Abstract: P75

Shortening and calcium transport in epicardial and endocardial ventricular myocytes from the streptozotocin-induced diabetic rat

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Background/Introduction: Diabetes mellitus (DM) is a serious global health problem. According to the International Diabetes Federation Atlas 2015 the estimated number of people with DM worldwide is expected to increase from 415 million in 2015 to 642 million in 2040. Cardiovascular complications are the major cause of morbidity and mortality in diabetic patients. Electromechanical function is frequently compromised in the diabetic heart.

Purpose: To investigate the regional effects of DM on shortening and calcium (Ca2+) transport in epicardial (EPI) and endocardial (ENDO) myocytes from the left ventricle of streptozotocin (STZ) - induced diabetic rat.

Methods: Diabetes was induced in adult male rats with a single injection of STZ/citrate buffer (60 mg/kg body weight, ip). Age-matched controls received citrate buffer alone. Experiments were performed after 5 months of treatment. EPI and ENDO myocytes were isolated from left ventricle. Shortening and intracellular Ca2+ were measured in fura-2 loaded, electrically stimulated myocytes, at 35-36 °C, by video edge detection and fluorescence photometry, respectively. In some experiments the voltage-dependence of the Ca2+ transient was assessed by simultaneous measurement of L-type Ca2+ current and intracellular Ca2+ current in fura-2 loaded myocytes, by whole-cell patch clamp and fluorescence photometry, respectively.

Results: Diabetes was characterized by a 5-fold increase in blood glucose. Surface area was significantly (P<0.05) reduced in EPI myocytes from STZ compared to control heart. Time to peak (TPK) shortening was significantly prolonged in EPI (102±5 ms, n=40 cells) and ENDO (100±4 ms, n=33 cells) myocytes from STZ compared to respective controls (77±2 ms, n=52 cells and 82±3 ms, n=52 cells). Time to half (THALF) relaxation of shortening was significantly prolonged only in EPI (67±6 ms, n=40 cells) myocytes from STZ compared to control (47±2 ms, n=52 cells). TPK to peak Ca2+ transient was also prolonged in EPI (63±2 ms, n=53 cells) and ENDO (69±2 ms, n=58 cells) myocytes from STZ compared to respective controls (53±1 ms, n=58 cells and 60±1 ms, n=57 cells). THALF decay of the Ca2+ transient was prolonged only in ENDO (210±7 ms, n=59 cells) myocytes from STZ compared to control (165±6 ms, n=57 cells) heart. Amplitude of the Ca2+ transient was not significantly (P>0.05) altered in EPI and ENDO myocytes from STZ compared to control heart. Interestingly, under experimental conditions where L-type Ca2+ current and intracellular Ca2+ were measured simultaneously, the amplitude of L-type Ca2+ current was not significantly altered however, the amplitude of the Ca2+ transient was significantly increased in EPI and ENDO myocytes from STZ compared to respective controls.

Conclusion(s): Intracellular Ca2+ transport is variously affected depending on region of the ventricle and...
experimental conditions in the STZ-induced diabetic rat.