Influence of obesity and epicardial fat on the progression of electrical and structural remodeling in a canine obese rapid atrial pacing model

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Funding Acknowledgement: Type of funding source: Public grant(s) – National budget only. Main funding source(s): Grant-in-Aid for Scientific Research (KAKENHI)

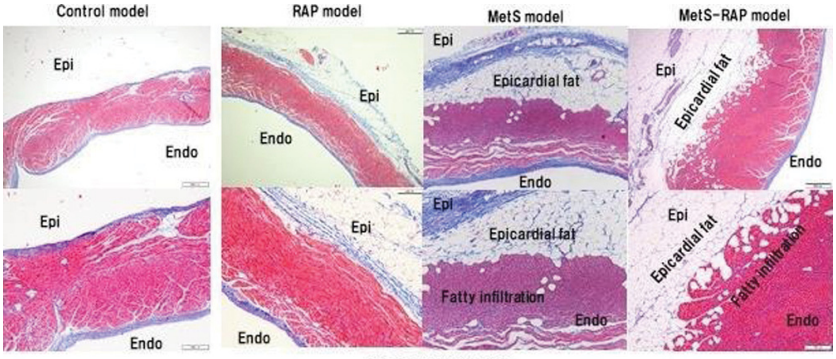
Background: Metabolic syndrome is a cluster of conditions including obesity, insulin resistance, hypertension, and abnormal cholesterol, which increases the cardiovascular risk. Metabolic syndrome or obesity has been reported to provide systemic inflammation and oxidative stress. Increased epicardial fat volume is a manifestation of obesity or metabolic syndrome. Those systemic and local conditions related to obesity or metabolic syndrome have been linking to the risk of atrial fibrillation (AF). The underlying mechanisms of obesity linking epicardial fat to AF progression have not been fully examined.

Purpose: To investigate the impact of obesity linked to epicardial fat on electrophysiologic and anatomical AF substrates.

Methods: Twenty dogs aged 3 years were divided into four groups (n=5 per each): normal diet for over 20 weeks (control group [median body weight: 12.0 kg]), rapid atrial pacing (RAP) for last 4–15 (median 8) weeks during a normal diet for the same period (RAP group [10.5 kg]), high-fat diet (HFD) maintained for over 20 weeks without RAP (MetS group [16.0 kg]), and RAP for last 4–12 (median 6) weeks during HFD maintained for 24 weeks (MetS-RAP group [17.0 kg]), respectively. Activation/voltage maps of the atria during sinus rhythm were created with Ensite NavX mapping system. The effective refractory period (ERP) at 5 left atrial (LA) and pulmonary vein (PV) sites (LA appendage [LAA], LA body, right and left superior PVs, and inferior PV), and AF inducibility by burst LAA pacing were determined. At study completion, hearts were excised for histopathological and gene expression analyses.

Results: The LA pressure was more significantly increased in MetS than the MetS-RAP, RAP, and control groups (22.5 [17–28.8] mmHg vs. 14.0 [10.5–16.3] mmHg, 10.5 [7.4–17.2] mmHg and 10.7 [9.6–13.5] mmHg, respectively, $P<0.05$). The LA/PV ERP at a basic cycle length of 400 ms was shorter in the MetS-RAP and RAP than MetS and control groups (118±39 ms and 122±44 ms vs. 136±18 ms and 155±39 ms, respectively, $P<0.05$). Short duration AF was more induced in the MetS and MetS-RAP than RAP and control groups (3 [0–5.5] sec and 2 [0.5–3.5] sec vs. 0 [0–4.5] sec and 0 [0–0] sec, $P<0.05$). Histological examinations showed the fatty infiltration extending from epicardial fat increased more in the Mets and Mets-RAP than RAP and control groups (Figure). The Fibronectin 1 and collagen I/III mRNA levels increased more in the MetS-RAP and AF than MetS and control groups.

Conclusions: AF vulnerability was associated with increased LA pressures and fibrofatty infiltration from epicardial fat in the MetS group, and with fibrofatty infiltration from epicardial fat with subtle fibrosis in the MetS-RAP group. This suggested that fibrofatty infiltration and epicardial fat plays an important role in AF pathogenesis in obese patients.



Masson trichrome