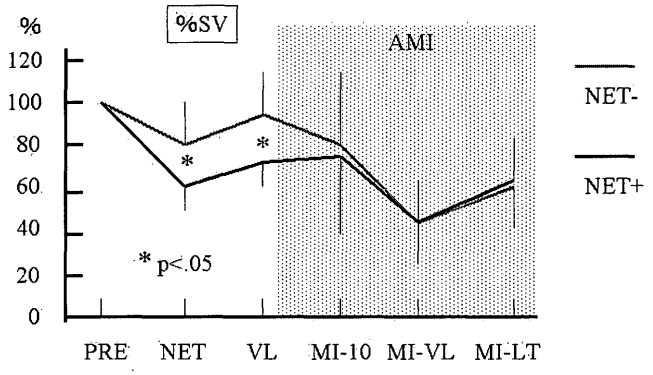
We previously reported the inhibition of granulation tissue cell apoptosis during the subacute stage of myocardial infarction (MI) improved left ventricular (LV) remodeling and dysfunction at the chronic stage. It was also reported that granulocyte colony-stimulating factor (G-CSF), which can mobilize multipotent progenitor cells into the peripheral blood, improved post-MI LV remodeling and function possibly via regenerating myocardium. We examined here the combined effect of soluble Fas (sFas), an apoptosis inhibitor, and G-CSF on post-MI LV remodeling and heart failure. On the 3rd day of MI, the mice were randomly assigned into 4 groups. In Group 1 (combination therapy), an adenovirus encoding sFas (Ad.sFas) was injected into the himdlimb muscles, and G-CSF (100 microg/kg/day) was intraperitoneally injected for 5 days. In Group 2, Ad.sFas alone, and in Group 3, G-CSF alone was similarly given. In Group 4 as a control, an adenovirus encoding LacZ gene and distilled water was injected. According to echocardiography and cardiac catheterization, Group 1 was found best in alleviating post-MI left ventricular remodeling and dysfunction. Groups 2 and 3 were the second best. Thus, an efficacy was evident of the combined anti-apoptosis and regeneration therapies during the subacute stage of MI for LV remodeling and heart failure at the chronic stage. This novel therapeutic concept may be applied for management of patients with post-MI heart failure.

PE-387

Passive Cardiomyoplasty with Nonviable Mesh Prevents Ventricular Dilatation and Function After Myocardial Infarction

[1]Akira Kawaguchi
[2]Akio Kishida, [3]Tetsuji Yamaoka
[1]Cardiovascular Surgery, Tokai University School of Medicine, Isehara, [2]National Cardiovascular Center, Research Institute, Suita, [3]Faculty of Textile Science, Kyoto Institute of Technology, Kyoto

Objectives. We tested the girdling effect of synthetic nonviable net after acute myocardial infarction (AMI). **Methods/Results.** Pressure-volume-loops were analyzed before (PRE), net around the heart (NET), intravenous volume-load (VL), 10-minutes after AMI (MI-10), repeated volume-load (MI-VL) and 40-minutes after AMI (MI-LT) in rats with (NET+, n=10) and without a net around the heart (NET-, n=10). Left ventricular size and function analyzed under standardized loading condition disclosed that ischemic increase in ventricular end-diastolic and end-systolic volumes were significantly suppressed in the same degree after AMI in NET+ rats, resulting in preserved stroke volume (SV: Figure) and significantly improved ejection fraction. **Conclusion.** Static cardiomyoplasty with a nonviable net may prevent ventricular remodeling after AMI without reducing ventricular function in the rat. Net elasticity needs to be adjusted for optimal girdling effect.



PE-388

Urinary 8-hydroxy-2'-deoxyguanosine to urinary creatinine ratio are correlation with severity of cardiac function in patients with Old Myocardial Infarction.

Yasuhiro Nagayoshi
Hirofumi Soejima, Shinzo Miyamoto, Sunao Kojima, Jun Hokamaki, Hidetomo Maruyoshi, Takashi Kudoh, Tomohiro Sakamoto, Michihiro Yoshimura, Hisao Ogawa
Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto

Background. Oxidative stress contributes to atherosclerosis and the development of ventricular dysfunction in the patients with Coronary Artery Disease. Urinary 8-hydroxy-2'-deoxyguanosine to creatinine ratio (8-OHdG/CRE) has been considered as systematic marker of oxidative stress. We investigated the relationships between urinary 8-OHdG/CRE levels and cardiac function in Old Myocardial Infarction (OMI). Methods. We measured urinary 8-OHdG/CRE levels in 44 patients with OMI and 28 patients with chest pain syndrome. Result. Urinary 8-OHdG/CRE levels (mean ± SEM ng/mg creatinine) in patients with New York Heart Association (NYHA) classes III-IV (n=7, 36.3 ± 5.6) were higher than those in controls (n=28, 13.0 ± 1.2, $p<0.0001$). Urinary 8-OHdG/CRE levels in NYHA II (n=18, 24.1 ± 2.9) were higher than those in controls ($p<0.0005$). The urinary 8-OHdG levels were negatively correlated with left ventricular ejection fraction ($r=-0.483$, $p<0.0001$) and the levels were positively correlated with LVEDP ($r=0.431$, $p<0.001$), PCWP ($r=0.585$, $p<0.0001$), and BNP ($r=0.311$, $p<0.05$). The urinary 8-OHdG levels tended to correlate with numbers of coronary artery disease, and the levels in 3-vessel disease group (n=16, 43.4 ± 12.4) were higher than the levels in controls (n=28, 13.0 ± 1.2, $p<0.001$) and one-vessel disease group (n=13, 20.9 ± 7.9, $p<0.05$). Conclusion. These results indicated that urinary 8-OHdG/CRE ratios are in-