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CIRCULATING MATRIX METALLOPROTEINASE-3 IS ASSOCIATED WITH VENTRICULAR ARRHYTHMIAS IN HYPERTROPHIC CARDIOMYOPATHY

ACC Poster Contributions
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Background: Myocardial samples from HCM patients demonstrate extensive interstitial fibrosis. Fibrosis seen on cardiac MRI (cMRI) has been tied to ventricular arrhythmia, but small foci and diffuse fibrosis are not seen on cMRI.. Since circulating MMP concentrations can be markers of myocardial fibrosis, we tested the hypothesis that MMPs are markers of ventricular arrhythmia in hypertrophic cardiomyopathy.

Methods: Plasma MMP 1,2,3,9 and TIMP 1,2,4 were measured in 45 HCM patients(20% female, median age 17years [IQR 15-20]), using multiplexed ELISA. Patients with syndromic HCM or other MMP altering conditions were excluded. Participants were grouped by history of serious ventricular arrhythmia (VA) versus without(NoVA). Ventricular arrhythmia history was limited to cardiac arrest, sustained VT/VF/appropriate implanted cardiac defibrillator (ICD) discharge, or syncope likely due to ventricular arrhythmia only. MMP differences between VA and NoVA were examined nonparametrically. In secondary analyses, linear regression assessed relations between MMP levels and ventricular arrhythmia, with adjustment for interventricular septum thickness above 3cm, family history of sudden death, and presence of ICD. As sensitivity analysis, age was substituted for ICD in the regression model.

Results: The 14 VA patients were older than 31 NoVA patients(Median 19 vs 17 years, p=0.03). All 14 VA and 12 NoVA patients had ICD. Family history of sudden death was present in 2 VA and 5 NoVA. Of the 19 NoVA patients with gadolinium-cMRI, 15 had evidence of fibrosis. MMP3 was significantly higher in the VA group (VA median 12.9 [IQR 5.7-16.7] mcg/mL vs NoVA 5.8 [IQR 3.7-10.0 mcg/mL]; p=0.01). On multivariable analysis, VA was independently associated with MMP3 levels (standardized ☒ 0.368, p=0.03). Adjustment for age attenuated this association.

Conclusions: Circulating MMP3 is elevated in HCM patients with ventricular arrhythmia. Due to lack of serious ventricular arrhythmia in our younger patients, we cannot exclude age related confounding. Future work could investigate this marker in adults with HCM and the utility of this marker for prospective prediction of ventricular arrhythmia in children.