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Next Generation Sequencing Panel for Muscular Dystrophies and Hereditary Myopathies: Diagnostic Yield on Fifty-One Families from a Single Center Cross-Sectional Study

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Introduction and Objectives: Due to the great clinical and genetic heterogeneity of muscular dystrophies (MD) and hereditary myopathies (HM) next-generation sequencing (NGS) genetic studies might be cost and time-effective diagnostic approaches for these diseases. We aimed 1) to evaluate the diagnostic yield of a NGS panel of 39 genes, and 3) to provide insights about the epidemiological profile of MD/HM in Rio Grande do Sul, Brazil.

Material and Methods: Index cases from consecutive families with clinical/neurophysiological suspicion of MD/HM were recruited in this single center study. NGS panel of 39 frequent MD/HM related-genes was performed with Ion Torrent-PGM.

Results: Amongst the 51 index cases, we obtained an overall diagnostic yield of 64.7%(33/51), a definitive diagnosis in 39.2%(20/51) and at least a possible diagnosis in other 25.4%(13/51) cases. Diagnostic yield for limb girdle muscular dystrophy (LGMD) was 58.3%(14/24), with 6 LGMD2A(25%); 4 LGMD2B(16.6%) and 1 for each LGMD2D, LGMD2G, LGMD2K and 1 *RYR1*-related disorder. For congenital muscular dystrophy and myopathy the diagnostic yield was 66.6%(10/15), 2 cases of *RYR1*, 1 case of each *LAMA2, COL6A2, NEB, SEPN1* and *POMGNT1*-related disorders. For muscle diseases with prominent joint contractures, the diagnostic yield was 80%(8/10). There was no difference in the diagnostic yield of patients with family history/consanguinity from isolated cases.

Conclusions: A likely molecular diagnosis was obtained in almost two-thirds of index cases with the NGS panel, indicating that this should be a first-tier approach in the investigation for MD/HM. The most frequent types of MD/HM in Southern Brazil were LGMD2A and LGMD2B.

Keywords: Muscular dystrophies; Hereditary myopathies; Next generation sequencing panel;

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