

ALTERATIONS TO THE ATRIAL EXTRACELLULAR MATRIX IN AGEING AND HEART FAILURE

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Left atrial (LA) structural remodelling is a feature of both heart failure (HF) and ageing. We have previously demonstrated that extracellular matrix (ECM) remodelling in HF is age-dependent in the left ventricle. However whether similar age-dependent alterations are present in the left atria (LA) in HF remains to be determined.

An ovine model of ageing was used in this study (young, 18 months and aged, >8 years) and HF was induced by rapid ventricular pacing (RVP) in both groups. Echocardiography performed on conscious animals demonstrated an increase in LA dimension with age and as a result of RVP (all $p < 0.05$). Unlike in the ventricle, elastin was histologically quantifiable in the LA. Collagen:elastin ratio was increased after RVP in both young and aged animals but not due to ageing alone. Zymographic matrix metalloproteinase-2 (MMP-2) activity was increased after RVP in young ($p < 0.01$) and in aged ($p < 0.05$), but not as a result of ageing alone. Protein levels of the tissue inhibitor of metalloproteinases (TIMPs) were quantified by immunoblotting. In ageing, augmented TIMP-3 protein was detected ($p < 0.01$), whereas after RVP levels of TIMP-1 and TIMP-2 were decreased in both young and aged hearts (all $p < 0.05$).

Results suggest that whilst gross LA remodelling (dilatation) occurs with both ageing and HF in the sheep, the changes to ECM content and degradative capacity which occur with RVP are not seen with ageing alone. Future experiments will focus on changes to atrial collagen processing and maturation in ageing and HF.

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