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Troponin I And Its Relation To Disease Severity In Paediatric Hypertrophic Cardiomyopathy- Sarah Watson- University College London

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Introduction:

Hypertrophic cardiomyopathy (HCM) is a genetic disorder that is characterized by left ventricular hypertrophy unexplained by secondary causes, and a non-dilated left ventricle with preserved or increased ejection fraction. It is commonly asymmetric with the most severe hypertrophy involving the basal interventricular septum. Left ventricular outflow tract obstruction is present at rest in about one third of the patients, and can be provoked in another third. The histologic features of HCM include myocyte hypertrophy and disarray, as well as interstitial fibrosis. The hypertrophy is also frequently associated with left ventricular diastolic dysfunction. In the majority of patients, HCM has a relatively benign course. However, HCM is also an important cause of sudden cardiac death, particularly in adolescents and young adults. Nonsustained ventricular tachycardia, syncope, a family history of sudden cardiac death, and severe cardiac hypertrophy are major risk factors for sudden cardiac death. This complication can usually be averted by implantation of a cardioverter-defibrillator in appropriate high-risk patients. Atrial fibrillation is also a common complication and is not well tolerated.

Troponin is associated with increased risk of adverse outcomes and correlates with multiple parameters of disease severity in adults with hypertrophic cardiomyopathy (HCM). However, prognostic and staging markers in adults are not always of value in children with HCM. This study assessed the ability of troponin I (TnI) to predict clinical variables in a paediatric cohort of HCM and compare this to well-established biomarker, NT-proBNP.TnI and NT-proBNP were measured in forty-nine patients with HCM [10.69±5.34 years old, 32 (65.31%) male] and elevated TnI is defined as ≥34ng/L (99th percentile reference limit). Evaluation included ECG, echocardiography, ambulatory ECG [19 (38.78%)], ICD interrogation [9 (18.37%)], exercise testing [19 (38.78%)], and cardiac magnetic resonance (CMR) imaging [16 (32.65%)].TnI was detected in 19 (38.78%) and ≥34 ng/L in 14 (28.57%). There were significant differences in maximum wall thickness (MWT) z-score, E/E', mitral E-wave deceleration time, and CMR-assessed LV mass index between patients with TnI<34ng/L and TnI≥34ng/L. Continuous TnI, but not NT-proBNP, correlated with global longitudinal strain (rs=0.62, p<0.001), and there were significant differences in TnI levels in patients with ST-segment changes, and late gadolinium enhancement. Both biomarkers correlated with MWT z-score and E/E', although correlations were stronger for NT-proBNP. Multivariate analysis revealed TnI was an independent predictor of MWT and LV mass index.Troponin is a reliable biomarker to identify features of HCM (extreme hypertrophy and diastolic dysfunction) and may be an additive monitoring parameter in children. However, the utility beyond NT-proBNP, and the ability to identify subclinical ischaemia and fibrosis is uncertain. HCM is usually inherited as an autosomal dominant trait caused by mutations in genes that encode proteins of the cardiac sarcomere.7–10 Based on the assumption that locus and allelic heterogeneity have different effects on myocyte structure and function, it has been hypothesized that individual mutations are associated with specific phenotypes.10–15 If this is correct, then mutation analysis could be used to guide therapy (eg, prophylactic implantation of implantable cardioverter-defibrillators) and counseling strategies for families. One of the first reported genotype-phenotype associations in HCM

was a high prevalence of sudden cardiac death in young carriers of mutations in the cardiac troponin T gene (TNNT2),9,16–18 paradoxically in the presence of only mild left ventricular hypertrophy.19,20 Although this finding has been used in subsequent consensus management guidelines for HCM, studies examining the natural history of troponin T gene mutations are limited by the small size of patient cohorts (often single families), cross-sectional study design, and a lack of data on disease expression in relatives. The aim of this study was to examine clinical outcomes in a relatively large cohort of patients and relatives with mutations in the cardiac troponin T gene.