Slowness Predicts Mortality: A Comparative Analysis of Walking Speed And Moberg Picking-Up Tests

Meyer May-Lucie

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Unisanté, Centre Universitaire de Médecine Générale et Santé Publique
Centre Hospitalier Universitaire Vaudois, Département d'Oncologie

Slowness Predicts Mortality: A Comparative Analysis of Walking Speed And Moberg Picking-Up Tests

THESE

préparée sous la direction de la Professeure Brigitte Santos-Eggimann
avec la co-direction du Docteur Andreas Hottinger

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

May-Lucie MEYER

Médecin diplômée de la Confédération Suisse
Originaire de Krummenau (SG) et Triegen (LU)

Lausanne
2021

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur.trice de thèse	Prof. **Brigitte Santos-Eggimann**
Co-Directeur.trice de thèse	Dr **Andreas Hottinger**
Expert.e	Prof. **Christophe Büla**
Vice-Directeur de l'Ecole doctorale	Prof. **John Prior**

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Madame May-Lucie Meyer

intitulée

Slowness Predicts Mortality: A Comparative Analysis of Walking Speed And Moberg Picking-Up Tests

Lausanne, le 8 juin 2021

pour Le Doyen
de la Faculté de Biologie et de Médecine

Monsieur le Professeur John Prior
Vice-Directeur de l'Ecole doctorale

Analyse comparative de la vitesse de marche et du test de Moberg comme prédicteurs de la mortalité

Contexte et objectif : Le ralentissement moteur est l'une des cinq composantes du phénotype de fragilité décrit par L. Fried et al. en 2001, dont l'intérêt est largement reconnu en médecine gériatrique. En pratique, un test de la vitesse de marche (VM) est utilisé pour objectiver la lenteur lors de l'évaluation de la fragilité des personnes âgées, et il est aujourd'hui établi qu'une VM basse est un facteur prédicteur de mortalité.
La VM peut cependant parfois s'avérer difficile à mesurer, pour des raisons médicales ou logistiques, et il n'existe à ce jour pas d'alternative reconnue pour évaluer la lenteur comme composante de la fragilité lorsqu'un test de marche n'est pas réalisable.
Dans cette circonstance, nous nous sommes intéressés au test de Moberg (Moberg Picking-Up Test, MPUT), initialement développé pour évaluer la fonction motrice de la main. Ce test chronométré peut aussi servir de mesure de la lenteur motrice. Dans une étude récente, une corrélation modérée mais significative a été observée entre la VM et le temps mesuré au MPUT.
Le but de notre travail était de comparer la relation entre lenteur et mortalité lorsque la lenteur est définie sur la base d'un test de Moberg ou sur celle d'un test de marche.

Méthodes : Le design est observationnel, de cohorte prospective. L'échantillon est constitué de 4731 personnes non-institutionnalisées, recrutées aléatoirement en 2004, 2009 et 2014 dans l'étude Lausanne cohorte 65+ (Lc65), dont les performances aux deux tests, MPUT et VM, ont été mesurées à l'âge de 66 à 71 ans.
Pour chacun des deux tests, la lenteur a été définie par un temps d'exécution supérieur au percentile 80, conformément à la définition du ralentissement moteur dans le phénotype de fragilité de Fried et al. Des analyses de survie ont comparé l'évolution des personnes selon ce seuil à 4 ans, 9 ans et 14 ans. Des analyses multivariables ont été conduites en recourant au modèle de régression de Cox, contrôlant l'âge, le sexe, la taille et la force de préhension. La capacité prédictive du MPUT et de la VM a été évaluée par le C de Harrell dans les modèles ajustés.

Résultats : Un test de MPUT ou de VM plus lent s'est révélé être associé à la mortalité à 4, 9 et 14 ans ($p<.001$). Les courbes de survie ont montré des taux de survie plus faibles lorque le temps de réalisation était supérieur au percentile 80 pour les deux tests ($p<.001$), quelle que soit la durée du suivi. Les modèles de Cox ont mis en évidence un risque de mortalité plus élevé au-dessus de ce seuil à 4 ans (Hazard ratio [intervalle de confiance de 95 %]) : MPUT 2.1 [1.5-3.0] ; VM 2.2 [1.5-3.1]), à 9 ans (MPUT 1.7 [1.3-2.3] ; VM 2.0 [1.5-2.6]) et à 14 ans (MPUT 1.8 [1.4-2.3] ; VM 1.8 [1.4-2.4]) (tous $p<.001$). Les deux tests ont montré une capacité prédictive similaire (Harrell's C : MPUT entre 61% et 68%, VM entre 62% et 69%).

Conclusions et implications : La lenteur au test de Moberg est associée à une augmentation de la mortalité à court et à long terme chez les personnes âgées non-institutionnalisées. La capacité de ce test à prédire la mortalité est similaire à celle d'un test de marche. Le test de Moberg pourrait offrir une alternative lorsqu'un test de marche ne peut pas être réalisé, permettant ainsi de minimiser le biais dû à l'exclusion systématique de tels cas observé dans de nombreuses études cliniques.

MOTS CLÉS : Vitesse de marche, Test de Moberg, Mortalité, Lenteur, Fragilité

JAMDA xxx (2021) 1–6

JAMDA

journal homepage: www.jamda.com

Original Study

Slowness Predicts Mortality: A Comparative Analysis of Walking Speed and Moberg Picking-Up Tests

May-Lucie Meyer MSc [a,*], Sarah Fustinoni BSc [b], Yves Henchoz PhD [b], Andreas F. Hottinger MD, PhD [a,c], Brigitte Santos-Eggimann MD, MPH, DrPH [b]

[a] Department of Oncology, University of Lausanne Hospital Center (CHUV) & University of Lausanne, Lausanne, Switzerland
[b] Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland
[c] Department of Clinical Neurosciences, University of Lausanne Hospital Center (CHUV) & University of Lausanne, Lausanne, Switzerland

Keywords:
Walking speed
Moberg picking-up test
mortality
slowness
frailty

A B S T R A C T

Objectives: Slow walking speed (WS) is predictive of mortality but may be difficult to measure, which compromises the assessment of frailty, based on Fried et al's phenotype. The timed Moberg picking-up test (MPUT), developed to evaluate hand's function, was found moderately but significantly correlated with WS. We compared the relationship between slowness, assessed by MPUT and WS tests, and mortality.
Design: Observational (prospective cohort study).
Setting and Participants: 4731 community-dwelling adults included in 2004, 2009, or 2014 in the ongoing Lausanne cohort 65+ (Lc65+) were assessed at the age of 66-71 years.
Method: Mortality was compared for individuals above and below percentile 80 of MPUT, and respectively WS performance time, according to the Fried criterion. Multivariable analyses using Cox's regression models were adjusted for age, sex, height and grip strength. The predictive capability of MPUT and WS was assessed in adjusted models using Harrell *C*.
Results: Slowness in MPUT and in WS test was associated with mortality at 4, 9, and 14 years ($P < .001$). Survival curves showed lower survival rates in the highest percentile for both tests ($P < .001$), regardless of the follow-up period. Cox models indicated a higher risk of death at 4 years [adjusted hazard ratio (95% confidence interval): MPUT, 2.1 (1.5-3.0); WS, 2.2 (1.5-3.1)], 9 years [MPUT 1.7 (1.3-2.3); WS 2.0 (1.5-2.6)] and 14 years [MPUT 1.8 (1.4-2.3); WS 1.8 (1.4-2.4)] for participants above the 80th percentile (all $P < .001$). The 2 tests had similar predictive capability (Harrell *C*: MPUT, between 61% and 68%; WS, between 62% and 69%).
Conclusions and Implications: Poor performance in MPUT is associated with increased mortality at the short and long term among community-dwelling older adults. This alternative to WS in the assessment of slowness has similar predictive capability for mortality and avoids biased estimates because of nonrandom exclusion of individuals unable to complete WS.

Population is aging in the majority of countries worldwide. As the population gets older, the increased incidence of chronic diseases leads to an augmentation in functional decline, which is a major concern and remains poorly addressed. In the last 2 decades, the concept of frailty emerged, described by geriatricians as a pathologic state of low functional reserve of multiple organs or systems that can turn to disability when stressful adverse events happen.[1,2]

In 2001, Fried et al[3] proposed a clinical definition of frailty. They described a phenotype characterized by 5 dimensions: denutrition, exhaustion, muscular weakness, motor slowness, and reduced physical activity. This phenotype was shown to be preceding functional decline in population-based studies,[3–5] and recent developments of

The Lc65+ study has been supported by the University of Lausanne Center for Primary Care and Public Health (Unisanté), Switzerland; University of Lausanne Hospital Center; Canton de Vaud Department of Public Health; City of Lausanne; Loterie Romande (research grants 2006-2008 and 2018-2019); Lausanne University Faculty of Biology and Medicine, Switzerland (multidisciplinary research grant 2006); Swiss National Foundation for Scientific Research, Switzerland (grant 3247B0-120795/1); and Fondation Médecine Sociale et Préventive, Lausanne, Switzerland. The sponsors had no role in the design, methods, subject recruitment, data collections, analysis, and preparation of the paper.
The authors declare no conflicts of interest.
* Address correspondence to May-Lucie Meyer, MSc, Department of Oncology, University of Lausanne Hospital Center (CHUV), Rue du Bugnon 46, CH-1011 Lausanne, Switzerland.
E-mail address: may-lucie.meyer@chuv.ch (M.-L. Meyer).

https://doi.org/10.1016/j.jamda.2021.02.028

research suggested an association with adverse outcomes in clinical settings, as it was also linked, among others, with surgical complications[6] or with mortality in patients with cancer.[7] In the process of operationalizing each frailty phenotype's dimension by measurable criteria, Fried et al separated participants according to the sex-specific 80th percentile (p80) for continuous variables. The time to perform a walking test at usual pace was dichotomized, and slowness was defined by a time > p80.

Since the early work conducted in the Cardiovascular Health Study, walking speed has been shown to be linked independently with the following complications in older adults: disability,[8,9] falls,[9] hospitalization/institutionalization,[9] cardiovascular disease,[10–12] and early death.[9–14] Nevertheless, walking speed is not the easiest parameter to assess, particularly in the clinical practice or in studies of diseased patients. Most important, the person has to be able to walk and it takes time and space to measure walking speed. People who are disabled or walk with aid are therefore often excluded from the studies.[15,16] This is unfortunate, as the excluded ones are potentially more at risk to be frail. In a cohort of older Mexican Americans, 30% of participants did not complete the walking test, in nearly half of the cases because they refused or were unable to walk. Nontested participants were older and more likely to be depressed, cognitively impaired, or disabled.[17] The inability to test walking speed is even higher in hospitalized patients. In a recent study, 38% of eligible persons did not complete the test, mostly for safety reasons.[18] Therefore, the development of alternative tests to measure slowness is essential, especially when walking speed cannot be assessed.

The Moberg picking-up test (MPUT) was first described in 1958. It was developed in the setting of rehabilitation to evaluate the impact of sensory deficits over the motor function of the hand.[19] The test is performed by picking up several small objects to put them in a box, and the time to complete the task is measured. This test has then been used to assess hand function in patients with rheumatologic conditions.[20] It was also shown to be a functional test with good test-retest reliability in healthy subjects[21,22] and in patients with carpal tunnel syndrome.[23] As a timed test of a mobility task, it might also be considered as a measure of slowness in general populations, with the advantage of being easily achievable, and not requiring an adapted environment. Participants do not need to be able to walk, and the cognitive ability and strength required to perform this test are minimal. Both walking speed and MPUT data were collected in a cohort of community-dwelling cohort of older adults. Analyses showed significant, albeit moderate, correlation between the 2 tests.[24] The extent to which the MPUT performance is associated with mortality remains to be investigated.

The aims of our study were to assess the prospective relationship between MPUT and mortality in a population of older adults and to compare the performance of MPUT and walking speed as predictors of mortality.

Method

Study Population

Data used in the current research come from the Lausanne cohort 65+ (Lc65+), an ongoing population-based longitudinal study of older adults living, at baseline, in the community in the city of Lausanne (Switzerland). The project is described in detail elsewhere.[25] In brief, participants were recruited by postal questionnaire in 3 waves (2004, 2009, and 2014). They participated in an examination performed by trained medical assistants the following year, at an age ranging between 66 and 71 years. The current study used data from the initial examination. Eligible participants for the principal analysis were those who had completed an MPUT and a walking speed (WS) test during their baseline appointment at the study center. The follow-up included continuous registration of deaths. The Lc65+ study protocol (no. 19/04) and periodic updates received approval from the ethics committee for human research of the Canton of Vaud; participants provided their informed consent.

Mortality Assessment

Occurrence and date of deaths from the initial assessment through the end of the follow-up were ascertained from the registry of the Canton of Vaud population office. Vital status was unknown among dropout participants who have left the Canton of Vaud during the follow-up; consequently, their follow-up was censored at the date of the last contact.

Explanatory Variables

The MPUT was assessed by the time in seconds to pick up 12 small objects scattered on a table in front of seated participants with the dominant hand and to place them into a box as quickly as possible.[24] WS was assessed by the time in seconds to walk a 20-m distance at usual pace in a quiet, well-lit corridor. MPUT and WS were dichotomized, according to the sex-specific p80 distribution in the study samples, into normal/fast (≤p80) vs slow (>p80), according to the approach of Fried et al.[3]

Covariates

Adjustment variables included age at baseline examination, sex, and physical characteristics that may influence the MPUT or WS performance (height and muscular strength). Height was measured in centimeters, and muscular strength was assessed by grip strength recorded in pounds using: in 2005 a Baseline® hydraulic dynamometer (Fabrication Enterprises Inc., Irvington, NY); in 2010 a Saehan® hydraulic dynamometer (Saehan corp., Changwon, S. Korea); in 2015 a Saehan® digital dynamometer (Saehan corp., Changwon, S. Korea).

Statistical Analysis

Analyses were conducted on the samples of participants who completed both the MPUT and WS test. Applying an outlier detection approach for skewed data,[26] extreme outliers for MPUT and WS were identified and not included in the analyses. Descriptive statistics were used to summarize the population baseline characteristics. Times to perform MPUT or WS were compared according to the vital status at the end of follow-up using Student *t* test. Unadjusted Kaplan Meier curves were performed according to the p80 of distribution of each test and compared using log-rank test.

Mortality was analyzed over a 4-year follow-up period for individuals enrolled in all 3 Lc65+ enrollment waves (2004, 2009, and 2014); over a 9-year follow-up period for those enrolled in 2004 and 2009; and over a 14-year period for those enrolled in 2004.

We used Cox regression analyses to assess, in separate models, the association between each of the 2 explanatory variables and the mortality outcome. Model 1 estimated the crude association of times to perform the test and mortality. Model 2 controlled the confounding effect of age, sex, and height. In order to isolate the independent association between slowness and mortality, model 3 further adjusted for grip strength to control the test force component, as grip strength is also known to be a predictor of mortality.[27] Linearity of continuous covariates was verified using fractional polynomials. The proportionality assumption was tested including time-dependent covariates in the model (tvc option in Stata), which were defined as an interaction term between each variable in the model and the logarithm of time. Only the sex in the 9-year analysis appeared as a nonproportional predictor, and the corresponding time-dependent covariate was kept

in the models. Absence of significant interactions between the main explanatory variable and sex were tested and confirmed. The predictive capability of multivariable Cox models was evaluated using Harrell *C* index.

A first analysis focused on the association between MPUT, and respectively WS, and the occurrence of death within the 4 years following baseline assessment for individuals included in the 3 recruitment waves. A second analysis concentrated on the occurrence of mortality over a 9-year period (recruitment waves 2004 and 2009) and the whole available follow-up period, that is, 14 years (recruitment wave 2004), respectively. A sensitivity analysis including participants who had completed only 1 of the 2 tests (MPUT but not WS in most cases) was performed.

Finally, a subgroup analysis was performed on participants who completed the Moberg picking-up test (MPUT) and not the walking speed test (hereafter "MPUT only") either at baseline or at any of the follow-up triennial examinations. The MPUT time at examination was dichotomized according to the sex-specific cut-off of the general study population set at the 80th percentile, as in our principal analysis. Mortality after each "MPUT only" examination was assessed in the following 3 years. Stata vce(cluster) option was used to take multiple observations into account. Model 1 adjusted for age; model 2 adjusted for age, sex, and height, and model 3 further adjusted for grip strength.

Results

Overall, 4731 persons were enrolled in the Lc65+ cohort, of whom 4655 were eligible for a baseline examination including performance tests the next year (after exclusion of 54 cases for death, 7 for severe cognitive impairment, 2 for end-of-life situation, and 13 for administrative reasons) and 3890 accepted. Of these, 3781 participants (97.2% of examinations) performed both MPUT and WS tests and were included in the principal analysis. Outlier analysis resulted in further exclusion of 16 persons for the 4-year analysis (n = 3765), 11 for the 9-year analysis (n = 2481), and 13 for the 14-year analysis (n = 1242). Most of the extreme outliers concerned the WS test. Lost participants, censored in survival analysis, represented 0.6% of the sample at 4 years (n = 22), 1.5% at 9 years (n = 36), and 1.9% at 14 years (n = 24).

The main characteristics of the participants are listed in Table 1. All 3 study samples included predominantly women. Mean age was 69 years. About one-quarter of the participants were prefrail or frail. Mortality was 3.5% at 4 years, 10.4% at 9 years, and 23.4% at 14 years.

Participants with performance times higher than p80 had a higher mortality both for MPUT (at 4 years: 6.2% vs 2.8%, 9 years: 16.1% vs 8.9%, 14 years: 34.8% vs 20.5%, all $P < .001$) and for WS (at 4 years: 6.3% vs 2.8%, 9 years: 18.1% vs 8.4%, 14 years: 36.4% vs 20.1%, all $P < .001$). The mean time recorded for MPUT and WS test completion was significantly higher among dead participants, as compared to survivors, whatever the duration of the follow-up time (Supplementary Table S1). As shown in Table 2, mortality rates in person-years were significantly higher among the slowest participants in both tests over the 3 follow-up periods. Kaplan-Meier survival curves (Figure 1) illustrate the differential evolution of the slowest participants, both tests being significantly discriminant ($P < .001$) at 4, 9, and 14 years. Crude hazard ratios at 4, 9, and 14 years were 2.2, 1.9, and 1.9 for MPUT and 2.3, 2.3, and 2.1 for the WS test (Table 3). The divergence between curves determined by p80 increased with time, and the evolution of individuals above and below p80 was similar for the 2 tests. Results of additional analyses (Supplementary Figure S1) contrasted individuals with performance times below p80 for the 2 tests, slow in MPUT, in WS test, and in the 2 tests. The curves for slowness in only 1 test superimposed in 4- and 9-year follow-up, showing an intermediate position between those of participants slow in no test, who had the highest survival, and slow in both tests, who experienced the most adverse evolution. The 2 intermediate curves diverged slightly at the end of the observation period in 9- and 14-year survival analyses.

Table 1
Baseline Characteristics of Participants Followed Over 4, 9 and 14 Years

	4-y Follow-up* (n = 3765)	9-y Follow-up† (n = 2481)	14-y Follow-up‡ (n = 1243)
Follow-up time, y			
Mean ± SD	3.9 ± 0.4	8.6 ± 1.4	12.7 ± 2.9
Range	0.2-4.0	0.4-9.0	0.5-14.0
Person-years	14,790	21,281	15,827
Age, y, mean ± SD	68.9 ± 1.5	68.9 ± 1.5	69.0 ± 1.4
Sex: female n (%)	2176 (57.8)	1461 (58.9)	726 (58.4)
Moberg picking-up time, s			
Mean ± SD	13.1 ± 2.8	13.5 ± 2.8	13.9 ± 2.8
Range	7.1-28.7	7.9-30.1	7.9-26.8
Percentile 80, male; female	15.5; 14.5	16.0; 15.0	16.4; 15.3
20-m walk time, s			
Mean ± SD	16.6 ± 3.1	17.0 ± 3.2	17.9 ± 3.1
Range	9.4-37.6	9.4-37.6	11.1-33.8
Percentile 80, male; female	17.7; 19.0	18.1; 19.6	18.9; 20.4
Prefrail or frail phenotype§, n (%)	1059 (28.4)	684 (27.8)	327 (26.6)
Mortality			
n (%)	132 (3.5)	257 (10.4)	291 (23.4)
Rate (/1000 person-years)	8.9	12.1	18.4

*Individuals enrolled in recruitment waves 2004, 2009, and 2014; lost participants represented 0.6% of the sample at 4 years (n = 22).

†Individuals enrolled in recruitment waves 2004 and 2009 only; lost participants represented 1.5% of the sample at 9 years (n = 36).

‡Individuals enrolled in recruitment wave 2004 only; lost participants represented 1.9% of the sample at 14 years (n = 24).

§Operationalization of Fried frailty criteria in the Lc65+ study was described in the study protocol of the Lc65+ cohort.[25]

In multivariable analyses (Table 3), associations remained significant after adjusting for age, sex, and height and with further adjustment for grip strength. Although hazard ratios were slightly stronger for WS than for MPUT in the models of 9- and 14-year mortality, additional control for grip strength reduced the effect of slowness as measured by WS in the 14-year analysis, leading to a same estimate for both tests (hazard ratio 1.8, 95% CI 1.4-2.3, for MPUT and 1.8, 95% CI 1.4-2.4, for WS). The predictive capability of adjusted models was similar for MPUT and WS tests in analyses at 4, 9, and 14 years, with a Harrell *C* between 0.61 and 0.69 indicating an acceptable discrimination.

Sensitivity analyses were conducted on 3877 participants who performed at least 1 of the 2 tests, including 94 cases with missing WS and 2 cases with missing MPUT. After outlier analysis, we excluded 4 cases, leaving 3873 observations. All survival analyses at 4, 9, and 14 years produced similar estimates of the effect and predictive capability of both tests. A comparison of times to perform the MPUT showed that participants who did not complete the WS test at baseline were significantly slower (n = 90, mean ± SD: 14.7 ± 3.8 seconds)

Table 2
Mortality Rate (/1000 Person-Years) at 4, 9, and 14 Years, According to the Sex-Specific 80th Percentile Threshold of Times to Perform the Moberg Picking-Up Test and the 20-m Walking Test

	4-y Follow-up	9-y Follow-up	14-y Follow-up
Moberg picking-up test			
Time ≤80th percentile	7.2 (5.8-8.9)	10.3 (8.9-12.0)	15.9 (13.9-18.3)
Time >80th percentile	16.0 (12.0-21.3)	19.3 (15.5-24.0)	28.7 (23.3-35.4)
20-m walk test			
Time ≤80th percentile	7.1 (5.7-8.8)	9.7 (8.4-11.3)	15.5 (13.5-17.8)
Time >80th percentile	16.4 (12.3-21.7)	21.8 (17.7-26.8)	30.8 (25.1-37.9)

Values within parentheses are 95% CIs.

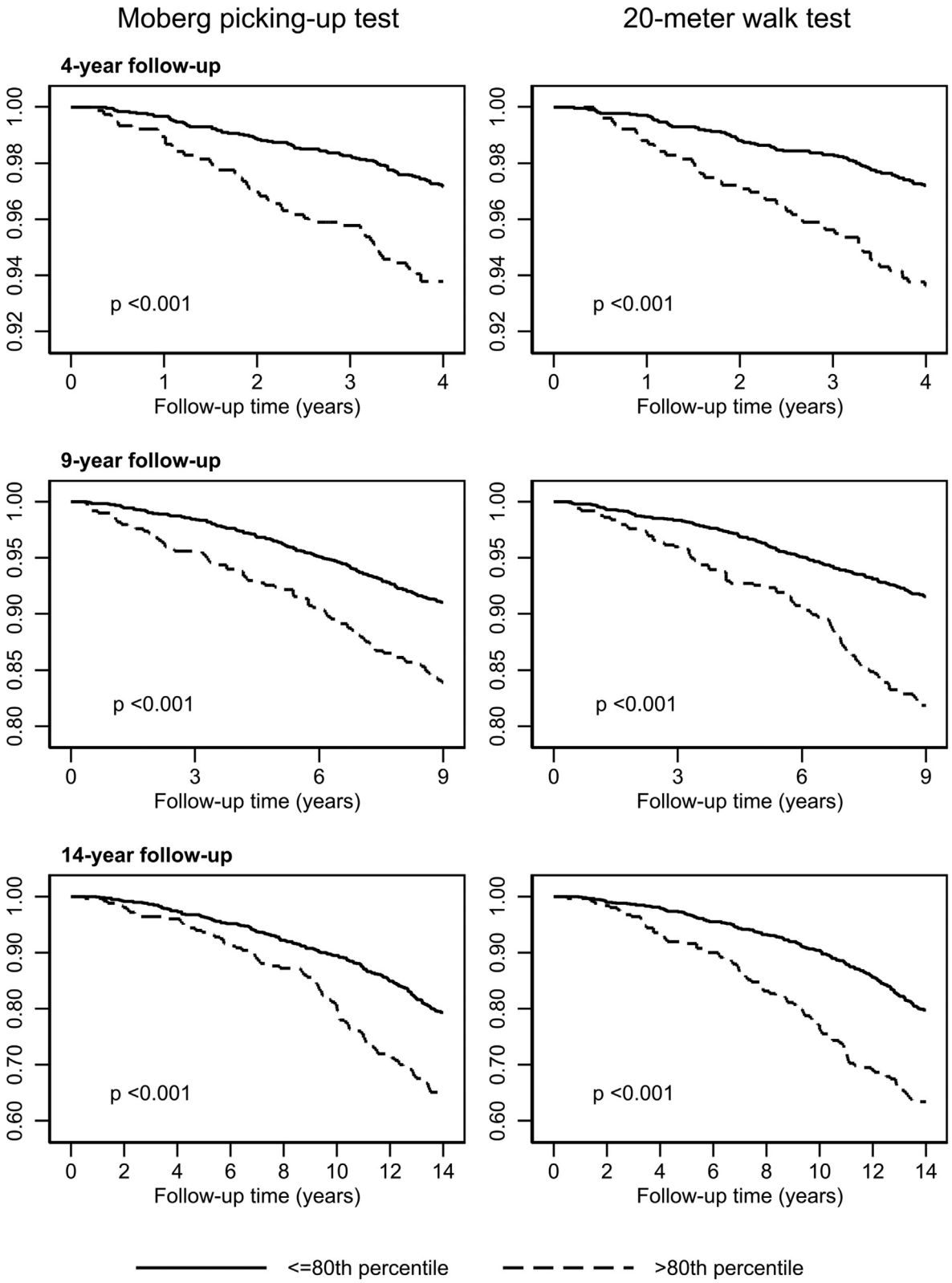


Fig. 1. Kaplan-Meier survival curves at 4, 9, and 14 years according to MPUT and 20-m walk times (sex-specific cut-off set at percentile 80 of the time distribution).

Table 3
Cox Regression Models of Mortality Over 4, 9, and 14 Years

	4-y Follow-up, HR (95% CI)	9-y Follow-up, HR (95% CI)	14-y Follow-up, HR (95% CI)
Moberg picking-up time, s			
Crude	2.2† (1.6-3.2)	1.9† (1.4-2.5)	1.9† (1.5-2.4)
Age, sex, height adjusted	2.2† (1.6-3.2)	1.8† (1.4-2.4)	1.8† (1.4-2.3)
Age, sex, height, GS adjusted	2.1† (1.4-3.0)	1.7† (1.3-2.3)	1.8† (1.4-2.3)
Harrell *C* (95% CI)*	0.68 (0.64-0.73)	0.64 (0.60-0.67)	0.61 (0.58-0.65)
20-m walk time, s			
Crude	2.3† (1.6-3.3)	2.3† (1.7-2.9)	2.1† (1.6-2.7)
Age, sex, height adjusted	2.3† (1.6-3.3)	2.2† (1.7-2.8)	2.0† (1.5-2.5)
Age, sex, height, GS adjusted	2.2† (1.5-3.1)	2.0† (1.5-2.6)	1.8† (1.4-2.4)
Harrell *C* (95% CI)*	0.69 (0.65-0.73)	0.65 (0.62-0.68)	0.62 (0.59-0.65)

Abbreviations: GS, grip strength; HR, hazard ratio.
Crude and adjusted estimates of the effect of slowness (sex-specific time percentile >80) in Moberg picking-up test and 20-m walking test are presented.
*Model adjusted for age, sex, height, and grip strength.
†$P < .001$.

than WS test completers (n = 3776, mean ± SD: 13.1 ± 2.8 seconds) ($P < .001$).

In the subgroup analysis of "MPUT only" cases, the MPUT p80 hazard ratio was 2.32 [95% confidence interval (CI) 1.32-4.07, $P = .003$] in model 1 (n = 320), 2.18 (95% CI 1.18-4.05, $P = .013$) in model 2 (n = 299), and 1.93 (95% CI 1.03-3.63, $P = .040$) in model 3 (n = 297). The Harrell *C* was 0.67 (95% CI 0.59-0.75) in model 3.

Discussion

We found a significant association between a poor MPUT performance and mortality among community-dwelling older adults. This positive association was similar to the one found in the same study population between slow WS and mortality. This was also the case among participants who completed MPUT but not WS test. The association with mortality was observed for the 2 tests both at short and longer term. The 2 measures of slowness had similar predictive capability. Individuals cumulating long times in both tests had the lowest probability of survival.

It has already been shown that the MPUT was influenced by age,[28] but to our knowledge there is no other study that used the MPUT as a predictor of mortality. However, several studies investigated the relationship between WS and mortality. Three meta-analyses recently explored this association. The first showed a pooled effect size over a mean follow-up of 5 years close to that found in our study.[14] Studenski et al[13] also described the capability of WS to predict mortality in populations who were generally older and at higher risk of dying. More recently, Veronese et al[11] confirmed these results while reporting a weaker association of WS with mortality in studies of community-dwelling populations.

We also note that among people who did not complete the walking test, the association with mortality was similar with the entire study population, which reinforces the interest of the MPUT as an alternative to the walking test, when the latter cannot be performed.

The hazard ratio of both tests decreases over time, with lower values in the analysis at 14 years. This attenuation seems slightly lower for the WS. The overall decrease in the prediction of mortality over time is probably explained by the fact that some good performers will become frail later on. This also raises the question of how often performance tests should be performed.

In our study, the participants who could not perform one of the 2 tests were almost exclusively noncompleters for the WS test. This observation confirms the hypothesis that feasibility is higher for MPUT than for WS. Although their proportion was low in this well-functioning, community-dwelling population assessed early after retirement age, those who did not complete the WS test were characterized by a significantly poorer performance in MPUT. This observation confirms the risk of bias due to the selective exclusion of frail individuals when slowness assessment is based only on a WS test. Keeping these individuals by performing an MPUT minimizes this bias.

Strengths of this study included a large sample of older community-dwelling adults who performed MPUT and WS tests during the same assessment, and a long follow-up period. Our results show that slowness can be assessed by an alternative test among individuals who could not perform a WS test, which may avoid the risk of bias related to their exclusion in studies of frailty. A sensitivity analysis including noncompleters of either one of the 2 tests allowed to consolidate our results. Finally, adjusting for grip strength in our last model provided an insight on the mechanisms (slowness vs muscular strength) linking the tests and the outcome. It may, however, represent an overadjustment in the study of the relationship between MPUT or WS and mortality, which is the first concern in the clinical practice.

This study was limited by the narrow age range of study participants, and our results cannot be extrapolated to very old, frailer adults. The mortality rate at 4 years was low in this community-dwelling population but longer follow-up periods, conducted in subsamples of our study population, increased the frequency of the outcome. The observed long-term effects of slowness on mortality were highly significant despite a smaller sample size. Previous analyses of Lc65+ data showed that all timed tests improved over time across cohorts of individuals born before, during, and at the end of World War II.[29] This appears in current analyses showing higher mean times in our study sample for the longer-term analyses that included only the first Lc65+ cohort, with participants born before the war. Although the 14-year mortality analysis was limited to individuals of the first cohort, associations found in this subsample were consistent with shorter-term observations. Finally, we compared 2 tests, MPUT and WS, that inform not only on slowness but also on other determinants of the performance, such as muscular strength or fingertip sensitivity. The Lc65+ study provided for multivariable adjustment a measurement of grip strength, an indicator of muscular strength widely used in geriatric research. Additional control based on a measure of lower limb strength independent of time would be particularly appropriate in analyses implying WS. The MPUT uses small objects and therefore evaluates fine motor skills in addition to slowness. An adaptation of the test with objects that are easier to grasp might somehow be more representative of slowness and minimize the effect of sensory defects or deformations of fingertips.

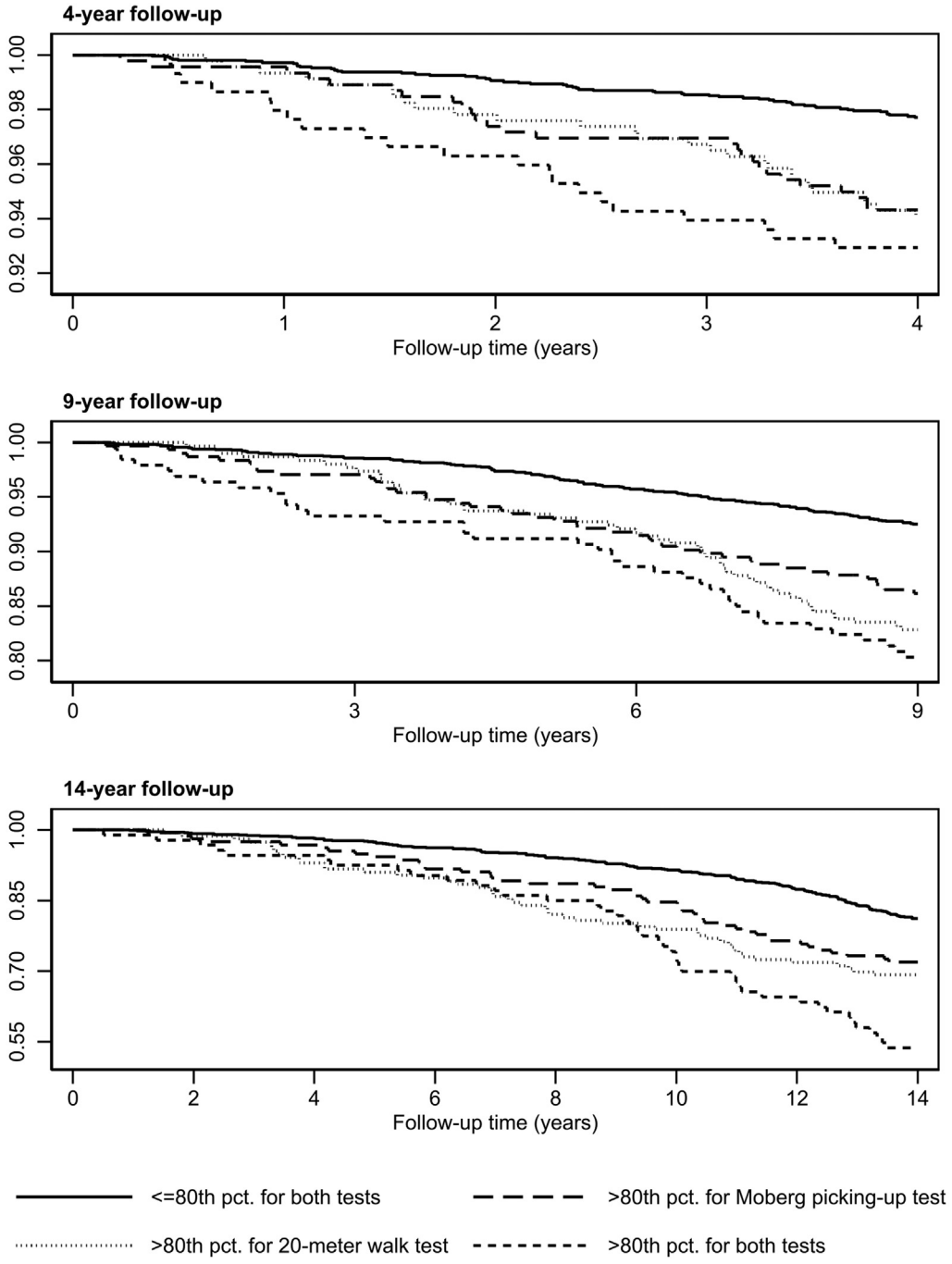
Conclusion and Implications

This study suggests that a poor performance in the MPUT is a risk factor for mortality in the short and longer term among community-dwelling persons aged 66 to 71 years. This test may contribute to the assessment of the slowness component of the Fried frailty phenotype when a WS test is not feasible, which is the case of a non-negligible proportion of older adults, and avoid biased estimates due to the nonrandom exclusion of the slowest individuals in frailty studies. Further research should explore the relation between the MPUT and mortality in other settings such as hospitals or nursing homes, and attempt to improve the test as a measure of slowness by reducing the potential impact of fingertip impairment. Finally, the MPUT may not be the only or the best test to replace the walking test. However, MPUT's feasibility in case of lower limb impairment or its ease of completion with respect to standard conditions in a variety of settings are interesting qualities. In a context of scarce research on alternatives to the walking speed as a slowness measure in frailty assessment, we believe that investigating other tests, including MPUT,

is important. Future studies investigating other alternatives should be encouraged.

References

1. Xue QL. The frailty syndrome: Definition and natural history. Clin Geriatr Med 2011;27:1–15.
2. Walston J, Hadley EC, Ferrucci L, et al. Research agenda for frailty in older adults: Toward a better understanding of physiology and etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. J Am Geriatr Soc 2006;54:991–1001.
3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–M156.
4. Bandeen-Roche K, Xue Q-L, Ferrucci L, et al. Phenotype of frailty: Characterization in the women's health and aging studies. J Gerontol 2006;61:262–266.
5. Woods NF, LaCroix AZ, Gray SL, et al. Frailty: Emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. J Am Geriatr Soc 2005;53:1321–1330.
6. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 2010;210:901–908.
7. Ngo-Huang A, Holmes HM, des Bordes JKA, et al. Association between frailty syndrome and survival in patients with pancreatic adenocarcinoma. Cancer Med 2019;8:2867–2876.
8. Perera S, Patel KV, Rosano C, et al. Gait speed predicts incident disability: A pooled analysis. J Gerontol A Biol Sci Med Sci 2016;71:63–71.
9. Pamoukdjian F, Paillaud E, Zelek L, et al. Measurement of gait speed in older adults to identify complications associated with frailty: A systematic review. J Geriatr Oncol 2015;6:484–496.
10. Yates T, Zaccardi F, Dhalwani NN, et al. Association of walking pace and handgrip strength with all-cause, cardiovascular, and cancer mortality: A UK Biobank observational study. Eur Heart J 2017;38:3232–3240.
11. Veronese N, Stubbs B, Volpato S, et al. Association between gait speed with mortality, cardiovascular disease and cancer: A systematic review and meta-analysis of prospective cohort studies. J Am Med Dir Assoc 2018;19:981–988.e7.
12. Chainani V, Shaharyar S, Dave K, et al. Objective measures of the frailty syndrome (hand grip strength and gait speed) and cardiovascular mortality: A systematic review. Int J Cardiol 2016;215:487–493.
13. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA 2011;305:50–58.
14. Cooper R, Kuh D, Hardy R, et al. Objectively measured physical capability levels and mortality: Systematic review and meta-analysis. BMJ 2010;341:c4467.
15. Hsu CL, Liang CK, Liao MC, et al. Slow gait speed as a predictor of 1-year cognitive decline in a veterans' retirement community in southern Taiwan. Geriatr Gerontol Int 2017;17(suppl 1):14–19.
16. Dommershuijsen LJ, Isik BM, Darweesh SKL, et al. Unravelling the association between gait and mortality—One step at a time. J Gerontol A Biol Sci Med Sci 2020;75:1184–1190.
17. Cesari M, Pahor M, Marzetti E, et al. Self-assessed health status, walking speed and mortality in older Mexican-Americans. Gerontology 2009;55:194–201.
18. Ostir GV, Berges IM, Ottenbacher KJ, et al. Gait speed and dismobility in older adults. Arch Phys Med Rehabil 2015;96:1641–1645.
19. Moberg E. Objective methods for determining the functional value of sensibility in the hand. J Bone Joint Surg Br 1958;40-B:454–476.
20. Stamm T, Mathis M, Aletaha D, et al. Mapping hand functioning in hand osteoarthritis: Comparing self-report instruments with a comprehensive hand function test. Arthritis Rheum 2007;57:1230–1237.
21. Ng CL, Ho DD, Chow SP. The Moberg pickup test: Results of testing with a standard protocol. J Hand Ther 1999;12:309–312.
22. D'souza SA, Kishan V. Moberg pick-up test (Indian version): Test-retest reliability and normative values for Indian adults of 30 to 60 years. Ind J Occup Ther 2010;XLII:9–12.
23. Amirjani N, Ashworth NL, Olson JL, et al. Discriminative validity and test-retest reliability of the Dellon-modified Moberg pick-up test in carpal tunnel syndrome patients. J Peripher Nerv Syst 2011;16:51–58.
24. Santos-Eggimann B, Ballan K, Fustinoni S, Bula C. Measuring slowness in old age: Times to perform Moberg picking-up and walking speed tests. J Am Med Dir Assoc 2020;21:1729–1734.e2.
25. Santos-Eggimann B, Karmaniola A, Seematter-Bagnoud L, et al. The Lausanne cohort Lc65+: A population-based prospective study of the manifestations, determinants and outcomes of frailty. BMC Geriatr 2008;8:20.
26. Hubert M, Van der Veeken S. Outlier detection for skewed data. J Chemometrics 2008;22:235–246.
27. Celis-Morales CA, Welsh P, Lyall DM, et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: Prospective cohort study of half a million UK Biobank participants. BMJ 2018;361:k1651.
28. Amirjani N, Ashworth NL, Gordon T, et al. Normative values and the effects of age, gender, and handedness on the Moberg Pick-Up Test. Muscle Nerve 2007;35:788–792.
29. Henchoz Y, Bula C, von Gunten A, et al. Trends in physical and cognitive performance among community-dwelling older adults in Switzerland. J Gerontol A Biol Sci Med Sci 2020;75:2347–2353.



Supplementary Figure S1. Unadjusted Kaplan-Meier Survival curves according to 80th percentile (pct) of time to perform Moberg picking-up test and 20-m walk test.

Supplementary Table S1
MPUT and 20-m Walk Times (Seconds) of Surviving and Dead Subjects Included in 4-, 9-, and 14-Year Follow-up

Length of Follow-up	Survival	Death	*P* Value
4 y			
n	3633	132	
Moberg picking-up time, mean ± SD	13.0 ± 2.7	14.4 ± 3.9	<.001
20-m walk time, mean ± SD	16.5 ± 3.1	17.7 ± 3.6	<.001
9 y			
n	2224	257	
Moberg picking-up time, mean ± SD	13.4 ± 2.7	14.6 ± 3.4	<.001
20-m walk time, mean ± SD	16.8 ± 3.1	18.1 ± 3.9	<.001
14 y			
n	952	291	
Moberg picking-up time, mean ± SD	13.6 ± 2.6	14.8 ± 3.2	<.001
20-m walk time, mean ± SD	17.6 ± 3.0	18.6 ± 3.3	<.001

Imprimé à Lausanne en 4 exemplaires, le 24.07.2021