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Assessing Disability in MS Patients with the SNRS and CombiWISE Tools

Dr. Wilner:

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and joining me today to discuss his study on disability assessment in patients who are severely affected by multiple sclerosis is lead author Dr. Dejan Jakimovski. In addition to being a Research Assistant Professor in the Department of Neurology at the University of Buffalo, Dr. Jakimovski is the Clinical Research Unit Director at the Buffalo Neuroimaging Center. He also presented this research at the joint 2023 ECTRIMS-ACTRIMS meeting in Milan, Italy.

Dr. Jakimovski, it's great to have you with us today.

Dr. Jakimovski:

Thank you, Dr. Wilner. The pleasure is all mine.

Dr. Wilner:

So let's start with some background, Dr. Jakimovski. Can you tell us what prompted you to conduct this research that focused on assessing patients severely affected by MS?

Dr. Jakimovski:

So this is an excellent question given that there's such a significant shift in the epidemiology of the multiple sclerosis population right now towards an older group. Given that we've been very successful in how we treat and rehabilitate our people with multiple sclerosis, they tend to have longer longevity and better quality of life. That being said, a very small population of people with MS, around 1 to 5 percent, have a very severe disease that creates such a physical and cognitive disability that they're mostly marginalized, and they're usually placed within special facilities, like the Boston Home that we're going to talk about today, and they are rarely A) investigated and B) part of any clinical trials or investigation that could be part of the general MS research. So we wanted to fill this gap and actually address something in the literature and in our knowledge for people that really were not part of any research studies up to this time.

Dr. Wilner:

So these are patients, most of whom have had multiple sclerosis for a long time and accumulated significant disability. Is that correct?

Dr. Jakimovski:

There are two types of subgroups that are part of this study. One is the patients that you just mentioned: people who had multiple sclerosis for many years, 30 to 40 years, and chronically have led to accumulation to this disability. However, there is also a group of what is called an aggressive multiple sclerosis where, over a very short period of time, patients will deteriorate at a quick trajectory and lead to having such a disability over 5, 10, or 15 years when compared to someone who had the disease for 40 years. So there are these two subgroups that are part of the study and usually are in the facilities like the Boston Home.

Dr. Wilner:

Which criteria did you use to determine which patients exactly should be in the study?

Dr. Jakimovski:

The study design has a control arm that is also crucial in understanding the findings of the study. So the study was conceptualized in a way where we contacted the people at the Boston Home and the patients that are located in the Boston Home, and we wanted to create the best control arm as we could potentially do. So this control arm was located here in Buffalo at our University of Buffalo at the Jacobs MS Center for Treatment and Research, and we devised it in a certain way where we had to match—we call them twin patients—where a patient from the Boston Home with significantly more disability will be matched to a patient from Buffalo that had the same age ± 2 years, the same amount of disease duration ± 2 years, and the same sex. And we wanted to see—if everything else is equal, if both

patients were diagnosed around the same time and around the same age—why is the fact that one person had such a different trajectory in their disease that he would have had more disability and eventually be at the Boston Home?

In terms of the disability scales, we used an EDSS score of 7.5 or 8 as the criteria for our Boston Home people. These were wheelchair or bedridden patients that are not necessarily physically able to ambulate, and we compared them to significantly less disabled people from the Buffalo group as our two major comparison groups.

As part of the eligibility, of course, all people were diagnosed based on the latest McDonald criteria for MS diagnosis. They had to have an MRI as part of their study, and they would have to provide a consent to participate in this study or their legal proxy would provide a consent for them to be included in the study.

Dr. Wilner:

Okay. So you've identified who's going to be in this study. What were your methods?

Dr. Jakimovski:

So this was the major development part of the study. These people have such a significant disability that sometimes they're not even able to communicate back to the investigators and to myself. This also comes into play when you're trying to evaluate their physical disability, their cognitive disability, and actually communicate with these patients. The traditionally used and current gold standard of disability measures in multiple sclerosis is called the Extended Disability Status Scale, or EDSS score. It has been used for 30 years so far, and it's part of any clinical trial. However, if we look at the later scores within the score, we see that there is very little differentiation among the people with very high disability level. So even if you go to a place like the Boston Home and you can physically see that there's such a difference among how they're being affected by the fact that they're not ambulatory, they're being grouped by this score into single or half a point different score, and on paper, these people will not be differentiated in terms of their disability with the current score that we use as our gold standards.

So we tried to research and implement any other neurological scaling systems in these patients and create better differentiation among them when we used to compare them to our control group and later correlate to their MRI outcomes. Several of those scores included Multiple Sclerosis Severity Scale that incorporates the amount of disease duration that the patient had until it led to certain disability. We had the age-related MS Severity Score and two more scores, which are the Scripps Neurological Rating Status and the CombiWISE score that incorporates cognitive function, lower extremity function, hand function or manual dexterity function, and the full neurological examination that creates a single-digit score that ranges much wider than the EDSS score itself. And we wanted to see out of these scores in the literature which score is probably the best to investigate patients like this that have never been investigated before.

Dr. Wilner:

For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and I'm speaking with Dr. Dejan Jakimovski about his study on disability assessment and quantification in patients severely affected by multiple sclerosis. Let's turn our attention to the results. What did you find?

Dr. Jakimovski:

Yes. So we found that the Scripps Neurological Rating System—and this score was used 30 years ago as part of one of the first secondary progressive MS trials in the late '90s on cladribine—and the CombiWISE score, which incorporates disabilities from multiple aspects of the disease, had much better correlation with MRI outcomes, such as the amount of lesion volume on the scan and the amount of atrophy as measured as whole brain volume or gray matter atrophy within these patients. So now we are kind of bridging this so-called clinical radiological paradox that sometimes exists in multiple sclerosis where patients would have such a significant disability that is measured in the clinic, but then their MRI would show no changes whatsoever and vice versa; MRI had such a substantial amount of changes, but the patient does not have any physical disability. And by using these scores, we were able to bridge this gap closer that the new scores in these people better correlated with their MRI outcomes versus the current gold standard of the EDSS score that is currently used.

Dr. Wilner:

So given these findings, how might this line of research impact the way we manage patients with severe MS in the clinic?

Dr. Jakimovski:

The severely affected multiple sclerosis patients, since they might become part of future research, this study urges researchers and clinicians to enroll these patients in clinical trials and enroll these patients into their studies. We are showing that not necessarily the current gold standard that works very well in our so-called less disabled MS patients might not be the best option of how we can quantify their disability. And in a very near future, knowing the current trajectory of our disease-modifying therapy development and improvement in how we treat patients—and maybe we're going to have a future breakthrough in terms of therapy of multiple sclerosis—

we wanted to select certain scores or certain ways we measure their disability so if we intervene with such a future intervention, we will be able to measure how much of that change has occurred due to the intervention. So maybe EDSS score might not be as responsive to treatment and doesn't measure how much we have achieved by treating these people and other scores that have more flexibility and don't have that much of a ceiling effect may help us determine the amount of change due to therapy. So this is looking forward into what if we include these patients, how do we assess them, and how much of the change we could expect and actually measure using our tools today.

Dr. Wilner:

So, lastly, Dr. Jakimovski, do you have any other comments you'd like to share with our audience today?

Dr. Jakimovski:

Yes. I would definitely like to acknowledge the patients first and then the staff at the Boston Home facility. This is one rare facility. I think there are only a few in the United States that are like this. And this is not your typical tertiary care facility. This is a very specialized facility only for the care of severely affected multiple sclerosis patients. And the patients that are there are receiving state-of-the-art care. I wish we could have more of that research and capability for everyone that might need it.

Without their cooperation and without their family cooperation, none of these studies would have been possible. And in the very near future, we'll come up with a lot more work of how could you potentially investigate the cognitive abilities within a person who is noncommunicable or bedridden and how can we potentially bring the tools that everyday MS patients have, like an MRI scanner, to their bedside and be able to have a much more comprehensive assessment going forward and incorporate this group of people who have been marginalized before into our MS research every day.

Dr. Wilner:

Well, with those final comments in mind, I want to thank my guest, Dr. Dejan Jakimovski, for sharing his insights on the intricacies of assessing disability in the most severe group of patients with MS. Dr. Jakimovski, it was great speaking with you today.

Dr. Jakimovski:

Thank you very much. I truly enjoyed this interview.

Dr. Wilner:

For ReachMD, I'm Dr. Andrew Wilner. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.