Non-Severe MR pre-LVAD

Abstract 4 Figure 1

Severe MR pre-LVAD

Abstract 4 Figure 2

end-systolic volume: 107 ± 41 vs 96 ± 59 ml/m²; $p=0.348$) and LV ejection fraction (17 ± 9 vs $17 \pm 7\%$; $p=1.0$). Severe MR patients had significantly greater ($p<0.001$) MR by proximal isovolumetric surface area (0.93 ± 0.27 vs 0.60 ± 0.16 cm), vena contracta (0.79 ± 0.32 vs 0.57 ± 0.18 cm), regurgitant volume (47 ± 25 vs 24 ± 12 ml), and fraction (54 ± 15 vs $37 \pm 13\%$). Follow-up echocardiography was performed at a median 222 days (range 356 days). Patients who received cardiac transplantation were excluded. Relative severities of MR at follow-up were: none=12 (46%), mild=8 (31%), moderate=5 (19%), severe=1 (4%) amongst patients with severe MR pre-LVAD, and none=55 (58%), mild=26 (27%), moderate=13 (14%), severe=1 (1%) amongst patients with non-severe MR pre-LVAD (figure 1). Within 12m, after excluding patients who underwent cardiac transplantation (severe MR $n=4$; non-severe MR $n=2$), rates of HF hospitalisation [5/25 (20%) vs 16/104 (15%); $p=0.575$] and all-cause mortality [2/25 (18%) vs 22/104 (21%); $p=0.129$] were similar, irrespective of pre-LVAD MR severity. No patient who died during follow-up had severe MR prior to death.

Conclusion LVAD improves severe MR in 96% of cases, resulting in 1-year rates of HF hospitalisation and mortality similar to patients without severe MR pre-LVAD. These data suggest mitral valve surgery at time of LVAD implantation is not warranted.

Conflict of Interest None

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EXAGGERATED ELASTIN TURNOVER IN CHILDHOOD AND ADOLESCENCE IN MARFAN SYNDROME - CORRELATION WITH AGE - NEW INSIGHTS FROM THE AIMS TRIAL

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Background Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder caused by mutations in the Fibrillin1 gene (FBN1) that leads to impaired elastin formation and extra-cellular matrix homeostasis. Elastin synthesis and related lamellae formation in the aorta is completed in the newborn. Thereafter further elastin turnover is thought to be minimal during life. Elastin homeostasis is little studied in patients with MFS who have been reported to have reduced elastin in their aorta and are at risk of aortic dilatation and consequent life-threatening dissection. It is not clear if elastin loss is due to reduced elastin formation in utero or accelerated degradation during life. However, aortopathy develops early in MFS with 70% of patients developing aortic dilatation by the age of 20. Therefore, the longitudinal and circumferential aortic growth that occurs in childhood may involve elastic lamellae remodelling that is impaired in MFS. Desmosine is the cross-link component in the elastin molecule and is exclusively released from mature elastin breakdown, thus is a physiologically relevant biomarker of elastin turnover. We hypothesize that physiologic aortic growth is associated with elastic lamellae remodelling and increased elastin turnover, detected by elevated plasma desmosine (pDES), and that elastin turnover is exaggerated during the fast-growing period in MFS.

Purpose The aims of this study were 1. to investigate the relationship between elastin turnover and age in the control subjects, 2. to compare the elastin turnover in MFS with control subjects.

Methods pDES was measured by stable isotope dilution LC-MS/MS in 113 MFS subjects (48% male, mean age 18.2 ± 9.4 (SD) years), mean aortic root 33.8 ± 2.1 mm and Z-score 3.4 ± 2.1 in the AIMS trial at baseline before intervention, and in 109 healthy controls (46% male, mean age 26.1 ± 9.5 years).

Results pDES levels were associated positively with age, body surface area and negatively with diastolic BP in the control group ($p=0.05$ and 0.21 respectively after correcting for age). In MFS subjects pDES also positively correlated with age and male sex ($p<0.05$). Interestingly, the age-dependent association with pDES showed a peak distribution in both control and MFS groups (figure 1) where teenage children expressed the highest pDES levels. MFS subjects had significantly higher

Abstract 5 Figure 1

Abstract 5 Figure 2

pDES compared to controls before the age of 20 ($p=0.01$) but in adulthood, there was no difference (figure 2).

Conclusion Elastin turnover is highly dynamic before early adulthood, and peaks in adolescence and is exaggerated in MFS, suggesting that this period of growth is critical in developing aortopathy.

Conflict of Interest None

6 CLINICAL PRESENTATION AND OUTCOMES OF CHILDHOOD HYPERTROPHIC CARDIOMYOPATHY ASSOCIATED WITH FRIEDREICH'S ATAXIA: A NATIONAL COHORT STUDY

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Introduction Hypertrophic cardiomyopathy (HCM) is a common manifestation and important predictor of morbidity and mortality in children with Friedreich's ataxia (FA). HCM is present in up to 85% of FA patients however despite this, the clinical spectrum and phenotype is poorly described in children. This has important implications for long-term follow-up and management of children with this disease.

The aim of this study was to describe the clinical characteristics and outcomes in a well-characterised longitudinal cohort of children with FA-HCM in the United Kingdom (UK) over four decades.

Methods Demographic and clinical data for all children (<18 years) diagnosed with FA-HCM between 1980-2017 were retrospectively collected from 11 out of 13 UK paediatric cardiology centres.

Results 78 patients with FA-HCM were identified (male $n=45$, 58%) with a mean age at baseline evaluation of 10.9 years (± 3.1). HCM diagnosis was within one year of cardiac referral in 29 (69.4%), but preceded the diagnosis of FA in 4 (5.3%). At baseline, 65 (90.3%) had concentric left ventricular (LV) hypertrophy with a mean maximal left ventricular wall thickness 12.8mm (± 2.6 , range 8-19mm). Six patients (12.5%, $n=49$) had LV systolic impairment. Over a median follow up of 5.1 years (IQR 2.4-7.3), eight (10.5%) had documented supraventricular arrhythmias [atrial fibrillation ($n=3$), atrial flutter ($n=1$), atrial ectopic tachycardia ($n=1$) and unspecified supraventricular tachycardia ($n=3$)] and four (7.8%) had non-sustained ventricular tachycardia. There were no differences in baseline clinical characteristics between patients with and without atrial arrhythmias, but a higher proportion had impaired systolic function at last clinical review ($n=3$, 37.5% vs $n=1$, 1.4%, p value <0.001). Forty (56.3%) were started on medications for cardiac symptoms, one underwent cardiac transplantation (aged 4 years, prior to diagnosis of FA) and 8 patients (10.6%) died [atrial-arrhythmia related ($n=2$); heart-failure related ($n=1$); non-cardiac ($n=2$); or unknown cause ($n=3$)]. There were no sudden cardiac deaths. Freedom from death or transplantation at 10 years was 80.8% (95% CI 62.5-90.8). No demographic or baseline clinical characteristics, including MLVWT at baseline, predicted transplant-free survival on univariable analysis (table 1).

Conclusions This national study of childhood FA-HCM is the largest cohort reported to date and describes a high prevalence of atrial arrhythmias and early progression to end-stage disease. Overall mortality is similar to that reported in non-syndromic childhood HCM but no patients died suddenly.

Conflict of Interest None

Abstract 6 Table 1 Univariate cox regression analysis for predictors of outcomes

Clinical predictor	Mortality or cardiac transplantation	Atrial arrhythmia		
	Hazard ratio (95% CI)	P Value	Hazard ratio (95% CI)	P Value
Male gender	0.495 (0.11-2.21)	0.357	0.483 (0.11 - 2.11)	0.324
Any symptoms at baseline	1.053 (0.19-5.79)	0.953	0.904 (0.16 - 4.95)	0.907
Heart failure symptoms	0.888 (0.11 – 7.41)	0.912	0.862 (0.11 – 7.02)	0.887
Increasing LVMWT	0.735 (0.49 -1.10)	0.089	0.946 (0.72 – 1.24)	0.687
Increasing LVOT gradient	0.956 (0.80 - 1.14)	0.516	0.936 (0.75 – 1.17)	0.418
Impaired LV systolic function	3.162 (0.52 – 19.11)	0.237	1.360 (0.15- 12.20)	0.790
Impaired LV diastolic function	NA	NA	1.620 (0.17 – 15.75)	0.690
Atrial arrhythmia	1.834 (0.37-9.12)	0.482	NA	NA

CI= confidence interval, LVMWT = left ventricular maximal wall thickness, LVOT =left ventricular outflow tract