Diagnostic performance and reference values of novel biomarkers of heart failure in children and adolescents

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Introduction: Biomarkers play a pivotal role in the management of heart failure (HF). In adults, several parameters are known to provide accurate information on diagnosis, prognosis and treatment response. However, reference values and insights from validation studies in adults cannot be extrapolated to the paediatric age group as it differs substantially from the adult population in pathophysiology, comorbidity and compensatory reserve.
Our aim was to assess the diagnostic performance of 3 novel biomarkers in paediatric HF and to elucidate their accuracy differentially in patients with cardiomyopathy (CMP) and congenital heart disease (CHD), respectively. Reference data from healthy children are presented.
Methods: Mid-regional pro Atrial Natriuretic Peptide (MRproANP), sST2 and Growth Differentiating Factor 15 (GDF15) were measured cross sectionally in 111 HF patients and 87 controls (mean age 7.9 ± 5.9 years; range 5 days to 24 years). N terminal pro B Natriuretic Peptide (NTproBNP) was used as a reference standard. A receiver operating characteristic (ROC) was plotted to assess the diagnostic performance of the novel biomarkers alone or in combination with NTproBNP. This was performed in all patients and, separately, for subgroups of patients with CHD (n=68) and CMP (n=43). In 38 patients with dilated CMP, left ventricular ejection fraction (LVEF) and diastolic volume were measured by echocardiography or magnetic resonance imaging. Associations with biomarker levels were assessed by logistic regression analysis.
Results: MRproANP and NTproBNP showed good diagnostic accuracy in the general population as well as in the CMP and CHD subgroups. By contrast, GDF15 and sST2 did not perform sufficiently. None of the novel parameters improved the accuracy of NTproBNP alone when combined with it. In the subgroup with dilated CMP, only NTproBNP was associated with an impaired LVEF. Moreover, NTproBNP and sST2 were predictive of left ventricular dilatation.
Conclusions: MRproANP can detect HF with accuracy comparable to that of the reference standard, NTproBNP. This was was the case in, both, CHD and CMP as the causal diagnosis. By contrast, neither sST2 nor GDF15 were of any diagnostic usefulness, alone or in combination with NTproBNP.