Comorbidity increases the risk of hospitalizations in MS

Prevention opportunities

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Comorbidity is pervasive throughout health care, affecting the health status of patients, influencing treatment decisions and the resulting outcomes. A recent review of disease multimorbidity patterns showed nonrandom associations for 3 groups: cardiovascular and metabolic diseases, mental health problems, and musculoskeletal disorders.[1] Comorbid conditions are frequent in chronic conditions such as multiple sclerosis (MS). In fact, Marrie et al.[2] have shown that vascular comorbidities are detectable as early as the time of diagnosis, evidenced by greater self-reported disability in patients with one or more such comorbidities. These authors have also shown that the presence of vascular comorbidities over the course of the disease are associated with a shorter time to impaired ambulation requiring gait assistance of about 6 years.[3] Despite the recognized importance of comorbidity, the routine assessment of comorbidities has not been fully appreciated nor implemented in clinical practice.

Understanding how a given comorbid condition is related to the disease of interest is not always clear-cut. For example, in MS, comorbid depression may be related to therapy (e.g., interferon-β or corticosteroids), or may be a reaction to a chronic, disabling condition or part of the pathogenic disease process itself.[4] Moreover, with the advent of more powerful immune-modulating therapies for MS, infections, cardiovascular conditions, and endocrine disorders are more commonly seen.[5]

In this issue of *Neurology*®, Marrie et al.[6] continue their programmatic approach to investigating the effects of comorbidity in MS. In this article, they assess the association of comorbidity on hospitalization in 4,875 patients with MS compared to 24,533 controls matched on sex, year of birth, and region. Using case algorithms applied to the claims-based databases from Manitoba, they identified MS cases[7] and the following comorbidities: hypertension, diabetes, hyperlipidemia, ischemic heart disease, fibromyalgia, autoimmune thyroid disease, migraine, depression, anxiety, and bipolar disorder. This limited set of comorbidities was chosen based on associations with other outcomes in MS or because of a high prevalence in the MS population. Linear regression was used to assess the association between comorbidity status and hospitalization (all-cause, MS-specific, non-MS-related) adjusting for age, sex, and socioeconomic status.

Among the number of analyses reported in this study, the primary findings were that patients with MS with comorbidities had a 3-fold higher all-cause hospitalization rate than those without comorbidity. In the general population, those with comorbidity had a 6-fold higher hospitalization rate. After adjustment, this comparative rate of hospitalization based on comorbidity status was smaller, but remained. Thus, the presence of comorbidity was associated with an increased rate of all-cause hospitalizations in both populations, but the effect was higher in the matched population than in the MS cohort. The latter may suggest that comorbidity is better managed in the MS population due to their greater contact with the health care system. It should also be noted that the patients with MS were 3.5 years younger ($p < 0.001$) at the time of first hospitalization compared to controls, which may have contributed to a lower hospitalization rate overall among the patients with MS.

Surprisingly, comorbidity status was not associated with MS-specific hospitalizations as the authors had hypothesized. This study had sufficient sample size and employed appropriate statistical techniques, suggesting the latter finding is real and is in need of further investigation. It would have been helpful to have had data on functional status and disease severity in the analysis. Even though there were statistical differences in the prevalence of the comorbidities measured between patients with MS and their controls, the actual differences were small except for depression and fibromyalgia. Since both of these conditions are predominantly managed on an outpatient basis, one would not predict them to be associated with a higher MS-specific hospitalization rate, or

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all-cause hospitalization for that matter. Inclusion of other comorbidities more germane to the MS disease process (e.g., urinary tract infections) may have shown a positive association with MS-specific hospitalizations. The question of whether comorbidity is associated with an increased rate of MS-related hospitalizations is unresolved and will have to await future research for clarification.

While the major finding of this study is intuitively obvious, that the presence of the measured comorbidities is associated with increased all-cause hospitalizations, it provides additional objective evidence of the need to prevent and treat comorbidities in patients with MS. A recent clinical practice guideline on the assessment and management of psychiatric disorders in patients with MS is a welcome resource in this regard.[8] Still more work is needed to find optimal treatment strategies and coordinated care models that will reduce the burden of comorbid disease in MS.

A challenge for researchers and clinicians alike is how to appropriately measure comorbidity status. Many comorbidity measures exist but they employ a limited number of conditions that are exclusively chronic in nature or rely on claims data and are not easily implemented in a clinic setting. Thus, development of better measures of comorbidity is one area that should be addressed in the near future. Such measures should not be restricted only to chronic conditions, as acute conditions (e.g., pneumonia, bone fractures) can have a marked effect on the health and quality of life of patients with MS.

Marrie et al. have shown that the presence of the measured comorbidities is associated with an increased rate of all-cause hospitalization. This is an outcome that clinicians, patients, and hospital administrators would agree is something to be avoided. The author's recommendation to prevent and manage comorbidity in patients with MS is wise advice. Successful management of comorbidity will likely have benefits beyond lowering hospitalization, such as maintaining a higher functional status and enhanced quality of life.

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