

**Mitochondrial Disorders at Lurie Children's Hospital:
Addressing the Need for a Comprehensive Database**
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Background: Mitochondrial medicine is in an era of rapidly expanding knowledge. Mitochondrial disorders are now known to be one of the commonest forms of inherited disease. The genotypic and phenotypic heterogeneity of these disorders is extensive, encroaching on the level of precision medicine. Efficient characterization of these complex disorders is a barrier to the continued growth of the field, such as the eventual development of targeted therapeutics.

Objectives: 1) Demonstrate the need for a comprehensive database of patients with mitochondrial disorders at Lurie Children's Hospital (LCH). 2) Define a cohort of patients with mitochondrial disorders at LCH. 3) Create a database integrating hospital, clinical and genetic information for this cohort. 4) Conduct initial analysis of the data to characterize the clinical severity of mitochondrial disorders.

Design/Methods: This is an IRB approved retrospective review of specific patient charts within the LCH Epic database from 1986-2018. 1) An initial search was conducted using ICD codes referring to possible mitochondrial disorders. 2) A second search word-matched a two-clinician derived list of mitochondrial disease terms within problem and diagnosis lists. Resulting charts were divided into two categories – those detected using specific mitochondrial terms versus broad metabolic terms. Three clinicians reviewed the resulting charts and classified them by likelihood of true mitochondrial disease based on clinical impression documented by experts and genetic testing results. The charts were then re-grouped into true mitochondrial disease (Mito+) and non-mitochondrial disease (Mito-). 3) Specific hospital, clinical, and testing information for these groups was compiled. 4) A severity scoring tool was designed by two clinicians; data analysis (Chi square, Kaplan-Meier) was conducted using Microsoft Excel.

Results: 1) There are more than 46 described mitochondrial diseases; only 9 ICD codes specifically refer to such diagnoses. The use of these codes has increased >15-fold over the past 30 years at LCH. Search by ICD code resulted in 2,588 patients with possible mitochondrial disorders. 2) Search by word matching within problem and diagnosis list resulted in 548 patients. On three clinician review, 79 of 332 (23.8%) charts resulting from the use of specific mitochondrial terms were Mito+, whereas 2 of 216 (0.93%) charts resulting from the use of broad metabolic terms were Mito+, $p < 0.01$. Specific mitochondrial term search had a sensitivity of 97.5% (specificity 48%, PPV 25.4%, NPV 99.1%). 3) We created a database of 81 Mito+ and 446 Mito- that includes genetic information as well as a range of clinical descriptors. 4) Chi-square analysis demonstrates Mito+ is significantly more clinically severe (46%) than Mito- (25%), $p < 0.01$. Twenty-year survival is significantly reduced in Mito+ (79%) versus Mito- (95%), $p < 0.01$.

Conclusions: 1) ICD code search is currently an inadequate method for detecting mitochondrial disease patients within the Epic database of LCH. 2) Searching Epic with specific language is a more sensitive technique for detecting such patients. 3) We have designed the first database of mitochondrial disease patients at LCH that integrates hospital, clinical, and genetic information. 4) Initial analysis demonstrates that mitochondrial disorders are significantly more clinically severe and have significantly reduced 20-year survival than the control population.