of collateral vessels and exertion of ischemic preconditioning, but irreversible ischemia damages the heart such as necrosis or apoptosis. In the mice heart, it is impossible to create low coronary flow (reversible) conditions, leading us to use canine hearts. However, it has been also difficult to examine the multiple gene expressions in canine hearts. To solve this difficulty, we succeeded in the development of canine microarray, and tested the ability of this method to distinguish 21000 probe but essential NO-dependent gene expressions and pathophysiological conditions of the heart. About sixty cardiovascular related genes were cloned using PCR method from our newly developed beagle dog cDNA library, and spotted on CMT-GAPS slides. PCR fragments were chosen to amplify the specific, non-overlapping open-reading frame of each cDNA. From the arrays, we analyzed the expression profile of canine myocardium in two protocols, 1) necrotic myocardium caused by total LAD ligation for 3 hours (equal to mice necrosis model), and 2) ischemic myocardium of 50% LAD blood flow reduction (equal to angina pectoris of human). Three hours after 60% coronary flow reduction, cardiovascular related genes were changed rapidly and the number of upregulated genes was much more than the case of complete coronary occlusion. These genes included eNOS-nucleotidase, endothelin-1, PAI-1, AT1 and AT2 receptors, PKC e. However, in the necrotic tissue, these gene expressions was almost lost. This indicates that ischemic damage without necrosis affects the gene expressions strongly on the survived myocardium than fatally damaged myocardium. These data suggest that canine microarray provide the novel tool to access the precise molecular events following the changes in physiological conditions.

1099-29  Reduction of Myocardial Infarct Size by a HMG CoA- Reductase Inhibitor in Normocholesterolemic Rats
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Background: In addition to their lipid lowering properties, statins improve endothelial function by increasing the activity of endothelial nitric oxide synthase (eNOS). We hypothesized, that by this mechanism statins may protect the myocardium from ischemic injury.

Methods: Anesthetized rats underwent 30 min of coronary artery occlusion (CAO) followed by 180 min of reperfusion. Heart rate and arterial blood pressures were continuously monitored throughout the experiments. Plasma cholesterol concentrations were determined at the end of the experiments. Infarct size was measured by TTC staining expressed as percentage of area at risk. Myocardial eNOS activity was measured by densitometry. The experiments were repeated in healthy and cholesterol fed rats.

Results and Conclusion: Thus, we conclude that a novel antagonist of both GP IIb/IIIa and vitronectin receptors appears to inhibit the formation of thromboembol or thrombosis.

1099-30 Simvastatin Restores Endothelial Nitric Oxide Mediated Vasorelaxation in Large Arteries After Myocardial Infarction
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Congestive heart failure (CHF) after myocardial infarction (MI) is associated with diminished endothelial nitric oxide (NO)-mediated vasorelaxation. The 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors have been shown to modulate vascular tone, independent of their effects on lipid lowering. We hypothesized that simvastatin restores NO-dependent vasorelaxation after MI, produced by coronary artery ligation, via upregulation of endothelial nitric oxide synthase (eNOS). We found that compared to normal arterial tissue incubated with culture medium only, incubation with 0.1 mM of simvastatin for 24 hours enhanced acetylcholine (ACH)-mediated vasorelaxation (P<0.05) with peak relaxations at 10-7 M (62±11% to 33±7.7%, n=6). Compared to untreated rats, simvastatin increased eNOS protein content by over 200% (82±14.0% vs 21±6.7% , P<0.05, respectively). In endothelial cells in culture, 10 mM and 20 mM of simvastatin increased eNOS levels by 114±39.8% and 212±79.9% respectively (P<0.05). Also, it increased NO production (P<0.05), respectively. In CHF rats treated by oral gavage with simvastatin (20 mg/kg/day) for 2 weeks, both groups demonstrated complete return of transmural microvascular blood flow. The area at risk remained akinetic in all groups throughout the study. At eight weeks LV end-systolic volume increased by 134% in control animals and by 114% in group 2 but was unchanged in group 1. Conclusion: Early microvascular reflow dramatically improves post-infarction LV remodeling independent of myocardial salvage.

1099-31 Inhibitory Effects of the Novel Antagonist of Both GP IIb/IIIa and Vitronectin Receptors on Formation of Coronary Thromboemboli Caused by an Inhibition of Adenosine Receptors During Coronary Hypoperfusion in Dogs
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Background: Platelet glycoprotein (GP) IIb/IIIa is a membrane receptor for fibrinogen and von Willebrand factor, which plays an important role in blood coagulation. We have previously reported that adenosine inhibits P-selectin-dependent formation of coronary thromboemboli during hypoperfusion in dogs, we examined whether the GP IIb/IIIa antagonist, an GP IIb/IIIa receptor antagonist, was infused during coronary hypoperfusion (18.2 ml/100gm, 20 % of the control), coronary blood flow decreased gradually and approached almost zero (3.4 ml/100gm) 20 min after its administration. Histological examination revealed thromboemboli in the small coronary vessels. During hypoperfusion in the presence of 8-SPT, the GP IIb/IIIa antagonist reduced the formation of thromboemboli, and improved contractile (fractional shortening, -7.1 to -1.0 %, P<0.05), and metabolic dysfunction (lactate extraction ratio, -70 to -54 %, P<0.05) of the myocardium.

Conclusion: Thus, we conclude that a novel antagonist of both GP IIb/IIIa and vitronectin receptors attenuates platelet aggregation and the worsening of the severity of myocardial ischemia caused by the inhibition of adenosine receptors. These findings were important in showing the linkages between the signals of adenosine receptors and GP IIb/IIIa or vitronectin receptors in platelet or coronary endothelial cells.

1099-32 Early Microvascular Reflow Status After Infarct Reperfusion Determines Outcome of Postinfarction Remodeling Independent of Myocardial Salvage

Background: Prompt opening of the infarct related artery is the treatment of choice for acute myocardial infarction (MI). A beneficial effect on left ventricular (LV) function often results even in patients in which little myocardium is salvage. We hypothesized that this phenomenon is dependent on adequate early microvascular perfusion. METHODS: Six sheep were subjected to 1 hour of ischemia followed by reperfusion (group 1). Six sheep underwent 6 hours of ischemia followed by reperfusion (group 2) and 7 sheep were infused without reperfusion (control). The ischemic region in all animals was 23% of the LV mass at the apex. Microvascular reflow was studied using LV long axis real time three-dimensional echocardiography and microscopic visualization during coronary reperfusion and at 2, 5, and 8 weeks. Echocardiography was used to assess changes in LV size and regional function throughout the study period. RESULTS: During coronary occlusion all animals demonstrated complete microvascular ischemia. After 30 minutes of coronary reperfusion, group 1 animals demonstrated microvascular reflow of the area at risk while group 2 animals demonstrated complete transmural non-reflow. At 2 weeks, both groups demonstrated complete return of transmural microvascular blood flow that persisted throughout the remainder of the study. Control animals never achieved reflow in the infarct region. The area at risk remained akinetic in all groups throughout the study. CONCLUSION: Early microvascular reflow dramatically improves post-infarction LV remodeling independent of myocardial salvage.

1099-33 Impaired Healing in Factor XIII KO Mice After Myocardial Infarction Assessed by Magnetic Resonance Imaging

Background: Clotting factor XIII has been shown to have a role in wound healing. We therefore studied healing after coronary artery ligation in FVIII KO and wild type mice. Methods: Magnetic Resonance Imaging was done 2 days after MI in a T 7-Biospec using an ECG-triggered Cine-FLASH-sequence; slice thickness 1 mm, echo-time 1.2 ms, acquisition 230 mm, flip angle 90°, single or multiple slices, images, through plane (EP), wall thickness (WT) and -thickening (SW) and LV mass were determined. To minimize bleeding from the thoracotomy wound, FXIII-free fibrin glue was applied.

Results and Conclusion: All FXIII KO mice died within 3 to 5 days after MI, whereas wild type mice, that survived surgery, did not die. Administration of MI was not different between groups, but systolic global and regional function was impaired when compared to wildtype. Unchanged RV volumes suggest that hemorrhage from thoracotomy was not