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Diabetic Alterations in Cardiac Sarcoplasmic Reticulum Ca^{2+}-ATPase and Phospholamban Protein Expression

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Diabetic cardiomyopathy has been suggested to be caused by abnormal intracellular Ca^{2+} homeostasis in the myocardium, which is partly due to a defect in calcium transport by the cardiac sarcoplasmic reticulum (SR). In the present study, the underlying mechanism for this functional derangement was investigated with respect to SR Ca^{2+}-ATPase and phospholamban (PLB, the inhibitor of SR Ca^{2+}-ATPase). The maximal Ca^{2+} uptake and the affinity of Ca^{2+}-ATPase for Ca^{2+} were decreased, and exogenous phosphorylation level of PLB was higher in streptozotocin-induced diabetic rat SR. Levels of both mRNA and protein of PLB were significantly increased in the diabetic hearts, whereas those of SR Ca^{2+}-ATPase were significantly decreased. Consequently, the relative PLB/Ca^{2+}-ATPase ratio was 1.88 in the diabetic hearts, and these changes were correlated with changes in the rates of SR Ca^{2+} uptake. However, phosphatase pretreatment of PLB for dephosphorylation of the sites phosphorylated *in vivo* did not change the levels of subsequent PLB phosphorylation in either control or diabetic rat hearts. The above data indicated that the increased PLB phosphorylation was not due to autonomic dysfunction but possibly due to increased PLB expression. These findings suggest that reduction of the SR Ca^{2+}-ATPase level would contribute to decreased rates of SR Ca^{2+} uptake and that this function is further impaired by the enhanced inhibition by PLB due to its increased expression in the diabetic heart.