平成 30 年度学位申請論文

Moderate to vigorous physical activity predicts mobility decline in community-dwelling elderly women aged 75 years and above: a cohort study

（地域在住後期女性において中等強度以上の活動時間は移動能力低下を予測する：コホート研究）

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Abstract

【Background】

Early detection and prevention of declining mobility function are important for older women aged 75 years and above from the viewpoint of preventive care because of the high prevalence of frailty. Beneficial effects of physical activity (PA) on mobility function in old age has been examined, however, there is little evidence for recommendations of moderate to vigorous PA (MVPA), generally defined as an activity with an intensity of >3 metabolic equivalents, in older population aged 75 years and above. On the other hand, usual walking speed (UWS) has been widely used as the screening test of mobility function, however, its measurement is often not feasible in community settings such as the individual's home or health checkup sites. A simple surrogate indicator of UWS that can be evaluated with less space compared to UWS could be useful for assessing mobility function at such places.

【Study 1】

<Aims> To examine 1) whether objectively measured MVPA predicts the onset of decline in mobility function, and 2) the possible cut-off value of MVPA in Japanese community-dwelling older women aged 75 years and above.

<Methods> This prospective cohort study included 330 community-dwelling Japanese women aged 75 years and above and excluded those who need a walk device or assistance in their daily

living. MVPA and light-intensity PA (LPA) were evaluated using a uniaxial accelerometer for seven consecutive days. Mobility decline was defined as the need of walking device or assistance during 2-year follow-up. Variables with a $P < 0.1$ in comparison of characteristics between those with and without mobility decline were considered potential confounders.

<Results> Results of logistic regression analysis showed the inverse relationship between MVPA and onset of mobility decline independent of LPA and other potential confounding factors (adjusted odds ratio (OR) = 0.93 per 1 min/d, 95% confidence interval (CI) = 0.88-0.99; $P = 0.017$). On the other hand, LPA was not associated with mobility decline after controlling MVPA and confounders (adjusted OR = 0.99 per 1 min/d, 95% CI = 0.96-1.01; $P = 0.245$). Receiver operating characteristic (ROC) analysis identified 7.9 min/d of MVPA as a possible cut-off value of MVPA for predicting mobility decline onset.

<Discussion> The main finding of Study 1 was that MVPA independently predicted the onset of mobility decline during two years after baseline survey, whereas LPA was not. These results suggest the importance of promoting MVPA for preserving mobility function in old age. A possible cut-off value of MVPA for predicting mobility decline was approximately 60 min/wk and this volume is less than the current recommendation by World Health Organization (150 min/wk). However, the target volume of MVPA may differ depending on target population and outcome. Therefore, further studies are needed to confirm the generalizability of our findings.

【Study 2】

<Aims> 1) To explore simple surrogate indicators of usual walking speed (UWS) in community-dwelling older individuals based on comprehensive assessment of physical and psychophysiological function in a cross-sectional analysis, and 2) to compare the predictive accuracy for mobility decline with UWS in a longitudinal analysis.

<Methods> A cross-sectional analysis (n = 516) and a longitudinal analysis (n = 458) were performed in Study 2. The UWS and candidates of surrogate indicators of UWS including physical and psychophysiological function were evaluated at baseline survey. The presence of mobility decline, defined as the need of walking device or assistance, was assessed after two years.

<Results> Cross-sectional analysis using the baseline data showed that maximum step length (MSL) had the most favorable correlation among measured variables. The linear regression model using MSL, age and gender provided adjusted R^2 of 0.426 for predicting UWS. ROC analysis also showed the favorable predictive ability of MSL for slow UWS. Are under the curves (AUC) for UWS <0.8 m/sec and <1.0 m/sec were 0.908 (95% CI 0.811-1.000) and 0.883 (95% CI 0.832-0.933), respectively. In longitudinal analysis, MSL showed the similar predictive accuracy for the onset of mobility decline to UWS (AUC, 0.813 (95% CI 0.752-0.874) vs 0.808 (95% CI 0.747-0.869), *P* <0.892).

<Discussion> In Study 2, surrogate indicators of UWS were examined for the screening of mobility function in the community settings. As a result, MSL had the favorable correlation with UWS and also the similar predictive ability for mobility decline to UWS. The measurement of UWS is often not feasible at the individual's home or health checkup sites. These results suggest that MSL could be the surrogate of UWS when it cannot be measured due to limited space.

【Conclusions】

This study demonstrated the independent relationship of MVPA and mobility decline by a prospective design, suggesting that promoting MVPA may be a key to maintain mobility function in older individuals aged 75years and above. Additionally, MSL may serve as the surrogate indicator of UWS, a representative measure of mobility function in old age, when UWS cannot be evaluated due to a lack of space. The generalizability of our findings should be examined by further studies due to selection bias and relatively small sample size. Nevertheless, our findings are expected to contribute to early detection and prevention of mobility decline in community-dwelling older population.

要旨

【背景】

移動能力低下の早期発見と予防は、高齢期の介護予防において重要である。特に、75歳以上の後期高齢者女性では、身体的虚弱の存在率や障害発生率が男性や前期高齢者と比較して高く、介護予防の観点からその重要性は増す。身体活動は高齢期の移動能力維持に寄与することが報告されているが、3メッツ以上の身体活動を指す中等度強度以上の身体活動（moderate to vigorous physical activity : MVPA）を後期高齢者で推奨するエビデンスは十分でなく、さらなる研究が必要である。一方、移動能力の代表的なスクリーニング指標である歩行速度は、在宅や健康診断など測定スペースの限られた環境では評価が難しい。そのため、少ないスペースで測定可能な簡易指標があれば、そのような環境においても移動能力をスクリーニングすることが可能となる。

【研究1】

<目的>　地域在住後期高齢女性において、１）MVPA が移動能力低下を予測するか否かを調査し、２）移動能力維持の目標となるカットオフ値を算出すること。

<方法>　本研究は前向きコホート研究であり、日本人の地域在住後期高齢女性（75 歳以上）330名を対象とした。ベースライン調査時点で、日常生活に歩行補助具または介助が必要な者は除外した。MVPA と低強度身体活動時間（light-intensity physical activity :

LPA）は単軸加速度計を用いて連続 7 日間測定した。研究アウトカムである移動能力低下は、2 年後の追跡調査時点で、歩行補助具または介助が必要な状態になっている場合と定義した。アウトカムの有無での対象特性比較において、*P* <0.1 だった変数を潜在的な交絡因子とみなし、移動能力低下の発生をアウトカムとしたロジスティック回帰分析に身体活動量指標とともに投入した。

<結果>　ロジスティック回帰分析の結果、MVPA と移動能力低下の発生は負の関連を示し、この関連は LPA や潜在的な交絡因子とは独立していた（調整済みオッズ比 = 0.93 per 1 min/d, 95%信頼区間 = 0.88-0.99; *P* = 0.017）。一方で LPA は、MVPA と交絡因子で調整後、 移動能力低下と有意な関連を示さなかった（調整済みオッズ比 = 0.99 per 1 min/d, 95%信頼区間 = 0.96-1.01; *P* = 0.245）。Receiver operating characteristic analysis（ROC 解析）の結果、2 年後の移動能力低下を予測する MVPA のカットオフ値は 7.9 min/d であった。

<考察>　研究 1 では、MVPA が 2 年後の移動能力低下と有意に関連し、この関連は LPA や交絡因子とは独立していた。一方で、LPA と移動能力低下は有意な関連を認めなかった。本結果は、高齢期の移動能力維持における MVPA の促進の重要性を示唆している。また、移動能力低下を予測する MVPA のカットオフ値は、週当たり約 60 分と算出された。この値は現在の世界保健機関による推奨量の週当たり 150 分よりも少ないが、MVPA の目標量は対象とする集団やアウトカムによって異なる可能性がある。そのため、我々

の研究結果の一般化可能性についてさらなる研究が必要である。

【研究 2】

<目的>　地域在住高齢者を対象として、1）身体機能や精神心理学的機能の簡便な測定に基づき、普通歩行速度の代替指標を横断的に探索し、2）その後の縦断的解析において移動低下発生の予測能を普通歩行速度と比較すること。

<方法>　本研究は、横断的解析（n = 516）と縦断的解析（n = 458）により実施した。普通歩行速度と普通歩行速度の代替指標となる候補変数をベースライン調査において網羅的に測定した。研究 1 と同様に、移動能力低下の定義は歩行補助具の使用または歩行介助の有無とし、ベースライン調査から 2 年後に追跡調査を行った。

<結果>　ベースライン調査を用いた横断的解析において、最大一歩幅が全測定指標中で最も良好な普通歩行速度との相関を示した。最大一歩幅、年齢、性別を用いた線形回帰モデルの自由度調整済み R^2 は 0.426 であった。普通歩行速度低下をアウトカムとした ROC 解析においても、最大一歩幅は優れた予測能を示し、普通歩行速度 <0.8 m/sec、<1.0 m/sec を予測する曲線下面積はそれぞれ 0.908（95%信頼区間 0.811-1.000）、0.883（95%信頼区間 0.832-0.933）であった。2 年間の追跡調査データを用いた縦断的調査において、最大一歩幅と普通歩行速度の移動能力低下の予測能は同等であった（曲線下面積はそれぞれ 0.813（95%信頼区間 0.752-0.874）、0.808（95%信頼区間 0.747-0.869）、*P* <0.892)。

<考察>　普通歩行速度は高齢者の移動能力評価に広く用いられている。しかしながら、測定スペースが障壁となり測定困難な場合も少なくない。研究 2 では、在宅や健康診断のようなスペースの限られた環境でも適用可能な、普通歩行速度の簡便な代替指標を探索した。その結果、最大一歩幅が全測定指標の中で最も普通歩行速度と良好な相関を示し、将来の移動能力低下の予測能に関しても、普通歩行速度と同等であることが分かった。本研究結果は、最大一歩幅が普通歩行速度の代替指標として利用可能なことを示唆している。

【結論】

研究 1 では、前向きコホート研究によって、MVPA と移動能力低下の独立した関連を示した。この結果は、MVPA の促進が後期高齢者の移動能力維持の鍵となる可能性を示唆している。加えて、研究 2 では、最大一歩幅が普通歩行速度の代替指標として役立つ可能性を示唆した。普通歩行速度は高齢者の移動能力を反映する代表的な指標であるが、在宅や健康診断など測定スペースの限られたケースでは、最大一歩幅を移動能力のスクリーニングに利用可能なことが示唆された。本研究結果は、地域在住高齢者における、移動能力の早期発見と予防に寄与することが期待される。

I. Introduction

Decline in mobility function among older individuals predicts adverse health outcomes such as disability and mortality[1]. Especially, older women aged 75 years and above have a higher prevalence of physical frailty[2]. Additionally, risk of disability incident is higher in older women than men or younger individuals[3]. These evidence suggest that early detection and prevention of declining mobility function are important for older women aged 75 years and above from the viewpoint of preventive care.

Physical activity (PA) has been reported to be one of the modifiable risk factors of declined walking speed and disability in older people[4]. Added to this, the causal relationship of promoting PA and reduced risk of mobility limitation has been reported by a randomized controlled trial[5]. From the above, promotion of PA has a possibility to be a key strategy to prevent mobility limitation in old age. Yet, there is a lack of data to build robust evidence on the association of PA with mobility function in older individuals aged 75 years and above[6].

Moderate to vigorous PA (MVPA) is generally defined as an activity with an intensity of 3 or more metabolic equivalents[7] and has positive effects on health outcomes in old age such as muscle mass[8,9], fall[10], and mortality[11]. A recent study demonstrated the inverse relationship of disability with higher-intensity exercise but not with duration of exercise[12]. In this previous study[12], however, PA was assessed using a questionnaire and did not measure potential confounders including muscle strength, depression and joint pain. Therefore, further studies that include objective measurement of PA and adjustment of potential confounders are needed to confirm the beneficial effects of intensity of PA on physical health in old age.

For this reason, we previously performed a cross-sectional study to examine the relationship between MVPA measured using accelerometer and slow walking speed among community-dwelling older women aged 75 years and above[6]. In this study, we found an independent relationship between MVPA and slow walking speed defined as <1.0 m/sec even when adjusting for possible confounders, whereas step count was not related to slow walking speed after controlling MVPA. This result has been supported by another recent study that showed an independent association between objectively-measured moderate-intensity PA and measures of physical performance in older subjects aged 65 years and above[13]. However, the relationship between MVPA and a change in mobility function was not investigated in these studies because of the cross-sectional design. Hence, we performed a prospective cohort study to examine 1) whether objectively measured MVPA predicts the onset of decline in mobility function, and 2) the possible cut-off value of MVPA in Japanese community-dwelling older women (Study 1).

We also conducted Study 2 along with Study 1 to discuss the methodology for early prediction of mobility limitation. Walking speed is a representative measure of mobility function that is reliable and easily evaluated[14]. Measurement of usual walking speed (UWS) has been recommended the physical performance assessment for diagnosing sarcopenia[15,16]. Additionally, slow UWS has been used for defining frailty based on frailty phenotype[17]. However, UWS measurement is often difficult at community settings such as homes or health checkup sites because UWS assessment generally requires 4 to 10-meter walkway[18]. Indeed, a previous study in Japan reported that the Timed-up and Go test could not be performed at home in 87 out of 111 older individuals using long-term care insurance because of there was not enough space for testing[19]. From this result, even the 4-meter walk test is not likely feasible at most individuals' homes in Japan because the Timed Up and Go test needs space for setting a chair and 3-meter walkway. Thus, surrogate indicators of UWS that can be measured with limited space will contribute to finding those with risk of mobility limitation or diagnosing sarcopenia or frailty in community settings.

Walking speed is correlated with various measures related to physical function[20–24]. In addition, psychophysiological indicators[25–27] and a level of activity of daily living[28] have been reported to be associated with walking speed. Most of these correlates of walking speed can be easily measured and are likely to become surrogate indicators of UWS. Study 2, therefore, aimed to explore simple surrogate indicators of UWS.

II. Study 1: Association of moderate to vigorous physical activity with onset of mobility limitation

Purpose

The aim of Study 1 was to examine 1) whether objectively measured MVPA predicts the onset of decline in mobility function, and 2) the possible cut-off value of MVPA in Japanese community-dwelling older women

Materials and Methods

Study design and subjects

This study was a prospective cohort study performed as part of a cohort study in our laboratory at the Graduate School of Medicine, Nagoya University, Japan. The inclusion criterion of the main cohort study was community-dwelling older people. Exclusion criterion was those who were not able to access a health checkup at Nagoya University Daiko Campus from their homes. We recruited participants were from senior citizen’s clubs in Nagoya city and asked them to register for the Research of Health Promotion at Nagoya University. The registered volunteers provided written informed consent for participating in this study, and were invited for the health examination via mail every two years.

The present study included women participants aged 75 years and above who participated in the examination conducted in 2012 or 2013. Exclusion criterion was a lack of ability to walk independently without walking device or assistance at the baseline survey. The study protocol was approved by the Ethic Committee of the School of Health Sciences at Nagoya University (approval number: 2012-0131).

Study outcome

The study outcome was a decline in mobility function within two years after the baseline survey. Outcome survey was conducted by the follow-up examination of the main cohort study and telephonic interviews. The study outcome was defied as either the inability to walk without a walking device in their daily life or the need of assistance or watching for going out due to physical or health problem.

Mobility limitation is generally defined according to the ability for walking a certain distance (e.g., 400 meter or one-fourth of a mile) or climbing stairs without resting[29]. However, our study subjects were aged 75 years and above who might not have enough cognitive or executive function for estimating their walking distance. Considering this point, we consider the need of walking device or assistance in their daily life as the study outcome.

Measurement of physical activity

All PA measurements were performed in autumn (September to November) in order to avoid seasonal effects. A uniaxial accelerometer (Kenz Lifecoder, Suzuken Co., Ltd., Nagoya, Japan) was used and step counts and intensity of PA for each participant were recorded.

The device categorizes the intensity of PA into 11 levels (0, 0.5, 1-9) based on the acceleration pattern. The relationship between these accelerometer levels and metabolic equivalents during treadmill walking have examined by a previous study[30]. This study reveled that an accelerometer level >4 corresponded to >3 metabolic equivalents. In reference to this data, PA with an accelerometer level >4 from this device has been used for MVPA measurement among individuals in a wide age range[31–33]. An accelerometer level of 0 means no movement and that of 0.5 indicates slight body or arm movement. Therefore, PA with an accelerometer level of 1 to 3 was defined as light-intensity PA (LPA).

Each participant was instructed to wear the accelerometer around the waist for seven consecutive days, except during bathing, swimming, and sleeping. Added to this, we asked them to continue normal activities of daily living during the measurement period. They were also blinded to their recoded PA to avoid stimulating their PA in daily living.

Valid days for analysis and the mean duration of MVPA and LPA were determined according to the previous reports[34]. We defined a valid day as >10 h/d of monitor wear and the wear time was determined by substracting the nonwear time (an interval of at least 20 consecutive minutes of 0 accelerometer level) from 24 h[35]. The mean duration of MVPA and

LPA per day were calculated from five or more valid days. Data with four or less of valid days was considered missing data.

Demographic characteristics

Age and comorbidities of each participant were collected using a self-administered questionnaire. Body mass index was calculated as body weight (kg) divided by the square of height (m). Using their prescriptions, we counted the number of prescribed medications. The back or joint pain was also assessed using a self-administered questionnaire (none, rarely, sometimes, always). “Sometimes” or “always” were considered the presence of pain with reference to a previous study[36].

Potential confounders

As the representative measure of muscle strength, grip strength was assessed by trained physical therapist using a Jamar hydraulic dynamometer (Sammons Preston, USA) set at the second handle position[37]. The participants were asked to sit with the wrist in a neutral position and elbow flexed at 90°. Two trials for each hand were performed and the strongest value was used for the analysis[38]. The Trail Making Test (TMT)[39] was used for evaluating executive brain function. The TMT is a visual task to connect circles by drawing a line from one point to the next as quickly as possible. The TMT part A requires the subjects to draw lines to connect consecutively numbered circles (1–25) and the part B asks them to connect the same number of circles in an alternating sequence of numbers and letters in the Japanese-character order. The time to complete the part B minus that to complete the part A (ΔTMT) was calculated as the measure of executive brain function[40]. The 5-item Geriatric Depression Scale (GDS-5)[41] was used for assessing depressive state. The GDS-5 is a questionnaire assessing depressive symptom by five items and the score of ≥ 2 points indicates the presence of depression.

Statistical analysis

Participants who were lost to follow-up after two years were excluded. Participant characteristics between those with and without the study outcome were compared using the Mann-Whitney U test or chi-square test. After that, logistic regression analysis was performed to assess the relationship between the study outcome and MVPA or LPA. Variables with a *P*-value <0.1 in the Mann-Whitney U test or chi-square test were considered potential confounders and entered into the logistic regression analysis as independent variables.

There were missing data in several variables. First, we performed logistic regression analysis in those without missing data. Then, sensitivity analysis, the logistic regression analysis was performed including all participants including those with missing data. In the sensitivity analysis, missing values were imputed using the median for continuous variables and the most frequent category for categorical variables. At last, receiver operating characteristic (ROC) curve analysis was performed to identify the cut-off value of MVPA for predicting the study outcome, if MVPA was associated with the study outcome in the logistic regression analysis. All statistical analyses were carried out with Stata 14 (Stata Corporation, Texas, USA). A *P* value of <0.05 was considered significant.

Results

Of 345 women participants who were able to walk without a walking device or assistance at baseline survey, 330 participants were included in the present analysis (Figure 1). After two years follow-up, 37 participants (11.2%) experienced the study outcome defined as the need of walking device or assistance in their daily living. Table 1 shows the detailed information regarding the study outcome.

Participant characteristics based on the presence of the study outcome are shown in Table 2. Of the 330 participants included in this study, valid PA data were obtained from 300 participants (seven days, n=161; six days, n=130; five days, n=9). Participants who experienced the study outcome had older age (P <0.001), more prescribed medications (P = 0.005), weaker grip strength (P <0.001), and longer ΔTMT (P = 0.002) than those without the study outcome. There were also significant differences in MVPA (P <0.001) and LPA (P <0.001) between the groups. Depression was tended to be frequent among those with the study outcome (*P* = 0.078).

Table 3 shows the results of the complete data analysis of logistic regression analysis. Both MVPA and LPA were negatively associated with the study outcome independent of potential confounders. (MVPA: adjusted odds ratio (OR) = 0.92 per 1 min/d, 95% confidence interval (CI) = 0.87-0.97; *P* = 0.004, LPA: adjusted OR = 0.97 per 1 min/d, 95% CI = 0.95-0.99; *P* = 0.023). Furthermore, the association between MVPA and study outcome remained after adjusting for LPA (adjusted OR = 0.93 per 1 min/d, 95% CI = 0.88-0.99; *P* = 0.017), whereas the relationship of LPA with study outcome was not significant after adjusting for MVPA (adjusted OR = 0.99 per 1 min/d, 95% CI = 0.96-1.01; *P* = 0.245). Table 4 shows the results of the sensitivity analysis, indicating that the inverse relationship between MVPA and study outcome was also observed when including all participants.

Result of ROC curve analysis is presented in Figure 2. The ROC analysis identified a 7.9 min/d of MVPA as the optimal predictive value for predicting the decline in mobility function, with a sensitivity of 72.4% and a specificity of 74.3%; the AUC was 0.773 (95% CI = 0.666-0.881; *P* < 0.001).

Discussion

In this study, we examined the relationship between objectively measured MVPA and onset of mobility decline, defined as the future need of walking device or assistance in daily living among community-dwelling older women aged 75 years and above. As a result, daily MVPA predicted the study outcome independent of LPA and potential confounders, suggesting that MVPA may be a key to maintain mobility function in this population.

Thirty-seven of the 330 participants required the walking device or assistance in their daily living during two years after baseline survey (11.2%). A previous study reported that 3.9% of older Japanese individuals experienced the disability incident, defined as the care-needs certification in the national long-term care insurance system, during two years[42]. Despite of the different definition of the study outcome, a relatively high incident ratio of mobility decline may be caused by the inclusion of older women aged 75 years and above in our cohort study.

A previous meta-analysis of observational studies demonstrated the inverse relationship between PA and disability onset[43]. Additionally, a large randomized controlled trial reported the effects of promoting moderate-intensity PA on reduced risk of mobility limitation[5]. These reports suggest the causal relationship between promoting PA and reduced risk of mobility decline. However, further studies are needed to confirm whether promoting MVPA should be recommended for older individuals aged 75 years and above. In this study, therefore, the longitudinal relationship between MVPA and mobility decline was investigated among this population. As a result, daily MVPA predicted the future need of walking device or assistance independent of LPA, but LPA did not. These results suggest the importance of PA intensity for preserving mobility function.

A possible cut-off value of MVPA for predicting mobility decline was 7.9 min/d in this study. This amount is less than 150 min/wk, which is a current recommendation by the World Health Organization[44]. However, the target volume of MVPA may differ depending on the target population. A previous cohort study reported that ≥ 15 min/d of MVPA contributed to reduced probability of declining muscle mass during 5 years among older individuals[8]. Another cross-sectional study identified 107.4 min/wk as a cut-off value for predicting the presence of mobility limitation in older women[45]. Our data suggested that a possible target volume of MVPA for preserving mobility function was approximately 60 min/wk in older women aged 75 years and above. The generalizability of our findings should be examined by further studies because this study was performed among healthy volunteers.

There exist several possible mechanisms that explain the relationship between high MVPA and reduced risk of mobility decline. First, daily MVPA has a possibility to preserve muscle mass and strength which have a close relationship with mobility function[46]. Previous studies have demonstrated the inverse relationship of MVPA with loss of lean body mass[8] and risk of sarcopenia[9]. Another possible mechanism is the favorable effects of PA on peripheral nerve function. A previous study in diabetic patients showed that long-term moderate- to high-intensity brisk walking improved peripheral nerve function[47]. Daily MVPA may affect mobility function via peripheral nerve function because peripheral nerve function is related to walking ability.

In addition to the above physiological mechanisms, decreased social participation resulted from low PA may play a role in declining mobility function. Level of social participation outside home has an inverse relationship with onset and progression of disability[48]. A previous study reported that moderate-intensity PA but not light-intensity PA was correlated with the area a person moves though in daily living in old age[49]. These results suggest that declined MVPA has a possibility to result in mobility decline caused by a negative cycle of decreased life-space mobility and social participation.

This study has several limitations that should be discussed. First, the participants of this study were healthy volunteers recruited at senior citizen’s clubs. This may cause selection bias and limited generalizability of our findings. Second, wearing accelerometer might stimulate participants’ PA, resulting in overestimation of their PA. This may affect the cut-off value of MVPA identified in this study. Third, there may be other unknown confounders such as education level or living circumstance. Finally, the causal relationship should be examined by a future intervention study. Nevertheless, our findings have clinical significance in that a preventive effect of MVPA on mobility decline in older women aged 75 years and above was implied.

Summary of Study 1

In Study 1, the relationship between daily MVPA and change in mobility function, defined as the future need of walking device or assistance, was examined by a prospective design among community-dwelling older women aged 75 years and above. As a result, objectively measured MVPA predicted the mobility decline independent of LPA and confounding factors, whereas LPA did not. Our findings suggest that 60 min/wk could be a target volume of daily MVPA for preserving mobility function in this population. The generalizability of our results should be confirmed by further studies because of the relatively small sample size in the present study.

This article was published in Biomed Research International in 2018, entitled “Predicting the Future Need of Walking Device or Assistance by Moderate to Vigorous Physical Activiry: A 2-year Prospective Study of Women Aged 75 Years and Above.”

(Biomed Res Int 2018;2018:1340479. doi:10.1155/2018/1340479)

Figures

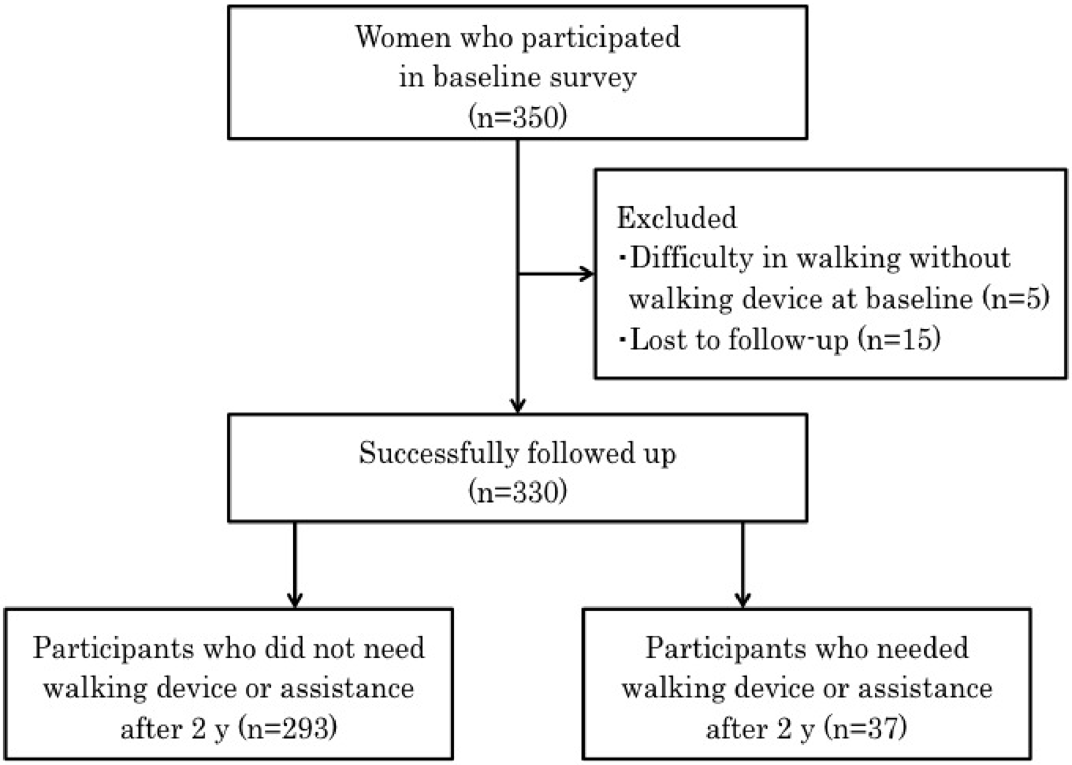

Figure 1. Flow diagram of the study participants

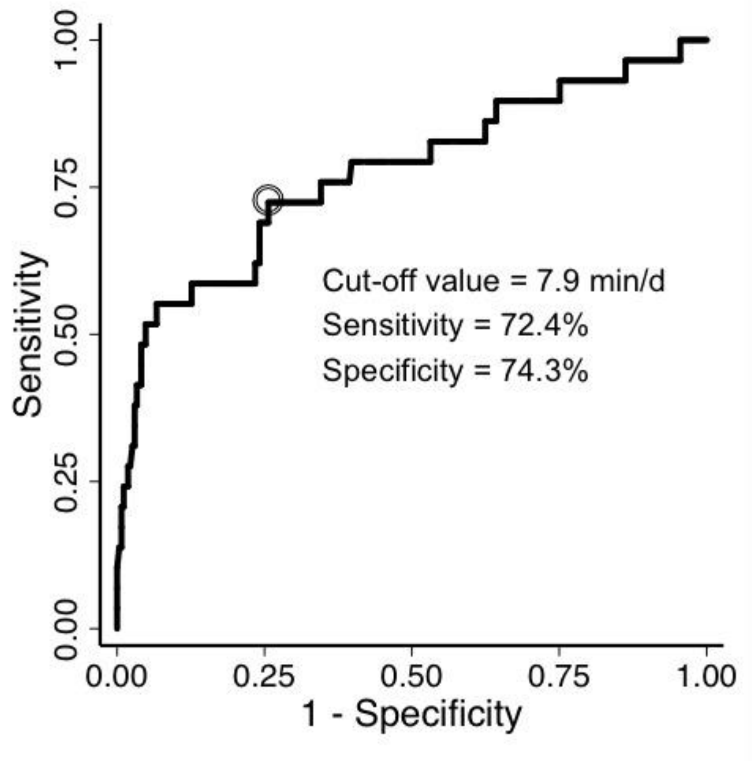

Figure 2. Receiver operating characteristic curve analysis for predicting the need of walking device or assistance by moderate to vigorous physical activity

Are under the curve was 0.773 (95% confidence interval: 0.666-0.881).

Tables

Table 1. Detail information of study outcome

	Number of participants who newly required walking device or assistance after 2 years	
	In a house	Outside
Need of walking device	16	28
Need of assistance for walking	10	20

Table 2. Participant characteristics and comparison of characteristics of those with and without the study outcome

Variables	Overall (N=330)	n	Participants without outcome (n=293)	n	Participants with outcome (n=37)	n	*P*
Age, years	79 [77-82]	330	79 [77-82]	293	83 [78-85]	37	<0.001
BMI, kg/m^2	21.6 [19.6-23.9]	330	21.6 [19.7-24.0]	293	21.6 [18.3-23.2]	37	0.243
Hypertension, n (%)	168 (50.9)	330	149 (45.2)	293	19 (51.4)	37	0.938
Diabetes, n (%)	47 (14.2)	330	41 (14.0)	293	6 (16.2)	37	0.685
Dyslipidemia, n (%)	147 (44.5)	330	135 (46.1)	293	12 (32.4)	37	0.118
Stroke, n (%)	14 (4.2)	330	12 (4.1)	293	2 (5.4)	37	0.669
Heart disease, n (%)	28 (8.5)	330	23 (7.8)	293	5 (13.5)	37	0.235
Prescribed medication, number	1 [1-4]	330	1 [1-4]	293	4 [1-6]	37	0.005
Pain, n (%)	83 (25.2)	330	70 (24.0)	293	13 (35.1)	37	0.141
Grip strength, kg	20[18-22]	327	20 [18-23]	291	18 [16-20]	36	<0.001
ΔTMT, sec	78.0 [57.0-125.7]	327	75.8 [54.2-117.1]	291	126.3 [74.5-188.2]	36	0.002
Depression, n (%)	55 (16.7)	328	45 (15.3)	291	10 (27.0)	37	0.078
MVPA	13.8 [6.3-24.0]	300	14.6 [7.7-24.7]	269	2.1 [0.5-10.7]	31	<0.001
LPA	50.5 [39.1-63.4]	300	51.2 [40.3-63.9]	269	39.3 [22.6-51.7]	31	0.002

Continuous variables are shown by median [interquartile range].

BMI, body mass index; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; LPA, light-intensity physical activity

Table 3. Results of the logistic regression analysis in those with complete data

	Model 1			Model 2			Model 3		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Age, per 1 year	1.16	[1.03-1.31]	0.016	1.15	[1.03-1.30]	0.014	1.14	[1.01-1.29]	0.032
Prescribed medications, per 1 medication	1.09	[0.95-1.26]	0.213	1.12	[0.98-1.28]	0.089	1.09	[0.95-1.25]	0.197
Grip strength, per 1 kg	0.93	[0.82-1.06]	0.279	0.91	[0.80-1.03]	0.141	0.91	[0.81-1.05]	0.213
ΔTMT, per 1 sec	1.00	[0.99-1.01]	0.107	1.00	[0.99-1.01]	0.189	1.00	[0.99-1.01]	0.153
Depression, yes	1.55	[0.56-4.25]	0.397	1.75	[0.65-4.73]	0.271	1.56	[0.56-4.31]	0.390
MVPA, per 1min/d	0.92	[0.87-0.97]	0.004		-		0.93	[0.88-0.99]	0.017
LPA, per 1 min/d		-		0.97	[0.95-0.99]	0.023	0.99	[0.96-1.01]	0.245

Dependent variable: Need of walking device or assistance

OR, odds ratio; CI, confidence interval; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; LPA, light-intensity physical activity

Table 4. Results of the sensitivity analysis including all participants

	Model 1			Model 2			Model 3		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Age, per 1 year	1.13	[1.02-1.27]	0.018	1.14	[1.02-1.26]	0.016	1.13	[1.01-1.25]	0.032
Prescribed medications, per 1 medication	1.09	[0.97-1.23]	0.136	1.12	[0.99-1.26]	0.053	1.10	[0.97-1.24]	0.126
Grip strength, per 1 kg	0.91	[0.81-1.01]	0.081	0.89	[0.79-0.99]	0.041	0.89	[0.80-1.00]	0.059
ΔTMT, per 1 sec	1.01	[1.00-1.01]	0.011	1.00	[1.00-1.01]	0.026	1.01	[1.00-1.01]	0.017
Depression, yes	1.33	[0.54-3.26]	0.534	1.43	[0.59-3.47]	0.431	1.33	[0.54-3.26]	0.535
MVPA, per 1min/d	0.93	[0.89-0.98]	0.004		-		0.94	[0.90-0.99]	0.017
LPA, per 1 min/d		-		0.97	[0.95-0.99]	0.030	0.99	[0.96-1.01]	0.255

Dependent variable: Need of walking device or assistance

OR, odds ratio; CI, confidence interval; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; LPA, light-intensity physical activity

III. Study 2: Estimation of usual walking speed using simple measurements

Purpose

The aim of Study 2 was to explore simple surrogate indicators of UWS in community-dwelling older individuals based on comprehensive assessment of physical and psychological function in a cross-sectional analysis, and to compare the predictive accuracy for mobility decline with UWS in a longitudinal analysis.

Materials and Methods

Study design and subjects

A cross-sectional analysis and a longitudinal analysis were performed in Study 2. This was a secondary study of a cohort study in our laboratory at the Graduate School of Medicine, Nagoya University, Japan. The inclusion criterion of the main cohort study was community-dwelling older people. Exclusion criterion was those who were not able to access a health checkup at Nagoya University Daiko Campus from their homes. We recruited participants were from senior citizen's clubs in Nagoya city and asked them to register for the Research of Health Promotion at Nagoya University. The registered volunteers provided written informed consent for participating in this study, and were invited for the health examination via mail every two years.

The present study included those aged 65 years and above who participated in the examination in 2012 or 2013. The study protocol was approved by the Ethic Committee of the

School of Health Sciences at Nagoya University (approval number: 2012-0131).

Measurement of usual walking speed

The UWS was measured using a 14-m walkway and calculated over a 10-m distance between the 2- and 12-m marks of the 14-m walkway[50]. The test was performed twice by trained physical therapists, and the faster result was used for the analysis. A previous study showed the strong reliability of 10-meter and 4-meter walk tests in older individuals and the good agreement between the two tests[51]. On the other hand, this study also reported the larger difference in UWS measured using a stopwatch versus using an automatic timer in 4-meter walk test than 10-meter test. In particular, this difference was more remarkably observed among those with faster walking speed compared with others[51]. Therefore, the UWS in the present study was measured using 10-meter walk way because of the inclusion of relatively healthy volunteers.

Measurements of physical function

Grip strength and knee extensor isometric strength (KEIS) were measured as representative indicators of muscle strength. Grip strength was assessed by trained physical therapist using a Jamar hydraulic dynamometer (Sammons Preston, USA) set at the second handle position[37]. The participants were asked to sit with the wrist in a neutral position and elbow flexed at 90°[37].

Two trials for each hand were performed and the strongest value was used for the analysis[38]. KEIS was measured using a handheld dynamometer (μ-tas F1, Anima, Japan), in a seated position with the knee and hip joints at 90° of flexion. Two trials for each side were conducted and the strongest value to body weight (% body weight) was used for the analysis.

Maximum step length (MSL) and functional reach test (FRT) were measured for physical performance. MSL was measured according to previous studies[24,52,53]. The subject was asked to step forward with one leg as far as possible and subsequently bring the other leg to the first leg in one step without using a walking aid or assistance. MSL was calculated as the distance between the initial and final positions. Two trials for each leg were performed and the mean value of the longest distances for each leg was used for the analysis. In addition to the absolute value of MSL, the ratio of MSL to height (%MSL) was calculated (MSL (m)/height (m)×100). The FRT was measured using a modified method (mFRT) according to a previous study[54]. A pointing stick that expands and contracts smoothly was used for the mFRT measurement. The participant was asked to stand in front of the wall and held a pointing stick in the dominant hand, with 90° of shoulder flexion and the tip of the pointing stick in contact with the wall. Then, the participant was asked to sway forward as far as possible in the same way as the original FRT[55]. The shortened length of the pointing stick was measured, and the longer length in two trials was used for the analysis.

Measurements of psychophysiological function

Cognitive state, executive brain function and depressive state were assessed. Cognitive state was assessed using Mini-Mental State Examination (MMSE)[56], a standard test for global cognitive function including orientation, attention, language and recall. Executive brain function was assessed using TMT[39], as well as Study 1. The time to complete the part B minus that to complete the part A (ΔTMT) was used for the measure of executive brain function[40]. The GDS-5 was used for assessing depressive state and the score of ≥2 points was considered the presence of depression[41], as well as Study 1.

Measurement of activity of daily living

Performance Measure for Activity of Daily Living-8 (PMADL-8)[57] was used. This questionnaire is composed of 8 items potentially requiring activity of daily living (ADL). The PMADL-8 was developed among patients with chronic heart failure to assess difficulties in performing ADL. Each item was answered using a 4-category Lickert scale. The score range is 8 to 32 and higher score means more severer functional limitation. The PMADL-8 has also been reported to associate with eligibility level of long-term care, grip strength, social participation and depressive state among in older individuals who use home help service in Japan[58].

Definition of mobility decline

A decline in mobility function during two years after the baseline survey was considered a study outcome for longitudinal analysis, as well as Study 1. Outcome survey was conducted by the follow-up examination of the main cohort study and telephonic interviews. The study outcome was defied as either the inability to walk without a walking device in their daily life or the need of assistance or watching for going out due to physical or health problem.

Demographic characteristics

Age and comorbidities of each participant were collected using a self-administered questionnaire. Body mass index was calculated as body weight (kg) divided by the square of height (m).

Statistical analysis

Continuous variables with or without normal distribution were described as mean ± standard deviation or median [interquartile range (IQR)]. The normal distribution for each continuous variable was assessed using the Shapiro-Wilk test.

The present study included both cross-sectional analysis using the baseline data and longitudinal analysis using 2-year follow-up data. In cross-sectional analysis, predictive accuracy of each variable for UWS was assessed using linear regression analysis. The regression model was made using age, gender and one of the measured variables. The variable with the most favorable adjusted R^2 was considered the possible surrogate indicator for UWS. Then, ROC analysis was used for predicting slow UWS by the selected surrogate indicator. The slow UWS was defined as <0.8 m/sec or <1.0 m/sec, which have been used for diagnosing sarcopenia[16] or physical frailty[59,60] in Japanese older population, respectively.

After performing the cross-sectional analysis, a longitudinal analysis was conducted for assessing the predictive ability of the surrogate indicator for mobility decline onset. The predictive accuracy of the UWS and the surrogate indicator for mobility decline was compared using the ROC analysis. The area under the curve (AUC) for each independent variable was calculated and the method of DeLong et al.[61] was used to compare them.

All statistical analyses were carried out with Stata 14 (Stata Corporation, Texas, USA). A *P* value of <0.05 was considered significant.

Results

A total of 516 participants [median age (IQR) 79 (76-82) years] were included in this study. Forty-eight participants were lost to follow-up and excluded from the longitudinal analysis (Figure 1). Participant characteristics are presented in Table 1.

Table 2 shows the results of linear regression analysis. Estimation model including absolute value of MSL, age and gender provided the best predictive accuracy (adjusted R^2=0.426). Scatter plots of UWS and MSL based on age and gender are presented in Figure 2. Figure 3 shows the results of the ROC analysis for predicting slow UWS by MSL. The area under the curves for predicting <0.8 m/sec and <1.0 m/sec were 0.908 (95% CI 0.811-1.000) and 0.883 (95% CI 0.832-0.933), respectively. Cut-off values for <0.8 m/sec and <1.0 m/sec were identified as 75.8 cm and 81.1 cm, respectively.

After excluding those with mobility decline at baseline survey and lost to follow-up, 458 participants were included in the longitudinal analysis (Figure 1). During the follow-up, eight deaths occurred and all cases were considered the onset of mobility decline after confirming the mobility limitation onset before they died by telephonic interview with their family. As a result, 51 participants developed mobility decline during 2-year follow-up. Figure 4 shows the results of the ROC analysis comparing the predictive accuracy of UWS and MSL for mobility decline. There was no difference between their AUCs for the study outcome (P <0.892).

Discussion

In Study 2, simple surrogate indicators of the UWS were examined based on simple measurements of physical and psychophysiological function among community-dwelling older individuals. As a result, MSL was identified as the indicator with the most favorable correlation to UWS and also having the similar predictive ability for mobility decline to UWS. Because MSL can be measured with less space compared to UWS, MSL may serve as a surrogate indicator of UWS when UWS cannot be measured due to a limited space such as the individual's home or health checkup examination.

The MSL has been reported to be associated with mobility function[22–24] and to predict falls[23,52,62], implying the possibility of MSL to be a surrogate indicator of UWS. However, the direct relationship between MSL and UWS has not been well examined. The present study demonstrated the strong correlation of MSL with UWS and the favorable predictive accuracy of estimation formula using MSL, age and gender. The similarity of the movements of walking and MSL testing may explain the closer relationship between UWS and MSL compared to other measured variables. We also performed the ROC analysis for predicting slow UWS by MSL. The adjusted R^2 of 0.426 of the estimation formula may not be sufficient to predict the absolute value of UWS, however, the results of the ROC analysis suggest the usefulness of MSL for diagnosing sarcopenia and physical frailty. A low positive predictive value of MSL for UWS <0.8 m/sec may be caused by the low prevalence of participants with UWS <0.8 m/sec, suggesting the necessity for including more frail participants to identify more appropriate cut-off value for UWS <0.8 m/sec. Another finding of this study was the similar predictive abilities of MSL and UWS for future mobility decline. Previous studies reported the predictive ability of MSL for falls in older individuals[23,52,62], and our data are consistent with them. The results of the ROC analysis in the present study suggest that MSL serves as a surrogate indicator of UWS in terms of assessing the risk of future mobility decline.

Safety of measurement should also be discussed in order to consider MSL as the surrogate of UWS. We did not observe any adverse events such as falls or joint pain occurrence at the baseline survey. The good feasibility and safety of self-measurements of MSL at home were demonstrated by previous studies among healthy older subjects[53,63]. The feasibility, validity and reliability were also reported among older individuals with mean age of 82±4.1 years[24], indicating the safety of MSL in a geriatric population. Additionally, the range of MSL in our participants was approximately 0.5 to 1.0 m, suggesting that MSL could be a useful screening test at home.

To date, there is little consensus about the method for MSL measurement. Results of linear regression analysis in this study demonstrated the slightly favorable adjusted R^2 of the absolute value of MSL compared to %MSL. Because the height of the subject is sometimes not available at home, absolute value of MSL seems more useful in the community settings. In addition to the calculation of MSL, the measurement protocol also varies among previous studies. In this study, the participants were asked to step forward maximally with one leg and bring the other leg up to the same point in one step, as well as several previous study[24,52,53].

Using this protocol, the examiner can measure the MSL easily after completing the stepping motion. As described before, the feasibility of self-measurement of MSL by this protocol has been report, indicating the simplicity and usefulness of the screening test at home[53,63].

This study has several limitations that should be discussed. First, the participants of this study were healthy volunteers recruited at senior citizen's clubs. This may cause selection bias and limited generalizability of our findings. Second, the number of the participants with UWS <0.8 m/sec were limited, suggesting the necessity of involving frailer subjects to establish the predictive validity of MSL for this level of UWS. Finally, the small number of men subjects may cause results to be biased towards women. Nevertheless, our findings still have clinical importance by showing the usefulness of MSL as a possible surrogate indicator of UWS in community settings.

Summary of Study 2

In Study 2, surrogate indicators of UWS were examined by cross-sectional and longitudinal analyses. As a result, MSL showed the most favorable predictive accuracy for UWS and the similar predictive ability for future mobility decline to UWS.

This article was published in Aging Clinical Experimental Research, entitled "Estimation of reduced walking speed using simple measurements of physical and psychological function in community-dwelling elderly people: a cross-sectional and longitudinal study.”

(Aging Clin Exp Res, in press. doi:10.1007/s40520-018-0938-5)

Figures

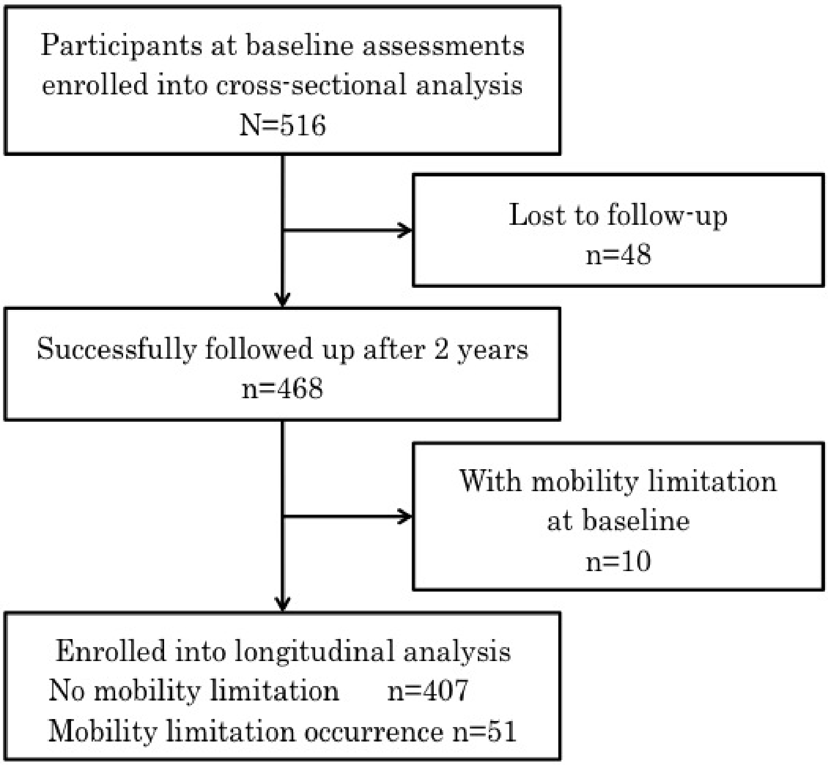

Figure 1. Flow diagram of the study participants

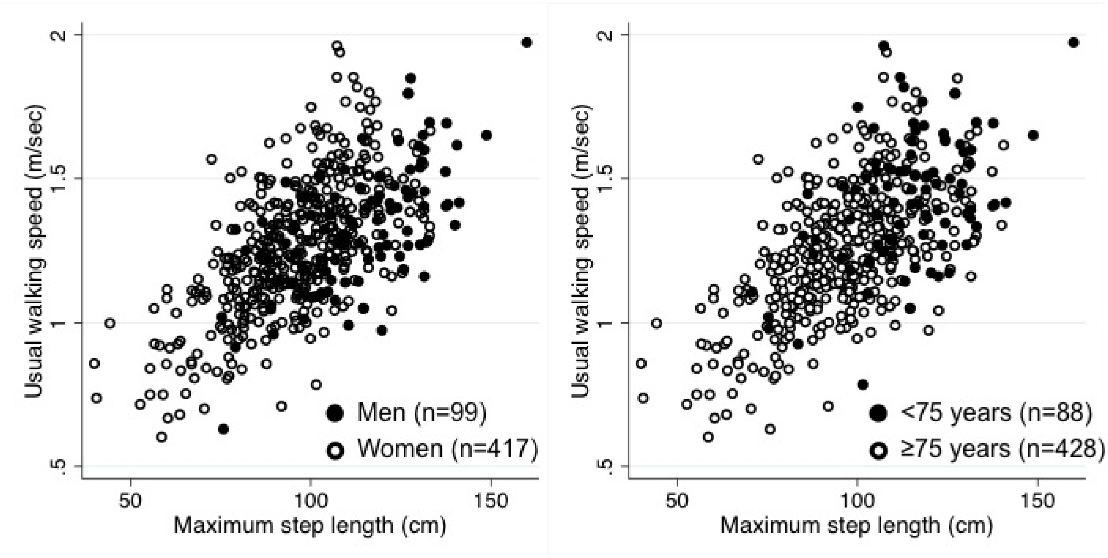

Figure 2. Correlation between usual walking speed and maximum step length

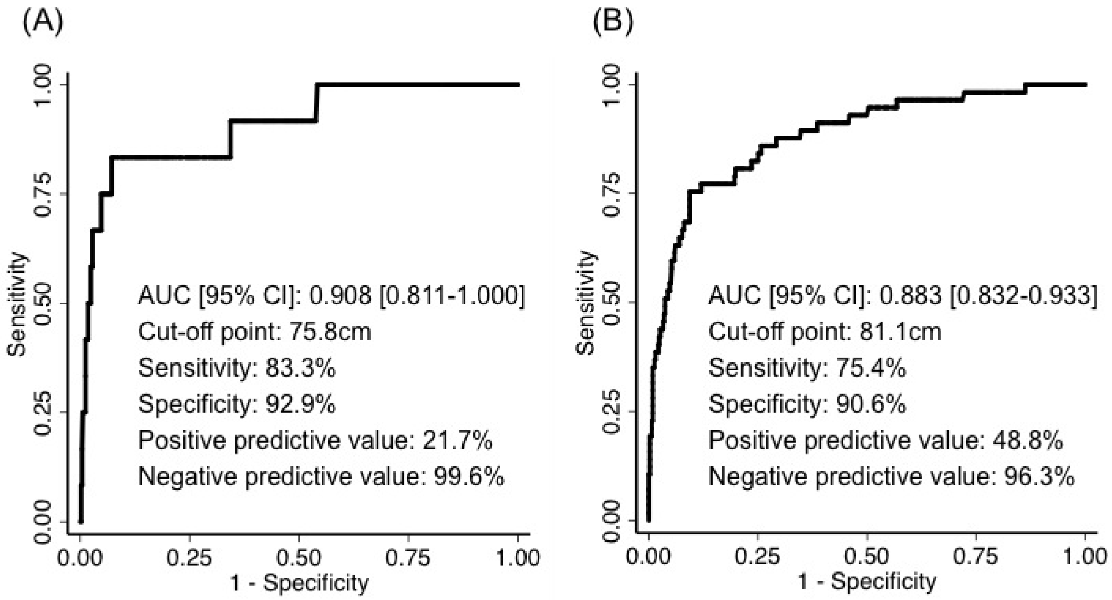

Figure 3. Results of receiver operating characteristics curve analysis for predicting declined usual walking speed using maximum step length

Dependent variables are <0.8 m/s (A) and <1.0 m/s (B), respectively.

AUC, are under the curve; CI, confidence interval

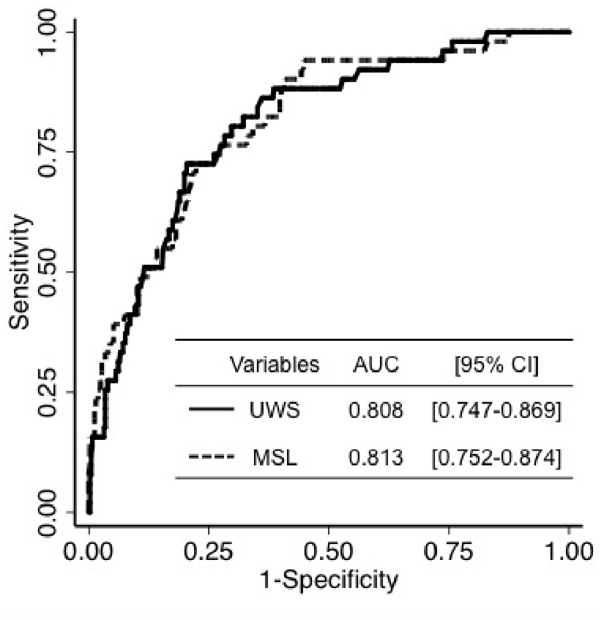

Figure 4. Results of receiver operating characteristic analysis for predicting mobility limitation (longitudinal analysis).

There is no significant difference between AUCs of UWS and MSL (*P* = 0.892). The cut-off values were 1.13 m/s for UWS (sensitivity: 72.6%, specificity: 79.6%, positive predictive value: 29.6%, negative predictive value: 95.0%) and 87.8 cm for MSL (sensitivity: 72.6%, specificity: 77.6%, positive predictive value: 28.3%, negative predictive value: 95.4%).

AUC, area under the curve; CI, confidence interval; UWS, usual walking speed; MSL, maximum step length

Tables

Table 1. Participant characteristics.

Age (years)	79 [76-82]
Women, %	80.8
Body mass index (kg/m^2)	21.6 [19.6-23.9]
Hypertension, %	49.6
Diabetes, %	13.4
Dyslipidemia, %	40.7
Stroke, %	4.8
Cardiac disease, %	7.6
Grip strength (kg)	
Men	33.2±6.2
Women	21.0±4.2
Knee extensor isometric strength (%body weight)	42.8±13.1
Maximum step length (cm)	93.2 [82.4-102.6]
%Maximum step length (%height)	63.3 [56.2-69.3]
Modified functional reach test (cm)	33.7 [30.3-37.2]
PMADL-8 (points)	16 [11-20]
Mini-Mental State Examination (points)	29 [27-30]
ΔTrail Making Test (sec)	70.6 [50.3-111.6]
5-item Geriatric Depression Scale (points)	1 [1-2]
Usual walking speed (m/sec)	1.27 ±0.23
<0.8 m/sec	2.4
<1.0 m/sec	11.0

Continuous variables are shown by mean±standard deviation or median [interquartile range]. Categorical variables are shown by n (%). PMADL-8, Performance Measure of Activity in Daily Living-8

Table 2. Results of linear regression analysis with usual walking speed as a dependent variable

Model	Variable	Regression coefficient	[95% CI]	Standardized beta	*p*	Adjusted R^2
1	Grip strength (kg)	0.013	[0.008, 0.016]	0.364	<0.001	0.244
	Age (years)	-0.014	[-0.018, -0.010]	-0.314	<0.001	
	Women	0.093	[0.026, 0.161]	0.158	0.007	
	Intercept	1.911	[1.490, 2.332]			
2	KEIS (%)	0.006	[0.004, 0.007]	0.320	<0.001	0.267
	Age (years)	-0.015	[-0.019, -0.012]	-0.350	<0.001	
	Women	0.027	[-0.022, 0.076]	0.047	0.274	
	Intercept	2.200	[1.881, 2.521]			
3	MSL (m)	0.785	[0.678, 0.893]	0.622	<0.001	0.426
	Age (years)	-0.006	[-0.009, -0.002]	-0.125	0.002	
	Women	0.082	[0.039, 0.125]	0.138	<0.001	
	Intercept	0.789	[0.417, 1.160]			
4	%MSL (%)	0.012	[0.010, 0.014]	0.545	<0.001	0.410
	Age (years)	-0.008	[-0.011, -0.004]	-0.178	<0.001	
	Women	0.009	[-0.031, 0050]	0.156	0.654	
	Intercept	1.084	[0.732, 1.437]			
5	mFRT (cm)	0.013	[0.010, 0.016]	0.318	<0.001	0.271
	Age (years)	-0.014	[-0.017, -0.010]	-0.309	<0.001	
	Women	-0.005	[-0.051, 0.041]	-0.009	0.827	
	Intercept	1.909	[1.542, 2.277]			
6	PMADL-8 (points)	-0.017	[-0.021, -0.015]	-0.456	<0.001	0.360
	Age (years)	-0.014	[-0.018, -0.010]	-0.292	<0.001	
	Women	-0.023	[-0.067, 0.021]	-0.041	0.298	
	Intercept	2.695	[2.402, 2.987]			
7	MMSE (points)	-0.008	[-0.003, -0.001]	0.072	0.076	0.199
	Age (years)	-0.018	[-0.019, -0.012]	-0.414	<0.001	
	Women	-0.054	[-0.090, 0.001]	-0.091	0.023	
	Intercept	2.605	[2.426, 2.992]			
8	ΔTMT (10 sec)	-0.004	[-0.007, -0.002]	-0.130	0.002	0.207
	Age (years)	-0.017	[-0.021, -0.014]	-0.388	<0.001	
	Women	-0.050	[-0.096, -0.005]	-0.085	0.031	
	Intercept	2.715	[2.474, 3.046]			
9	GDS-5 (points)	-0.036	[-0.058, -0.015]	-0.129	0.001	0.210
	Age (years)	-0.019	[-0.022, -0.015]	-0.416	<0.001	
	Women	-0.052	[-0.098, -0.007]	-0.089	0.024	
	Intercept	2.878	[2.600, 3.156]			

CI, confidence interval; KEIS, knee extensor isometric strength; MSL, maximum step length; mFRT, modified functional reach test; PMADL-8, Performance Measure of Activity in Daily Living-8; MMSE, Mini Mental State Examination; TMT, Trail Making Test; GDS-5, 5-item geriatric depression scale

IV. General discussion and Conclusions

Early detection and prevention of declining mobility function are important for older women aged 75 years and above from the viewpoint of preventive care. Promoting PA has been reported to have the beneficial effects on mobility function in old age, however, there is a lack of evidence for recommendations of MVPA in older population aged 75 years and above. In Study 1, we performed prospective cohort study and demonstrated the inverse relationship between MVPA and mobility decline, defined as the need of walking device or assistance in daily living, during two years after baseline survey. A possible cut-off value of MVPA for predicting mobility decline was approximately 60 min/wk. The generalizability of these findings should be examined by further large cohort studies. In Study 2, surrogate indicators of UWS were examined for the screening of mobility function in the community settings. The cross-sectional analysis demonstrated the favorable correlation between MSL and UWS. In the longitudinal analysis, MSL showed the similar predictive accuracy for future onset of mobility decline to UWS, suggesting that MSL could be the surrogate indicator of UWS where UWS cannot be measured due to a limited space such as the individual’s home or health checkup sites. Our findings are expected to contribute to early detection and prevention of mobility decline in community-dwelling older population.

V. Acknowledgements

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VI. References

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