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Short communication

Pericardial adipose and aromatase: A new translational target for aging, obesity and arrhythmogenesis?

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ABSTRACT

A correlation exists between the extent of pericardial adipose and atrial fibrillation (AF) risk, though the underlying mechanisms remain unclear. Selected adipose depots express high levels of aromatase, capable of converting androgens to estrogens – no studies have investigated aromatase occurrence/expression regulation in pericardial adipose. The Women's Health Initiative reported that estrogen-only therapy in women elevated AF incidence, indicating augmented estrogenic influence may exacerbate cardiac vulnerability. The aim of this study was to identify the occurrence of pericardial adipose aromatase, evaluate the age- and sex-dependency of local cardiac steroid synthesis capacity and seek preliminary experimental evidence of a link between pericardial adipose aromatase capacity and arrhythmogenic vulnerability. Both human atrial appendage and epicardial adipose exhibited immunoblot aromatase expression. In rodents, myocardium and pericardial adipose aromatase expression increased > 20-fold relative to young controls. Comparing young, aged and aged-high fat diet animals, a significant positive correlation was determined between the total aromatase content of pericardial adipose and the occurrence/duration of triggered atrial arrhythmias. Incidence and duration of arrhythmias were increased in hearts perfused with 17β-estradiol. This study provides novel report of pericardial adipose aromatase expression. We show that aromatase expression is remarkably upregulated with aging, and aromatase estrogen conversion capacity significantly elevated with obesity-related cardiac adiposity. Our studies suggest an association between adiposity, aromatase estrogenic capacity and atrial arrhythmogenicity – additional investigation is required to establish causality. The potential impact of these findings may be considerable, and suggests that focus on local cardiac steroid conversion (rather than systemic levels) may yield translational outcomes.

1. Introduction

Adipose is a major endocrine organ which releases a range of bioactive agents [1].

Selected adipose depots have been established as sites of sex steroid metabolism [1]. Subcutaneous and visceral adipose express high levels of aromatase, capable of converting androgens to estrogens [1]. No studies to date have investigated aromatase occurrence or expression regulation in pericardial adipose. Aging and obesity are both associated with a marked increase in pericardial adipose deposition, and represent significant cardiac risk factors [2]. With ongoing rises in obesity rate and life expectancy, there is considerable interest in identifying the underlying cellular mechanisms by which pericardial adipose accumulation may exert pathogenic influence.

Clinically, a correlation between the extent of pericardial adipose (constituting both epicardial and paracardial) and atrial fibrillation

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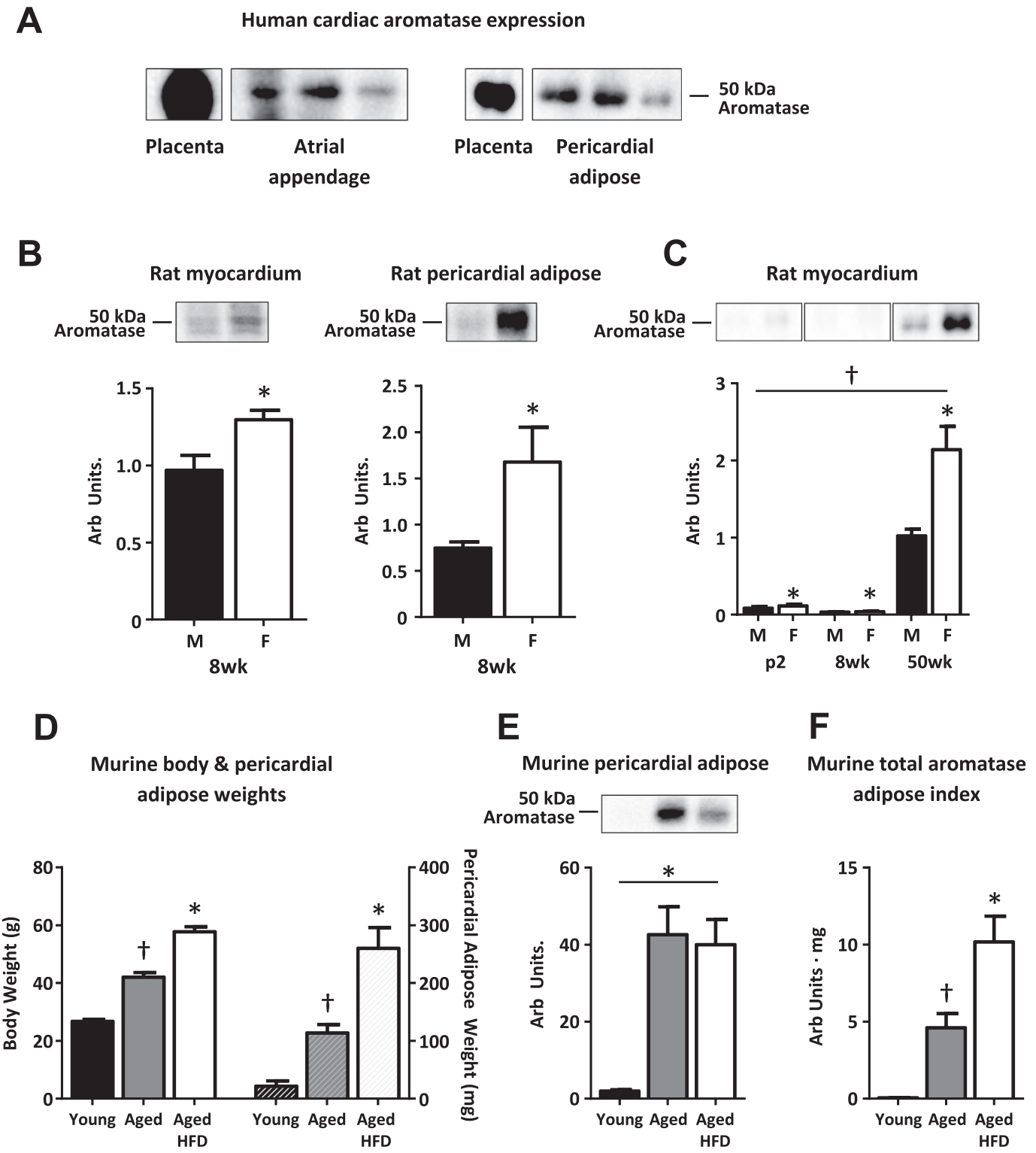

Fig. 1. Aromatase protein is expressed in human and rodent myocardial and pericardial adipose tissue.
A. Representative immunoblot images of aromatase expression in human atrial appendage and pericardial adipose. Human placenta was used as a positive control. B. Immunoblot quantification of aromatase expression in myocardium ($n = 5$, $^*p < 0.05$ Student's *t*-test) and pericardial adipose from 8 week male (M) and female (F) rats ($n = 6$, $^*p < 0.05$ Student's *t*-test). C. Developmental differences in male/female rat myocardium aromatase expression at postnatal day 2 ('p2'), 8 weeks and 50 weeks of age ($n = 6$–8, $p < 0.05$ sex-effect (*) and age-effect (†) by ANOVA). D. Body and pericardial adipose weights in 'Young' (14 weeks), 'Aged' (60 weeks) and high fat diet (HFD) male mice ($n = 6$–8, $p < 0.05$ (ANOVA with LSD post-hoc) vs. Young (†) and vs. Aged (*)). E. Mouse pericardial adipose aromatase expression ($n = 6$–8, $^*p < 0.05$ age-effect by ANOVA). F. Index of total aromatase capacity within the mouse pericardial adipose depots ($n = 6$–8, $p < 0.05$ (ANOVA with LSD post-hoc) vs. Young (†) and vs. Aged (*)).

(AF) risk has now been established [2]. AF is the most common sustained arrhythmia, and is particularly prevalent in the aged population [3]. Cather ablation procedures have been successful in treating paroxysmal AF, though high rates for repeat procedures highlight the necessity for new adjunct therapies or stand-alone preventative measures.

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