Blood Pressure and Disability

Novus Orsa

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Disability has been defined as an inability to perform an action in a way that is consistent with the purpose of an organ or an organ system. Preclinical disability, often detected by self-report instruments, is the term for functional limitations that are not clinically diagnosed but nonetheless represent a transition between impairment and disability. Disability is a major public health problem, yet there is little information currently available with respect to the role of blood pressure (BP) in its development.

It is clear that hypertension-associated diseases and events, eg, stroke, myocardial infarction, angina pectoris, heart failure, and peripheral vascular disease, are risk factors for disability. Considerably less attention has been focused on the more direct associations between hypertension and disability. In 1985, hypertension was related to disability in the Framingham Heart Study. Nine years later, Hubert and Fries reported an association between the diagnosis of hypertension and disability in a university runners club.

Thirteen years later, in this issue of Hypertension, Hajjar et al report a statistically significant association between hypertension and disability and concurrent and prospective associations between systolic BP and disability among 999 stroke-free men and women participating in the Charleston Heart Study, 39% of whom were African American. Concurrently and prospectively measured systolic BP values were positively related to increasing disability as assessed by 3 functional measures: (1) Nagi’s Congruency in Medical and Self-Assessment of Disability Scale; (2) the Rosow-Breslaw Scale; and (3) the Katz Activities of Daily Living Scale. Thus, demonstration of a “dose-response” relationship between BP and multiple functional disability measures may be expected to stimulate a timely succession of studies, especially because many unanswered and important questions are raised about possible mechanisms. Hajjar et al suggest the following candidate mechanisms for the positive association between systolic BP and increments in disability over time: white matter hyperintensities in the brain, cerebrovascular function, overall lean muscle mass, inflammation or changes in the renin angiotensin system, and cognitive function. The complexity of understanding these mechanisms may be illustrated by considering cognition as just 1 example of a variable intervening between BP and disability.

With respect to cognition, the emphasis on executive functioning (planning, organizing, and properly sequencing activities) and fluid intellect (problem solving) is well placed, because adequate performance in these domains is necessary to meet the heavy demands of managing one’s work and personal affairs, as well as everyday life demands, such as shopping, cooking, house management, and dressing. Thus, although each of the proposed mechanisms deserves comment, we will focus on cognitive functioning for 2 reasons: we can illustrate the complexity involved in identifying mechanisms intervening between BP and disability, and studies of cognition and disability present interesting challenges in terms of the methodologic development of psychometric scales to assess these constructs, as well as their independent evaluation. One especially important challenge is to develop pure measures of disability that do not involve items (questions) that reflect cognitive deficit or depression.

Disability is a major predictor of functional disability and is related to BP as a cause, an effect, or both. In fact, interference with activities of daily living is itself a diagnostic criterion for dementia. However, modest changes in cognition may herald dementia years before it appears and may also play a direct causal role in disability in nondemented individuals.

Data on cognitive deficit and change were not available in the Charleston study sample, so these variables could not be included in the statistical models used by Hajjar et al. Future studies should add statistical controls for cognition, but more complex modeling will be necessary to understand the underlying mechanisms linking BP, cognition, and disability.

A simple model for the role of executive functioning as an intervening or mediator variable is shown in the Figure, panel A. However, the literature clearly indicates that vascular lesions in the brain are mediators of both cognition and disability. Thus, we have the model illustrated in the Figure, panel B. However, because vascular lesions relate to disability independent of cognition, we may modify the model again (Figure, panel C). Consideration of the literature on BP and social-psychological variables leads to even more complex models (Figure, panel D), eg, BP, cognition, and disability are related to social activity, sleep disturbance, and depressed mood. Fortunately, we have statistical modeling procedures available that allow comparisons among these models in terms of parsimony and predictive validity.

As an example of the literature relevant to these models, a review by Inzitari et al indicates that the vast majority of subjects fitting the criteria for the preclinical stage of cogni-

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tive and functional impairment have subcortical small vessel disease causing changes in the brain white matter.\textsuperscript{1} Persons manifesting small vessel disease on brain imaging often exhibit subtle cognitive changes over time, accompanied by functional disabilities that may not be readily apparent in everyday life. Moreover, white matter lesions are related to subtle deficits in executive performance but also to gait disorders and falls in older persons.\textsuperscript{1}

Identification of another risk factor for disability, in this case, hypertension, may be considered bad news. However, the study by Hajjar et al\textsuperscript{2} also offers good news. A successfully treated cohort of study participants for whom BP was reduced to normal levels on antihypertensive drugs did not show decline in functional abilities compared with normotensive subjects. This result needs to be replicated with a larger sample of controlled hypertensive subjects, as indicated by the authors, and with less stringent criteria for BP control.

Assuming replication, other questions arise, eg, is it the lowering of BP or the medication used to lower the BP that results in a reduction in disability? One may be inclined to postulate the former, because many antihypertensive medications have been associated with preclinical functional disability as adverse effects.\textsuperscript{4,8} The benefits of treatment may outweigh its adverse effects.

On the other hand, some antihypertensive drugs may serve to attenuate, delay, or prevent disability.\textsuperscript{4,8} For example, in persons with heart failure, angiotensin-converting enzyme inhibitors have been shown to be associated with a decreased rate of decline in physical function for persons with heart failure.\textsuperscript{8} After this study, Onder et al\textsuperscript{9} investigated the association between angiotensin-converting enzyme inhibitors and physical performance and muscle strength in women free of heart failure and compared 4 groups: patients on angiotensin-converting enzyme inhibitors, patients treated with other antihypertensive medications continuously, patients treated with other antihypertensive medications irregularly, and patients with normal BP. Over 3 years, decline in muscle and knee extensor strength was statistically significantly lower in patients who had been treated with angiotensin-converting enzyme inhibitors as compared with the other cohorts.

Given the complexities of sorting out dosages from drug action and the widespread use of polypharmacy, the avenue to understanding which antihypertensive medications are of direct value in attenuating disability may require the inclusion of measures of disability in clinical trials. Clearly, many follow-up studies can be generated from the work of Hajjar et al.\textsuperscript{2} Because of this work, we are beginning again (\textit{novus orsa}) with studies leading to a better understanding of the role of hypertension and antihypertensive treatment in the course and prevention of disability.

"The beginning is the most important part of the work."
—Plato, \textit{The Republic}

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