

## Predictive Factors for Hospitalized and Institutionalized Care-giving of the Aged Patients with Diabetes Mellitus in Japan

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### ABSTRACT

To identify predictive factors for hospitalized and institutionalized care-giving among a group of aged patients with diabetes mellitus in Japan, retrospective chart review was performed in 288 diabetic subjects aged 65 years or older. Independent variables, based on the chart review, were age, sex, diagnosis, diabetic control and complications. Comprehensive geriatric assessment was performed to obtain information on the functional capacity and demographic variables, including physical and mental function, and socioeconomic status. 131 diabetic patients were considered as frail elderly and characterized for their higher age, longer duration of diabetes, higher frequency of insulin use, lower cognitive function, and lower QOL, in comparison with those of non-frail patients. All non-frail diabetic patients were independently treated at their homes, while 38 subjects out of 131 frail diabetic patients were hospitalized or institutionalized. Apparent clinical features of hospitalized/institutionalized patients were higher age, higher serum creatinine, and higher prevalence of stroke episodes, advanced cognitive decline and absence of key caregiver in the family members, in comparison with those of in-home frail diabetic patients. The predicted probabilities from the multivariate logistic regression analysis in predicting hospitalized and institutionalized care-giving were as follows:  $\text{Log } p/(1 - p) = -19.801x_1 - 54.269x_2 + 721.405$ ; where  $x_1$  = cognitive function (score),  $x_2$  = social support (score). Receiver operating characteristic curve analysis revealed a satisfactory discrimination for hospitalized and institutionalized care-giving in frail diabetic elderly with 92.9% of sensitivity and 91.4% of specificity, when the cutoff point of the model was set at 0.992. We concluded that cognitive decline and low social support are the predictive for hospital and institutional care-giving, and that demographic and mental information as well as diagnostic data should be analyzed to predict the hospitalization/institutionalization among frail diabetic elderly.

### INTRODUCTION

Successful management of diabetes mellitus in the elderly population is a major public health challenge. The aging population (over 65 years) now makes up 23.1% of the overall

population in Japan, and the prevalence of diabetes in this population is over 16% (1). Along with the increasing duration of diabetes in the elderly, diabetes-related complications frequently occur and propagated: not only vascular complications such as diabetic foot, retinopathy, and nephropathy, but also age-associated illness and frail homeostasis, which produce a high rate of disablement and decay of quality of life. The complexity of physical and mental disability, coupled with the vulnerability to frailty often disturbs the day to day diabetes self-management at their homes. In the previous reports (2-4), diabetes is a significant predictor for the institutionalization among the frail elderly; the aged diabetic patients are 1.8 times more likely to enter a nursing home (2). Therefore, for the achievement of successful medical treatment of diabetic elderly, the cooperative long-term caregiving should be conducted, involving community-based and institutional care services.

Japan moved toward socialization of care for the frail elderly by initiating public, mandatory long-term care insurance in 2000. Everyone aged 65 and older is eligible for benefits based strictly on physical and mental disability. The long-term care insurance covers chronic-care beds in hospital, institutional and community-based caregiving. By improving the health outcomes, community-based caregiving can reduce the cost of the frail elderly, and the ability to identify patients who are at high risk for hospitalization and institutionalization could be useful not only in setting the medical treatment of the frail elderly, but also in developing policy for the long-term care insurance. Several studies have looked at factors that might predict hospitalization among populations of community dwelling older adults (5, 6) hospitalized patients (7), and those with dementia (8). However, information on the hospitalized and institutionalized care-giving of frail elderly with diabetes is scarce.

The present study attempts to identify predictive factors for hospitalized and institutionalized care-giving among the elderly with diabetes. For this purpose, we reviewed the charts of diabetic elderly who were treated at the Kobe University Hospital. Relationship between medical, functional and demographic variables of the diabetic elderly and the subsequent hospitalization and institutionalization was examined.

## MATERIAL AND METHODS

### Participants

Retrospective medical chart of 288 patients aged 65 years or older with known diabetes mellitus (164 women; mean age,  $72.8 \pm 7.7$  years) were reviewed. This study was conducted from 2006-2009. The institutional review boards of Kobe University Hospital approved the research protocol, and written informed consent was obtained from each patient and his or her family members. All subjects met the criteria of diabetes from Japan Diabetes Society (9). At entry into this study, geriatricians routinely examined all patients to estimate diabetic control and complications, and assessed the functional and socioeconomic status. Professionals in neurology, psychiatrics, orthopedics, urology, and ophthalmology examined their specific problems.

Among 288 diabetic elderly, 131 patients were considered as frail elderly by their chief physicians. In this study, frail elderly was defined as persons who are vulnerable and at high risk of a range of adverse health outcomes, such as dependency, institutionalization, falls, injuries, acute illness, hospitalization, slow recovery from illness and mortality, and also included persons who have relatively preserved physical function, but easily become supported or cared condition (so-called "specified elderly individuals") in the modified Japanese long-term care insurance (10). Frail diabetic patients often had nonlocalizing or

## HOSPITALIZED CARE-GIVING OF DIABETIC ELDERLY

constitutional symptoms such as weakness, fatigue, poor appetite, undernutrition, and/or dehydration.

### Measurements of diabetic control and complications

Glycemic control and diabetes-related complications were analyzed by data chart. Fasting and postprandial blood glucose and HbA<sub>1c</sub> examined diabetic control in each individual. Information on duration of diabetes and on pharmacological therapeutics for diabetes was obtained. Diabetic retinopathy was classified into three subclasses, normal, nonproliferative, and proliferative diabetic retinopathy. Diabetic neuropathy was diagnosed by subjective symptoms and by objective examinations; autonomic function was tested by beat to beat variation test and Schellong test, and conduction velocity of the peripheral nerve was measured. Based on these observations, diabetic peripheral neuropathy was classified into three subclasses, normal, asymptomatic, and symptomatic neuropathy. Renal complication of diabetes was estimated by quantification of serum creatinine and Urea-N in dialyzed and non-dialyzed patients. Abnormal findings in electrocardiogram, chest X-ray, and cardio-echogram diagnosed coronary artery disease and congestive heart failure. Previous stroke episodes were re-evaluated by neurological examinations and presence of the cerebral vascular disease was investigated by MRI brain scanning.

### Assessment of functional and socioeconomic status

Information on physical, mental, and demographic status among the aged diabetic patients was collected through personal interviews and supplemented by corroborative data from nursing staff. Comprehensive Geriatric Assessment Form, a standardized data sheet was completed by the physicians and clinical psychologists (11, 12). Geriatric assessment consisted of following 8 examinations, which were shown to be important predictors of institutionalization (4): physical measurements, basic activities of daily living (ADLs), instrumental ADLs, cognitive function, quality of life (QOL), depression, and socioeconomic status. Functional measurements included visual acuity, auditory acuity, communication, and bladder incontinence. Each of the dichotomous variables was coded so that 3=normal, 2=slightly disturbed, 1=severely disturbed, 0=functionally disrupted. Ability of communication was tested to ask every subject to read a short paragraph and answer questions about the paragraph. Basic ADLs were determined using the Barthel index, including the ability for bathing, dressing, toileting, transferring, and eating. Instrumental ADLs were estimated by Roken score, established in the Tokyo Metropolitan Geriatric Hospital, Japan (13), which referred to going outside the home, shopping for groceries, preparing meals, managing finances, reading the newspapers and magazines, interests in health management, and communicating to family members and friends. For the self-administered screening instruments for depression, we used geriatric depression scale-15 (14). For measuring the cognitive function, mini-mental state examination (MMSE) was used (15). QOL was tested by the questionnaires of Morale scale of the Philadelphia Geriatric Center (16). To evaluate the socioeconomic status, we used the elderly diabetes impact scales (17). For caregiving conditions, 8 positive questionnaires and 4 negative questionnaires were asked, to know presence of and relationship with a key caregiver. Information on economical status was obtained from the patients and their caregivers, and coded so that 4=excellent, 3=good enough for daily life, 2=partially shortened, 1=asking for assistance.

### Statistical analysis

Data were reported as mean  $\pm$  SD. Two-tailed Student's t-test and  $\chi^2$  test were used to compare the variables between the frail and non-frail diabetic groups, and between the

institutionalized and in-home diabetic patients. Logistic regression analysis was employed to determine the predictive factors for institutionalization in frail diabetic elderly. Any significant items were entered into a multivariate logistic regression, using stepwise selection with an inclusion criteria of  $p < 0.05$  and exclusion criteria of  $p > 0.1$ . Using a developed model, a receiver operating characteristic (ROC) curve was constructed to test the relationship between sensitivity and specificity using varying cutoff points of the model for predicting hospitalized/institutionalized care-giving. The area under the curve was calculated. Statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The level of significance was set at  $p < 0.05$  for all statistical analyses.

### RESULTS

Clinical characteristics of frail diabetic patients were shown in Tables I-III. Frail elderly were significantly older and had longer duration of diabetes than non-frail diabetic patients. However, there was no significant difference in gender (Table I). Type 1 diabetes was significantly frequent in the frailty group. Insulin user was more predominant in frail subjects than in non-frail patients. In the frail diabetic patients, HbA<sub>1c</sub> levels were significantly higher than those in the non-frail group.

Table I. Clinical profiles of the non- frail and frail diabetic elderly

	Non-frail	Frail
Number (M/F)	157 (68/89)	131 (56/75)
Age (year)	70.3 ± 6.3	75.3 ± 9.0*
Duration of diabetes (years)	13.8 ± 9.3	18.1 ± 12.6*
Type 1 diabetes (%)	1.6	10.2 *
Insulin use (%)	22.9	43.5 *
HbA <sub>1c</sub> (%)	7.4 ± 1.4	7.9 ± 1.1 *
Fasting blood glucose (mg/dl)	162 ± 60	168 ± 73

Data are presented as mean ± SD. Student's t-test and  $\chi^2$  test were used to compare the variables between non-frail and frail patients. \* $P < 0.05$ .

Underlying causes of the frailty in 131 aged diabetic patients were shown in Table II. Most common complication among the frail subjects was cognitive impairment including all types of dementia (30.5%), followed by visual disturbances (15.3%), depression (13.7%), cerebrovascular disease (13.7%), and end-stage renal disease (12.2%). MMSE of the frail diabetic subjects was 21.0 ± 4.5, as shown in Table III, and thirty-two subjects of the frail diabetic patients were diagnosed as dementia. Visual disturbance was mostly due to diabetic retinopathy and/or cataracts. Coronary artery disease, congestive heart failure, and Parkinsonism were also frequently observed in the frail subjects. 5 frail patients had orthopedic disturbances such as hip and knee joints instability.

## HOSPITALIZED CARE-GIVING OF DIABETIC ELDERLY

Table II. Underlying causes of frailty in 131 diabetic elderly

	Number (%)
Cognitive decline and Dementia	40 (30.5)
Visual disturbances	20 (15.3)
Depression and Other psychiatric disorders	18 (13.7)
Cerebrovascular disease	18 (13.7)
End-stage renal disease	16 (12.2)
Coronary artery disease and congestive heart disease	9 (6.9)
Parkinsonism	5 (3.8)
Orthopedic disturbances	5 (3.8)

Incidence of frailty is shown as a number of patients (%).

Table III. Comprehensive geriatric assessment in non-frail and frail diabetic elderly

	Non-frail	Frail
Number (M/F)	157 (68/89)	131 (56/75)
Physical measurements ( /12)	11.9 ± 0.3	11.3 ± 0.9
Basic ADL ( /20)	19.6 ± 2.2	18.1 ± 3.0
Instrumental ADL ( /13)	10.6 ± 2.3	9.9 ± 3.1
Cognitive function ( /30)	24.8 ± 2.7	21.0 ± 4.5*
QOL ( /17)	12.4 ± 3.1	11.3 ± 3.2*
Depression ( /15)	4.2 ± 2.2	4.1 ± 3.5
Social support ( /12)	9.3 ± 1.3	7.3 ± 3.3
Economic status ( /4)	3.2 ± 0.4	3.2 ± 0.9

Data are presented as mean ± SD. Student's t-test and  $\chi^2$  test was used to compare the variables between non-frail and frail patients. \*P<0.05. Functional measurements included visual acuity, auditory acuity, communication, and bladder incontinence. Basic ADL and instrumental ADL were determined using the Barthel index and the Roken score, respectively. For measuring the cognitive function, mini-mental state examination was used. QOL was tested by the questionnaires of Morale scale of the Philadelphia Geriatric Center. Screening of depression was evaluated by geriatric depression scale-15. To evaluate the socioeconomic status, the elderly diabetes impact scales was used.

Demographic and functional status was assessed by comprehensive geriatric assessment (Table III). Of the physical measurements, visual acuity was slightly depressed in the frail subjects, other functional measurements including auditory acuity, communication, and bladder incontinence, were not different between non-frail and frail subjects (data not shown).

Basic ADLs and instrumental ADLs tended to decrease in the frail diabetic patients, which did not reach statistical significance in this study. MMSE of the frail diabetic patients was significantly lower than that of non-frail subjects. Depression was screened by the GDS-15, in which more than 5 positive answers were reported to indicate the possible geriatric depression (18). Scores of GDS-15 in frail and non-frail diabetic patients of this study were not elevated. Although an association between diabetes and depression has been recently postulated (19), our diabetic patients did not seem depressive, but rather in reasonably self-satisfactory condition. QOL was measured by Philadelphia Morale scale, and an average QOL was reported approximately 4 through 7 (20). QOL of our frail diabetic patients was slightly lower than that of non-frail diabetic patients. Socioeconomic status was not different between non-frail and frail diabetic elderly.

Table IV. Clinical profiles of in-home and institutionalized patients with diabetes mellitus

	In-home	Hospitalized/ Institutionalized
Number (M/F)	93 (40/53)	38 (16/22)
Age (year)	73.0±9.2	81.2±4.9*
DM duration (years)	17.8±13.3	18.7±10.9
HbA <sub>1c</sub> (%)	7.8±1.0	8.2±1.3
Blood glucose (mg/dl)		
Fasting	165±77	173.7±68
Postprandial	259±76	285±80
Insulin use (%)	45.2	39.5
Proliferative retinopathy (%)	38.0	44.0
Symptomatic neuropathy (%)	75.5	69.7
Dialysis treatment (%)	11.4	23.7
Serum creatinine (mg/dl)	1.3±1.4	2.4±2.8*
Cerebrovascular diseases (%)	12.0	41.1*
Coronary artery disease and heart failure (%)	21.1	27.3
Peripheral vascular disease (%)	9.5	23.1

Data are presented as mean±SD. Student's t-test and  $\chi^2$  test were used to compare the variables between in-home and institutionalized patients. \*P<0.05. Diabetic retinopathy was classified into three subclasses, normal, nonproliferative, and proliferative diabetic retinopathy. Diabetic neuropathy was diagnosed by subjective symptoms and by objective examinations. Previous stroke episodes were re-evaluated by neurological examinations and presence of the cerebral vascular disease was investigated by MRI brain scanning. Abnormal findings in electrocardiogram, chest X-ray, and cardio-echogram diagnosed coronary artery disease and congestive heart failure.

All of 157 non-frail diabetic patients were independently living at their homes, whereas thirty-eight out of 131 frail diabetic patients (29%) required hospitalized/institutionalized care-giving. Next, we compared the medical, functional, and demographic variables of in-home and of hospitalized/institutionalized patients among frail diabetic subjects (Tables IV and V). Hospitalized/institutionalized patients were older than in-home subjects, while difference in gender was not significant (female gender was 57.0% and 57.9% in in-home and hospitalized/institutionalized patients, respectively). Blood glucose and HbA<sub>1c</sub> levels were considerably higher in the hospitalized/institutionalized patients, but the difference in the glycemic control did not reach statistical significance. Prevalence of proliferative retinopathy and symptomatic neuropathy tended to be equally common among frail diabetic patients. In contrast, diabetic nephropathy was more propagated in the hospitalized/institutionalized diabetic patients. One fourth of the

## HOSPITALIZED CARE-GIVING OF DIABETIC ELDERLY

hospitalized/institutionalized patients received dialysis treatment, and mean concentration of serum creatinine was significantly higher in hospitalized/institutionalized patients than in in-home patients. Of the macroangiopathic disease, cerebrovascular disease was more prevalent in the hospitalized/institutionalized patients, while coronary artery disease and peripheral vascular disease were not different between in-home and hospitalized/institutionalized patients.

Comprehensive geriatric assessment in the hospitalized/institutionalized patients with diabetes demonstrated that physical measurements including visual acuity, auditory acuity, communication, and bladder incontinence were not different, compared with those of in-home patients (data not shown). Basic and instrumental ADLs tended to decrease in the frail diabetic subjects with hospitalized/institutionalized care-giving, however, which did not reach statistical significance in the study. (Table V). In the super-old individuals aged 85 or over, basic ADL of the hospitalized/institutionalized patients was significantly impaired than that of in-home frail elderly (13.1±3.4 and 16.8±4.5, respectively) and instrumental ADL of the hospitalized/institutionalized patients was also lower than that of in-home frail elderly (5.2±4.0 and 9.0±4.2 in the respective group, P<0.05). In contrast, basic and instrumental ADLs of young-old (65-74 years old) and old-old (75-84 years old) were not altered between in-home and hospitalized/institutionalized patients. Cognitive function of the hospitalized/institutionalized patients was more seriously impaired than that of in-home frail elderly. However, scores of GDS-15 and Morale scale were similar in the in-home and hospitalized/ institutionalized patients. Social support for the hospitalized/institutionalized patients was significantly decreased and the presence of a caregiver in their family members was apparently lower in the hospitalized/institutionalized patients than in in-home patients (50.0% and 90.0%, respectively). Economic status did no differ between the in-home and the hospitalized/institutionalized elderly with diabetic mellitus.

**Table V.** Comprehensive geriatric assessment in the in-home and institutionalized patients

	In-home	Hospitalized/ Institutionalized
<b>Number(M/F)</b>	<b>93 (40/53)</b>	<b>38 (16/22)</b>
<b>Physical measurements ( /12)</b>	<b>11.3±0.9</b>	<b>11.2±1.0</b>
<b>Basic ADL ( /20)</b>	<b>18.4±2.7</b>	<b>17.3±3.5</b>
<b>Instrumental ADL ( /13)</b>	<b>10.3±3.0</b>	<b>9.0±3.5</b>
<b>Cognitive function ( /30)</b>	<b>22.2±4.2</b>	<b>17.7±3.6*</b>
<b>QOL ( /17)</b>	<b>11.4±3.1</b>	<b>10.9±3.6</b>
<b>Depression ( /15)</b>	<b>4.0±3.2</b>	<b>4.4±4.1</b>
<b>Social support ( /12)</b>	<b>8.7±1.9</b>	<b>2.4±2.2 *</b>
<b>Economic status ( /4)</b>	<b>3.3±0.7</b>	<b>2.4±1.6</b>

Data are presented as mean± SD. Student's t-test and  $\chi^2$  test was used to compare the variables between in-home and institutionalized patients. \* P<0.05. Physical measurements, basic ADL, instrumental ADLs, cognitive function, QOL, depression, socioeconomic support were determined as described for Table III.

Finally, to develop a model for predicting the hospitalized/institutionalized care-giving in frail diabetic elderly using stepwise selection, clinical variables that were shown to be different at  $p < 0.05$  (Tables IV and V) were entered into a multivariate logistic regression. This showed that cognitive dysfunction and low social support were predictive factors for hospitalization/institutionalization in frail diabetic elderly subjects. The predicted probabilities from the multivariate logistic regression analysis in predicting hospitalized/institutionalized care-giving were as follows:  $\text{Log } p/(1 - p) = -19.801x_1 + 54.269x_2 + 721.405$ ; where  $x_1 = \text{MMSE (score)}$ ,  $x_2 = \text{social support (score)}$ . ROC analysis revealed a satisfactory discrimination for hospitalization/institutionalization in frail diabetic elderly subjects with a sensitivity of 92.9% and a specificity of 91.4%, when the cutoff point of the model was set at 0.992.

## DISCUSSION

This study first indicated that factors to predict hospitalized/institutionalized care-giving of frail diabetic elderly are cognitive decline and low social support, namely absence of a caregiver in the family members. These results indicated that cognitive dysfunction with changes in self-care behavior and treatment of diabetes may increase the use of care beds in hospital and institutional caregiving when social support is limited. In contrast, clinical features of frailty of diabetic elderly including aging, longer duration of diabetes, insulin use and decreased QOL were not critical for hospitalized/institutionalized care-giving.

Of the physical measurements, visual activity, auditory acuity, communication, and bladder incontinence did not differ between in-home and hospitalized/institutionalized frail diabetic patients. Basic and instrumental ADLs of the hospitalized/institutionalized super-old patients aged 85 or over were significantly impaired, but ADLs of the overall frail subjects were not changed in this study, which presumably due to the relatively preserved physical activities of the younger frail diabetic elderly. Our results in diabetic subjects were consistent to the previous reports that ADLs were not significantly associated with nursing home replacement (2), at least in the young-old and old-old diabetic populations. Among the general population, physical and mental disabilities have consistently been found to be the primary predictor for nursing home placement (2, 6-8, 21). However, in the selected frail elderly, the relative importance of functional limitations was lessened or even insignificant if caregiver conditions were taken into account (22). Follow-up of frail subjects recruited to the National Long-Term Care Survey (2-year mortality: 22%; 2-year nursing home replacement rate: 8%) showed that caregiver burden was the strongest predictor among the variables and that ability to perform ADLs was not associated with institutionalization (21). Follow-up studies of demented individuals (1.5-year nursing home placement rate: 51%) also indicated that the predictive power of caregiver burden was stronger than ADL level of the care receivers (22).

Recent population-based cohort studies have suggested that older subjects with diabetes have an increased risk of dementia (23, 24). A critical review of 19 controlled studies concluded that sufficient evidence exists to link cognitive dysfunction with type 2 diabetes (24). We have reported the characteristics of cognitive dysfunction of Japanese diabetic patients (25-27). In this study, we found that lower MMSE was closely related to hospitalized/institutionalized care-giving in frail diabetic elderly. Our results confirmed to earlier studies that found that cognitive impairment is important in predicting institutionalization (3, 4). Sinclair *et al.* provided evidence that demonstrates that subjects with lower MMSE required significantly more assistance with personal care behavior, and were more likely to have been institutionalized (28). In addition, physical function was more



## HOSPITALIZED CARE-GIVING OF DIABETIC ELDERLY

compromised in those with cognitive impairment. In this connection, it should be noted that our hospitalized/institutionalized patients were not so severely demented and maintained relatively preserved physical activities. However, even mild to moderate cognitive decline often disturbs the treatment of diabetes, including medication, exercise and diet therapy. Importantly, chronic hyperglycemia further worsens the cognitive dysfunction vice versa. Thus, it would seem more likely that the cognitive deterioration leads to poor self-management of diabetes, resulting in the increased need for hospitalized/institutionalized care-giving.

Another critical factor for hospitalized/institutionalized care-giving in diabetic elderly was caregiver issues, namely increased caregiver burden. Tsuji et al (2) pointed out three caregiver characteristics for the strong predictors of the nursing home placement: living separate from the patients, having time conflicts attribute to work, and being stressed by caregiving. In addition, they suggested that having a secondary caregiver in the family tended to decrease and using a formal caregiver tended to increase the risk of nursing home replacement (2). Although these findings were obtained in the general frail elderly in the defined area of southeast Baltimore, U.S., we felt that this was the case in Kobe, Japan. Therefore, clinicians must be alert to caregivers' burden, and have to pay much attention to use a formal caregiver under the long-term care insurance.

A major limitation of this study among diabetic elderly is the nature of the study population, who entered into this study at the Kobe University Hospital. Elderly subjects participating in research are likely to have lots of health problems, including a series of diabetes-related complications and age-associated illness. On the other hand, most diabetic elderly recruited in this study were highly motivated for receiving careful medical follow-up of diabetes. In fact, our diabetic patients seemed in reasonably self-satisfactory conditions and not depressive. These characteristics of our diabetic population were advantageous to investigate the possible risk factors of hospitalized/institutionalized care-giving, although we have to be cautious to consider the risk in general diabetic population. Second limitation is the reliability to assess physical activity, because we obtained information on ADLs from the patients themselves. Patients with dementia often overestimate their functional abilities. In this respect, it should be mentioned that the capacity for self-observation is considerably preserved in patients with mild to moderate dementia, although a decline in patient self-reporting on this issue is less dramatic than that seen in family reports (29, 30).

As noted, Japan started mandatory long-term care insurance in 2000. In respect of long-term care insurance, institutionalization is defined as entry into nursing homes or health facilities for the elderly and hospitalization is defined as entry into designated care beds in hospitals. In the nursing homes, frail elderly can be placed for long, but with limited medical facilities. Health facilities for the elderly can provide rehabilitation toward the independent self-care management for the frail elderly. Medical treatment can be provided in the care beds in hospitals, but only for the limited term. For the institutionalized patients with diabetes, medical follow-up for glycemic control and diabetes-related complications is additionally required, when compared with that for non-diabetic frail elderly. In particular, diabetes-specific medical requirements such as daily insulin injection, continuous dialysis therapy, and functional rehabilitation are often limiting factors for the institutionalization. These medical requirements for institutionalization in the frail elderly with diabetes should be overcome in near future.

Conclusively, cognitive decline and low social support are the predictive factors for hospitalized/institutionalized care-giving in diabetic elderly. We believe the current study emphasizes an obvious but critical fact, when caring for disabled and dependent diabetic

patients, clinicians should be sensitive to the people on whom they depend. The present study also indicated that the subsequent risk for hospitalization/institutionalization could be predicted at the time of entry into in-home care program by comprehensive understanding of risk, including medical problems, mental status, and social factors of the frail diabetic elderly.

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## HOSPITALIZED CARE-GIVING OF DIABETIC ELDERLY

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ORIGINAL ARTICLE

Risk factors for a 6-year decline  
in physical disability and  
functional limitations among  
elderly people with type 2  
diabetes in the Japanese elderly  
diabetes intervention trial

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**Aim:** Type 2 diabetes increases the risk of disability. The purpose of this study was to  
clarify the explanatory factors for disability in Japanese diabetic elderly.

**Methods:** The 6-year decline in physical disability and functional limitations was  
investigated among 317 elderly people with type 2 diabetes recruited in a large-scale  
prospective study of the Japanese Elderly Diabetes Intervention Trial. Information about  
diabetes, blood examinations and complications was obtained, and basic activities of  
daily living (ADL) and instrumental ADL (IADL) were assessed by total score of the  
Barthel index and the Tokyo Metropolitan Institute of Gerontology Index of Compe-  
tence, respectively.

**Results:** After 6 years of follow up, 13.6% of patients had developed a new ADL dis-  
ability and 38.3% had developed a new functional impairment. In the 65–74 years age  
group, basic ADL decreased only in males, whereas females became functionally impaired.  
In the 75–84 years age group, basic and IADL decreased in both males and females. Older  
age and metabolic syndrome were prognostic for impairment of basic ADL, whereas  
baseline IADL problems, lower cognitive function, physical inactivity and insulin therapy  
were significant predictors of a future decline in the IADL.

**Conclusion:** This study identified several factors predicting the future decline of basic  
ADL and IADL in diabetic elderly patients, and provided a conceptual framework that  
might help to clarify the pathways leading to disability. Because the specific causes of each

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T Sakurai *et al.*

functional problem are modifiable, comprehensive treatment and care are needed to allow Japanese diabetic elderly patients to have more favorable living conditions. *Geriatr Gerontol Int* 2012; 12 ○○: ○○-○○.

**Keywords:** activities of daily living, disability, elderly, longitudinal observation study, type 2 diabetes.

## Introduction

As the population ages, disability becomes one of the greater individual and societal burdens. The pathway to disability has a complex nature compromising the effects of aging itself, lifestyle factors and medical conditions.<sup>1</sup> Although the benefits of improved socioeconomic conditions and medical care have prolonged the total life expectancy, this is not the case for active life expectancy.

In Japan, the prevalence of diabetes is rapidly increasing, particularly in the older age groups. It has been postulated that type 2 diabetes is a risk factor for physical and functional disability.<sup>2-12</sup> Elderly diabetic patients have significantly greater difficulty in walking, climbing stairs or doing housework, and perform worse on physical performance tests, such as walking speed, muscle strength, chair stand and tandem stand evaluations.<sup>2-8</sup> Kalyani *et al.* have found that diabetic elderly patients are more likely to have a higher degree of difficulty in carrying out leisure and social activity tasks.<sup>11</sup> The higher prevalence of functional disability in elderly diabetes patients might be a result of diabetes-related comorbidities, such as cardiovascular complications, vision loss, obesity, arthritis and chronic hyperglycemia.<sup>5,13,14</sup> However, these factors do not consistently explain the association of diabetes with disability. This inconsistency with the previous studies might be a result of the variability in the measures of disability or the limited number of physical tasks and comorbidities examined in these studies. Information that specifically addresses the association of the psychological aspects of diabetes with disability has been limited.

The purpose of the present study was to clarify the explanatory factors for disability in elderly Japanese diabetic patients. We carried out a large-scale prospective study of the Japanese Elderly Diabetes Intervention Trial (J-EDIT) and examined the 6-year decline related to physical disability and functional limitations among elderly people with type 2 diabetes. We hypothesized that the profile of risk factors for basic activities of daily living (ADL) would differ from that for the instrumental ADL (IADL), and that identifying the factors related to the disablement process at different stages could help to understand how diabetes leads to disability. We herein: (i) compared the sex differences in the prevalence of physical disability and functional limitations in two age groups (a younger and older elderly population), and (ii)

determined the factors predicting a future decline in the basic ADL and IADL in elderly patients with type 2 diabetes.

## Methods

### Participants

The J-EDIT started in 2001 with an enrolment of 1173 diabetic patients aged 65 years or over and with serum glycated hemoglobin (HbA<sub>1c</sub>) levels of 7.4% from 39 institutions in Japan. The J-EDIT protocol, which is in accordance with the provisions of the Declaration of Helsinki, received ethics approval from the institutional review boards of all of the participating institutions. Written informed consent was obtained from all patients. The details of the J-EDIT have been described previously.<sup>15-18</sup> We carried out a survey of the basic ADL and IADL in 2000-2001 (baseline) and again in 2006-2007. All examinations relevant to the present study were completed by 317 individuals (137 males), including 236 patients in the younger elderly group (65-74 years-of-age) and 81 in the older elderly group (75-84 years-of-age). The remaining patients were excluded because, their data were missing. Some of diabetic participants who had stroke, cardiovascular disease and the other comorbidities could not complete the present study.

### Assessment of diabetes mellitus and complications

Information about diabetes mellitus, blood examinations and complications was obtained from clinical charts as described elsewhere.<sup>15-18</sup> Briefly, blood samples were taken by venipuncture after an overnight fast to assess the blood levels of glucose, HbA<sub>1c</sub>, total cholesterol, triglycerides, high-density lipoprotein (HDL)-cholesterol and albumin. Insulin resistance was assessed by means of the homeostasis model assessment (HOMA) formula: fasting insulin ( $\mu$ U/mL)  $\times$  fasting glucose (mg/dL) / 405.<sup>19</sup> This method was not applicable to patients treated with insulin. The HbA<sub>1c</sub> levels are expressed in the National Glycohemoglobin Standardization Program units.<sup>20</sup> Diabetic vascular complications were assessed based on the existence of nephropathy, retinopathy, neuropathy, coronary heart disease (CHD) and stroke.<sup>15,18</sup> Proliferative retinopathy was diagnosed fundoscopically through the dilated pupils by experienced ophthalmologists. Persistent

Risk for physical and functional disabilities

proteinuria was defined as albumin-to-creatinine ratio > 300 µg/mg or urinary protein > 30 mg/dL. Neuropathy was diagnosed for loss of Achilles tendon reflex and/or neuropathic symptoms including paresthesia. Stroke events were defined as a constellation of neurological deficits of sudden or rapid onset for which there was no apparent cause other than a vascular accident, and confirmed by either brain computed tomography or magnetic resonance imaging. Cases with asymptomatic lesions detected by brain imaging were not included.

**Cardiovascular risk factors and treatment**

Several cardiovascular risk factors, such as hypertension and dyslipidemia, were defined as shown in the previous J-EDIT reports.<sup>15,18</sup> For metabolic syndrome (MetS), two different sets of criteria were applied; MetS by the International Diabetes Federation (IDF), and by the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI). According to the IDF criteria, there is a strong correlation between abdominal obesity and insulin resistance, which makes the presence of abdominal obesity a condition required for a diagnosis of MetS.<sup>21</sup> In contrast, the AHA/NHLBI has introduced alternative criteria, which have the advantage of avoiding the emphasis on a single cause.<sup>22</sup>

Drinking and smoking habits were assessed by a questionnaire, which asked about the patients' current smoking and drinking (an excessive alcohol intake of more than 37.8 g of ethanol a day). Physical activity was evaluated by the index developed by Baecke *et al.*<sup>23</sup> Aortic calcification of atherosclerotic lesions was determined from chest X-rays by expert physicians.

Information about insulin therapy and the use of oral antihyperglycemic drugs, antihypertensive drugs, statins, anticoagulants, and antiplatelet drugs were also obtained from the clinical charts.

**Measurements of functional disability, cognitive function and mood**

We used comprehensive geriatric assessment batteries to examine the disability, mood and cognitive function of the patients.<sup>24</sup> The Barthel index and the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence were used to measure the basic ADL and IADL, respectively.<sup>25,26</sup> The Barthel index asks about 10 items of ADL (grooming, feeding, fecal incontinence, urinary incontinence, toilet use, transfers [bed to chair and back], walking, dressing, climbing stairs and bathing), and whether each of these could be accomplished without help, with partial help or with complete help.<sup>25</sup> The TMIG Index of Competence is composed of five questions inquiring about instrumental independence, four about intellectual activity, and four about social roles.<sup>26</sup> The global cognitive function and depres-

sive mood were measured by the Mini-Mental State Examination (MMSE) and Geriatric Depression Scale (15 items), respectively.<sup>27,28</sup>

**Statistical analysis**

The data are presented as the means ± SD or as percentages unless otherwise specified. Differences between the baseline and sixth year basic ADL and IADL were tested by a *t*-test and McNemar's test. Predictive factors for the 6-year decline in scores of the Barthel index and TMIG Index of Competence were explored by simple regression analyses calculating the odds ratios (OR) and the lower and upper bounds of the 95% confidence interval (CI). Any items selected in the simple regression (*P* < 0.2) were then entered into a multivariate logistic regression to develop a model to predict the 6-year decline of ADL and IADL, using stepwise selection with an inclusion criterion of *P* < 0.2 and an exclusion criterion of *P* > 0.2. The SAS software package (Version 9.2; SAS, Cary, NC, USA) was used for the analyses, and *P* < 0.05 was considered to be significant.

**Results**

**Clinical features of the study participants and ADL disability**

The baseline characteristics of elderly diabetic patients are shown in Table 1. The participants were divided into two age groups (65–74 years and 75–84 years), and the mean scores of the basic ADL and IADL for each group are shown in Table 2. After 6 years of follow up in 317 patients, 13.6% of patients had developed a new ADL disability and 38.3% had developed new functional impairments. In males, the basic ADL significantly decreased in both the younger group (65–74 years) and the older group (75–84 years). In females, the basic ADL only decreased in the older age group (Table 2). Bathing activity tended to decline in both genders (Fig. 1). In contrast, the IADL scores of the males did not decline significantly in those aged 65–74 years, whereas reduction of the IADL in female patients was significant in both age groups. Impaired activity for shopping was observed in the younger female group, followed by functional disability for going out, cooking, paying and financing in the older female group (Fig. 2).

**Factors predicting physical disability and functional limitations**

The factors predicting a 6-year decline in the scores of the Barthel index and TMIG Index of Competence were explored by the simple regression analyses, and a large

T Sakurai *et al.*

**Table 1** Demographic and clinical characteristics of older Japanese adults with type 2 diabetes at baseline (2001), Japanese Elderly Diabetes Intervention Trial

	Total	Female	Male
<i>n</i>	317	178	139
<b>Demographics</b>			
Age (years)	71.1 (4.5)	71.3 (4.5)	70.8 (4.5)
Systolic blood pressure (mmHg)	135.3 (15.4)	134.8 (15.3)	136.0 (15.6)
Diastolic blood pressure (mmHg)	74.7 (9.3)	73.7 (9.0)	75.9 (9.6)
BMI (kg/m <sup>2</sup> )	23.7 (3.4)	23.9(3.8)	23.4 (2.9)
HbA <sub>1c</sub> (%)	8.5 (0.8)	8.5 (0.9)	8.4 (0.8)
Fasting plasma glucose (mg/dL)	166 (47)	163 (47)	169 (48)
Fasting plasma insulin (μU/mL)	8.9 (7.8)	9.1 (7.9)	8.6 (7.6)
HOMA-IR	4.32 (5.28)	4.14 (4.55)	4.55 (6.13)
Serum cholesterol (mg/dL)	203 (34)	213 (35)	191 (28)
Serum triglycerides (mg/dL)	130 (72)	131 (70)	128 (75)
Serum HDL-C (mg/dL)	56 (17)	59 (18)	51 (14)
Albumin (g/dL)	4.2 (0.3)	4.2 (0.4)	4.3 (0.3)
Hypoglycemic episodes (%)	28	32	23
Diabetic retinopathy, proliferative (%)	6	7	5
Diabetic nephropathy, persistent proteinuria (%)	15	10	21
Peripheral neuropathy (%)	63	64	63
Current smoker (%)	17	4	32
Drinking habit (%)	45	0	99
Physical activity (Baecke score)	9.2 (2.3)	9.3 (2.2)	8.9 (2.5)
Cognitive function (MMSE score)	28.4 (2.5)	28.4 (2.7)	28.5 (2.1)
<b>Comorbidities</b>			
Hypertension (%)	68	68	68
Dyslipidemia (%)	60	50	73
Cerebrovascular disease (%)	10	7	14
Coronary artery disease (%)	14	13	14
Metabolic syndrome (IDF) (%)	34	19	55
Metabolic syndrome (AHA/NHLBI) (%)	52	44	63
Atrial fibrillation (%)	1.3	0.6	2.2
Aortic calcification (%)	30	36	23
Cataract (%)	32	41	23
<b>Medication use</b>			
Use of insulin / use of oral anti-hyperglycemic drugs / no use (%)	29 / 60 / 11	30 / 61 / 9	27 / 61 / 12
Use of anti-hypertensive drugs (%)	43	42	45
Use of a statin (%)	59	49	72
Use of anti-coagulation drugs (%)	1.6	1.1	2.2
Use of anti-platelet drugs (%)	24	22	28

The data are the means (SD) or percentages unless otherwise indicated. AHA/NHLBI, American Heart Association and the National Heart, Lung, and Blood Institute; BMI, body mass index, HbA<sub>1c</sub>, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IDF, International Diabetes Federation.

number of baseline variables were observed to be correlated with the development of disabilities (Table 3). Advanced age, cerebrovascular disease, AHA/NHLBI-MetS and physical inactivity correlated to basic ADL impairment, whereas aging, hypertension, cataract, persistent proteinuria, cognitive decline, physical inactivity and insulin use associated with future decline of IADL ( $P < 0.05$ ). Next, a multivariate stepwise regression analysis was applied to identify the responsible factors

for impairment of ADL and IADL (Table 4). The patients' age and sex were consistently entered as confounders, together with possible associating factors, as shown in Table 3 ( $P < 0.2$ ). Baseline score of Barthel index and that of TMIG Index of Competence were also entered as a possible factor related to the impairment of the basic ADL and IADL impairment, respectively. As a result, we observed that an older age and AHA/NHLBI-MetS were independently prognostic for impairment of

Risk for physical and functional disabilities

Table 2 Changes in the activities of daily living disability during the 6-year follow-up period

	Basic ADL		6th year	Mean changes in the Barthel Index	P-value	n	Instrumental ADL <sup>†</sup>		Mean changes of the TMIG Index of Competence	P-value
	1st year	n					1st year	6th year		
Males										
65-74 years	106	19.82 (0.83)	19.54 (1.79)	-0.42 (1.93)	0.029	107	11.59 (2.22)	11.41 (2.87)	-0.36 (2.25)	0.097
75-84 years	33	19.86 (0.6)	19.31 (1.77)	-0.64 (1.71)	0.040	33	11.49 (2.31)	10.5 (3.03)	-1.24 (2.76)	0.015
Females										
65-74 years	130	19.82 (0.86)	19.73 (1.21)	0.02 (0.51)	0.733	123	11.86 (1.99)	11.43 (2.79)	-0.46 (2.14)	0.020
75-84 years	48	19.57 (1.92)	19.11 (2.17)	-0.65 (1.99)	0.030	48	11.24 (2.48)	8.86 (4.12)	-2.35 (3.26)	<.0001

<sup>†</sup>Instrumental activities of daily living (ADL) denotes the total score of Tokyo Metropolitan Institute of Gerontology (TMIG) index. The data are the means (SD).

the basic ADL (Table 4). In contrast, lower baseline score of TMIG Index of Competence, lower cognitive function, physical inactivity and insulin therapy were significant independent predictors of a future decline of the IADL (Table 4). Although the TMIG Index of Competence showed a broader range of activity in daily life for the elderly than the narrowly defined IADL, the aforementioned results were substantially similar when we only used the subscale of the IADL in the TMIG score.

Discussion

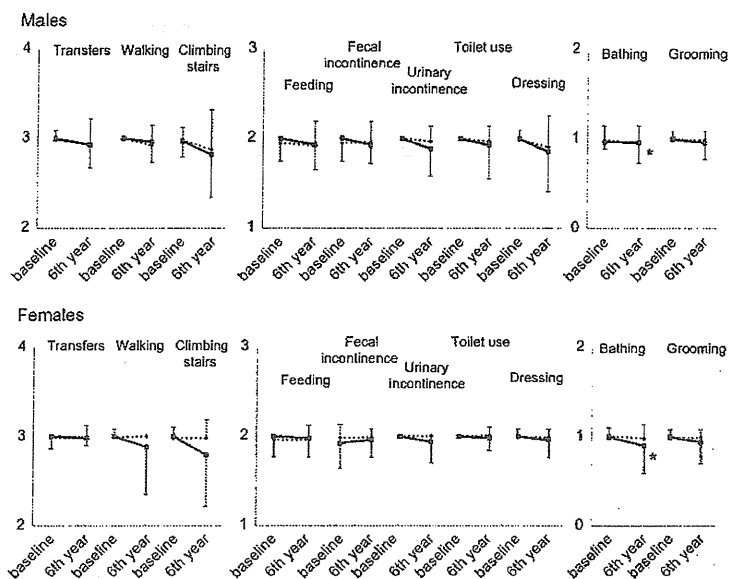
This is the first study to show the factors predicted to affect the active life expectancy of Japanese elderly patients with type 2 diabetes based on a longitudinal study. In the younger age group, the basic ADL decreased in males, whereas females became functionally impaired. In the 75-84-year-old population, both males and females lost both basic ADL and IADL functions. As prognostic factors for future disabilities, IADL dependence at baseline, lower cognitive function, physical inactivity and insulin use were responsible for IADL impairment, whereas age and AHA/NHLBI-defined MetS led to increased basic ADL disability. Of interest, the blood glucose levels, insulin sensitivity and diabetic vascular complications were not directly linked to the development of new ADL disability.<sup>29,30</sup> These results showed that different factors limit the rate of physical disability and functional limitations in diabetic elderly patients, suggesting the importance of the total management of diabetic elderly, including vascular risk factors, cognitive function, physical activity and administration of insulin therapy, in order to sustain their health and improve their likelihood of being able to live independently.

The strengths of the present study include the representative nature of the cohort, the longitudinal study design, the detailed assessment of a large number of diabetes-related variables and the long duration of follow up. The main limitation was that the study participants who did not return for follow-up assessment were excluded. Therefore, the present study might underestimate the impact of stroke, cardiovascular disease, and other serious comorbidities on the physical disability and functional limitations of elderly diabetic patients. Second, the J-EDIT did not evaluate all of the factors that could influence the ADL and IADL.<sup>30-32</sup> Information about the chronic musculoskeletal condition and a range of social, economic and behavioral parameters were limited in the current study. Detailed observations will be required to detect every responsible factor related to disability in elderly diabetic patients.

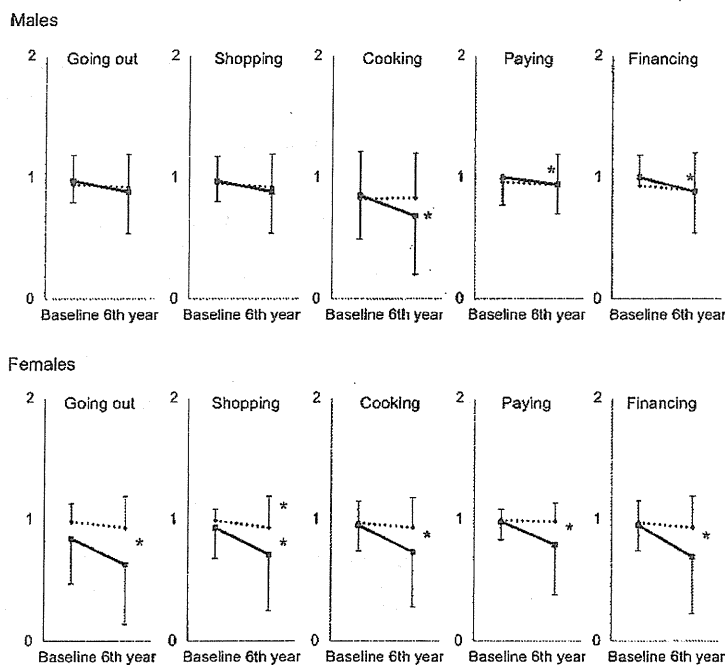
With regard to the factors predicting disability in the community-dwelling elderly people, age, cognitive



T Sakurai et al.



**Figure 1** Changes of basic activity of daily living items during the 6-year follow-up period in Japanese elderly with type 2 diabetes. Alteration of subscales of the Barthel index in the baseline and the sixth year assessment in the younger elderly group (65–74 years) and the older elderly group (75–84 years) are shown by the dotted and straight lines, respectively. Vertical bar represents standard deviation. Asterisks denote the significant difference between baseline and sixth year ( $P < 0.05$ , McNemar's test). Bathing activity tended to decline in both sexes.



**Figure 2** Progressive impairment of instrumental activity of daily living during the 6-year observation. Changes of five questions inquiring about instrumental independence of the Tokyo Metropolitan Institute of Gerontology Index of Competence in the baseline and the sixth year assessment of two age groups (65–74 years and 75–84 years) are shown by the dotted and straight lines, respectively. Vertical bar represent standard deviation. Asterisks denote the significant difference between baseline and sixth year ( $P < 0.05$ ). Cooking, paying and financing tended to decline in males of the older group, whereas impaired activity for shopping was observed in the younger female group, followed by functional disability for going out, cooking, paying and financing in the older female group.

function, self-rated health and visual impairment were previously shown to have strong-to-moderate evidence for an association, whereas sex had weak evidence.<sup>1</sup> In contrast, gender-specific risks for impaired ADL and

functional limitations have been suggested.<sup>33,34</sup> For males, the risk of ADL impairment is mainly associated with the disease burden, whereas for females, social vulnerability and functional capacities were more

Risk for physical and functional disabilities

**Table 3** The results of a univariate analysis of variables associated with impairment of basic and instrumental activities of daily living

Effect	Basic ADL				Instrumental ADL <sup>†</sup>			
	OR	Lower CI	Upper CI	P-value	OR	Lower CI	Upper CI	P-value
Age	1.082	1.009	1.161	0.027	1.105	1.048	1.164	0.000
Male sex	1.746	0.914	3.338	0.092	0.868	0.548	1.376	0.547
BMI	0.991	0.902	1.089	0.857	1.033	0.965	1.105	0.348
HbA1c (%)	1.070	0.733	1.561	0.726	0.895	0.677	1.184	0.437
HOMA-IR	1.014	0.950	1.082	0.685	1.006	0.955	1.059	0.827
Albumin (g/dL)	0.950	0.371	2.432	0.916	0.820	0.414	1.624	0.569
Hypertension	0.964	0.485	1.915	0.916	2.083	1.247	3.481	0.005
Dyslipidemia	1.097	0.562	2.139	0.787	0.909	0.570	1.451	0.690
Hypoglycemic episodes	0.804	0.359	1.797	0.594	1.058	0.608	1.841	0.841
Cerebrovascular disease	3.471	1.512	7.968	0.003	1.349	0.624	2.915	0.446
Coronary heart disease	1.039	0.410	2.632	0.936	0.845	0.431	1.657	0.624
Atrial fibrillation	2.056	0.209	20.228	0.537	0.404	0.045	3.661	0.420
Aortic calcification	1.185	0.573	2.449	0.647	1.080	0.609	1.915	0.792
Metabolic syndrome (IDF)	1.864	0.937	3.706	0.076	1.365	0.832	2.242	0.218
Metabolic syndrome (AHA/NHLBI)	3.399	1.549	7.462	0.002	1.295	0.806	2.082	0.285
Cataract	0.889	0.386	2.046	0.782	1.990	1.117	3.547	0.020
Diabetic retinopathy, proliferative	1.983	0.613	6.417	0.253	1.317	0.476	3.649	0.596
Diabetic nephropathy, persistent proteinuria	1.138	0.474	2.732	0.773	2.702	1.408	5.184	0.003
Peripheral neuropathy	0.736	0.380	1.425	0.364	1.621	0.991	2.651	0.054
Current smoker	1.723	0.784	3.785	0.175	1.222	0.660	2.262	0.523
Drinking habit	0.000	0.000		0.991	0.000	0.000		0.986
Basic ADL (Barthel Index)	0.866	0.356	2.105	0.751	-	-	-	-
IADL (TMIG Index of Competence)	-	-	-	-	1.005	0.893	1.129	0.939
Depressive state	0.992	0.832	1.182	0.927	1.069	0.947	1.206	0.282
Cognitive function	0.901	0.806	1.007	0.066	0.835	0.747	0.932	0.001
Physical activity	0.843	0.734	0.968	0.015	0.838	0.755	0.929	0.001
Use of insulin	2.199	0.462	10.479	0.322	2.653	1.083	6.498	0.033
Use of anti-hyperglycemic drugs	2.962	0.674	13.018	0.151	1.972	0.847	4.594	0.115
Use of anti-hypertensive drugs	1.152	0.604	2.197	0.667	0.702	0.440	1.119	0.137
Use of a statin	1.064	0.551	2.053	0.853	0.880	0.553	1.400	0.589
Use of anti-coagulation drugs	4.374	0.709	26.973	0.112	3.298	0.595	18.292	0.172
Use of anti-platelet drugs	1.815	0.912	3.611	0.090	1.033	0.612	1.742	0.904

<sup>†</sup>Instrumental activities of daily living (ADL) denotes the total score of Tokyo Metropolitan Institute of Gerontology (TMIG) index. Lower and upper confidence intervals (CI), lower and upper bounds of the 95% CI. AHA/NHLBI, American Heart Association and the National Heart, Lung, and Blood Institute; BMI, body mass index, HbA<sub>1c</sub>, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IADL, instrumental activities of daily living; IDF, International Diabetes Federation; OR, odds ratio.

important. In the younger group evaluated in the present study, males were more likely to lose their physical ADL and females were more likely to develop impaired IADL. Vascular complications and the other comorbidities of diabetes might impair the physical activity in males, whereas female might be more resistant to such critical events.<sup>1,33,34</sup>

The present study, together with the previous literature, showed that cognitive decline has a potent impact on IADL impairment.<sup>1</sup> Cognitive decline in patients

with type 2 diabetes has been attracting increasing attention, because diabetes increases the risk of cognitive dysfunction and new-onset dementia.<sup>35,36</sup> Cognitive decline causes serious difficulties in the independent self-care of aged people. Poor adherence to diabetes treatment easily disrupts diet control, exercise and medication, resulting in extreme hyperglycemia and hypoglycemia, which in turn further deteriorate cognitive functioning.<sup>35</sup> New strategies for preventing cognitive decline and controlling the diabetic state are

T Sakurai *et al.*

**Table 4** Predictive factors for a 6-year decline in the scores of the basic and instrumental activities of daily living

	OR	Lower CI	Upper CI	P-value
<b>Basic ADL</b>				
Age	1.087	1.002	1.179	0.046
Male sex	1.323	0.612	2.862	0.477
Cerebrovascular disease	2.121	0.759	5.933	0.152
Metabolic syndrome (AHA/NHLBI)	3.382	1.416	8.074	0.006
Cognitive function	0.892	0.766	1.039	0.142
<b>Instrumental ADL<sup>†</sup></b>				
Age	1.007	0.934	1.086	0.855
Male sex	1.121	0.582	2.157	0.733
Cataract	1.887	0.911	3.909	0.088
TMIG Index of competence score at baseline	1.390	1.113	1.735	0.004
Cognitive function	0.824	0.685	0.990	0.039
Physical activity	0.862	0.745	0.999	0.049
Use of insulin	4.575	1.328	15.762	0.016
Use of oral anti-hyperglycemic drugs	2.149	0.666	6.938	0.201

<sup>†</sup>Instrumental activities of daily living (ADL) denotes the total score of Tokyo Metropolitan Institute of Gerontology (TMIG) index. Lower and upper confidence intervals (CI), lower and upper bounds of the 95% confidence interval; AHA/NHLBI, American Heart Association and the National Heart, Lung, and Blood Institute; OR, odds ratio;

therefore required to delay the progression of functional disability in elderly people with diabetes.

One of the most important findings of the present study was that higher physical activity is beneficial for the prevention of functional limitations in older diabetic adults.<sup>30</sup> The Baecke index determines the physical activity at work, sport and leisure time.<sup>23</sup> Exercise is important to improve glycemic control by improving insulin sensitivity, and, enhancing cardiovascular function, lowering blood pressure and improving the lipid profile in patients with diabetes. In the elderly patients, loss of muscle strength is a major limiting factor that determines their chances of living an independent life.<sup>37</sup> An association of exercise with cognitive ability has been also shown.<sup>39</sup> In this connection, physical and mental disability might result in a lower level of physical activity participation. It is reported that older age ( $\geq 75$  years), female sex, and having obesity, disability or coronary heart disease were significant predictors of low adherence to physical activity, whereas advanced educational status was associated with greater participation to physical activity in USA older adults with diabetes.<sup>13,40</sup> Thus, public health campaigns targeted at increasing the amount of physical activity in elderly patients with diabetes could have a profound effect to prolong the healthy life expectancy.

To our surprise, there was a substantial impact of insulin treatment on the IADL impairment in the present study participants. Two previous studies have

shown an association of insulin therapy with reduced mobility in patients with type 2 diabetes.<sup>9,30</sup> However, why the baseline use of insulin therapy predicted IADL impairment is unclear. It seems likely that the muscle strength might be lower in patients receiving insulin treatment, or that the administration of insulin therapy might affect the quality of life of the aged patients, which might cause difficulties in maintaining their instrumental independence, intellectual activity and normal social roles.<sup>41</sup>

Besides aging, AHA/NHLBI-MetS was a significant predictor for impairment of the ADL. Although the effects of each individual cardiovascular risk factor did not reach statistical significance in the current study, the risks became more powerful when they were combined. In the reports from the NIPPON-DATA, stroke was the main cause of impaired ADL in Japan.<sup>42-44</sup> Hypertension, a leading risk factor for stroke, adversely affected the ADL in the Framingham Disability Study.<sup>45</sup> Our current observations did not disclose the impact of stroke and hypertension on ADL disability, but metabolic risk factor clustering was prognostic for a future decline of the basic ADL. The precise roles of the insulin resistance associated with MetS for ADL impairment should be further investigated in elderly patients with type 2 diabetes.<sup>46</sup>

The present J-EDIT study showed that different factors predict the future decline of the basic ADL and IADL in elderly diabetic patients, and provided a

Risk for physical and functional disabilities

conceptual framework that might help to clarify the pathways leading to disability. Among the predictive factors for disability, metabolic risk factor clustering, cognitive function, physical inactivity and insulin therapy were clinically relevant. The specific causes of each functional problem are largely modifiable, and thus, comprehensive care and treatment plans are required to allow Japanese diabetic elderly patients to have more favorable living conditions.

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### Disclosure statement

The authors declare no conflict of interest.

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