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“UPDATES IN THE MANAGEMENT OF RELAPSING MULTIPLE SCLEROSIS”

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What changes have been made to the 2017 McDonald criteria for diagnosing multiple sclerosis?

Patricia K. Coyle, MD: First of all, they added cortical lesions to juxtacortical lesions as a dissemination-in-space site. Second, you can count symptomatic lesions, as well as asymptomatic lesions. Third, they gave a second way to make a definite diagnosis of multiple sclerosis [MS] with a single attack of a clinically isolated syndrome. You must have ruled out other possibilities, but if you meet dissemination in space by MRI criteria and you have CSF [cerebrospinal fluid]–specific oligoclonal bands, you can qualify for a definite diagnosis with 1 attack. That was brand-new. The criteria elevated CSF-specific oligoclonal bands. That is the key test and is even above the IgG index.

View video: neurologylive.com/ms-peer-exchange-1
Misdiagnosis of Multiple Sclerosis

In creating criteria, what concerns came into play regarding misdiagnosis?

Mark Freedman, MD, MSc: This was a huge question that came up repeatedly, and we had to emphasize the point that the diagnostic criteria were being driven by accuracy. That means we’re not willing to sacrifice specificity for sensitivity. The last thing you want to do is put an MS [multiple sclerosis] label on someone when it doesn’t belong. That usually leads to treatments that are not going to work and delay in the appropriate diagnosis and most appropriate therapy.

We erred on the side of specificity, knowing full well that there are some patients who probably have MS but may not meet the McDonald criteria. The advice is, if they haven’t met the criteria, they probably will. That means improved vigilance, repeated testing, maybe repeating the [lumbar puncture], and repeating even the MRIs at an earlier date than expected to show that the activity is consistent with multiple sclerosis. We do not want to miss another entity.

View video: neurologylive.com/ms-peer-exchange-3
Managing Multiple Sclerosis Begins at Diagnosis

BY GINA BATTAGLIA, PHD

RECENT UPDATES TO DIAGNOSTIC CRITERIA for multiple sclerosis (MS) aim to improve accuracy of and reduce delays in diagnosis, according to a panel of experts who participated in a virtual Neurology Live® Peer Exchange on October 23, 2020. Session moderator Fred D. Lublin, MD, and the rest of the panel discussed recently updated criteria for diagnosis and general strategies for management and follow-up of patients receiving a diagnoses of or suspected of having MS.

The McDonald criteria, first published in 2001 by the International Panel on MS Diagnosis, were the first diagnostic criteria to incorporate MRI. They effectively “brought MRI into the modern era of diagnosis of MS,” said Lublin. The most recent revision of the McDonald criteria in 2017 provided additional avenues for diagnosing cases that involve a typical clinically isolated syndrome. These criteria state that cerebrospinal fluid (CSF)–specific oligoclonal bands can be used in place of MRI lesions to fulfill the criteria for dissemination in time, symptomatic MRI lesions (with the exception of optic nerve lesions for patients with optic neuritis) can be used in addition to asymptomatic lesions to demonstrate dissemination in space or time, and cortical lesions and juxtacortical lesions can be used to fulfill criteria for dissemination in space.

Additional recommendations from the panel of experts who developed the criteria included the use of brain MRI during the diagnostic process (if feasible), analysis of CSF and serum in pairs to confirm that the oligoclonal bands are present only in the CSF, and indication of the MS course at the time of diagnosis and periodic reevaluation over time.

Scott D. Newsome, DO, noted that the expanded criteria for dissemination in space can help differentiate between MS and either neurosarcoidosis or neuromyelitis optica; this expedites diagnosis and initiation of therapy. “We know from clinical trials that the earlier you can get people on therapy, the better they will do long term,” said Newsome.

Mark Freedman, MD, MSc, also pointed out that although the 2017 updates expanded the criteria for diagnosing MS, they also aimed to reduce misdiagnosis of MS in patients with conditions that have a similar presentation.

“The last thing you want to do is put [an] MS label on somebody when it doesn’t belong. That usually leads to treatments that are not going to work, delay in the appropriate diagnosis, and delay in the most appropriate therapy,” said Freedman, who was among the authors of the Lancet Neurology paper that summarized the 2017 revisions.

Freedman added that the 2017 criteria aimed to maximize specificity, even if that means missing some patients with MS in initial evaluations. The criteria also recommended increased vigilance and repeated testing with lumbar puncture and MRI for patients with an unclear diagnosis, to promptly identify the correct clinical entity.

Patricia K. Coyle, MD, agreed that misdiagnosis is an important concern. She recommended a robust evaluation that includes imaging of the brain and spinal cord, lumbar puncture to analyze the CSF, and optical coherence tomography. Additionally, this should be accompanied by immunoglobulin G tests for aquaporin-4 and myelin oligodendrocyte glycoprotein (MOG) to rule out neuromyelitis optica and MOG antibody disorders, respectively.

Freedman added that CSF analysis can play a key role in diagnosis for patients who have not had a clear-cut demyelinating event or who have inconclusive MRI results. In addition, it has a high negative predictive value in patients who received a misdiagnosis of MS. “If they’ve had so-called established MS for years and the CSF is negative by the standardized tests…that’s a red flag to me in someone who supposedly has established disease,” said Freedman.

According to Coyle, CSF–specific oligoclonal bands are often present early in the prodromal stage and generally do not disappear over time; therefore, she repeats lumbar punctures for patients with signs and symptoms of MS to see if CSF–specific oligoclonal bands eventually appear. She does the same in patients with oligoclonal bands and a suspected misdiagnosis of MS to see if the bands disappear.

Although the 2017 McDonald criteria have not influenced the panelists’ treatment decisions, Coyle and Newsome said that the criteria have allowed them to make MS diagnoses sooner. Newsome added that they may have the greatest utility for providers who are not specialists in MS, such as general neurologists.

After diagnosing MS and using the clinical examination features and test results to get an overview of the patient’s prognosis, choosing an agent appropriate to the patient’s prognosis is the next step in management, according to Freedman. “Optimally, we would stop the disease in its tracks, but we all know that none of the medications are able to do..."
that unless you go to the very extreme, which is to replace their immune system, which is not appropriate for most patients,” he said.

Freedman said that assessing the treatment response and determining the threshold for switching therapies continues to be a big challenge, particularly for progressive forms of MS. “We now have some therapies, but it behooves us to try to figure out whether we’re winning or losing the battle, knowing full well in the trials with these drugs that the progression is expected,” he said. “We need some other measure that tells us that we’re doing something to [treat the] disease, and this is where I think...the evolving biomarkers, like measuring neurofilament lights or even now the [glial fibrillary acid protein] marker in the serum, might help us to know [if we] are getting at the progressive nature of the disease with our therapies.”

Lublin concluded that in addition to offering disease-modifying therapies to patients with MS, providing holistic care should remain at the forefront of MS management. Offering symptomatic therapies, understanding a patient’s management of social issues, and knowing how they interact with their environment are all important because of the multiple symptoms, impairments, and disabilities that may be present, he explained. “My colleague, Steven Krieger, MD, likes to say that no matter where you are in the spectrum of MS, there’s always something that the [MS treatment] center can do to make someone’s life better,” said Lublin.

REFERENCES

Living With Multiple Sclerosis Involves Balancing Quality of Life

BY GINA BATTAGLIA, PHD

ISSUES RELATED TO QUALITY OF LIFE are often the primary concern of patients with multiple sclerosis (MS). Employing a holistic approach that includes lifestyle modifications and medical therapies should be a key focus among patients and providers, according to session moderator Fred D. Lublin, MD, and a panel of experts on MS who participated in a virtual Neurology Live® Peer Exchange on October 23, 2020.

Although quality of life is a major worry of patients with MS, patients may not understand that the efficacy of disease-modifying therapy (DMT) is often unrelated to their quality of life, said Mark Freedman, MD, MSc. “Often, there’s a big disconnect between the actual disease process and many of the day-to-day symptoms patients are having,” he said. “We have to pay attention to those day-to-day symptoms [that] are impairing their quality of life.”
Scott D. Newsome, DO, added that day-to-day issues often affect patients even if objective measures such as MRI indicate their disease is stable. “I would tell the patient, ‘You’re absolutely doing great. This medication that we chose for you is doing what we hoped it would do for you,’” he related. “Then the patient would say to me, ‘Well, Doc, what about my fatigue? What about my cognitive fogging that has led to unemployment now? What about these day-to-day issues that I’m experiencing that are the bigger problem?’ That was a real eye-opener for me in treating people and in trying to take that into the framework of the comprehensive care model.”

According to Lublin, smoking and dietary habits, as well as annual neuropsychological evaluation, also should be addressed with patients. “The patient has to understand that there’s more to the care than DMTs and that they shouldn’t expect more from the DMT than it can do,” he said.

Fatigue is a particularly common and debilitating symptom. It can manifest from sources such as thyroid disease, anemia, respiratory difficulties, depression, sleep disorders, physical disabilities, and medication, so management requires a multimodality approach, according to Patricia K. Coyle, MD. She added that management of “the mysterious primary MS fatigue” can be particularly challenging because its pathogenesis is unclear. To assess the contribution of different factors to the patient’s fatigue, Coyle said that she asks patients and their family members how their fatigue affects their everyday activities; she also screens patients for depression, asks questions related to sleep hygiene, evaluates their medications, and discusses strategies for accommodating strenuous activities, such as adding rest periods.

Although multiple medications are often used by providers to improve fatigue, TRIUMPHANT-MS (NCT03185065), a randomized, placebo-controlled, crossover, 4-sequence, 4-period, double-blind, multicenter trial, showed that compared with placebo, amantadine, modafinil, and methylphenidate were not superior for improving the Modified Fatigue Impact Scale score, and a higher proportion of patients reported adverse events while taking each of the active agents.1

“It was interesting because it was like, ‘Oh my gosh, I use these medicines all the time in patients’ and [these data show that] it’s like a flip of a coin [regarding] which of these medicines will help,’” said Newsome. He added that the trial was relatively small and short in duration.

Overall, Newsome said, the TRIUMPHANT-MS trial results have not changed his current practice because amantadine, modafinil, and methylphenidate are the only options for patients outside of lifestyle modification. “Right now, we need further data,” he said. “We need a larger study to prove that there’s not a subgroup of people who would respond to the therapies that were studied.”

Freedman added that regular exercise should be a central focus for reducing fatigue with MS and would likely boost the benefit of a pharmacologic agent. “The data [are] coming in regularly that it doesn’t matter how you do it, and it doesn’t matter at what stage you’re doing it...there is an established benefit of exercise at every level, and one of the factors that’s been impacted by exercise is fatigue,” he said.

Freedman also said that the heterogeneity of fatigue makes it difficult to assess benefits of a single medication. “There are probably [some] patients who truly are in need of a booster for their wakefulness, and that’s where these drugs with amphetamine bases are probably going to have some benefit,” he noted. “But their downside is that they can cause insomnia, and that just may worsen the sleep problem.”

The effect of new DMTs on quality-of-life measures such as fatigue has also been a focus of recent clinical trials such as OPTIMUM (NCT02425644), a multicenter, randomized, active-controlled trial that aimed to compare the efficacy and safety of ponesimod with teriflunomide in patients with relapsing multiple sclerosis. The primary end point was annualized relapse rate over a 108-week period; however, Freedman, a member of the trial’s steering committee, noted that observed differences in relapse rates among sphingosine-1-phosphate receptor agonists are generally small and may not be clinically meaningful.

Therefore, he and his colleagues decided to include fatigue-related symptoms, which were measured by the symptoms domain of the Fatigue Symptoms and Impact Questionnaire – Relapsing Multiple Sclerosis (FSIQ-RMS), as a secondary outcome measure.

“The thought was: Let’s go after an important patient-related outcome that is undertreated and for which there is a huge unmet need...[Fatigue is] probably, if not the No. 1, close to the No. 1 reason [patients] are dropping out of gainful employment. They’re not able to meet the needs of their lives, not only at work but [also] at home, and it’s a huge dent in quality of life,” Freedman said.

Data presented in 2019 at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis showed a significant reduction in annualized relapse rate and improvement in fatigue symptoms at week 108 with ponesimod.2 According to a news release from ponesimod’s manufacturer, OPTIMUM was the first trial in which one drug’s effects on the FSIQ-RMS, when used as a prespecified end point, were shown to be statistically significant over those of an active comparator.2 Freedman added that the effects on fatigue appeared to improve over the course of the study, suggesting that ponesimod may target the primary fatigue that is typically difficult to manage.

Newsome concluded that the OPTIMUM findings highlight the importance of continuing to evaluate patient-reported outcomes when studying new DMTs for MS. “In general, we need to continue to look at [patient-reported outcomes] in clinical trials because, at least in my practice, there was that disconnect for me between what the patient was experiencing and what I was seeing,” he stated.

For a full list of references, see the article on NeurologyLive.com.
Experts Consider First-line Therapies for MS Treatment

BY MATT HOFFMAN

WHEN DECIDING ON A first-line therapy for patients with multiple sclerosis (MS), the treating physician has much to consider, from the individual prognosis to the state of disease. Additionally, according to a panel of experts led by Fred D. Lublin, MD, participating in a NeurologyLive® Peer Exchange on October 23, 2020, patient preference is a critical issue to incorporate into this process.

Preference can be affected by concerns about safety, insurance challenges, and plans for future pregnancy, among others. Many factors, Lublin noted, beyond those involved in simply identifying a therapy that is likely to be effective, influence the decision. Trying an agent and later reassessing it can be viable for some patients but not ideal for all. Additionally, as Scott D. Newsome, DO, explained, the lack of an ultimate biomarker for individuals leads physicians to choose which clinical factor offers the highest level of confidence in a given treatment.

“I try to use clinical and paraclinical factors of what I call ‘badness’ in determining the direction of treatment,” Newsome said. “There are emerging data from observational studies that are pointing toward being more aggressive up front in treating MS. In my practice, I haven’t prescribed a self-administered injectable therapy in a very long time for that reason.”

Newsome explained that his standard practice is to go with an oral or infusible therapy, which provides him a low threshold to escalate to an exclusively infusible therapy. That escalation, he noted, can occur as early as the first year of treatment, as long as patients are compliant and have been treated for 6 or more months.

“Do I have a high level of confidence that the escalation is going to put someone in a better place, from a disability perspective, 20 years down the road? I don’t think we have data to support that. However, the observational studies hint toward that from the MS-based cohort,” Newsome said.

ANTI-CD20 MONOCLONAL ANTIBODIES

Some of the highest-efficacy therapies available to physicians treating MS are the anti-CD20 monoclonal antibodies, including ocrelizumab (Ocrevus; Genentech) and ofatumumab (Kesimpta; Novartis).

The pivotal trials of ocrelizumab offered clear evidence on all markers of disease activity that this agent was superior to interferon in treating patients. The annualized relapse rate (ARR) was close to 50% in favor of ocrelizumab, Newsome pointed out, adding that new gadolinium-enhancing (Gd+) lesions were strongly suppressed by the therapy, favoring it upward of 90%.

Ofatumumab, on the other hand, was compared with teriflunomide (Aubagio; Sanofi-Genzyme) but showed similar results in terms of suppression of ARR into the 50th percentile, as well as greater-than-90th percentile suppression of Gd+ lesions.

“At least in the short term, and probably in the intermediate term, we know that the B-cell–depleting therapies do a much better job in suppressing the inflammatory disease activity,” Newsome said. “That includes relapses, Gd+ lesions, and T2 lesions, which may speak to those observational studies. They’re compelling enough for me to think about using the B-cell–depleting therapies as a first line.”

One caveat with the use of B-cell therapies, Mark Freedman, MD, MSc, pointed out, is the untold story concerning how long B-cell suppression needs to occur to obtain a long-term response. “You may not need to maintain the barrage against the B cells year after year. There may be a point where you can stop and still glean the benefit from those early treatments,” Freedman said.

Newsome noted that data on rituximab have suggested that physicians can treat patients up front with a similar protocol for a couple of years before cutting back on the frequency or the dosing.

IMMUNE RECONSTITUTION THERAPY

A notion exists in MS treatment with immune reconstitution agents that a certain dosage of therapy can control disease, and it can be given like a cancer therapy in select treatment groups. One such agent is part of the physician’s toolbox in the United States: cladribine (Mavenclad; EMD Serono).

“The overall results from the clinical end point were that the people who had 4 successive years of cladribine were
Do I have a high level of confidence that escalation is going to put someone in a better place, from a disability perspective, 20 years down the road? I don’t think we have data to support that.

— Scott D. Newsome, DO

no better clinically than those who had only 2 years and then 2 years of placebo,” Freedman explained. “This tells you that the up-front treatment has some durability, and we’ve seen the same thing with alemtuzumab. That is the other prototypic induction agent with which you knock down the immune system, allow it to recover over time, and then watch for the durability of the response. That’s the uniqueness of cladribine.”

Cladribine is utilized with a dose induction, which requires following the patients for a few years, but it does offer the option to retreat if necessary. A caution put forward by the panelists included that these therapies are not cures: Even in terms of reconstituting the immune system, data do not yet support the notion that no other therapy will be required. They do, however, offer an interesting advantage for patients who may be considering pregnancy, Newsome said.

“Cladribine is a very interesting agent,” Patricia K. Coyle, MD, concurred. “I consider it the most efficacious of the oral therapies. It’s not as efficacious as the monoclonal antibodies. The greatest difficulty is that in the United States, the label says you give your 2 courses and then they’re silent. That’s a big issue. That needs to be resolved.”

S1P RECEPTOR MODULATORS
Another group of therapies available for consideration consists of the sphingosine-1-phosphate (S1P) receptor modulators, a class that includes 3 agents: fingolimod (Gilenya; Novartis), siponimod (Mayzent; Novartis), and ozanimod (Zeposia; Bristol Meyers Squibb). A fourth, ponesimod, is likely on the way.

“Fingolimod was the first-in-class S1P receptor modulator, and it hits S1P receptors 1, 3, 4, and 5,” Coyle noted. “Both of [the others] are aimed at S1P receptors 1 and 5. They deliberately got rid of receptor 3 targeting, which is enriched in the cardiac tissue, in the hopes of getting away from the first-dose, 6-hour observation. Both of them, for the most part, offer you that.”

Coyle explained that with siponimod and ozanimod, most individuals do not require formal dose escalation. The former, however, offers a small advantage in that it has also been assessed in patients with secondary progressive MS who were experiencing gradual worsening.

“The primary outcome was confirmed disability progression at 3 months. This is a progressive population, and they met that primary outcome. They weren’t knock-your-socks-off data…[but] I was impressed with this study,” Coyle said. She compared this with fingolimod’s phase 3 trial, in which a secondary progressive outcome was met but approval for that indication was not granted. Siponimod, though, was approved for relapsing forms of MS, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive MS.

Ozanimod, Coyle noted, is particularly intriguing because it breaks down into 2 active metabolites. These metabolites have a longer half-life, which lengthens the washout time.

“The label has a bit of a concern about other drugs like MAO [monoamine oxidase] inhibitors and anything that might cause a serotonin surge. I would think about avoiding those. We need better data there,” Coyle said.
Panelists Look Ahead to the Future of MS Treatment

BY MATT HOFFMAN

THE CARE OF PATIENTS WITH multiple sclerosis (MS) has advanced at remarkable speed over the past few decades. This has pushed 4 major themes to the forefront of the landscape: newly available treatments, the incorporation of novel and innovative technologies in diagnosis and management, the transformation of communication with a new generation of patients, and the use of technology for next-generation care.

These innovations have led to, arguably, a turning point in the treatment of MS. Physicians feel a brighter future is ahead for MS treatment, although they have not solved every problem, and more approved, effective symptomatic therapies are needed for the many patients who continue to struggle with symptoms that greatly affect their quality of life and, sometimes, employment. These issues can include fatigue, neuropathic pain, and cognitive difficulties. Nonetheless, the field appears poised to advance significantly in the coming years.

In a NeurologyLive® Peer Exchange held October 23, 2020, a panel of experts in the care of patients with MS, moderated by Fred D. Lublin, MD, discussed these topics and shared their insights into potential advances, as well as what challenges remain unaddressed.

“In the United States, we have 25 distinct agents for relapsing forms of MS covering 10 mechanisms of action,” Patricia K. Coyle, MD, explained. “What we don’t have are a lot of treatments for the neurodegenerative phase of MS and progressive MS. That is an ongoing key focus, and it’s very likely that neurodegeneration has to be hit from the earliest time point; ideally, even before there is clinically apparent progression. We’re going to see a real emphasis on that.”

Additionally, she and the other panelists, including Scott D. Newsome, DO, noted that the landscape is without any meaningful strategies to repair the central nervous system (CNS). This, Coyle said, includes remyelination and cell-based strategies to induce axonal sprouting. Very recently, opicinumab, a CNS-repair therapy developed by Biogen, was discontinued after failing to reach main and secondary end points in a phase 2 study.

“That’s off the table, with regard to CNS repair. This is a focus. It’s very promising that we have multiple studies in MS looking at CNS repair, but that’s a big deficit,” Coyle
said, adding that the needs extend beyond just CNS repair. The field, she said, needs neuroprotection agents, more treatments for progressive MS, and neurodegenerative strategies to combat disease progression.

Notably, those strategies will need to be employed early on, and along with them, physicians will need to ensure the promotion of wellness programs and recognize the severity of comorbid conditions in MS, in order to properly identify and optimally manage them. “With that, the individual with MS will age better,” Coyle said.

For Mark Freedman, MD, MSc, the future of MS treatment also includes what he calls the “highest efficacy” treatment: bone marrow transplantation. Although its use in MS is increasingly common around the world, it is still not widely applied. There is some recognition of its benefit in a select group of patients with early and aggressive disease, however.

An ongoing US study “will no doubt prove [bone marrow transplantation] is better than any of the other higher-efficacy therapies, when appropriately applied to the right patient group. It’s an option on the table for certain types of people,” Freedman said.

Additionally, Freedman and the rest of the panel pointed to the ongoing and evolving use of biomarkers to inform treatment outcomes as a point of focus for the coming years. One such biomarker, neurofilament light (NfL), has “gone beyond an experimental type,” and the back-and-forth conversation around its use is no longer relevant, Freedman said.

“It should be commonplace,” opined Freedman. “These assays are readily available. They’re giving you some information about what kind of axonal damage is occurring ‘under the water.’ In the appropriate patient who is young and has no confounders that might lead to the destruction of axons, neurofilament light is cheap and easy to do. It’s a blood test. You can do it on a regular basis and get at the entire brain.”

Freedman explained that routine MRI offers a small look at the spinal cord and the cervical spine, but if there’s damage anywhere, it gives rise to the axonal loss that can be measured with NfL. “That’s a biomarker moving forward, which you’ll see adopted quite readily. It’s another piece that can help inform, not only on prognosis, because we’ve seen those data, but also on monitoring treatment response,” he added.

Newsome and Freedman also noted that a recent study explored the combination of interferon beta and teriflunomide (Aubagio; Sanofi-Genzyme), which produced a 90% suppression of gadolinium-enhancing lesions. Achieving this, using 2 drugs that are relatively safe, Freedman explained, may warrant exploration of combination therapy in the future.

“I’ll throw in this idea of wanting to have individual prognostication,” Lublin concluded. “We’re good at prognosticating for groups, and we’re terrible at prognosticating for individuals. Biomarkers may be a part of that, but we need to build some individual metrics for a given individual, which will then inform our choice of therapies.”
Fatigue Plays a Key Role in Multiple Sclerosis Daily Functioning

Patients with lower levels of disability tended to report fatigue as the most impactful symptom in daily life.

BY MARCO MEGLIO

FATIGUE OCCURS IN MOST PATIENTS who have relapsing multiple sclerosis (MS) and it can influence daily functioning, according to findings presented in September at MS Virtual 2020, the 8th Joint ECTRIMS-ACTRIMS meeting.¹

Through data presented by Lindsey L. Lair, MD, senior global medical affairs leader—neuroscience at Janssen Pharmaceuticals, investigators sought to measure MS fatigue and its impact on daily life in a real-world population. They used a survey specific to relapsing MS (RMS): the Fatigue Symptoms and Impacts Questionnaire – Relapsing Multiple Sclerosis (FSIQ-RMS).

Higher scores in a range from 0 to 100 indicated greater severity. Findings from the cohort of 142 patients with RMS revealed that fatigue levels are severe, with a mean FSIQ-RMS symptom domain score of 59.5 during a 7-day period.

Demographic and clinical questionnaires that included disease history and status, sleep, and social and emotional function were completed by the participants along with the FSIQ-RMS, which was administered daily for 7 days. Physical, cognitive/emotional, and coping subdomain scores were 45.1, 44.9, and 50.6, respectively, following the 7-day period.

Walking difficulties and fatigue were recorded as the 2 symptoms with the most impact on daily functioning. Notably, 56% of the patient population experienced fatigue prior to their MS diagnosis.

In total, 72% of patients were not currently relapsing and had a mean fatigue symptom domain score of 56.2 compared with a mean score of 68.0 in those who had an active relapse. Lair and colleagues also noted that fatigue was rated the most impactful symptom on daily life by those with lower disability.

Patients without depression, who represented 56% of the population, still reported mean fatigue symptom domain scores of 53.7 compared with 67.0 in those with depression. Among those who reported a sleep disorder, 72% of the population, the mean fatigue symptom domain score was 58.1. In contrast, those without a sleep disorder recorded a 63.3 mean fatigue symptom domain score.

The most common triggering factor for fatigue was heat exposure, which occurred in 82% of patients.

Disability and economic burden have both been associated with higher levels of fatigue in patients with MS. Results of another study presented at MS Virtual 2020 revealed that patients with relapsing-remitting MS who were stratified by high levels of fatigue had greater comorbidity and economic burdens compared with those with MS who had low levels of fatigue.²

The data from that study showed that in patients with relapsing-remitting MS, the annualized number of outpatient visits, emergency department visits, and hospitalizations were greater for those with high levels of fatigue compared with those with low levels of fatigue.

AMY SULLIVAN, PsyD, ABPP: Personalized Approach to Fatigue in Multiple Sclerosis

Amy Sullivan, PsyD, ABPP, director of behavioral medicine at Mellen Center for Multiple Sclerosis (MS) Treatment and Research at Cleveland Clinic, sat down with Neurology Live® last year at the 2019 Annual Meeting of the Consortium of Multiple Sclerosis Centers and discussed how she approaches fatigue in MS from a behavioral standpoint.

View video: neurologylive.com/ms-fatigue

For a full list of references, see the article on NeurologyLive.com.
Patients With High Levels of Fatigue Face Greater Disability, Economic Burden

Among patients with relapsing multiple sclerosis, those experiencing greater fatigue were less likely to be employed full time than those reporting more energy.

BY MARCO MEGLIO

NEW FINDINGS SHOW THAT PATIENTS with relapsing-remitting multiple sclerosis (RRMS) who were stratified by high levels of fatigue (RRMS + HF) had greater comorbidity and economic burdens compared with those with low fatigue (RRMS + LF) and individuals without MS. The results of the cross-sectional study were presented in September at MS Virtual 2020, the 8th Joint ECTRIMS-ACTRIMS meeting.

Hoa H. Le, PhD, associate director of real world value and evidence at Janssen Pharmaceuticals, presented the findings and noted that they can facilitate identification of patients with MS who may require additional treatment and support to manage MS-related fatigue. The data showed that the annualized number of outpatient visits (mean, 15.5; SD, ±15.4), emergency department visits (1.3 ± 3.5), and hospitalizations (0.9 ± 2.6) were greater for those with RRMS+HF compared with those with RRMS+LF (11.5 ± 17.6, 0.7 ± 2.0, and 0.4 ± 1.6, respectively) and those without MS (7.4 ± 11.3, 0.5 ± 2.5, and 0.4 ± 2.8, respectively).

To fully describe demographics, comorbidities, and health care resources of adults with RRMS with low levels and high levels of fatigue, investigators analyzed the data of 123 respondents with RRMS + HF, 375 with RRMS+LF, and 145,669 non-MS controls. The mean age among the 3 groups was similar; women made up 75%, 74%, and 55% of the groups, respectively.

Annual medical costs of $19,508 (± $43,614) were recorded for those with RRMS+HF compared with $10,406 (± $28,081) for those with RRMS+LF and $8493 (± $45,661) for those without MS. Full-time employment was reported in 18%, 31%, and 43% of those with RRMS+HF, RRMS+LF, and non-MS participants, respectively. Notably, those with RRMS + HF were more likely to have lower annual household income.

Higher Charlson Comorbidity Index scores were reported by patients with RRMS+HF (mean, 1.2; SD, ± 1.8) compared with RRMS+LF (0.7 ± 2.9) and those without MS (0.4 ± 1.0). Additionally, long-term disability was reported in 38%, 14%, and 3% of patients within each group, respectively.

Depression was reported in 65% of patients with RRMS+HF compared with 33% of those with RRMS + LF and 20% of healthy controls. Furthermore, investigators noted that anxiety was more commonly reported in those with RRMS+HF than in patients with RRMS + LF and individuals without MS (48% vs 25% and 19%, respectively). Insomnia was also reported in 26% of patients with RRMS + HF, 16% with RRMS + LF, and 8% of those without MS.

The economic burden associated with MS has been well documented. Recent data collected from the Harvey L. Neiman Health Policy Institute, in a study of 243 patients with MS, showed that more than 75% face financial toxicity, with higher risk for patients with MS who have lower financial self-efficacy and prior relapse history.

The Neiman data showed that decreases in income after receiving an MS diagnosis were reported by 56.2% of patients, with 37.1% experiencing a decrease greater than 20% of their income. The investigators of that study noted that approximately 67.0% of patients used at least 1 financial coping strategy in response to financial burden from treatment expenses. Furthermore, 50.4% of those cut their spending on leisure activities, and 40.2% withdrew money from savings accounts and 34.8% reduced basic spending.

For a full list of references, see the article on NeurologyLive.com.

More on NEUROLOGYLIVE.COM

No Relief: Rising MS Drug Prices

Neurology Live® spoke with Daniel M. Hartung, PharmD, MPH, associate professor of pharmacy at Oregon State University College of Pharmacy, to discuss his findings from a report on rising spending in the US Medicaid program on disease-modifying therapies for multiple sclerosis, and the unique nature of their prices in the United States.

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Progressive and Relapsing-Remitting Multiple Sclerosis Share Similar Fatigue Severity

Future research may help better characterize whether fatigue interventions aimed at one patient population may be effective in the other.

BY MARCO MEGLIO

NO BETWEEN-GROUP DIFFERENCES in mean fatigue severity or interference exist among persons with progressive multiple sclerosis (MS) or relapsing-remitting MS (RRMS), according to study results presented in September at MS Virtual 2020, the 8th Joint ECTRIMS-ACTRIMS meeting.

Tracy Herring, PhD, senior fellow at the University of Washington Multiple Sclerosis Rehabilitation & Wellness Research Center, who presented the data, noted that “given the similarity between fatigue and its correlates for both progressive and relapsing forms of MS, future research should consider if the interventions that work for fatigue management in people with relapsing forms of MS work similarly for people with progressive forms of MS.”

The study, which included 573 community-dwelling individuals with MS, looked at outcome measures such as fatigue severity and fatigue interference and used t test and χ² analyses to compare group differences.

Investigators also used multiple regression analysis to examine the extent to which the association of risk factors with fatigue severity and interference are moderated by MS subtype. They found that longer MS disease duration was associated with lower mean fatigue severity (B = –0.082; t = –3.637; P < .001) for persons with progressive MS compared with persons with RRMS (B = –0.025; t = –1.900; P = .058).

In an effort to identify common demographic risk factors, Herring and colleagues found that having a college degree or higher was associated with greater fatigue interference in persons with progressive MS (B = 2.90; t = 2.28; P = .023) compared with persons with RRMS (B = –0.17; t = –0.22; P = .825).

As the investigators previously noted, future studies will confirm whether interventions for patients with progressive MS can be used for those with RRMS. Fatigue increase has been documented as a major symptom that can affect quality of life for those with MS.

Findings from another study presented at MS Virtual 2020 revealed that patients with RRMS who were stratified by high levels of fatigue (RRMS+HF) had greater comorbidity and economic burdens compared with those with low fatigue (RRMS+LF) and individuals without MS.

The data showed that the annualized number of outpatient visits (mean, 15.5; SD ± 15.4), emergency department visits (1.3 ± 3.5), and hospitalizations (0.9 ± 2.6) were greater for those with RRMS+HF compared with those with RRMS+LF (11.5 ± 17.6, 0.7 ± 2.0, and 0.4 ± 1.6, respectively) and those without MS (7.4 ± 11.3, 0.5 ± 2.5, and 0.4 ± 2.8, respectively).

REFERENCES


TOP TWEETS

The Notorious EEG
(M. Scott Perry MD)
@TheNotoriousEEG
Enjoyed speaking with @neurology_live about one of my favorite topics!! #Dravet

Diamond Headache
@diamondheadache
Check out Dr. Diamond in the latest episode of #MindMoments @neurology_live by @byMattHoffman

TouretteAssn
@TouretteAssn
Dr. @MichaelOkun, @TouretteAssn Medical Advisory Board member and executive director of the Norman Fixel Institute for Neurological Diseases at @UFHealth, recently spoke with @neurology_live about holding insurance companies accountable in the care process for patients with neurological disorders.

Andrea Quattrone
@andreaquattro
Here I answer some questions by @_vic_j from @neurology_live about our new simple biomarker for #parkinson and #PSP. The second part of the interview in the comments.

NEUROLOGYLIVE VIDEOS

BENJAMIN M. SEGAL, MD: ESCALATION VERSUS INDUCTION IN MS
One of the leading topics of conversation in the multiple sclerosis (MS) community has been the induction versus escalation therapeutic approach. At this year’s joint ECTRIMS-ACTRIMS meeting, MS Virtual 2020, Benjamin M. Segal, MD, chair, Department of Neurology, and director, Neuroscience Research Institute, The Ohio State University, offered NeurologyLive® an overview of this debate.

LEAH CROLL, MD: IMPORTANCE OF MENTAL HEALTH OF CLINICIANS DURING COVID-19 PANDEMIC
Leah Croll, MD, a neurology resident at NYU Langone, and other members her department recently compiled a survey for all neurology faculty and house staff to better understand the psychosocial impact the pandemic has had on categories such as fear, depression, and anxiety. Here, she discusses the results.

MASCULINITY AND MULTIPLE SCLEROSIS
This episode, “Masculinity and Multiple Sclerosis,” features an interview with Bryan Davis, PsyD, MS, clinical health psychology fellow at Mellen Center for Multiple Sclerosis Treatment and Research at Cleveland Clinic. Davis offers his takeaways from a recent research project that set out to explore the impact of gender norms and masculinity on men with multiple sclerosis.

CAPITALIZING ON COLLABORATION IN NEUROLOGY CARE
This episode features an interview with Paul Fisher, MD, and Gerald Grant, MD, FACS, both of the Brain and Behavior Center at Stanford Children’s Health. The pair discusses how their team is bolstering the use of multidisciplinary care and harnessing advances in science to improve the care of children with neurologic disease.
Even patients taking a DMT can experience MS fatigue\textsuperscript{1,2}.

This symptom is highly prevalent, can occur early in the disease course, and may worsen over time.\textsuperscript{1,2}

The American Academy of Neurology (AAN) recommends using a validated fatigue rating instrument when identifying and managing fatigue.

The measurement of both maintenance and improvement of fatigue over a 12-month period may be useful when evaluating fatigue in patients with MS.\textsuperscript{3}

Discover potential mechanisms of MS fatigue, how to recognize it, and the effect it can have on your patients.

Visit \texttt{MoreToMS.com/more} to learn more.


MS = multiple sclerosis; DMT = disease-modifying therapy.

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