Gait Speed, Body Composition, and Dementia. The EPIDOS-Toulouse Cohort

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Background. Slow gait speed (GS) predicts dementia, but this association might be mediated by body composition parameters like total fat mass (TFM) or total lean mass (TLM). The aim of the study was to evaluate whether GS, TLM, and TFM were associated factors with an increased risk for subsequent dementia in community-dwelling older women.

Methods. A case–control study was nested in the EPIDemiologie de l’OSTéoporose cohort. GS (at usual pace more than 6 m), TLM, and TFM (assessed by dual energy x-ray absorptiometry) were measured at baseline. Cognitive performance was evaluated at baseline and at 7 years of follow-up. The presence of dementia was assured by two blinded memory experts based on best practice and validated criteria. Multivariate logistic regression models assessed the association of GS, TLM, and TFM with dementia risk.

Results. Of the initial 1,462 women, 75 years old and older, 647 (43.4%) were cognitively intact at baseline and had a full cognitive assessment at 7 years (145 of them developed dementia). Controlled for covariates (demographics, physical activity, self-reported disabilities, and comorbidities), GS was an independent associated factor for subsequent dementia as a continuous variable (odds ratio [OR] 2.28, 95% CI: 1.32–3.94) and as a categorized variable (OR 2.38, 95% CI: 1.28–4.43 highest vs lowest quartile). Neither interaction with GS nor a statistically significant association with dementia as a continuous variable (odds ratio [OR] 2.28, 95% CI: 1.32–3.94) and as a categorized variable (OR 2.38, 95% CI: 1.28–4.43 highest vs lowest quartile). Neither interaction with GS nor a statistically significant association with dementia risk was found for TLM and TFM.

Conclusions. GS was an independent associated factor for subsequent dementia not mediated by TLM or TFM.

Key Words: Dementia—Gait speed—Body composition—Alzheimer’s disease.

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HABITUAL gait speed (GS; assessed over a short distance) has shown to be predictive of a wide range of critical health outcomes including survival, health care use, subsequent mobility disability, and dementia (1–4). Despite consistent results across studies, none of these were controlled for body composition parameters such as fat mass (FM) or muscle mass (MM). To control for these parameters, when assessing dementia risk, seems advisable as high FM and low MM are associated with poor physical performances, including GS (4–7), and plausible metabolic pathways suggest direct links with increased dementia risk.

Several common mediators underlying increased adiposity and dementia can be proposed. Insulin resistance with hyperinsulinemia (main consequences of adiposity) is related to a higher risk of Alzheimer’s disease (AD) and is supposed to be the most plausible direct mechanism linking adiposity to AD (8). Surrogates of obesity, like body mass index or waist circumference, have been associated with dementia (8,9). Advanced glycation end products (AGEs), direct products of insulin resistance and diabetes, are present in senile plaques and neurofibrillary tangles, the pathologic hallmarks of AD (10). Receptors for AGEs have been found to be specific cell surface receptors for beta-amyloid, allowing for amyloid aggregation and stimulation of an immune inflammatory response that triggers many characteristics of AD pathology (11). Finally, the adipose tissue not only generates a series of adipokines that are important in metabolism but also produces pro-inflammatory cytokines. Leptin, an adipocyte-derived hormone, has recently been proposed as a plausible biological link between increasing adiposity, insulin resistance, decreasing MM, and dementia (12–15). Finally, the low subclinical systemic inflammation observed in older people with increased circulating cytokines, like tumor necrosis factor-α or interleukin-6,
have also been associated with increased risk of dementia (16,17). As stated before, these cytokines might be liberated by adipose tissue (including the adipose tissue surrounding and infiltrating muscle) so that adiposity might play a crucial role in dementia development. Moreover, leptin has similar structural and functional characteristics to cytokines, sharing post-receptor pathways (18).

Recent studies also highlight associations between reduced MM and brain atrophy in early AD and cognitive functioning (19,20). Common metabolic pathways underlying MM and dementia could be suggested. The low subclinical pro-inflammatory state present in older adults influences the balance between muscle protein synthesis and breakdown and could be the mediator between decreased MM (21,22), poor physical functioning (23), and the incidence of dementia (16,22). Leptin has been proposed as the plausible mediator for decreased MM and dementia (18). Muscle anabolism, low physical performance, and decreased MM are influenced by vitamin D, which possesses a nuclear receptor in muscular cells (24). Moreover, recent evidence highlights the association of vitamin D with cognitive decline (25). Currently, a huge body of evidence links increased MM with increased physical activity and prevention of late-life cognitive decline (26,27). Physical exercising has a preventive effect on the inflammatory pathway. These effects may be mediated by activation of insulin-like growth factor-1, vascular endothelial growth factor, brain-derived neurotrophic factor, and endorphins (28).

Finally, special attention should be given to intramuscular adipose tissue (IMAT). Fat infiltration has been observed to be related to age and higher adiposity and to be associated with poorer physical performance and decreased MM (6). Even more, subclinical local inflammation, as evaluated by IL-6 gene expression, was positively associated with the degree of IMAT (13). Thus, the resulting subclinical inflammation due to IMAT could be related to decreased MM, poor physical performance, and increased risk of dementia.

Therefore, it could be hypothesized that the increased risk of dementia, in the presence of slow GS, could be mainly due to impaired body composition parameters. Increased FM or decreased MM could be the cause behind slow GS and be directly responsible for an increased risk of dementia. The purpose of the present case–control study nested in the EPIDemioLOGie de l’OSTéoporose (EPIDOS) cohort was to evaluate if baseline slow GS and body composition parameters (FM and MM) were independent associated factors for an increased risk of dementia and if the body composition parameters mediated the association of GS with subsequent dementia.

**METHODS**

**EPIDOS Cohort**

The EPIDOS study was a French observational prospective multicenter cohort study designed to evaluate risk factors for hip fractures among community-dwelling women aged 75 years and older. Detailed information about the study has been previously published (29). Briefly, between January 1992 and January 1994, 7,598 women, in 5 French cities, volunteered to participate. Women unable to walk autonomously (walking aids allowed), with a history of femoral neck fracture, hip replacement, or were institutionalized were excluded. The local ethics committee of the participating centers approved the study, and each woman signed informed consent. An additional study of dementia risk factors in 1999–2000 was proposed to the volunteers from Toulouse. In this new investigation, data on cognitive performances were collected during a standardized interview by trained investigators (30).

**Study Sample**

The totality of the 1,462 women from the EPIDOS study cohort at Toulouse were contacted and 714 (48.8% of the initial cohort) agreed and signed informed consent to participate in the additional follow-up study, 414 participants (28.3%) were lost to follow-up, 193 died (13.2%), and 141 withdrew consent (9.6%).

Baseline cognitive impairment was ascertained using the Short Portable Mental Status Questionnaire (SPMSQ; 31). The SPMSQ, a 10-item questionnaire, was developed to detect the presence of cognitive impairment in community-dwelling older adults. The validated cutoff value for normal cognitive functioning is a score of 8 or above (32–34). For the present analyses, only participants free from baseline cognitive impairment were included. Therefore, of the 264 participants who developed dementia or mild cognitive impairment (MCI), 66 had to be excluded as baseline cognitive status could not be assured. The participants with no cognitive impairment after 7 years of follow-up were considered cognitively intact at baseline, as dementia is a progressive and nonreversible disease. Only one participant had no baseline GS assessment and was also excluded. So, the final study sample consisted of 647 participants cognitively intact at baseline, with full data on GS and cognitive performances at 7 years of follow-up (see Figure 1).

**Baseline Assessment of Covariates**

The standardized examination was performed by trained nurses and included a structured questionnaire (demographics, self-reported disabilities, and comorbidities), a clinical examination, and the assessment of physical performances.

Educational level was assessed as a dichotomous variable indicating receipt of the French certificate of elementary school education. Self-reported diseases like hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, depression, pain and its localization, and history of fracture (other than hip fracture) were recorded at
baseline. The total number of comorbidities for each patient was retained for the present analyses. The presence of Parkinson’s disease (PD) and the cardiovascular disease risk factors (CVDRF) hypertension, diabetes, and obesity were also considered independently due to the association with low GS and the risk of developing dementia (35). Other disorders that could eventually affect GS without increasing the risk of cognitive decline (ie severe osteoarthritis, recent joint replacement, or peripheral neuropathy) were not specifically taken into account in analyses (other than including the condition in the comorbidity variable). Participants presenting these disorders were excluded from the EPIDOS cohort only when coexisting with severe disability (29). Dressing, toileting, and mobility were assessed for basic activities of daily living (ADL) and categorized as a dichotomous variable, independent or not, for all the three items (36). The eight items of the Lawton’s instrumental activities of daily living (IADL) scale were also assessed as a dichotomous variable (presence of 0 or ≥1 incapacity in performing the eight items; 37). Participants reported in a structured questionnaire whether they practiced recreational activities such as walking, gymnastics, cycling, swimming, or gardening. Type, frequency, and duration of each activity were recorded. As performed in a previous paper, the variable “physically active” was constructed to obtain approximately the fittest 20% of the study sample (this was equivalent to a participant practicing at least one activity for at least 1 hour a week for the past month or more; 4).
Baseline Assessment of Body Composition

Whole-body composition was estimated using a dual energy x-ray absorptiometry (DXA) scanner (QDR 4500 W Hologic, Waltham, MA; 38,39). DXA measurements were performed by a trained technician, and the DXA machine was regularly calibrated. As done in previous surveys and based on distribution characteristics of the sample, total fat mass (TFM) and total lean mass (TLM; measured in kilograms) were categorized in quartiles (20). Data on the validity of body composition parameters of the EPIDOS-Toulouse cohort have previously been published (40).

Assessment of Cognitive Performances After 7 Years of Follow-up

As stated before, baseline cognitive impairment was ascertained using the SPMSQ with a score of 8 or above as the validated cutoff value for normal cognitive functioning. At the seventh year of follow-up, all cases of dementia were recorded during a single structured and standardized home-based interview. During this visit, cognitive performances were assessed with the Mini-Mental State Examination (41), the Grober and Buschke (42), and the IADL tests. In a double-blind manner, two memory specialists established the diagnosis of dementia. Clinical suspicion of dementia was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, criteria (43). Probable or possible AD was diagnosed according to the criteria of the National Institute of Neurological and Communicative Disorders/Alzheimer’s Disease and Related Disorders Association working group (44). Computed tomography reports or the images themselves, when available, were reviewed to rule out reversible causes of dementia or contribute to the diagnosis of dementia subtypes (ie cortical and subcortical atrophy or infarcts, intracerebral lesions [tumors or hematomas], white matter lesions, and presence of enlarged ventricles; 45). Participants were classified into three groups: normal cognitive function, MCI, and dementia (categorizing subtypes of dementia, ie AD, vascular or mixed dementia, dementia with Lewy bodies, frontotemporal dementia, and Parkinson dementia when possible; 46,47).

Baseline Assessment of GS

A standardized assessment of GS was performed at baseline (3). Participants were asked to perform a 6-m walk at their usual pace; walking aids were allowed. Timing began when the command was given, and time in seconds needed to complete the 6-m walk was recorded. The faster of two walks was retained for the present analysis. GS (calculated as meters per second) was used as a continuous variable and was categorized in quartiles based on the sample distribution.

Continuous variables were compared by Student’s t test and categorical variables using chi-square statistics in univariate analyses.

A multiple logistic regression model (backward stepwise) was constructed (containing all covariates with p < .30 in univariate analyses) to assess the independent association of the two GS variables (continuous and categorized in quartiles), TFM, and TLM with subsequent dementia risk. The best performers (faster GSs) were chosen as reference categories. The model was fitted using the maximum likelihood method, and the null hypothesis of backward stepwise models was verified with a likelihood ratio test. In a supplementary analysis, the same model was also constructed for the 71 participants who developed AD.

The existence of interaction between GS and TLM and TFM was tested using the Mantel–Haenzel test for homogeneity for odds ratios (ORs), and sensitivity analyses were conducted to evaluate whether a potential bias could be introduced by excluding MCI participants from the analyses. Two scenarios, with the strongest possible hypothesis that all the MCI participants progressed to dementia (scenario 1) or that none of the participant progressed to dementia (scenario 2), were assessed with GS, TFM, and TLM as independent variables in both models (48).

RESULTS

Of the 647 women included in the present analyses (43.4% of the EPIDOS-Toulouse cohort), 449 (69.4%) remained dementia free, 145 (22.4%) developed dementia (with 71 cases of probable AD, 2 mixed dementia, 1 vascular dementia, and 1 subcortical dementia), and 53 (8.2%) developed MCI after 7 years of follow-up (Figure 1). After the standardized home-based interview, 70 participants could not be categorized by the memory experts other than suffering from dementia.

Of the initial cohort of 1,462 participants, 748 (51.2%) women were not enrolled in the additional follow-up (193 died [13.2%], 141 withdrew from the study [9.6%], and 414 [28.3%] were lost to follow-up). The baseline analyses of these women showed that they were older (p < .001), had a lower educational level (p < .001), were less physically active (p < .01), suffered more from ADL (p < .05) and IADL (p < .01) impairments, and had a significant lower GS (p < .001).

No interaction could be evidenced between GS across quartiles of TLM or TFM (p = .88 and p = .14, respectively), so no stratification of models was necessary.

Table 1 lists the baseline characteristics and unadjusted OR of the participants by dementia status. A statistically significant difference of 0.1 ms⁻¹ in habitual GS can be appreciated between the two groups. Only 37 participants expressed important mobility impairments (all participants were autonomous for dressing and toileting), and 11 participants had three or more IADL difficulties representing
Table 1. Baseline Characteristics by Follow-up Status

<table>
<thead>
<tr>
<th>Variables, n (%)</th>
<th>Dementia Free* (n = 449)</th>
<th>Dementia* (n = 145)</th>
<th>p Value†</th>
<th>OR (95% CI) Unadjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;80</td>
<td>274 (61.0)</td>
<td>58 (40.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>≥80</td>
<td>175 (39.0)</td>
<td>87 (60.0)</td>
<td>2.3 (1.6–3.4)</td>
</tr>
<tr>
<td>French certificate of living arrangements</td>
<td>Yes</td>
<td>400 (89.1)</td>
<td>118 (81.4)</td>
<td>.016</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>49 (10.9)</td>
<td>27 (18.6)</td>
<td>1.9 (1.1–3.1)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>26 (5.8)</td>
<td>11 (7.6)</td>
<td>.699</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>166 (37.0)</td>
<td>48 (33.1)</td>
<td>0.7 (0.3–1.5)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>177 (39.4)</td>
<td>62 (42.8)</td>
<td>0.8 (0.4–1.8)</td>
</tr>
<tr>
<td></td>
<td>≥3</td>
<td>80 (17.8)</td>
<td>24 (16.5)</td>
<td>0.7 (0.3–1.6)</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>No</td>
<td>439 (97.8)</td>
<td>140 (96.6)</td>
<td>.378</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>10 (2.2)</td>
<td>5 (3.4)</td>
<td>1.6 (0.5–4.7)</td>
</tr>
<tr>
<td>ADL (three items)</td>
<td>Autonomous</td>
<td>427 (95.1)</td>
<td>130 (89.7)</td>
<td>.018</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>22 (4.9)</td>
<td>15 (10.3)</td>
<td>2.2 (1.1–4.4)</td>
</tr>
<tr>
<td>IADL (eight items)</td>
<td>No incapacity</td>
<td>408 (90.9)</td>
<td>121 (83.4)</td>
<td>.013</td>
</tr>
<tr>
<td></td>
<td>≥ 1 incapacity</td>
<td>41 (9.1)</td>
<td>24 (16.6)</td>
<td>2.0 (1.1–3.4)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Yes</td>
<td>119 (26.6)</td>
<td>25 (17.4)</td>
<td>.025</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>329 (73.4)</td>
<td>119 (82.6)</td>
<td>1.7 (1.1–2.8)</td>
</tr>
<tr>
<td>BMI</td>
<td>Normal (&lt;25)†</td>
<td>252 (56.1)</td>
<td>79 (54.9)</td>
<td>.389</td>
</tr>
<tr>
<td></td>
<td>Overweight (&gt;25–30)</td>
<td>158 (35.2)</td>
<td>47 (32.6)</td>
<td>0.9 (0.6–1.4)</td>
</tr>
<tr>
<td></td>
<td>Obese (&gt;30)</td>
<td>39 (8.7)</td>
<td>18 (12.5)</td>
<td>1.5 (0.8–2.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes</td>
<td>205 (45.7)</td>
<td>72 (49.7)</td>
<td>.401</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>244 (54.3)</td>
<td>73 (50.3)</td>
<td>1.17 (0.81–1.71)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>20 (4.5)</td>
<td>138 (95.5)</td>
<td>.855</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>428 (95.5)</td>
<td>7 (4.8)</td>
<td>1.09 (0.45–2.62)</td>
</tr>
<tr>
<td>Fat mass (kg), in quartiles</td>
<td>(26.81–max)</td>
<td>101 (23.7)</td>
<td>30 (23.1)</td>
<td>.301</td>
</tr>
<tr>
<td></td>
<td>(21.63–26.81)</td>
<td>109 (23.7)</td>
<td>35 (26.9)</td>
<td>1.1 (0.6–1.9)</td>
</tr>
<tr>
<td></td>
<td>(16.63–21.63)</td>
<td>112 (26.3)</td>
<td>25 (19.2)</td>
<td>0.8 (0.4–1.4)</td>
</tr>
<tr>
<td></td>
<td>(min–16.63)</td>
<td>104 (24.4)</td>
<td>40 (30.8)</td>
<td>1.3 (0.7–2.2)</td>
</tr>
<tr>
<td>Lean mass (kg), in quartiles</td>
<td>(37.57–max)</td>
<td>94 (21.2)</td>
<td>27 (20.8)</td>
<td>.124</td>
</tr>
<tr>
<td></td>
<td>(34.9–37.57)</td>
<td>93 (21.8)</td>
<td>39 (30.0)</td>
<td>1.5 (0.8–2.6)</td>
</tr>
<tr>
<td></td>
<td>(32.5–34.9)</td>
<td>95 (23.2)</td>
<td>32 (24.6)</td>
<td>1.2 (0.7–2.1)</td>
</tr>
<tr>
<td></td>
<td>(min–32.5)</td>
<td>144 (33.8)</td>
<td>32 (24.6)</td>
<td>0.8 (0.4–1.4)</td>
</tr>
<tr>
<td>GS (ms⁻¹)</td>
<td>&gt;0.92 ms⁻¹</td>
<td>153 (34.1)</td>
<td>27 (18.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>GS, in quartiles</td>
<td>&gt;0.92 to &lt;0.98 ms⁻¹</td>
<td>130 (28.9)</td>
<td>31 (21.4)</td>
<td>1.4 (0.8–2.4)</td>
</tr>
<tr>
<td></td>
<td>&gt;0.67 to &lt;0.92 ms⁻¹</td>
<td>92 (20.5)</td>
<td>44 (30.3)</td>
<td>2.7 (1.6–4.7)</td>
</tr>
<tr>
<td></td>
<td>≤0.67 ms⁻¹</td>
<td>74 (16.5)</td>
<td>43 (29.7)</td>
<td>3.3 (1.9–5.7)</td>
</tr>
</tbody>
</table>

Notes: *Results are presented as number (percentage) or mean ± standard deviation. BMI = body mass index; ADL = basic activities of daily living (dressing, toileting, and mobility); GS = gait speed; IADL = instrumental activities of daily living; OR = odds ratio. Bold values are statistically significant p values.

†Based on Student’s t test or chi-square statistics as appropriate.

‡See text for list of comorbidities.

§Underweight is included in normal BMI class.

In the multiple logistic regression models of the supplementary analysis of 71 cases of AD (adjusted for age), GS proved to be the strongest independent associated factor for AD risk with an OR of 3.38 (95% CI: 1.80–6.33) as a continuous variable (meters per second). Once more, no statistical significant association could be demonstrated for TLM with OR of 0.57 (95% CI: 0.24–1.34) and TFM with OR of 2.12 (95% CI: 0.90–4.99; comparing highest vs lowest quartile) with subsequent AD risk in this additional analysis.

Finally, the sensitivity analyses showed a nonstatistically significant variation in OR estimation of GS (comparing highest vs lowest quartile) in scenario 1 (all MCI convert to dementia), with OR of 2.36 (95% CI: 1.39–4.02), and an autonomous community-dwelling population. No association with PD or CVDRF could be evidenced.

Table 2 lists the OR of multivariate analyses. In the backward stepwise logistic regression models, GS was an independent associated factor for increased dementia risk with an OR of 2.28 (95% CI: 1.32–3.94) as a continuous variable (meters per second) and an OR of 2.38 (95% CI: 1.28–4.43) when comparing the highest versus lowest quartile. No statistical association of TLM and TFM with subsequent dementia risk could be demonstrated in both models, with OR of 0.67 (95% CI: 0.35–1.29) and OR of 1.60 (95% CI: 0.85–3.01), respectively (in the model with GS as a continuous variable).
Table 2. Association of Usual Gait Speed (GS) and Body Composition with Dementia Risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>Full Model*</th>
<th>Stepwise Backward Model†</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS, Continuous variable (ms⁻¹)</td>
<td>2.00 (1.08–3.68)</td>
<td>2.28 (1.32–3.94)</td>
</tr>
<tr>
<td>Age (&gt;80 years)</td>
<td>2.02 (1.31–3.13)</td>
<td>2.09 (1.35–3.22)</td>
</tr>
<tr>
<td>TLM (kg), highest vs lowest quartile</td>
<td>0.69 (0.36–1.33)</td>
<td>0.67 (0.35–1.29)</td>
</tr>
<tr>
<td>TFM (kg), highest vs lowest quartile</td>
<td>1.61 (0.86–3.05)</td>
<td>1.60 (0.85–3.01)</td>
</tr>
<tr>
<td>GS, highest vs lowest quartile</td>
<td>2.04 (1.06–3.92)</td>
<td>2.38 (1.28–4.43)</td>
</tr>
<tr>
<td>Age (&gt;80 years)</td>
<td>2.07 (1.33–3.22)</td>
<td>2.15 (1.39–3.33)</td>
</tr>
<tr>
<td>TLM (kg), highest vs lowest quartile</td>
<td>0.69 (0.35–1.33)</td>
<td>0.67 (0.35–1.28)</td>
</tr>
<tr>
<td>TFM (kg), highest vs lowest quartile</td>
<td>1.57 (0.84–3.03)</td>
<td>1.57 (0.83–2.97)</td>
</tr>
</tbody>
</table>

Notes: OR = odds ratio; TLM = total lean mass; TFM = total fat mass. Bold values identify statistically significant odds ratios.

* Initial logistic regression model containing all covariates with p < .30 in univariate analyses: gait speed, TLM, TFM, age, living arrangements, French certificate of education, basic activities of daily living impairment, instrumental activities of daily living impairment, and physical activity. Only variables of interest are shown.

† Final backward stepwise logistic regression model illustrating the independent associated variables with an increased risk of dementia. Adjusted for TLM and TFM.

Discussion

After 7 years of follow-up, of the 647 participants, 145 developed dementia (with 71 cases of AD). Habitual GS was associated with an increased 7-year risk of dementia. Neither interaction with GS nor a statistical significant association with subsequent dementia was found for TLM and TFM. Supplementary analyses with AD patients confirmed the main results, and sensitivity analyses using MCI proved robustness of models. Based on the current research hypothesis, no further analyses searching for an association between GS and MCI were performed.

Regarding GS, the present findings are consistent with prior surveys reporting the association between decreased GS and dementia. Indeed, in dementia-free community-dwelling older adults, habitual GS (measured in quartiles, as a continuous variable or with a specific threshold) has proven to be a consistent risk factor for incident dementia or MCI in multiple cross-sectional and longitudinal studies (1,2,49,50). A limit of these results is that no quantitative or qualitative analyses of GS were performed. Abnormalities in gait, other than speed, have shown to predict MCI and dementia, especially non-Alzheimer’s dementia. The absence of a clinical characterization (ie, neurological gait, extrapyramidal features, and unsteady gait) could underestimate the odds of impaired GS, especially in non-Alzheimer’s dementia (51–53).

Only age was found to be another independent associated factor. As reported in literature, advancing age is the most consistent risk factor for dementia (54,55). The current findings, illustrating that GS and age present similar odds, suggest that the association of GS with subsequent dementia could be as strong as age.

The originality of the present study relies on the fact that the models were adjusted for TFM and TLM, and to the authors knowledge, it is the first study to control for these variables, the association of GS with subsequent risk of dementia. The two body composition variables slightly attenuated the odds of GS but were not found to be independent associated factors and did not interact with GS. Even if plausible mechanisms have been evoked, the present analyses could not evidence a relationship of TFM and TLM with increased risk of dementia, and so the association of GS with dementia was not mediated by the latter. Only scarce evidence exists to compare the current findings. The association between cognitive decline and low lean mass was previously found in 7,105 women of the French EPIDOS cohort (20), but this link could not be confirmed in a recent Chinese study where only men showed a statistical significant association (56). Both studies used DXA to assess lean mass, analyzed body composition in quartiles, and performed cross-sectional logistic regression analyses. No evidence of longitudinal data could be retrieved, so that the present study could not be compared. It could be possible that (the same as for mobility disability) body composition parameters do not predict risk of dementia even if cross-sectional associations are found (57).

A main limitation in the interpretation of these results is that DXA was only performed at baseline, so that changes over time in TFM or TLM could be associated to an increased risk of dementia. In a recent study of more than 4,300 ambulatory older adults, 68% of the study participants showed more than 5% change in TFM (loss in 31% and gain in 37%) and 23% showed a 5% change in TLM (loss in 20% and gain in 3%) over a 4- to 5-year period (58). This dynamic nature of body composition parameters could challenge the actual results (with only one measure at baseline and dementia assessed 7 years later). Only repeated DXA assessment and performing a time-dependent analysis involving the body composition parameters could solve this issue.

Another main limitation of the present study is that dementia diagnosis was performed only at the seventh year of follow-up. Thus, the relative risk of GS, TLM, or TFM and the incidence of dementia could not be assessed. However, the study was prospective, and the cognitive status of women was assessed at baseline and after 7 years. Therefore, a nested case–control study was possible, and the odds of GS and body composition parameters could be assessed for subsequent risk of dementia.

Statistical power needs to be addressed to justify the non-association, and the study could be underpowered due to a small study sample. Although the maximum of efforts were performed to include all participants in the additional follow-up...
study, only 714 (48.8%) of the participants of the initial Toulouse cohort were reassessed after 7 years with present analyses performed on 647 participants (43.4% of inception cohort). The analyses of the excluded population highlighted factors that have been shown in previous studies to be risk factors for dementia. Having lost 50% of the study population (and knowing that the attrition might be due to the presence of the study-dependent variable), the validity and inference of the results might be limited, but this is true for all dementia trials involving older adults where attrition is as high as 25%–50% in the first year of follow-up (59,60).

Concerning longitudinal data of older adults, a “survivor effect” is generally present, and it is possible that the population continuing their participation after 7 years is a much healthier population at baseline. This survivor effect underestimates the odds of GS as slower baseline performers might have been lost to follow-up or might have died during the 7-year period. The survivor effect also underestimates the odds of TLM and TFM. These parameters have been associated with mortality and adverse health events so that impaired baseline TFM or TLM could have led to increased attrition over 7 years. The resulting underestimation of their odds could dampen the potential association with dementia.

**Conclusions**

In this cohort of community-dwelling autonomous elderly women, GS was an independent associated factor with an increased risk for dementia and AD after 7 years of follow-up even after adjustment of covariates that included body composition parameters. This association was as strong as age, the most consistent risk factor for dementia and AD. Body composition parameters (TLM and TFM) failed to be associated to subsequent dementia and could not mediate the association of GS. More survey needs to be performed on body composition parameters before concluding that these variables are not associated with dementia.

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**References**


