Sarcomere Lengthening Decreases the Rate of Cross-Bridge Cycling. Implications for the Inhomogeneous Myocardium.

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ABSTRACT. The effects of stretch, encountered in weak areas of inhomogeneous myocardium, on force development and energy consumption, are not well understood. We hypothesize that the cross-bridge (XB) strong to weak transition (weakening) rate increases with the shortening velocity, and decreases during stretch. The hypothesis reproduces cardiac basic properties such as the force-velocity relationship, the cardiac elastance and the linear dependence of energy consumption on the generated mechanical energy. This study investigates the dependence of XB kinetic rates on the XB strain (displacement) and strain rate (velocity), during stretch. Trabeculae were isolated from rat right ventricles. Sarcomere length was measured by laser diffraction and controlled by a fast servomotor. The number of strong XB (N_{XB}) was evaluated by fast (120Hz) and small (3-5nm) oscillations. Stretches at different velocities (0-2.4μ/s) and instants were imposed on isometric twitches. Faster stretches yielded larger forces. A tight linear correlation between force and stiffness (N_{XB}) was obtained, implying that the force increased due to the increase in N_{XB}. The rates of the normalized stress and stiffness development were linear functions of the sarcomere lengthening velocity. The phenomenon can not be attributed to the Force-length relationship since fast stretches (>1.6μ/sec) double the force and the stiffness with only small sarcomere lengthening. The results thus strongly support the hypothesis that stretch decreases the rate of XB weakening in a velocity dependent manner. The implications are relevant to ischemic or failing heart, where there is strong inhomogeneity in the structural and mechanical properties of the myocardium, and a nonuniform control of the excitation-contraction coupling. This inhomogeneity causes stretching of the weaker segments, during cardiac contraction. A decreased XB weakening rate during stretch yields a protective effect by reducing energy consumption (decrease in the XB cycling rate) while increasing force generation capability by prolonging the time over which the XBs are in the strong state. On the negative side, the stretch produces the post-systolic shortening observed in ischemic regions and impairs the diastolic function, since the energy stored in the stretched XBs is released late at early diastole and produces shortening instead of an increase in the cardiac wall compliance.

KEYWORDS. Stretch, cross-bridge dynamics, force enhancement, energy, post-systolic shortening

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