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Functional Alterations of Sarcoplasmic Reticulum Ca^{2+} Release Channel in Streptozotocin-induced Diabetic Rat Heart

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Our previous studies showed that the relaxation defect of diabetic heart was due to the changes in the expressional levels of SR Ca^{2+}–ATPase and PLB. In the diabetic heart contractile abnormalities were also observed, and one of the mechanisms for these changes could include alterations in the expression and/or activity levels of various Ca^{2+} regulatory proteins involving cardiac contraction. In the present study, quantitative changes in the expression of SR Ca^{2+} release channel (RyR) and sarcolemmal L-type Ca^{2+} channel (DHPR), and the functional consequences of these changes in diabetic heart were investigated. The levels of protein and mRNA of the RyR in diabetic hearts were comparable to those of the controls. However, SR Ca^{2+} release and the binding capacity of ryanodine were significantly decreased in diabetic hearts, and electrophysiological data confirmed the above findings. In the diabetic heart, open probability and the mean opening time of the RyR were markedly decreased. Furthermore, the protein level of the DHPR and the binding capacity of nitrendipine in the diabetic hearts were not different as compared to those of the control. Thus, one of the deranged steps in controlling cytoplasmic Ca^{2+} concentrations during cardiac contraction in the diabetic heart appears to reside in the SR release. The Ca^{2+} release through the RyR appears to be impaired but this was only functional without involving the transcriptional or translational steps. In conclusion, in diabetic hearts, Ca^{2+} release processes are impaired, which are likely to lead to functional derangement of contraction of heart.