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ORIGINAL ARTICLE

Influence of mild cognitive impairment on activities of daily living in patients with cardiovascular disease

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Abstract

Activities of daily living (ADL) are maintained in patients with mild cognitive impairment (MCI), but, in patients with cardiovascular disease, ADL may have already declined. MCI combined with cardiac disease may accentuate the decline of ADL in these patients. Because the relationship between MCI and ADL in patients with cardiovascular disease is unclear, we examined the associations between MCI and ADL in these patients. We conducted a cross-sectional study of 114 patients with cardiovascular disease but without probable dementia. MCI was estimated with the Japanese version of the Montreal Cognitive Assessment (MoCA-J). We classified patients into the normal cognitive group and MCI group, and compared their clinical characteristics, physical function [Short Physical Performance Battery (SPPB), gait speed, handgrip strength, and knee extensor muscle strength], and ADL [via the Functional Independence Measure (FIM)]. We used logistic regression analysis to evaluate the specific association between MCI and ADL. The incidence of MCI was 36.0%. Significant differences between the two groups were identified for age, body mass index, estimated glomerular filtration rate, albumin, dyslipidemia, educational background, SPPB, gait speed, handgrip strength, and FIM. However, after adjustment for covariates, only FIM was significantly associated with MCI (odds ratio 0.74, 95% confidence interval 0.65–0.84, $p < 0.001$). ADL was the only independent factor significantly associated with MCI in patients with cardiovascular disease. ADL may be hindered in these patients, even at an early stage of MCI. Therefore, early intervention is necessary to prevent ADL decline from the time of MCI onset or before.

Keywords Mild cognitive impairment · Activities of daily living · Cardiovascular disease · Montreal cognitive assessment · Physical function

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Introduction

Japan's average life expectancy is now the highest in the world [1]. In addition, the numbers of elderly patients with heart disease and with dementia in Japan are increasing and are becoming public health problems [2, 3]. Dementia is becoming a progressively widespread problem, especially in elderly people. Cognitive impairment is generally defined as a decline in memory functions, and the seriousness of the impairment can range from mild cognitive impairment (MCI) to dementia.

Worldwide, MCI is thought to be a transitional state between the normal declines in cognitive function that occurs with aging and dementia [4]. Worldwide, 5–10% of healthy elderly people with MCI will develop dementia [5]. Aging, low educational background, hypertension [6], and cardiovascular disease [7, 8] are reported as risk factors for MCI. Cardiovascular disease is strongly associated with cognitive dysfunction: 55.6% of patients with acute myocardial infarction are reported to develop it [9]. Cerebral hypoperfusion [10], reduced hippocampal volume [11], and increased formation if senile plaques in cerebral cortical areas [12] are also associated with the cognitive impairment occurring with cardiovascular disease. Moreover, cognitive dysfunction in patients with heart disease is associated with increased short-term progression to death and hospital readmission [13], functional disability [14], reduced adherence to self-care behaviors [15], and decline in the quality of life [16].

The most commonly utilized criteria for MCI indicate that activities of daily living (ADL) such as dressing, eating, toileting, and transfers are maintained in patients with MCI [17]; however, instrumental activities of daily living (IADL) such as using public transportation, managing finances, or shopping are impaired in these patients [18]. ADL are considered low-demanding activities that include self-maintenance skills, whereas IADL are considered more complex instrumental functions that require more complex consideration [19]. Nevertheless, ADL may involve many processes, from perception to cognition, instead of simple motor output only. Moreover, in patients with cardiovascular disease, it is reported that physical function and cognitive function have already declined [20–22] and that decreased physical function and cognitive function itself can lead to ADL impairment [23].

In this way, patients with cardiovascular disease are at high risk for the decline of ADL, and ADL of these patients may be hindered even at an early stage of MCI. However, the relationship between MCI and ADL in patients with cardiovascular disease is unclear. Thus, we hypothesized that ADL would decline in MCI patients with cardiovascular disease and that ADL would be associated with MCI in these patients. The purpose of the present study was, thus, to examine the associations between MCI and ADL in these patients.

Methods

Study population

The present cross-sectional study comprised 916 consecutive patients with coronary artery disease (CAD) with acute myocardial infarction, acute coronary syndrome, and unstable and stable angina who were admitted to the Sakakibara Heart Institute of Okayama from May 2018 to December 2018. Of these patients, those who underwent rehabilitation and were admitted for more than 2 days, except those admitted for 1 night and 2 days for percutaneous coronary intervention were included. Exclusion criteria included patients who did not give informed consent, underwent coronary artery bypass surgery, had mental disease (schizophrenia, bipolar disorder, and intellectual disability), experienced a cerebral vascular accident, could not walk without total assistance, had probable dementia as indicated by a Mini-Mental State Examination (MMSE) score below 24 [24, 25], and died in hospital.

Clinical characteristics of the patients

Medical records were retrospectively reviewed to collect data on the clinical characteristics of the patients. Baseline characteristics assessed included age, sex, body mass index (BMI), educational background (categorized as > 13 years), diagnosis, the number of significant stenosis of the coronary arteries ($\geq$ 75%; especially left main trunk, $\geq$ 50%), treatments, left-ventricular ejection fraction (LVEF) as calculated with the Simpson method for cardiac echocardiography, maximum creatine kinase-myocardial band (CK-MB), estimated glomerular filtration rate (eGFR), serum albumin levels, comorbidities, and medications. Laboratory and cardiac echocardiography data were evaluated just prior to patient discharge.

Measurement of cognitive function

The Japanese version of the Montreal Cognitive Assessment (MoCA-J) [26] and the MMSE were used to measure cognitive function in the patients [24, 25]. Assessments of cognitive function were conducted by a physical therapist at the time of discharge, when the patients were in a stable general condition, and which was approximately 2 weeks after hospital admission or the percutaneous coronary intervention.

The MoCA-J is used to screen persons with MCI and was reported to have a sensitivity of 93% and specificity of 87%

in finding MCI [26]. Multiple cognitive domains are measured by the MoCA-J, which include visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. An MoCA-J cut-off point of 26 was previously used to define MCI [26], and thus, we defined patients with MCI as having an MoCA-J score < 26 and those with normal cognitive function as having an MoCA-J score ≥ 26.

Although the MMSE is used globally as a screening tool for dementia [25], it is not sensitive enough to discover early cognitive decline associated with MCI [27]. Thus, we used the MMSE as a means to select the patients with probable dementia, who were then excluded. A MMSE cut-off score of < 24 was used to define probable dementia [25].

Measurement of ADL

ADL was measured with the Functional Independence Measure (FIM). The FIM is an 18-item instrument reflecting the ADL of patients with disabilities [28]. It is divided into the motor domain (13 items: eating; grooming; bathing; dressing upper body; dressing lower body; toileting; bladder management; bowel management; transfer to bed, chair, or wheelchair; transfer to toilet; transfer to tub or shower; walking/wheelchair; and stairs) and the cognitive domain (5 items: comprehension, expression, social interaction, problem solving, and memory). The FIM's 7-point ordinal scale indicates the burden of care, with 1 point indicating total assistance; 2 points, maximal assistance; 3 points, moderate assistance; 4 points, minimal contact assistance; 5 points, supervision; 6 points, modified independence; and 7 points, complete independence. The FIM score ranges from a minimum of 18 points to a maximum of 126 points. A physical therapist measured the FIM at the time of discharge.

Measurement of physical function

The Short Physical Performance Battery (SPPB), gait speed, handgrip strength, and knee extensor muscle strength were used as indices of physical function. All physical function assessments were measured by a physical therapist from the time of discharge.

The SPPB is a physical ability test that assesses the ability to balance, 4-m walking time, and time required to stand-up over five repetitions [29]. Test scores range from 0 points (inability to complete the task) to 4 points (highest level of performance), and the sum of the scores (0–12 points) was measured.

To measure gait speed, patients performed two 4-m gait trials at their usual walking pace on a flat floor. Gait speed is calculated as the time taken (s) to complete the 4-m distance (m/s). The highest speed from the two trials was used in this study [30].

Handgrip strength was measured with a grip strength dynamometer (T.K.K.5401; Takei Scientific Instruments Co., Ltd., Niigata, Japan). Patients were seated in a chair with the dynamometer set at the second grip position (patients' shoulders neutral and elbows at 90° flexion, and forearms neutral in supination/pronation) to avoid the Valsalva effect. The higher of two measured values was recorded, and the right- and left-hand values were averaged to obtain the handgrip strength (kg) in this study [30].

Knee extensor muscle strength was measured with a hand-held dynamometer (μ-Tas F-1; ANIMA Co., Ltd., Tokyo, Japan). After the patient assumed a seated position on a chair, the sensor pad was attached to the front of the patient's distal lower leg, and the length of the belt was adjusted with the knee and hip at 80–90° of flexion. Maximum knee extension muscle strength was measured for approximately 5 s to avoid a Valsalva effect. Two measurements were taken, and the highest value (kg) normalized to body weight (kgf/kg) for the right and left leg was used in this study [30].

Statistical analysis

Patient characteristics and measured outcomes are shown as percentages for the categorical variables and as the mean ± standard deviation for the continuous variables. Unpaired *t* tests, Welch tests, Mann–Whitney *U* tests, and Chi-square tests were used to evaluate differences in patients' characteristics and in measured outcomes between the MCI and normal cognitive function groups.

The relation between MCI and ADL was clarified with logistic regression analysis, with the dependent variable being MCI and the independent variables being patient characteristics, physical function, and ADL. The factors that were characteristics of the patients, as guided by significant findings on univariate analyses, were the covariates entered.

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

This study was approved by the Sakakibara Heart Institute of Okayama Ethics Committee (Approval No. A2018-0401), and informed consent was obtained from each patient. The present study complied with the principles of the Declaration of Helsinki regarding investigations in human subjects.

Results

Clinical characteristics

A flowchart of patients included in this study is shown in Fig. 1. Of the 916 consecutive patients with CAD, 307 met the inclusion criteria, but 193 patients were subsequently excluded due to the reasons, as shown in Fig. 1. Therefore, 114 patients were ultimately included in our final analysis and were divided into the normal cognitive function group and MCI group.

In this study, 73 patients (64.0%) were included in the normal cognitive function group and 41 patients (36.0%) in the MCI group. The patients' clinical characteristics can be compared between the two groups in Table 1. Compared to the patients in the normal cognitive function group, those in the MCI group were significantly older and had a lower BMI, lower eGFR, lower serum albumin levels, lower dyslipidemia, lower educational background, lower MoCA-J, lower SPPB, slower gait speed, lower handgrip strength, lower FIM score, and lower motor and cognitive FIM scores ($p < 0.05$).

Relationship between MCI and ADL

The results of the logistic regression analysis are shown in Table 2. After significant independent variables and covariates were identified in the univariate analysis, the multivariate analysis showed only FIM to be associated with MCI after adjustment for covariates (odds ratio 0.74, 95% confidence interval 0.65–0.84, and $p < 0.001$).

Discussion

This is the first study, to our knowledge, to show an association between MCI and ADL in patients with cardiovascular disease. ADL was found to be significantly associated with MCI in patients with cardiovascular disease after adjustment for covariates.

The incidence of MCI in Japanese community-dwelling older adults reported in one study was 18.8% [31], whereas, in our cohort, the incidence of MCI was 36.0%. A possible explanation for the higher incidence in the present study is that patients with cardiovascular disease are at high risk for MCI. The incidence of dementia was reported to be higher in cardiovascular disease patients [32], and another study reported that CAD may lead to dementia, because it was found to be associated with small vessel disease in the brain [33]. Thus, our cohort may have included patients with a relatively high risk of MCI.

The MCI patients with cardiovascular disease were significantly older and had a lower BMI, lower eGFR, lower serum albumin levels, lower dyslipidemia, lower educational background, and lower MoCA-J than those in the normal

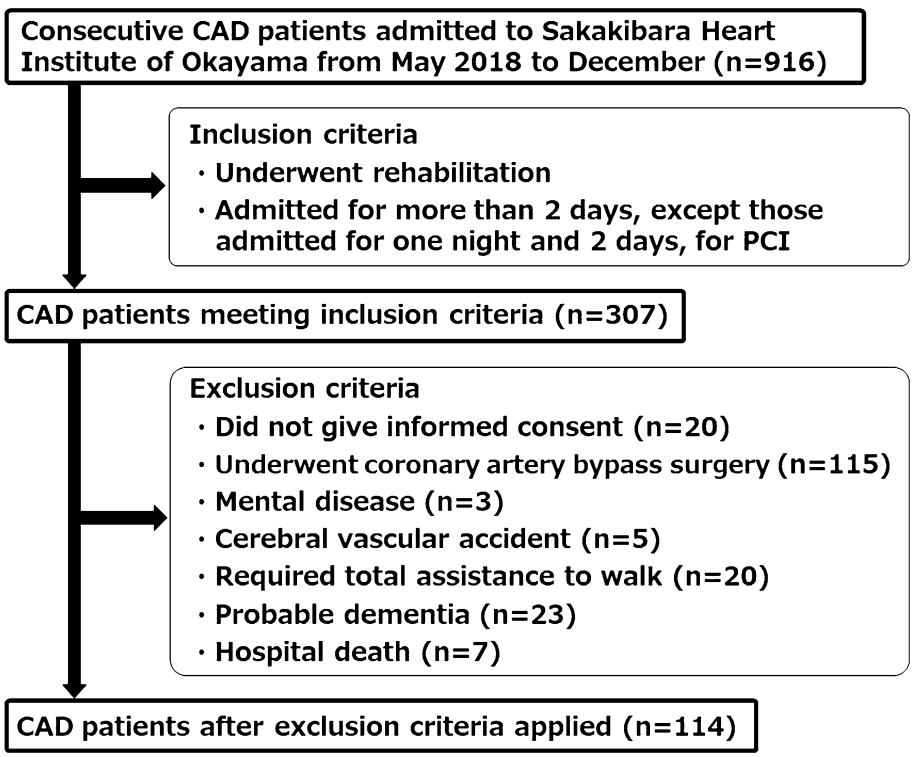

Fig. 1 Flowchart of patient selection. *CAD* coronary artery disease, *PCI* percutaneous coronary intervention

Table 1 Patients' characteristics in the normal cognitive function group and MCI group

	Normal cognitive function group ($n=73$)	MCI group ($n=41$)	t, χ^2, Z value	p value
Age (years)	65.8 ± 11.4	75.7 ± 10.6	0.43	< 0.001
Male [n (%)]	63 (86)	32 (78)	1.29	0.26
BMI (kg/m^2)	24.8 ± 4.0	22.9 ± 3.9	0.22	0.02
Diagnosis [n (%)]			0.47	0.79
Acute myocardial infarction	37 (51)	21 (51)		
Acute coronary syndrome	6 (8)	2 (5)		
Angina	30 (41)	18 (44)		
Significant stenosis of the coronary arteries [n (%)]			0.15	0.93
1-vessel disease	36 (49)	19 (46)		
2-vessel disease	23 (32)	13 (32)		
3-vessel disease	14 (19)	9 (22)		
Treatment [n (%)]			< 0.01	0.95
Percutaneous coronary intervention	62 (85)	35 (85)		
Medication	11 (15)	6 (15)		
LVEF (%)	53.5 ± 10.2	54.0 ± 13.6	0.07	0.46
Laboratory data				
Maximum CK-MB (IU/L)	119.9 ± 178.1	108.2 ± 138.5	0.02	0.87
eGFR (mL/min/1.73 m^2)	52.9 ± 21.7	43.6 ± 20.1	0.23	0.01
Albumin (g/dL)	3.6 ± 0.5	3.4 ± 0.4	2.04	0.04
Comorbidities [n (%)]				
Hypertension	40 (55)	23 (56)	0.02	0.89
Dyslipidemia	42 (58)	15 (37)	4.61	0.03
Diabetes	31 (43)	16 (39)	0.13	0.72
Medication [n (%)]				
ACE inhibitor	33 (45)	20 (49)	0.14	0.71
ARB	26 (36)	13 (32)	0.18	0.67
β-blocker	59 (81)	30 (73)	0.90	0.34
Diuretics	18 (25)	15 (37)	1.82	0.18
Calcium antagonist	20 (27)	11 (27)	< 0.01	0.95
Anticholinergics	0 (0)	0 (0)		
Benzodiazepines	6 (8)	7 (17)	2.04	0.15
Analgesics	4 (5)	1 (2)	0.58	0.45
Education background				
> 13 years (%)	29 (40)	6 (15)	7.77	0.005
MoCA-J (points)	27.7 ± 1.4	22.0 ± 2.6	0.83	< 0.001
Physical function				
SPPB (points)	11.6 ± 1.0	10.2 ± 2.3	0.44	< 0.001
Gait speed (m/s)	1.1 ± 0.2	0.8 ± 0.2	0.45	< 0.001
Handgrip strength (kg)	30.9 ± 9.0	23.6 ± 8.2	4.29	< 0.001
Knee extensor muscle strength (kgf/kg)	0.5 ± 0.2	0.4 ± 0.2	1.67	0.10
ADL				
FIM score (points)	123.5 ± 3.9	116.2 ± 6.7	0.66	< 0.001
Motor FIM score (points)	89.1 ± 3.2	85.9 ± 5.6	0.43	< 0.001
Cognitive FIM score (points)	34.4 ± 1.2	30.3 ± 2.2	0.78	< 0.001

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

MCI mild cognitive impairment, *BMI* body mass index, *LVEF* left-ventricular ejection fraction, *CK-MB* creatine kinase-myocardial band, *eGFR* glomerular filtration rate, *ACE* angiotensin-converting enzyme, *ARB* angiotensin receptor blocker, *MoCA-J* Japanese version of the Montreal Cognitive Assessment, *SPPB* short physical performance battery, *ADL* activities of daily living, *FIM* functional independence measure

Table 2 Univariate and multivariate analyses for the association between MCI and ADL in patients with cardiovascular disease

Variable	Univariate model		Multivariate model	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.09 (1.04–1.14)	< 0.001		
BMI	0.88 (0.78–0.98)	0.99	0.89 (0.77–1.02)	0.09
eGFR	0.98 (0.96–1.00)	0.03		
Albumin	0.41 (0.17–0.99)	0.047		
Dyslipidemia	0.43 (0.19–0.94)	0.03		
SPPB	0.53 (0.37–0.75)	< 0.001		
Gait speed	0.01 (0.001–0.08)	< 0.001		
Handgrip strength	0.91 (0.87–0.96)	< 0.001		
FIM	0.73 (0.64–0.83)	< 0.001	0.74 (0.65–0.84)	< 0.001

cognitive function group. These findings largely agreed with the characteristics of patients with MCI who were readmitted to hospital in the previous studies [6, 34–36]. In past studies, it was reported that aging [6], low nutrient states [34, 35], renal impairment [36], and educational background [6] were associated with MCI. Therefore, it may be possible to partly generalize the characteristics of the MCI patients with cardiovascular disease.

The MCI patients with cardiovascular disease had significantly lower SPPB, slower gait speed, lower handgrip strength, lower FIM, and lower motor and cognitive FIM scores than those in the normal cognitive function group. It was reported that physical function correlates closely with cognitive function [37–39]. In past studies, low moving ability [37, 38] and low handgrip strength [39] were correlated with cognitive decline, and patient frailty and cognitive decline were reported as causative factors of the decline in ADL [40]. Thus, physical function and ADL of the MCI patients with cardiovascular disease were lower than those with normal cognitive function.

ADL was an independent predictor of MCI in this study. Recently, other studies have investigated the relationship between ADL and the early continuum of cognitive decline [41]. Moreover, we measured ADL using the FIM, which is divided into motor and cognitive domains [28]. In the present study, the MCI patients with cardiovascular disease had lower moving ability and lower handgrip strength, and these declines in physical function influenced the motor domain of the FIM. Furthermore, the items in the cognitive domain in the FIM require advanced cognitive functions. The characteristics of MCI patients were reported to be deterioration of memory, attention, and cognitive function beyond what would be expected based on patient age and educational background [42]. Thus, these findings could explain why ADL was strongly associated with MCI in the present study.

The meaning of the association found between ADL and MCI was that simple ADL could be affected by the slight cognitive deficits usually found at the MCI stage. It was reported that IADL require more complex neuropsychological processing capacity than simple ADL [43], and IADL can be impaired before the onset of dementia and should, therefore, be included in the diagnosis of MCI [44]. However, simple ADL can be impaired at the MCI stage in patients with cardiovascular disease. Thus, our results agree with the conceptualization that motor activity as a complex activity involves many processes from perception to cognition, instead of simple motor output alone [45]. Moreover, it was reported that microvascular brain pathology was associated with motor impairment late in life [46], and brain imaging studies have also linked nonspecific white matter hyperintensities, commonly thought of as surrogates for small vessel disease, with impaired physical functioning and disability [47, 48]. In this way, MCI could interfere with the execution of simple ADL in patient with cardiovascular disease.

The present study has several clinical implications. Early diagnosis of MCI in the daily clinical setting is difficult. Thus, we should consider the presence of MCI in patients with cardiovascular disease showing a decline in ADL. Moreover, ADL may be hindered in these patients, even at an early stage of MCI. Therefore, early intervention is necessary to prevent ADL decline from the time of MCI onset or before.

There are several limitations in this study. This was a single-center cross-sectional study with a small sample size. Because of the strict inclusion and exclusion criteria, only 13% (114/916) of the hospitalized patients with cardiovascular disease could be enrolled as study subjects. Thus, generalizability of the results may be limited. Regarding cognitive function assessment, the setting for the assessment of cognitive function assessment may not have been the most appropriate, especially considering that the patients had previously undergone percutaneous coronary intervention, which is a potentially stressful event that can cause anxiety. Second, the assessment of cognitive function was limited to a single screening tool, and the evaluation was performed by a nonspecialist. Usually, a complete battery of neuropsychological tests is performed for a full diagnosis of MCI.

Moreover, we did not evaluate whether the MCI patients had amnesia. Third, no imaging data were analyzed. Regarding ADL assessment, we measured ADL using the FIM, which is a common scale used to evaluate ADL. However, because the FIM includes a cognitive section, using the FIM to evaluate the associations between MCI and ADL might have affected our results. Moreover, the reason for the association between MCI and ADL decline remains unclear. Furthermore, the influence of changes in factors such as cognitive function and ADL over time is unknown. Thus, these issues remain to be resolved in future studies.

Conclusions

ADL was the only independent factor significantly associated with MCI in patients with cardiovascular disease. Because ADL may be hindered in these patients even at an early stage of MCI, early intervention is necessary to prevent a decline in ADL from the time of MCI onset or before.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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