Cardiac remodelling in heart failure progression

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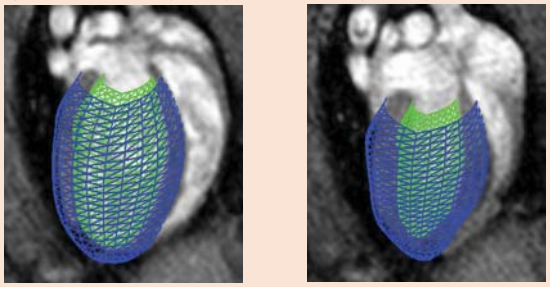
Introduction

- Heart failure (HF): cardiac output does not meet the requirements of the body.
- HF results from maladaptive cardiac remodelling which includes changes in **geometry**, **structure** and **function**
- Aim: improve understanding of the development of HF by investigating the inter-relationships of these three aspects of remodelling.

Method

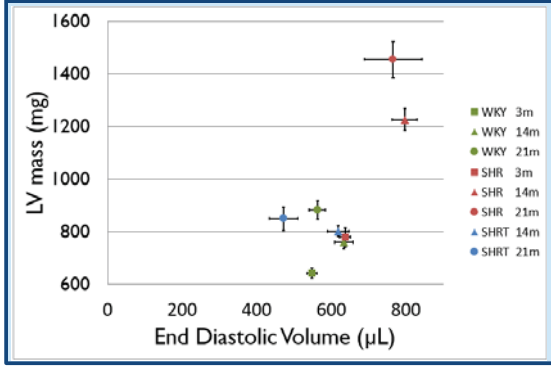
- Investigated three groups of rats at 3, 14 and 21 months of age:

1. Control group: Wistar Kyoto rats (WKY)
2. Hypertensive group: Spontaneously Hypertensive Rat (SHR)
3. Treatment group: SHR undergoing angiotensin-converting-enzyme inhibitor (ACEi) treatment (SHRT)



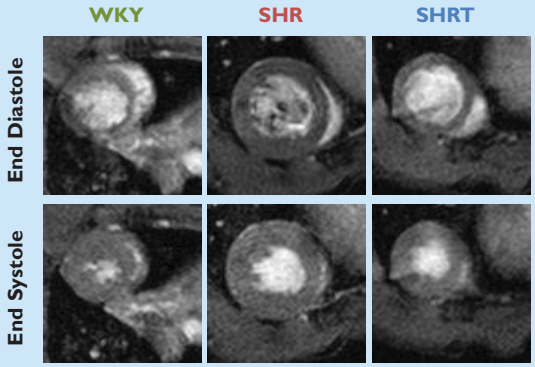
Models of the epicardial and endocardial surfaces are fitted to MR images at ED (left) and ES (right) in order to calculate geometric and functional metrics.

Geometric remodelling



Left: LV mass increased with age for all groups. WKY maintained EDV and SHRT had decreased EDV with age, while SHR showed increased EDV with age.

Right: Short axis MR images at end-diastole (ED) and end-systole (ES) showing differences in cardiac geometry. SHR had larger lumens as well as thicker walls.

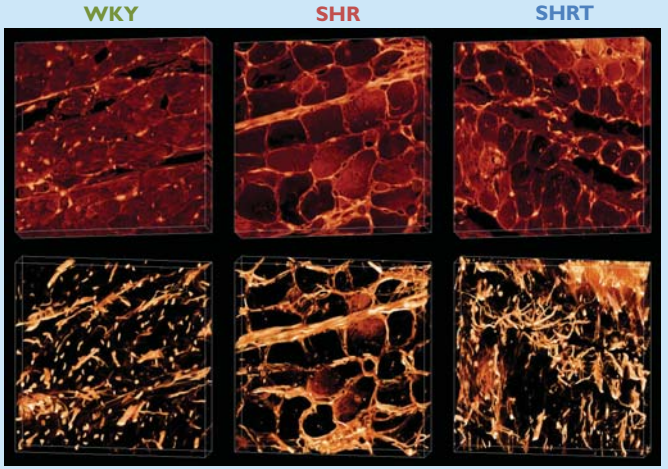


Structural remodelling

LV midwall blocks (200 × 200 × 40 μm³ at 0.4 μm resolution) from adult hearts were stained for collagen and imaged using confocal microscopy.

Top row: Myocytes (red) and collagen (yellow). Myocyte size was both larger and more variable in SHR and SHRT.

Bottom: Collagen only. SHR and SHRT both showed increased endomysial collagen compared with WKY. Laminar clefts in the SHR were fused by perimysial collagen, but laminae were separate in the WKY and SHRT.



Results and Discussion

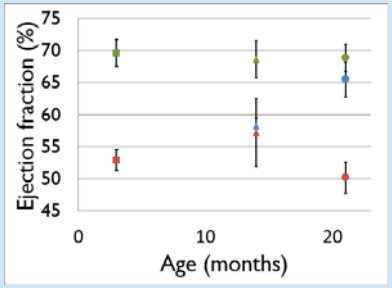
Geometry-Function relationship

- **SHR have larger hearts** relative to normal as evidenced by increases in both LV mass and EDV.
- Although hypertrophy is evident, it is **not clearly concentric hypertrophy** as LV mass and EDV increase concurrently.
- The increased EDV contributes to SHR having a **decreased extent of ejection** (reduced EF at all time-points).
- **ACEi treatment offsets the geometric remodelling**, reducing both LV mass and EDV to near-normal, which accounts for the normal EF at 21 months.

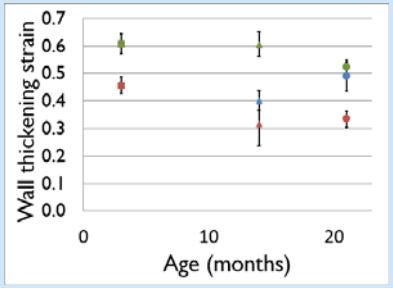
Structure-Function relationship

- **SHR show altered myocardial collagen** arrangement compared to WKY, particularly the increased deposition of collagen in the laminar cleft.
- The increased laminar collagen present in SHR **alters the ability of the myocardium to fully thicken** by inhibiting the relative shear of myocardial laminae.
- Evidenced by decreased wall thickening strain in SHR at all time-points.
- **ACEi treatment reduces collagen deposition** in the laminar clefts compared to SHR.
- **SHRT group exhibit normal wall thickening** at 21 months of age.

Functional remodelling



At 14m SHR and SHRT had reduced EF compared to normal, but at 21m SHR exhibit reduced EF while SHRT had normal EF.



At all time-points SHR showed decreased wall thickening strain compared with WKY. SHRT showed normal wall thickening at 21 months.