7 RELATION BETWEEN N-TERMINAL PRO B-TYPE NATRIURETIC PEPTIDE (NT-PROBNP) AND DISEASE SEVERITY IN PAEDIATRIC HYPERTROPHIC CARDIOMYOPATHY

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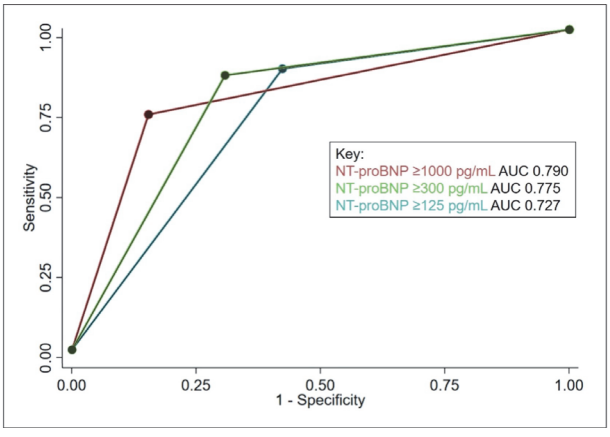
Introduction N-terminal pro B-type natriuretic peptide (NT-proBNP) is associated with an increased risk of mortality and heart failure related adverse events in adults with hypertrophic cardiomyopathy (HCM). Elevated NT-proBNP levels have been correlated with multiple subjective and objective parameters of HCM severity including dyspnoea and left ventricular maximal wall thickness (LVMWT). However, robust prognostic markers in adults may not be reliable for children with HCM in whom disease severity assessment is challenging. No studies have yet evaluated utility of NT-proBNP in children with HCM.

Thus, the objective of this study was to assess associations of NT-proBNP with conventional markers of disease severity and predictive ability of NT-proBNP in a paediatric HCM cohort.

Methods Plasma NT-proBNP levels were measured in eighty consecutive patients [23 (28.8%) females; median age: 12.3 years (interquartile range (IQR): 6.4-16.0); 37 (46.3%) sarcomeric aetiology]. Contemporaneous data from conventional clinical evaluation was used to establish disease severity including electrocardiography, echocardiography, tissue Doppler imaging, magnetic resonance imaging (MRI) and cardiopulmonary exercise testing.

Results Median NT-proBNP concentration was 1104.5 pg/mL (range: 20–11206 pg/mL and IQR: 108.5–2613.5 pg/mL). NT-proBNP levels correlated with: QTc (ρ= 0.445, p<0.01); septal thickness z-score (ρ=0.618, p<0.001); MLVWT z-score (ρ=0.582, p<0.001); lateral S' (ρ=–0.668, p<0.001); septal E/E' (ρ=0.609, p<0.001); MRI MWT (ρ=0.773, p<0.001; indexed LV mass (ρ=0.576, p<0.001) and peak systolic blood pressure (ρ=–0.605, p<0.001). There were weak associations between NT-proBNP and aetiology or subjective symptoms including palpitations and chest pain (p>0.05).

NT-proBNP levels were higher in patients who were: female; dyspnoeic (defined as Ross/NYHA Class ≥II); prescribed cardioactive medication and had an implantable cardioverter defibrillator (p<0.05).Lateral S' (β = –0.306, p=0.001) and MLVWT (β = 0.217, p = 0.013) were independent predictors of NT-proBNP in multivariate analysis. At a cut-off point of 300 pg/ml, NT-proBNP had a positive predictive value of 84% and a negative predictive value of 72% for predicting septal E/E'>10 (Area under the curve = 0.775 (p<0.001)) (See figure 1).



Abstract 7 Figure 1 Receiver operator characteristic (ROC) curves of NT-proBNP cut-offs for predicting septal E/E'>10, a marker of diastolic dysfunction, in children with hypertrophic cardiomyopathy. True-positive rate (sensitivity), false positive rate (1-specificity) and area under the curve (AUC) are displayed for the following cut-offs; NT-proBNP ≥1000 pg/ml (red), NT-proBNP ≥300 pg/ml (green) and NT-proBNP ≥125 pg/ml (blue)

Conclusions NT-proBNP levels correlate with parameters of disease severity in paediatric HCM including measures of diastolic dysfunction (septal E/E') and systolic dysfunction (lateral S'). NT-proBNP measurement may be an effective adjunct for monitoring disease severity in children, particularly when conventional clinical evaluation is challenging. Future studies in larger cohorts of children are needed to explore prognostic value.

Conflict of Interest None

8 SINGLE-CELL RNA SEQUENCING REVEALS CARDIAC CELL-SPECIFIC TRANSCRIPTOMIC CHANGES IN DILATED CARDIOMYOPATHY

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Introduction Dilated cardiomyopathy (DCM) is the most common cause of heart failure (HF), with a complex aetiology including lifestyle and genetic factors involving pathological changes in multiple cardiac cell types. The ability of single-cell RNA sequencing (scRNA-Seq) to measure gene expression in thousands of individual cells simultaneously provides a way to study the differing pathological changes in cell types within complex tissues. We aimed to detect celltype-specific transcriptomic alterations implicated in DCM through an integrated analysis of publicly available adult heart scRNA-Seq datasets that leveraged recent advancements in single-cell analytical tools.

Methods scRNA-Seq data from an adult human HF dataset containing DCM (n=5) and control (n=14) samples were retrieved from Gene Expression Omnibus (GSE109816, GSE121893) and subjected to an updated bioinformatic workflow. Unsupervised clustering analysis of 10,242 cells was paired with reference celltype mapping from Heart Cell Atlas data to produce a more comprehensive annotation of the HF dataset. Differential expression analysis was performed between DCM and control cells to identify celltype-specific transcriptomic changes in DCM. Bulk RNA-seq was performed on adult human DCM (n=9) and control (n=9) heart tissue to detect whole-tissue changes. Genes differentially expressed in bulk and single-cell data were intersected to generate a list of putative DCM-linked genes, validated in vitro by RT-qPCR in human cardiac fibroblasts.

Results Our single-cell workflow resolved 8 distinct cell populations in the heart, 4 of which were not reported in the original publication associated with the data. The validity of these cell populations was strongly supported by the similarity of their transcriptomic profiles with those of the recently