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Mild Cognitive Impairment Status and Mobility Performance: An Analysis From the Boston RISE Study

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Background. The prevalence of mild cognitive impairment (MCI) and mobility limitations is high among older adults. The aim of this study was to investigate the association between MCI status and both performance-based and self-report measures of mobility in community-dwelling older adults.

Methods. An analysis was conducted on baseline data from the Boston Rehabilitative Impairment Study in the Elderly study, a cohort study of 430 primary care patients aged 65 or older. Neuropsychological tests identified participants with MCI and further subclassified those with impairment in memory domains (aMCI), nonmemory domains (naMCI), and multiple domains (mdMCI). Linear regression models were used to assess the association between MCI status and mobility performance in the Habitual Gait Speed, Figure of 8 Walk, Short Physical Performance Battery, and self-reported Late Life Function and Disability Instrument's Basic Lower Extremity and Advanced Lower Extremity function scales.

Results. Participants had a mean age of 76.6 years, and 42% were characterized with MCI. Participants with MCI performed significantly worse than participants without MCI (No-MCI) on all performance and self-report measures ($p < .01$). All MCI subtypes performed significantly worse than No-MCI on all mobility measures ($p < .05$) except for aMCI versus No-MCI on the Figure of 8 Walk ($p = .054$) and Basic Lower Extremity ($p = .11$). Moreover, compared with aMCI, mdMCI manifested worse performance on the Figure of 8 Walk and Short Physical Performance Battery, and naMCI manifested worse performance on Short Physical Performance Battery and Basic Lower Extremity.

Conclusions. Among older community-dwelling primary care patients, performance on a broad range of mobility measures was worse among those with MCI, appearing poorest among those with nonmemory MCI.

Key Words: Cognition—Functional performance—Successful aging.

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FOR community-dwelling older adults, both cognitive impairments and mobility limitations are highly prevalent and can interfere with the ability to maintain independent living (1–3). It is estimated that among adults aged 65 or older, the prevalence of mild cognitive impairment (MCI) is between 10% and 20%, and the prevalence of mobility problems is equally as high (4,5).

MCI is defined as cognitive decline greater than that expected for one's age and education level, but which does not interfere appreciably with daily function (5,6). MCI is a well-known risk factor for dementia (7,8), with an annual conversion rate from MCI to dementia around 15% (8). Moreover, people with MCI are at increased risk of mobility decline, falls, and institutionalization (2,7,9).

Studies evaluating gait parameters indicate that cognitive function and mobility are linked. In a review, Monterro-Odasso and coworkers (9) highlighted that many of the brain regions (eg, hippocampus) affected by cognitive impairment also mediate aspects of mobility. It is also recognized that altered mobility performance precedes the behavioral manifestation of MCI (10). Therefore, mobility tests may serve as assessment tools for patients who either manifest, or are at risk for, developing cognitive impairment. A wide variety of clinical tests evaluates mobility by physical performance or self-report measures. However, few studies have contrasted how performance on these different mobility tests varies with MCI status and with specific MCI subtypes. One study that evaluated differences in gait analysis findings among different subtypes of MCI found

that different gait parameters were associated with amnestic MCI compared with nonamnestic MCI (11). Also, among older adults with MCI, executive function deficits are associated with poorer mobility performance and future risk for falls (12,13). By definition, nonamnestic MCI is largely influenced by executive function impairments, which suggests that these individuals may be at a heightened risk for poor mobility status and fall risk. Lastly, recent studies suggest that specific cognitive domains may be preferentially influential to specific mobility tests (14,15). However, these findings did not account for MCI status.

MCI is considered a subclinical state, which may remain unreported or undetected for a period of time. The first clinician to address these concerns is commonly the primary care practitioner (8). If mobility tests are to be considered as screening tools for incipient cognitive impairment (eg, MCI), then it will be essential to better understand the association between cognitive status and mobility performance. Also, it will be clinically important to evaluate these associations within primary care settings. Thus, based on the current evidence and the importance of screening for MCI within primary care settings, we investigated the association between cognitive function and mobility among older primary care patients, and more specifically the association between mobility and both MCI and MCI subtypes. We hypothesized (1) that participants with cognitive impairment, consistent with a diagnosis of MCI, would manifest greater limitation in performance-based and self-report measures of mobility than participants who did not meet diagnostic criteria for MCI (ie, cognitively intact); (2) that these associations would be maintained for all MCI subtypes; and (3) lastly that participants with nonamnestic MCI would manifest worse performance than those with amnestic MCI.

Methods

Study Design and Participants

A cross-sectional analysis was conducted using baseline data collected as part of the Boston Rehabilitative Impairment Study in the Elderly (Boston RISE), a cohort study of 430 community-dwelling and independent ambulating primary care patients aged 65 or older. The Boston RISE methods have been described in detail elsewhere (16). Briefly, participants were recruited through primary care practices at Massachusetts General Hospital and Brigham and Women's Hospital, two large academic medical centers located in Boston, Massachusetts. Eligible participants were identified through a Partners HealthCare patient database and telephone screening interviews and were invited to an initial screening and assessment visit. Potential subject were subsequently invited to undergo supplementary screening tests. Inclusion criteria were community-dwelling older adults, aged 65 or older, ability to understand and communicate in English, and self-reported difficulty with walking half a mile (6 blocks) or climbing one flight of stairs (10 steps). Patients were excluded for the presence of a terminal disease, significant visual impairment, uncontrolled hypertension, amputation of a lower extremity, use of supplemental oxygen, myocardial infarction or major surgery in the previous 6 months, planned major surgery, planned move from the Boston area within 2 years, cognitive impairment of significant severity as to likely reflect dementia (defined as Mini Mental State Examination [MMSE] score <18) (17), and Short Physical Performance Battery [SPPB] score less than 4 (18). Recruitment was based upon U.S. Census data 2000, to ensure an inclusion representing the ethnic, racial, and gender distribution of older adults residing within a 10-mile radius of our center. All of the methods of the Boston RISE study were approved by the Institutional Review Board of Spaulding Rehabilitation Hospital. Participants gave written informed consent before participation, and study procedures were approved by the Spaulding Rehabilitation Hospital Institutional Review Board.

Measures

The baseline assessments included a physical examination, a medical history questionnaire, the Self-Administered Comorbidity Questionnaire that assesses 13 comorbidities and has been validated for epidemiological trials among older adults (19), demographics, neuropsychological testing, physical performance testing, and questionnaires on functional ability.

Neuropsychological tests were used to evaluate cognitive performance and to characterize participants with MCI. Moreover, MCI was further subclassified as impairment in memory domains versus nonmemory domains using the current framework on MCI (20). Both self-report and performance-based mobility measures were used to investigate the association between MCI domains and mobility.

Cognitive measures.—Trail Making test.—The Trail Making test is a well established reliable and valid assessment of executive function that measures cognitive abilities of sequencing, visual scanning, processing speed, shifting attention, and cognitive flexibility (21,22). The test is administered in two parts, A and B, in which the participant is asked to connect circled numbers and letters. Both tests are sensitive to cognitive decline (21,22). Time to complete each test was recorded, and faster completion times indicate better performance (21,22).

Digit Symbol Substitution test.—The Digit Symbol Substitution test is a subtest of the Wechsler Adult Intelligence scale (23). The test is a measure of processing speed and visual–spatial skills, has an executive function component assessing sustained attention, and has good test–retest reliability (intraclass correlation coefficient = 0.80) (21). The test consists of a series of numbers and

corresponding symbols. The participant was asked to fill in a response form with as many corresponding symbols to numbers as possible in 90 seconds. The number of correct number–symbol matches was recorded with a higher score indicating better performance.

Hopkins Verbal Learning Test, Revised.—The Hopkins Verbal Learning Test, Revised (HVLT-R) is a valid test of verbal memory and learning (24). The test includes a list of 12 words of concrete objects that are read aloud by the examiner across three learning trials (25). The scores derived from the test are (a) total recall, the total number of words correctly recalled on trials 1–3; (b) delayed recall, the number of words correctly recalled after 20–25 minutes; and (c) recognition discrimination, the number of true responses minus the number of false responses on a subsequent recognition task (25). The HVLT-R is a valid instrument for clinical and research-based neuropsychological assessment with elderly patients (24).

Mild cognitive impairment.—The identification of participants meeting the diagnostic criteria for MCI was based on performance on the neuropsychological tests. The raw scores of each test were converted into age-adjusted standardized scores (z scores) based on published normative data from healthy age matched peers (23,26–28). Use of standardized scores allowed for comparisons across cognitive measures, cognitive domains, and across age groups. Consistent with previous studies, we used a cutoff of 1.5 *SD* below the age-adjusted means to identify impaired performance on a given cognitive measure (7,29). MCI was defined as an impairment (ie, $z < -1.5$) on two subtests within the neuropsychological test battery (HVLT-R total recall, HVLT-R delayed recall, HVLT-R recognition discrimination, Digit Symbol Substitution test, Trails A, and Trails B) (30). All participants were identified as either cognitively intact (No-MCI) or as having cognitive impairment (MCI).

MCI has been classified into two subtypes, amnestic and nonamnestic MCI, and further into single or multiple domain categories (5,30,31). Amnestic MCI denotes impairment within the cognitive domain of memory but not of sufficient severity to meet the diagnostic criteria for dementia, accompanied by preserved executive function, attention, language, and visual–spatial skills. In contrast, nonamnestic MCI denotes intact performance within the domain of memory but with impairment in at least one of the other cognitive domains (5).

The subtest scores of the HVLT-R (total recall, delayed recall, recognition discrimination) were used to define memory impairment, and the subtest scores of the Trail Making test and the Digit Symbol Substitution test (Trails A, Trails B, and Digit Symbol Substitution test) were used to define nonmemory impairment. Participants identified as having MCI were classified into one of three groups as follows: (a) single domain amnestic MCI (aMCI) if at least two tests within the memory domain were impaired (ie, $z < -1.5$) and no other cognitive impairments were identified, (b) multiple domain amnestic MCI (mdMCI) if memory and nonmemory domains were impaired, or (c) nonamnestic MCI (naMCI) if two tests within the nonmemory domain were impaired (6,30).

Measures of mobility.—Habitual Gait Speed.—Habitual Gait Speed (HGS) tested straight path walking and was measured by asking participants to walk a 4-m straight walk at their usual pace starting from a standing position (18,32). HGS is a valid and reliable measure in community-dwelling older adults (33,34) and is predictive of disability and adverse outcomes (10,34–36). Clinically meaningful differences for HGS are reported as 0.03–0.05 m/s (minimal difference) and 0.08 m/s (substantial difference) (37).

Figure of 8 Walk.—The Figure of 8 Walk (F8W) tested curved path walking (38). Participants were timed while walking in a figure of 8 pattern at their usual pace around two cones 1.5 m (5 feet) apart (39). The F8W has good test–retest reliability (intraclass correlation coefficient = 0.84) and interrater reliability (intraclass correlation coefficient = 0.90) and is a valid measure of walking skills among older adults (39).

Short Physical Performance Battery.—The SPPB is a reliable and valid measure of lower extremity performance and predictive for subsequent disability, mortality, and institutionalization among community-dwelling older adults (18,32). The SPPB is a composite score of standing balance, walking speed and the ability to rise from a chair. Each test is scored between 0 to 4 points with a maximum total score of 12. Clinically meaningful differences for the SPPB have been reported as 0.3–0.8 points (minimal difference) and 0.8–1.5 points (substantial difference) (37).

Late Life Function and Disability Index.—The Late Life Function and Disability Index assesses functioning in a variety of daily activities (40) and is associated with performance-based measures of function (41). The function component of the Late Life Function and Disability Index assesses self-reported difficulty in performing 32 physical activities. Scores on the Late Life Function and Disability Index are transformed to scaled scores (0–100) with higher scores indicating better levels of functioning (40). The subdomains of basic lower extremity (BLE) function and advanced lower extremity function were used in this study. BLE consists of 14 items including the ability to walk around the home, and advanced lower extremity consists of 11 items including abilities such as hiking a few miles. The Late Life Function and Disability Index has been validated in different cohorts of older adults (40–42).

Statistics

Descriptive analyses are presented as means with standard deviations for continuous variables and as frequencies

and percentages for categorical variables. For determining differences between two groups (MCI vs No-MCI), the Student's *t* test was used for normally distributed continuous variables, the Mann–Whitney *U* test for nonnormally distributed continuous variables, and the χ^2 test for categorical variables. Associations between each mobility measure and cognitive status were examined by analysis of variance and analysis of covariance comparing MCI versus No-MCI. First, we adjusted for gender, race, and education. Second, cognitive status was entered into similar models as a categorical variable (aMCI, mdMCI, naMCI, and No-MCI), and estimates for differences in physical performance measures between all MCI categories were calculated. Goodness of fit was investigated and physical performance measures were log-transformed where necessary. The F8W was transformed, and transformation was successful in achieving a normal distribution. Coefficients from these models are given as back-transformed 2^{β}-coefficients. As part of a post hoc analysis, we also adjusted for current health status and chronic conditions. Also, in an additional analysis, we included baseline MMSE status as a categorical variable to explore whether the distribution of low MMSE (MMSE < 24) significantly modified the association between the respective MCI subtypes and mobility. An alpha value of 0.05 was used to determine statistical significance. Data were analyzed using SAS 9.2 (SAS Institute Inc., Cary, NC).

Results

Baseline Characteristics

The 430 participants had an average age of 76.6 (*SD* = 7 years), two thirds were women, 16% had aMCI, 23% had mdMCI, and 4% had naMCI. Participants with MCI did not differ from those without MCI according to age, gender, and body mass index ($p > .05$), but a significant difference was seen in race, education, and current health status, whereby MCI was associated with poorer self-rated health ($p < .01$; Table 1).

MCI Versus No-MCI

Participants with MCI performed significantly worse in tests of mobility performance than participants without MCI (eg, HGS: $\beta = -0.13$, $p < .01$; SPPB: $\beta = -1.39$, $p < .01$), and these relationships were unchanged after adjusting for sex, race, and education ($p < .01$; Table 2). Similar results were observed in the associations of MCI with self-reported functional performance. Goodness of fit was acceptable for all measures except the F8W, which was log-transformed resulting in normally, distributed residuals.

MCI Subtypes Versus No-MCI

All MCI subtypes performed significantly worse than No-MCI on all mobility measures ($p < .05$), after adjusting for gender, race, and education, except for aMCI, which did not differ from No-MCI on F8W and BLE (Table 3).

Comparisons Between MCI Subtypes

Compared with patients with amnestic MCI, those with nonamnestic MCI performed more poorly on a number of mobility tests, for example, the SPPB ($p = .01$) and BLE ($p = .04$), and borderline significance was seen in both walking tests, for HGS ($p = .08$) and F8W ($p = .08$). Similarly, compared with patients with aMCI, those with mdMCI performed 21% worse on F8W ($2^{\beta} = 1.21$; $p < .001$) and scored 1.07 points lower on SPPB ($\beta = 1.07$, $p < .01$; Table 3). No statistically significant differences were observed between mdMCI and naMCI.

All multiple models were evaluated with the addition of current health status as an adjustment variable. The major findings were not materially altered; however, the β-estimates were diminished, and the difference in BLE between aMCI and naMCI was no longer statistically significant ($\beta = 5.53$, $p = .11$; Supplementary Appendix 1). Similar findings were observed after adjusting for chronic conditions instead of health status. Also, adjustment for MMSE categories did not materially alter our findings.

Discussion

To our knowledge, this is the first investigation to compare primary care patients with and without MCI across a broad range of mobility measures. The major findings of our study are (a) patients with MCI manifested consistently worse mobility performance compared with those without MCI across both performance-based and self-report measures of mobility and (b) when evaluating patients by MCI subtypes in relation to no MCI, these same associations held, though important differences were observed with use of certain mobility outcomes and among comparisons between certain MCI subtypes.

Our findings are consistent with prior studies reporting associations between MCI and gait speed (10,11) and add to the existing literature by showing associations between MCI and a broader range of mobility measures, including both performance-based and self-report measures. The fact that these relationships held within both performance-based and self-reported mobility outcomes is important as performance-based and self-reported functional measures have been demonstrated to assess different aspects of an individual's functioning (43). Interestingly, in differentiating MCI from No-MCI (Table 2), differences in HGS (0.12 m/s) and SPPB (1.35 points) surpassed clinically meaningful thresholds (37), which emphasizes the possible suitability of these measures as supplemental screening tools in MCI. Clinically meaningful differences have not yet been defined for F8W, BLE, and advanced lower extremity.

In general, subtypes of MCI performed worse than No-MCI on most mobility measures. Moreover, consistent

Table 1. Baseline Characteristics of Boston RISE Participants Based Upon MCI Status

		MCI Subtypes			
	No-MCI; *N* = 249	aMCI; *N* = 68	mdMCI; *N* = 98	naMCI; *N* = 15	*p* Value
Demographics					
Age	76.5±6.7	77.1±6.8	76.7±8.0	74.2±6.0	.52
Gender, female % (*n*)	69.1 (172)	70.6 (48)	60.2 (59)	80 (12)	.25
BMI	29.2±5.9	30.1±5.6	29.4±7.2	31.6±5.0	.40
Race, white% (*n*)	90.8 (226)	86.8 (59)	65.3 (64)	40 (6)	<.001
Education % (*n*)					
< High school	6.8 (17)	8.8 (6)	25.5 (25)	40 (6)	<.001
High school	24.9 (62)	38.2 (26)	39.8 (39)	20 (3)	
Graduate	37.8 (94)	33.8 (23)	20.4 (20)	20 (3)	
Post graduate	30.5 (76)	19.1 (13)	14.3 (14)	20 (3)	
Current Health, % (*n*)					
Poor–fair	13.2 (33)	17.7 (12)	27.5 (27)	46.7 (7)	<.001
Good	47.4 (118)	48.5 (33)	49.0 (48)	40.0 (6)	
Very good–excellent	39.4 (98)	33.8 (23)	23.5 (23)	13.3 (2)	
Number of chronic conditions	4.0±1.9	3.5±1.7	4.2±1.8	4.9±2.1	.02
MMSE	28.2±1.6	27.8±1.6	25.5±2.9	25.9±3.1	<.001
18–23, % (*n*)	1.2 (3)	4.4 (3)	23.5 (23)	13.3 (2)	<.001
24–30, % (*n*)	98.8 (246)	95.6 (65)	76.5 (75)	86.7 (13)	
Cognitive measures					
Trail Making test, A (s)	42.4±15.2	41.5±10.7	73.3±32.1	94.4±34.4	<.001
Trail Making test, B (s)	109.2±52.7	115.5±41.8	246.6±68-9	275.4±38.1	<.001
DSST (points)	40.7±4.5	14.5±3.4	13.7±3.3	20.4±2.0	<.001
HVLT (words)					
Total recall	21.8±4.5	14.5±3.4	13.7±3.3	20.4±2.0	<.001
Delayed recall	7.4±2.4	3.3±2.0	3.0±2.2	7.1±1.7	<.001
Recognition discrimination	10.4±1.4	7.9±1.8	7.9±2.6	10.7±1.2	<.001
Self-reported mobility					
BLE (0–100)	67.9±11.4	65.0±12.6	63.2±12.8	57.4±9.6	<.001
ALE (0–100)	44.3±13.9	38.7±14.1	38.8±15.7	33.7±16.4	<.001
Performance-based mobility					
SPPB (0–12)	9.3±2.1	8.5±2.0	7.6±2.4	7.2±2.4	<.001
HGS (m/s)	0.96±0.2	0.87±0.2	0.87±0.2	0.76±0.21	<.001
F8W (s)	8.18±2.4	8.83±2.7	10.74±4.0	10.74±5.5	<.001

Notes: MCI = mild cognitive impairment; No-MCI = no MCI; aMCI = single domain amnestic MCI; mdMCI = multiple domain amnestic MCI; naMCI = non-amnestic MCI; BMI = body mass index; MMSE = Mini Mental State Examination; DSST = the Digit Symbol Substitution test; HVLT = the Hopkins Verbal Learning test; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function; SPPB = Short Physical Performance Battery; HGS = Habitual Gait Speed; F8W = Figure of 8 Walk. *p* Values are given for a comparison across all four groups. *N* = 430 for all parameters (*N* = 429 for BMI).

Table 2. Mean Difference Given as Betas, 95% Confidence Intervals, and *p* Values From Multiple Regression models Demonstrating the Difference in Mobility Between Those With MCI and Without MCI Among Boston RISE Participants

	Unadjusted Model		Adjusted Model 1*	
	β (CI)	*p* Value	β (CI)	*p* Value
HGS (m/s)	−0.13 (−0.17; −0.10)	<.001	−0.12 (−0.16; −0.07)	<.001
F8W (s)†	1.19 (1.13; 1.27)	<.001	1.19 (1.13; 1.27)	<.001
SPPB (4–12)	−1.39 (−1.80; −0.98)	<.001	−1.35 (−1.80; −0.90)	<.001
BLE	−4.55 (−6.84; −2.25)	<.001	−4.06 (−6.48; −1.65)	.001
ALE	−5.97 (−8.74; −3.20)	<.001	−5.57 (−8.43; −2.71)	<.001

Notes: MCI = mild cognitive impairment; CI = confidence interval; HGS = Habitual Gait Speed; F8W = Figure of 8 Walk; SPPB = Short Physical Performance Battery; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function.

*Adjusted for sex, race, and education.

†F8W was log2-transformed. Results are given as 2^{β}–coefficients.

with the findings seen between those with and without MCI, the differences in HGS (≥0.09 m/s) and SPPB (≥0.71 points) surpassed the threshold of clinical meaningfulness when comparing each of the subtypes of MCI to those without MCI. In addition, some of the mobility measures differed between specific MCI subtypes. Participants with nonamnestic MCI performed significantly worse on SPPB and BLE than participants with amnestic MCI.

Table 3. Mean Difference Given as Betas, 95% Confidence Intervals, and *p* Values From Multiple Regression Model Demonstrating the Difference in Mobility Between MCI Subtypes and Those Without MCI as well as the Difference Between Single Amnestic MCI and Nonamnestic MCI Among Boston RISE Participants

	HGS (m/s)		F8W (s)*		SPPB (points)		BLE		ALE	
	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value
aMCI vs No-MCI	−0.09 (−0.14; −0.03)	<.01	1.08 (1.00; 1.17)	.054	−0.71 (−1.30; −0.13)	.02	−2.57 (−5.74; 0.60)	.11	−4.89 (−8.66; −1.12)	.01
naMCI vs No-MCI	−0.19 (−0.30; −0.08)	<.001	1.26 (1.07; 1.47)	<.01	−2.29 (−3.46; −1.11)	<.001	−9.75 (−16.16; −3.34)	<.01	−10.50 (−18.11; −2.88)	.01
mdMCI vs No-MCI	−0.13 (−0.19; −0.08)	<.001	1.31 (1.21; 1.40)	<.001	−1.79 (−2.34; −1.24)	<.001	−4.62 (−7.62; −1.63)	<.01	−5.52 (−9.08; −1.96)	<.01
naMCI vs aMCI	−0.11 (−0.22; 0.01)	.08	1.16 (0.98; 1.38)	.08	−1.57 (−2.82; −0.33)	.01	−7.18 (−13.98; −0.38)	.04	−5.61 (−13.69; 2.47)	.17
mdMCI vs aMCI	−0.05 (−0.11; 0.22)	.15	1.21 (1.10; 1.33)	<.001	−1.07 (−1.76; −0.39)	<.01	−2.05 (−5.80; 1.70)	.28	−0.63 (−5.09; 3.82)	.78
mdMCI vs naMCI	0.06 (−0.05; 0.17)	.32	1.04 (0.89; 1.22)	.61	0.50 (−0.69; 1.69)	.41	5.13 (−1.34; 11.60)	.12	4.98 (−2.71; 12.67)	.20

Notes: MCI = mild cognitive impairment; No-MCI = no MCI; aMCI = single domain amnestic MCI; mdMCI = mixed domain amnestic MCI; naMCI = nonamnestic MCI; HGS = habitual gait speed; F8W = Figure of 8 Walk; SPPB = Short Physical Performance Battery; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function; CI = confidence interval. The model was adjusted for sex, race, and education.
*F8W was log2-transformed. Results are given as 2^{β}–coefficients.

Further, participants with multiple MCI performed worse on F8W and SPPB than those with amnestic MCI alone. Thus, older persons with nonamnestic impairments, characterized by problems with processing speed and executive function, performed worse on mobility measures including performance-based tests and self-report measures. These findings are consistent both with a study by Bombin and coworkers (44), indicating that people with multiple domain MCI are more impaired than those with amnestic MCI and with prior studies linking executive dysfunction to disability (11,12,45). Also, in prior studies, F8W has been linked to visual scanning and set-shifting abilities (14) and HGS performance to executive function (9,12). These findings suggest that HGS and F8W may be linked to distinct patterns of cognitive impairment. Also, poorer mobility among different MCI subtypes may be due to greater severity or different patterns of peripheral neuromuscular impairments that underlie mobility. This was demonstrated in an analysis of gait analysis parameters conducted by Verghese and coworkers (11). They found that nonamnestic MCI was more related to gait parameters associated with pace of walking, whereas amnestic MCI was more associated with rhythm and variability parameters. Our study adds to this evidence by including a variety of both performance-based and self-reported mobility tests compared with a clinical assessment of one aspect of mobility, that being gait. An investigation of the severity and pattern of peripheral neuromuscular attributes, like that performed by Verghese and coworkers, was beyond the scope of this investigation but can be evaluated within future analyses of the Boston RISE cohort.

Of note, those with naMCI reported poorer health status and manifested more chronic conditions than other subtypes, which may explain their poorer performance. However, after adjusting for current health status, naMCI still performed significantly worse than aMCI on the more complex performance-based mobility measure, SPPB, suggesting that part of the difference in performance between the two groups is likely due to different cognitive deficits.

Our results have important clinical implications. Within a population-based study of community-dwelling older adults (26), the prevalence of coexisting cognitive impairment and slow gait was 7%. Our findings suggest that the rate of cognitive impairment is much higher among primary care patients undergoing screening for mobility problems. Given the likely progression from MCI to dementia (8) and the knowledge that coexisting cognitive impairment and mobility limitations increases the risk of institutionalization(3), early detection of these patients is critical for initiating preventative and ameliorative therapies. One mode of therapy that can improve mobility is exercise and rehabilitative care (46,47). However, patients with cognitive disabilities have commonly been excluded from large clinical trials evaluating exercise or rehabilitative care as therapies for preventing functional decline (47,48). Rehabilitative

therapy requires a capacity to learn; yet, learning may be challenged if MCI is present. Therefore, rehabilitative care paradigms for older adults with mobility problems should be developed that account for common types of MCI and the specific cognitive deficits indicated.

Limitations

Our study is cross-sectional and therefore we cannot infer a causal association between cognitive impairment and mobility limitations. Furthermore, the study was observational and therefore we might have missed some confounders. However, the estimates did not change meaningfully when adjusting for known confounders. The standardized scores used in the determination of MCI were not adjusted for education, which could influence the association between MCI and function. However, we did adjust for education in the multiple regression analyses. Our sample size was small for some MCI subtypes and corresponding analyses may not have been sufficiently powered to observe true differences between these groups. However, even given these small sample sizes, the differences between subgroups were statistically significant, and our hypotheses were predefined. Our study sample is representative of older adults, who had at least some evidence of mobility problems and were living within a 10-mile radius of our center, and may not generalize to older adults residing in other regions. It is possible that our sample included some individuals with mild dementia. However, we attempted to screen out those with moderate to severe dementia by using a MMSE cut point of 18 and our entry criteria required participants to have the ability to live and function independently in the community. Moreover, when adjusting for MMSE as part of a post hoc analysis, the findings were not materially altered, suggesting the burden of cognitive impairment had a minimal influence on the findings. Lastly, the neuropsychological battery utilized was circumscribed and did not evaluate other aspects of cognition that may be relevant to mobility (ie, visuoconstructional skills). Thus, there is the possibility that some individuals were misclassified with regard to MCI subtype. Despite these potential limitations, our study provides a unique contribution to the literature because of its design within primary care and use of a broad range of clinically feasible mobility measures.

Conclusions

Among older primary care patients, performance on a broad range of mobility measures is associated with MCI status. Performance is worse among those with MCI, and these differences extend across different MCI subtypes, appearing to be poorest among those with nonamnestic MCI.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/.

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References

1. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011;305:50–58.
2. Dewey ME, Saz P. Dementia, cognitive impairment and mortality in persons aged 65 and over living in the community: a systematic review of the literature. *Int J Geriatr Psychiatry*. 2001;16:751–761.
3. von Bonsdorff M, Rantanen T, Laukkanen P, Suutama T, Heikkinen E. Mobility limitations and cognitive deficits as predictors of institutionalization among community-dwelling older people. *Gerontology*. 2006;52:359–365.
4. Federal Interagency Forum on Aging Related Statistics. *Older Americans 2010: Key Indicators of Well-being*. Washington, DC: US Government Printing Office; 2010.
5. Petersen RC. Clinical practice. Mild cognitive impairment. *N Engl J Med*. 2011;364:2227–2234.
6. Petersen RC. Mild cognitive impairment: current research and clinical implications. *Semin Neurol*. 2007;27:22–31.
7. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol*. 1999;56:303–308.
8. Ritchie K. Mild cognitive impairment: an epidemiological perspective. *Dialogues Clin Neurosci*. 2004;6:401–408.
9. Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and cognition: a complementary approach to understanding brain function and the risk of falling. *J Am Geriatr Soc*. 2012;60:2127–2136.
10. Buracchio T, Dodge HH, Howieson D, Wasserman D, Kaye J. The trajectory of gait speed preceding mild cognitive impairment. *Arch Neurol*. 2010;67:980–986.
11. Verghese J, Robbins M, Holtzer R, et al. Gait dysfunction in mild cognitive impairment syndromes. *J Am Geriatr Soc*. 2008;56:1244–1251.
12. McGough EL, Kelly VE, Logsdon RG, et al. Associations between physical performance and executive function in older adults with mild cognitive impairment: gait speed and the timed "up & go" test. *Phys Ther*. 2011;91:1198–1207.
13. Mirelman A, Herman T, Brozgol M, et al. Executive function and falls in older adults: new findings from a five-year prospective study link fall risk to cognition. *PLoS One*. 2012;7:e40297.
14. Lowry KA, Brach JS, Nebes RD, Studenski SA, VanSwearingen JM. Contributions of cognitive function to straight- and curved-path walking in older adults. *Arch Phys Med Rehabil*. 2012;93:802–807.
15. Odonkor CA, Thomas JC, Holt N, et al. A comparison of straight- and curved-path walking tests among mobility-limited older adults. *J Gerontol A Biol Sci Med Sci*. 2013;68:1532–1539.
16. Holt NE, Percac-Lima S, Kurlinski LA, et al. The Boston Rehabilitative Impairment Study of the Elderly: a description of methods. *Arch Phys Med Rehabil*. 2013;94:347–355.
17. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189–198.
18. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49:M85–M94.
19. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum*. 2003;49:156–163.
20. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment–beyond controversies, towards a consensus: report of the International

Working Group on Mild Cognitive Impairment. *J Intern Med*. 2004;256:240–246.
21. Lezak MD, Howieson DB, Loring DW, Hannay JH, Fischer JS. *Neuropsychological Assessment*. 4th ed. New York: Oxford University Press; 2004.
22. Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. *Nat Protoc*. 2006;1:2277–2281.
23. Wechsler D. *Wechsler Adult Intelligence Scale – Third Edition: Administration and Scoring Manual*. San Antonio, TX: The Psychological Corporation; 1997.
24. Shapiro AM, Benedict RH, Schretlen D, Brandt J. Construct and concurrent validity of the Hopkins Verbal Learning Test-revised. *Clin Neuropsychol*. 1999;13:348–358.
25. Benedict RHB, Schretlen D, Groninger L, Brandt J. Hopkins Verbal Learning Test – revised: normative data and analysis of inter-form and test-retest reliability. *Clin Neuropsychol*. 1998;12:43–55.
26. Ivnik R, Malec J, Smith G, Tangalos E, Peterson R. Neuropsychological tests' norms above age 55: COWAT, BNT, MAE Token, WRAT-R Reading, AMNART, STROOP, TMT and JLO. *Clin Neuropsychol*. 1996;10:262–278.
27. Brandt J, Benedict, R. *Hopkins Verbal Learning Test – Revised: Professional Manual*. Lutz, FL: Psychological Assessment Resources; 2001.
28. Brandt J, Benedict, R. *Hopkins Verbal Learning Test – Revised/ Brief Visuospatial Memory Test – Revised: Professional Manual Supplement*. Lutz, FL: Psychological Assessment Resources; 2007.
29. Verghese J, Wang C, Lipton RB, Holtzer R. Motoric cognitive risk syndrome and the risk of dementia. *J Gerontol A Biol Sci Med Sci*. 2013;68:412–418.
30. Jak AJ, Bondi MW, Delano-Wood L, et al. Quantification of five neuropsychological approaches to defining mild cognitive impairment. *Am J Geriatr Psychiatry*. 2009;17:368–375.
31. Petersen RC, Morris JC. Mild cognitive impairment as a clinical entity and treatment target. *Arch Neurol*. 2005;62:1160–1163; discussion 1167.
32. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci*. 2000;55:M221–M231.
33. Rydwik E, Bergland A, Forsén L, Frändin K. Investigation into the reliability and validity of the measurement of elderly people's clinical walking speed: a systematic review. *Physiother Theory Pract*. 2012;28:238–256.
34. Tager IB, Swanson A, Satariano WA. Reliability of physical performance and self-reported functional measures in an older population. *J Gerontol A Biol Sci Med Sci*. 1998;53:M295–M300.
35. Mielke MM, Roberts RO, Savica R, et al. Assessing the temporal relationship between cognition and gait: slow gait predicts cognitive decline in the Mayo Clinic Study of Aging. *J Gerontol A Biol Sci Med Sci*. 2013;68:929–937.
36. Toots A, Rosendahl E, Lundin-Olsson L, Nordström P, Gustafson Y, Littbrand H. Usual gait speed independently predicts mortality in very old people: a population-based study. *J Am Med Dir Assoc*. 2013;14:529.e1–529.e6.
37. Kwon S, Perera S, Pahor M, et al. What is a meaningful change in physical performance? Findings from a clinical trial in older adults (the LIFE-P study). *J Nutr Health Aging*. 2009;13:538–544.
38. Courtine G, Schieppati M. Human walking along a curved path. I. Body trajectory, segment orientation and the effect of vision. *Eur J Neurosci*. 2003;18:177–190.
39. Hess RJ, Brach JS, Piva SR, VanSwearingen JM. Walking skill can be assessed in older adults: validity of the Figure-of-8 Walk test. *Phys Ther*. 2010;90:89–99.
40. Haley SM, Jette AM, Coster WJ, et al. Late Life Function and Disability Instrument: II. Development and evaluation of the function component. *J Gerontol A Biol Sci Med Sci*. 2002;57:M217–M222.
41. Sayers SP, Jette AM, Haley SM, Heeren TC, Guralnik JM, Fielding RA. Validation of the Late-Life Function and Disability Instrument. *J Am Geriatr Soc*. 2004;52:1554–1559.
42. Jette AM, Haley SM, Coster WJ, et al. Late life function and disability instrument: I. Development and evaluation of the disability component. *J Gerontol A Biol Sci Med Sci*. 2002;57:M209–M216.
43. Bean JF, Olveczky DD, Kiely DK, LaRose SI, Jette AM. Performance-based versus patient-reported physical function: what are the underlying predictors? *Phys Ther*. 2011;91:1804–1811.
44. Bombin I, Santiago-Ramajo S, Garolera M, et al. Functional impairment as a defining feature of: amnestic MCI cognitive, emotional, and demographic correlates. *Int Psychogeriatr*. 2012;24:1494–1504.
45. Rosano C, Simonsick EM, Harris TB, et al. Association between physical and cognitive function in healthy elderly: the health, aging and body composition study. *Neuroepidemiology*. 2005;24:8–14.
46. Uemura K, Shimada H, Makizako H, et al. Cognitive function affects trainability for physical performance in exercise intervention among older adults with mild cognitive impairment. *Clin Interv Aging*. 2013;8:97–102.
47. Heyn PC, Johnson KE, Kramer AF. Endurance and strength training outcomes on cognitively impaired and cognitively intact older adults: a meta-analysis. *J Nutr Health Aging*. 2008;12:401–409.
48. Courtney MD, Edwards HE, Chang AM, et al. Improved functional ability and independence in activities of daily living for older adults at high risk of hospital readmission: a randomized controlled trial. *J Eval Clin Pract*. 2012;18:128–134.