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Gait speed, life-space mobility and mild cognitive impairment in patients with coronary artery disease

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Abstract

Slow gait speed and restricted life-space mobility predict cognitive decline and dementia in healthy older adults, yet the relation between gait speed or life-space mobility and cognitive function remains poorly understood in patients with coronary artery disease (CAD). We therefore examined the following relations: that between gait speed and cognitive function, and mild cognitive impairment (MCI) and that between life-space mobility and cognitive function, and MCI. We conducted a cross-sectional study of 240 non-dementia patients who met the study criteria from 2132 consecutive CAD patients. MCI was estimated with the Japanese version of the Montreal Cognitive Assessment (MoCA-J). Gait speed was measured to perform gait trials at the patients' usual walking pace, and life-space mobility was evaluated using the Life-Space Assessment (LSA). We investigated the relation between gait speed or life-space mobility and cognitive function by Pearson correlation analysis, whereas multivariable logistic regression analysis was conducted for detecting MCI. Gait speed and LSA scores were positively associated with the MoCA-J score ($r = 0.54$, $p < 0.001$ and $r = 0.44$, $p < 0.001$, respectively), and both were independently associated with MCI in the multivariable logistic regression analysis (odds ratio, 0.007; $p < 0.001$, and odds ratio, 0.98; $p = 0.038$, respectively). Cognitive impairment can be easily detected by assessment of gait speed and life-space mobility. Interventions to improve gait

speed and life-space mobility may lead to improvement of cognitive function and MCI in patients with CAD.

Keywords: Cognitive function; Coronary artery disease; Gait speed; Life-space mobility; Mild cognitive impairment.

Introduction

Because Japan has the highest life expectancy in the world and a sustainable low birth rate, the aging of Japan's population is advancing [1]. The resulting increased numbers of older Japanese patients with cardiovascular disease and patients with dementia are becoming a public health problem [2,3]. The Japanese government has required measures to deal with these difficult problems.

Mild cognitive impairment (MCI) is known to be a transitional state between the normal cognitive declines that occur with aging and dementia [4]. In addition, the presence of motoric cognitive risk syndrome (MCR) has been proposed as a pre-dementia syndrome [5]. MCR is characterized by cognitive complaints and slow gait [5]. Both cognitive complaints and slow gait speed predict cognitive decline, but the combination of both is a stronger predictor of the development of future dementia in community-dwelling older adults [6,7]. Moreover, a meta-analysis showed that MCR was significantly associated with cardiovascular diseases, hypertension, diabetes, stroke, and obesity [8]. These findings suggested that a vascular mechanism might underlie the pathophysiologic basis of MCR. Nevertheless, the relationship between MCI and gait speed is unclear in patients with cardiovascular disease. Of note, it was reported that older adults with MCI showed decreased life-space mobility compared with those without MCI [9]. Furthermore,

cognitive executive functions and physical factors have been reported to predict life-space mobility in community-dwelling older adults [10], but it remains unclear whether their association is as strong among older people with cardiovascular disease.

From these points of view, it is important to clarify the relationship between gait speed or life-space mobility and cognitive function or MCI in patients with coronary artery disease (CAD). Thus, we hypothesized that there would be greater declines in gait speed and life-space mobility in CAD patients with MCI than in those without MCI and that gait speed and life-space mobility would be strongly associated with cognitive function and MCI in patients with CAD.

Therefore, the purposes of the present study were to determine the following: (1) the differences in gait speed and life-space mobility in patients with or without MCI; (2) the relationship between gait speed and cognitive function, and MCI; (3) the relationship between life-space mobility and cognitive function, and MCI; and (4) the cutoff values of gait speed and life-space mobility that could potentially predict MCI in patients with CAD.

Methods

Study population

We examined the data of 2132 consecutive patients with CAD who were treated at the

Sakakibara Heart Institute of Okayama from May 2018 to December 2019, including those with acute myocardial infarction, stable and unstable angina, and acute coronary syndrome. We included patients who received rehabilitation and were hospitalized for more than two days, except those hospitalized for only one night and two days, to undergo percutaneous coronary intervention (PCI) [11]. We excluded patients who did not give informed consent, underwent coronary artery bypass surgery, had mental disease, experienced a cerebral vascular accident, could not walk without total assistance, had probable dementia as shown by a Mini-Mental State Examination (MMSE) score <24 [12,13], died in hospital, and had missing data [11].

Clinical characteristics of the patients

Patient characteristics were retrospectively evaluated from the medical records. Baseline characteristics evaluated included age, sex, body mass index (BMI), educational background (categorized as >13 years of schooling), living alone, diagnosis, number of significant coronary artery stenoses (≥75%; especially left main trunk stenosis ≥50%), treatments, left ventricular ejection fraction (LVEF) as calculated with the modified Simpson method for cardiac echocardiography, maximum serum levels of creatine kinase-myocardial band, hemoglobin, albumin, and HbA1c, estimated glomerular filtration rate

(eGFR), comorbidities, and medications. The laboratory and echocardiographic data obtained just prior to patient discharge were evaluated from the patients' medical records [11].

Measurement of cognitive function

We used the Japanese version of the Montreal Cognitive Assessment (MoCA-J) [14] and the MMSE [12,13] to evaluate cognitive function in the patients [11]. The MoCA-J is used to evaluate multiple cognitive domains, such as visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation [14]. The scoring ranges from 0 to 30 points with higher scores indicating better cognitive function. The MoCA-J is also used to identify persons with MCI, for which it was reported to have a sensitivity of 93% and specificity of 87% [14]. A cutoff score of 26 for the MoCA-J was previously used to define MCI [14], and thus we defined patients with MCI as having a MoCA-J score <26 and those without MCI as having a MoCA-J score ≥26 [11].

Although the MMSE is used as a screening tool for dementia globally [13], it is not sensitive enough to screen for early cognitive decline associated with MCI [15]. Thus, we used the MMSE only as a means to choose the patients with probable dementia for exclusion [11]. A MMSE cutoff score of <24 was used to define probable dementia [13]. A

physical therapist assessed cognitive function at the time of discharge.

Measurement of gait speed and life-space mobility

We measured gait speed by performing two 4-m gait trials at the patients' usual walking pace on a flat floor [16]. Gait speed is calculated as the time taken in seconds to complete the 4-m distance (m/s). The highest speed from the two trials was used in this study. A physical therapist evaluated gait speed at the time of discharge.

We used the Life-Space Assessment (LSA) [17] to evaluate life-space mobility. The LSA is a self-reported questionnaire in which patients report the distance and frequency of movement within a life-space level during the past four weeks. The LSA score consists of three items (five life-space levels, the frequency of movement, and levels of independence), and ranges from 0 to 120 points with higher scores indicating greater mobility. The LSA is a reliable assessment shown to be sensitive in older adults with and without cognitive impairment [17,18].

Statistical analysis

Patient characteristics and evaluated outcomes are shown as percentages for the categorical variables and as the mean ± standard deviation for the continuous variables. The unpaired *t*-

test, Mann-Whitney U test, and χ^2 test were used as appropriate to evaluate differences in patients' characteristics and in measured outcomes between the MCI and non-MCI groups. Pearson correlation analysis was used to test the relations between gait speed and MoCA-J scores and between LSA scores and MoCA-J scores. Univariable and multivariable logistic regression analyses were used to clarify the relation between MCI and gait speed or life-space mobility, with the dependent variable being MCI and the independent variables being patient characteristics, gait speed, and LSA score. Receiver operating characteristic (ROC) curve analysis was used to construct areas under the curve (AUC) to calculate the optimal cutoff values of gait speed and LSA scores for prediction of MCI. AUC values of >0.9 indicate high accuracy, 0.7–0.9 indicate moderate accuracy, and <0.7 indicate low accuracy [19]. The overall level of statistical significance was set at 0.05. Statistical analyses were performed with R ver. 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Ethical considerations

The Sakakibara Heart Institute of Okayama Ethics Committee approved this study (approval no. A2018-0401), and we obtained informed consent from each patient. We complied with the principles of the 1975 Declaration of Helsinki regarding investigations in human subjects.

Results

Clinical characteristics

A flowchart of the patients included in this study is shown in Figure 1. Of the 2132 consecutive patients with CAD, 744 met the inclusion criteria, but 504 patients were subsequently excluded. Ultimately, 240 patients were included in our final analysis and were divided into the non-MCI group (n = 160) and the MCI group (n = 80). Compared to the patients in the non-MCI group, those in the MCI group were significantly older, less frequently male, had lower BMI, lower rates of PCI, lower serum levels of hemoglobin and albumin, lower eGFR, lower rates of β-blocker use, higher rates of benzodiazepines use, lower educational background, and lower MoCA-J score (Table 1).

Differences in gait speed and life-space mobility between groups

Gait speed was significantly slower and LSA scores were significantly lower in the MCI group than those in the non-MCI group (Table 1).

Relation between gait speed or life-space mobility and cognitive function

Pearson correlation analysis showed that both gait speed and LSA scores were positively

associated with the MoCA-J score (r = 0.54, $p < 0.001$ and r = 0.44, $p < 0.001$, respectively).

Relation between gait speed or life-space mobility and MCI

After the significant independent variables and covariates were identified in the univariable analysis, the multivariable logistic regression analysis showed age (odds ratio [OR], 1.08; 95% confidence interval [CI]: 1.04–1.12; p < 0.001), gait speed (OR, 0.007; 95% CI: 0.0009–0.006; p < 0.001), and LSA score (OR, 0.98; 95% CI: 0.96–0.999; p = 0.038) to be significantly associated with MCI after adjustment for covariates (Table 2).

Cutoff points of gait speed and life-space mobility for prediction of MCI

The ROC curve analysis showed that the AUCs for gait speed and LSA score as predictors of MCI were 0.83 (95% CI: 0.78–0.89) and 0.76 (95% CI: 0.72–0.80), respectively. The optimal cutoff values of gait speed and LSA score were 0.97 m/s and 92 points, respectively. The respective sensitivity and specificity for the prediction of MCI by gait speed were 77% and 78%, and those by LSA score were 73% and 70% (Figure 2).

Discussion

To the best of our knowledge, this is the first study to show a relationship between gait speed or life-space mobility and cognitive function or MCI in CAD patients. Gait speed was significantly slower and life-space mobility was significantly lower in the CAD patients with MCI than those in the patients without MCI in this study. Moreover, gait speed and life-space mobility in the CAD patients were found to be significantly associated with cognitive function and independently associated with MCI after adjustment for covariates. The results of multivariable logistic regression analysis showed that the non-MCI group was the reference group, and the odds were for having MCI. The odds for gait speed (OR, 0.007; 95% CI: 0.0009–0.006; $p < 0.001$) and for life-space mobility (OR, 0.98; 95% CI: 0.96–0.999; $p = 0.038$) indicated that both were negatively associated with the incidence of MCI in CAD patients. Thus, the OR of gait speed indicated that slow gait speed would increase the odds of having MCI by 142.86 times, and the OR of life-space mobility indicated that restricted life-space mobility would increase the odds of having MCI by 1.02 times.

It was reported that gait speed and decline in gait speed were strongly associated with the decline of cognitive function and the incidence of dementia in older adults [20,21]. Similarly, we found that gait speed was moderately associated with the decline of cognitive function and the incidence of MCI in the CAD patients. These results showed gait speed to

be one important factor in identifying early cognitive decline in patients with CAD. Slow gait speed is one of the components of MCR [5], and MCR (characterized by subjective memory complaints and slow gait speed) can occur during the long preclinical phase and increase the risk of progression to MCI and dementia [22]. The cutoff value we determined for gait speed might partly indicate that a CAD patient may be in the transitional stage from MCR to MCI. Furthermore, we showed the cutoff value for gait speed determined by ROC curve analysis that can predict MCI to be 0.97 m/s (sensitivity, 77%; specificity, 78%; AUC = 0.83). Because this cutoff value for gait speed indicates moderate accuracy [19], it could potentially be useful in ascertaining the transitional stage from MCR to MCI in patients with CAD.

Life-space mobility is reported to be associated with increased risk of cognitive decline, MCI, and dementia in older people [23]. Similarly, we found that life-space mobility was moderately associated with the decline of cognitive function and the incidence of MCI in the CAD patients, indicating that life-space mobility may be one important factor in identifying early cognitive decline in patients with CAD. Moreover, a reduction in life-space mobility in older adults with MCI might be caused by altered functional architecture of the brain [24]. A previous study reported that the default-mode network and sensory-motor network were associated with life-space mobility and cognitive decline [24]. Life-

space mobility indicates the spatial expanse of personal life and social function [17]. Thus, the assessment of life-space mobility is important in recognizing the spatial expanse of personal life and in screening cognitive function and cognitive impairment in CAD patients. Furthermore, because our cutoff value for the LSA score that can predict MCI is 92 points (sensitivity, 73%; specificity, 70%; AUC = 0.76 [indicating moderate accuracy [19]]), , this value could be potentially useful in screening cognitive function and MCI in patients with CAD.

Our study showed a relationship between gait speed or life-space mobility and cognitive impairment and indicated that the effects of these factors on cognitive impairment might reflect their involvement in the frailty cycle comprised of physical frailty, social frailty, and cognitive frailty. Recently, frail older patients have been shown to have multi-domain risk factors related to physical, social, and cognitive health and that multi-domain interventions have the potential to improve these factors [25]. Our study indicated that poorer mobility might lead to poorer cognition, and vice versa. Thus, interventions to improve gait speed and life-space mobility may lead to the improvement of cognitive impairment and issues related to frailty in CAD patients. Similarly, interventions to improve cognitive function may likewise lead to improved mobility in these patients.

Our findings in CAD patients with MCI largely agreed with the characteristics of MCI

patients reported in previous studies [26–30] and thus may partially reflect the characteristics of CAD patients with MCI. The independent association of gait speed and LSA with MCI even after adjustment for age indicates the great clinical importance of assessing these two factors.

There are several limitations in this study. This is a single-center, cross-sectional study with small sample size. Therefore, generalizability of the results may be limited. Evaluation of cognitive function was limited to a single screening tool, and imaging data were not analyzed. Moreover, the influence of changes in factors such as gait speed and life-space mobility and cognitive function over time is unknown. Therefore, further longitudinal studies are needed to clarify the relation between gait speed or life-space mobility and cognitive function and MCI in patients with CAD.

Conclusions

Gait speed and life-space mobility were significantly associated with cognitive function and independently associated with MCI in the patients with CAD. Assessment of gait speed and life-space mobility may be useful in identifying the presence of cognitive impairment, and interventions for gait speed and life-space mobility may lead to the improvement of cognitive function and MCI in patients with CAD.

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Compliance with Ethical Standards

Conflicts of interest

All authors declare no conflicts of interest in relation to the work reported in this manuscript.

References

1. Arai H, Ouchi Y, Toba K, Endo T, Shimokado K, Tsubota K, Matsuo S, Mori H, Yumura W, Yokode M, Rakugi H, Ohshima S (2015) Japan as the front-runner of super-aged societies: perspectives from medicine and medical care in Japan. Geriatr Gerontol Int 15:673–687

2. Okura Y, Ramadan MM, Ohno Y, Mitsuma W, Tanaka K, Ito M, Suzuki K, Tanabe N, Kodama M, Aizawa Y (2008) Impending epidemic: future projection of heart failure in Japan to the year 2055. Circ J 72:489–491

3. Sekita A, Ninomiya T, Tanizaki Y, Doi Y, Hata J, Yonemoto K, Arima H, Sasaki K, Iida M, Iwaki T, Kanba S, Kiyohara Y (2010) Trends in prevalence of Alzheimer's disease and vascular dementia in a Japanese community: the Hisayama Study. Acta Psychiatr Scand 122:319–325

4. Gauthier S, Reisberg B, Zaudig M, Petersen RC, Ritchie K, Broich K, Belleville S, Brodaty H, Bennett D, Chertkow H, Cummings JL, de Leon M, Feldman H, Ganguli M, Hampel H, Scheltens P, Tierney MC, Whitehouse P, Winblad B, International Psychogeriatric Association Expert Conference on mild cognitive impairment (2006) Mild cognitive impairment. Lancet 367:1262–1270

5. Verghese J, Wang C, Lipton RB, Holtzer R (2013) Motoric cognitive risk syndrome

and the risk of dementia. J Gerontol A Biol Sci Med Sci 68:412–418

6. Verghese J, Annweiler C, Ayers E, Barzilai N, Beauchet O, Bennett DA, Bridenbaugh SA, Buchman AS, Callisaya ML, Camicioli R, Capistrant B, Chatterji S, De Cock AM, Ferrucci L, Giladi N, Guralnik JM, Hausdorff JM, Holtzer R, Kim KW, Kowal P, Kressig RW, Lim JY, Lord S, Meguro K, Montero-Odasso M, Muir-Hunter SW, Noone ML, Rochester L, Srikanth V, Wang C (2014) Motoric cognitive risk syndrome: multicountry prevalence and dementia risk. Neurology 83:718–726

7. Cohen JA, Verghese J, Zwerling JL (2016) Cognition and gait in older people. Maturitas 93:73–77

8. Beauchet O, Sekhon H, Barden J, Liu-Ambrose T, Chester VL, Szturm T, Grenier S, Léonard G, Bherer L, Allali G (2018) Association of motoric cognitive risk syndrome with cardiovascular disease and risk factors: results from an original study and meta-analysis. J Alzheimers Dis 64:875–887

9. O'Connor ML, Edwards JD, Wadley VG, Crowe M (2010) Changes in mobility among older adults with psychometrically defined mild cognitive impairment. J Gerontol B Psychol Sci Soc Sci 65B:306–316

10. Poranen-Clark T, von Bonsdorff MB, Rantakokko M, Portegijs E, Eronen J, Kauppinen M, Eriksson JG, Rantanen T, Viljanen A (2018) Executive function and

life-space mobility in old age. Aging Clin Exp Res 30:145–151

11. Ishihara K, Izawa KP, Kitamura M, Shimogai T, Kanejima Y, Morisawa T, Shimizu I (2020) Pinch strength is associated with the prevalence of mild cognitive impairment in patients with cardiovascular disease. J Cardiol 75:594–599

12. Folstein MF, Folstein SE, McHugh PR (1975) “Mini-mental state”: A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12:189–198

13. Anthony JC, LeResche L, Niaz U, von Korff MR, Folstein MF (1982) Limits of the ’Mini-Mental State’ as a screening test for dementia and delirium among hospital patients. Psychol Med 12:397–408

14. Fujiwara Y, Suzuki H, Yasunaga M, Sugiyama M, Ijuin M, Sakuma N, Inagaki H, Iwasa H, Ura C, Yatomi N, Ishii K, Tokumaru AM, Homma A, Nasreddine Z, Shinkai S (2010) Brief screening tool for mild cognitive impairment in older Japanese: Validation of the Japanese version of the Montreal Cognitive Assessment. Geriatr Gerontol Int 10:225–232

15. Tang-Wai DF, Knopman DS, Geda YE, Edland SD, Smith GE, Ivnik RJ, Tangalos EG, Boeve BF, Petersen RC (2003) Comparison of the Short Test of Mental Status and the Mini-Mental State Examination in mild cognitive impairment. Arch Neurol

60:1777–1781

16. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB (1994) A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 49:M85–94

17. Baker PS, Bodner EV, Allman RM (2003) Measuring life-space mobility in community-dwelling older adults. J Am Geriatr Soc 51:1610–1614

18. Ullrich P, Werner C, Bongartz M, Kiss R, Bauer J, Hauer K (2019) Validation of a modified Life-Space Assessment in multimorbid older persons with cognitive impairment. Gerontologist 59:e66–e75

19. Akobeng AK (2007) Understanding diagnostic tests 3: receiver operating characteristic curves. Acta Paediatr 96:644–647

20. Fitzpatrick AL, Buchanan CK, Nahin RL, Dekosky ST, Atkinson HH, Carlson MC, Williamson JD (2007) Associations of gait speed and other measures of physical function with cognition in a healthy cohort of elderly persons. J Gerontol A Biol Sci Med Sci 62:1244–1251

21. Dumurgier J, Artaud F, Touraine C, Rouaud O, Tavernier B, Dufouil C, Singh-Manoux A, Tzourio C, Elbaz A (2017) Gait speed and decline in gait speed as

predictors of incident dementia. J Gerontol A Biol Sci Med Sci 72:655–661

22. Semba RD, Tian Q, Carlson MC, Xue QL, Ferrucci L (2020) Motoric cognitive risk syndrome: integration of two early harbingers of dementia in older adults. Ageing Res Rev 58:101022

23. James BD, Boyle PA, Buchman AS, Barnes LL, Bennett DA (2011) Life space and risk of Alzheimer disease, mild cognitive impairment, and cognitive decline in old age. Am J Geriatr Psychiatry 19:961–969

24. Hsu CL, Crockett R, Chan P, Brinke LT, Doherty S, Liu-Ambrose T (2020) Functional connectivity underpinning changes in life-space mobility in older adults with mild cognitive impairment: a 12-month prospective study. Behav Brain Res 378:112216

25. Lee H, Lee E, Jang IY (2020) Frailty and comprehensive geriatric assessment. J Korean Med Sci 35:e16

26. Cronk BB, Johnson DK, Burns JM (2010) Alzheimer's Disease Neuroimaging Initiative, Body mass index and cognitive decline in mild cognitive impairment. Alzheimer Dis Assoc Disord 24:126–130

27. Luck T, Luppa M, Briel S, Riedel-Heller SG (2010) Incidence of mild cognitive impairment: A systematic review. Dement Geriatr Cogn Disord 29:164–175

28. Taniguchi Y, Shinkai S, Nishi M, Murayama H, Nofuji Y, Yoshida H, Fujiwara Y (2014) Nutritional biomarkers and subsequent cognitive decline among community-dwelling older Japanese: a prospective study. J Gerontol A Biol Sci Med Sci 69:1276–1283

29. Iwata A, Iwatsubo T, Ihara R, Suzuki K, Matsuyama Y, Tomita N, Arai H, Ishii K, Senda M, Ito K, Ikeuchi T, Kuwano R, Matsuda H (2018) Effects of sex, educational background, and chronic kidney disease grading on longitudinal cognitive and functional decline in patients in the Japanese Alzheimer's Disease Neuroimaging Initiative study. Alzheimers Dement (N Y) 4:765–774

30. Picton JD, Marino AB, Nealy KL (2018) Benzodiazepine use and cognitive decline in the elderly. Am J Health Syst Pharm 75:e6–e12

Figure legend

Fig. 1. Flow chart of patient selection. CAD, coronary artery disease; PCI, percutaneous coronary intervention.

Fig. 2. Receiver operating characteristic curves for gait speed and Life-Space Assessment (LSA) scores to predict the incidence of mild cognitive impairment (MCI) in patients with coronary artery disease. a) The area under the curve (AUC) for gait speed is 0.83 with the cutoff value set at 0.97 m/s for prediction of the incidence of MCI (sensitivity, 77%; specificity, 78%). b) The AUC for the LSA score is 0.76 with the cutoff value set at 92 points for prediction of the incidence of MCI (sensitivity, 73%; specificity, 70%).

Consecutive CAD patients admitted to Sakakibara Heart Institute of Okayama from May 2018 to December 2019 (n=2132)

Inclusion criteria

- Underwent rehabilitation
- Admitted for more than 2 days, except those admitted for only one night and 2 days, for PCI

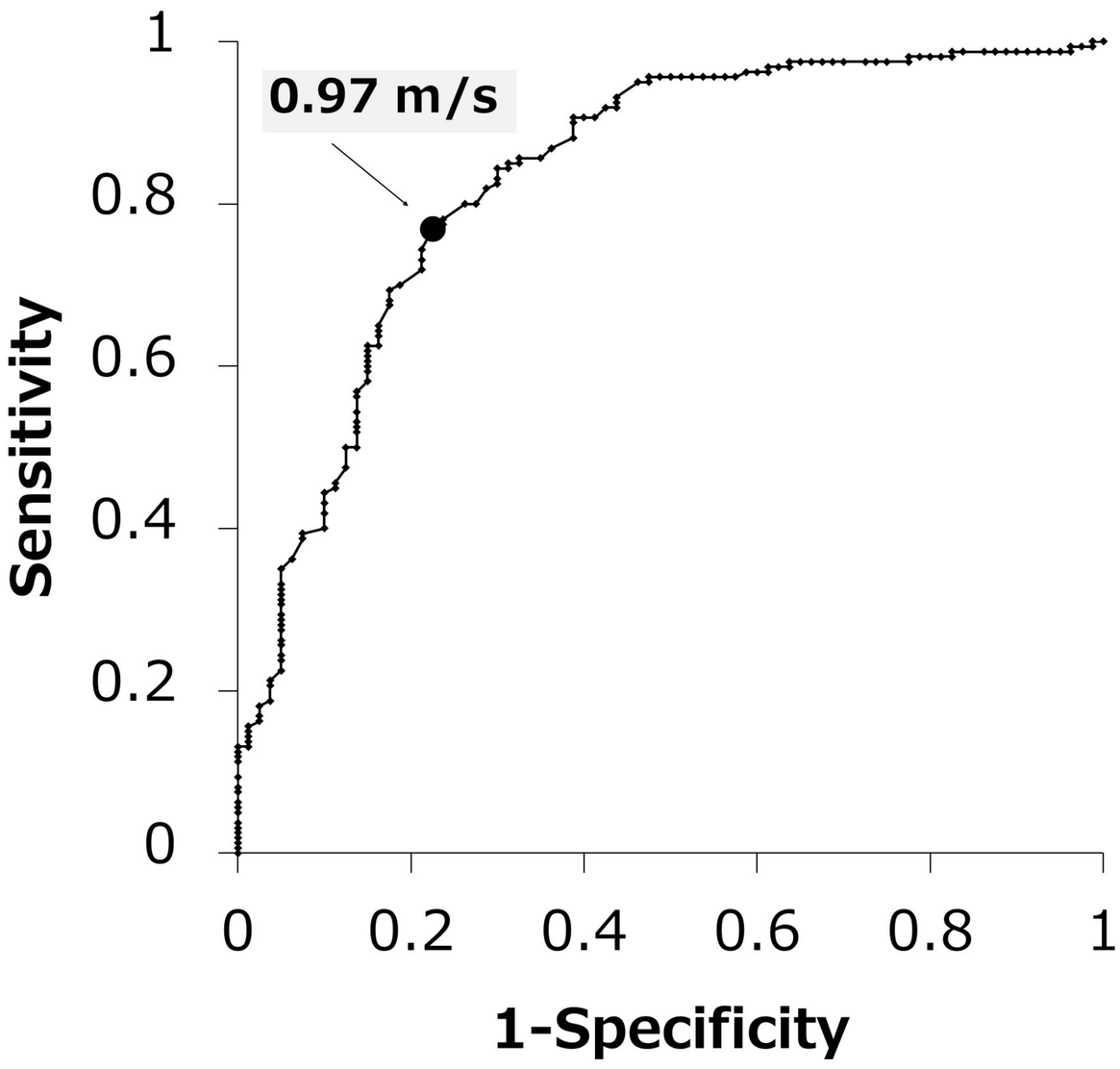
CAD patients meeting inclusion criteria (n=744)

Exclusion criteria

- Did not give informed consent (n=82)
- Underwent coronary artery bypass surgery (n=287)
- Mental disease (n=8)
- Cerebral vascular accident (n=16)
- Required total assistance to walk (n=36)
- Probable dementia (n=58)
- Hospital death (n=14)
- Missing data: gait speed (n=3)

CAD patients after exclusion criteria applied (n=240)

a


1
0.8
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Sensitivity
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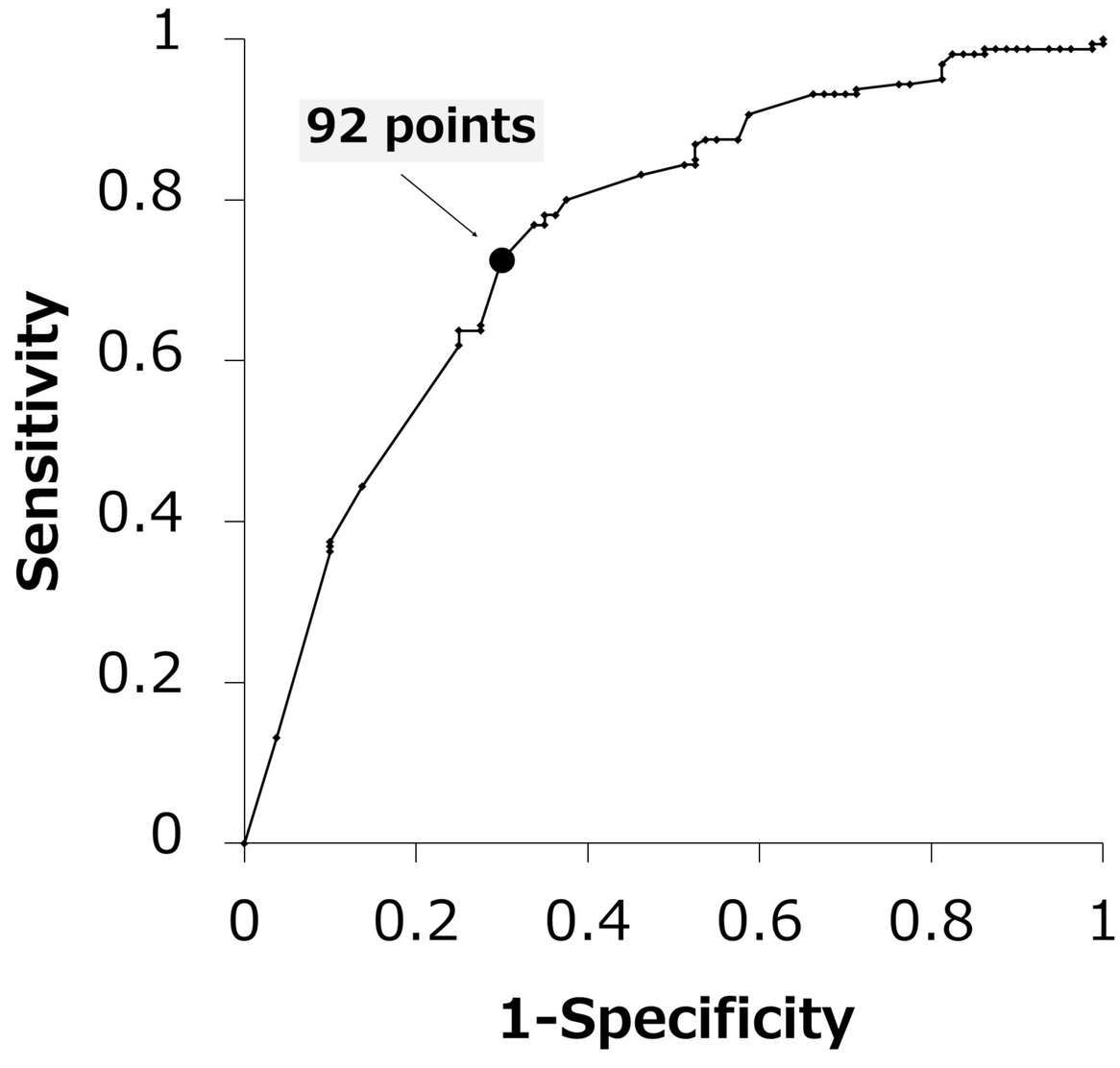
1-Specificity

b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Sensitivity
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Table 1

Clinical characteristics, gait speed, and life-space mobility of patients with and without MCI.

	Non-MCI group (n=160)	MCI group (n=80)	t, χ^2, or Z value	p value
Age (years)	63.5 ± 11.7	76.3 ± 9.2	0.51	<0.001
Male sex, n (%)	134 (84)	58 (73)	4.22†	0.04
BMI (kg/m^2)	24.4 ± 3.8	22.5 ± 3.4	0.23	<0.001
Diagnosis, n (%)			3.23†	0.20
Acute myocardial infarction	110 (69)	47 (59)		
Acute coronary syndrome	6 (4)	2 (3)		
Angina	44 (28)	31 (39)		
Significant coronary artery stenosis, n (%)			0.40†	0.82
1-vessel disease	81 (51)	41 (51)		
2-vessel disease	48 (30)	26 (33)		
3-vessel disease	31 (19)	13 (16)		
Treatment, n (%)			3.96†	0.047
PCI	146 (91)	66 (83)		

Medication	14 (9)	14 (18)		
LVEF (%)	51.8 ± 10.7	52.9 ± 13.8	0.08	0.20
Laboratory data				
Maximum CK-MB (IU/L)	169.0 ± 204.7	125.7 ± 161.4	0.09	0.18
Hemoglobin (g/dL)	13.0 ± 1.7	12.1 ± 1.8	3.92*	<0.001
eGFR (mL/min/1.73 m^2)	55.8 ± 21.2	47.5 ± 19.9	0.21	0.001
Albumin (g/dL)	3.6 ± 0.5	3.4 ± 0.4	3.08*	0.002
HbA1c (%)	6.5 ± 1.5	6.5 ± 1.1	0.06	0.33
Comorbidities, n (%)				
Hypertension	78 (49)	47 (59)	2.14†	0.14
Dyslipidemia	80 (50)	32 (40)	2.14†	0.14
Diabetes	63 (39)	37 (46)	1.04†	0.31
Chronic respiratory disease	1 (1)	2 (3)	1.52†	0.22
Orthopedics disease	22 (14)	15 (19)	1.02†	0.31
Medications, n (%)				
ACE inhibitor	79 (49)	36 (45)	0.41†	0.52
ARB	48 (30)	24 (30)	0†	1
β-blocker	136 (85)	59 (74)	4.43†	0.04

Nitrates	21 (13)	5 (6)	2.61†	0.11
Calcium antagonist	35 (22)	18 (23)	0.01†	0.91
Anticholinergics	0 (0)	0 (0)		
Benzodiazepines	7 (4)	9 (11)	4.05†	0.04
Analgesics	11 (7)	7 (9)	0.27†	0.60
Educational background				
>13 years (%)	66 (41)	14 (18)	13.54†	<0.001
MoCA-J (points)	28.0 ± 1.3	21.6 ± 2.9	0.82	<0.001
Living alone (%)	35 (22)	15 (19)	0.32†	0.57
Gait speed (m/s)	1.1 ± 0.2	0.8 ± 0.2	0.54	<0.001
LSA (points)	97.3 ± 18.1	78.4 ± 22.1	0.42	<0.001

Date are presented as mean ± standard deviation or number (%).

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; CK-MB, creatine kinase-myocardial band; eGFR, estimated glomerular filtration rate; LSA, Life-Space Assessment; LVEF, left ventricular ejection fraction; MCI, mild cognitive impairment; MoCA-J, Japanese version of the Montreal Cognitive Assessment; PCI, percutaneous coronary intervention.

* t value, † χ^2 value.

Table 2

Univariate and multivariable logistic regression analysis of patients with MCI.

Variable	Univariate model		Multivariable model	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.12 (1.08-1.16)	<0.001	1.08 (1.04-1.12)	<0.001
Male sex	0.51 (0.27-0.98)	0.042		
BMI	0.86 (0.79-0.93)	<0.001		
Treatment	0.45 (0.20-1.00)	0.051		
Hemoglobin	0.74 (0.63-0.87)	<0.001		
eGFR	0.98 (0.97-0.99)	0.005		
Albumin	0.39 (0.21-0.72)	0.003		
β-blocker	0.50 (0.26-0.96)	0.037		
Benzodiazepines	2.77 (0.99-7.74)	0.052		
Gait speed	0.001 (0.0002-0.008)	<0.001	0.007 (0.0009-0.06)	<0.001
LSA	0.95 (0.94-0.97)	<0.001	0.98 (0.96-0.999)	0.038

BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; LSA, Life-Space Assessment; MCI, mild cognitive impairment; OR, odds ratio.

Logistic regression analyses were conducted with MCI present/MCI absent as the dependent variable. Clinical characteristics, gait speed, and LSA were included as independent variables. The multivariable model was developed by forward stepwise variable selection.