Accelerated Cure Project for MS | July 2018

Accelerating research towards a cure for multiple sclerosis

Hypertension in those with MS

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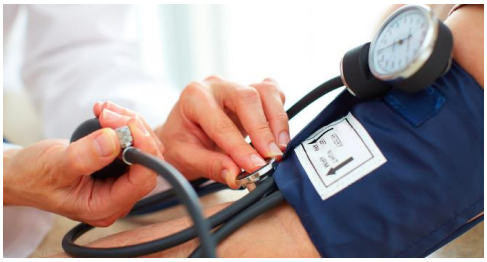
Multiple sclerosis (MS) can be very challenging at times, and it is increasingly evident that persons with MS (PwMS) commonly have other medical conditions. These comorbid conditions, especially *modifiable* ones, may add substantially to the difficulties PwMS encounter on a daily basis - thus, comorbidities in PwMS is a very hot research topic. Some research questions include investigating the role of comorbidities on the progression of MS, on the effectiveness of disease modifying therapies (DMTs), on the adherence of PwMS to DMTs, and on incurring healthcare debt. This month there were several studies looking at comorbidities in MS, but there were two studies that focused on characterizing *modifiable* comorbidities in MS.

The first study is actually a study I conducted with data from the Accelerated Cure Project (ACP) Repository, where we sought to describe the burden of cardiovascular conditions in MS, neuromyelitis optica and transverse myelitis – all demyelinating diseases.[1] The rationale for this study was to determine how common cardiovascular

conditions are when accounting for various factors that might influence cardiovascular disease risk and demyelinating disease risk (i.e. smoking). We call these factors confounders because differences in the distribution of these factors between the groups being compared may generate false results – therefore we need to *adjust* for these factors. There have been several prior studies looking at how common cardiovascular diseases were in PwMS, but the results were mixed – and one reason for the variation in results may have been the inability to *adjust* for *confounders*. Here is where the ACP resource is invaluable, as detailed information for several possible confounders were collected, including smoking history, history of obesity, socioeconomic status, and family medical history. For this study, there were 1,548 PwMS, 306 neuromyelitis optica cases, 145 transverse myelitis cases, and 677 controls (individuals without a demyelinating disease). After *adjusting* for the possible confounders, the burden of **hypertension** was approximately **30-50%** higher in PwMS than in the control population. Other cardiovascular conditions (heart disease, high cholesterol, and type 2 diabetes) were *as common* in individuals with demyelinating diseases as the control population. Interestingly, we observed no differences in the age of cardiovascular disease onset across the groups. This study was unique for it is one of the first studies of cardiovascular diseases in neuromyelitis optica and transverse myelitis, and the first study to comprehensively adjust for established cardiovascular risk factors – therefore, we are more confident that the observed association is a true relationship.



The second study aimed to describe the impact of hypertension on brain integrity in PwMS.[2] The researchers recruited 95 MS patients seen at a neurology clinic in Argentina. Blood pressure was measured; brain magnetic resonance imaging (MRI) images were used to determine the number of lesions, lesion volume load, and brain atrophy; and diffusion tensor imaging assessed brain white matter integrity by measuring the diffusion of water in myelinated tissue (white tracts). 71% of the patients in the study had above normal blood pressure. In a statistical analysis *adjusting* for age, gender, smoking status, DMT use, anti-hypertensive medication use, and serum vitamin D levels, increased blood pressure was significantly associated with reduced integrity in the white matter of three regions of the brain: precuneus, middle cingulate gyrus, posterior cingulate gyrus. Similarly, increased blood pressure was associated with brain atrophy in three frontal areas: orbital gyrus,

medial frontal cortex, and subcallosal area. Interestingly, blood pressure was not associated with lesion number or size.

The underlying mechanisms mediating these findings are not yet known, but we can say that hypertension is elevated in those with MS and that hypertension *may* impact brain integrity and brain atrophy. There is evidence that elevated blood pressure increases blood flow in the brain, which may play a role in promoting inflammation.[3] We also know that high blood pressure impacts the blood-brain barrier, which in MS is disrupted – which may allow for damaging immune cells to cross into the central nervous system. There is much work that can build on these two studies, but in the least, hypertension is modifiable and can be well managed through the use of many anti-hypertensive medications. So, in any event, it's further evidence to skip the salt in the kitchen.

1. https://www.ncbi.nlm.nih.gov/pubmed/30014877
2. https://www.ncbi.nlm.nih.gov/pubmed/29988562
3. https://www.ncbi.nlm.nih.gov/pubmed/23760630