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## Original Article

# Identification of Undetected Dementia and Hypoglycemic Risk Using the Dementia Assessment Sheet for Community-Based Integrated Care System 21-Items in the Glycohemoglobin-Guided Management of Elderly Individuals with Diabetes: An Exploratory Study

Takuma Yasuda<sup>a, #</sup>, Takaaki Murakami<sup>a, b, #</sup>, Yoko Ueba<sup>a</sup>, Haruka Fujita<sup>a</sup>, Masaki Fujimura<sup>a</sup>, Tomonobu Hatoko<sup>a</sup>, Yugo Kanai<sup>a</sup>, Eisaku Mori<sup>a</sup>, Shin Yonemitsu<sup>a</sup>, Shogo Oki<sup>a</sup>, Seiji Muro<sup>a, †</sup>

<sup>a</sup> Department of Diabetes and Endocrinology, Osaka Red Cross Hospital, 5-30 Fudegasaki-cho, Tennoji-ku, Osaka, Japan, <sup>b</sup> Department of Diabetes, Endocrinology and Nutrition, Graduate School of Medicine, Kyoto University, 54 Kawara-cho, Shogoin, Sakyo-ku, Kyoto, Japan

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## SUMMARY

**Background:** Assessing cognitive function and the risk of hypoglycemia among older individuals with diabetes is an ongoing challenge. Although the Japan Diabetes Society/Japan Geriatrics Society Joint Committee has already provided recommendations for glycemic control in older individuals with diabetes, its usefulness in clinical settings remains unclear.

**Methods:** A retrospective, single-center study was conducted on 616 outpatients aged over 65 years at Osaka Red Cross Hospital, Japan. They were assessed for glycemic control and cognitive function using the Dementia Assessment Sheet for Community-based Integrated Care System 21-items (DASC-21). Patients were categorized into three groups based on cognitive function, and each group was divided into six subcategories based on recommended therapeutic regimens.

**Results:** Ninety-eight patients treated with insulin, sulfonylurea, or glinide were identified using DASC-21 and classified into categories IIB and IIIB. The number of hypoglycemic events was divided according to the lower limit of the recommended glycohemoglobin (HbA1c) value. However, the results did not significantly differ. Notably, in 7 of 9 IIIB patients who with hypoglycemic events, their DASC-21 scores reached up to 36. This suggests that the physicians had not identified the risk of dementia before conducting the assessment using DASC-21, which might result in continuous therapy for diabetes including daily multiple insulin injections.

**Conclusions:** Physicians can overlook the risk of hypoglycemia and cognitive impairment thereby failing to optimize diabetic therapies among older individuals if DASC-21 is not used during assessments in daily diabetic care.

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## 1. Introduction

Globally, the aging process in patients with diabetes mellitus has been arduous, and Japan is no exception.<sup>1</sup> Management strategies to reduce the risks of hypoglycemia are urgently needed because the incidence of hypoglycemic events is highest in older diabetic patients.<sup>2</sup> There is a strong correlation between hypoglycemia and cognitive dysfunction.<sup>3</sup> Thus, screening for cognitive decline among older patients is a clinical imperative to prevent hypoglycemic events.

Recently, the Japan Diabetes Society (JDS)/Japan Geriatrics Society (JGS) Joint Committee confirmed the glycemic targets for older individuals with diabetes based on their activities of daily living (ADL), cognitive function, and therapeutic agents.<sup>4</sup> The lower limit of the recommended glycohemoglobin (HbA1c) level was set for patients treated with hypoglycemic agents, such as insulin, sulfonylurea, and glinide, which could exacerbate the risk of hypoglycemia.

The International Diabetes Federation (IDF) has shown that a 7.0% lower limit in HbA1c level can effectively manage older patients with type 2 diabetes.<sup>5</sup>

The Dementia Assessment Sheet for Community-based Integrated Care System 21-items (DASC-21) is a simple, fast, and easy-to-use assessment tool.<sup>6,7</sup> Although the JDS/JGS Joint Committee has recommended its use for the assessment of cognitive function, its clinical efficacy is unclear because of difficulty in suspecting cognitive dysfunction in diabetic clinics.<sup>8</sup>

This study aimed to assess the efficacy of DASC-21 in clinical settings; we focused on investigating the risk of hypoglycemia in patients with substantial cognitive dysfunction who were receiving hypoglycemic agents.

## 2. Methods

### 2.1. Participants

In this retrospective, single-center study, we enrolled all pa-

\* Corresponding author. Department of Diabetes and Endocrinology, Osaka Red Cross Hospital, 5-30 Fudegasaki-cho, Tennoji-ku, Osaka, 5438555, Japan.

E-mail address: [muro@osaka-med.jrc.or.jp](mailto:muro@osaka-med.jrc.or.jp) (S. Muro)

<sup>#</sup> Takuma Yasuda and Takaaki Murakami were equally contributed to this work.

tients aged over 65 years who presented with diabetes and whose cognitive function was assessed at the outpatient clinic of the Department of Diabetes and Endocrinology, Osaka Red Cross Hospital (Osaka, Japan) between March 14 and April 30 in 2017. We recorded sex, age, diagnosis, type and duration of diabetes, laboratory data, C peptide index, self-monitoring blood glucose (SMBG) levels, hypoglycemic agents used, and DASC-21 scores. This study was approved by the ethics committee of Osaka Red Cross Hospital (registry no. 906).

## 2.2. Assessment of cognitive function using DASC-21

DASC-21 comprises 21 individual questions,<sup>6</sup> each on a 4-point scale providing a total score range of 21–84. A higher score indicates worse cognitive impairment, a total score above 31 indicates a risk for dementia, and a score of 3 or 4 in each item indicates impairment. The scores were significantly correlated to the Clinical Dementia Rating.<sup>6,7</sup> We only assessed patients who consented to answer the questions in DASC-21, and patients who responded to all 21 questions were categorized according to the recommendation of the JDS/JGS Joint Committee.<sup>4</sup>

## 2.3. Allocation of patients based on cognitive function and therapeutic agents

Participants were categorized into three and two groups based on their cognitive function and therapeutic agents, respectively (Table 1). Category II patients had a total score above 31 and a score of 1 or 2 in all items concerning remote memory, space orientation, social common sense, and physical ADL. Patients with a total DASC-21 score below 31 but with a score of 3 or 4 in at least one item in the instrumental activities of daily living were also allocated to category II. Category III patients had a total score above 31 and a score of 3 or 4 in at least one item in the remote memory, space orientation, social common sense, and physical ADL question category. Patients with a total DASC-21 score below 31 but with a score of 3 or 4 in at least one item in the physical ADL category were also allocated to category III. Patients who were treated with insulin, sulfonylurea, or glinide were placed in group B, whereas others were assigned to group A. All patients were subcategorized according to their HbA1c levels relative to the range recommended by the JDS/JGS Joint Committee. This study focused on patients in IIB and IIIB, who may be at higher risk of hypoglycemia than those in other groups.

## 2.4. Definition of hypoglycemia

Based on the statement of the American Diabetes Association, we defined hypoglycemia as blood or plasma glucose level below 70 mg/dL based on SMBG or laboratory test findings or both.<sup>9</sup> We collected data about SMBG from the electronic medical records 1 month before the patients' visits. Hypoglycemia was considered mild when it improved without any assistance from another person and severe when it required help from another person.

## 2.5. Statistical analysis

Data are presented as mean  $\pm$  SD. We used unpaired student's *t*-test and Mann-Whitney U test for continuous variables. We used the chi-square test and Fisher's exact test for binary variables. Additionally, a two-sided *p* value less than 0.05 was considered statistically significant. The area under the receiver operating characteristic curve (AUROC) was evaluated to determine the predictive factors of hypoglycemic events within a month before the visit. The superior cutoff value was defined as the point with the larger Youden index. The AUROC values above 0.9 had high accuracy, and those between 0.7–0.9 and 0.5–0.7 had moderate and low accuracy, respectively.<sup>10</sup> The JMP version 14.0.1 (SAS Institute, Cary, NC) was used to perform all statistical analyses.

## 3. Results

### 3.1. Characteristics of the patients

During the study period, 928 outpatients aged over 65 years visited our clinic, and 660 of them answered all the questions in DASC-21. Of these patients, 616 had laboratory data during the study period, and 366 (59.4%) of them were men. The average age of the patients was  $73.5 \pm 6.0$  years; HbA1c level,  $7.50 \pm 1.02\%$ ; glycoalbumin level,  $21.2 \pm 4.7\%$ ; Hb level,  $13.3 \pm 1.7$  g/dL; and estimated glomerular filtration rate,  $60.3 \pm 18.9$  mL/min/1.73 m<sup>2</sup>. Table 1 presents the categorization of patients based on their cognitive function and therapeutic agents used. Although the participants in categories IIB and IIIB were assumed to be at a higher risk for hypoglycemia and required more clinical care, the ratio of patients whose HbA1c levels were below the lower limit of the recommendation was higher in IIB and IIIB than in IB. Thus, we analyzed IIB and IIIB as a group with the risk of hypoglycemia and dementia, which

**Table 1**  
Number of patients according to the DASC-21 score, therapeutic regimen, and HbA1c level.

	Category I	Category II	Category III
<b>Group A<sup>†</sup></b>			
Total	138	11	7
Above the recommendation	67 (48.6%)	3 (27.3%)	3 (42.9%)
Within the recommendation	71 (51.4%)	8 (72.7%)	4 (57.1%)
Recommended HbA1c (%) <sup>§</sup>	< 7.0	< 7.0	< 8.0
<b>Group B<sup>‡</sup></b>			
Total	362	66	32
Above the recommendation	172 (47.5%)	18 (27.3%)	5 (15.6%)
Within the recommendation	148 (40.9%)	35 (53.0%)	13 (40.6%)
Below the recommendation	42 (11.6%)	13 (19.7%)	14 (43.8%)
Recommended HbA1c (%) <sup>§</sup>	Age < 75: 6.5–7.4 Age $\geq$ 75: 7.0–7.9	7.0–7.9	7.5–8.4

DASC-21, Dementia Assessment Sheet for Community-based Integrated Care System 21-items; HbA1c, glycohemoglobin.

<sup>†</sup> Group A includes patients who were treated without insulin, sulfonylurea, or glinide. <sup>‡</sup> Group B includes patients treated with insulin, sulfonylurea, or glinide. <sup>§</sup> Japan Diabetes Society (JDS) / Japan Geriatrics Society (JGS) Joint Committee on Improving Care for Elderly Patients with Diabetes. Glycemic targets for elderly patients with diabetes. *J Diabetes Investig.* 2017;8:126–128.

had not been fully recognized in daily diabetic care.

### 3.2. Profile of patients in groups IIB and IIIB

A total of 98 patients in categories IIB and IIIB were sub-categorized according to the lower limit of the recommended HbA1c level provided by the JDS/JGS Joint Committee (Table 2). Patients with HbA1c levels below the lower limit of the recommended value were more likely to have a higher total DASC-21 score than those with levels above the lower limit. However, the difference was not significant in both groups. Of 98 patients, 22 had mild hypoglycemic events; however, none of the patients experienced severe hypoglycemia.

### 3.3. Clinical factors for predicting hypoglycemia in IIB and IIIB

Based on the comparison between patients with and without hypoglycemia, we performed a logistic regression analysis of variables correlated to hypoglycemia, which included daily insulin dosage, daily frequency of insulin injections, and weekly frequency of SMBG (Table 3). Additionally, we considered age, HbA1c levels, and total DASC-21 score as variables correlated to hypoglycemia because these were considered indicative factors of glycemic control based on the recommendation of the JDS/JGS Joint Committee. The analyses were performed for all patients in the IIB and IIIB categories

**Table 2**

The profile of patients in IIB and IIIB divided according to the recommended HbA1c level.

	All (n = 98)	HbA1c below the lower limit of recommendation (n = 27)	HbA1c above the lower limit of recommendation (n = 71)	p value
Male (%)	65.3	74.1	62.0	0.26
Age (years)	76.1 ± 6.4	76.0 ± 6.9	76.1 ± 6.2	0.89
HbA1c (%)	7.56 ± 1.06	6.45 ± 0.64	7.98 ± 0.87	< 0.01
Diabetes duration (years)	19.6 ± 11.9	21.2 ± 12.6	19.0 ± 11.5	0.42
Type 2 (%)	87.8	92.6	85.9	0.30
Glycoalbumin (%)	22.5 ± 4.3	20.2 ± 3.6	23.4 ± 4.2	< 0.01
C peptide (ng/mL)	2.40 ± 2.16	2.55 ± 1.80	2.34 ± 2.26	0.78
Plasma glucose (mg/dL)	201.3 ± 102.8	240.1 ± 138.2	188.0 ± 83.3	0.94
CPI	1.16 ± 0.79	1.11 ± 0.66	1.18 ± 0.84	0.46
Hb (g/dL)	12.6 ± 1.8	11.7 ± 2.0	12.9 ± 1.6	< 0.01
eGFR (mL/min/1.73 m <sup>2</sup> )	53.9 ± 22.0	45.9 ± 24.0	57.0 ± 20.4	0.03
Total score of DASC 21	34.7 ± 10.0	38.6 ± 12.8	33.2 ± 8.2	0.12
Insulin (%)	82.7	88.9	80.3	0.25
Sulfonylurea (%)	17.3	7.4	21.1	0.09
Glinide (%)	13.3	11.1	14.1	0.49
Daily doses of insulin (units)	21.0 ± 16.7	21.2 ± 14.7	21.0 ± 17.4	0.95
Patients with hypoglycemia (%)	22.4	18.5	23.9	0.57
Frequency of hypoglycemia within 1 month	0.76 ± 2.91	0.67 ± 2.11	0.79 ± 3.19	0.59
Patients with SMBG (%)	76.5	81.5	74.6	0.48
Weekly frequency of SMBG	11.3 ± 8.9	12.3 ± 9.2	10.9 ± 8.7	0.48
Frequency of hypoglycemia per SMBG	0.014 ± 0.037	0.011 ± 0.020	0.015 ± 0.042	0.72

HbA1c, glycohemoglobin; CPI, C peptide index; Hb, hemoglobin; eGFR, estimated glomerular filtration rate; DASC-21, Dementia Assessment Sheet for Community-based Integrated Care System 21-items; SMBG, self-monitoring of blood glucose.

**Table 3**

AUROC values to predict hypoglycemia in IIB and IIIB.

	All (n = 98)	Below the lower limit of recommendation (n = 27)	Above the lower limit of recommendation (n = 71)
Age (years)	0.53 (81) [0.59]	0.54 (76) [0.93]	0.55 (81) [0.50]
HbA1c (%)	0.54 (7.8) [0.39]	0.56 (6.3) [0.90]	0.62 (7.7) [0.07]
Total score of DASC-21	0.55 (36) [0.74]	0.71 (33) [0.05]	0.53 (28) [0.25]
HbA1c and total score of DASC-21	0.56 [0.64]	0.71 [0.14]	0.66 [0.05]
Daily doses of insulin (units)	0.71 (18) [< 0.01]	0.82 (30) [0.01]	0.68 (15) [0.08]
Daily frequency of insulin injection	0.69 (1) [< 0.01]	0.71 (3) [0.16]	0.70 (1) [0.01]
Weekly frequency of SMBG	0.70 (13) [< 0.01]	0.69 (18) [0.07]	0.71 (13) [< 0.01]

AUROC, area under the receiver operating characteristic curve; HbA1c, glycohemoglobin; DASC-21, Dementia Assessment Sheet for Community-based Integrated Care System 21-items; SMBG, self-monitoring of blood glucose.

The numbers in the parentheses and brackets indicate cutoff values and p values, respectively.

and for those with HbA1c levels greater and less than the lower limit of the recommended value.

In all patients, the AUROC values for age, HbA1c, total DASC-21 score, the combination of HbA1c and total DASC-21 score ranged from 0.50 to 0.70. Moreover, the AUROC values for daily insulin dosage, daily frequency of insulin injection, and weekly frequency of SMBG reached approximately 0.70. There was no significant difference in each analysis. The AUROC values for the total DASC-21 score and a combination of HbA1c and total DASC-21 score were lower in patients with HbA1c levels above the lower limit of the recommended value than in those with HbA1c below the lower limit.

3.4. Distribution of treatment and hypoglycemic events in IIIB

Although patients in group IIIB should have been provided with utmost care for hypoglycemia in clinical settings, the ratio of patients whose HbA1c levels were below the lower limit of the recommended value in IIIB was higher than those in group IIB (Table 1). Hence, we focused on IIIB patients. Figure 1a depicts the correlation between HbA1c levels and total DASC-21 score for patients in group IIIB. Of 32 patients, the treatment was multiple daily injections (MDI) in 9, basal insulin with or without oral antidiabetic drug (OAD) in 7, other insulin regimens in 13, and OAD alone in 3 patients. Of 32 patients, 9 (28.1%) had hypoglycemic events, and the treatment was MDI in 6, basal insulin without OAD in 1, and other insulin regimens in 2.

Of 9 patients who developed hypoglycemia, 7 had impairment in less than 4 of 21 items in DASC-21 and their diabetologists had not been able to identify the risk of cognitive impairment prior to the use of DASC-21; their total scores ranged from 31 to 36, indicating milder cognitive decline than other patients in group IIIB. Of the 7 patients with hypoglycemia and a total score below 36, 5 were treated with MDI.

3.5. Predictors of hypoglycemia in patients with low DASC-21 scores

We performed logistic regression analysis to determine the efficacy of DASC-21 in predicting hypoglycemia based on the HbA1c levels of patients in IIIB group. Based on the distribution of hypoglycemic patients irrespective of HbA1c levels (Figure 1a), patients in IIIB group were divided into two groups based on their total score above or below 36 (Figure 1b). The AUROC values for the HbA1c level were 0.88 in patients with a total score above 36 (cutoff value, 7.7%; sensitivity, 100.0%; and specificity, 75.0%) and 0.49 in patients with a total score below 36 (cutoff value, 6.7%; sensitivity, 100.0%; and specificity, 28.6%).

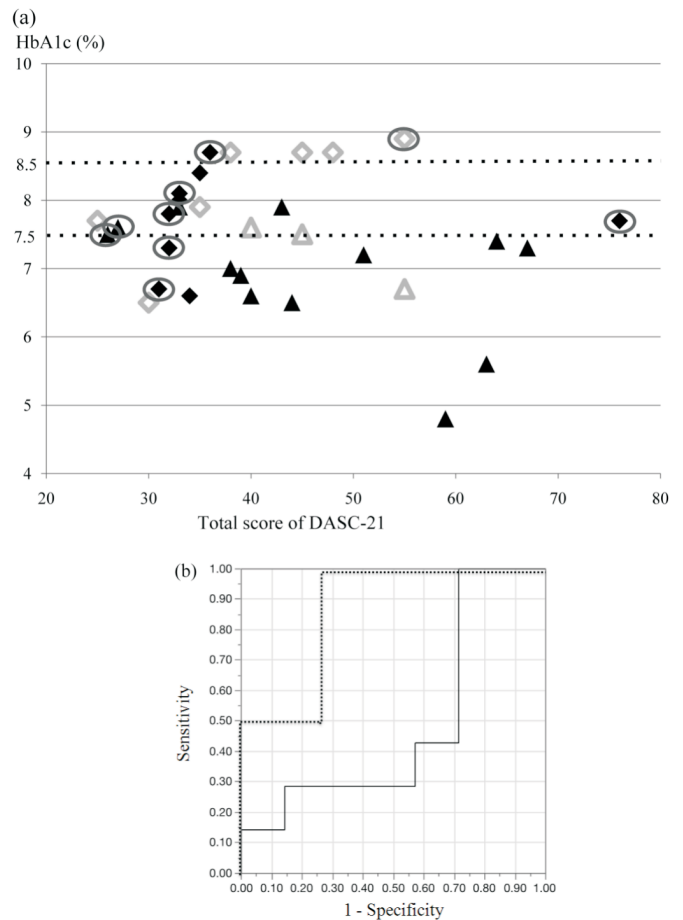
4. Discussion

The prevention of hypoglycemia in older patients with diabetes is an important clinical issue. This study showed that without DASC-21 application, the development of hypoglycemia did not differ between patients who were grouped according to the lower limit of the recommended HbA1c levels. However, individuals presenting with hypoglycemia were more likely to have dementia with relatively low DASC-21 scores, and most were on MDI. Patients with dementia with relatively low DASC-21 scores exhibited lower hypoglycemic predictive values of HbA1c levels.

This study shows that DASC-21 can help clinicians identify

cognitive impairment and the risk of hypoglycemia in older patients with diabetes, which was important in setting the individual targets for HbA1c. Most patients in group IIIB with hypoglycemia had impairment in less than 4 of the 21 items in DASC-21, indicating the possibility that diabetologists could not identify the risk of dementia prior to using DASC-21 during assessment. Additionally, this study revealed that the estimation of hypoglycemia using the HbA1c level was more challenging in those with relatively low DASC-21 scores among patients in IIIB group. Thus, in managing HbA1c-guided glycemic control, clinicians should suspect dementia in older patients and use a screening tool such as DASC-21 for assessing cognitive impairment in daily diabetic care.

Moreover, the continuous use of MDI without adequate de-



**Figure 1.** (a) The distribution of the HbA1c level and total DASC-21 score in IIIB. The correlation between the HbA1c levels and the total DASC-21 score among 32 patients in IIIB. A higher score of DASC-21 indicated higher severity of cognitive impairment, and a total score above 31 indicated a risk for dementia. Of 9 patients who had hypoglycemia, 5 patients had total scores of DASC-21 of patients from 31–36, indicating milder cognitive decline than other patients under IIIB. Moreover, 6 patients who were treated with MDI had hypoglycemia no matter whether their HbA1c levels were within the recommendation. Black square, patients treated with MDI; gray square, patients treated with basal insulin (with or without OAD); black triangle, patients treated with other insulin regimens; gray triangle, patients treated only with OAD; gray circle, patients whose SMBG levels or plasma glucose levels were lower than 70 mg/dL within 1 month before visit. HbA1c, glycohemoglobin; DASC-21, Dementia Assessment Sheet for Community-based Integrated Care System 21-items; MDI, multiple-dose injection; OAD, oral antidiabetic drug; SMBG, self-monitoring of blood glucose. (b) The predicted risk of hypoglycemia according to the total DASC-21 score in IIIB. Patients were divided according to the total DASC-21 score, and the data were analyzed using a logistic regression model. Solid line: the risk in patients with total scores of DASC-21 ≤ 36; dotted line: the risk in patients with total scores of DASC-21 > 36. DASC-21, Dementia Assessment Sheet for Community-based Integrated Care System 21-items.

mentia screening could be a risk factor for hypoglycemia. In this study, though none of the 9 patients in IIIB who were on MDI underwent sick day, 6 of them had hypoglycemic events. Therefore, automatically continuing MDI without identifying cognitive impairment may lead to potential hypoglycemic events (Figure 1a). Routine screening of cognitive impairment using DASC-21 may be effective for the optimization of individual treatment. In addition, a previous study showed that in elderly diabetics, basal insulin therapy with OAD provided similar glycemetic control to younger diabetics, and the rate of hypoglycemic events was not statistically different between the elderly and younger patients.<sup>11</sup> Hence, physicians should consider switching from MDI to basal insulin therapy with OAD in patients with dementia.

Moreover, HbA1c level alone might not be a reliable indicator of the risk of hypoglycemia in some patients. In this study, the ratio of patients who experienced hypoglycemic events did not differ between both patients with HbA1c levels below and above the lower limit of the recommended value, whereas the frequency of hypoglycemia within 1 month and hypoglycemic events based on SMBG findings did not differ between both groups (Table 2). Moreover, the AUROC values for the indicators, including HbA1c level and total DASC-21 score, were relatively insufficient in patients in IIB and IIIB groups (Table 3). In addition, though the lower limit of recommended HbA1c level by the JDS/JGS Joint Committee is 7.5% for patients with moderate or severe dementia, the IDF recommendation is 7.0%.<sup>4,5</sup> This indicates that when physicians refer to the IDF guideline, it may be necessary to give more attention on the risk of hypoglycemia and use an optimal screening tool for assessing cognitive impairment.

The recommendation of the JDS/JGS Joint Committee emphasized that a glycemetic target should be set for each old patient to prevent severe hypoglycemia,<sup>4</sup> which was also supported by our findings. A recent study suggested that increasing the target HbA1c level may not effectively prevent hypoglycemia in older adults.<sup>12</sup> In addition, a previous report has indicated that polypharmacy is an important factor in diabetes-related comorbidity;<sup>13</sup> thus, we should determine the individual target of HbA1c levels by evaluating cognitive function as the JDS/JGS Joint Committee recommended.

This study had some limitations. First, only 616 of 928 older patients answered all the questions, which suggests the need for a simplified DASC-21 or a new tool. Accordingly, the DASC-8, which was reported after the end of this study, could be used instead of DASC-21.<sup>7</sup> The use of DASC-8 for categorization might reduce the risk of overlooking mild cognitive impairment.

Second, the frequency of SMBG might have affected the recognition of hypoglycemic events, although we also evaluated its influence on our data (Table 3). Moreover, we may underestimate asymptomatic hypoglycemia in patients who did not use SMBG. For further studies, performing continuous glucose monitoring or SMBG in patients with OADs could be an option.

In conclusion, the use of DASC-21 identified the risk of clinically

unrecognized hypoglycemia and cognitive impairment among older patients with diabetes. We also showed that continuing MDI in older individuals with diabetes, particularly those with relatively low DASC-21 scores, might lead to hypoglycemia if patients are not screened for cognitive impairment. Therefore, clinicians should adequately use a screening tool for assessing cognitive impairment in daily diabetic care.

## Conflicts of interest

None.

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