PRESENTING AUTHOR'S NAME & RESEARCH TITLE

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Reliance on cooperative mechanisms in the mammalian heart

PURPOSE/BACKGROUND

Ca^{2+} binding to troponin C (TnC) and myosin cross-bridge binding to actin act in a synergistic cooperative manner to modulate myocardial contraction and relaxation. The responsiveness of the myocardial thin filament to the activating effects of Ca^{2+} and myosin cross-bridge binding (i.e., cooperative profile) have been well-characterized in small mammals especially mice. Given the ten-fold difference in resting heart rates and twitch kinetics between small and large mammals, it is unlikely that the cooperative profile is identical in these two instances.

MATERIALS & METHODS

To test the idea that the cooperative profie is a species-dependent property of mammalian myocardium, we measured the Ca^{2+}-dependencies of steady-state force and the rate constant of force redevelopment (*k*tr) in murine and porcine permeabilized ventricular myocardium.

RESULTS

While murine myocardium exhibited a steep activation-dependence of *k*tr (i.e., from 3.9 ± 0.7 sec^{-1} at pCa 6.0 to 29.8 ± 2.1 sec^{-1} at pCa 4.5), the activation-dependent profile of *k*tr was significantly reduced in porcine ventricular myocardium (i.e., from 2.1 ± 0.2 sec^{-1} at pCa 6.1, to 0.9 ± 0.1 sec^{-1} at pCa 5.8, and 2.9 ± 0.2 sec^{-1} at pCa 4.5). Further insight into the cooperative profile was attained by examining force-pCa and *k*tr-pCa relationships. In the murine myocardium, the pCa_{50} for *k*tr was right-shifted compared to the pCa_{50} for force (i.e., $\Delta pCa_{50} = 0.17 \pm 0.01$, $P<0.05$). Thus, a higher $[Ca^{2+}]$ was required to achieve half-maximal activation of *k*tr, meaning that increases in steady-state force occurred well before increases in the rate of force redevelopment were observed. In porcine myocardium, we observed a tighter coupling of the force-pCa and ktr-pCa relationships, as evidenced by near maximal rates of force redevelopment at low levels of Ca^{2+} activation.

DISCUSSION/CONCLUSION

These results demonstrate that the cooperative profile is a species-dependent dynamic property of the mammalian heart. Such a mechanism suggests a molecular basis for beat-to-beat synchronization of ventricular contractility and circulatory demand across species.