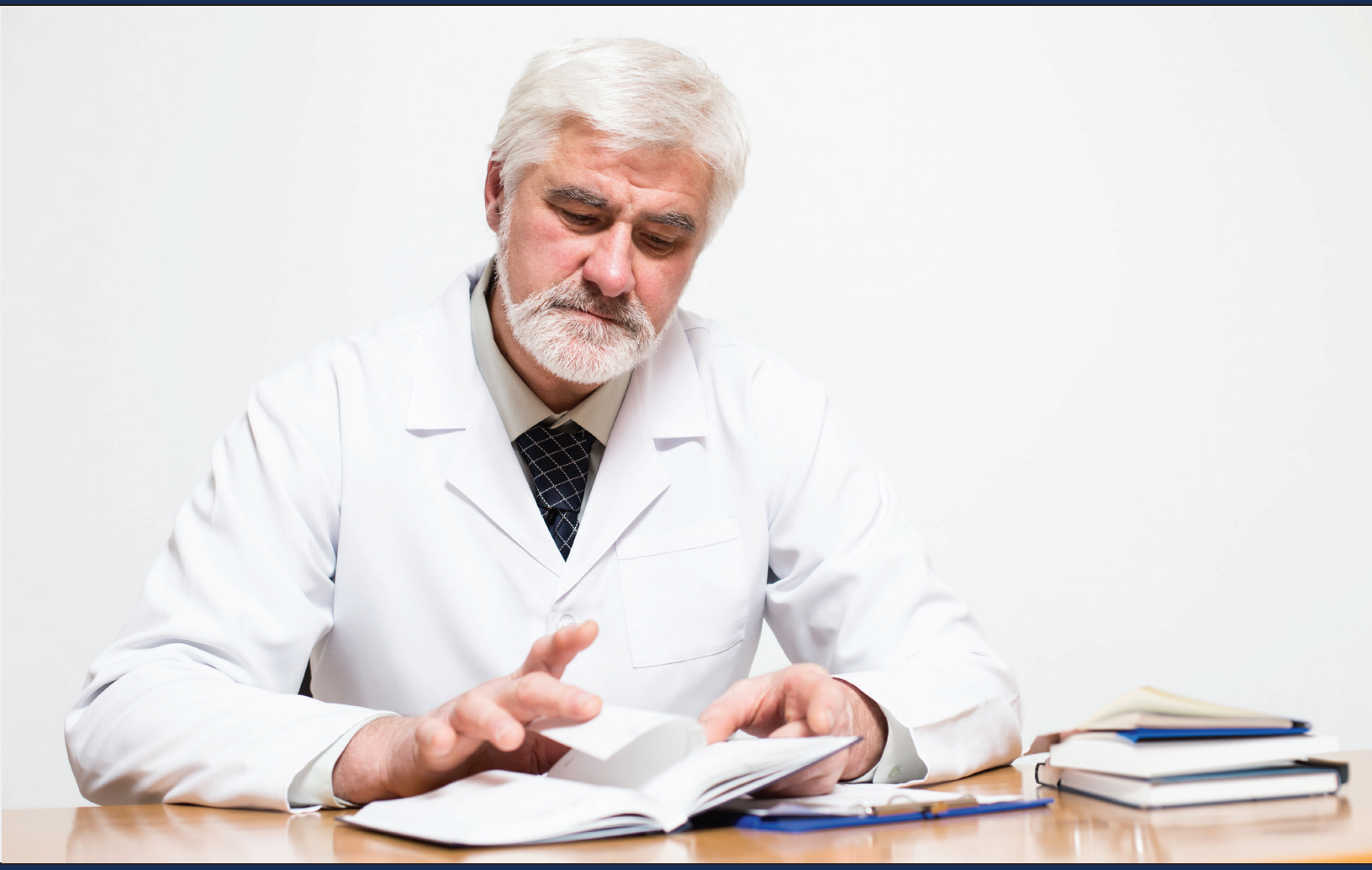
News Science Anthology

January - December 2023



Article Summaries From the
AANEM News Science Editorial Board

AANEM
American Association of Neuromuscular

News Science
Editorial Board

Anthology of NSEB Journal Article Summaries and Comments
January - December 2023

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Jan. 11, 2023

Hetherington-Rauth M, Magalhães JP, Alcazar J, et al. Relative sit-to-stand muscle power predicts an older adult's physical independence at age of 90 yrs beyond that of relative handgrip strength, physical activity, and sedentary time: A cross-sectional analysis. *Am J Phys Med Rehabil.* 2022;101(11):995-1000. doi:10.1097/PHM.0000000000001945

Submitted by: Joshua Wilson, MD

Edited by: Nakul Katyal, MD

Summary: Functional decline associated with advanced age results in significant morbidity and mortality, in addition to increased demand on healthcare systems. Models and testing to predict functional decline help healthcare systems direct resources to vulnerable individuals that are at risk of future loss of independence.

The authors build on previous studies showing muscle power to be a greater predictor of age-related decline compared to evaluation using muscle strength or mass-based metrics. Using a cross-sectional study of 1,748 Portuguese adults over > 65 years old, they conducted multi-logistical regression analysis to compared standardized handgrip strength, sit-to-stand (STS) and sedentary time as predictors of moderate-high function at 90 years of age using the Composite Physical Functional (CPF) scale. Power analyses found that relative STS power assessment was a stronger predictor of anticipated independence at the age of 90 compared to sedentary time and commonly used handgrip testing.

They compared relative STS power quartiles demonstrating a graded response with prediction of a moderate-high functioning status at the age of 90. With an odds ratio up to 11.48 using the 4th quartile of relative STS strength.

Using receiver operator characteristic curve analysis, they determined optimal cut-off values for relative STS power based on both sex and age that would predict independence at the age of 90. From this analysis, they derived an equation using individual age, gender, and relative STS power to predict the risk of losing independence later in life.

Comments: The authors cite that their findings were limited by being a cross-sectional study, and their reliance on using CPF self-reported scales. They believe that they have shown that relative STS strength out-performed handgrip as predictor for age associated functional decline. Furthermore, their analysis provided optimized cutoffs to screen individuals for future functional decline.

This study provided benefit by helping to establish a screening test that is easy to use and does not require the use of specialized equipment. Areas for further exploration would include the use of prospective studies to assess the outcomes of this predictive model once the individuals have reached the age 90. If use of relative STS power were to be shown to successfully predict independence in advanced age, then future studies should focus on modalities and timing of interventions to prevent such functional declines.

Article of Similar Interest: Alcazar J, Alegre LM, Van Roie E, et al. Relative sit-to-stand power: aging trajectories, functionally relevant cut-off points, and normative data in a large European cohort. *J Cachexia Sarcopenia Muscle.* 2021;12(4):921-932. doi:10.1002/jcsm.12737

Damato V, Spagni G, Monte G, et al. Clinical value of cell-based assays in the characterisation of seronegative myasthenia gravis. *J Neurol Neurosurg Psychiatry.* 2022;93(9):995-1000. doi:10.1136/jnnp-2022-329284

Submitted by: Pritikanta Paul, MD

Edited by: Nakul Katyal, MD

Summary: Although autoantibody testing is critical for the diagnosis of myasthenia gravis (MG) in current clinical practice, the test can be negative in up to 10% of cases of generalized MG and up to 50% of cases of ocular MG. These seronegative patients often have delayed diagnosis and potentially can have an erroneous diagnosis. A cell-based assay (CBA) can improve the diagnostic yield of the antibody testing when compared to standardized commercially available radioimmunoassay (RIA) but it is mostly restricted to research institutions. This study retrospectively looked at consecutive MG patients in a single tertiary referral center to assess the clinical significance of CBA approach and compared with cases positive for AChR and MuSK tested by RIA.

Stored sera of 82 patients with diagnosis of seronegative MG (SNMG) were tested by live-CBA. Nearly one-third (N=23) tested positive for either AChR or MuSK antibodies, but none tested positive for LRP4. CBA- positive AChR patients were majority early-onset (<50 yrs age), frequently ocular, and most had mild disease course when compared with RIA-positive AChR patients. CBA- positive MuSK antibodies had milder disease course than RIA-positive MuSK cases. Patients who received early immunotherapy achieved a better outcome than those in whom immunotherapy was delayed.

Some of the major limitations of the study include retrospective nature, testing of samples of patients while on immunotherapy, as well as limited data on the genetic testing for the seronegative patients. However, this study highlights the importance of including CBAs in diagnostic workup for MG.

Comments: While use of live-CBAs is currently restricted to research settings currently, given the requirement of expertise and cell-culture facilities, a fixed-CBA could be a reasonable alternative based on a recent study. Further well designed studies are required to explore the diagnostic utility and feasibility of CBA in MG diagnosis without use of radiolabeled ligands.

Article of Similar Interest: Spagni G, Gastaldi M, Businaro P, et al. Comparison of Fixed and Live Cell-Based Assay for the Detection of AChR and MuSK Antibodies in Myasthenia Gravis. *Neurol Neuroimmunol Neuroinflamm.* 2022;10(1):e200038. Published 2022 Oct 21. doi:10.1212/NXI.0000000000200038

Feb. 22, 2023

Prada V, Laurà M, Zuccarino R, Reilly MM, Shy ME. Virtual charcot-marie-tooth examination score: A validated virtual evaluation for people with charcot-marie-tooth disease. *Neurol Clin Pract.* 2022;12(5):e98-e104. doi:10.1212/CPJ.0000000000200070

Submitted by: Nakul Katyal, MD

Edited by: Eman Tawfik, MD

Summary: The Charcot-Marie-Tooth (CMT) Examination Score Version 2 (CMTESv2) is used in clinical practice to measure impairment in patients with CMT. However, the CMTES requires an in-person visit, which may not be possible for all CMT patients. This study evaluated a virtual form of CMTES (vCMTES) as a remote clinical outcome assessment tool to measure impairment in CMT patients. The pinprick and vibration domains of CMTESv2 are replaced with light touch and position sensation in the vCMTES. The patient can perform these domains remotely either independently or with the help of an assistant while being observed by the clinic evaluator.

Sixty-four patients with genetically confirmed CMT were evaluated using the vCMTES and CMTESv2 scale, in-person and remotely. During the first in-person visit, both CMTESv2 and the vCMTES scales were performed. Fifty-three patients were re-evaluated virtually 3 weeks after the initial examination. Moreover, 10 patients were evaluated virtually twice by two different evaluators, 5 days apart to evaluate intra-examiner variability and for test-retest assessment. CMTESv2 correlated strongly with the vCMTES conducted both in-person and virtually ($p < 0.0001$) and similar results were obtained comparing symptoms score items, sensory items, and motor items. The authors concluded that vCMTES was reproducible and reliable as a clinical outcome assessment for CMT.

Comments: The strong correlation that was observed in this study between the vCMTES and conventional CMTSv2, conducted in-person and virtually denotes that vCMTES could serve as a reliable outcome assessment measure. However, further studies are needed to assess its reproducibility with disease progression and different CMT subtypes.

March 8, 2023

Kim KH, Kim SW, Cho J, Chung HY, Shin HY. Anti-titin antibody is associated with more frequent hospitalization to manage thymoma-associated myasthenia gravis. *Front Neurol.* 2022;13:978997. Published 2022 Oct 5. doi:10.3389/fneur.2022.978997

Submitted by: Nakul Katyal MD

Edited by: Eman Tawfik, MD

Summary: Anti-titin antibodies are anti-striational antibodies associated with thymoma-associated myasthenia gravis (MG). Anti-titin antibodies have been previously linked to severity of MG, but its relation to clinical worsening is not clear. Thus, the authors in this study aimed to evaluate whether the patients with anti-titin antibody are more frequently hospitalized to manage thymoma-associated MG than those patients without anti-titin antibody.

Patients with thymoma-associated MG who were tested for anti-titin antibody were retrospectively included. Parameters including disease severity, treatments, MG-related annual hospitalization rate, and emergency room visit rate were compared between the patients with anti-titin antibody and those without anti-titin antibody.

Thirty-one (48.4%) of the 64 included patients were positive for anti-titin antibody (titin+ group) and 33 (51.6%) patients were negative (titin- group). A total of 92 hospitalizations and 52 ER visits were observed during the study period. Main cause of MG-related admission was symptom aggravation (97.8%), followed by management of medication toxicity (2.2%), while the main cause of MG-related ER visit was dyspnea or chest discomfort (61.5%), followed by limb weakness (19.2%) and bulbar symptoms (9.6%).

The annual rate of MG-related hospitalization and ER visit were significantly higher in the titin positive group [0.2 (0.1-0.6) and 0.1 (0-0.2) per year, respectively] than those in the titin negative group [0 (0-0.2) and 0 (0-0) per year, $p = 0.004$ and $p = 0.006$, respectively]. Positive anti-titin antibody was significantly associated with multiple admissions [odds ratio (OR) 4.11, 95% CI 1.05-16.03] compared to the titin negative group.

Comments: Although the association of anti-titin antibody and thymoma is well reported, controversy remains in the association between the presence of anti-titin antibody and the severity of MG. In this study, the authors observed that the presence of anti-titin antibody is associated with more frequent hospitalization and ER visits. Thus serological testing of anti-titin antibody can be utilized as a clinical indicator of disease relapse. However, given the study limitations which include the retrospective nature and the non-uniformity of timing of antibody testing, further studies are required to elucidate a causal relationship between the anti-titin antibody positivity and hospitalization associated with MG.

March 22, 2023

Zhang X, Kira JI, Ogata H, et al. Anti-LGI4 antibody is a novel juxtaparanodal autoantibody for chronic inflammatory demyelinating polyneuropathy. *Neurol Neuroimmunol Neuroinflamm*. 2023;10(2):e200081. Published 2023 Jan 11. doi:10.1212/NXI.0000000000200081

Submitted by: Pritikanta Paul, MD

Edited by: Nakul Katyal, MD

Summary: In this single-centered study, 113 anti-NF155 and anti-CNTN1 antibody–negative chronic inflammatory demyelinating polyneuropathy (CIDP) patients were enrolled and the reactivity of sera from these patients against mouse dorsal root ganglion (DRG) and sciatic nerves was surveyed. The objective of this was to identify novel nodal autoantibodies in CIDP. Western blotting, indirect immunofluorescence, and cell-based RNA interference assays were used to identify target antigens. Sera from four patients reacted to juxtaparanodal regions of nodes of Ranvier in the sciatic nerve fibers and DRG satellite glia. Majority of these antibodies were IgG4 type. The identified candidate antigen was leucine-rich repeat LGI family member 4 (LGI4). The authors noted, patients with anti-LGI4 antibody positivity tended to have relatively old age at onset with subacute presentation involving both motor and sensory and very high levels of CSF protein. Intravenous immunoglobulin (IVIG) was only partially effective.

The authors concluded a small proportion of patients with CIDP have IgG4 antibodies against LGI4 have subacute onset of symptoms mimicking Guillain-Barré syndrome but have severe sensory impairment in addition to weakness.

Comments: This study identifies a novel nodal autoantibody in CIDP. That adds to our knowledge on autoimmune nodopathies, and warrants further studies to elaborate on these findings.

April 5, 2023

Karasu AU, Karataş L, Yıldız Y, Günendi Z. Natural course of muscular strength, physical performance, and musculoskeletal symptoms in hospitalized patients with COVID-19. *Arch Phys Med Rehabil.* 2023;104(1):18-26. doi:10.1016/j.apmr.2022.09.001

Submitted by: Joshua Wilson, MD

Edited by: Nakul Katyal, MD

Summary: The clinical presentation of acute novel coronavirus 19 (COVID-19) is often quite heterogeneous ranging from asymptomatic infections to acute hypoxic respiratory failure. COVID has been shown to impact multiple tissue types leading to widespread multi-organ dysfunction. Furthermore, the acute illness can be followed by a prolonged convalescent period with persistent symptoms of cough, fatigue, generalized weakness, and muscle pain, part of a so-called "long haul COVID."

The study's authors investigated the long-term effects of COVID in 76 adult patients (aged >18 years) admitted to the hospital with confirmed COVID infections. Participants were separated by disease severity into mild, moderate, and severe infections based on clinical and radiographic findings. Factors such as the fraction of inspired oxygen (FiO2), oxygen saturation (SpO2), hand grip strength (HGS), five times sit-to-stand test (5XSTS), modified borg scale for rest and activities of daily living (mBorg-rest, mBorg-ADL), Barthel index and myalgia- VAS score were compared at baseline, one week, three weeks and 12 weeks.

At baseline, there was a significant difference in FiO2, SpO2, 5XSTS, mBorg-rest, and mBorg-ADL between disease severity groups. Within-group analysis showed significant improvement with time in moderate and severe disease groups, including HGS, 5XSTS, mBorg-rest, and mBorg-ADL. At the 12-week follow-up, FiO2 and m-borg rest and ADL scale differences between groups resolved; however, differences remained with 5XSTS and SpO2.

The results of the study show that acute coronavirus infection impacts oxygen saturation, requirements, perceived physical exertion, and physical performance. This difference was affected by disease severity. Fortunately, patients with higher levels of disease severity did show significant improvements, but at nearly three months post-infection, there remained deficits in physical performance.

Comments: Despite the reduction of COVID infections experienced by the global population, infections continue to spread at a basal rate. Identifying so-called long-haul COVID syndromes helps to characterize persistent physical impairments that limit patient reintegration into their daily activities and social roles. Studies such as this one help to highlight patient risk factors for developing persistent deficits that could help future target rehabilitative efforts.

April 19, 2023

Nishikawa Y, Holobar A, Watanabe K, et al. Detecting motor unit abnormalities in amyotrophic lateral sclerosis using high-density surface EMG. *Clin Neurophysiol.* 2022;142:262-272. doi:10.1016/j.clinph.2022.06.016

Submitted by: Eman Tawfik, MD

Edited by: Nakul Katyal, MD

Summary: In this study, the authors evaluated motor unit (MU) abnormalities in patients with amyotrophic lateral sclerosis (ALS) using quantitative non-invasive high density-surface EMG.

The inclusion criteria included patients with ALS diagnosed using the Awaji criteria and the needle EMG study showed motor unit action potentials (MUAPs) in their vastus lateralis. The control group included age-matched healthy volunteers. Patients with lower limb injury, dementia, myositis, spinal muscular atrophy, and dystonia were also included. The disease severity was graded using the ALS Functional Rating Scale-Revised (ALSFRS-R).

The high density surface EMG was recorded from the vastus lateralis 10 minutes after submaximal ramp-up contraction task. The EMG signal was recorded from the weaker side in ALS patients and from the dominant side in the control group while performing the ramp and hold contraction task (ramp up to 30% maximum volume contraction (MVC) in 15 s, sustained contraction for 15 s, and ramp down in 15 s). The number of motor units, mean firing rate, recruitment threshold (= the force level (%MVC) at the first firing of each MU, coefficient of variation of the MU firing rate (= the ratio of standard deviations and the mean values of the MU firing rates), MU firing rate at recruitment, and motoneurons excitability were calculated.

In ALS patients, the number of MUs were significantly lower and the mean firing rate, recruitment threshold, coefficient of variation of the MU firing rate, MU firing rate at recruitment, and motoneurons excitability were significantly higher, compared to the controls. Moreover, the number of MU, MU firing rate, recruitment threshold, and MU firing rate at recruitment were significantly correlated with disease severity. The findings denote compensatory increase in motorneuron excitability at recruitment secondary to neurodegeneration.

Comments: This article is interesting for several reasons: it demonstrates the pattern of firing rate abnormality in ALS patients and the feasibility of the using non-invasive surface EMG in detection of this abnormality, and highlights the relation between the firing rate abnormality and disease severity which may help in disease prognostication. The methodology is well-conducted, and the study has a practical implication.

May 3, 2023

Can Ebru Bekircan-Kurt, Megan A Waldrop, Anne M Connolly, Jerry R Mendell. Treatment for spinal muscular atrophy using onasemnogene abeparvovec. *touchREVIEWS in Neurology* 2022;18(2): 133-41.

Submitted by: Justin Willer, MD

Edited by: Eman Tawfik, MD

Summary: The article summarizes the development, safety, and efficacy of intravenously administered drugs using the Adeno-associated virus vector for spinal muscular atrophy (SMA) type 1 and intrathecal administration for SMA type 2.

The article discusses several clinical trials. The SART trial was groundbreaking. Based on its positive results, the FDA approved onasemnogene abeparvovec gene therapy for SMA on 24 May 2019. The STRIVE trial included patients aged 6 months or fewer with 1 or 2 copies of SMN2. Endpoints were independent sitting for > 30 seconds per Bayley-II at 18 months and survival at 14 months. Thirteen patients in the treatment group achieved sitting > 30 seconds versus none in the control group, and 18 patients did not use ventilatory support. On the other hand, the STRONG trial was performed to address the drug use in SMA-2. Patients were between 6 and 12 months and able to sit unassisted for 10 seconds but were not able to walk or stand. Patients were given prophylactic prednisolone (1 mg/kg/day) 24 hours prior to intrathecal delivery that was maintained for about 30 days. The STEER trial has now started in patients with SMN type 2.

The review also briefly discusses two additional pharmacologic agents, nusinersen and risdiplam, which are clinically approved as alternative treatments. Nusinersen is administrated intrathecally, and was approved by the FDA under the brand name Spinraza®. In the ENDEAR trial, it was found that a significantly higher percentage of infants treated with nusinersen had a motor milestone response.

Risdiplam is the only orally administered medication for SMA and is approved by the FDA under the name Evrysdi®. It is a pre-mRNA splicing modifier that increases production of the SMN protein. Its efficacy results from its unique SMN2 pre-mRNA binding sites: a 5' splice site in intron 7 and exonic splicing enhancer in exon 7. This increases levels of full-length SMN mRNA and protein. The authors conclude that risdiplam is an important alternative to nusinersen in patients with SMA type 1 for patients who cannot receive first line gene therapy (those with AAV antibodies).

Comments: This is an excellent article on the pathophysiology of SMA, the underlying genetic defects, and the basis for treatment with a review of the available agents.

May 17, 2023

Tan HHG, Westeneng HJ, Nitert AD, et al. MRI clustering reveals three ALS subtypes with unique neurodegeneration patterns. *Ann Neurol.* 2022;92(6):1030-1045. doi:10.1002/ana.26488

Submitted by: Raymond Rosales, MD, PhD

Edited by: Eman Tawfik, MD

Summary: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease in which patients are confronted with speech impairment, muscle wasting and weakness, and eventually respiratory insufficiency and death. The purpose of this study was to identify subtypes of ALS by comparing patterns of neurodegeneration using brain magnetic resonance imaging (MRI) and explore their phenotypes. The study included 488 ALS patients and 338 control subjects.

MRI clustering algorithm divided patients with ALS into three subgroups. All subgroups displayed involvement of the precentral gyrus, and each has a unique neurodegeneration pattern, and is associated with distinct clinical characteristics and cognitive profiles. The three subgroups are: (1) pure motor involvement (pure motor cluster [PM]), (2) orbitofrontal and temporal involvement (frontotemporal cluster [FT]), and (3) involvement of the posterior cingulate cortex, parietal white matter, temporal operculum, and cerebellum (cingulate-parietal–temporal cluster [CPT]).

Comments: With the increase in knowledge over the years, the remarkable heterogeneity of ALS is becoming more apparent in many aspects of the disease, such as the primary disease site, progression rate, the presence of cognitive and behavioral impairment, genetic predisposition, and pathophysiological processes. Life expectancy is also highly variable, ranging from a few months to more than 10 years. This heterogeneity means that providing an accurate prognosis is complicated for clinicians and, as a result, leaves patients with uncertainty about their future. To advance our understanding of ALS, it is crucial to get to the core of this heterogeneity because it seems highly likely that treatments will need to be tailored to individual patient characteristics. Neuroimaging may help shed the light on ALS heterogenicity as demonstrated in this study.

May 31, 2023

Sia T, Connors KA, Morgan P. Physical activity in people with motor neuron disease: Validity of the physical activity scale for the elderly as a measuring tool. *Arch Phys Med Rehabil.* 2023;104(1):102-107. doi:10.1016/j.apmr.2022.09.007

Submitted by: Rebecca O'Bryan, MD

Edited by: Eman Tawfik, MD

Summary: This prospective, observational study investigated the physical activity scale for the elderly (PASE) as a tool to measure physical activity in patients with motor neuron disease (MND). The PASE is a brief questionnaire that assesses the type, frequency, duration, and intensity of the physical activities chosen by the patient over the previous week to assign a score ranging from 0-793, with higher scores indicating greater physical activity.

The authors aimed to compare the PASE with amyotrophic lateral sclerosis functional rating scale (ALSFRS-R), and to identify the demographic and clinical factors that predict physical activity participation. The study included 190 patients with MND. The results showed that engagement of patients with MND in physical activity is generally low, with median PASE score of 57. The PASE had a fair-moderate correlation with ALSFRS-R (rho .607). The most frequently chosen physical activities for patients with MND were activities around home, and the biggest barrier to participation is fatigue.

Comments: This article suggests another tool to assess physical function in patients with MND. The study shows relationship to disease severity to be the strongest predictor of physical activity, which is to be expected. The suggested PASE tool being brief and easily administered facilitates its application in daily clinical practice.

June 14, 2023

Liu A, Jia X, Zhang L, et al. Diagnostic performance of preoperative ultrasound for traumatic brachial plexus root injury: A comparison study with an electrophysiology study. *Front Neurol.* 2023;13:1077830. doi: 10.3389/fneur.2022.1077830.

Submitted by: Nakul Katyal, MD

Edited by: Eman Tawfik, MD

Summary: This retrospective study aimed to investigate the diagnostic performance of preoperative ultrasound (US) compared with electrophysiology study (EPS) in the assessment of traumatic brachial plexus (BP) root injury. Patients with suspected traumatic BP root injury who underwent preoperative US and EPS examination were included in the analysis. Each BP root was assessed via US and EPS as either completely or incompletely injured.

A total of 49 patients with traumatic BP injury who underwent surgical exploration were included. Surgical exploration confirmed 89 completely injured BP roots in 28 patients, US correctly detected 80 completely injured BP roots (sensitivity, 0.899; specificity, 0.981; PPV, 0.964; NPV, 0.944; accuracy, 0.951), whereas EPS correctly detected 75 completely injured BP roots (sensitivity, 0.843; specificity, 0.929; PPV, 0.872; NPV, 0.912; accuracy, 0.898). The US showed significantly higher accuracy than EPS. When combining US and EPS for completely injured BP root detection, the sensitivity of the inclusive combination (US or EPS) was significantly higher than EPS alone, and the specificity of the exclusive combination (US and EPS) was significantly higher than EPS alone.

Comments: Preoperative assessment for traumatic BP injury is vital for clinicians to establish a treatment strategy. The electrodiagnostic studies play a pivotal role in this assessment, but US has emerged as a valuable complementary tool. However, literature comparing the diagnostic performance of US and EPS in patients with BP injury is limited. This study highlights the diagnostic accuracy of the US in detection of complete BP root injury, both in isolation and in combination with EPS. The results add to the growing body of literature supporting the use of neuromuscular US in clinical practice The main study limitations included the retrospective nature of the analysis and the inclusion of only severe BPI cases requiring surgical intervention. The performances of US or the combined use of US and EPS needs to be further investigated in a medium or minor level of BP injury.

June 28, 2023

Can Ebru Bekircan-Kurt, Megan A Waldrop, Anne M Connolly, Jerry R Mendell. Treatment for spinal muscular atrophy using onasemnogene abeparvovec. *touchREVIEWS in Neurology 2022*;18(2): 133-41.

Submitted by: Justin Willer, MD

Edited by: Eman Tawfik, MD

Summary: The article summarizes the development, safety, and efficacy of intravenously administered drugs using the Adeno-associated virus vector for spinal muscular atrophy (SMA) type 1 and intrathecal administration for SMA type 2.

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Risdiplam is the only orally administered medication for SMA and is approved by the FDA under the name Evrysdi®. It is a pre-mRNA splicing modifier that increase production of the SMN protein. Its efficacy results from its unique SMN2 pre-mRNA binding sites: a 5' splice site in intron 7 and exonic splicing enhancer in exon 7. This increases levels of full-length SMN mRNA and protein. The authors conclude that risdiplam is an important alternative to nusinersen in patients with SMA type 1 for patients who cannot receive first line gene therapy (those with AAV antibodies).

Comments: This is an excellent article on the pathophysiology of SMA, the underlying genetic defects, and the basis for treatment with a review of the available agents.

July 12, 2023

Lindgren U, Pullerits R, Lindberg C, Oldfors A. Epidemiology, survival, and clinical characteristics of inclusion body myositis. *Ann Neurol.* 2022;92(2):201-212. doi:10.1002/ana.26412

Submitted by: Raymond Rosales, MD, PhD

Edited by: Eman Tawfik, MD

Summary: In this study, the authors conducted a population-based study on inclusion body myositis (IBM) with the primary aims to define the disease prevalence, survival rate, and incidence, and to investigate the symptom profiles associated with disease duration and sex over a 33-year period. A total of 128 patients fulfilled the clinicopathological definition of IBM. The disease prevalence was 32 per million inhabitants, 19 per million women, and 45 per million men. The mean incidence was 2.5 per million inhabitants and year. Mean age at symptom onset was 64.4 years with quadriceps weakness being the most common presenting symptom followed by finger flexor weakness. Dysphagia was a common presenting symptom being more frequent in women (23%) than men (10%). The results also revealed decreased survival rate (mean survival was 14 years from symptom onset), and marked sex differences in both prevalence and clinical manifestations.

Autoantibodies to cytosolic 50-nucleotidase 1A were found in 40% of IBM patients and 3.6% of the controls. A total of 22% had one or more malignancies, compared to the risk of malignancy before 75 years of age in the Western Region, Sweden, during the years 2012 to 2016 of 30.6% for men and 28.3% for women.

Comments: Due to the protractive course and lack of response to immunosuppressive treatment, IBM has a major impact on the activity of daily living in a substantial group of elderly individuals. This emphasizes the importance of knowledge of the diagnosis and typical symptoms and signs to decrease the frequent marked delay in disease diagnosis. Increased awareness of treatable common complications, such as swallowing problems and respiratory dysfunction, as well as sex differences, is important and may improve the impaired survival rate.

July 26, 2023

Reyes-Leiva D, López-Contreras J, Moga E, et al. Immune response and safety of Sars-Cov-2 Mrna-1273 vaccine in patients with myasthenia gravis. *Neurol Neuroimmunol Neuroinflamm.* 2022;9(4):e200002. Published 2022 Jun 21. doi:10.1212/NXI.0000000000200002

Submitted by: Nakul Katyal, MD

Edited by: Eman Tawfik, MD

Summary: This prospective study investigated the safety profile of mRNA-1273 vaccine and its ability to induce humoral and cellular responses in patients with myasthenia gravis (MG).

The study included 100 unvaccinated patients with stable MG scheduled for mRNA-1273 vaccine during the vaccine campaign from April to November 2021. Patients with significant clinical or therapeutic changes in the previous 6 months were excluded. The primary outcomes were clinically significant changes in MG symptoms after vaccination, adverse events (AEs), and seroconversion and T-cell immune response rates. The MG activities of daily life (MG-ADL) score was recorded at baseline and 1 week after the first and second doses. Humoral and cellular immune responses after vaccination were assessed using a spike-antibody ELISA and interferon gamma release assay in plasma.

Ninety-nine patients completed the full vaccination schedule, and 98 had 2 blood samples taken. A statistically significant worsening of symptoms was identified after the first and second doses of the mRNA-1273 vaccine, but this was not clinically relevant and was self-limited (Mean MG-ADL at baseline 2.34 (3.22), 1 week post first dose: 2.65 (3.52), 1 week post second dose: 2.72 (3.57; n= 99). Mild AEs occurred in 14 patients after the first dose and in 21 patients after the second dose. Eighty-seven patients developed a humoral response, and 72 patients showed a T-cell response after vaccination. A combined therapy with prednisone and other immunosuppressive drugs correlated with a lower seroconversion ratio and a lower T-cell response ratio.

Comments: Evidence regarding the safety and efficacy of mRNA vaccines in patients with MG after immunosuppressive therapies is limited. Physicians often come across the question of COVID vaccine's safety in patients with MG and its efficacy in patients with autoimmune disease taking immunosuppressive therapies. This article provides class IV evidence regarding safety of mRNA-1273 vaccination in patients with MG. Most of the patients achieved high cellular or immune response levels. The main study limitations are the lack of a control group and the exclusion of patients with recent clinical or therapeutic changes.

Aug. 9, 2023

Keller CW, Chuquisana O, Derdelinckx J, et al. Impaired B cell expression of the inhibitory Fcγ receptor IIB in myasthenia gravis. *Ann Neurol.* 2022;92(6):1046-1051. doi:10.1002/ana.26507

Submitted by: Raymond Rosales, MD, PhD

Edited by: Eman Tawfik, MD

Summary: Myasthenia gravis (MG) is an autoimmune disease in which pathogenic immunoglobulin G antibodies (Abs) bind to acetylcholine receptors (AChR) (or to functionally related molecules at the neuromuscular junction). B cell expression of the inhibitory immunoglobulin G receptor, Fc-gamma receptor (FcγR) IIB, maintains peripheral immune tolerance, and its absence renders B cells hyper-responsive to auto-antigen. In this study, the authors report that FcγRIIB expression levels are substantially reduced in B lineage cells derived from immunotherapy-naïve patients with ACHR-AB+ early-onset MG. In contrast, genetic variants associated with impaired FcγRIIB expression are not enriched in MG, indicating posttranscriptional dysregulation. The authors suggest that FcγRIIB-targeting therapies could have therapeutic benefits in AChR-Ab+ MG.

Comments:

1. The present study provides evidence for lower expression of the inhibitory FcγRIIB on B lineage cells in AChR-Ab+ patients with early-onset MG.
2. The present results warrant further investigations; for example, to correlate FcγRIIB expression profiles with clinical disease severity parameters in larger cohorts of MG subtypes.
3. The unique inhibitory features of the B cell inhibitory Fcγ R can be exploited by novel therapeutic platforms, such as B-specific Abs, which crosslink the Fcγ RIIB with BCR complex-associated molecules, such as CD19 or CD79B. These strategies were found to highly effective in suppressing humoral autoimmunity and disease development in animal models.

Aug. 23, 2023

Kim GM, Powell JE, Lacey SA, Butkus JA, Smith DG. Current and emerging prostheses for partial hand amputation: A narrative review. *PM R.* 2023;15(3):392-401. doi:10.1002/pmrj.12764

Submitted by: Oksana Sayko, MD

Edited by: Pritikanta Paul, MD

Summary: Partial hand amputation leads to significant impacts on a person's life, causing a wide range of functional losses. Various partial hand prosthetic devices exist, differing in function and appearance. However, there is no ideal replacement for the lost hand. Often, those with partial hand amputation need multiple prosthetic devices. This review examines and compares different prosthetic choices, including passive, body-powered, activity-specific, and externally powered options.

Passive prostheses do not provide active movement but are designed to look like natural hand and fingers. Although passive partial hand prostheses lack active movement, such as a grip or release, they still do provide support for pushing, pulling, or holding objects. Realistic silicone partial hand prostheses can offer impressive cosmetic results. They are offered by various companies and are typically suction fitting.

Among trans-radial amputees, there is an abundance of activity-specific prosthetic tools utilized for activities of daily living, sports, and occupation.

Body-powered prostheses harness power from the residual limb using a system of cables, spring, and harnesses. Loss of function from multiple digital amputations or partial hand amputation presents unique challenges for prosthetic design and implementation, and this is frequently addressed using body-powered prostheses. Some body-powered prostheses are driven by the residual hand itself, rather than a more proximal aspect of the limb.

Externally powered prostheses utilize motor and batteries to provide movement and power to the prosthesis. Although externally powered prosthetic hands have been commercially available for decades, externally powered digit systems have been challenged by their innate spatial limitations. The externally powered prosthesis typically allows substantially stronger grip strength with less physiological cost on the surrounding joints. This type of prostheses typically uses signals from the user's muscle activation to predict their intention to control the hand. Among the commercially available ones, surface electromyography (EMG) or myoelectrode, is more frequently used due to its portability and non-invasiveness.

Comments: To choose the best prosthesis amongst many options for patients with partial hand amputation, it is vital to consider the patient's current functional levels, impact of the aesthetic loss and disfigurement, and desired functional and aesthetic goals while being cognizant of the benefits and limitations. Individuals with partial hand amputation may need multiple devices to address their needs. Finally, it is important to work in a multidisciplinary setting with physiatrists, hand surgeons, occupational therapists, and prosthetists.

Sept. 6, 2023

Sharma P, Naglah A, Aslan S, et al. Preservation of functional descending input to paralyzed upper extremity muscles in motor complete cervical spinal cord injury. *Clin Neurophysiol.* 2023;150:56-68. doi:10.1016/j.clinph.2023.03.003

Submitted by: Eman Tawfik, MD

Edited by: Pritikanta Paul, MD

Summary: According to the widely used American Spinal Injury Association (ASIA) impairment scale (AIS), complete spinal cord injury (SCI) is characterized by complete absence of sensory and motor function below the injury level. However, voluntary activation of paralyzed lower limbs muscles in patients with complete SCI has been previously observed. Whether similar activation of paralyzed upper limb muscles in complete cervical SCI is possible or not has not been proven.

In this study, the authors investigated neurophysiological evidence of motor involvement in clinically paralyzed muscles in patients with complete cervical SCI using surface EMG.

Eighteen individuals with motor complete cervical SCI and five age-matched non- injured individuals were recruited. EMG activity was recorded from biceps brachii (BB), triceps brachii (TB), extensor carpi radialis (ECR), flexor digitorum (FD), and abductor digiti minimi (ADM) using surface EMG. The participants were instructed to perform a controlled and isolated 3- second movement trials with full force, termed 'events' for each muscle against manual resistance resulting in no visible movement of the target muscle.

Surface EMG activity was recorded from the clinically paralyzed muscles (FD, ADM). Moreover, greater activation of the paralyzed muscles was observed when the patients were instructed to perform events involving relatively proximally innervated non-paralyzed muscles (BB, ECR, TB). These findings indicate presence of residual pathways across the injury establishing supra-lesional control over the sub-lesional neural circuitry. The greater activation of the paralyzed muscles during events involving the non-paralyzed muscles can be considered as reinforcement techniques which are known to facilitate the spinal cord excitability below the injury level.

Comments: A profound and disabling injury, complete SCI significantly affects patients' lives, often leading to diminished hope for recovery. This study revealed presence of voluntary subclinical muscle activation through surface EMG recordings in paralyzed muscles. These findings shed light on neurophysiological changes in upper limb muscles after clinically complete motor loss and offer insights for creating neuromodulation rehabilitation strategies to enhance upper limb recovery after cervical SCIs.

The limitation includes small number of the recruited patients. Therefore, larger scale studies are needed. Further investigation of the effect of neuromodulation techniques and spinal cord stimulation on the EMG activity of the paralyzed muscles is also warranted.

Moschovos C, Tsivgoulis G, Ghika A, et al. Image analysis can reliably quantify median nerve echogenicity and texture changes in patients with carpal tunnel syndrome. *Clin Neurophysiol.* 2023;149:61-69. doi:10.1016/j.clinph.2023.02.171

Submitted by: Eman Tawfik, MD

Edited by: Pritikanta Paul, MD

Summary: Neuromuscular ultrasound (US) has emerged as a useful adjunct diagnostic tool in peripheral nerve disorders. The nerve cross-sectional area (CSA) is the most sensitive and reliable sonographic parameter used in clinical practice. Nevertheless, other parameters such as nerve echotexture and mobility are also important. Typical median nerve echotexture changes in carpal tunnel syndrome (CTS) are hypoechogenicity and partial or complete loss of the honeycomb fascicular pattern. These echotexture changes are usually qualitatively assessed by the sonographer depending on visual assessment. However, this method is subjective. Therefore, the authors in this study aimed to assess the reliability and diagnostic accuracy of two quantitative methods as objective methods to assess median nerve echotexture changes in patients with CTS compared to controls.

The study was conducted on two group of participants: Group 1: < 65 years old and Group 2: > 65 years old. Group 1 included 19 healthy volunteers and 37 consecutive patients with electrodiagnostic (EDX)-proven CTS, while Group 2 included 20 healthy volunteers, 20 consecutive patients with EDX-proven CTS, and an additional 30 elderly patients with CTS from the database. Patients with secondary CTS (e.g., tenosynovitis detected in US) were excluded.

The median nerve was scanned at the level of carpal tunnel inlet and the captured image was analyzed. Median nerve brightness, gray level co-occurrence matrix (GLCM), and percentage of the hypoechoic area of the median nerve were calculated using offline software and compared with subjective assessment of the US image and CSA measurement.

In younger patients, GLCM measures were of equivalent diagnostic accuracy to nerve CSA (AUC = 0.97). In older patients, image analysis measures were equivalent or superior to subjective visual analysis and showed similar diagnostic accuracy to CSA (AUC for brightness = 0.88). Moreover, image analysis was abnormal in many older patients with normal CSA values. No difference in image analysis measures was found between groups with mild, moderate, and severe CTS.

Comments: This study establishes the usefulness of an objective method to assess nerve echotexture in CTS. This study is in keeping with the current trend in the neuromuscular US research to quantify the sonographic parameters that are usually subjectively assessed. This study's merits encompass its broad demographic coverage, encompassing both young and elderly individuals, maintaining consistent US settings throughout measurements, and ensuring that the sonographer remained unaware of the EDX results. The limitations include the exclusion of patients with secondary CTS, the assessment of the nerve only at the carpal tunnel inlet, and the retrospective analysis of the data of some patients (30 elderly patients).

Oct. 4, 2023

Alazzam AM, Goldsmith JA, Khalil RE, et al. Denervation impacts muscle quality and knee bone mineral density after spinal cord injury. *Spinal Cord.* 2023 Apr;61(4):276-284. doi: 10.1038/s41393-023-00885-3. Epub 2023 Mar 10. PMID: 36899099.

Submitted by: Nandita Keole, MD

Edited by: Pritikanta Paul, MD

Summary: Conducted at a single center, this cross-sectional study aimed to compare muscle size, body composition, bone mineral density (BMD), and metabolic profiles between two groups: individuals with spinal cord injury (SCI) characterized by denervation lower motor neuron (LMN) and those with innervation upper motor neuron (UMN).

Body composition, BMD, muscle size, and metabolic parameters were collected in 16 persons with chronic SCI (n = 8 denervated, n = 8 innervated) using dual-energy x-ray absorptiometry (DXA), magnetic resonance imaging (MRI), and fasting blood samples. Basal metabolic rate (BMR) was measured by indirect calorimetry. On assessment with the American Spinal Injury Association Impairment Scale (AIS) [Grade A is complete loss of motor and sensory function below level of injury and Grade E is normal motor and sensory function], seven participants in the denervated group were A and one was C. In the UMN injury group three participants were AIS A, two AIS B, and three AIS C. Percent differences of the whole thigh muscle cross-sectional area (CSA; 38%), knee extensor CSA (49%), vasti CSA (49%), and rectus femoris CSA (61%) were smaller in the denervated group ($p < 0.05$). Leg lean mass was also lower (28%) in the denervated group ($p < 0.05$). Whole muscle intramuscular fat (IMF%; 15.5%), knee extensor IMF% (22%), and % fat mass (10.9%) were significantly greater in the denervated group ($p < 0.05$). Knee distal femur and proximal tibia BMD were lower in the denervated group, 18–22% and 17–23%; $p < 0.05$. Certain indices of metabolic profile were more favorable in the denervated group though were not significant.

SCI results in skeletal muscle atrophy and dramatic changes in body composition. LMN injury results in denervation of the lower extremity muscles which exacerbates atrophy. Denervated participants exhibited lower leg lean mass and muscle CSA, greater muscle IMF, and reduced knee BMD compared to innervated (UMN injury) participants. Future research is needed to explore therapeutic treatments for the denervated muscles after SCI.

Comments: This highlights musculoskeletal changes in a lesser reviewed subpopulation in SCI patients. Level of lesion alone does not help differentiate UMN and LMN patients. This article highlights some gaps in knowledge for the LMN SCI patients and will influence plan of care and education with regards to therapy and activity. It would be interesting to see if LMN patients may derive more benefits from robotic assisted exoskeletons.

Oct. 18, 2023

Agergaard J, Yamin Ali Khan B, Engell-Sørensen T, et al. Myopathy as a cause of Long COVID fatigue: Evidence from quantitative and single fiber EMG and muscle histopathology. *Clin Neurophysiol.* 2023;148:65-75. doi:10.1016/j.clinph.2023.01.010

Submitted by: Eman Tawfik, MD

Edited by: Pritikanta Paul, MD

Summary: Long COVID is a long-term disabling sequalae of COVID-19 infection in hospitalized patients as well as in patients with mild symptoms. A common presenting symptom is physical fatigue. The author of this study previously reported myopathic changes in quantitative EMG (qEMG) and pathological changes in muscle biopsies of a small group of long COVID patients with fatigue. In this study, the authors investigated the clinical and electrodiagnostic features in a larger cohort of long COVID patients to explore whether myopathy and neuromuscular transmission failure are common causes of post-COVID fatigue.

The patients were recruited from a post-COVID clinic in Denmark from December 2020 to March 2022. Patients with impaired daily function and physical/muscular fatigue, myalgia, or reduced muscle force who were referred for qEMG were included. Critically ill patients and patients with known neurological disease were excluded.

All patients underwent motor nerve conduction studies (NCSs) of the tibial and peroneal nerves and sensory NCS of the peroneal and sural nerves, repetitive nerve stimulation (RNS) of the median and spinal accessory nerves, qEMG of the biceps, vastus medialis, and tibialis anterior muscles using concentric needle, and single fiber EMG (sfEMG) of the tibialis anterior and later extensor digitorum communis muscles. Additionally, muscle biopsy from the biceps brachii with examination using light and electron microscopy was performed.

A total of 84 patients meeting the study's inclusion criteria were enrolled. None of these patients exhibited abnormal nerve conduction studies (NCSs) or repetitive nerve stimulation (RNS) results. In 52% of the patients, there was a reduction in the mean duration of motor unit potential (MUP) in at least one muscle. Additionally, an increase in mean jitter was noted in 17% of the patients, specifically in the tibialis anterior muscle, and in 25% of the patients in the extensor digitorum communis muscles. The heightened jitter was observed in patients with or without myopathic quantitative electromyography (qEMG) findings. Furthermore, muscle biopsies revealed the presence of damaged terminal nerves and motor endplates, accompanied by an abundance of basal lamina material. The post-synaptic cleft displayed atrophy with short clefts and coarse crests.

The authors suggested that sfEMG changes may be due to motor endplate pathology. The myopathic changes being observed in > 50% of the patients could be the underlying cause of fatigue in long COVID patients.

Comments: The article provides valuable insight into the electrophysiological abnormalities in long COVID patients with physical fatigue. The myopathic changes in >50% patients with long COVID fatigue symptoms are of particular interest. It would be interesting to perform muscle ultrasound examinations and correlate the structural changes observed with ultrasound and the electrophysiological and muscle biopsy findings.

Iannibelli E, Gibertini S, Cheli M, et al. VCP-related myopathy: A case series and a review of literature. *Acta Myol.* 2023;42(1):2-13. Published 2023 Mar 31. doi:10.36185/2532-1900-2444

Submitted by: Justin Willer, MD

Edited by: Pritikanta Paul, MD

Summary: Valosin containing protein (VCP) controls the ubiquitin proteasome system, endolysosomal sorting, and autophagy. Frontotemporal dementia, inclusion body myopathy, and Paget's disease of bone all have been related to dominant missense mutations in the VCP gene causing a multisystem proteinopathy.

In this study, the authors describe a series of five patients with VCP mutations, a majority with lower limb weakness with distal predominance. Beevor's sign suggesting lower abdominal muscle weakness was noted in two patients never described before in VCP related myopathy. One patient also had upper limb proximal muscle weakness and mild tongue and orbicularis oculi muscle weakness. Only one patient also had mild length-dependent sensory predominant peripheral neuropathy. Three patients had elevated creatine kinase (CK), two patients had cardiac involvement, and one had restrictive lung disease with concomitant obstructive lung disease. EMG showed abnormal spontaneous activity and complex repetitive discharges. A myopathic pattern was noted in 4/5 patients combined with neurogenic findings in two patients.

Muscle biopsy showed fiber degeneration and regeneration and rimmed vacuoles in most. Muscle imaging showed fatty replacement primarily in adductor magnus, vastus intermedius and medialis, and tibialis anterior and medial gastrocnemius. Genetic testing revealed VCP mutations all reported as pathogenic in the literature.

The authors summarize that the findings indicate that VCP gene mutations might lead to a primarily skeletal muscle-related phenotype, without affecting the central nervous system, contrary to some previous reports. Further research is needed to fully comprehend the wide-ranging and distinct clinical phenotypes associated with these mutations.

Comments: This disease affects the peripheral nervous system at multiple levels. This is an intriguing manner that single gene VCP mutation impacts various aspects of the nervous system, encompassing proximal myopathy, distal myopathy, as well as involvement of upper motor neurons.

Loser V, Benkert P, Vicino A, et al. Serum neurofilament light chain as a reliable biomarker of hereditary transthyretin-related amyloidosis-A Swiss reference center experience. *J Peripher Nerv Syst.* 2023;28(1):86-97. doi:10.1111/jns.12524

Submitted by: Nakul Katyal, MD

Edited by: Pritikanta Paul, MD

Summary: In this prospective study, the authors aimed to determine if serum neurofilament light chain (sNfL) is a reliable and early biomarker of peripheral neuropathy in hereditary transthyretin-related (hATTR) amyloidosis.

A total of 20 hATTR patients, 14 symptomatic and 6 asymptomatic were included and assessed at baseline and after 1 year. Patients over 18 years old who were carriers of a pathogenic TTR mutation were enrolled in this study. Patients were considered asymptomatic if they had either no clinical symptoms or mild subjective isolated sensory symptoms with normal nerve conduction study (NCS) and electrochemical skin conductance. In addition to detailed clinical assessment, electrochemical skin conductance measurement, NCSs, and sNfL levels were measured for all patients. hATTR patient sNFLs were also compared with 4,532 healthy controls.

At baseline, the median sNfL concentration was 3.6 times greater in hATTR patients with symptoms compared to those without symptoms ($P = 0.003$). There was no difference noted in sNfL levels between asymptomatic patients and healthy controls, but significant difference noted between symptomatic and healthy controls. Additionally, significant correlation between sNfL levels and disease severity scores were noted, with the strongest being with the Neuropathy Impairment score (NIS). Two patients treated with patisiran had a reduction in sNfL levels. The authors concluded sNfL appears to be a dependable biomarker for gauging peripheral neuropathy severity in hATTR amyloidosis, capable of discerning between asymptomatic and symptomatic patients and holds promise as a potential biomarker for identifying disease onset and evaluating treatment response.

Comments: This study presents intriguing insights into the potential of sNfL as a biomarker for peripheral neuropathy in hATTR amyloidosis. According to this study, sNfL shows promise as a dependable marker to differentiate between asymptomatic and symptomatic patients. However, notable limitations include small sample size, as well as the brief duration of follow-up. Larger studies with longer longitudinal follow-up are required to further explore these findings.

Nov. 29, 2023

Picelli A, Di Censo R, Zadra A, Faccioli S, Smania N, Filippetti M. Management of spastic equinovarus foot in children with cerebral palsy: An evaluation of anatomical landmarks for selective nerve blocks of the tibial nerve motor branches. *J Rehabil Med.* 2023;55:jrm00370. Published 2023 Feb 20. doi:10.2340/jrm.v55.4538

Submitted by: Rebecca O'Bryan, MD

Summary: This is a small observational study of 24 children aged 6-16 with cerebral palsy (CP) to define landmarks of tibial motor nerve branches for selective motor nerve blocks of the gastrocnemii, soleus, and tibialis posterior muscles to manage spastic equinovarus foot. Muscle spasticity was graded using the Modifed Ashworth Scale, as well as spastic calf via the Tardieu scale. Patients had never received botulinum toxin previously. The authors performed selective diagnostic nerve block of tibial motor nerve branches. Landmarks were targeted using ultrasound (US) and the location of motor branches was defined a as percentage of the affected leg length. Mean coordinates were: for the gastrocnemius medialis 2.5 ± 1.2% vertical (proximal), 1.0 ± 0.7% horizontal (medial), 1.5 ± 0.4% deep; for the gastrocnemius lateralis 2.3 ± 1.4% vertical (proximal), 1.1 ± 0.9% horizontal (lateral), 1.6 ± 0.4% deep; for the soleus 2.1 ± 0.9% vertical (distal), 0.9 ± 0.7% horizontal (lateral), 2.2 ± 0.6% deep; and for the tibialis posterior 2.6 ± 1.2% vertical (distal), 1.3 ± 1.1% horizontal (lateral), 3.0 ± 0.7% deep. A significant correlation was found between the association of ankle dorsiflexion passive range of motion and the vertical coordinate for the gastrocnemius lateralis motor nerve branch.

Comments: This is a very small, limited study, but the use of diagnostic nerve block (DNB) to determine spasticity vs contracture is a useful tool in evaluating candidacy for botulinum toxin. Use of landmarks with US in addition to EMG guidance may enhance targeting the motor branches of the tibial nerve in children with CP, in the context of less experience ultrasonographers. This study would be most relevant in providing some useful landmarks for those who are new to utilizing US in identifying the tibial motor nerve for DNB. This may be a helpful supplement for those currently using only EMG guidance, who would like to supplement their localization with US.

Dec. 13, 2023

Molinares D, Parke S, Yadav R, Liu D, Williams J, Bruera E. Knowledge, attitudes, and beliefs of oncology trainees on function and cancer rehabilitation medicine. *PM R.* 2023;15(8):982-989. doi:10.1002/pmrj.12881

Submitted by: Oksana Sayko, MD

Edited by: Nandita Keole, MD

Summary: Enhancing functionality is linked to decreased morbidity and mortality among individuals living with cancer. Cancer rehabilitation medicine (CRM) emphasizes elevating functionality in this patient population. However, a notable impediment to patients availing themselves of CRM services lies in the insufficient number of referrals originating from oncology providers. Addressing this challenge necessitates an exploration of the perspectives held by oncology trainees. Unraveling their knowledge, attitudes, and beliefs concerning the significance of function and the role played by CRM is imperative. This understanding is pivotal in mitigating educational gaps and improving patients' access to rehabilitation services.

This study, conducted at a comprehensive cancer center in the US, involved sending a survey to 197 postgraduate oncology trainees who spent at least 1 day a week providing patient care. The response rate was 67% (n = 132). Of the 132 responses, 126 were included in the results. All respondents expressed the significance of addressing function in the care of cancer patients. The vast majority (94%) acknowledged the positive impact of enhanced function on treatment tolerance, while 84% believed it contributes to improved survival rates. Notably, 80% considered the presence of CRM physicians crucial, and 88% emphasized the importance of having an inpatient rehabilitation unit within the oncological setting.

Despite this acknowledgment, a striking pattern emerged concerning referrals - the majority (more than 75%) admitted to referring fewer than a quarter of their patients to such services. This trend persisted even when respondents acknowledged the pivotal role of both CRM physicians and inpatient rehabilitation units in cancer care. Interestingly, participants with previous exposure to PM&R were markedly more inclined to consult PM&R services compared to their counterparts without PM&R exposure ($p = .005$). This suggests a potential correlation between familiarity with PM&R and increased likelihood of patient referrals to CRM services.

Furthermore, a notable 81% of oncology trainees expressed the belief that education in CRM should be an integral part of their oncology training. This underscores a recognized need for enhanced education in CRM within the oncology community.

Comments: Reaching functional independence is an important aspect of cancer patients' recovery. Rehabilitation education should be included in oncology training programs.

Thomma RCM, Fokke C, Walgaard C, et al. High and persistent Anti-GM1 antibody titers are associated with poor clinical recovery in Guillain-Barré syndrome. *Neurol Neuroimmunol Neuroinflamm.* 2023;10(4):e200107. Published 2023 Apr 14. doi:10.1212/NXI.0000000000200107

Submitted by: Nakul Katyal MD

Edited by: Joshua Wilson, MD

Summary: This study investigated the relationship between the serum antibody titers of ganglioside GM1 and outcomes in patients with Guillain-Barre syndrome (GBS). Patients who met the criteria for GBS were included if hospitalized within 2 weeks from the onset of weakness and unable to walk 10 meters independently. Serum anti-GM1 antibody titers were collected at study enrollment and during a 6-month follow-up appointment.

Anti-GM1 antibodies were detected in 78 (20.7%) out of 377 patients. Out of those that tested positive, 30 (38.5%) were positive for IgG alone, 24 (30.8%) were positive for IgM alone, and 24 (30.8%) were positive for both IgG and IgM. At entry, antibody titers were higher for the IgG isotype (median: 1,600, range: 100–51,200) than for the IgM isotype (median: 200, range: 100–25,600). Although all antibody titers declined during follow-up, there was considerable variation in titer course between individual patients. A subset of anti–GM1-positive patients had persistent anti-GM1 antibodies at 3 months (n = 27/43) and 6 months (n = 19/41).

Patient titers were considered high if greater than the median titer. For patients with a high anti-GM1 IgG and IgM titers at entry, recovery was slower and less complete than anti–GM1-negative patients. High vs low IgG titers, but not IgM titers, were independently associated with poor outcomes when corrected for known prognostic factors (age of onset, preceding diarrhea, and MRC sum score). Among patients with a high anti-GM1 IgG titer at entry, a slow titer decline was associated with poor outcomes at 4 weeks and 6 months. Persistent high IgG titers at 3 and 6 months were associated with poor outcomes at 6 months.

Comments: In this study, high anti-GM1 IgG and IgM titers at entry and a persistent high anti-GM1 IgG antibody titer during follow-up were associated with poor clinical outcomes in patients with GBS. The continued presence of these antibodies suggests an ongoing production beyond the acute phase of GBS, potentially predisposing to poor outcomes. The study had several limitations, including patients with relatively severe GBS, effects of IVIG treatment on GM1 antibody titers, and lack of analysis of IgG subtypes, which may influence its pathogenic effect.

Monitoring anti-GM1 antibodies during the disease course could identify patients needing additional treatment. However, further research is necessary to determine if these persistent antibodies are pathogenic and whether targeting their persistence could be a viable treatment approach.

The study highlights the role of GM1 antibody persistence as a potential factor with prognostic implications for patients with GBS. The study brings up a significant question for future research: whether individuals with GBS who have both persistent GM1 antibody levels and poor outcomes might gain advantages from additional therapeutic interventions. Nevertheless, this aspect still requires further investigation.

Article of Similar Interest: Koga M. Multifaceted features of immunoglobulin G anti-GM1 antibodies in Guillain-Barré syndrome. Clin Exp Neuroimmunology. 2021;12(3):150-157. doi: 10.1111/cen3.12653


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