Small Vessel Disease and Dietary Salt Intake: Cross-Sectional Study and Systematic Review

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Background: Higher dietary salt intake increases the risk of stroke and may increase white matter hyperintensity (WMH) volume. We hypothesized that a long-term higher salt intake may be associated with other features of small vessel disease (SVD). *Methods:* We recruited consecutive patients with mild stroke presenting to the Lothian regional stroke service. We performed brain magnetic resonance imaging, obtained a basic dietary salt history, and measured the urinary sodium/creatinine ratio. We also carried out a systematic review to put the study in the context of other studies in the field. *Results:* We recruited 250 patients, 112 with lacunar stroke and 138 with cortical stroke, with a median age of 67.5 years. After adjustment for risk factors, including age and hypertension, patients who had not reduced their salt intake in the long term were more likely to have lacunar stroke (odds ratio [OR], 1.90; 95% confidence interval [CI], 1.10-3.29), lacune(s) (OR, 2.06; 95% CI, 1.09-3.99), microbleed(s) (OR, 3.4; 95% CI, 1.54, 8.21), severe WMHs (OR, 2.45; 95% CI 1.34-4.57), and worse SVD scores (OR, 2.17; 95% CI, 1.22-3.9). There was limited association between SVD and current salt intake or urinary sodium/creatinine ratio. Our systematic review found no previously published studies of dietary salt and SVD. *Conclusion:* The association between dietary salt and

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background SVD is a promising indication of a potential neglected contributory factor for SVD. These results should be replicated in larger, long-term studies using the recognized gold-standard measures of dietary sodium. **Key Words:** Dietary salt—urinary sodium/creatinine ratio—white matter lesions—acute stroke.

Introduction

Cerebral small vessel disease (SVD) is common and clinically important: it is responsible for dementia,[1] depression,[2] physical disability,[3] and one fifth of all strokes.[4] On pathology, there is an intrinsic disease of the small deep-penetrating arteries with appearances described as segmental arteriolar disorganization, fibrinoid necrosis, and lipohylinosis.[5] However, the etiology is unclear: while common vascular risk factors such as hypertension are very important, they only account for a small proportion of the variance in SVD features.[6]

Previously, we found that increased dietary salt intake was associated with greater white matter hyperintensity (WMH) volumes, a key feature of SVD.[7] Dietary salt also increases the risk of any type of stroke: in 19 cohort studies (n > 170,000 participants), the relative risk of stroke was 1.23 (95% confidence interval [CI], 1.06-1.4) for higher versus lower salt intake,[8] confirmed in the North Manhattan Stroke Study, which found a 17% increase in the 10-year stroke risk for each additional 500 mg of daily dietary sodium.[9]

To further examine the potential relationship between dietary salt intake and SVD clinical and imaging features, we performed a cross-sectional study in patients presenting with minor stroke and a systematic review of the existing literature.

Materials and Methods

We recruited consecutive inpatients and outpatients presenting to our regional stroke service with a minor ischemic stroke from May 2010 to May 2012. We defined "minor" as a stroke with a National Institutes of Health Stroke Scale (NIHSS) score of 7 or lower at assessment and which was not anticipated to cause impairment in activities of daily living. The detailed recruitment and data collection procedure have been published previously.[7,10]

The study was approved by the Lothian Ethics of Medical Research Committee (REC 09/81,101/54) and National Health Service Lothian Research and Development Office (2009/W/NEU/14) according to the Health Research Authority, United Kingdom, which uses the Declaration of Helsinki 1975 (revised in 1983), and all patients gave written informed consent.

All patients underwent magnetic resonance imaging (MRI) as soon as possible after presentation (1.5 Tesla GE Scanner, General Electric Medical Systems, Milwaukee, USA) with T1, T2, T2*, fluid-attenuated inversion recovery, and diffusion-weighted imaging sequences.

An experienced neuroradiologist (J.M.W.) reviewed all imaging and classed the stroke lesion as "lacunar" or "cortical" blind to clinical features; if no lesion was present, the stroke syndrome was classified on clinical findings based on the Bamford Classification.[7] We defined hypertension as either a previous diagnosis of hypertension made prior to the stroke or a diagnosis of hypertension made after presentation with stroke. All patients had blood pressure (BP) recordings made during their NHS clinical care. We recorded deep and periventricular WMHs on the Fazekas Scale, and a total SVD burden score (0-4) that incorporates microbleeds, lacunes, periventricular spaces in the basal ganglia, and WMH, as described previously,[11] classifying severe WMHs as a periventricular Fazekas score of 3 and/or a deep Fazekas score of 2-3.

We assessed dietary salt intake during patient recruitment with the following questions. The first 2 questions were adapted from a widely used validated food frequency questionnaire,[12] and the third question we derived ourselves as there was no widely used validated question to estimate if dietary salt intake had reduced during adult life:

a. *"Do you/your partner add salt to your food during cooking": Always/Often/Occasionally/Rarely/Never*
b. *"Do you add salt to your food at the table": Always/Often/Occasionally/Rarely/Never*
c. *"Have you reduced the amount of salt that you add to your food, during cooking or at the table, since age 20": No take more salt/Yes, I take less salt/I take the same amount of salt.*

These questions were chosen pragmatically to identify patients who were likely to have a higher salt intake from those who on average were likely to have a lower salt intake, rather than to quantify lifetime salt intake. The gold-standard measurement of current dietary salt with a detailed food frequency questionnaire or 24-hour urine would have been impractical in the context of a large study of patients with a recent stroke.

We measured the urinary sodium : creatinine ratio on an early-morning urine specimen obtained a minimum of 1 month post–index stroke using the standard hospital biochemistry laboratory procedures.