discordant results and 6 with mimics (1 systemic disease, 2 congenital myasthenic syndromes and 2 neurogenic diseases), we had a cohort of 105 subjects with NGS-confirmed myopathy. The male-female ratio was 1.8 with a mean age of 20.55 ±13.82 (range 0 to 57) years. Family history was positive in 23 (21.9%) and consanguineous parentage was reported in 20 (19.04%). 58 (55.24%) patients had first-decade onset, 25 (23.81) second decade, while 22 (20.95%) had symptoms after 20 years of age. The most common genetic subgroups were limb girdle muscular dystrophies (36, 34.29%) with recessive mutations in all but 4. *DYSF* (10), *CAPN3* (9) and *SGCA* (4) were the most common recessive dystrophies. Dystrophinopathies with point mutations in 15, collagenopathies in 7, *GNE* in 10, *LMNA* in 3 and *TTN* in 2 constituted the other major dystrophies. Non-dystrophic myotonia and periodic paralysis syndromes were confirmed in 10 patients with SCN4A in 5, CLCN1 in 4 and CACNA1S in 1. Congenital myopathies were diagnosed in 14 (RYR1 in 5, MTM1 in 2, MYH2 in 2 being the commonest) and metabolic and mitochondrial myopathies in 9. Mutations were homozygous in 42 (40%), heterozygous in 25 (23.81 %), compound heterozygous in 22 (20.95%), hemizygous in 15 (14.29%) and homoplasmic in 1. Among a total of 127 variants, 45 (35.43%) were classified as pathogenic, 35 (37.56%) as likely pathogenic and 47 (37.01%) as VUS by ACMG criteria. Homozygous and compound heterozygous mutations were more commonly pathogenic or likely pathogenic. In this cohort of NGS-confirmed genetic myopathies, recessive variants in *DYSF*, *CAPN3*, *GNE*, *SGCA* and *RYR1* and hemizygous mutations in DMD were the most common. The overall yield of genetic testing and diagnostic yield for a pathogenic or likely pathogenic variant was to the tune of two thirds in the tested and genetically proven groups, respectively. Resources should be mobilized to reach the large subgroup that remains untested.

http://dx.doi.org/10.1016/j.nmd.2023.07.182

P183

The genetic profile of childhood neuromuscular disorders: a single center experience

O. Tezel [1], G. Öztürk [2], O. Ünver [2], H. Polat [3], A. Ayaz [4], S Aksoy Özcan [2], D. Türkdoğan [2]
[1] *Marmara University School of Medicine, Dept Paediatrics, Istanbul, Turkey;* [2] *Marmara University School of Medicine, Dept Paediatrics, Div Paediatric Neurology, Istanbul, Turkey;* [3] *Marmara Univ Sch Medicine, Dept Medical Genetics, Istanbul, Turkey;* [4] *İstanbul Medipol Univ Sch Medicine, Genetic Diseases Assessment Center, Dept Medical Genetics, Istanbul, Turkey*

Neuromuscular Diseases are a heterogeneous group of childhood disorders, and differential diagnosis can be challenging. Although there is no definitive treatment for the most of this group of diseases, early diagnosis is important with the development of new treatment methods. In this study, we aimed to draw attention to the importance of new generation genetic tests in diagnosing neuromuscular diseases. In this retrospective study, we reviewed the records of 800 patients with suspected neuromuscular diseases followed in the Neuromuscular Clinic of Marmara University Pendik Training and Research Hospital between December 2011 and January 2023 according to their demographic, clinical and genetic characteristics. Patients who were diagnosed with Duchenne muscular dystrophy and spinal muscular atrophy with targeted gene testing were excluded from the study. The results of targeted gene testing, clinical exome sequencing (CES), whole exome sequencing (WES) and mitochondrial genome analysis were analysed. Cases with positive results were classified as variants of unknown significance (VUS), likely pathogenic (LP), and pathogenic (P). A total of 349 patients were diagnosed with neuromuscular diseases. The classification was as follows: 163 (47%) had myopathy, 147 (42%) had neuropathy, 39 had myasthenia (11%). Genetic analysis was sent from 146 patients. Of these, 27 were single gene analysis, 81 were CES, 45 were WES, and 5 were mitochondrial genome analysis. A total of 114 patients (78%) had a specific diagnosis. 24 patients were diagnosed with single gene analysis, 52 patients with CES, 36 patients with WES, and 2 patients with mitochondrial genome analysis. The genetic results were reevaluated by two paediatric neurologists and a medical geneticist. The diagnostic rates of the genetic tests performed are 88%, 64%, 80% and 40%, respectively, when VUS results were included. The most common causative genes were PMP22 (10), CAPN3 (7), COLQ (7) and FXN (6). Genetic analysis has been shown to be very valuable and rapid in diagnosing neuromuscular diseases. Early genetic evaluation of patients who apply to the clinic with the suspicion of a neuromuscular disease is important as it will shorten the diagnosis process, eliminate the need for painful procedures such as muscle biopsy or needle EMG, which the paediatric patient group avoids, and enable rapid initiation of treatment in selected patients. We believe that this result can be strengthened by more extensive studies on next generation genetic analysis in neuromuscular diseases.

http://dx.doi.org/10.1016/j.nmd.2023.07.183

P184

Revealing myopathy spectrum: integrating transcriptional and clinical features of human skeletal muscles with varying health conditions

H. Zhong [1], M. Johari [2,3], S. Katayama [2,4], A. Oghabian [2,5], V. Sian [6], P. Jonson [2,7], P. Hackman [2,8], M. Savarese [2,7], B. Udd [2,9]
[1] *Huashan Rare Disease Center and Dept Neurology, Huashan Hospital, Fudan University, Shanghai, China;* [2] *Folkhälsan Research Center, Helsinki, Finland;* [3] *Harry Perkins Inst Med Res, Nedlands, Australia;* [4] *Dept Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden;* [5] *Obesity Research Unit, Research Program for Clin & Molec Metabolism, Fac Medicine, Univ Helsinki, Finland;* [6] *Dept of Precision Medicine, "Luigi Vanvitelli" Univ Campania, Naples, Italy;* [7] *Dept Medl & Clin Genetics, Univ Helsinki, Finland;* [8] *Medicum, Univ Helsinki, Finland;* [9] *Tampere Univ Hosp Dept of Musculoskeletal Diseases, Tampere, Finland*

The rarity of different myopathies has limited the scope of myopathy studies. Many published myopathy data, which are scattered in different databases, remains to be integrated. To address this issue, this study aimed to integrate local and online human skeletal muscle data and explore the relationships between transcriptional data and corresponding clinical features. A total of 1221 bulk RNA-sequencing (RNA-seq) data from human skeletal muscles were integrated from three sources: GTEx database (n = 803), GEO database (n = 291), and Helsinki (n = 127). The phenotypes included 15 different myopathies and 8 controls with varying health conditions, with 9231 muscle-related genes analysed. Techniques including batch adjustment, dimensional reduction, and tissue deconvolution were applied to analyse the dataset. Integration visualization explicitly exhibited a continuous spectrum ranging from very healthy muscles to diseased, wasting, and myopathy muscles. This spectrum order consistently preserved when clinical features (e.g., MRI fat quantification, pathology scores, CTG repeats, and functional scores) were mapped to different myopathies, which was validated in facioscapulohumeral muscular dystrophy (n = 60), congenital myotonic dystrophy (n = 29), and limb-girdle muscular dystrophy R12 (n = 41). Tissue deconvolution utilizing two different muscular single-cell datasets (52804 cells) revealed more fibrosis/immune infiltration and less vasculature in myopathy muscles. By selecting pathologically healthier muscles from fast death (e.g., car accident) donors (n = 234) from the GTEx database as unprecedented controls, common and unique pathways of different myopathies were revealed in differential expression analyses. In conclusion, this integration study proves the continuous process of myopathy progression and provides a new perspective to investigate myopathies.

http://dx.doi.org/10.1016/j.nmd.2023.07.184

P185

Global carrier frequency and genetic prevalence of autosomal-recessive genetic neuromuscular disorders

S. Kim [1], J. Park [2], H. Park [1], Y. Choi [1]
[1] *Department of Neurology, Gangnam Severance Hospital, Yonsei University College of Medicine, Eonju-ro, Gangnam-gu, South Korea;* [2] *Departments of Neurology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, South Korea*

Genetic neuromuscular disorders (NMDs) are clinically and genetically heterogeneous disorders that primarily affect peripheral nerve, muscle, and neuromuscular junctions. Epidemiological investigations for rare diseases are performed using the clinical and genetic information of patients. However, recent studies have been conducted to estimate the prevalence of autosomal-recessive Mendelian disorders based on the carrier frequency using a huge amount of genetic information of the general population. In this study, we analyzed carrier frequency and predicted genetic prevalence of autosomal-recessive NMDs to use genetic information from the Genome Aggregation Database (gnomAD). We selected 270 autosomal-recessive NMD genes based on GeneTable of neuromuscular Disorders (https://musclegenetable.fr). We found 336,273 DNA variants on the gnomAD v2.1.1 (https://gnomad.broadinstitute.org/). Then, we collected information about each of the variants from scientific literatures, ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/), HGMD (http://www.hgmd.cf.ac.uk/ac/), and LOVD (https://databases.lovd.nl/shared/genes) regarding the following parameters: segregation analysis (was it performed? was the family size large enough?), availability of biochemical analyses supporting pathogenicity, presence of the variant in patients vs. controls, and biallelically vs. monoallelically. The following groups were included in the manual analysis: truncating variants with allele frequency >0.005, truncating variants affecting the beginning or the end of the ORF, and nontruncating variants with contradicting predictions in Databases such as HGMD, ClinVar, and LOVD. We identified pathogenic/likely pathogenic variants according to the guidelines of American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Then, we assessed carrier frequency and predicted genetic prevalence of pathogenic variants in autosomal-recessive NMDs. We identified 11,110 gnomAD pathogenic variants including 3,885 variants in literature and 7,225 novel variants. The total carrier frequency was 17.0% and the