zymographic gelatinase assay and Western blotting were employed to detect the gelatinase A (MMP-2) abundance. In addition, protein expressions of MMP-1, -2, -3 and membranous type-1 MMP were significantly increased by BNP, while MMP-9 and MMP-13 were down-regulated. The QMRT analogue 6-bromomidamide (10 nM), mimicked BNP's effect, whereas inhibition of protein kinase G (PKG) by KT5823 (5 nM) significantly (p<0.05) attenuated BNP-induced zymographic MMP-2 abundance. ET-1 (10^{-7} mol/L) down-regulated the zymographic MMP-2 abundance and BNP reversed the action of ET-1, while TNF-alpha (10^{-9} mol/L) increased BNP-induced zymographic MMP-2 abundance in a synergistic manner.

Conclusions: This study reports that BNP increases MMPs via QMRT-PKG signaling. In addition, cross-talk between BNP and ET-1, TNF-alpha results in different biological effects. These findings indicate that BNP participates in the remodeling of myocardial structure in the progression of heart failure via the control of cardiac fibroblast function.

409-3 Identification of Differential Gene Expression Patterns in Patients With End-Stage Ischemic and Nonischemic Cardiomyopathies

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Background: End-stage cardiomyopathy (ESC) is associated with altered expressions of multiple genes. Unloading by the left ventricular assist device (LVAD) which results in recovery of hemodynamic and cellular abnormalities may lead to further dynamic gene expression changes.

Methods: A microarray technique representing approximately 2/3 of known human genome (22283 genes, Attechyme) was used to probe paired left ventricular samples from 15 patients (7 ischemic, 8 non-ischemic, on LVAD for 1 to 22 months) obtained at LVAD implant and transplantation; real-time polymerase chain reaction (RT-PCR) was used to further confirm selected gene transcript changes.

Results: At a p value of <0.01, at least 196 genes encompassing both cell structure proteins and subcellular signaling proteins regulating intracellular, metabolic, myocardial hypertrophy, and apoptosis were differentially expressed between ischemic and nonischemic ESC. In ischemic ESC, LVAD support resulted in increase of 68 genes and decrease of 81 genes. In non-ischemic ESC, LVAD support resulted in increase of 50 genes and decrease of 25 genes. Five genes (Proprotein convertase subtilisin/kexin type-1, Interleukin-33, Interleukin-10, Interleukin-4, and Interleukin-13) were identified as key effectors of ESC.

Conclusion: In ischemic ESC, LVAD support may induce cellular and subcellular signaling pathways regulating intracellular, metabolic, myocardial hypertrophy, and apoptosis.

409-2 Antibiotic Property of Brain Natriuretic Peptide in Cardiac Fibroblistes: Cross-Talk Action With Endothelin-1 and Tumor Necrosis Factor on the Induction of Matrix Metalloproteinases

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Background: Cardiac fibroblasts (CFs) produce extracellular matrix (ECM) proteins and participate in the remodeling of the heart. Brain natriuretic peptide (BNP) is known to be activated in heart failure, and inhibit cellular proliferation; however, it is unknown if BNP participates in the degradation of ECM turnover. To understand the role of BNP as an anti-fibrotic factor in the progression of heart failure, we examined the effect of BNP on its signaling system on the activation of matrix metalloproteinases (MMPs), a key enzyme for the degradation of ECM proteins. In addition, we looked at the interactions between BNP and a fibrotic factor, endothelin-1 (ET-1), and a pro-inflammatory cytokine, TNF-alpha.

Methods: CFs isolated from normal adult canine ventricles were used. Techniques for zymographic gelatinase assay and Western blotting were employed to detect the gelatinase abundance and the protein levels for MMPs, respectively.

Results: One micro mol/L BNP significantly (p<0.01) enhanced zymographic gelatinase A (MMP-2) abundance. In addition, protein expressions of MMP-1, -2, -3 and membranous type-1 MMP were significantly increased by BNP, while MMP-9 and MMP-13 were down-regulated. The QMRT analogue 6-bromomidamide (10 nM), mimicked BNP's effect, whereas inhibition of protein kinase G (PKG) by KT5823 (5 nM) significantly (p<0.05) attenuated BNP-induced zymographic MMP-2 abundance. ET-1 (10^{-7} mol/L) down-regulated the zymographic MMP-2 abundance and BNP reversed the action of ET-1, while TNF-alpha (10^{-9} mol/L) increased BNP-induced zymographic MMP-2 abundance in a synergistic manner.

Conclusions: This study reports that BNP increases MMPs via QMRT-PKG signaling. In addition, cross-talk between BNP and ET-1, TNF-alpha results in different biological effects. These findings indicate that BNP participates in the remodeling of myocardial structure in the progression of heart failure via the control of cardiac fibroblast function.