Prevalence of genetic disorders in critically ill children requiring intensive care

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Introduction: Genetic disorders are among the most common causes of infant morbidity and mortality. Rapid advancements in whole genome sequencing (WGS) techniques enable the revision of diagnostic pathways with application of WGS as a first-tier test for critically ill children and the implementation of WGS in newborn screening (NBS). This monocentric retrospective study aims at evaluating the prevalence of genetic disorders in a German pediatric intensive care unit and the presumed diagnostic and therapeutic benefits of WGS for this patient group.

Methods: To achieve this goal, we evaluated comprehensive health data of critically ill children aged < 7 years, who required intensive care for at least 24 hours in the years 2017-2019.

Results: Of the 809 evaluated children, 238 (29.4%) were found to have a confirmed (n=136; 16.8%) or suspected (n=102; 12.6%) genetic disorder. The group of patients with a genetically confirmed diagnosis covered a broad spectrum of etiologies and clinical symptoms. More than half of them (n=76; 55.9%) were already symptomatic at birth (median age at disease onset 0 days, range 0-2083), but diagnostic delays were high (median delay 77 days, range 0-1888) regardless of age at first symptoms. Mathematic modeling elucidated that time to diagnosis would have been shortened by both (ultra-)rapid WGS in symptomatic children and WGS-based NBS (in up to 75% respectively 64% of cases).

Conclusion: (Ultra-)rapid WGS in combination with WGS for NBS should be considered a powerful two-pronged public health strategy to shorten diagnostic pathways for children with life-threatening genetic disorders, thereby improving health and guiding therapeutic decision-making.