ACHD/Valve Disease/Pericardial Disease/Cardiomyopathy

1 INVASIVE AND NON-INVASIVE QUANTIFICATION OF MYOCARDIAL FIBROSIS IN PRIMARY MITRAL REGURGITATION: PROGNOSTIC IMPLICATIONS FOR POST-OPERATIVE REMODELLING, SYMPTOM BURDEN AND EXERCISE CAPACITY

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10.1136/heartjnl-2020-BCS.1

Chronic primary mitral regurgitation (MR) exposes the left ventricle (LV) to volume overload and is associated with evidence of fibrosis on non-invasive imaging. It is not known whether fibrosis predicts outcome from surgery. This study aimed to 1) quantify myocardial fibrosis on histology and non-invasive imaging, 2) investigate any association between fibrosis and LV size and function, 3) determine the impact of fibrosis on post-operative outcome.

Methods In a prospective observational multicentre study, 105 patients with severe MR (N=65/32/8 NYHA Class I/II/III respectively; mean age 63.1±13.4years; male 73%; VO2max 91.2±22.4%) had multiparametric cardiac magnetic resonance (CMR), symptom assessment (Minnesota Living with Heart Failure Questionnaire (MLHFQ)) and cardiopulmonary exercise testing before and at 6-9 months following repair. Patients consented for up to 3 intraoperative LV biopsies for histological collagen volume fraction (CVF) quantification.

Results 234 LV biopsies were collected from 86 patients with median CVF of 14.6%[IQR 7.4-20.3]. Fibrosis was present even in NYHA Class I patients (13.6%[6.3-18.8]), and was significantly higher than the 3.3%[2.6-6.1] obtained from 8 autopsy controls without cardiac disease (P<0.001).

Pre-operatively, there was no relationship between CVF and LV size, systolic function, ECV, late gadolinium enhancement, although CVF did correlate with MLHFQ (R=0.23, P=0.034). Conversely, ECV correlated with systolic (LVEF Rho=-0.22, P=0.029; LVESVi Rho 0.22, P=0.025, GCS Rho=0.31, P=0.002) and diastolic function (E/e' R=0.25, P=0.022), exercise capacity (%VO2max R=-0.22, P=0.030), with borderline correlation to MLHFQ (R=0.19, P=0.058).

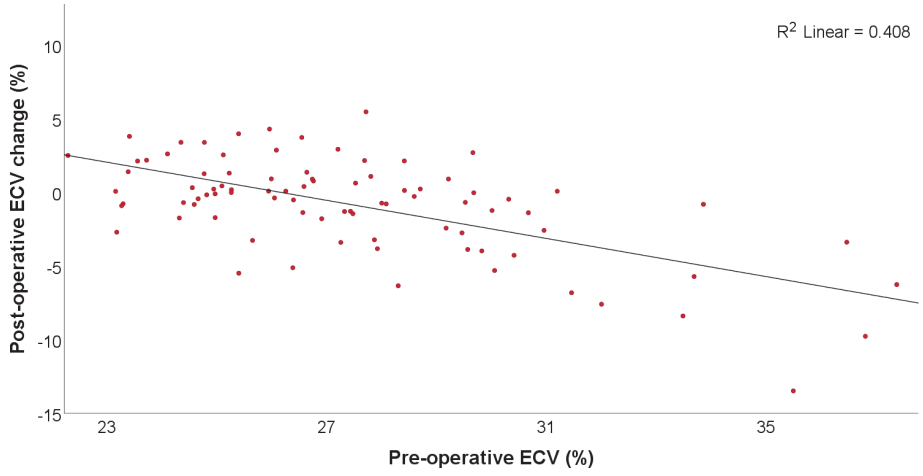
Abstract 1 Table 1 Comparison of pre-operative and post-operative CMR parameters. P values are derived from paired T test.

	Pre-operative(n=105)	Post-operative (n=93)	P
LVEF (%)	69.1±8.0	63.3±8.3	**<0.001**
LVEDVi (ml/m^2)	102.9±22.4	71.8±16.6	**<0.001**
LVESVi (ml/m^2)	32.2±11.8	26.9±10.8	**<0.001**
LVMi (g/m^2)	68.6±13.5	60.2±11.3	**<0.001**
RVEF (%)	56.4±8.7	56.8±7.1	0.654
RVEDVi (ml/m^2)	71.0±15.0	68.0±13.6	**0.026**
RVESVi (ml/m^2)	31.2±10.0	29.5±8.3	**0.036**
ECV (%)	27.4±3.3	26.6±2.8	**0.027**

Following surgery, although LVEF remained >50% in all but 6 patients (LVEF pre 69.1±8.0 vs post 63.3±8.3%, P<0.001), there was a reduction in ECV (27.4±3.3 vs 26.6 ±2.8%, P=0.027) that was proportionate to its pre-operative expansion (figure 1), suggesting that fibrosis was reversible within our patients. Neither histological CVF nor ECV predicted change in LVESVi, LVEF, symptom burden or exercise capacity following repair. GCS was an independent predictor of post-operative LVESVi and LVEF on multiple linear regression models. Whilst improvements in symptom burden and exercise capacity was observed in NYHA II-III patients, this sub-group of patients failed to achieve the same level of fitness and symptom-free status as NYHA I patients (VO2max 92.2±18.8% vs 102.9±21.1%, P=0.017; MLHFQ 12[5-26] vs 3[0-10], P<0.001).

Conclusions Myocardial fibrosis is present in primary MR, before the onset of symptoms. Due to its patchy nature, ECV but not fibrosis on histology is a better marker of pre-operative myocardial function and symptom status. Despite ECV reduction following successful MR surgery, symptomatic patients fail to regain exercise fitness and symptom-free status – providing further support for the benefits of early surgery.

Conflict of Interest None



Abstract 1 Figure 1