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Gait speed has comparable prognostic capability to six-minute walk distance in older patients with cardiovascular disease

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Abstract

Background: Although gait speed and six-minute walk distance are used to assess functional capacity in older patients with cardiovascular disease, their prognostic capabilities have not been directly compared.

Methods: The study population was identified from the Kitasato University Cardiac Rehabilitation Database and consisted of 1474 patients $\geq$60 years old with a mean age of 72.2 ± 7.1 years that underwent evaluation of both usual gait speed and six-minute walk distance in routine geriatric assessment between 1 June 2008–30 September 2015. Both gait speed and six-minute walk distance were determined on the same day at hospital discharge.

Results: Mean gait speed and six-minute walk distance in the whole population were 1.04 m/s and 381 m, respectively, and were strongly positively correlated ($r = 0.80$, $p < 0.001$). A total of 180 deaths occurred during a follow-up of 2.3 ± 1.9 years. After adjusting for confounding factors, both gait speed (adjusted hazard ratio per 0.1 m/s increase: 0.87, 95% confidence interval: 0.81–0.93, $p < 0.001$) and six-minute walk distance (adjusted hazard ratio per 10-metre increase: 0.96, 95% confidence interval: 0.94–0.97, $p < 0.001$) were independent predictors of all-cause mortality. There was no significant difference in prognostic capability between gait speed and six-minute walk distance (c-index: 0.64 (95% confidence interval: 0.60–0.69) and 0.66 (95% confidence interval: 0.61–0.70), respectively, $p = 0.357$).

Conclusions: Gait speed and six-minute walk distance showed similar prognostic predictive ability for all-cause mortality in older cardiovascular disease patients, indicating the potential utility of gait speed as a simple risk stratification tool in older cardiovascular disease patients.

Keywords

Six-minute walk distance, gait speed, prognosis, elderly, sarcopenia, frailty, cardiovascular, coronary artery disease, heart failure, cardiac surgery

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Introduction

With the aging of the population, sarcopenia and frailty are becoming major issues in cardiovascular medicine.[1] Sarcopenia and frailty have been indicated as reliable markers of poor prognosis among older patients with

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cardiovascular disease (CVD).[1–4] Importantly, the number of patients with sarcopenia has been predicted to increase over the next 30 years.[5] Therefore, clinically relevant physical function tests for older patients are urgently required.

The six-minute walk distance (6MWD) is often used to assess functional capacity in a wide range of populations.[6,7] Several studies demonstrated its ability to predict outcome in patients with CVD, including heart failure,[7,8] coronary artery disease,[9] and those undergoing cardiac surgery.[6,10] However, measurement of 6MWD requires a long walking track, which is not always feasible in a smaller office practices or home care settings.

Gait speed, measured as the time required to walk a short distance at a comfortable pace, is another commonly used test to screen for physical function and sarcopenia/frailty.[1] Gait speed has also been shown to predict morbidity and mortality in various populations, including elderly patients with CVD.[2,11–13] Indeed, some authors have suggested that gait speed should be considered as the sixth vital sign and assessed clinically along with breathing, temperature, heart rate, pain, and color.[14] Gait speed requires little space, time, or training, making it a suitable routine measure in both clinical and research settings. Importantly, several studies have indicated that the single measurement of gait speed outperformed other multicomponent frailty scales in predicting outcomes.[3,15]

To date, however, no direct comparisons of the prognostic capabilities of gait speed and 6MWD have been reported, although both tests examine the walking ability of patients. This study was performed to compare the prognostic capabilities of gait speed and 6MWD in older patients with CVD.

Methods

Study population

The study population was identified in the Kitasato University Cardiac Rehabilitation Database and consisted of 1474 patients $\geq$60 years old who underwent evaluation of both usual gait speed and 6MWD in routine geriatric assessment between 1 June 2008–30 September 2015. A flow diagram of the study population is shown in the Supplementary Material, Figure 1. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki, and was approved by the Ethics Committee of Kitasato University Hospital (B16-108).

Data collection

Data on all variables were collected from electronic medical records. Clinical details of presentation, as well as demographic, biochemical, and echocardiographic data, were recorded. Height was measured to the nearest 0.1 cm using a stadiometer and weight was determined to the nearest 0.1 kg using a calibrated weighing scale at hospital discharge. Body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared. Blood pressure and heart rate were measured at hospital discharge. Estimated glomerular filtration rate (eGFR) was defined according to the formula recommended by the Japanese Society of Nephrology.[16]

The endpoint of this study was all-cause mortality, and the time for the endpoint was calculated as the number of days from the date of 6MWD and gait speed measurements to the date of events.

6MWD and gait speed measurement

6MWD and gait speed were evaluated on the same day at hospital discharge, and electrocardiographic data were monitored continuously via telemetry. Both tests were performed only once for all patients. The 6MWD was measured according to standard guidelines at hospital discharge.[17] Patients were allowed to use assistive devices for the walking test. Patients were asked to walk at their own pace from chair-to-chair, but were instructed to cover as much distance as possible during the allotted time of six minutes. Patients were allowed to stop and rest during the test but were instructed to resume walking as soon as they were able. Standardized verbal encouragement was provided every one minute. Coaching and enthusiastic urging were prohibited. After six minutes, patients were instructed to stop walking, and the distance covered was recorded.

For measurement of usual gait speed, the patients were asked to walk at their usual speed, and were timed over the 10 m of the walkway. Participants were allowed to use walking aids, such as a cane, during the test. Gait speed has high test–retest reliability in older adults with intraclass correlation coefficient >0.9.[18]

Statistical analysis

Continuous variables are expressed as means (standard deviation). Categorical variables are expressed as numbers and percentages. We divided the cohort into three groups according to the tertiles of 6MWD and gait speed. Baseline characteristics were compared by one-way analysis of variance or Fisher's exact test where appropriate.

Linear regression was used to evaluate the relations between 6MWD and gait speed. Receiver-operating characteristic (ROC) curves were also used to describe the ability of gait speed to discriminate established

6MWD cut-off values of 300 m[19–21] and 400 m.[22,23] In the ROC curve for gait speed, a value below than the cut-off was considered positive and other values were considered negative. Predictive value was determined by determining the sensitivity and specificity for various cut-offs. The optimal cut-off for gait speed was defined as the value nearest to the northwest point of the ROC curve.

We calculated the cumulative incidence of mortality during follow-up according to tertiles of 6MWD and gait speed with Kaplan–Meier curves. Intergroup differences were estimated by the log-rank test. Univariate and multivariate Cox regression analyses were performed to evaluate the prognostic capabilities of 6MWD and gait speed. Multivariate analyses were adjusted for age, male sex, BMI, systolic blood pressure, acute coronary syndrome, heart failure, cardiac surgery, serum albumin, hemoglobin, low-density lipoprotein (LDL) cholesterol, eGFR, hypertension, diabetes mellitus, current smoking, prior myocardial infarction, and prior hospitalization due to heart failure.

We constructed ROC curves to compare the predictive capabilities of 6MWD and gait speed for mortality. The areas under the curve (AUCs) were compared according to the method of DeLong et al.[24] To assess the potential effect modification on the prognostic capabilities of 6MWD and gait speed, we performed subgroup analyses across gender and major diagnostic categories, including acute coronary syndrome, heart failure, and cardiac surgery.

The dose–response associations between 6MWD, gait speed, and mortality risk were examined using a Cox regression model with spline functions with four knots at quartiles of the independent variable.

A two-tailed p value <0.05 was taken to indicate statistical significance. Analyses were performed using SPSS 22.0 (IBM Corporation, New York, USA), STATA version 13.0 (StataCorp, College Station, Texas, USA), and R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population

Table 1 shows the baseline characteristics for all subjects and for groups stratified by 6MWD and gait speed. The mean age of the study population was 72.2 years and 68% of the patients were male. The reasons for hospitalization were acute heart failure (38.5%), cardiac surgery (26.5%), acute coronary syndrome (21.7%), and other clinical entities (13.3%). There were no patients in whom only one of either gait speed or 6MWD could be evaluated. The mean 6MWD and gait speed were 381 m and 1.04 m/s, respectively. Low 6MWD and gait speed were associated with older age, lower BMI, female sex, higher percentage of heart failure, diabetes mellitus, prior hospitalization due to heart failure, and lower albumin, hemoglobin, eGFR, and LDL cholesterol levels.

Associations between 6MWD and gait speed. The correlations between 6MWD and gait speed in the full sample and stratified by gender are shown in the Supplementary Material, Figure 2. Gait speed had strong positive correlation with 6MWD ($r = 0.81$, 0.76, and 0.80, for female, male and all-cohort, $p < 0.001$ for all). Supplementary Material, Figure 3 shows the ROC curves for gait speed as a predictor of 6MWD < 300 m and <400 m. Gait speed showed high discriminative performance for prediction of each 6MWD threshold (AUC for 6MWD <300 m: 0.93, 95% confidence interval (CI): 0.91–0.94, AUC for 6MWD<400 m: 0.90, 95% CI: 0.88–0.91). Gait speed of <0.90 m/s and <1.05 m/s were identified as optimal cut-off points for prediction of 6MWD <300 m and <400 m, respectively, with sensitivity and specificity values both above 80%.

Associations between 6MWD, gait speed, and all-cause mortality. A total of 180 deaths occurred in the study population over a mean follow-up of 2.3 ± 1.9 years. The Kaplan–Meier survival curves plotting tertiles of 6MWD or gait speed showed that both low 6MWD and slow gait speed were associated with all-cause death (Figure 1) (log rank: $p < 0.001$ for both). In univariate and multivariate Cox regression analyses for all-cause mortality, both 6MWD and gait speed were significant predictors of mortality (Supplementary Material, Table).

Prognostic capabilities of 6MWD and gait speed

ROC analysis for all-cause mortality was performed to compare the prognostic predictive capability of 6MWD and gait speed. The AUCs on ROC analysis were 0.66 (95% CI: 0.61–0.70) for 6MWD and 0.64 (95% CI: 0.60–0.69) for gait speed (Figure 2(a)). There was no significant difference between the AUCs of 6MWD and gait speed ($p = 0.357$). The AUCs of 6MWD and gait speed were similar across major diagnostic categories and gender (Figure 2(b)).

Figure 3 shows the dose–response associations of 6MWD and gait speed with mortality. Mortality risk increased with decreasing 6MWD and gait speed, with an inverse J-shaped association.

Table 1. Baseline characteristics.

Variable	All	6MWD tertile				Gait speed tertile			
		Low	Mid	High		Slow	Mod	Fast	
n	1474	492	497	485	*p* Value	496	489	489	*p* Value
Age, years	72.2 ± 7.1	76.5 ± 7.0	71.5 ± 6.3	68.5 ± 5.6	<0.001	76.1 ± 7.2	71.8 ± 6.6	68.7 ± 5.5	<0.001
Male sex, no. (%)	1002 (68)	255 (52)	341 (69)	406 (84)	<0.001	272 (55)	329 (67)	401 (82)	<0.001
Body mass index, kg/m^2	22.3 ± 3.6	21.8 ± 4.0	22.4 ± 3.8	22.7 ± 3.0	0.001	21.9 ± 4.1	22.6 ± 3.6	22.4 ± 3.0	0.011
Blood pressure, mm Hg									
Systolic	125 ± 30	124 ± 29	126 ± 29	124 ± 31	0.351	123 ± 29	126 ± 29	125 ± 31	0.212
Diastolic	70 ± 18	68 ± 18	71 ± 17	71 ± 19	0.083	68 ± 18	70 ± 18	71 ± 18	0.088
Heart rate, /min	78 ± 20	78 ± 20	78 ± 18	77 ± 21	0.796	77 ± 19	79 ± 20	77 ± 20	0.252
Diagnosis, no. (%)					<0.001				<0.001
Acute coronary syndrome	320 (22)	53 (11)	91 (18)	176 (36)		61 (12)	103 (21)	156 (32)	
Heart failure	567 (39)	251 (51)	181 (36)	135 (28)		245 (49)	183 (37)	139 (28)	
Cardiac surgery	391 (27)	126 (26)	151 (30)	114 (24)		128 (26)	132 (27)	131 (27)	
Others	196 (13)	62 (13)	74 (15)	60 (12)		62 (13)	71 (15)	63 (13)	
History of disease, no. (%)									
Hypertension	1049 (71)	362 (74)	350 (70)	337 (70)	0.334	362 (73)	342 (70)	345 (71)	0.536
Diabetes mellitus	594 (40)	222 (45)	209 (42)	163 (34)	0.001	216 (44)	203 (42)	175 (36)	0.037
Dyslipidemia	791 (54)	239 (49)	275 (55)	277 (57)	0.018	251 (51)	271 (55)	269 (55)	0.243
Prior heart failure	368 (25)	169 (34)	129 (26)	70 (14)	<0.001	175 (35)	113 (23)	80 (16)	<0.001
Prior myocardial infarction	269 (18)	104 (21)	80 (16)	85 (18)	0.107	98 (20)	86 (18)	85 (17)	0.564
Smoking, no. (%)	240 (16)	45 (9)	74 (15)	121 (25)	<0.001	51 (10)	67 (14)	122 (25)	<0.001
Left ventricular ejection fraction, %	52.7 ± 15.4	52.1 ± 16.5	53.2 ± 14.5	53.0 ± 15.1	0.049	52.0 ± 16.1	53.5 ± 14.8	52.7 ± 15.3	0.031
Albumin, g/dl	3.6 ± 0.5	3.4 ± 0.5	3.5 ± 0.5	3.7 ± 0.4	<0.001	3.4 ± 0.5	3.6 ± 0.5	3.7 ± 0.5	<0.001
Hemoglobin, g/dl	11.9 ± 2.0	11.3 ± 1.9	11.8 ± 2.0	12.8 ± 1.9	<0.001	11.3 ± 1.9	11.9 ± 2.0	12.6 ± 1.9	<0.001
eGFR, ml/min/1.73 m^2	51.1 ± 20.6	44.5 ± 21.2	52.5 ± 21.5	56.4 ± 17	<0.001	45.4 ± 21.7	52.0 ± 20.7	56.0 ± 17.9	<0.001
LDL-cholesterol, mg/dl	92 ± 29	88 ± 29	93 ± 31	94 ± 28	0.001	89 ± 30	91 ± 28	96 ± 29	0.001

6MWD: six-minute walk distance; eGFR: estimated glomerular filtration rate; LDL: low-density lipoprotein.
Values are mean ± standard deviation (SD) or percentage of total.

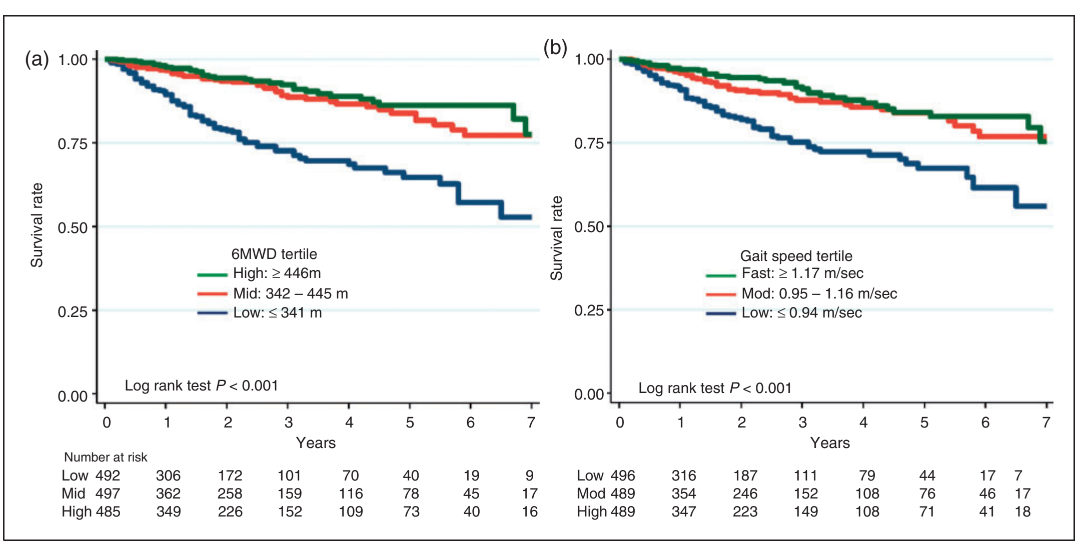

Figure 1. Kaplan–Meier curves for all-cause death according to tertiles of six-minute walk distance (6MWD) (a) and gait speed (b).

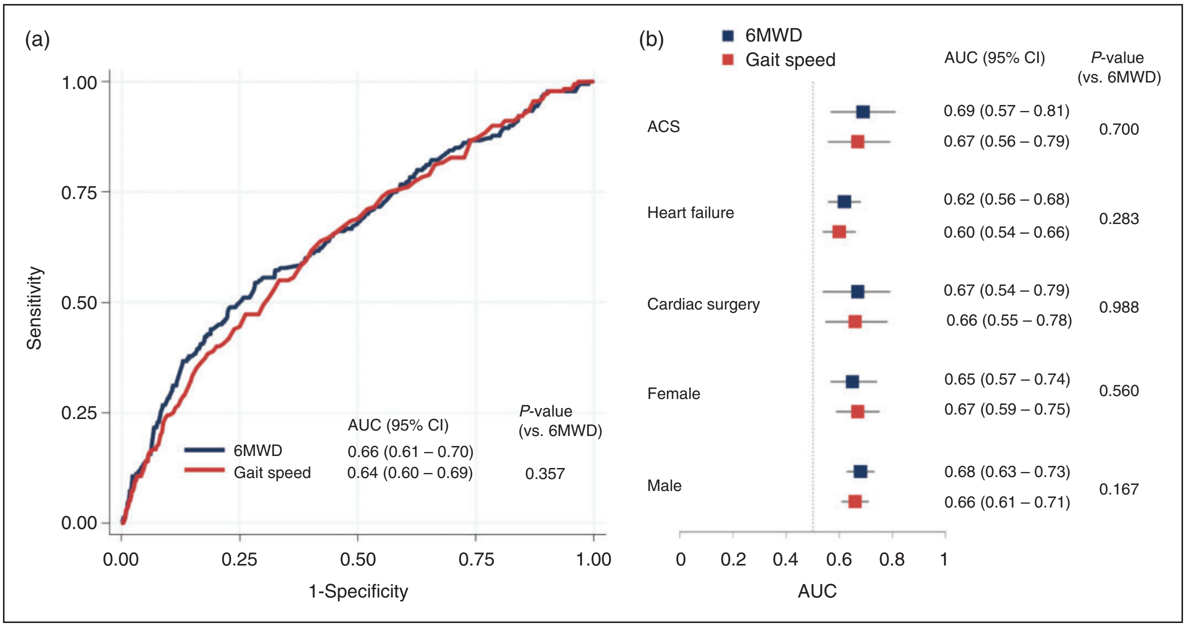

Figure 2. Comparison of prognostic capabilities of six-minute walk distance (6MWD) versus gait speed in all subjects (a) and various subgroups (b).
ACS: acute coronary syndrome; AUC: area under the curve; CI: confidence interval.

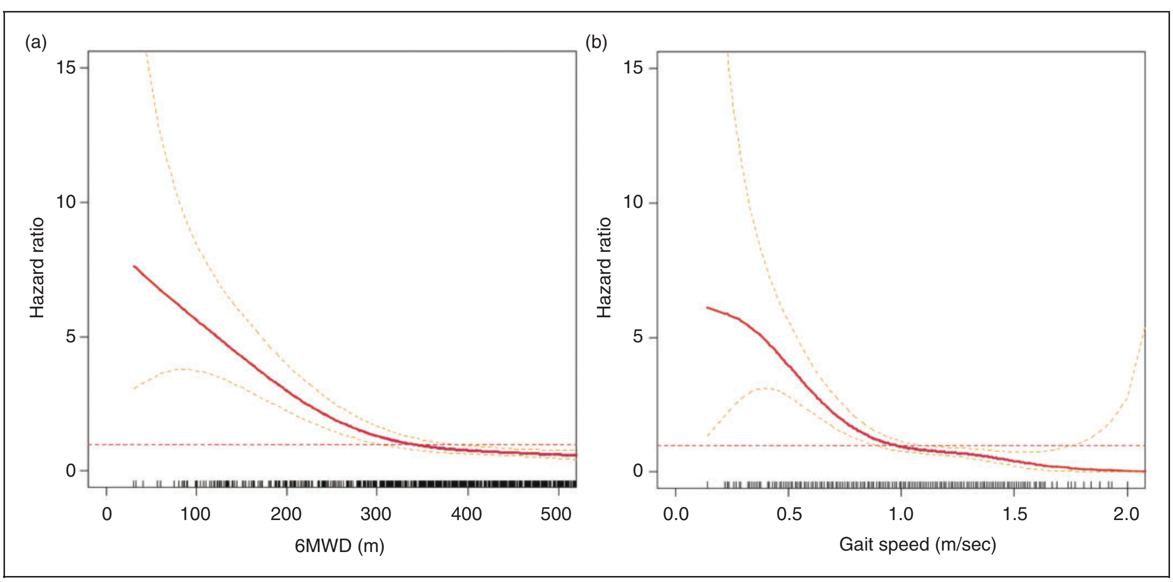

Figure 3. Dose–response associations of six-minute walk distance (6MWD) (a) and gait speed (b) with all-cause mortality.

Discussion

The primary findings of our study were as follows: (a) gait speed showed a strong positive correlation with 6MWD in older patients with CVD; (b) 6MWD and gait speed were both independent predictors of mortality; (c) the prognostic capabilities of gait speed were comparable to those of 6MWD in both all-CVD cohort and across various disease subgroups. These results suggest that gait speed, which is a quickly and repeatedly measurable metric, can be a useful risk stratification tool for older CVD patients.

The 6MWD is a widely used tool to assess functional capacity in a wide range of populations, including CVD patients. Several studies demonstrated its ability to predict outcome including heart failure,[7,8] coronary artery disease,[9] and those undergoing cardiac surgery.[6,10]

It has also been suggested that the prognostic utility of 6MWD is comparable to that of cardiopulmonary exercise testing.[25] On the other hand, gait speed has also been shown to predict morbidity and mortality in community-dwelling elderly populations,[12] those with acute coronary syndrome,[2] heart failure,[13] and patients undergoing transcatheter aortic valve replacement,[26] percutaneous coronary intervention,[27] or cardiac surgery.[11] However, no direct comparisons of prognostic capability between 6MWD and gait speed have been reported. In this study, gait speed showed prognostic capability comparable to 6MWD in both all-cohort and various subgroups, including acute coronary syndrome, heart failure, and post-cardiac surgery. To our knowledge, this is the first study to show similar prognostic capabilities of gait speed and 6MWD in older patients with CVD.

The mechanism underlying the association between slow gait speed and mortality may involve sarcopenia/frailty and exercise capacity. With the aging of the population, it is becoming increasingly important to integrate sarcopenia/frailty as a vital sign in older patients to guide management and coordinate better care.[28] The current criteria require measurement of gait speed to identify sarcopenia/frailty,[1,29] and gait speed is the most suitable functional test for pharmacological trials in frail older adults.[30] Both skeletal muscle mass and muscle strength are significant determinants of gait speed in patients with CVD, and higher values of both have been shown to have protective effects against CVD.[4,31,32] In addition, both muscle mass and strength are strongly correlated with circulating inflammatory markers in patients with chronic diseases.[33,34] The results of the present study indicated that gait speed was lowest in older patients, and slow gait was seen more often in women with higher prevalence rates of previous heart failure and impaired nutritional status. These multiple comorbidities and frailty likely contribute to morbidity and mortality. Other possible mechanisms involve the associations of gait speed or sarcopenia and exercise capacity. Exercise capacity is one of the strongest predictors of mortality in healthy individuals and patients with CVD.[35,36] The results of the present study indicated that gait speed has a strong positive correlation with 6MWD ($r = 0.80$), and gait speed predicted established critical cut-off points of 6MWD < 300 m[19–21] and 400 m[22,23] with sensitivity and specificity values above 80%. Previously, we demonstrated that quadriceps strength was a strong predictor of exercise capacity and mortality in patients with coronary artery disease.[33,37] These data and those of the present study indicate that sarcopenia/frailty is a critical determinant of exercise capacity and prognosis, and also support the results of comparable prognostic capability of gait speed to 6MWD in elderly patients with CVD.

Measurement of gait speed over a short distance has the advantages of both rapidity and simplicity, requiring only a stopwatch and having a typical assessment time of 1–2 min. The test is also easy for patients to understand, and the short distance involved may allay their fears associated with maximal or near-maximal tests. Furthermore, the test requires little space, and is therefore suitable for most clinical environments. Conversely, the 6MWD test requires significant space, which may be problematic for smaller office practices or home care settings. Shimada et al. compared several physical performance tests to predict the need for help with personal care in 10,351 adults aged ≥65 years.[38] The usual gait speed showed a stronger correlation with the requirement for personal care assistance than other performance measures (odds ratio = 5.9; AUC = 0.92–0.94). Gait speed can be measured reliably, and is a sensitive, quick, and a simple tool.[38] Therefore, gait speed measurement can be used as a risk stratification tool and to evaluate the effects of clinical care and interventions in clinical settings.

Our study had several limitations. First, this was a retrospective study with limited follow-up. Second, we measured 6MWD and gait speed only once; repeated measurements would have provided information about the prognostic power of 6MWD and gait speed changes over time. Third, some factors associated with mortality of CVD patients, such as socioeconomic and psychological status, were not examined. Finally, multiple testing was conducted in this study, which may increase the false-positive (type I error) rate.

Conclusion

Gait speed provided prognostic capability comparable to 6MWD in both all-cohort and across various subgroups. These observations indicated the potential utility of gait speed as a simple risk stratification tool in older CVD patients.

Author contribution

KK, NH, AMa, TM, and JA contributed to the conception or design of the work. KK, NH, YM, AMe, UC, RM, KN, ST, EM, CN, and MT contributed to the acquisition, analysis, or interpretation of data for the work. KK and YM drafted the manuscript. NH, AMe, UC, RM, KN, ST, EM, CN, MT, AMa, TM, and JA critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of conflicting interests

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