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Editor's Choice

Research Article

Gait Speed and Decline in Gait Speed as Predictors of Incident Dementia

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Abstract

Background: Slow gait is common in dementia, but it remains unknown whether the slowing happens many years prior to dementia onset. We therefore examined the relationship between slow baseline gait speed (GS), change in GS, and the hazard of incident dementia in a community dwelling of elderly people.

Methods: A total of 3,663 participants dementia-free at baseline (mean age, 73.5 years) were followed up for 9 years from a prospective cohort (Three-City study, France) for incident dementia (all-cause, Alzheimer's disease, vascular dementia, and other causes). GS over 6 m was assessed 4 times over the follow-up using two photoelectric cells. We used a multistate model to estimate the hazard ratio (HR) of dementia for baseline GS and tested a washout period of 4 to 7 years. The role of GS change between 65 and 85 years was examined using linear mixed models and joint models for survival and longitudinal data.

Results: A total of 296 participants developed dementia during the follow-up. In age/sex-adjusted models, 1-*SD* (0.204 m/s) lower GS was associated with an increased hazard of dementia (HR = 1.59, 95% confidence interval [CI] = 1.39, 1.81, $p < .001$), with associations evident when gait assessments were taken from 4 years (HR = 1.46; CI = 1.26, 1.68) and 7 years (HR=1.30; CI = 1.00, 1.70) prior to dementia onset. Independently of baseline GS, those with a steeper decline had a higher hazard of dementia (HR per 1 *SD* [0.007 m/s/year] decrease = 3.39 [1.37–8.43], $p = .009$).

Conclusions: Gait is slower up to 7 years prior to clinical onset of dementia. Decline in GS is also more accelerated, suggesting strong links between cognitive and motor function in older adults.

Keywords: Gait—Dementia—Epidemiology—Alzheimer's disease

Human gait is highly complex, involving the peripheral and central nervous system, including motor, sensory, sensorial, and neurocognitive pathways (1), and gait dysfunction is common in the elderly people (2). Gait speed (GS) is a simple and reliable measure that can provide similar information regarding risk of subsequent outcomes (falls, hospitalization, disability, and mortality) as a more comprehensive summary measure of physical performance such as the short physical performance battery or the timed up and go (3,4) and can be easily assessed in primary care settings and large population-based studies. Slow GS is associated with several adverse outcomes, including disability (5) and death (6), leading it to be proposed as a new "vital sign" in older adults (7). However, the generalization of GS in clinical settings is hampered by marked heterogeneity in methods used to measure it (8).

The association between gait and cognition is complex (9,10). In cross-sectional studies, slow speed is associated with poor cognitive

function (11), mild cognitive impairment (12), and dementia (13). Longitudinal data also suggest faster subsequent cognitive decline in those with slow GS (14,15). In community-dwelling elderly people, gait abnormalities are associated with the risk of mild cognitive impairment (16,17) and dementia (18). The "motoric cognitive risk" syndrome, defined as cognitive complaints accompanied with slow GS, is useful in identifying older adults at risk of dementia (19). However, the extent to which decline in GS is evident prior to cognitive decline remains unclear.

We investigated the association between GS and dementia using repeated gait assessments before dementia onset. This approach allowed us to examine whether decline in GS for 9 years is associated with an increased hazard of dementia, independently of GS at baseline.

Methods

Study Population

The 3C study is a prospective cohort of community-dwelling persons ≥65 years living in three French cities (Bordeaux, Dijon, and Montpellier) (20). A specific substudy on motor function was undertaken in Dijon (n = 4,931), where GS was measured at the study center in individuals ≤85 years at baseline (1999–2000). After the baseline examination, participants ≤85 years were invited to the study center to be interviewed in-person and for clinical assessment after 4 years (Wave 2, 2003–2004), 7 years (Wave 4, 2006–2007), and 9 years (Wave 5, 2008–2009), whereas those older than 85 years were seen at home. The study protocol was approved by the ethical committee of the Kremlin-Bicêtre University Hospital (France), and all participants gave written informed consent.

Gait Speed

GS was measured at baseline and at Waves 2, 4, and 5 in participants not less than 85 years who attended the study center; it was not assessed in those seen at home. Two photoelectric cells were connected to a chronometer and placed in a corridor 6 m apart. Participants were asked to walk at usual pace and were asked to start walking 3 m before the start line. They were allowed to use their usual walking aids if needed.

Dementia

Diagnosis of dementia at baseline and each follow-up examination was undertaken using a standardized three-step procedure, as previously reported (20). First, trained neuropsychologists administered an extensive battery of neuropsychological tests (20). Second, all participants suspected of having dementia based on their neuropsychological evaluation, using age- and education-specific cutoffs for the Mini-Mental State Examination (MMSE), Benton Visual Retention Test, and Isaac Set Test were examined by a physician. Third, an independent committee of expert neurologists reviewed all suspected cases of dementia and reached a consensus on diagnosis and etiology using standard criteria (21).

Covariates

Baseline sociodemographic measures included age, sex, education (no education to primary school, secondary school, high school, and university degree), and marital status (married; divorced, separated, widowed; and single). An unhealthy behavior score (22) was established as the number of unhealthy behaviors (range 0–4) using measures from study baseline: low-to-intermediate physical activity (walking <1 hour per day and/or exercising <1 time per week); consumption of fruits and vegetables less than once per day; current or recent smoker (quit smoking <15 years before baseline); and never, former, or heavy drinker (>21 alcoholic drinks per week for men, >14 for women).

Anthropometric measures included body mass index (BMI) and height. Weight was measured during clinical examinations (baseline, 89%; Wave 4, 67%; Wave 5, 91%; Wave 6, 81%) or self-reported otherwise during interviews at all waves. Height was measured (>99%) or self-reported (<1%) at baseline and measured at Wave 4. BMI (kg/m^2) was calculated as weight divided by height squared; baseline height was used to compute BMI at baseline and Waves 1 and 2, and height from Wave 4 was used to compute BMI at Waves 4 to 6.

The following covariates were assessed at study baseline and at each visit. Depressive symptomatology was measured using the Center for Epidemiologic Studies Depression Scale, with scores ≥16 corresponding to high depressive symptoms. Use of psychotropic drugs (antidepressants, anxiolytics, benzodiazepines, and hypnotics) was recorded. Cognition was taken into account in multivariable analyses using the Trail Making Test part B (TMT-B), which reflects executive function and was not included in the diagnosis of dementia. Trauma included history of bone fracture or recurrent falls (≥2 falls) over the 2 years preceding each visit. Chronic conditions included self-reported diabetes mellitus, Parkinson's disease, dyspnea (classes II–IV of the New York Heart Association classification), regular use of nonsteroidal anti-inflammatory drugs for joint pain, and knee or hip replacement for osteoarthritis. Cardiovascular disease and risk factors included stroke, coronary heart disease, lower limb arteritis, hypertension (systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or antihypertensive medication), and lipid-lowering drugs as a surrogate for hypercholesterolemia. Expert committees validated incident stroke and coronary heart disease events using hospital and other medical records.

DNA was extracted from white blood cells. Apolipoprotein E genotyping was carried out at Lille Genopole.

Statistical Analysis

Participants with dementia and conditions that cause gait impairment (Parkinson's disease, stroke, and hip fracture) at baseline were excluded from the analysis (Supplementary Figure 1). Participants' characteristics at baseline were described overall and according to baseline GS (<1 m/s vs. ≥1 m/s) and dementia status at the end of the follow-up using age- and sex-adjusted linear regression models and the Mantel–Haenszel χ^2 test.

Baseline GS and hazard of dementia

The association between baseline GS and the hazard of dementia was examined using a multistate (illness–death) model. Standard survival analysis requires the time to onset of disease to be known precisely for subjects with incident disease. However, in cohort studies, the diagnosis may be made at intermittent follow-up visits: time to onset is said to be interval censored between the diagnostic visit and the previous one. The Cox model does not handle interval censoring, and usual approaches to define time to onset (time at diagnosis and midpoint between diagnostic visit and the previous one) lead to biased effect estimates and underestimate standard errors, in particular if follow-up intervals are wide and variable. Death introduces another important difficulty when interval censoring is present: because disease status is determined intermittently, it is usually unknown whether subjects developed the

disease between their last visit alive (when they were disease-free) and death; not taking this into account leads to underestimate disease incidence, in particular when the follow-up intervals are wide and disease is associated with increased mortality. Multistate models for interval-censored data allow subjects to develop the disease between the last visit and death and provide more accurate estimates of the association of exposure with disease, when exposure is also associated with death and follow-up intervals are wide; in these situations, it has been recommended that multistate models for interval-censored data should be preferred to the standard Cox regression approach (9). Three baseline transitions (*no-dementia* to *dementia*, *no-dementia* to *death*, and *dementia* to *death*) and the effect of covariates were estimated using a penalized likelihood approach (23). GS was first modeled as a continuous variable (1-*SD* lower speed, *SD* = 0.204 m/s). We then estimated the hazard of dementia for slow speed using an a priori cutoff of 1.0 m/s that has been recommended for use in clinical practice (24). We also explored whether this threshold was suitable for dementia by examining the HRs and log-likelihood of models with thresholds from 0.60 to 1.35 m/s. All analyses were adjusted for age and sex, as they are strongly associated with GS.

Analyses were undertaken with all-cause dementia as the main outcome and then restricted to those with Alzheimer's disease (AD) and vascular dementia. Analyses were also repeated by progressively excluding dementia cases diagnosed at the second and fourth waves, in order to estimate the lag between the diagnosis of dementia and slowing of gait.

Change in GS and hazard of dementia

We then examined the association of change in GS with dementia onset between 65 and 85 years. Participants who developed conditions causing gait impairment (stroke, Parkinson's disease, and hip fracture) during the follow-up contributed to the analyses only while they were free of these conditions. We used two complementary approaches.

First, we used a linear mixed model with the intercept and slope fitted as random effects using a backward time scale in order to compare change in GS in those who developed dementia and those who did not. We repeated these analyses for change in cognition (MMSE and TMT-B) for comparison. The MMSE was transformed in order to normalize its distribution (25). Circularity is one limitation for analyses using the MMSE, as it was used for the diagnosis of dementia (TMT-B was not). Test scores were standardized to *z*-scores (mean = 0, *SD* = 1) using the baseline mean and SD values to allow comparisons.

Second, we used a joint modeling approach in order to estimate the association between change in GS (a longitudinal process) and dementia (time to event) by jointly estimating the parameters of a linear mixed model and a survival model. We used a Weibull function for the survival component with age as the time scale, adjusted for sex. We modeled the time to dementia onset as a function of the random intercept (ie, baseline speed) and slope of change in GS.

Role of covariates in explaining the association between GS and dementia

GS is a marker of general health that is associated with many characteristics that contribute to explain its association with outcomes such as dementia, disability, or death. We therefore examined the extent to which the association of baseline or change in GS with dementia is explained by covariates (education, height and BMI, health behaviors, cardiovascular risk factors, chronic conditions, cognitive function, and apolipoprotein E ε4 allele); the percentage reduction in HRs was estimated as $100 \times \left(\log \mathrm{HR}_{\text{Reference model}} - \log \mathrm{HR}_{\text{Model } i}\right) / \log \mathrm{HR}_{\text{Reference model}}$.

Two-tailed values of $p \leq .05$ were considered statistically significant. Analyses were performed using SAS 9.2 (SAS Institute, Cary, NC), the *SmoothHazard* package in R, v3.2.1 (R-Foundation for Statistical Computing, Vienna, Austria), and the *stjm* command in Stata 13 (StataCorp LP, College Station, TX).

Results

Of the 4,421 participants aged 65–85 years at baseline, 136 were excluded due to conditions that cause gait impairment (Parkinson's disease, *n* = 53; recent hip fracture, *n* = 12; disabling stroke, *n* = 44) or prevalent dementia (*n* = 38). We also excluded 498 participants without a GS measurement, 122 participants lost to follow-up, and 2 participants who did not have a date of death. Analyses are based on 3,663 participants (Supplementary Figure 1). Those excluded (*n* = 622) were older ($p < .001$) but did not differ on gender or education; dementia status at the end of the follow-up was known for 471 (76%) of these participants and their age-adjusted hazard for all-cause dementia ($p = .42$) and AD ($p = .40$) was similar to participants included in the analyses.

Baseline GS and Hazard of Dementia

During 24,061 person-years of follow-up (median duration, 7.8 years, *SD* = 2.7), 296 participants developed dementia (incidence: 12.3/1,000 person-years); 76% (*n* = 226) of these had AD, 7% (*n* = 20) vascular dementia, and 17% (*n* = 50) mixed/other types of dementia. Five hundred fifty eight participants died without dementia, and 64 died after a dementia diagnosis.

In age- and sex-adjusted analyses, those who developed dementia had slower baseline GS; lower education and cognitive function; and were more likely to have depressive symptoms, diabetes mellitus, coronary heart disease, to use psychotropic drugs, and to carry the apolipoprotein E ε4 allele compared with those who remained dementia-free (Table 1). Participants who walked slower at baseline were older, more often women, and more likely to have higher BMI, depressive symptoms, diabetes, and hypercholesterolemia than those who walked faster. They also had lower education, lower cognitive function (assessed by the MMSE and TMT-B) and physical activity, and used nonsteroidal anti-inflammatory drugs or psychotropic drugs more frequently.

One-*SD* lower GS was associated with a 59% increased hazard of dementia (Table 2). The log-likelihood of models with GS dichotomized using increasing thresholds suggests 1.0 m/s to be the optimal cutoff (Supplementary Figure 2). Slow speed (<1 m/s) was associated with a twofold increased hazard of dementia (HR = 2.28, 95% CI = 1.76, 2.96; Table 2; Supplementary Figure 3). This association was similar for AD (HR = 2.08, 95% CI = 1.55, 2.80) but stronger for vascular dementia (HR = 12.11, 95% CI = 4.04, 36.31). The association was somewhat stronger in younger than older participants (Table 2).

In analyses excluding incident dementia cases in the first 4 years of follow-up (Table 2), HRs for slow GS (<1 m/s) decreased compared with the main analyses, but remained statistically significant. Analyses excluding the first 7 years suggested a weaker and borderline significant association.

The role of baseline covariates in explaining the relationship between baseline GS and incident dementia is presented in

Table 1. Baseline Characteristics of the Study Population

Baseline Characteristics	Overall (*N* = 3,663)	Dementia at the End of the Follow-up			Baseline GS		
		No (*N* = 3,367)	Yes (*N* = 296)	*p*	≥1m/s (*N* = 2,612)	<1m/s (*N* = 1,051)	*p*†
Age, years, mean (*SD*)	73.5 (4.7)	73.3 (4.6)	76.5 (4.6)	<.001	72.8 (4.5)	75.5 (4.6)	<.001
Women, *n* (%)	2,267 (61.9)	2,091 (62.1)	176 (59.5)	.24	1,478 (56.6)	789 (75.1)	<.001
Marital status, *n* (%)				.57			.01
Married	2,179 (59.6)	2,015 (59.9)	164 (55.6)		1,659 (63.5)	520 (49.7)	
Divorced, separated, or widowed	1,172 (32.0)	1,063 (31.6)	109 (36.9)		756 (28.9)	416 (39.7)	
Single	308 (8.4)	286 (8.5)	22 (7.5)		197 (7.5)	111 (10.6)	
Education, *n* (%)				.003			<.001
No education or primary school	749 (20.5)	658 (19.5)	91 (30.7)		476 (18.2)	273 (26.0)	
Secondary school	1,591 (43.4)	1,476 (43.9)	115 (38.9)		1,097 (42.0)	494 (47.0)	
High school	696 (19.0)	655 (19.5)	41 (13.9)		532 (20.4)	164 (15.6)	
University degree	626 (17.1)	577 (17.1)	49 (16.6)		506 (19.4)	120 (11.4)	
Number of unhealthy behaviors, *n* (%)‡				.04			<.001
0	217 (5.9)	205 (6.1)	12 (4.1)		184 (7.0)	33 (3.1)	
1	915 (25.0)	864 (25.7)	51 (17.2)		704 (27.0)	211 (20.1)	
2	1511 (41.3)	1369 (40.7)	142 (48.0)		1031 (39.5)	480 (45.7)	
≥3	895 (24.4)	816 (24.2)	79 (26.7)		602 (23)	293 (27.9)	
BMI, kg/m^2, mean (*SD*)	25.7 (4.0)	25.7 (4.0)	26.0 (4.2)	.10	25.4 (3.7)	26.6 (4.6)	<.001
Height, cm, mean (*SD*)	161.7 (8.9)	161.8 (8.8)	160.7 (8.7)	.04	162.8 (8.7)	158.9 (8.2)	<.001
Trail Making Test, part B, mean (*SD*)§	2.3 (1.2)	2.3 (1.2)	1.6 (1.0)	<.001	2.4 (1.3)	1.9 (1.1)	<.001
Mini-Mental State Examination, mean (*SD*)	27.5 (1.9)	27.6 (1.8)	26.4 (2.1)	<.001	27.6 (1.8)	27.1 (2.0)	<.001
Depressive symptoms, *n* (%)	836 (22.8)	740 (22.0)	96 (32.4)	<.001	490 (18.8)	346 (32.9)	<.001
Psychotropic drugs use, *n* (%)	1,163 (31.7)	1,035 (30.7)	128 (43.2)	.001	716 (27.4)	447 (42.5)	<.001
Bone fracture, *n* (%)	203 (5.5)	182 (5.4)	21 (7.1)	.62	122 (4.7)	81 (7.7)	<.001
Falls, *n* (%)	427 (11.7)	366 (10.9)	61 (20.6)	<.001	246 (9.4)	181 (17.2)	<.001
Diabetes, *n* (%)	342 (9.3)	300 (8.9)	42 (14.2)	.003	225 (8.6)	117 (11.1)	<.001
Dyspnea, *n* (%)	385 (10.5)	340 (10.1)	45 (15.2)	.15	188 (7.2)	197 (18.7)	<.001
NSAIDs for joint pain, *n* (%)	551 (15.1)	505 (15.0)	46 (15.5)	.98	326 (12.5)	225 (21.5)	<.001
Knee/hip replacement for osteoarthritis, *n* (%)	202 (5.5)	179 (5.3)	23 (7.8)	.14	121 (4.6)	81 (7.7)	<.001
Cardiovascular disease, *n* (%)	639 (17.4)	562 (16.7)	77 (26.0)	.01	432 (16.5)	207 (19.7)	<.001
Hypertension, *n* (%)	2,908 (79.4)	2,663 (79.1)	245 (82.8)	.88	2,020 (77.3)	888 (84.5)	<.001
Hypercholesterolemia, *n* (%)	1,316 (35.9)	1,202 (35.7)	114 (38.5)	.16	944 (36.1)	372 (35.4)	.09
APOE ε4 allele, *n* (%)	783 (22.0)	699 (21.3)	84 (29.7)	<.001	572 (22.5)	211 (20.6)	.77
GS, m/s, mean (*SD*)	1.08 (0.20)	1.09 (0.20)	0.99 (0.20)	<.001	1.18 (0.14)	0.84 (0.11)	<.001
GS < 1 m/s, *n* (%)	1,051 (28.7)	909 (27.0)	142 (48.0)	<.001	—	—	—

Notes: GS = gait speed; BMI = body mass index; NSAIDs = nonsteroidal anti-inflammatory drugs; APOE = apolipoprotein E.

*Mantel–Haenszel χ^2 test adjusted for age and sex.

†Analysis of covariance adjusted for age and sex, with GS as a continuous dependent variable.

‡Low-to-intermediate physical activity; consumption of fruits and vegetables less than once per day; current or recent exsmoker; never, former, or heavy drinker.

§Number of correct connections per 10 s.

Supplementary Table 2. Cognitive function explained the largest proportion of the association between GS and dementia: adjustment for the TMT-B reduced the association by 18%; adjustment for the MMSE led to similar results. Health behaviors, anthropometric characteristics, and depressive symptoms also played an important role. Chronic conditions, apolipoprotein E ε4 allele, and cardiovascular disease had a marginal effect. All covariates considered together explained ~35% of the association of GS with dementia and AD.

Change in GS and Hazard of Dementia

These analyses included 137 dementia cases and 3526 non cases. The annual rate of decline of GS was 80% greater in participants who developed dementia (–0.09 *SD*, corresponding to –0.018 m/s/y, 95% CI = –0.025, –0.011) than in those who did not (–0.05 *SD*, corresponding to –0.010 m/s/y, 95% CI = –0.011, –0.009; p = .024; Figure 1; Supplementary Table 1). After adjustment for the TMT-B, the difference in the slope of change of GS between demented and nondemented participants remained significant (p = .05). The difference of 0.008 m/s/y was equivalent to the effect of 1 year of age (Supplementary Table 1) and also similar to the SD of the random slope of change in GS (0.007 m/s/y; Supplementary Table 3). The difference between demented and nondemented participants was significant at dementia onset (t = 0, –0.11 m/s, p < .0001) and 7 years (t = –7, –0.05 m/s, p = .008) but not 9 years prior to dementia onset (t = –9, –0.03 m/s, p = .15). Figure 1 shows a very similar pattern for TMT-B (difference in slopes between demented and nondemented participants of –0.04 *SD*, 95% CI = –0.07, –0.01), while the difference was more pronounced for the MMSE (–0.07 *SD*, 95% CI = –0.10, –0.04).

After taking into account the association with baseline GS (HR per 1-*SD* [0.14m/s] decrease = 1.47, 95% CI = 1.05, 2.08, p = .026), those with more pronounced decline in GS had an increased hazard

Table 2. Association Between Baseline GS and Incident Dementia

	All-cause Dementia				Alzheimer's Disease			
GS, m/s	*n**	HR (95% CI)	*p*	*p*†	*n**	HR (95% CI)	*p*	*p*†
Overall (*N* = 3,663)								
Continuous, per *SD*‡	296	1.59 (1.39, 1.81)	<.001		226	1.47 (1.27, 1.71)	<.001	
≥1 m/s, *N* = 2,612	154	Reference	—		119	Reference	—	
<1 m/s, *N* = 1,051	142	2.28 (1.76, 2.96)	<.001		107	2.08 (1.55, 2.80)	<.001	
Age at baseline ≤ 73 y (*N* = 1,801)								
Continuous, per *SD*‡	67	2.43 (1.88, 3.15)	<.001		47	2.29 (1.61, 3.25)	<.001	
≥1 m/s, *N* = 1,470	46	Reference	—		34	Reference	—	
<1 m/s, *N* = 331	21	2.56 (1.45, 4.53)	.001		13	2.04 (1.00, 4.15)	.05	
Age at baseline ≥ 73 y (*N* = 1,862)								
Continuous, per *SD*‡	229	1.45 (1.26, 1.67)	<.001	.04	179	1.38 (1.18, 1.63)	<.001	.30
≥1 m/s, *N* = 1,142	108	Reference	—		85	Reference	—	
<1 m/s, *N* = 720	121	2.11 (1.58, 2.82)	<.001	0.52	94	1.99 (1.44, 2.77)	<.001	0.95
Exclusion of the first 4 y of follow-up (cases diagnosed at first or second waves, *N* = 2,558)								
Continuous, per *SD*‡	216	1.46 (1.26, 1.68)	<0.001		171	1.45 (1.24, 1.71)	<0.001	
≥1m/s, *N* = 1,930	117	Reference	—		93	Reference	—	
<1m/s, *N* = 628	99	2.01 (1.50, 2.70)	<.001		78	1.93 (1.39, 2.69)	<.001	
Exclusion of the first 7 y of follow-up (cases diagnosed between first and fourth waves, *N* = 1,918)								
Continuous, per *SD*‡	64	1.30 (1.00, 1.70)	.05		54	1.31 (0.97, 1.75)	.07	
≥1 m/s, *N* = 1,502	37	Reference	—		30	Reference	—	
<1m/s, *N* = 416	27	1.61 (0.95, 2.75)	.08		24	1.68 (0.93, 3.02)	.09	

Notes: HR = hazard ratios; CI = confidence interval. HR and 95% CI adjusted for sex were computed using an multistate model with age as the time scale.
*Number of incident cases of dementia over the follow-up.
†The values of *p* for interaction between GS and median age at baseline.
‡HR per decrease in 1 *SD* (0.204 m/s).

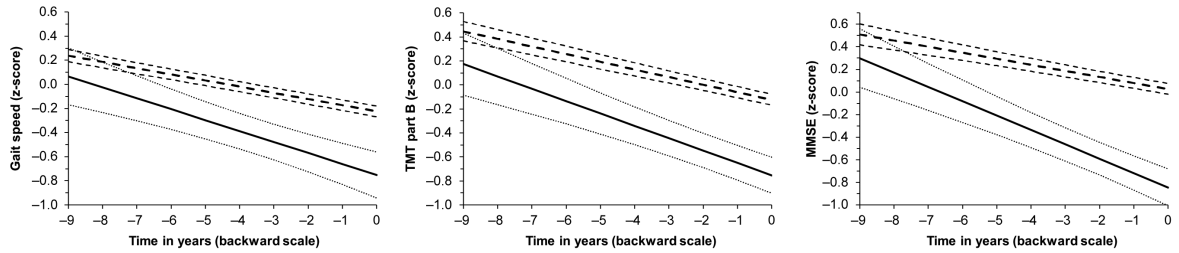

Figure 1. Predicted trajectories of GS, Trail Making Test part B, and Mini-Mental State Examination in Demented (solid line) and nondemented (dashed line) women aged 75 years at the end of follow-up. GS, Trail Making Test part B, and the transformed Mini-Mental State Examination were modeled using a linear mixed model including a random intercept and slope, with a backward time scale, and adjusted for age at t_0 and sex. Test scores were standardized to *z*-scores (mean = 0, *SD* = 1) using the baseline mean and SD values (Table 1). Dashed and dotted lines represent 95% confidence intervals.

of dementia (HR per 1-*SD* [0.007 m/s/y] decrease = 3.39, 95% CI = 1.37, 8.43, *p* = .009) and AD (HR = 2.85, 95% CI = 0.90, 9.04, *p* = .075). Cognitive function played the strongest role in this association, followed by depressive symptoms, chronic conditions, and cardiovascular disease and risk factors. All covariates considered together explained ~45% of the association for dementia and ~60% for AD (see Supplementary Table 3).

Discussion

In this large cohort of community-dwelling older persons, slow GS at the start of the study was associated with an increased risk of dementia over a 9 years follow-up. After taking into account the competing risk of death, participants walking slower than 1.0 m/s had a two-fold increased hazard of dementia compared with those who walked faster. These results were evident both for AD and vascular dementia. Remarkably, the baseline GS measure predicted dementia 7 years later, suggesting that slowing of gait is an early marker, present several years before diagnosis of dementia. We showed that independently of baseline GS, those who experienced a steeper decline over the follow-up also had an increased dementia risk. These novel findings suggest that slower GS is not only concomitant to onset of dementia but present in the years preceding dementia diagnosis and may be helpful for the early identification of elderly people at risk of becoming demented. The strengths of our study lie in its large size and long follow-up, the validation of incident dementia cases, the repeated GS assessments, and the use of sophisticated statistical methods (multistate models) that take into account both the interval-censored nature of the data and the competing risk of death. In addition to baseline GS, we also assessed the relationship between longitudinal change in GS and incident dementia. We validated the previously proposed GS cutoff of 1 m/s for dementia. Finally, by progressively excluding dementia cases diagnosed at the second and fourth waves, we determined that slower GS precedes dementia diagnosis by at least 7 years.

Previous studies, based on a variety of approaches, have found an association between gait characteristics and dementia.

Clinically defined gait abnormalities (18) or pace characteristics (26) have been associated with non-AD dementia. Extrapyramidal gait changes in combination with cognitive impairment are associated with dementia risk (27). Poor performance on physical functioning tasks are linked to an increased AD (28) and dementia risk (29). Our findings are consistent with evidence from longitudinal studies showing slower GS to be associated with faster subsequent cognitive decline (30) and mild cognitive impairment (17).

In addition to the longer follow-up, our study makes other important contributions compared with previous studies. Our use of a "washout" period of 4 to 7 years shows that GS is slowed many years prior to clinical onset of dementia. Our results are robust as we used multistate models, taking into account the competing risk of death and the interval-censored nature of the data that are preferable in this context to more conventional analytical approaches (9). Finally, by examining the effects of both baseline GS and change in GS, we were able to show their independent associations with dementia risk. Thus, our results suggest that both these measures are important in monitoring vulnerable older adults. The fact that the GS-dementia association was stronger in younger subjects may be due to selection effects, as slow GS is associated with increased mortality (31).

Our findings can be explained by several possible mechanisms. First, slow speed may be an early predementia symptom with the slowing of gait part of the process leading to dementia. Second, vascular risk factor (32) have been associated with poor motor function and dementia and in our analyses explained part of the association. Vascular risk factors are likely to play a role through vascular lesions of the brain (eg, stroke and white matter lesions (33)) that disrupt neuronal circuits involved in motor control (34). Third, unhealthy behaviors were associated with slow GS, and these behaviors may affect dementia risk (35).

Our findings need to be considered in light of some limitations. First, GS in our study was not measured in participants older than 85 years; findings on change in GS are therefore restricted to participants who developed dementia before that age. There is considerable interest in determining whether changes in cognitive function precede decline in motor function or vice versa or whether both functions decline in parallel (36). A recent review concluded that motor dysfunction predicts cognitive decline, while recognizing the fact that few studies had examined the association of cognition with subsequent changes in motor function (37).

In conclusion, our findings highlight the importance of repeated gait measures in the health assessment of older adults. GS is simple to measure in primary care settings and does not require special expertise or equipment. Our findings show that slow GS may help to identify persons at risk of dementia and underline the benefit of repeated measures in order to identify those with a steeper decline. Further research will be needed to determine the added value of GS in the prediction of dementia risk based on risk scores (38,39) and clinically relevant norms for gait in relation to dementia and other outcomes.

Supplementary Material

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

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Conflict of Interest

The authors have no conflict of interest to declare.

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