Why a Sex Difference in Age-Adjusted Relationship Between Height and Stroke Mortality?

To the Editor:

We read with interest the study by Hozawa et al., who concluded that height is inversely related to stroke mortality and that the relationship is statistically significant among women but not men when adjusted for age. The authors put forward several possible confounding factors including age effect and the impact of classic stroke risk factors. Adjusting for these variables, however, did not fully attenuate the relationship between height and stroke mortality in women. We feel that the following points need to be considered in order to better understand this age-adjusted sex difference in the relationship between height and stroke mortality.

Although the authors examined the possibility that systolic blood pressure may have been a confounding variable in the relationship between height and stroke mortality, the potential effect of pulse pressure (PP) was not analyzed. PP is an independent risk factor for stroke mortality. It is possible that differences in PP resulting from differences in arterial structure and function between the sexes could better explain this phenomenon.

It is increasingly being realized that abnormalities in large artery structure and function play an important role in the pathogenesis of vascular disease including stroke. PP is the pulsatile component of blood pressure generated through intermittent ventricular contraction. Whereas PP is influenced by several cardiac and vascular factors, its magnitude is predominantly determined by the cushioning capacity of arteries or arterial stiffness and the timing and intensity of pressure wave reflections. The latter results from the summation of a forward wave coming from the heart propagating at a given pulse wave velocity and a backward wave returning from points of arterial bifurcations (reflection points). Therefore, central arterial PP magnitude is ultimately the cushioning capacity of arteries or arterial stiffness and the distance from reflection sites either ‘real’ (physical distance to point of reflection) or ‘apparent’ whereby heightened pulse wave velocity attributable to increased arterial stiffness causes reflection points to appear closer.

In Hozawa’s study, the inverse relationship between stroke mortality and height was attenuated with age in men. As aging is associated with increased vessel stiffness, it could be that in older men, vessel stiffness is the more important determinant of PP and thereby stroke mortality. Conversely, because a significant factor in determining the physical distance to be traveled by the pulse wave and hence PP is physical stature, it is possible that this rather than vessel stiffness is the more important determinant of PP and thereby stroke mortality in women.

In addition, previous studies have shown that women have larger reflected waves than height and age-matched men. Thus, there are also unexplained sex differences in arterial structure and function that lead to increased wave reflection in women which may in part account for the apparent sex difference in height-adjusted stroke mortality observed by Hozawa.

In our view, future studies of sex-related differences in stroke risk and mortality should not only take height and ‘classic risk factors’ into account but also hemodynamic factors that influence PP. These surrogate measurements of large vessel structure and function should include aortic pulse wave velocity (stiffness) and pulse wave analysis (wave reflectance). Elucidating sex differences in arterial structure and function is important because this approach may have future therapeutic implications for stroke prevention.

Disclosures

None.

Thomas Walsh, MRCPI
Teresa Donnelly, MRCPI
Declan Lyons, MD
Clinical Age Assessment Unit
Department of Medicine
Mid-Western Regional Hospital & University of Limerick
Dooradoyle, Limerick, Ireland

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Thomas Walsh, Teresa Donnelly and Declan Lyons

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