



Comorbidity in Multiple Sclerosis

Some Answers, More Questions

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Guest Editor

This issue of the *International Journal of MS Care* (IJMSC) addresses the increasingly important issue of comorbidity and health behaviors in multiple sclerosis (MS). Many definitions of comorbidity exist, but commonly this refers to the total burden of chronic illness other than the disease of interest.¹ This encompasses the spectrum of psychiatric disorders, such as depression and anxiety, and medical disorders such as sleep disorders, hypertension, and hyperlipidemia. Over the last few years, investigators have highlighted the high prevalence of comorbidity in the MS population.² The most common comorbidities are depression, anxiety, hypertension, hyperlipidemia, and chronic lung disease.² These comorbidities are common even at the time of MS diagnosis; 19% of individuals have sought care for depression by this time, while 11.1% have sought care for anxiety,³ indicating that comorbidities are a concern throughout the disease course.

The presence of comorbid disease is a critical issue for clinicians given the breadth of adverse impacts with which it is associated. Comorbidity is associated with a longer delay between MS symptom onset and diagnosis, more severe disability at diagnosis even after accounting for diagnostic delays,⁴ greater disability progression,⁵ increased health-care utilization,⁶ and higher mortality.⁷ Despite our growing understanding of the effects of comorbidity in MS, important gaps persist in our knowledge about how best to identify these conditions

in clinical practice, and how they may influence treatment choices and treatment outcomes.

The timely recognition of comorbid conditions in clinical practice is paramount to initiating effective treatment of those conditions, and to preventing adverse effects of these conditions on MS. Depression is recognized to be common in MS, with a lifetime prevalence as high as 50%,⁸ and reduces health-related quality of life.⁹ Several screening tools with adequate sensitivity and specificity are available to assist clinicians in recognizing individuals with depression.¹⁰ However, this is not the case for anxiety. Anxiety is also quite common in MS, affecting over one-third of individuals. Like depression, anxiety adversely affects health-related quality of life,⁹ and may reduce the initiation of disease-modifying therapy.¹¹ Despite the relatively high prevalence of anxiety in MS and its adverse effects, much less effort has been devoted to identifying sound screening tools for anxiety that can be employed for use in clinical practice. Litster et al.¹² conducted a systematic review to evaluate the criterion validity of anxiety screening tools for measuring anxiety in MS. Strikingly, only four studies met their inclusion criteria, and only one tool, the Hospital Anxiety and Depression Scale, appeared to have adequate sensitivity and specificity. This highlights the need for further work in this area.

Gromisch et al.¹³ went beyond the tools available to assess the presence of depression, anxiety, and sleep disorders to evaluate what health-care providers are actually doing to assess these comorbidities in clinical practice. Using an online survey completed by 42 members of the Consortium of Multiple Sclerosis Centers, they found that nearly 93% asked about depression, and 81% asked about anxiety, but the use of validated tools to do so was infrequent. This highlights a gap in the implementation of available evidence.

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As interest in understanding the effects of comorbidity grows, so does the interest in developing new data sources to evaluate the effects of comorbidity in real world situations. Administrative health data constitute one such data source that increasingly has been used to study comorbidity in MS.¹⁴ Databases derived from electronic health records are a new and emerging and potentially powerful data source. They offer the potential to identify populations of individuals with particular conditions, their comorbidities, how they are treated, and their outcomes in a clinical setting rather than in the highly controlled setting of a clinical trial. While such uses are in their infancy, Mirsky et al.¹⁵ employed the Explorys Enterprise Performance Management database to re-address the question of whether use of disease-modifying therapies is associated with depression in the MS population.

In clinical trials of pharmacologic therapies, both disease-modifying and symptomatic, older individuals with MS and those with comorbidities are often excluded.¹⁶ While such exclusions may enhance the internal validity of these trials by reducing heterogeneity, control the sample sizes needed to detect an effect, and reduce concerns about safety, they have undesirable consequences. The findings from these clinical trials may lack generalizability, given that many individuals with MS are older and have comorbid conditions. Fakolade et al.¹⁷ illustrate that this problem extends to clinical trials of neurorehabilitation interventions in MS as well. Their scoping review included 54 randomized controlled trials, but most excluded individuals with comorbidity. This emphasizes the need for more pragmatic clinical trials of all interventions used in MS.

Finally, one of the best ways to address comorbidity in MS may be to prevent it altogether. While this is not possible for all comorbidities, modifiable health behaviors such as smoking, alcohol overuse, physical inactivity, obesity, and poor nutrition are risk factors for several common comorbidities in MS, including hypertension, diabetes, hyperlipidemia, ischemic heart disease, and chronic lung disease. Balto et al.¹⁸ report that over 85% of individuals with MS surveyed did not meet nutrition guidelines, and over 60% did not meet physical activity guidelines. The prevalence of smoking and alcohol overuse was much lower, suggesting that clinicians need to place more emphasis on helping their patients meet diet and activity guidelines.

We have learned a lot about health behaviors and comorbidity in the MS population, but this issue of the IJMSc indicates that there is much more work still to be done. □

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