Outcome in Paediatric Pulmonary Arterial Hypertension: a Systematic Review and Meta-Analysis

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Introduction: Current data on outcome and prognostic factors in children with pulmonary arterial hypertension (PAH) are derived from small patient series and contradictory findings have been reported. For the development of treatment strategies and guidelines, there is a high unmet need for an evidence-based recapitulation of prognostic factors. Therefore, the aim of this study was to combine the currently available data on prognostic factors in paediatric PAH by a systematic review of the literature and to summarize the prognostic value of currently reported prognostic factors using meta-analysis.

Methods: Medline, EMBASE and The Cochrane Library were searched at April 1st 2014 to identify original studies that described predictors of mortality or lung-transplantation exclusively in children with PAH. Titles and abstracts followed by full-text articles were screened by two independent reviewers. Eligible studies were required to report at least (1) data on mortality in paediatric PAH and (2) variables studied in relation to mortality. Hazard ratio’s (HR) and 95% confidence intervals (CI) were extracted or calculated from the papers. For variables studied in at least three non-overlapping cohorts, a combined HR was calculated using random-effects meta-analysis. Heterogeneity was assessed using Cohran’s Q-test and the I2-quantity.

Results: Of 1053 primarily identified articles, 25 were eligible for inclusion. In these paediatric studies, a total of 40 candidate prognostic factors was reported. 10 of these 40 candidate prognostic factors were studied in at least 3 cohorts, allowing for 10 separate meta-analyses involving up to 585 children. WHO-functional-class (HR=2.67, CI=1.49-4.80, p=0.001), (N-terminal-pro-) B-type natriuretic peptide (HR=3.24, CI=1.76-6.02, p<0.001), mean right atrial pressure (HR=1.12, CI=1.05-1.20, p=0.001), cardiac index (HR=0.66, CI=0.52-0.84, p=0.001), indexed pulmonary vascular resistance (HR=1.32, CI=1.17-1.48, p<0.001) and acute vasodilator response (HR=0.27, CI=0.14-0.54, p<0.001) were identified as significant prognostic factors in the absence of evidence for heterogeneity (Q-test p>0.10 and I2≤50% for all identified significant prognostic factors).

Conclusions: This systematic review combined with separate meta-analyses identifies 6 clinical variables that are consistently reported prognostic factors for outcome in paediatric PAH. These variables are useful clinical tools to assess prognosis and should be incorporated in treatment strategies and guidelines for the management of paediatric PAH.