More than 4 decades ago, Borhani reported excess stroke mortality risk in the southeastern states of the US, the “Stoke Belt”. Since then, none of the many reasons proposed adequately explained the phenomenon. Many studies have failed to adequately explain geographic differences in stroke risk using traditional stroke risk factors measured later in life. There are 3 possible reasons why the traditional stroke risk factors failed to account for the higher stroke risk in the Stroke Belt states. First, the measurement of the risk factors may be inadequate. For example, higher blood pressure level, the most important single determinant of stroke risk, was measured in previous studies at only 1 or even several points in time, usually in middle aged or older adults. The integrated level of blood pressure from childhood or young adulthood to older ages and their adverse effects on vascular disease may be a more important determinant. Second, previous studies typically did not take into account the differential effects of treatment of the risk factors, not only including the likelihood that individuals are placed on various therapies to lower blood pressure or other risk factors but also, most important, adherence to such therapies and reduction of these risk factors. Third, there may be other still unidentified risk factors more prevalent in the southeastern states that make them carry this high risk of stroke mortality to their residents.

Supporting the concept of duration of exposure, we have previously reported in older individuals from the Cardiovascular Health Study that higher white matter grade on brain MRI, a marker of cumulative exposure and control of several stroke risk factors, explained 25% of the observed differences in stroke incidence among the 4 centers of the study. Another approach to evaluating the concept of duration of exposure is to evaluate whether earlier life exposures in the Stroke Belt are associated with increased stroke risk. Using local state mortality data and 1990 US census data, a couple of US studies examined the relation between Stroke Belt early-life mortality data and 1990 US census data, a couple of US states had higher stroke mortality compared with those who were born in northeastern states. Three years later, Lackland and colleagues reported a graded risk of stroke mortality by birthplace, with the highest risk among individuals born in South Carolina (a prominent Stroke Belt state), intermediate risk in those born in the southeastern states other than South Carolina, and lowest risk in those born outside the southeastern states. The lower stroke risk among those born outside the southeast was greater in blacks than whites and in men than women.

These 2 studies were complementary in terms of reporting the importance of birthplace effect on stroke death later in life among those who migrated to a traditionally low stroke risk state (New York) and a traditionally high stroke risk state (South Carolina). However, because both studies were not designed to determine how birthplace affects stroke mortality, the question remains whether the excess stroke risk conferred by early childhood residence in the Stroke Belt states is mediated by socioeconomic status, behavioral norms, medical care, cardiovascular risk factors, or certain environmental exposures. Moreover, it is not clear whether those who were born and lived in the Stroke Belt carry excess risk than those who were born and migrated out of the Stroke Belt. Therefore, the study by Glymour and colleagues in the current issue of Stroke is a welcome addition to the literature on this interesting topic.

Glymour and colleagues analyzed data from the Health and Retirement Study (HRS). They compared the risk of first stroke in those who never lived in the Stroke Belt to those who lived there in childhood only, in adulthood only, and at both ages. Overall, they found higher stroke risk among those who lived in the Stroke Belt in childhood or both in childhood and adulthood (but not in adulthood only) compared with those who never lived there. The excess risk was not adequately explained by demographic characteristics, childhood and adult socioeconomic status, and adult cardiovascular risk factors.

HRS data have several strengths in addressing the above questions at least partially. HRS is a large (n=18 070), nationally representative, longitudinal study of white and black men and women 50 years or older. HRS includes information on place of residence in childhood and at study enrollment, comprehensive socioeconomic status assessments, and many stroke risk factors. The study has several major shortcomings that were acknowledged by the authors, including the self-reported nature of stroke outcome and predictors, lack of data on some important stroke risk factors such as levels of blood pressure and cholesterol, lack of data on place of residence between childhood and study enroll-
ment, and finally inadequate power of some subanalysis by sex and birth cohort.

The study by Glymour and colleagues is important in making a valuable contribution to our understanding of Stroke Belt etiology by suggesting that the determinants of high stroke risk probably begin in childhood. Unfortunately, the data cannot separate the above 3 critical hypotheses related to high stroke risk in the southeastern states. A next step, therefore, might be to focus efforts in trying to determine whether there are differences in stroke risk factors, particularly early onset ones, as well as micro- and macronutrients among children and young adults in the southeastern states compared with the rest of the nation. For example, there has been some suggestion that low birth weight, poor weight gain early in life and low parental socioeconomic status at the time of birth as measures of prenatal and early postnatal nutritional and environmental exposures, may be associated with an excess risk of stroke. Moreover, dietary factors such as high salt intake or low intake of potassium in childhood and young adulthood may be associated with an earlier onset of elevated blood pressure which could be associated with greater subclinical vascular disease and consequently stroke risk later in life. Increased left ventricular hypertrophy, microalbuminuria, elevated creatinine and cystatin-C levels and microvascular retinopathy in the eye may all be markers for long-standing elevated blood pressure and should be evaluated in further studies. In summary, the findings from this study and previous and ongoing studies to explain high stroke risk in the southeastern US suggest that greater emphasis is needed in studying the evolution of vascular disease in high and low risk areas in children and younger adults.

Disclosures

None.

References


Key Words: cerebrovascular diseases ■ children ■ epidemiology ■ etiology ■ geography ■ risk factors ■ mortality
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