Gender Related Differences in Local Ca^{2+} Release in Normal and Diabetic Rat Cardiomyocytes: Electrophysiological and Molecular Approach

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ABSTRACT: The present study was designed to determine whether the properties of local Ca^{2+} release and its related regulatory mechanisms might provide insight into the role of sex differences in heart functions of normal and streptozotocin (STZ; 50 mg/kg)-induced diabetic adult rats. Basal intracellular Ca^{2+} level ($[Ca^{2+}]_i$), left ventricular developed pressure (LVDP), rate change in developed pressure (+dP/dt) rate of change in relaxation (-dP/dt), and spatio-temporal parameters of $[Ca^{2+}]_i$ transients were found similar in normal male and female rats. On the other hand, all of the parameters of Ca^{2+} sparks in cardiomyocytes isolated from normal female rats were significantly different from those of the normal males. However, diabetes-induced depression in LVDP of male rats was 15% higher than the diabetic female rats while diabetes induced less depression (12%) in the amplitude of $[Ca^{2+}]_i$ transients in female than in males. Moreover, slow-downs in both +dP/dt and –dP/dt by diabetes were more significant (~20%) in the males than the females. In addition, spatio-temporal parameters of the Ca^{2+} sparks in cardiomyocytes isolated from normal female rats were also significantly different from those of the normal males. In addition, diabetes-induced depression in the amplitude of Ca^{2+} sparks was significantly different from the matched males whereas the other changes were similar in the two sexes. Levels of cardiac ryanodine receptors (RyR2) and FK506 binding protein 12.6 (FKBP12.6) of normal female rats were significantly higher than the aged- matched males diabetes induced less hyperphosphorylation level of RyR2 and less increase in basal $[Ca^{2+}]_i$ as well as less depression in Ca^{2+} loading of SR in the females compared to those of the males. Our data for local Ca^{2+} release and its related proteins can describe some of the mechanisms that may underlie sex-related differences, especially the female's advantage in the development of cardiac diseases.*Supported by TUBITAK-SBAG-3056 & Ankara Univ BAP20030809120***

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