—Original—

Use of the Japanese Version of the Montreal Cognitive Assessment to Estimate Cognitive Decline in Patients Aged 75 Years or Older with and without Type 2 Diabetes Mellitus

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Background: The number of people diagnosed with dementia worldwide is set to increase significantly. Patients with dementia often have comorbidities, particularly diabetes, and patients with type 2 diabetes mellitus (T2DM) have a high risk of cognitive decline. This study investigated whether older people with T2DM have disease-specific cognitive deficits.

Methods: The Montreal Cognitive Assessment is a well-known tool for examining mild cognitive impairment, and the modified Japanese version (MoCA-J) has been confirmed as effective. Using the MoCA-J, we assessed the cognitive function of Japanese adults aged ≥75 years with and without T2DM and analyzed the results.

Results: Thirty-three patients with T2DM and 23 non-DM patients completed the examination, and MoCA-J total scores differed between these groups (T2DM mean, 21.4 ± 3.5; non-DM mean, 23.5 ± 3.6). Only 9% of patients with T2DM and 39% of those with non-DM had scores ≥26, which is the cutoff point for mild cognitive impairment, although all patients were capable of self-care. Additionally, delayed recall scores were significantly lower for the older patients with T2DM had for the non-DM group.

Conclusions: Patients aged ≥75 years with T2DM might have worse cognition than those without T2 DM; the inability to perform delayed recall in T2DM patients suggests a decline in cognitive function. Therefore, patients aged ≥75 years with T2DM should receive explanations of their care that are individualized in relation to their cognitive status. (J Nippon Med Sch 2022; 89: 196–202)

Key words: Montreal Cognitive Assessment, elderly, type 2 diabetes mellitus

Introduction

The aging population rate is projected to increase worldwide by 17.8% by 2060 and will continue to rise significantly in the latter half of the 21st century[1]. In addition, the total number of people with dementia is projected to reach 82 million by 2030 and 152 million by 2050[2]. In Japan, 1 of 4 Japanese will be 75 years or older in 2025[3]. The number of people diagnosed with dementia is >4 million in Japan and is predicted to be 7 million by 2025. Furthermore, the number of older people with mild cognitive impairment (MCI) is estimated to be approximately 3.8 million[4] and is expected to continuing rising.

Diabetes is a common comorbidity for people living with dementia, and previous studies have shown that type 2 diabetes mellitus (T2DM) tends to accelerate cognitive decline[5–7]. Patients with diabetes who were hospi-

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talized for hypoglycemia had significantly lower scores on the Mini-Mental State Examination (MMSE) than did their peers without diabetes[8]. The MMSE has been used as a dementia-screening tool worldwide; however, it has been suggested that it is challenging to use the MMSE to identify MCI[9]. Therefore, a tool that can quickly identify MCI in clinical settings is desirable.

The Montreal Cognitive Assessment (MoCA) tool was developed by Nasreddine et al[10] and appears to be better than the MMSE for detecting MCI in middle-aged and older persons with T2DM[11]. Thus, the traditional method for diagnosing cognitive impairment with the MMSE may need to be replaced by MoCA screening to effectively identify affected persons with T2DM in the community[11]. The Japanese version of the MoCA (MoCA-J) was reported to have high sensitivity and specificity, making it an effective tool[12]. A systematic review indicated that patient nonadherence was associated with dementia, which was comorbid with T2DM[13]. However, it remains unclear whether a low MoCA-J score in patients with T2DM is associated with poor activities of daily living in those patients. Therefore, this study investigated whether MoCA-J total score and subdomain scores were relevant in assessing cognitive function and whether, among the comorbidities common in older people, T2DM most affects cognitive function. Furthermore, using the MoCA-J, we sought to investigate whether older people with T2DM had specific deficits in subdomain scores, as compared with patients without T2DM.

Materials and Methods

This study reviewed data from 1,668 patients with diabetes and nondiabetic diseases who were treated by 3 physicians at outpatient clinics in the Departments of Endocrinology, Nephrology and Cardiovascular Medicine of a medical school hospital in Chiba, Japan. T2DM was diagnosed according to the report of the committee on the classification and diagnostic criteria of diabetes mellitus by the Japan Diabetes Society[14,15]. The eligibility criteria were as follows: age 75 years or older, self-reliance in daily living, and use of Japanese as a first language.

To establish a rationale for using the MoCA-J, the content of the MoCA-J had to be written in a language that patients could understand. Thus, the MoCA-J was utilized as a tool for examining cognitive function. All eligible patients were individually recruited to participate in the study by their doctors at a routine clinic visit. The exclusion criteria were age <75 years, dependence on others for activities of daily living, and refusal to participate in the present research. These conditions (e.g., those with psychiatric disease, personality disorders, and unstable medical conditions) are not examples of declining to participate in the study. A researcher who is a member of the dementia patient support team in the hospital and a certified gerontological nursing specialist experienced in examining patients using the MoCA-J explained the study purpose to the participants and indicated that participation was voluntary. Written informed consent was obtained from all participants. In the period between March 2019 and March 2020, the researcher examined the patients individually using the MoCA-J in a private space, and the results were recorded as data.

During the study, 3 patients were newly diagnosed with dementia and were excluded (**Fig. 1**). Participant characteristics are shown in **Table 1**. HbA1c levels were determined with a high-performance liquid chromatography instrument (HLC723 G8; Tosoh, Co., Tokyo, Japan) and presented as the equivalent National Glycohemoglobin Standardization Program values. The formula established by the Japanese Society of Nephrology was used to calculate estimated glomerular filtration rate (eGFR)[16]. Complications of T2DM are shown in **Table 1** and include retinopathy (ophthalmologists performed fundoscopy after pupillary dilatation to diagnose retinopathy), as determined in accordance with the Davis classification, as follows: no diabetic retinopathy, simple diabetic retinopathy, preproliferative diabetic retinopathy, and proliferative diabetic retinopathy, including panretinal photocoagulation. Nephropathy was classified according to the Classification of Diabetic Nephropathy 2014 as Stage 1, urinary albumin excretion (UAE) <30 mg/g creatinine; Stage 2, UAE 30-299 mg/g creatinine; Stage 3, UAE ≥300 mg/g creatinine; Stage 4, estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2; and Stage 5, dialysis therapy. We calculated MoCA-J total and subdomain scores of the patients. The collected data were examined with the Student t-test and Wilcoxon test, and statistical significance was defined as $P < 0.05$. Statistical analyses were performed using JMP version 11. This study was approved by the Clinical Ethics Committee of Nippon Medical School, Tokyo, Japan (Approval No. 733-2).

Results

A total of 33 patients with T2DM and 23 patients with non-DM completed the examination. The patients had a mean age of 80.1 ± 4.5 years and included 35 men and 21 women. Patients with T2DM (80.3 ± 4.6 years) were designated as the T2DM group, and patients without T2DM

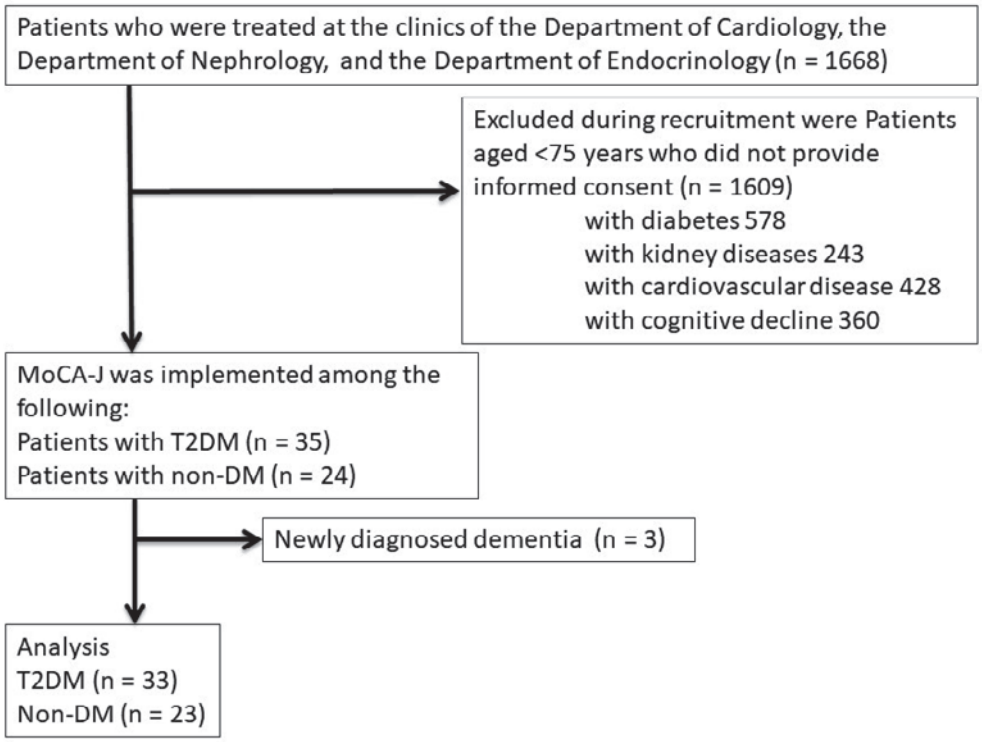

Fig. 1 Recruitment process.
The eligibility criteria were patients aged ≥75 years, patients who could perform daily self-care activities and patients who were Japanese. All patients were treated at the clinics of the Department of Cardiology, the Department of Nephrology, and the Department of Endocrinology of a medical school hospital in Japan.
The exclusion criteria were patients who were <75 years; who could not perform daily self-care activities; who declined to participate because they had dementia, unstable medical condition, psychiatric disease, mental retardation, personality disorder, malignant disease, and inability to understand the Japanese language. A total of 59 participants underwent the Japanese version of the Montreal Cognitive Assessment (MoCA-J). However, patients who were diagnosed with dementia after being recruited were also excluded. Finally, the data that were gathered from 56 participants were analyzed.

(79.9 ± 4.6 years) (e.g., those with congestive heart failure, angina pectoris, nephrotic syndrome) were designated as the non-DM disease group. There were no significant differences in age or eGFR between groups. However, we found a significant difference in body mass index (T2DM mean, 24.9±4.0; non-DM mean, 22.8±2.6) and MoCA-J total score between groups (T2DM mean, 21.4 ± 3.5; non-DM mean, 23.5 ± 3.6) (**Fig. 2**). There were no significant difference between groups in disease duration, HbA1c, number of diabetes complications, or total MoCA-J score (**Table 2, 3**). Furthermore, the total scores for 79% of patients with and without T2DM were lower than the cutoff point of 26 for MCI (median, 23; 75% quartile, 25, 25% quartile, 20; 95% confidential interval, 23.32-21.31). While only 9% of patients with T2DM had scores ≥26, 39% of patients without T2DM exceeded this threshold. We analyzed the cognitive domains assessed by the MoCA-J by using the following subdomains: visuospatial executive function, naming (3 animals), attention (forward order, backward order, tap with one's hand, calculation), language (repeat, fluency), abstractions, delayed recall, and orientation (**Table 2**). Although most subdomain scores were not statistically different between the T2DM and non-DM groups, delayed recall scores were significantly lower for the T2DM group than for the non-DM group (T2DM mean, 1.2±1.3; non-DM mean, 2.7 ±1.8; p <0.05; **Fig. 3**). In addition, patients with T2DM who were not receiving insulin therapy had significantly lower delayed recall scores than did those receiving insulin therapy (**Table 3**).

Discussion

Using the MoCA-J, we examined whether decline in cognition function differed between patients with and without T2DM. The results showed 2 significant findings. First, total scores were significantly lower in T2DM pa-

Table 1 Baseline characteristics (n = 56)

	T2DM (n = 33)	nonDM (n = 23)	p value*
Age (years)	80.3±4.6	79.9±4.6	0.7
Male/female	21/12	14/9	0.8
HbA1c	7.1±0.7	5.8±0.2	< 0.05**
estimated Glomerular Filtration Rate	51.0±20.4	40.9±22.7	0.08
BMI	24.9±4.0	22.8±2.6	< 0.05**
period of T2DM	19.6±14.71	0	
Agents (%)			
Antihypertensives would include:			
-Ca-antagonist	69.6	43.4	
-ARB	48.4	26.0	
-β-blocker	6.0	4.3	
-Anticoagulant	42.4	21.7	
-Diuretics	3.0	4.3	
-HMG-CoA reductase inhibitor	39.9	26	
Glucose-lowering agents would include:			
-DPP-4 inhibitor	42.4	0	
-Metformin	24.2	0	
-SGLT2	3.0	0	
-Sulfonylurea	3.0	0	
-Glinide	3.0	0	
-Insulin	57.5	0	
diabetic complications (n)			
with/without	31/2		
neuropathy	4		
retinopathy	15		
>stage2	15		

*p-value < 0.05 Values are expressed as means ± SD

**HbA1c and BMI show significant difference between groups with and without T2DM

tients than in non-DM patients. Second, the groups significantly differed in delayed recall, a subdomain of cognitive function estimated by the MoCA-J. In addition, the MoCA-J total scores of 79% of patients with and without T2DM were lower than the cutoff point of 26, which indicates MCI. In MCI, patients do not meet the criteria for dementia and their daily functioning is largely preserved, but they have experienced a change in cognition. The criteria for MCI are objective corroboration of whether function is relatively well preserved and whether the patient meets the criteria for dementia.

MCI can be classified as amnestic or non-amnestic; if MCI is non-amnestic, the clinician needs to determine the cause of the syndrome[17]. A previous study revealed that, as compared to people without diabetes, people with diabetes have a greater rate of decline in cognitive function and a greater risk of cognitive dysfunction[18]. Cognitive dysfunction should therefore be added to the list of chronic complications of diabetes[18]. The Japanese clinical practice guidelines for diabetes 2019 recommend that appropriate glycemic control be focused on ensuring safety, rather than strict glycemic control, in elderly patients with diabetes[15]. Currently, avoiding hypoglycemia is the treatment priority for elderly patients with diabetes, even when they cannot achieve their glycemic target[19]. Therefore, no patient in the present study experienced an episode of hypoglycemia, although we cannot exclude the possibility of asymptomatic hypoglycemia[15]. In the present study, we did not investigate plasma glucose levels in patients with diabetes. Instead, we estimated HbA1c level, which is a more stable index than fasting plasma glucose and is now considered a superior index of chronic hyperglycemia[14]. Although hypoglycemia can hasten cognitive decline in elderly people with diabetes mellitus, the relationship between diabetes and cognitive impairment is complicated and controversial[5,6]. In addition, the Mayo Clinic Study of Aging followed adults aged ≥70 years for a median of 5 years and found that the progression rate of MCI was just 5-6% per year[20]. In our study, it seems extraordinary that 79% of all patients and 61% of patients without DM could be categorized as having MCI. This apparent discrepancy may be attribut-

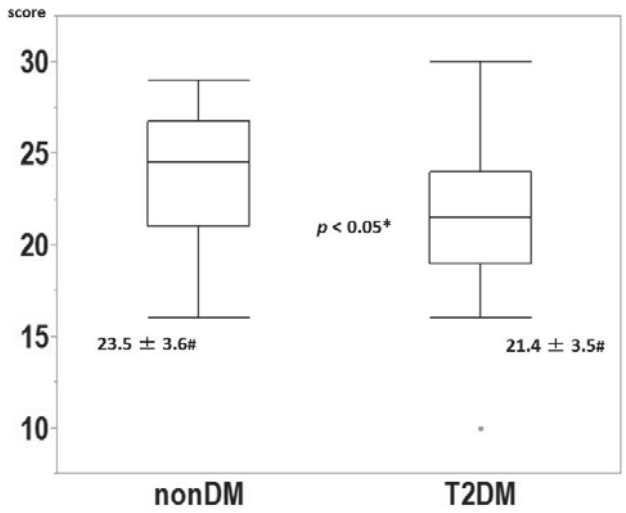

Fig. 2 Total scores of patients with and without type 2 diabetes mellitus (T2DM), estimated using the Japanese version of the Montreal Cognitive Assessment (MoCA-J).
The right side of the box plot indicates the total score for patients with T2DM while the left side is for the non-DM group. The vertical axis shows the MoCA-J total score.
*$p < 0.05$, indicates that there was significant difference between each score.
#Both groups showed total score that were less than the cut-off value, which indicated mild cognitive impairment (T2DM mean, 21.4 ± 3.5; non-DM mean, 23.5 ± 3.6).

able to differences in cognitive function tests. All the present participants were able to perform daily self-care activities, visit the hospital regularly, and cope independently with the process as outpatients. The MoCA-J might thus be able to detect slight derangement of cognitive function[11].

Age-related changes in memory (e.g., episodic, semantic, implicit, explicit, and prospective) and attention (e.g., selective attention, sustained attention, inhibition, and set switching) have been important topics in the field of cognitive aging[21]. One study reported that the discriminatory ability of the MoCA to diagnose MCI was superior to that of the standardized MMSE[21]. Specific difficulties in cognitive domains, like abstraction, executive function (clock drawing), visuospatial function, and delayed 5-word recall in MoCA, appear to make this test a better screening procedure for MCI[11]. That might the reason MoCA-J made a difference between the results of the study. Efforts to extend life expectancy are often addressed by receiving interdisciplinary treatment; that is, patients must understand complicated treatments and choose the most appropriate care by themselves[22]. Although many of the present patients with or without T2 DM had lower-than-normal MoCA-J scores, they were able to comprehend explanations they received regarding their care. Thus, our results suggest that patients aged ≥75 years with T2DM need to receive explanations that are individualized in relation to their cognitive status. Although cognitive impairment is common in patients with T2DM[18], we found no difference in any MoCA-J subdomain score except delayed recall scores between patients with and without T2DM, and between those receiving and not receiving insulin therapy for T2DM. Therefore, most subdomains, except delayed recall, are not specific to T2DM. Several studies of cognitive function have suggested that various subdomains are specifically affected by T2DM. Our results suggest that delayed recall, as estimated by the MoCA-J, is specific to cognitive decline in T2DM. This finding is consistent with the results of a study by Futamura et al[23]. In another study, impaired cognitive function in patients with diabetes was accompanied by reduced cerebral blood flow in the frontotemporal region, as determined by single photon emission computed tomography[24]. The temporal lobe is responsible for retaining memories, and the frontotemporal region is assumed to be responsible for the output of memories. Thus, the significant difference in delayed recall scores between patients with and without T2DM in this study suggests an association with T2DM.

The reason for the significant difference in delayed recall score in relation to receipt of insulin therapy is unclear. In clinical practice, the patient's capacity for self-management is a critical factor in selecting therapy, especially for older patients with T2DM. Daily insulin injections and self-monitoring of blood glucose require good cognitive function, and the result might reflect this. Another possibility is that insulin treatment has beneficial effects on brain function. Additional studies are necessary to test these hypotheses.

Conclusions

In persons aged ≥75 years, cognitive status may be worse in those with T2DM than in those with other chronic illnesses. Furthermore, patients aged ≥75 years with T2DM might have worse delayed recall, a subdomain of cognitive function. Therefore, when managing patients aged ≥75 years with T2DM, their cognitive status should be considered when providing individualized explanations of their care.

Table 2 Montreal Cognitive Assessment-Japanese version total score and subdomain scores in patients with and without Type 2 diabetes

		T2DM	non-DM	p-value
Total score	min/max	10/30	16/29	
mean± SD		21.4±3.5	23.5±3.6	< 0.05*
Total score > 26	n (%)	3 (9.3)	9 (39.1)	
Subdomain/score				
visuospatial executive function/5		3.5±1.0	3.7±1.0	0.3
naming/3		2.8±0.4	2.7±0.5	0.6
attention/5		4.6±1.2	4.8±1.0	0.5
forward order/1		0.9±0.3	0.9±0.2	0.9
backward order/1		0.8±0.3	0.8±0.3	0.6
tap with one's hand/1		0.8±0.3	0.9±0.2	0.3
caluculation/3		2.1±0.9	2.1±0.8	0.8
language/3		1.5±0.7	1.4±0.8	0.6
repeat/2		1.1±0.4	0.9±0.7	0.1
fluency/1		0.3±0.4	0.4±0.5	0.4
abstractions/2		1.8±0.4	1.9±0.2	0.4
delayed recall/5		1.2±1.3	2.7±1.8	< 0.05**
orientation/6		5.7±0.6	5.8±0.4	0.4
educational period Male/female	< 12 years	3/1	2/1	

*Total score showed minimum score and maximum score between T2DM and non-DM, Values are expressed as means ± SD, the ratio of more than 26 score, respectively. MoCA-J consists of the subdomain Scores. Total scores were significant difference between T2DM and non-DM.

**The delayed recall score of the T2DM group was significantly lower than those of non-DM group; the T2DM mean 1.2±1.36, the non-DM mean 2.78±1.80, $p < 0.05$.

Table 3 Montreal Cognitive Assessment-Japanese version total score and subdomain scores in patients with type 2 diabetes, by insulin treatment status

T2DM	insulin injection	non insulin	p-value
Total score min/max	10/30	16/26	
mean± SD	21±0.8	21±0.9	0.5
Sub domain/score			
visuospatial executive function/5	3.4±0.2	3.6±0.2	0.8
naming/3	2.8±0.1	2.8±0.1	0.9
attention/5	4.7±0.3	4.6±0.3	0.9
language/3	1.5±0.1	1.6±0.2	0.7
abstractions/2	1.8±0.1	1.9±1.7	0.7
delayed recall/5	1.8±0.3	0.6±0.3	<0.05***
orientation/6	5.5±0.1	5.7±0.1	0.4

***The delayed recall score of the non-insulin injection group was significantly lower than those of insulin-injection group with T2DM; the insulin injection 1.8±0.3, non-insulin injection 0.6±0.3

Limitations

This study was conducted in only one center, the sample size was small, and healthy older people were not included in the assessment. These limitations could have introduced sampling bias. Studies of larger samples are necessary to confirm our results. Because many factors affect cognitive aging[20], additional studies will be necessary. An ongoing study is investigating cognitive aging using the MoCA-J, including estimation of medication, habits, atherosclerosis, and socioeconomic status.

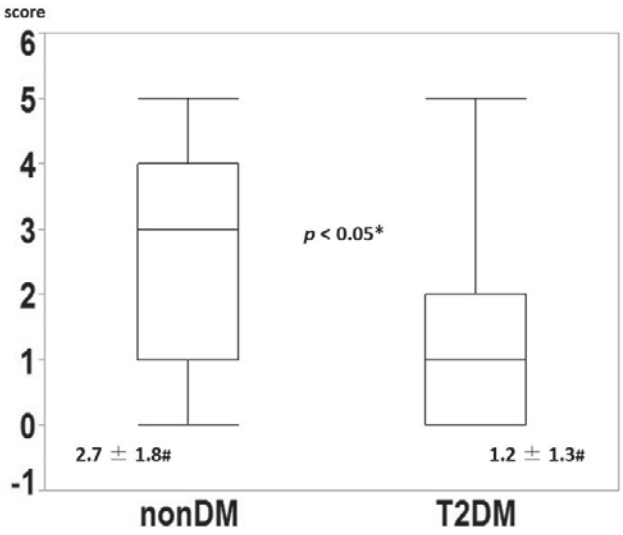

Fig. 3 Delayed recall Scores of patients with and without type 2 diabetes mellitus (T2DM).
*$p < 0.05$, indicating a significant difference between the T2DM and non-DM group. The vertical axis shows the delayed score estimated using the Japanese version of the Montreal Cognitive Assessment (MoCA-J).
#This indicates a delayed score, which is one of the subdomains of cognitive function in the MOCA-J. The mean score for the T2DM group was 1.2, and the standard deviation was 1.3. The mean score for the non-DM group was 2.7, and the standard deviation was 1.8.

Conflict of Interest: The authors declare no conflicts of interest associated with this manuscript.

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