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Neurology [ALERT®]

Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Back Pain-Related Disability and Lumbar Spine Imaging Changes

By Joshua Weaver, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: A population-based, prospective cohort study of women in the United Kingdom found no association between the number of lumbar segments with radiographic pathology and severity of back pain-related disability.

SOURCE: Chen L, Perera RS, Radojcic MR, et al. Association of lumbar spine radiographic changes with severity of back pain-related disability among middle-aged, community-dwelling women. *JAMA Netw Open* 2021;4:e2110715.

Low back pain is the leading cause of disability worldwide and is the most common reason for patients to see their primary care physician. Although most guidelines recommend imaging for back pain only when specific criteria, such as neurological deficits or an underlying condition, are met, lumbar spine imaging often is performed by doctors on patients who do not have these signs or symptoms. Questions remain regarding whether the presence and severity of degenerative changes seen on such imaging relates to the severity of disability that people experience.

In this study, 1,003 predominantly white women from a large practice in the United Kingdom were examined as an initial baseline. They had similar weight, height, and body mass index (BMI) compared to the general population. They were re-evaluated with questions regarding physical activity at year 6 and again at year 9, along with lateral lumbar spine radiographs to provide data for a cross-sectional analysis. The participants then were re-evaluated at year 15 for a longitudinal analysis.

The radiologist reviewing the radiographs was blinded to clinical information and patient identity. A validated grading scale known as Kellgren-Lawrence (K-L) was used to measure osteoarthritis at each lumbar disc level, and this was the primary exposure. As secondary

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exposures, a semi-quantitative assessment of both disc space narrowing and osteophytes at each lumbar segment was used. The primary outcome of back pain-related disability was assessed using a non-validated back pain questionnaire at years 9 and 15, with a score ranging from 0 to 16 (higher values correspond to more severe disability).

A total of 650 women were included at year 9 for the cross-sectional analysis, and a total of 443 were included at year 15 for the longitudinal analysis. More than 80% of women in both analyses had either never smoked tobacco or had quit. The mean BMI was 27. Just more than 67% of women in both analyses reported no back pain. More than three-fourths of participants reported jobs or housework that was "active" at least half the day; more than half reported no regular exercise.

Based on the K-L osteoarthritis grading scale, women who had one or more lumbar segments with K-L based changes were not statistically more likely to have more disability in both the cross-sectional and longitudinal analyses. This also was true when adjustments were made for physical activity. There was no trend between the number of segments involved and the severity of disability.

Similarly, there was no association between either the osteophyte grade-based score or the disc space narrowing grade-based score and the severity of back pain-related disability in both cross-sectional and longitudinal analyses. There were no interactions found with confounders such as age, BMI, or smoking status.

■ COMMENTARY

There have been mixed data in the literature regarding the association of findings on lower back imaging and back pain symptoms or disability. This is a large study that provides a detailed and quantified score of degenerative changes in the lumbar spine to examine — not only cross-sectionally but longitudinally — their association with back pain-related disability.

An important limitation of the study is its homogenous patient population of middle-aged white women in the United Kingdom, and these results may not be generalizable to different populations across the world. Another limitation in this study includes the lack of data on other radiographic features that might correlate to back pain or disability, such as spondylolisthesis or vertebral body height. Various anatomical features, such as central stenosis, foraminal stenosis, or nerve root impingement, would be better identified on computed tomography (CT) or magnetic resonance imaging (MRI) modalities.

Regardless, this is an important study that highlights the fact that degenerative changes seen on lower back imaging may not (and often do not) correlate with back pain-related disability. Thus, lumbar X-rays are not useful in making management decisions regarding pain control in this population. This ties in nicely with a prior study done in 2015 that looked at lumbar spine MRI imaging of asymptomatic people ranging from 20 to 90 years of age, finding that degenerative changes increased with age and were exceedingly common (e.g., in those age 60 years, 50% had facet degeneration, 69% had disc bulges, and 88% had disc degeneration) despite not causing pain.[1]

Future studies should include a more diverse patient population regarding age, gender, and race. The association between imaging findings and back pain, not just back pain-related disability, would be useful to explore. Other imaging features should be included, and although more costly, the use of MRI would provide more anatomical information potentially relevant to the cause of back pain and disability. ■

REFERENCE

1. Brinjikji W, Luetmer PH, Comstock B, et al. Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *AJNR Am J Neuroradiol* 2015;36:811-816.

ABSTRACT & COMMENTARY

Recovery of Consciousness After TBI: Who Recovers and When?

By Alexander E. Merkler, MD, MS

Assistant Professor of Neurology and Neuroscience, Weill Cornell Medical College, and Assistant Attending Neurologist, New York-Presbyterian Hospital

SYNOPSIS: The majority of patients with moderate to severe traumatic brain injury who survive and are treated in acute rehabilitation centers will recover consciousness.

SOURCE: Kowalski RG, Hammond FM, Weintraub AH, et al. Recovery of consciousness and functional outcome in moderate and severe traumatic brain injury. *JAMA Neurol* 2021;78:548-557.

There are approximately 2.9 million emergency department visits for head trauma each year in the United States. In addition, there are 61,000 traumatic brain injury (TBI)-related deaths in the United States each year. Most of these deaths were in patients who experienced a moderate to severe TBI.[1] The majority of this mortality may be a consequence of withdrawal of life-sustaining therapy, which in part may be caused by persistent disturbance in consciousness.[1] However, few data exist regarding the recovery of consciousness in patients with moderate to severe TBI.

In the current study, Kowalski et al evaluated the factors associated with recovery of consciousness and independence among patients with moderate to severe TBI using data from the Traumatic Brain Injury Model Systems National Database, a 30-year prospective, multiyear, longitudinal database.[2] A total of 17,470 patients with moderate to severe TBI were included in the study. The median age at injury was 39 years, and 74% were male. Among these patients, 57% had an initial loss of consciousness and 12% had a disorder of consciousness (defined as not following commands) by the time they were admitted to inpatient rehabilitation. Among these 2,058 patients who had a disorder of consciousness, 82% recovered consciousness during inpatient rehabilitation. Factors associated with recovery of consciousness included absence of intraventricular hemorrhage and intracranial mass effect. Among the patients admitted to inpatient rehabilitation with a disorder of consciousness, 40% became fully or semi-independent during inpatient rehabilitation. There were differences in outcomes across the 30-year study period.

■ COMMENTARY

This study adds to the growing body of data suggesting TBI is not a "one-size-fits-all" type of disorder. Prior work has shown that patients who seemingly do not appear conscious based on standard clinical tests may indeed have preserved covert consciousness.[3,4] The current paper suggests that consciousness may recover over time and that patients with moderate to severe TBI may have a good outcome yet. Making hasty, life-or-death decisions in patients with TBI may be a mistake.

Limitations of this study include the article's definition of a disorder of consciousness, which was based on the lack of ability to follow commands. It is possible that some patients determined to have a disorder of consciousness may not have been in a coma, but instead were aphasic or encephalopathic. Second, there may be a selection bias. Only patients who survived the acute hospitalizations and were discharged to inpatient rehabilitation were included in the analysis. Thus, it remains uncertain whether patients who died during the acute hospitalization or were sent to a non-rehabilitation center, such as a nursing home, would have regained consciousness. Finally, although the article contends that there may be a self-fulfilling prophecy of withdrawal of care in patients with TBI, this cannot be proven since the population included only patients who survived to inpatient rehabilitation. Thus, the chance of recovery of consciousness may have been significantly lower if all patients with moderate to severe TBI were followed.

Recovery of consciousness may be delayed in patients with moderate to severe TBI. Good outcomes still are possible even in patients with moderate to severe TBI with delayed recovery of consciousness. ■

REFERENCES

1. Centers for Disease Control and Prevention. Traumatic Brain Injury & Concussion. TBI Data. https://www.cdc.gov/traumaticbraininjury/data/

2. Kowalski RG, Hammond FM, Weintraub AH, et al. Recovery of consciousness and functional outcome in moderate and severe traumatic brain injury. *JAMA Neurol* 2021;78:548-557.
3. Edlow BL, Chatelle C, Spencer CA, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. *Brain* 2017;140:2399-2414.
4. Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. *N Engl J Med* 2010;362:579-589.

ABSTRACT & COMMENTARY

CSF Biomarkers May Distinguish MSA from Lewy-Body Alpha-Synucleinopathies Before the Onset of Debilitating Symptoms

By Harini Sarva, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: In patients with autonomic failure, the combination of elevated neurofilament light and alpha-synuclein oligomers in the cerebrospinal fluid can distinguish between multiple system atrophy and Parkinson's disease/dementia with Lewy bodies. Early diagnosis is critical for the development of treatment trials.

SOURCE: Singer W, Schmeichel AM, Shahnawaz M, et al. Alpha-synuclein oligomers and neurofilament light chain predict phenoconversion of pure autonomic failure. *Ann Neurol* 2021;89:1212-1220.

Thirty-two patients with clinically defined pure autonomic failure (PAF) using standardized tests, including thermoregulatory sweat test, were included in this prospective study. Baseline cerebrospinal fluid (CSF) samples were examined for neurofilament light chain and the presence of alpha-synuclein oligomers.

The majority of subjects were male with prominent symptoms of bladder and erectile dysfunction. In addition, rapid eye movement sleep behavior disorder (RBD) and anosmia or hyposmia were common. Patients were examined annually, and the mean follow-up time was 3.9 years. Nine patients phenoconverted to neurodegenerative disorders — multiple system atrophy (MSA) (5), Parkinson's disease (PD) (2), and dementia with Lewy bodies (DLB) (2). The time to conversion was one to two years for MSA and between one and three years for PD and DLB.

Those who converted to MSA had fewer complaints of impaired smell, shorter disease duration at the time of enrollment, and higher upright catecholamine levels. Two of these subjects who came to autopsy had pathologically confirmed MSA. All phenoconverters had subtle motor signs. All who had converted to MSA had elevated CSF neurofilament light chain levels compared to none of the PD or DLB phenoconverters. The alpha-synuclein oligomer assay demonstrated that those who converted to MSA had lower maximum thioflavin fluorescence than those who converted to PD/DLB, consistent with previous reports of established ranges for these disorders. The reaction kinetics also were distinct between MSA and the PD/DLB phenoconverters, with the reaction plateau occurring in the assay at an earlier time point for those who eventually developed MSA.

■ COMMENTARY

MSA is a devastating, progressive, fatal disease with diverse clinical phenotypes. Clinical diagnosis often is delayed without obvious autonomic dysfunction. No disease-specific therapies exist. MSA is pathologically distinct from PD and DLB and much rarer than either of these conditions. Developing treatment trials is challenging. Although clinical markers, such as the presence of RBD, subtle motor signs, and impaired smell, can aid in predicting conversion of prodromal alpha-synuclein pathology to full-blown disease, relying on clinical characteristics alone is insufficient to diagnose early stage disease. Failure to make an early and accurate diagnosis will limit the chances for disease modification.

Reliable CSF biomarkers, such as the combination of neurofilament light and alpha-synuclein oligomer, to accurately distinguish MSA from PD/DLB will not only aid in the prognostication and counseling of patients, but also will help in the development of therapeutics while patients still are in the prodromal phase of pure autonomic failure, which has limited alpha-synuclein pathology. Although the sample size of this study was

small and lacked extensive autopsy confirmation of diagnosis, the detailed evaluations, with both clinical and biomarker assessments, are strengths. Although distinguishing between PD and DLB still remains a challenge, the potential of CSF biomarkers in distinguishing between MSA and PD/DLB synucleinopathies can aid in improving the accurate and early diagnosis of patients who present with mild parkinsonian features. ■

ABSTRACT & COMMENTARY

Neuromuscular Complications of Graft-Versus-Host Disease

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: Graft-versus-host disease is common in allogeneic bone marrow recipients, but neuromuscular complications are unusual (8%). The most common neuromuscular complication is an immune-mediated myositis that responds to treatment with immunosuppressive therapies.

SOURCE: Saw JL, Sidiqi MH, Mauermann ML, et al. Immune-mediated neuromuscular complications of graft-versus-host disease. *Muscle Nerve* 2021;63:852-860.

Graft-versus-host disease (GVHD), seen in 30% to 70% of adult patients following allogeneic stem cell (bone marrow) transplantation, occurs when immune cells, transplanted from a non-identical donor, recognize the recipient as foreign. GVHD is divided into acute GVHD, occurring within the first 100 days and manifested by rash, nausea, vomiting, diarrhea, and rising bilirubin, and chronic GVHD, occurring later and affecting the skin (67%), mouth (60%), liver (52%), joints and fascia (48% each), gastrointestinal tract (30%), and genitalia (12%). Central and peripheral nervous system manifestations are uncommon in GVHD. Neuromuscular complications, reportedly seen in 8% of patients, were the subject of this study.

A retrospective chart review identified patients 18 years or older with a diagnosis of GVHD, seen between April 2013 and July 2018 at Mayo Clinic, Rochester, MN. Separately, patients with a new neuromuscular complication, including any variety of myopathy, myositis, myasthenia, neuropathy, radiculopathy, or plexopathy, were identified electronically. Lastly, chart review was undertaken to identify patients with a high suspicion of an immune-mediated neuromuscular complication. Patients were excluded if they failed to fulfill 2014 National Institutes of Health consensus criteria for GVHD, if they did not manifest at least one non-neurological complication of GVHD, or if they did not appear to have an immune-mediated process. An immune process was defined as histological evidence of myositis or elevated creatine kinase with fibrillation potentials on needle electromyography for myositis and clinical or electrophysiologic findings characteristic of immune or inflammatory neuropathy for neuropathy patients. Any patient with a neuromuscular junctionopathy was included.

[A retrospective chart review identified patients 18 years or older with a diagnosis of graft-versus-host disease, seen between April 2013 and July 2018 at Mayo Clinic, Rochester, MN. Separately, patients with a new neuromuscular complication were identified electronically.]

Among 688 patients with GVHD, 20 (2.9%) developed immune-mediated neuromuscular complications, including myositis (n = 17; 2.5%), manifested most often as proximal weakness with or without axial weakness (n = 12), axial weakness with head drop (n = 2), generalized weakness (n = 1), or predominant respiratory failure or skin induration with no weakness (n = 1 each). Neuropathy (n = 2; 0.3%) manifested as neuralgic amyotrophy or acute inflammatory demyelinating polyneuropathy (AIDP) in one patient each, and myasthenic syndrome (n = 1; 0.15%), manifested as fluctuating foot drop. Mean age at transplant

was 54 years, and mean age at neurological presentation was 55 years, a mean delay of 14 months, with male predominance (n = 13; 66%). Acute leukemia was the primary malignancy in 60% of subjects, with a lymphoproliferative disorder present in 20%, myelodysplastic syndrome in 15%, and a myeloproliferative disorder in one patient. Most patients (40%) had both acute and chronic GVHD at the onset of the neuromuscular condition, with 35% (n = 7) having acute GVHD and 25% (n = 5) having chronic GVHD.

Muscle biopsy in 11 patients demonstrated a predominantly macrophage, perimysial infiltration in 10 and an endomysial and perimysial lymphocytic infiltration in one. Treatment with immunosuppressive agents, including steroids alone or in combination with rituximab, intravenous immunoglobulin (IVIG), or tacrolimus, was given to 19 patients, all of whom responded. Eleven patients experienced subsequent GVHD flares requiring additional treatment, including sirolimus, cyclosporine, and mycophenolate mofetil. Over a median follow-up of 83 months, 35% (n = 7) died, five from GVHD, and two from infection. Myositis is the most common neuromuscular GVHD complication and usually is macrophage predominant.

■ COMMENTARY

Central nervous system complications of GVHD occur more commonly than those affecting the peripheral nervous system and include seizures, posterior reversible encephalopathy syndrome (PRES), and stroke. Electronic retrieval and review of articles between 1983 and 2017 using several databases, including Medline, revealed that although seizures were significantly associated with both acute and chronic GVHD, PRES was significantly associated with acute GVHD, whereas stroke was associated with chronic GVHD.[1] ■

REFERENCE

1. Sheikh MA, Im A, Ballen K, Hashmi SK. Association of graft-versus-host-disease with neurologic complications: Clinical paradigm and future directions. *Bone Marrow Transplant* 2021;56:1471-1473.

ABSTRACT & COMMENTARY

Dietary Modifications with Linoleic Acid Can Have an Effect on Gut and Brain Inflammation

By Ulrike W. Kaunzner, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: This study evaluated the use of dietary conjugated linoleic acid (CLA) supplementation to modulate the disease outcome in a spontaneous mouse model of central nervous system autoimmunity and also studied patients with relapsing-remitting multiple sclerosis receiving CLA supplementation. CLA may act as a modulator of the gut-brain axis by targeting immune cells in the gut, with a subsequent effect in the brain.

SOURCE: Fleck AK, Hucke S, Teipel F, et al. Dietary conjugated linoleic acid links reduced intestinal inflammation to amelioration of CNS autoimmunity. *Brain* 2021;144:1152-1166.

The etiology of multiple sclerosis (MS), a chronic inflammatory and demyelinating disorder of the central nervous system (CNS), is largely unknown, and a combination of genetic and environmental factors is thought to play a role. As more focus is put on the gut-brain axis, several influences, such as the type of diet, microbiome composite, vitamin D status, or nutrients, such as fatty acids, are discussed. So far, only a few clinical studies have been conducted with the aim to influence the diet or microbiome of MS patients. Study design, adherence to certain diets, and ethical aspects can make these types of studies difficult. Fleck et al designed a study supplementing conjugated linoleic acid (CLA) to assess the potential modification of the gut and immune cells in a spontaneous mouse model of MS, as well as in a pilot study in relapsing-remitting MS patients.

CLA is a naturally occurring fatty acid in the meat and dairy products of ruminants, which has a beneficial effect on inflammatory bowel disease when studied in animal models. This mechanism is thought to interact with the nuclear peroxisome proliferator-activated receptor (PPAR) family that

can be found in various tissues, such as $PPAR_{\alpha}$ in kidney and gut tissue or $PPAR_{\delta}$ in brain and adipose tissue. The anti-inflammatory properties of CLA also can ameliorate certain immune pathways, such as the anti-inflammatory cytokine interleukin 10 (IL-10), which can be low in MS patients.

In their study, Fleck et al show that CLA-enriched chow has a strong protective effect in a spontaneous mouse model of CNS autoimmunity. A reduction of intestinal inflammation was noticed, as well as a shift within the intestinal myeloid cells accompanied by an attenuation of intestinal barrier dysfunction. Furthermore, the researchers noticed enhanced production of anti-inflammatory IL-10 as well as suppression of T-cell proliferation. This suggests a major local innate immune response, with a subsequent beneficial effect on CNS autoimmunity. In addition, a proof-of-concept study was conducted on first-line disease-modifying treatment in 15 MS patients, who received dietary CLA for six months. A down-regulation of pro-inflammatory cell subsets and an increase in anti-inflammatory subsets was seen in the study.

■ COMMENTARY

This is a very important publication, since CLA seems to have a regulating effect on the intestinal barrier function and a concomitant ameliorating effect on CNS autoimmunity. These effects were not influenced by changes in the microbiome, indicating that the CLA effects are beyond a pure effect on the composite of the microbiota and might be associated with changes of immune cells in the intestinal wall itself.

Given the positive objective findings in this study and the observed positive effect in other diseases (e.g., atherosclerosis and Crohn's disease), a potential anti-inflammatory effect needs to be evaluated in a larger, randomized, placebo-controlled trial, examining levels of inflammation within MS patients, as well as investigating classical clinical and imaging endpoints. This potential study design also should investigate the confounding effect of disease-modifying treatments. Since this study focused on a small cohort of relapsing-remitting MS, and since the effect of CLA is thought to be the result of peripheral immune regulation, it also will be interesting to see if there is any effect in progressive MS patients, where inflammation is considered to be compartmentalized to the CNS itself.

The various pathways of communication between the gut and the brain immune system, altered by CLA, also will need further investigation to identify a potential target for better intervention. Moreover, the correct dosing of CLA and potential long-term side effects need to be established, since, as the authors pointed out, increased liver enzymes, triglycerides, and steatosis have been observed in other trials.

In conclusion, this is an important study, since dietary supplements, nutrients, or special diets are a frequent topic in the management of patients with MS. This study will widen the scope of discussion on the treatment of neurological disorders. Traditional medications can have a benefit on overall well-being and on the disease outcome. Nutritional supplements need to be discussed with caution until clear recommendations can be given based on clinical trials and other strong evidence of efficacy without significant side effects. ■

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CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss current scientific data regarding the diagnosis and treatment of neurological disease;
- discuss the pathogenesis and treatment of pain;
- describe the basic science of brain function;
- discuss new information regarding new drugs for commonly diagnosed neurological conditions and new uses for traditional drugs;
- identify nonclinical issues of importance for the neurologist.

CME QUESTIONS

1. Which of the following lumbar spine radiographic features is associated with back pain-related disability?
a. Osteoarthritis
b. Disc space narrowing
c. Posterior osteophytes
d. None of the above

2. A 42-year-old male is in a motor vehicle accident. He is found unconscious with a Glasgow Coma Scale score of 8 (E2 V2 M4). He does not follow commands. His computed tomography shows trace scattered subarachnoid hemorrhage. He is discharged to acute rehabilitation and is not following commands. Which of the following is true?
a. He likely will not regain the ability to follow commands and likely will remain dependent.
b. He likely will not regain the ability to follow commands and likely will become independent.
c. He likely will regain the ability to follow commands and likely will remain dependent.
d. He likely will regain the ability to follow commands and likely will become independent.

3. Which of the following statements about biomarkers in patients who present with pure autonomic failure is true?
a. Neurofilament light was elevated in Parkinson's disease/dementia with Lewy bodies (PD/DLB).
b. Neurofilament light was elevated in all patients who converted to multiple system atrophy.
c. Based on the biomarkers, there were more phenoconverters to PD/DLB.
d. Neurofilament light and the alpha-synuclein oligomer assays were useful in distinguishing between PD and DLB.

4. Which of the following is the most common neuromuscular manifestation of graft-versus-host disease?
a. Myositis
b. Acute inflammatory demyelinating polyneuropathy
c. Neuralgic amyotrophy
d. Myasthenia

5. Conjugated linoleic acid has been shown to have which of the following effects?
a. It has an anti-inflammatory effect in human autoimmune diseases.
b. It benefits patients with multiple sclerosis.
c. It reduces inflammatory bowel disease in rodent models.
d. It has no side effects when used in therapeutic trials.