(ΔpCa_{50}=0.08 ± 0.02), while no significant difference was present in sham hearts (ΔpCa_{50}=0.01 ± 0.02).
These measurements indicate that economy of myofilament contraction is reduced in post-MI remodeled myocardium.

3723-Pos
Myosin Heavy Chain Isoform Expression and Contractile Function in Mechanically Unloaded Left Ventricles Following Left Ventricular Assist Device (LVAD) Implantation
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The ventricles of human myocardium normally express low levels of α myosin heavy chain (MHC) on a predominately β MHC background. However, in heart failure the distribution changes to ~100% β MHC with virtually undetectable levels of α MHC, a change that has been associated with contractile dysfunction. In cases of severe failure, surgical implantation of a left ventricular assist device (LVAD) may be used as destination therapy and has been previously associated with improvements in contractile function in single myocytes. Here, we used post-LVAD myocardium in which the heart has been explanted for transplantation to test the hypothesis that mechanical unloading of ventricular myocardium increases contraction kinetics, possibly through the re-expression of α MHC. Measurements of the maximal rate of ATP utilization and isometric force in permeabilized multicellular preparations revealed no significant difference between failing myocardium prior to LVAD implantation (pre-LVAD) and post-LVAD myocardium. Tension cost, which is calculated as the rate of ATP utilization divided by the isometric force, was also similar between groups. For comparison, normal myocardium displayed maximal rates of ATP turnover that were approximately 2.5-fold greater than in pre- and post-LVAD myocardium. SDS-PAGE indicated virtually undetectable levels of α MHC in pre- and post-LVAD myocardium, while protein phosphorylation gels revealed significant differences in the basal level of phosphorylation of myosin binding protein-C, TnT, and TnI between both groups. These results suggest that while mechanical unloading of failing myocardium may not cause a re-expression of α MHC, improvements in contractile function following LVAD implantation may be associated in part with alterations in the phosphorylation status of key regulatory proteins. This work supported by NIH RO1-HL61635 (RLM).

3724-Pos
Myofibrillar Protein Expression and Contractility in Neonates and Infants with Congenital Right Ventricular Outflow Obstruction
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In this study we investigated the postnatal developmental changes in sarcomeric protein expression in parallel with contractile parameters in myofibrils isolated from small resections from the right ventricular (RV) outflow tract in 25 patients with Tetralogy of Fallot and related congenital heart diseases (CHD). These CHDs are associated with RV hypertrophy and outflow tract obstruction. The age of the patients ranged from 4 days to 38 months. The resections were procured during surgical correction of the cardiac malformation and would have been otherwise discarded. In the neonate (4 days old), the expression of slow skeletal TnI (ssTnI) and atrial light chain (ALC-1) was ~82% and ~50% respectively and declined to respectively < ~8% and ~3% at the age of 38 months. This down-regulation in ssTnI and ALC-1 expression correlated ($p<0.05$) with the decline in Ca^{2+}-sensitivity from $pCa_{50} = 5.95$ in the neonate to $pCa_{50} = 5.33$ in 38 months old infants. Neither contraction nor relaxation kinetics correlated with ssTnI expression. However, ALC-1 expression correlated positively with the activation kinetics, k_{ACT} and force redevelopment, k_{TR} ($r = 0.62$, $p<0.05$). The time course of relaxation is biphasic with an initial slow quasi-linear decay followed by a fast exponential decay. The rate constant of the fast exponential decay, k_{REL} correlated positively with ALC-1 expression ($r = 0.57$, $p<0.05$). In summary right ventricular hypertrophy associated with congenital heart disease does not prevent the developmental down-regulation of ssTnI and ALC-1 although we cannot exclude that this down-regulation occurs at a slower rate than in healthy infants. The change in ssTnI expression correlates with the expected decrease in Ca^{2+}-sensitivity while ALC-1 expression appears to modulate crossbridge turnover kinetics in agreement with studies in animals.

3725-Pos
Sex Dimorphic Myofilament Function and AMPK Expression in R403Q Hearts
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Male mice expressing an autosomal dominant mutation in alpha-myosin heavy chain (R403Q) develop hypertrophic cardiomyopathy characterized by progressive left-ventricular dilation and cardiac dysfunction whereas females do not. We wished to determine whether these sex dimorphisms were due to underlying differences in myofilament contractile function. Therefore, we determined the sensitivity of the myofilaments to Ca^{2+} in demembranated cardiac trabeculae (CT) from wild-type (WT) and R403Q male and female mice (10-12 months of age). We demonstrate that the R403Q mutation did not affect Ca^{2+}-sensitive tension development in CT from males. While Ca^{2+}-sensitivity was greater in both male WT and R403Q CT compared to WT females, they were less sensitive to Ca^{2+} than CT from female R403Q hearts. We also determined rates of tension redevelopment (k_{tr}) following a release-restretch protocol in CT from WT and R403Q male and female hearts at the same age. CT from R403Q male hearts exhibited an enhanced k_{tr} compared to WT males. The k_{tr} in WT female CT was similar to WT males. The k_{tr} in R403Q female CT measured between WT and R403Q males. We hypothesized that the sex dimorphisms in myofialment function reflect an increase in the energetic cost of contraction when expressing the R403Q mutation. Therefore, we measured levels of Adenosine monophosphate-activated kinase (AMPK), a central sensor of the cellular energy state. Total AMPK protein levels were significantly increased in 10-12 month male R403Q hearts compared to WT controls. Female R403Q hearts showed the opposite: total AMPKα expression was lower compared to WT controls. We conclude that (1) the increased Ca^{2+}-sensitivity may provide sufficient contractile support in female R403Q hearts maintaining a compensated state, and (2) the increased AMPK expression in male R403Q hearts is indicative of an increased energetic demand caused by the mutation.

3726-Pos
Intralipid Protects Cardiac Function of Late Pregnant Mice against Ischemia/Reperfusion Injury
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Female mouse hearts show better functional recovery after ischemia/reperfusion (I/R) injury compared with males. However, the vulnerability of isolated late pregnant (LP) hearts to I/R injury is unknown. Here we investigated the susceptibility of isolated mouse hearts in LP and postpartum (PP) to I/R injury. Isolated hearts (Langendorff) from female mice in diestrus stage (NP), LP, one day PP (PP1) and 7 day PP (PP7) were subjected to 20 minutes of global normothermic (37°C) ischemia followed by 40 minutes of reperfusion. The heart function was recorded throughout the experiments and infarct size was assessed by triphenyltetrazolium staining at the end of reperfusion. Although the function was similar in all 4 groups before ischemia, the functional recovery of LP hearts at the end of reperfusion was significantly lower compared to NP hearts; the rate pressure product (RPP) was reduced from 12926 ± 1479mmHg*beats/min in NP to 1614 ± 438mmHg*beats/min in LP mice. Interestingly, the RPP recovered partially in PP1 to 4716 ± 584mmHg*beats/min and almost fully back to NP levels one week PP. Consistent with the functional recovery findings, the infarct size was markedly larger in LP (59.7 ± 5.2%) compared with NP (15.2 ± 0.8%). The infarct size was restored partially in PP1 and fully back in PP7. Recently we have observed that Intralipid can protect the male mouse heart against I/R injury. To test whether Intralipid can improve the heart function in LP mice, 1% Intralipid was applied to isolated LP hearts at the onset of reperfusion. Intralipid treatment significantly improved the cardiac function of LP mice (RPP=11565 ± 1599mmHg*beats/min) and reduced the infarct size (17 ± 1.1%) to similar values as in NP. In conclusion, isolated LP hearts have high vulnerability to I/R injury and postischemic treatment with Intralipid can protect the heart against I/R injury.

3727-Pos
Intralipid Induces Cardioprotection against Ischemia-Reperfusion Injury by Inhibiting the Mitochondrial Permeability Transition Pore Opening Via the PI3K/AKT Pathway
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Acute myocardial infarction is a major cause of mortality, and the best hope of salvaging viable myocardium is by rapid cardiac reperfusion. A novel cardioprotective drug which could be applied at the time of reperfusion after acute infarction would be ideal. Here we tested the hypothesis that administration of Intralipid at the onset of reperfusion protects the heart against ischemia reperfusion (I/R) injury. Isolated hearts (Langendorff) from male mice were subjected to 20 minutes of global normothermic (37°C) ischemia followed by 40 minutes of reperfusion with Krebs Henseleit buffer (CTRL) or with additional 1% Intralipid (ILP). Postischemic treatment with Intralipid significantly improved the cardiac function; the rate pressure product (RPP) was increased from 3432 ± 334mmHg*beats/min in CTRL to 15405 ± 1011mmHg*beats/min in ILP. Consistent with the higher functional recovery in ILP, the infarct