

G-protein coupled receptor kinase expression in lymphocytes –a novel biomarker of left ventricular systolic function in heart failure patients [Abstract]

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Background: One key molecular event involved in the pathophysiology of systolic heart failure is myocardial β -adrenergic receptor (β -AR) desensitization and downregulation. G-protein coupled receptor kinase (GRK2) is believed to play a critical role in the phosphorylation of myocardial β -ARs, and GRK2 expression is elevated in failing human myocardium. Previous work has demonstrated that lymphocyte levels of GRK2 correlate with myocardial GRK2 expression, and reduced GRK2 expression in LVAD supported hearts is associated with improved β -AR signaling. To better define the role of GRK2 in heart failure, we examined GRK2 protein expression before and after cardiac transplantation. We also investigated GRK2 expression as a marker of allograft cellular rejection. **Methods:** We obtained peripheral blood from NYHA class IV patients (n=11) listed for heart transplantation at our institution before and at routine heart biopsy after transplant for one year. Lymphocytes were isolated with Ficoll-gradient, and GRK2 levels were determined by Western blotting and ELISA. We compared levels of GRK2 protein before transplant and at the first post-transplant biopsy. Levels of GRK2 were correlated with cardiac index. GRK2 expression was examined in an additional ten patients with evidence of rejection. **Results:** GRK2 expression significantly declined after heart transplant (mean GRK2 pre-transplant 13.41 ± 4.1 nmol/gram of protein vs. 5.31 ± 2.6 nmol/gram of protein post-transplant, $p=0.009$), corresponding to a 60% decrease in protein expression. Mean cardiac index was 1.8 l/min/m² pre-transplant. Post-transplant cardiac index was 3.0 l/min/m². GRK2 protein did not change significantly with rejection ($p = ns$). **Conclusions:** Our data provides additional evidence that GRK2 is a novel biomarker of myocardial function in end-stage heart failure. We saw a dramatic 60% decline in GRK2 expression after heart transplant correlating with an improved cardiac index. GRK2 expression was not reflective of allograft rejection in this group of patients. Further study is needed with a larger patient population to assess the role of GRK2 in the management of heart failure patients and transplant recipients.

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G-Protein Coupled Receptor Kinase Expression in Lymphocytes – A Novel Biomarker of Left Ventricular Systolic Function in Heart Failure Patients

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