Magnetic Resonance Abnormalities and Cardiovascular Disease in Older Adults

The Cardiovascular Health Study

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Background and Purpose

Cerebral magnetic resonance imaging often detects abnormalities whose significance is unknown. The prevalence and correlates of findings such as ventricular enlargement, sulcal widening, and increased white matter signal intensity were examined in 303 men and women aged 65 to 95 years participating in a multicenter study of cardiovascular disease.

Methods

Cerebral magnetic resonance imaging was performed and interpreted according to a standard protocol, and findings were correlated with measures of cardiovascular disease and its risk factors.

Results

Ventricular enlargement and sulcal widening were associated with prior stroke, hypertension, and white race (each P<.01). Extent of white matter hyperintensity was associated with age, prior stroke, hypertension, and use of diuretics (each P<.004). On multivariate analysis, age, male gender, white race, and prior stroke retained strong associations with increased ventricular and sulcal scores. After adjustment for age, prior stroke, and other risk factors, white matter hyperintensity was associated with atherosclerosis as measured by increased internal carotid artery thickness on ultrasound.

Conclusions

Cerebral atrophy and white matter hyperintensity are common in the elderly and are associated with age, prior stroke, and known cardiovascular risk factors. Though these findings have been suggested to represent normal aging, their wide variability and associations with cardiovascular disease argue against their inevitability with advancing age and support the need to identify modifiable risk factors for these abnormalities. (Stroke. 1994;25:318-327.)

Key Words

- epidemiology
- leukoencephalopathy
- magnetic resonance imaging
- risk factors

Magnetic resonance imaging (MRI) is widely used for the diagnosis of intracranial abnormalities in the elderly. During such use, MRI frequently detects other abnormalities of unknown significance that are often postulated to be related to cerebrovascular disease or chronic cerebral ischemia. Findings such as ventricular enlargement, sulcal widening, and cerebral white matter areas of increased T₂-weighted signal intensity on MRI have been strongly correlated with age, prior stroke, and hypertension.¹⁻⁷ Conversely, the very high prevalence of these abnormalities in elderly asymptomatic persons has led many to believe that they are a normal part of aging.⁸

Previous reports have been based primarily on clinical series and volunteer samples of relatively small size, which may be poorly generalized to a community-dwelling population. Examination of cardiovascular and cerebrovascular disease and their risk factors, other than stroke and hypertension, has been infrequent and nonstandardized.⁹ Few have investigated MRI associations with noninvasive measures of subclinical cardiovascular disease such as carotid ultrasonography and echocardiography.¹⁰

The Cardiovascular Health Study (CHS) is a population-based observational study of 5201 men and women aged 65 years and older from four US communities. Shortly after initiation of the study, cerebral MRI was performed in 100 subjects with a reported history of stroke and 203 age- and sex-matched control subjects to determine the feasibility of performing MRI in the entire eligible cohort. These data were analyzed to (1) describe prevalences of MRI-defined ventricular enlargement, sulcal widening, and cerebral white matter areas of increased signal intensity by age and gender; and (2) identify associations between MRI findings and cardiovascular disease and its risk factors.

Subjects and Methods

Data Collection

The CHS sample of 5201 men and women aged 65 and older was recruited from a random sample of the Health Care
Financing Administration (HCFA) Medicare eligibility lists in four US communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh (Allegheny County), Pennsylvania. Potential participants were excluded if they were institutionalized, wheelchair bound in the home, or currently under treatment for cancer. Details of the study design have been published.11 Eligible participants giving informed consent answered standard questionnaires on personal habits, transient symptoms (such as syncope, vertigo, and palpitations), cognitive function,12,13 family history, medication use, and medical history, including recent hospitalizations and prior diagnoses of cardiovascular and cerebrovascular diseases. Baseline recruitment and examination were conducted between June 1989 and May 1990.

Participants were asked to fast for 12 hours before their clinic visit. After a 5-minute rest, sitting blood pressure in the right arm was measured with an appropriately sized cuff and a random-zero sphygmomanometer. The average of two measurements was used for analysis. Duplicate measurements of supine blood pressure in both arms and both ankles were performed with a standard mercury sphygmomanometer and an in-office Doppler ultrasound probe. The ratio of these pressures (the ankle-arm systolic blood pressure ratio) was used as a measure of arterial occlusive disease in the lower extremities.14

Anthropometric measurements included weight and height in light clothing and no shoes. Twelve-lead resting electrocardiograms and venipuncture were performed early in the clinic visit. Multiple aliquots of plasma were prepared, frozen at −70°C, and shipped weekly on dry ice to a central laboratory. Fasting plasma lipid analyses included measurement of total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglycerides. Low-density lipoprotein cholesterol (LDL-C) was calculated according to the Friedewald equation.15 Coagulation rate measurements were made for common and internal carotid arteries. CHS ultrasound methods and initial quality control results have been published.16

M-mode echocardiography was used to measure dimensions of the left atrium and ventricle and thickness of the ventricular walls. Left ventricular mass was derived from the formula of Devereux and associates.17 Abnormalities of left ventricular ejection fraction, regional wall motion, and left atrial chamber size were detected on two-dimensional echocardiographic images by trained readers and were classified on a qualitative basis as normal, borderline, or abnormal. The borderline and abnormal classifications were combined into a single “abnormal” category for analysis. CHS echocardiographic methods and initial quality control results have been published.18

Study of the Feasibility of Magnetic Resonance Imaging

Approximately 18 months after the baseline examination, a study of cerebral MRI in 303 CHS participants aged 65 to 95 years was undertaken to evaluate the feasibility of performing MRI in the entire CHS cohort. The study was conducted between November 1991 and January 1992 and included 100 randomly selected participants who had reported a prior stroke and 203 persons who had not reported a stroke and had not suffered one during follow-up. These 203 control subjects were selected by stratifying the cohort into deciles of risk for prevalent stroke based on presence of hypertension, atrial fibrillation, and coronary heart disease and on levels of serum creatinine and common carotid wall thickness at baseline. A group of 101 controls was selected at random from the lowest risk decile and matched to prevalent stroke cases for gender and age within 5 years. A second group of 102 controls was selected at random from all other risk deciles combined and similarly matched to stroke cases for gender and age. Given the entry criteria into the study and the requirement for confirmed consent, prevalent and incident function scores in general were reasonably good (a mean Mini-Mental State score of 39 in the control group and 31 in the stroke group; a mean digit-symbol score of 32 in the control group and 31 in the stroke group; P<.001 for both comparisons), and few if any participants were frankly demented.

Magnetic resonance imaging was performed on General Electric or Picker 1.5 Tesla scanners at three of the four field centers and on a 0.35 Tesla Toshiba instrument at the fourth center. The first scanning sequence was a sagittal T1-weighted localized scan, with pulse repetition time (TR), 500 milliseconds; echo time (TE), 20 milliseconds; thickness, 5 mm; gap, 0; and matrix, 128 × 256. Midline images were used to identify the anterior commissure-posterior commissure (AC/PC) line on which subsequent oblique axial scans were aligned. The second series of axial spin density/T1-weighted scans was angled parallel to the AC/PC line, with TR, 3000 milliseconds; TE, 30/100, flow compensated; thickness, 5 mm; gap, 0; and matrix, 256 × 192; 1/2 ncs (1 ncs on 0.35 scanner) from vertex to skull base. The third series of axial T1-weighted scans was angled parallel to the AC/PC line, with TR, 500 milliseconds; TE, 20 milliseconds; thickness, 5 mm; gap, 0; and matrix, 256 × 192; 1 ncs (2 ncs on 0.35 Scanner) from vertex to skull base. Scans were archived on magnetic tape and sent to a central reading center for interpretation by neuroradiologists trained in the CHS protocol. Images were interpreted directly from a PDS-4 digital workstation (Vortech, Dallas, Tex) consisting of four 1024x1024 pixel monitors capable of displaying all 96 images simultaneously.

Cerebral ventricular size was assessed on a scale of 0 to 9 by comparison with a series of eight studies with successively increasing ventricular size ranging from small and presumably normal (grade 1) to severe enlargement (grade 8; Fig 1). Studies considered to have ventricles smaller than those in grade 1 received grade 0 and worse than grade 8 received grade 9. Similarly, sulcal widening was assessed by comparison with eight studies with successively increasing sulcal size, with grades 0 and 9 assigned as for ventricular size (Fig 2).

“White matter disease” was estimated as the total volume of periventricular and subcortical white matter–signal abnormality on spin density–weighted axial images by comparison with eight studies that successively increased from barely detectable white matter changes (grade 1) to extensive, confluent changes (grade 8). Studies with no white matter changes received grade 0, and those with changes worse than grade 8 received grade 9 (Fig 3). Abnormalities interpreted as representing areas of large vessel cerebral infarction or small vessel lacunar infarction were coded separately and excluded from this analysis. All studies were assessed without knowledge of any clinical information, including subject’s age, gender, case-control status, prior imaging findings, or other cardiovascular disease risk factors.

Definitions

Prevalent myocardial infarction, angina pectoris, congestive heart failure, stroke, transient ischemic attack, and peripheral vascular disease were defined as positive answers to the question, “Has a doctor ever told you that you had ...?” Confirmation of diagnosis was sought from review of hospital and physicians’ records. Prevalent disease was considered confirmed if review of hospital or physicians’ records showed a diagnosis of these conditions and nonconfirmed if not. Subjects with major Q-QS waves by Minnesota code20 on resting
electrocardiogram or with an ankle-arm index less than 0.8 were also considered to have prevalent myocardial infarction and prevalent peripheral vascular disease, respectively, regardless of reported history. Coronary heart disease included reported and confirmed (or silent) myocardial infarction and/or reported and confirmed angina and/or prior coronary revascularization procedures.

Diabetes was defined as self-report of physician-diagnosed diabetes, current use of insulin or oral hypoglycemic medication, a fasting glucose level of 140 mg/dL or greater, or a 2-hour post-load glucose level of 200 mg/dL or greater. Impaired glucose tolerance was defined as a fasting glucose level of less than 140 mg/dL and a 2-hour post-load glucose level of 140 mg/dL or greater in the absence of physician diagnosis of diabetes or use of glucose-lowering medications. Hypertension was defined as systolic blood pressure of 140 mm Hg or greater, diastolic blood pressure of 90 mm Hg or greater, or current use of antihypertensive medications. Borderline hypertension was defined as the subcategory of persons not on medications who had systolic pressures of 140 to 159 mm Hg and diastolic pressures of 90 to 94 mm Hg. Obesity was defined as greater than 20% above ideal body weight as defined by the Metropolitan Life Insurance Company.21

Statistical Analysis

Associations with MRI findings were assessed by \( \chi^2 \) analysis and \( t \) tests for categorical and continuous MRI variables, respectively. Relationships with 5-year age groups were assessed by \( \chi^2 \) test for trend for categorical variables and analysis of variance for continuous variables. Correlations between continuous variables were assessed with linear regression and correlation. Independence of associations with MRI findings was assessed by multiple regression. Because the coding of ventricular enlargement, sulcal widening, and white matter disease was arbitrary, for multiple regression analyses, these variables were recorded to their normal scores to fit the assumptions of the analysis.22 All analyses were performed using the STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES (SPSS).23

Results

Cerebral atrophy, as assessed by ventricular enlargement and sulcal widening, increased with age and was greater in men than in women (Table 1). Severity of white matter disease similarly increased with age and showed a nonsignificant trend toward being greater in women than in men. Ventricular enlargement was significantly greater in participants with reported history of stroke, particularly among women (Fig 4). Sulcal widening was also greater in participants with stroke (Fig 5), as was white matter disease severity (Fig 6). Mean white matter disease severity was 2.40 in those with prior stroke compared with 1.86 in control subjects without stroke; median severity was 2 in those with prior stroke compared with 1 in control subjects without stroke.

Associations With Cardiovascular Disease and Its Risk Factors

Ventricular enlargement was more severe in persons with prior stroke, diabetes, and hypertension (Table 2). Participants with nonconfirmed stroke had a mean ventricular score intermediate between those of confirmed strokes and control subjects without stroke. Participants with diabetes had ventricular scores greater than those of persons with impaired or normal glucose tolerance. Those with hypertension had higher ventricular and sulcal scores compared with those without hypertension. Subjects who were former smokers or had never smoked and white subjects also had significantly higher ventricular scores compared with current smokers and nonwhite subjects, respectively.

Mean sulcal score was higher in subjects with prior stroke, hypertension, and use of antihypertensive medications. Higher white matter disease grade was associated with prior stroke, hypertension, and use of antihypertensive medications.
pertensive medications. No association between ventricular or sulcal scores or white matter disease severity was noted with coronary disease, congestive failure, atrial fibrillation, carotid stenosis, abnormal left ventricular systolic wall motion or ejection fraction, or aspirin use.

Associations between MRI findings and continuous variables are shown in Table 3. Ventricular enlargement and sulcal widening were both significantly related to higher systolic blood pressure, creatinine, and carotid wall thicknesses. In addition, ventricular enlargement was related to higher electrocardiographic left ventricular mass and lower physical activity levels, whereas sulcal widening was also related to higher uric acid levels and lower ankle-arm indexes, spirometric lung volumes, and cognitive function scores. White matter disease severity showed associations similar to those of sulcal widening, except for absence of associations with uric acid and creatinine levels and presence of inverse associations with height and physical activity.

Independent associations between MRI findings and known risk factors and manifestations for cardiovascular disease were assessed by multiple linear regression (Table 4). Age, male gender, white race, and prior stroke were strongly associated with increased ventricular and sulcal scores. White matter disease severity was associated with prior stroke and increased internal carotid wall thickness and diastolic blood pressure, as well as diuretic use and lower LDL-C levels. It was not associated with gender after adjustment for age, prior stroke, and other factors.

Discussion

Prevalence and Correlates of Cerebral Atrophy

Some degree of cerebral atrophy, as defined by ventricular and sulcal size greater than those in our grade 1 images, was present in 301 of 303 participants in this feasibility study, including all but 2 participants without prior stroke. Ventricular and sulcal size increased with age and were greater in men independent of other factors such as race, prior stroke, and other manifestations and risk factors of cardiovascular disease. Prior stroke and white race were independently associated with increased ventricular and sulcal scores.

The associations of MRI findings with age in our data are similar to those reported previously. Advanced age has been shown to be associated with increased ventricular volume and decreased cerebral hemispheric volume in a large number of computed tomography (CT) and quantitative volumetric MRI studies. The mechanism of age-related increases in cerebral atrophy and ventricular size has not been clearly defined but has been suggested to be caused by declining cerebral perfusion. That age maintained a strong relation with measures of cortical atrophy in the current study after adjustment for a variety of other factors suggests either that age may directly effect such changes, or more likely, that other age-related factors yet to be identified may be responsible. It must be noted, however, that causal relations may be suggested but cannot be determined from cross-sectional data such as these.
Similarly, explanations for the observed gender differences in atrophy remain elusive, having variably been ascribed to greater degrees of atherosclerosis in men, to some protective effect of female sex hormones, or to differences in hematocrit or blood viscosity. Hormone replacement therapy has been shown to be associated with improved cardiovascular risk factor profiles and less evidence of subclinical atherosclerosis in older women, and these relations may also pertain to cerebral atrophy.

Hypertension, whether measured by diagnosis, medication use, or blood pressure level, was also associated with cerebral atrophy in the current study. The relations of systolic pressure to measures of cerebral atrophy were among the strongest demonstrated and may account in part for the associations of MRI findings with carotid wall thickness and left ventricular mass, both of which are related to blood pressure. Previous studies have demonstrated an association between hypertension and increased cerebral atrophy attributed to hypertension-related reductions in cerebral blood flow.

Cerebral atrophy has also been related to aortic atherosclerosis as measured by calcifications of the abdominal aorta visualized by CT. The ankle-arm index, a reliable measure of arterial occlusive disease in the lower extremities, demonstrated negative associations with sulcal widening and white matter disease severity on bivariate analysis in the current study and retained its negative relation with sulcal widening after

![Fig 3. Proton density-weighted images for grading white matter disease, ranging from barely detectable white matter changes (W1, upper left-hand corner) to extensive, confluent white matter changes (W8, lower right-hand corner).](image-url)
adjustment for other factors, which confirms these prior findings.

Prevalence and Correlates of White Matter Disease

White matter disease as detected by hyperintensity on spin density- and T2-weighted images, ranging from a few discrete punctate lesions to widely confluent areas, was present in 87% of all subjects in this study and in 83% of those without prior stroke. Severity of white matter disease increased strongly with age independently of other factors but was not associated with gender, though there was a nonsignificant trend toward increased severity in women after controlling for age. White matter disease severity was also independently associated with prior stroke, diastolic blood pressure, diuretic use, internal carotid wall thickness, and LDL-C level.

White matter foci of increased T2 signal intensity have previously been shown to be more common in persons with known cerebrovascular disease, hypertension, and advanced age. These foci appear to correspond pathologically to areas of gliosis and demyelination surrounding small vessels and are believed to be concentrated in the periventricular watershed areas between cortical penetrating and deep perforating vessels. Vascular changes accompanying these foci, such as tortuosity and sclerosis, are believed to be primarily caused by chronic hypertension, which leads to thickening of arteriolar walls and impaired diffusion of oxygen and nutrients to surrounding tissues.

Prior studies have reported prevalences of white matter disease from 30% to 92% in the elderly, with most reports exceeding 75%. The suggestion that women may have higher degrees of white matter disease than men is intriguing given the clearly increased prevalence of magnetic resonance measures of cerebral atrophy in men in the current study. A slight female predominance may be explained by the higher prevalence of hypertension among women in this study, since prevalence did not differ by gender in multivariate analysis.

Independent associations noted in the current study with diastolic pressure, diuretic use, and internal carotid thickness support a hypertension-related pathogenesis to these findings. Internal carotid thickness in particular may be an indicator of intracranial arteriosclerosis, though Fazekas et al did not find a difference in white matter disease prevalence by presence of extracranial carotid disease. This lack of association may have been caused by a less precise measure of carotid disease and smaller sample size than in the current study.

Limitations of Current Study

The relatively small size of the current study, though larger than many previously published series, limits power for assessing relations with MRI findings. This is particularly true for some of the less frequent cardiovascular conditions such as congestive failure, atrial fibrillation, and significant carotid stenosis, which were not present in high enough numbers to permit mean-
FIG 6. Bar graphs showing white matter disease severity by history of stroke in women and men.

meaningful examinations of these relations. Extension of the study to the full CHS cohort, designed to provide information on prevalence, correlates, and prognostic implications of MRI findings in more than 4000 participants, will permit more careful study of these associations. Because those data will not be complete until late in 1994, it seemed reasonable to provide preliminary data from these 303 participants at the present time.

The sample selected for the current study was, by design, heavily weighted toward those with prior stroke. Age- and gender-matching of controls resulted in a sample that was older (though only among women) and had a higher proportion of men than the full CHS cohort. Inasmuch as age and gender are related to cerebral atrophy and white matter disease, the prevalences in controls without stroke reported here will overestimate the true rates in the full CHS cohort and in the general population from which it was drawn. For these reasons, the prevalences of abnormalities demonstrated here should not be generalized to other populations without consideration of the biases inherent in this sample. Examination of associations, in contrast, is much less vulnerable to bias from biased sample selection, so the associations presented here may be more applicable to a general population.

Strengths of Current Study

Subjects in the current study are truly a population-based sample of community-dwelling individuals, having been selected at random for participation in CHS from HCFA eligibility lists in four geographic areas.

<table>
<thead>
<tr>
<th>Prior stroke</th>
<th>Ventricular Enlargement</th>
<th>Sulcal Widening</th>
<th>White Matter Disease Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>confirmed (n=55)</td>
<td>4.29</td>
<td>4.42</td>
<td>2.69</td>
</tr>
<tr>
<td>unconfirmed (n=45)</td>
<td>3.82</td>
<td>3.91</td>
<td>2.31</td>
</tr>
<tr>
<td>absent (n=203)</td>
<td>3.78</td>
<td>3.73</td>
<td>1.88</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;.03</td>
<td>&lt;.002</td>
<td>&lt;.004</td>
</tr>
<tr>
<td>Glucose tolerance</td>
<td>diabetes (n=76)</td>
<td>4.16</td>
<td>3.76</td>
</tr>
<tr>
<td>impaired (n=80)</td>
<td>3.95</td>
<td>3.99</td>
<td>2.30</td>
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<tr>
<td>normal (n=147)</td>
<td>3.89</td>
<td>4.03</td>
<td>1.86</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;.03</td>
<td>.3</td>
<td>.1</td>
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<tr>
<td>Hypertension</td>
<td>definite (n=106)</td>
<td>4.08</td>
<td>4.17</td>
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<tr>
<td>borderline (n=42)</td>
<td>4.14</td>
<td>4.12</td>
<td>2.12</td>
</tr>
<tr>
<td>normal (n=154)</td>
<td>3.66</td>
<td>3.60</td>
<td>1.75</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;.009</td>
<td>&lt;.0008</td>
<td>&lt;.0009</td>
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<tr>
<td>Any antihypertensive</td>
<td>present</td>
<td>3.97</td>
<td>4.13</td>
</tr>
<tr>
<td>absent</td>
<td>3.82</td>
<td>3.73</td>
<td>1.89</td>
</tr>
<tr>
<td>P value</td>
<td>.4</td>
<td>&lt;.009</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Diuretic use</td>
<td>present</td>
<td>3.98</td>
<td>3.95</td>
</tr>
<tr>
<td>absent</td>
<td>3.85</td>
<td>3.87</td>
<td>1.93</td>
</tr>
<tr>
<td>P value</td>
<td>.5</td>
<td>.7</td>
<td>.004</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>current (n=38)</td>
<td>3.37</td>
<td>3.71</td>
</tr>
<tr>
<td>former (n=139)</td>
<td>3.96</td>
<td>3.90</td>
<td>2.01</td>
</tr>
<tr>
<td>never (n=120)</td>
<td>3.98</td>
<td>3.93</td>
<td>2.21</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;.03</td>
<td>.7</td>
<td>.3</td>
</tr>
<tr>
<td>Race</td>
<td>black (n=14)</td>
<td>3.14</td>
<td>3.57</td>
</tr>
<tr>
<td>white (n=289)</td>
<td>3.92</td>
<td>2.90</td>
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</tr>
<tr>
<td>P value</td>
<td>&lt;.03</td>
<td>.4</td>
<td>.2</td>
</tr>
</tbody>
</table>

No associations noted for ventricular score, sulcal score, white matter grade with coronary disease, congestive failure, atrial fibrillation, carotid stenosis of 50% or greater, abnormal left ventricular systolic wall motion or left ventricular ejection fraction, aspirin use.

Though the design of the feasibility study produced further selection and resulting biases in this sample of participants, these biases can easily be quantified by comparison to the population-based sample from which they were drawn. For these reasons this report differs from previously reported series, which were drawn almost exclusively from clinical samples and were limited to a single geographic area.

A further strength of the current study is that all MRI studies were read centrally by one of two board-certified
### TABLE 3. Statistically Significant Correlation Coefficients of Continuous Variables With Findings From Magnetic Resonance Imaging

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ventricular Enlargement</th>
<th>Sulcal Widening</th>
<th>White Matter Disease Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>.24†</td>
<td>.25†</td>
<td>-.16*</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>.13†</td>
<td>.14‡</td>
<td>.20†</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum common carotid thickness (mm)</td>
<td>.17*</td>
<td>.22†</td>
<td>.13‡</td>
</tr>
<tr>
<td>Maximum internal carotid thickness (mm)</td>
<td>.13‡</td>
<td>.17*</td>
<td>.21†</td>
</tr>
<tr>
<td>Ankle-arm index</td>
<td></td>
<td>-.17*</td>
<td>-.14‡</td>
</tr>
<tr>
<td>LV mass on electrocardiogram (gm)</td>
<td>.18‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV, (L)</td>
<td></td>
<td>-.16*</td>
<td>-.15‡</td>
</tr>
<tr>
<td>FVC (L)</td>
<td></td>
<td>-.12‡</td>
<td>-.22†</td>
</tr>
<tr>
<td>Physical activity (kcal)</td>
<td>-.13†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive function score</td>
<td>-.10</td>
<td>-.16*</td>
<td>-.14‡</td>
</tr>
<tr>
<td>Digit-symbol score</td>
<td>-.11</td>
<td>-.22†</td>
<td>-.21†</td>
</tr>
</tbody>
</table>

**FEV, indicates forced expiratory volume in 1 second; and FVC, forced vital capacity.**

No associations with weight, diastolic pressure, alcohol intake, fibrinogen, factor VII, factor VIII, cholesterol, triglycerides, low-density lipoprotein cholesterol, glucose, insulin, albumin, hemoglobin, potassium, body mass index, left atrial dimension, or left ventricular mass measured by echocardiography.

* .001 < P < .01
† P < .0001
‡ .01 < P < .05

radiologists with neuroradiology subspecialty training at the CHS MRI Reading Center (Johns Hopkins University, Baltimore, Md). Ventricular size, sulcal size, and white matter disease were assessed on a 10-point scale which has been shown to be highly reproducible; duplicate readings did not vary by more than one point for any of the measures reported. In addition, MRI studies were performed according to a standard protocol at each field center during a 3-month period. Finally, a wealth of other data are available on CHS participants. Baseline and follow-up examinations have been extensive and have included questionnaire data, laboratory studies, and noninvasive testing. These data will be of great value in interpreting the prognostic significance of MRI findings and may help to elucidate the mechanisms of some of these changes.

### Conclusions

Cerebral atrophy and white matter disease were common among these elderly subjects and were strongly related to increased age, prior cerebrovascular disease, and hypertension. Though many authors have suggested

### TABLE 4. Multiple Linear Regression Analysis of Variables Associated With Magnetic Resonance Findings

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ventricular Enlargement</th>
<th>Sulcal Widening</th>
<th>White Matter Disease Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>β: 0.054 P: .001</td>
<td>β: 0.074 P: .001</td>
<td>β: 0.050 P: .001</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>β: 0.068 P: .04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>β: 0.660 P: .0001</td>
<td>β: 0.381 P: .0003</td>
<td></td>
</tr>
<tr>
<td>Potassium (mEq/dL)</td>
<td>β: -0.341 P: .008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>β: 0.215 P: .05</td>
<td>β: 0.291 P: .005</td>
<td>β: 0.299 P: .006</td>
</tr>
<tr>
<td>White race</td>
<td>β: 0.826 P: .0006</td>
<td>β: 0.604 P: .009</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>β: 0.006 P: .008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>β: 0.011 P: .02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic use</td>
<td>β: 0.251 P: .05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (m)</td>
<td>β: -0.017 P: .03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle-arm index</td>
<td>β: -0.648 P: .02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum internal carotid thickness (mm)</td>
<td>β: 0.147 P: .003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>β: -0.003 P: .03</td>
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</tbody>
</table>
these MRI findings to be normal concomitants of aging. The wide variability in presence and severity of these lesions in the current study and others argues against the inevitability of such abnormalities with advancing age. The danger of assuming that these changes represent "normal aging" is illustrated by the subsequent disproving of previous similar assertions about elevated systolic blood pressure and atherosclerosis. Should these findings be shown to be associated with increased risk of dementia, disability, and death, the value of possible preventive strategies should be examined. Although some risk factors for these abnormalities, such as age and gender, are not modifiable, others, such as hypertension and stroke, clearly are. The search should continue for other modifiable risk factors, and if these MRI abnormalities are related to disability and death, effective interventions should be developed to prevent their onset or slow their progression.

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Appendix

Participating Institutions and Principal Staff


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Magnetic resonance abnormalities and cardiovascular disease in older adults. The Cardiovascular Health Study.

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