CHARACTERISTICS OF ATRIAL SUBSTRATE AND INDUCIBILITY FOR ATRIAL FIBRILLATION IN HYPERCHOLESTEROLEMIA RABBITS

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Authors: Kun-Tai Lee, Wen-Ter Lai, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, ROC

Background: Hypercholesterolemia could increase the occurrence of atrial fibrillation (AF). The characteristics of atrial substrate for AF in hypercholesterolemia were not determined.

Methods: Five of 3-month-old, 2.5-3.0 Kg, male New Zealand White (NZW) Rabbits fed with standard chow were selected as a control group (CP). Another 5 of the same age, 2.8-3.4 Kg, rabbits fed with high cholesterol-contained chow for 2 months were selected as a hypercholesterolemia group (LP). All rabbits were anesthetized and ventilated on room air. After a median sternotomy, two plates with 4 electrodes are sutured at the right atrium appendage (RAA) and the left atrium appendage (LAA), respectively, for pacing and recording. The effective refractory period (ERP) of atrium was measured by S1-S2 method at a basic cycle length of 200 ms. The AF vulnerability was defined as the maximum duration of inducible repetitive atrial responses during determination of atrial ERP and by incremental atrial pacing with pacing cycle lengths from 200 ms to 100 ms. Atrial fibrosis areas were determined by Masson trichrome stained from atrial appendage. The expressions of connexin 43 (Cx43), connexin 40 (Cx40) and phosphorylated form of c-Jun N-terminal Kinase (P-JNK) in atrial tissues were determined by Western blot analysis.

Results: The serum cholesterol (1331.4±458.9 vs.50.6±8.0 mg/dl, P<0.01) and the AF vulnerability (30157±1020 vs.419±466 ms, P=0.02) were significantly higher in LP than in CP. As comparing with CP, the atrial expression of Cx43 (5.0-fold in LAA and 1.19-fold in RAA; P<0.05) and P-JNK (2.36-fold in LAA and 2.12-fold in RAA; P<0.05) were significantly increased and Cx40 (0.43-fold in LAA and 0.31-fold in RAA; P<0.05) was significantly decreased in LP. The ERPs of RAA and LAA (78±10 vs. 70±11.2 ms, P=0.61 and 88±10 vs. 90±12 ms, P= 0.51, respectively) and the distribution of fibrosis area (collagen area/muscle area: 0.07 ± 0.04 vs. 0.07±0.09, P=0.83 in LAA and 0.10±0.07 vs. 0.13±0.12, P=0.32 in RAA) were all not significantly different between LP and CP.

Conclusions: The alternations of expression of Cx43, Cx40 and P-JNK in atrial substrate of hypercholesterolemia rabbit may contribute to higher AF vulnerability.