

Theoretical Diagnostic Yield of a Rapid, Targeted Genetic Panel for Critically Ill Pediatric Patients and Newborns

Background

- In pediatric and neonatal intensive care units (PICUs/NICUs), rapidly identifying the cause of a newborn's illness is important for guiding healthcare management and improving health outcomes.
- Genetic disorders are a leading cause of infant mortality in NICUs.¹ Rapid exome (ES) and genome (GS) sequencing methods are increasingly being used in NICU/PICU settings, but these options are costly and may yield secondary findings.
- As an alternative to ES/GS, the investigators had previously developed a rapid, targeted genetic panel of 1,722 genes associated with congenital disorders.
- **Objective:** In this study, the investigators conducted a retrospective literature review to evaluate the theoretical diagnostic yield of the 1,722-gene panel compared to ES/GS.

Methods

- A retrospective literature review was conducted to identify ES and GS studies of predominantly pediatric and newborn populations.
- Genes with pathogenic or likely pathogenic variants in the identified studies were compared to those on the 1,722-gene panel.
 - The following were excluded: diagnoses of chromosome abnormalities and copy-number variants owing to inconsistent screening and reporting, and carrier status that did not contribute to a patient's phenotype.

Results

- Six ES and 3 GS studies were identified; cohorts ranged from 10 to 526 patients. Seven studies included patients 0 to 2 years of age²⁻⁸; 2 studies included patients up to adulthood.^{9,10}
- The theoretical diagnostic yield of the 1,722-gene panel was
 - 80% to 100% relative to individual ES studies
 - 90% to 100% relative to individual GS studies
- When ES and GS study data were combined, theoretical yield was
 - 85% when patients of all ages were included
 - 87% when patients 0 to 5 years of age were included
 - 89% when patients ≤ 1 year of age were included

Conclusions

- The theoretical diagnostic yield of the 1,722-gene panel suggests the panel may serve as an alternative to ES and GS for patients in PICU/NICU settings, especially in the age cohort (≤ 1 year of age) that the panel was designed for testing.
- A direct comparison of the gene panel to rapid ES and GS in newborns is warranted to determine the actual diagnostic yield of the panel. Future studies may also assess cost savings, time of detection, and clinical utility of the panel.

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