White Matter Hyperintensities Predict Functional Decline in Voiding, Mobility, and Cognition in Older Adults

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OBJECTIVES: To compare magnetic resonance imaging data with functional assessments of mobility, urinary control, and cognition to determine common or distinctive features in the distribution of brain white matter hyperintensities (WMHs) associated with functional decline and impairment.

DESIGN: Baseline data from subjects aged 75 to 89 enrolled in a longitudinal study. Assessors and subjects were blinded to group assignment.

SETTING: Healthy community-dwelling volunteers.

PARTICIPANTS: Ninety-nine subjects were enrolled using a balanced 3×3 matrix stratified according to age and mobility performance. Exclusion criteria were medication, systemic conditions, and neurological diseases that can compromise mobility.

MEASUREMENTS: WMHs were identified using a semiautomated segmentation method, and regional burdens were assessed using a white matter parcellation atlas. Quantitative measures of mobility, urinary incontinence (UI) severity, and executive function and processing speed were obtained.

RESULTS: WMHs occur predictably in predominantly periventricular areas. There were powerful correlations between total (tWMH) and regional (rWMH) WMH, with correlation coefficients of 0.5 to 0.9 for eight of 10 structures analyzed. tWMH predicted functional measures of UI, mobility, executive function, and processing speed nearly as well as the best regional measures. The total volume of WMHs independently explains 5% to 11% of the variability for mobility, UI severity, executive function, and processing speed and is a sensitive (0.7–0.8) predictor of functional decline. The odds of decline in each of the three functional domains was 1.5 to 2.4 times greater with each 1% increase in tWMH.

CONCLUSION: This work establishes the importance of brain WMH burden in three major geriatric syndromes. The findings support the inclusion of total WMH burden as a risk factor in the predictive and diagnostic criteria. **J Am Geriatr Soc 58:275–281, 2010.**

Key words: white matter hyperintensities; impaired function; impaired urinary function; functional decline in cognitive function; impaired mobility

Magnetic resonance imaging (MRI) has advanced understanding of diseases of the nervous system, particularly those involving brain white matter (WM). The detail seen on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences has allowed localization and quantification of the underlying disseminated focal WM abnormalities. WM hyperintensities (WMHs), commonly present on the MRI scans of older persons, were initially ignored but have subsequently been linked to hypertension and other vascular disease risk factors.[1] An increasing body of knowledge has associated these abnormalities with functional deterioration in mobility,[2,3] urinary control,[4] and cognition.[5] In three earlier reports, hypothesis-driven evaluations of WMH presence within brain regions known to be critical to mobility, cognition or voiding were presented.[6–8] These studies essentially confirmed the association between the functions and some of the proposed pathways. Although the three studies used different regional WMHs (rWMHs), the current study combines the subsets of rWMHs from each of the three. This cross-sectional study compares total WMHs (tWMHs) and rWMHs with one another and examines the relationship with functional assessments of the three geriatric syndromes. The goal was to define common or distinctive features in the distribution or volume of brain WMHs responsible for

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deterioration of these functions that lead to predictive or diagnostic criteria.

METHODS

Subjects

Ninety-nine subjects aged 75 to 89 were recruited from the community for a 4-year longitudinal study defining the relationship between WMH accrual and mobility impairment. From 312 individuals screened by telephone, 164 were eligible, consenting individuals, of whom 117 came for a physical examination performed by the senior investigator (LW), who also assessed the exclusion criteria: medication, systemic conditions (e.g., arthritis), and neurological diseases (e.g., Parkinson's disease) that can compromise mobility; cognitive impairment (Mini-Mental State Examination score <24); corrected distance vision worse than 20/70; unstable cardiovascular disease (e.g., unstable angina pectoris); pulmonary disease requiring oxygen; inability to walk 10 meters independently in less than 50 seconds; lower extremity amputation; weight greater than 113.5 kg (250 pounds); claustrophobia; presence of a pacemaker or other metallic device or implant; excessive alcohol intake; and expected life span less than 4 years. Seventeen subjects were excluded because of arthritis, Parkinson's disease, and claustrophobia and one because of a clinically silent tentorial meningioma. Subjects were enrolled using a balanced 3×3 matrix that stratified age (75–79, 80–84, and ≥ 85) and mobility performance in terms of Short Physical Performance Battery (SPPB) scores (11–12, 9–10, and <9). Subjects provided informed consent and then underwent physical, neurological, and cognitive assessment and brain MRI. Participants and assessors were blinded to clinical, mobility, and imaging outcomes. The protocol was approved by the institutional review board.

Assessment Tools

Severity of urinary incontinence (UI) was measured using the Urinary Incontinence Severity Index,[9] a validated self-reported instrument in which leakage is characterized as none, slight, moderate, or severe. This particular incontinence-related instrument was chosen because WMHs appear to be much more closely related to incontinence severity than to the presence of incontinence, category of incontinence, bother of incontinence, or ultimate effect on function.[8] Mobility was assessed using SPPB score,[10] Tinetti total score, and Tinetti gait score.[11] Laboratory testing of mobility performance included timed stair descent and self-paced maximum velocity. Measures of executive functioning included the Trail Making Test Part B (Trails B),[12] the Stroop Color and Word Test,[13] and the California Computerized Assessment Package (CalCAP) sequential reaction time (SQ1) (Norland Software, Los Angeles, CA).

Brain MRI and tWMH

A 3-Tesla Siemens Allegra (Erlangen, Germany) MRI system was used to acquire the following magnetic resonance brain scans: T1-weighted magnetization prepared rapid gradient echo (MPRAGE, 176 contiguous, 1-mm-thick axial slices, repetition time (TR)/echo time (TE) = 2,500/2.74 ms, time of inversion (TI) = 900 ms, matrix size = 256 $\times$ 208), T2-weighted 3D fast spin echo (T2, 176 contiguous, 1-mm-thick sagittal slices, TR/TE = 2,500/353 ms, matrix size = 256 $\times$ 220), and T2-weighted FLAIR (128 contiguous 1.3-mm-thick sagittal slices, TR/TE = 6,000/353 ms, TI = 2,200 ms, matrix size = 256 $\times$ 208). Image preprocessing included magnetic field–related signal inhomogeneities[14] and linear affine registration of FLAIR and T2 series to the MPRAGE series.[15] The skull-stripped intracranial cavity was outlined on the T2 series using an in-house program implemented in Matlab (Mathworks Inc., Natick, MA) and included the brain parenchyma and ventricles, as well as cortical cerebrospinal fluid. The MPRAGE and FLAIR series were used for automated identification of the WMH using two applications (FreeSurfer (http://surfer.nmr.mgh.harvard.edu/) and Slicer (http://www.slicer.org)). Specifically, the MPRAGE series was used as input in FreeSurfer,[16] and the MPRAGE and FLAIR series were used as inputs in the expectation maximization segmentation module of Slicer.[17] The WMH maps were combined into one using Matlab. (WMH spatial overlap between the maps had to be more than 10%, and WMH three voxels or smaller were excluded.) Final WMH maps were produced after review, which included manual correction of remaining false-positive and false-negative WMHs if present. WMH and intracranial cavity volumes for each subject were determined in Matlab and expressed as milliliters (number of voxels $\times$ voxel volume/1,000). To correct for head size difference, for each subject, total WMH volume was expressed as a percentage of the intracranial cavity volume.

Regional WMH

A WM parcellation atlas,[18] which provides a functional map of approximately 32% of total brain WM, was used for regional analysis. This atlas was first aligned to each subject's brain and then overlaid onto the tWMH map obtained using the segmentation method described above to identify WM regions of interest (ROIs).[7] The ROIs selected contained the following fiber tracts: anterior, superior, and posterior corona radiata; cingulate gyrus; genu, body, and splenium of corpus callosum; anterior and posterior limb of internal capsule; and superior longitudinal fasciculus. For ROIs with hemispheric distribution, the volumes were expressed as total after adding the left and right volumes together. rWMH was expressed as a fraction of the ROI by dividing the rWMH total volume (mL) by the total volume (mL) of the ROI.

Statistical Analysis

SAS version 9.1 (SAS Institute, Inc., Cary, NC) was used for the statistical analysis. Spearman correlations were calculated to measure the relationship between tWMH and regional WMHs. Regression models were used to compare the amount of variation explained by tWMH with that explained by the rWHMs. Dependent variables were five mobility measures (Tinetti total score, Tinetti gait score, SPPB score, time needed (seconds) to descend three stairs, self-paced maximum velocity (m/s)), UI severity, and three cognitive measures (Trails B, CalCAP SQ1, Stroop-color-word). Multivariate cumulative logit regression analysis was performed to evaluate MRI variables that significantly

contributed to prediction of the categorical UI severity. Linear regression analysis was used for all other dependent variables. Each model had one MRI variable, as well as age, sex, and BMI. BMI was replaced by education level (high school (HS) graduate vs not) in models for cognitive measures. To examine how well tWMH predicts functional decline, a sensitivity analysis was conducted, and receiver operating characteristic (ROC) curves were produced for each of the dependent variables. ROC curves plot sensitivity along the y-axis versus 1–specificity on the x-axis. Area under the ROC curve (AUC) was calculated and used to compare models. Maximum possible AUC is 1, so models with area closest to 1 were considered best. Possible confounders were age, sex, BMI, and education level (HS graduate or not). Final models for SPPB, Tinetti total score, and Tinetti gait score controlled for age. Models for UI, self-paced maximum velocity, and time required to walk down stairs controlled for sex, and cognitive models controlled for age and level of education. Functional decline was indicated by a Tinetti total score of 24 or less, a Tinetti gait score of 10 or less, and a SPPB score of 9 or less. Moderate and severe UI indicated impairment. Because most individuals performed in the normal range on the cognitive measures, and there was no normative data for the CalCAP RT measure for people in this age range, relative rather than normative based impairment was used. This was also done for self-paced maximum velocity and time needed to descend three stairs. Several cutoff points were compared as the markers for functional decline using percentiles from the sample. Logistic regression models were then fitted, and odds ratios were calculated. A two-tailed level of $\alpha \leq 0.05$ was the threshold for statistical significance.

RESULTS

Participant Characteristics

At baseline, 99 older subjects (mean age 82.1 ± 4.1, range 75–89) were enrolled, of whom 60% were female. Subjects were well-educated non-Hispanic whites, with only seven non-HS graduates. Moderate to severe UI was present in 38%. Mean instrumental activity of daily living (23.5 ± 1.1), Center for Epidemiologic Studies Depression Scale (8.2 ± 6.7), and Mini-Mental State Examination (28.4 ± 1.3) scores indicated that most were independent with normal affective and cognitive function. The average Tinetti total score was 25.8 ± 2.6. The mean tWMH was 1.00 ± 0.91% (range 0.02–4.23%). Sixty-four of the subjects were in the 0% to 1% range, 23 in the 1% to 2% range, six in the 2% to 3% range, and six were greater than 3%. The outcome variables and the WMHs are described in Table 1.

WMHs occur more frequently in the periventricular regions, with detectable presence in subcortical areas as well (Figure 1). The observed distribution suggests a progression of WMH in an outward direction. It was reasoned that the amount of WM damage at the regional level is probably highly related to the total quantity of WMH, which implies that an association observed between different functional impairments (cognitive, mobility, voiding, and regional WM lesion burden) could also be reflected in the association with total WMH burden. To test this hypothesis, the association between tWMH and rWMH burdens previously analyzed and relevant for aspects of cognitive, urinary, or mobility function was measured. Strong correlations (correlation coefficient s = 0.5–0.9) were found between tWMH and eight of the 10 structures analyzed; the other two structures had correlations of 0.20 and 0.30. This observation provides strong support for the hypothesis above.

Table 1. Descriptive Statistics for Outcome Variables and Brain Regions

Measure	N	Mean ± Standard Deviation	Range
Cognitive			
Trail Making Test Part B	98	125.3 ± 74.5	43.7–419.1
Stroop-Color-Word	98	26.6 ± 9.0	5–50
Sequential Process Time	96	610.8 ± 137.1	298–854
Mobility			
Short Physical Performance Battery (range 0–12)	99	9.2 ± 2.2	2–12
Tinetti total (range 0–28)	99	25.8 ± 2.6	14–28
Tinetti gait (range 0–12)	99	11 ± 2	3–12
Gait velocity	94	2.3 ± 0.5	1.0–3.6
Time require to descend three stairs	87	5.1 ± 1.1	2.5–7.7
WMH %			
tWMH*	99	1.0 ± 0.9	0.02–4.2
Anterior corona radiata†	99	8.4 ± 8.5	0.0–53.2
Anterior limb of internal capsule†	99	1.3 ± 4.0	0.0–34.6
Body of corpus callosum†	99	6.5 ± 6.2	0.0–31.4
Cingulate gyrus†	99	0.1 ± 0.3	0.0–2.3
Genu of corpus callosum†	99	6.2 ± 5.1	0.0–25.2
Posterior corona radiata†	99	23.4 ± 21.6	0.0–84.0
Posterior limb of internal capsule†	99	0.8 ± 4.7	0.0–44.7
Splenium of corpus callosum†	99	2.0 ± 2.8	0.0–12.6
Superior corona radiata†	99	8.8 ± 11.5	0.0–60.8
Superior longitudinal fasciculus†	99	3.3 ± 6.2	0.0–35.4

* Percentage of intracranial cavity.
† Percentage of region's volume.

All regression models were significant, with 4 degrees of freedom and *P*-values between .04 and <.001. The main focus was comparing the amount of variation explained by tWMH and rWMH in addition to age, sex, and BMI or education. UI severity had its strongest relationship with the rWMH in the superior corona radiata, although other structures were also significantly related (Table 2). tWMH was associated with UI severity almost as strongly as the best of the regional burdens. The rWMH in the splenium of corpus callosum showed the strongest association with mobility, as measured according to Tinetti total and gait scores, although tWMH had almost the same strength (Table 2). tWMH also showed a strong association with executive function and processing speed (Table 2). Thus, each of the three functional domains (mobility, cognition, and UI) were almost as strongly related to tWMH as to the individual rWMHs.

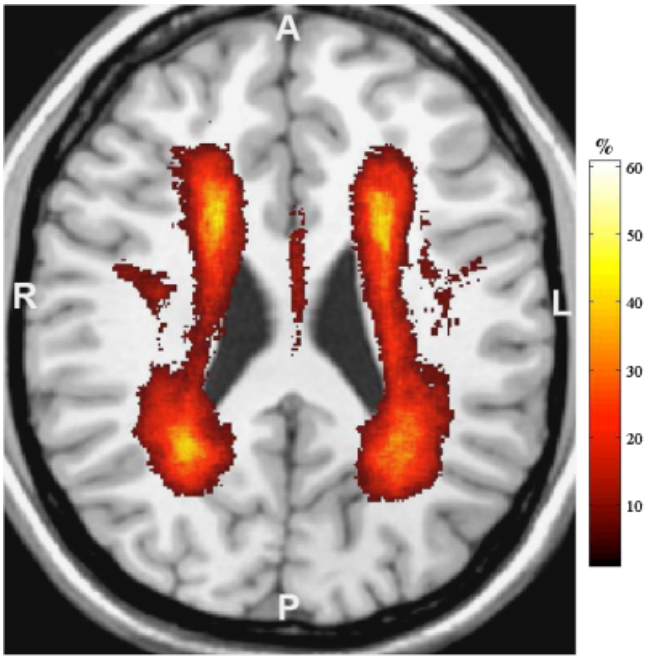

Figure 1. Distribution of white matter hyperintensities (WMHs) and their frequency in one slice as observed in the study subjects. The frequency map is overlaid on the reference brain obtained from the International Consortium on Brain Mapping, University of California at Los Angeles. The color bar indicates the percent of subjects with WMH in that voxel. A = anterior; P = posterior; L = left hemisphere; R = right hemisphere.

Because the rWMHs were strongly correlated with tWMH, and tWMH had almost as strong a relationship with the three functional domains as the rWMHs, the sensitivity of the dependent variables to changes in tWMH was next examined. Logistic regression models were fitted with tWMH predicting varying levels of decline or impairment for each of the dependent variables, and sensitivity and specificity were calculated. Different cut-off points were selected for each of the measures so that the sensitivity and specificity for different levels of function could be compared. Sensitivity varies with specificity, so Table 3 shows the highest sensitivity achieved at levels of specificity greater than 0.50, as well as the AUC for each model. Models with tWMH, age, and education level predicted a Trails B score of 148 or more with a sensitivity of 0.84 at a specificity of 0.54 and an AUC of 0.83. Education was not a significant predictor in these models, most likely because 93% of subjects were HS graduates. Two other cut-offs for Trails B score (slowest 10% and 30%) were also examined, but neither was as sensitive or specific. An SPPB score less than 11 was predicted with 0.79 sensitivity at a specificity of 0.56 and an AUC of 0.66 (not shown), but a SPPB score 9 or less, which is more indicative of impairment, had lower sensitivity, specificity, and AUC (0.71, 0.51, and 0.63). Moderate to severe UI was predicted with 0.81 sensitivity and 0.67 specificity with an AUC of 0.77.

To determine how well tWMH predicted functional decline or impairment in each of the domains, the odds ratios were calculated from the logistic regression models predicting functional decline or impairment. For dependent variables without established cutoffs for impairment (self-paced maximum velocity, SQ1, Trails B, Stroop-Color-Word), the cutoff was chosen from the model with the largest AUC. Table 4 shows the odds ratios. For each 1% increase in tWMH, subjects were 1.5 to 2.4 times as likely to have moderate to severe incontinence, a SPPB score of 9 or less, a Tinetti total score of 24 or less, a Tinetti gait score of 10 or less, a Stroop-Color-Word score of 24 or less, a SQ1 greater than 633, and a walking velocity less than 0.69 m/s.

DISCUSSION

WMHs observed using MRI have clinical relevance, because they are thought to represent tissue damage with potential effect on brain function. The type and extent of the impairment is, at least in part, linked to the specific pathways affected and the physiological effects of the diminished connectivity between various networks and neural structures. Because the relationship between the total amount of brain WMH and that in subregions affecting specific tracts is unknown, the usefulness of global lesion burden as an indicator reflective of damage in areas containing relevant pathways remains to be defined. The availability of quantitative global and regional measurements of WMH were used to assess this relationship. It was desired to produce a model for the contribution of each rWMH to each and all of the three functional domains of interest (executive functions, mobility, and UI), but tWMH unexpectedly added almost as much to the regression models as did the best of the rWMHs. The stereotyped nature of the distribution of rWMH, with the resulting high level of correlation between individual rWMHs and tWMH, readily explains the extent to which tWMH predicts functional decline or impairment. Moreover, the measurement of rWMH is highly technical, requiring the resources of an imaging research laboratory. By contrast, tWMH can readily be determined using published scales, thus serving as a diagnostic surrogate for rWMH but not necessarily as a substitute in a model of that function.

These findings show a strong association between tWMH and rWMH and demonstrate a significant predictive value of tWMH to functional deficit. These observations provide a basis for understanding the pattern and accrual of WMHs and help in explaining the often-reported relationship between the geriatric syndromes involving declines in cognitive domains, urinary function, and mobility.[19–22] Comparable accrual of WMHs in WM regions supporting these functional domains would explain these relationships, although the relationships also may be related to general brain connectivity.[7] The findings of the current study offer potential insights into earlier reports in which seemingly distinct conditions such as upper and lower extremity impairment, poor vision, sensory impairment, and depression may represent shared risk factors for UI, falling, and functional dependence.[19]

Subjects with dementia were excluded from this study, narrowing the range of cognitive function analyzed. Nevertheless, a relationship between processing speed and executive function and tWMH was demonstrated. It is the authors' clinical impression that, by itself, the volume of tWMH noted in the subjects is rarely associated with established dementia. By contrast, the relationship between

Table 2. Coefficient of Determination (r^2) Added by Brain Regions to Regression Models over Age, Sex, and Body Mass Index (BMI) or Education

	Mobility Measures					Cognitive Measures			
MRI Region	Tinetti Total	Tinetti Gait	Short Portable Performance Battery	Velocity	Down Stairs	Trails B	Sequential Processing Time	Stroop-Color-Word	Incontinence Severity*
Total white matter hyperintensity									
r^2	0.097	0.109	0.061	0.054	0.010	0.030	0.060	0.045	0.050
P-value	.001	.001	.01	.02	.66	.06	.009	.02	.02
Anterior corona radiata									
r^2	0.057	0.039	0.051	0.024	0.000	0.010	0.040	0.035	0.060
P-value	.01	.14	.02	.14	.85	.17	.03	.08	.02
Anterior limb of internal capsule									
r^2	0.017	0.019	0.051	0.024	0.010	0.000	0.000	0.015	0.030
P-value	.24	.80	.04	.28	.63	.55	.57	.35	.12
Body of corpus callosum									
r^2	0.077	0.099	0.061	0.044	0.000	0.020	0.040	0.025	0.030
P-value	.003	.003	.01	.046	.74	.10	.03	.10	.09
Cingulate gyrus									
r^2	0.107	0.099	0.061	0.014	0.020	−0.010	0.000	0.015	0.020
P-value	<.001	.002	.01	.52	.27	.93	.55	.34	.13
Genu of corpus callosum									
r^2	0.037	0.039	0.041	0.024	0.000	0.000	0.040	0.015	0.000
P-value	.06	.12	.04	.24	.84	.42	.04	.23	.82
Posterior corona radiata									
r^2	0.077	0.129	0.001	0.004	0.000	0.040	0.040	0.035	0.020
P-value	.003	<.001	.10	.06	.90	.02	.03	.06	.12
Posterior limb of internal capsule									
r^2	0.037	0.059	0.011	0.004	0.000	−0.010	0.020	0.015	0.050
P-value	.05	.03	.94	.79	.71	.84	.11	.18	.24
Splenium of corpus callosum									
r^2	0.137	0.129	0.111	0.084	0.060	0.040	0.080	0.085	0.030
P-value	<.001	<.001	.001	.004	.02	.02	.003	.003	.09
Superior corona radiata									
r^2	0.117	0.109	0.051	0.054	0.010	0.030	0.020	0.025	0.060
P-value	.001	.002	.02	.02	.32	.046	.09	.15	.008
Superior longitudinal fasciculus									
r^2	0.047	0.059	0.021	0.044	0.020	0.000	0.010	0.005	0.030
P-value	.03	.03	.22	.07	.27	.38	.28	.43	.09

All models controlled for age, sex. Mobility and incontinence models also controlled for BMI. Cognitive models also controlled for Education.

* Logistic regression.

P-values shown are for magnetic resonance imaging (MRI) region parameter estimates.

mobility and UI and tWMH is not only robust, but is also of clinical significance in these same subjects.

A predictable pattern of WMHs, in which tWMH relates to multiple functional domains, suggests the potential clinical value of methodologies capable of assessing tWMH. Three commonly used observational rating scales provide reliable cross-sectional assessment of hemispheric WMH burden, although their ability to measure change over time is limited. A fourth scale has been developed to measure change.[23] Even with these limitations, visual assessment of WMH burden is realistic in the short term, particularly if visual measures are validated against quantitative WMH.[23] This would allow clinicians to determine the importance of WMH in UI, mobility impairment, or cognitive slowing, ultimately leading to predictive and diagnostic criteria based on the overall quantity of WMHs. The value and importance of WMHs is best illustrated by noting that it independently determines 5% to 11% of the variability for mobility, 5% of the variability for UI, and 5% to 6% of the variability of executive function and processing speed (Table 2). These results are consistent with the recognized multifactorial complexity of common geriatric syndromes, in which no single risk factor is responsible for a large portion of the overall risk of developing the specific condition.[22]

Sensitivity in the 0.7 to 0.8 range supports the predictive value of WMH for cognitive, urinary, and mobility function, making this measurement a useful tool for fore-

Table 3. Sensitivity, Specificity, and Area Under the Receiver Operating Characteristic Curve (AUC)

Measure	Sensitivity/ Specificity	AUC
Moderate to severe incontinence	0.81/0.67	0.77
Short Physical Performance Battery score ≤9 (lowest 43%)	0.71/0.51	0.63
Tinetti total score ≤24 (lowest 24%)	0.83/0.63	0.79
Tinetti gait score ≤10 (lowest 27%)	0.73/0.53	0.69
Gait velocity≤0.69 m/s (slowest 50%)	0.77/0.54	0.71
Time needed to descend 3 stairs ≥6.2 seconds (slowest 50%)	0.67/0.60	0.65
Trail Making Test Part B score ≥148 (slowest 20%)	0.84/0.59	0.83
Stroop-Color-Word score ≤24 (lowest 40%)	0.83/0.54	0.71
California Computerized Assessment Package sequential reaction time ≥633 (slowest 40%)	0.76/0.62	0.70

casting function. Given that, for each 1% increase in tWMH there is an increase of 1.5 to 2.4 times the chance of diminished function in each of these domains. This indicates a major increase in risk across the 0% to 4.2% range. The mean tWMH of 1.0 in conjunction with median and 75th percentile tWMH values of 0.7 and 1.2 indicate a skewed distribution, with only 35 subjects above the mean. This suggests that the major burden of functional impairments linked to WM damage lies in subjects in the skewed WMH tail above the 1% mean (~ one-third of subjects).

Cerebral perfusion may dictate the stereotyped anatomic distribution of WMHs in the brain, with the most poorly perfused areas demonstrating the greatest tendency to develop WMHs.[24] The presence and severity of WMHs is related to age, with current severity best predicting future accrual.[25] The distribution of WMHs, and the relationship between their severity, age, and vascular disease risk factors, is consistent with the conclusion that abnormalities within brain microvascular may underlie WMHs. The pathophysiological mechanism, although probably related to changes within blood vessel walls, remains unclear. The increasing clinical importance of WMHs, as reported in this work, raises the importance of defining causation, as well as optimizing a risk factor abatement strategy, which minimizes the WMH accrual associated with functional deterioration.

Table 4. Logistic Regression Results with Total White Matter Hyperintensity Fraction Predicting Functional Decline

Outcome	Estimate	Standard Error	*P*-Value	Odds Ratio (95% Confidence Interval)
Moderate to severe incontinence	0.49	0.26	.06	1.63 (0.98–2.71)
Short Physical Performance Battery score ≤9	0.56	0.25	.03	1.75 (1.07–2.86)
Tinetti total score ≤24	0.69	0.27	.01	1.98 (1.17–3.38)
Tinetti gait score ≤10	0.58	0.25	.02	1.79 (1.11–2.9)
Gait velocity ≤0.69 m/s	0.88	0.34	.01	2.4 (1.23–4.68)
Time down stairs ≥6.2 seconds	0.52	0.33	.11	1.68 (0.88–3.21)
Trail Making Test Part B score ≥148	0.51	0.30	.09	1.66 (0.93–2.97)
Stroop-Color-Word score ≤24	0.61	0.27	.03	1.85 (1.08–3.16)
California Computerized Assessment Package sequential reaction time ≥633	0.51	0.25	.04	1.67 (1.03–2.7)

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