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REVIEW ARTICLE

Cognitive dysfunction: An emerging concept of a new diabetic complication in the elderly

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The incidence of type 2 diabetes mellitus (T2DM) has risen, and this trend is likely to continue. Recent advances suggest that T2DM is a risk factor for cognitive decline. We are now encountering novel complications of T2DM, namely cognitive dysfunction and dementia. Although the treatment strategy for diabetic patients with neurocognitive dysfunction has received a great deal of attention, the appropriate level of glycemic control for the prevention of the development and/or progression of cognitive decline in elderly diabetic patients remains to be elucidated. Another issue in diabetic treatment in patients with cognitive dysfunction is the selection of medicines. The best choice and combination of antidiabetic medications for the preservation of cognition should also be studied. Ample studies suggest that exercise helps to preserve cognitive function, although existing evidence does not necessarily indicate its effectiveness exclusively in diabetic patients. Exercise is a helpful non-pharmacological therapy. Considering the progressive aging of the worldwide population, more research to investigate the best way to manage this population is important. **Geriatr Gerontol Int 2013; 13: 28–34.**

Keywords: Alzheimer's disease type dementia, hypoglycemia, insulin resistance, neurocognitive assessment, vascular dementia.

Introduction

The incidence of type 2 diabetes mellitus(T2DM) has risen, and this trend is expected to continue.[1] Recent remarkable advances in pharmacological therapy in T2DM have resulted in a wide variety of treatments. Many large clinical trials have been carried out, and a variety of interventions are now available to prevent and treat the classic microvascular and macrovascular complications that occur with DM, so that people are living longer with the condition.[2] Recent studies suggested that T2DM is a risk factor for cognitive dysfunction and dementia in the elderly. With the increase in the number of elderly individuals with DM, the number of diabetic patients with cognitive dysfunction has been increasing. We are now encountering novel complications of T2DM that are not targeted by the current management strategies. As one of these new targets, cognitive impairment and dementia in patients with T2DM has generated a great deal of interest, and diabetic treatment in this population that takes brain protection into consideration should be provided.

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Cognitive impact of T2DM

Large epidemiological studies have shown the cognitive impacts of T2DM. In the Rotterdam Study,[3] T2DM patients showed an increased risk of developing dementia. The study also showed that patients treated with insulin were at a 4.3-fold higher relative risk for dementia. The Hisayama Study showed that the incidence of all-cause dementia, Alzheimer's disease (AD) and vascular dementia were significantly higher in patients with diabetes than in those with normal glucose tolerance[4] The same study showed that systemic insulin resistance was associated with the pathogenic process of AD, neuritic plaques formation.[5] The Religious Orders Study, which observed some 800 nuns and priests longitudinally for 9 years, showed that diabetic people had a 65% increased risk of developing AD.[6] The Honolulu Asia Aging Study, a cohort of Japanese Americans in Hawaii, showed that the diabetic population had a 1.8-fold higher risk of developing AD and a 2.3-fold risk of vascular dementia.[7,8]

Prospective trials also suggested that T2DM caused cognitive function to deteriorate in the elderly.

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A diagnosis of diabetes increased the odds of cognitive decline 1.2-fold to 1.7-fold (95% CI 1.3–2.3) in several neurocognitive assessments.[9] A recent systematic review of large prospective trials reported that T2DM increased the risk of AD by a factor of 1.59 (range 1.15–2.7).[10] Another systematic review reported that T2DM has a risk of vascular dementia of 2.0–4.2.[9,11]

The advances in the research in this field strongly suggest that T2DM is a risk factor for cognitive dysfunction or dementia.[12,13]

Assessment of diabetes-associated cognitive dysfunction

To screen patients with cognitive impairment, several neuropsychological assessment tools might be applied. The Mini-Mental State Examination (MMSE) is an assessment scale for global cognition including orientation, memory, calculation, verbal ability and constructional disability.[14] A full score is 30, and a cut-off point of 23 out of 24 is usually used for the screening of dementia. The MMSE subset analysis identified impaired attention and calculation as specific characteristics of DM patients,[15] whereas patients with AD had lower scores in temporal orientation and recall.[16]

As a part of a large cohort study of older DM patients (Japanese Research of Cholesterol and Diabetes Mellitus, UMIN000000516 Japan CDM), we carried out MMSE on diabetic patients aged older than 65 years in a diabetic outpatient clinic (52 males, 61 females; mean age 74.7 ± 4.6 years). Of these patients, 75 were aged less than 75 years (younger-old mean age 69.9 ± 4.7 years) and 38 patients were aged older than 75 years (older-old mean age 80.7 ± 4.4). In the younger-old group, 76.0% of patients (57/75) had a MMSE score of more than 24 (mean score 25.3 ± 4.7), and in the older-old group, 52.6% (20/38) had a MMSE score of more than 24 (mean score 24.2 ± 4.6). This small assessment showed that many diabetic patients had lower cognitive scores indicative of dementia, especially in the older-old.

Diabetes affects a wide range of cognitive domains.[17] Among the domains affected by T2DM, cognitive speed might provide early detection of diabetes-related cognitive decline[18,19] The digit symbol substitution test (DSST) is a test of cognitive speed that can be carried out relatively easily. It consists of a number (e.g. nine) of digit-symbol pairs (followed by a list of digits). Under each digit, the patient is asked to write down the corresponding symbol as quickly as possible. The number of correct symbols written within the allowed time (e.g. 90 or 120 s) is measured.

In clinical settings, the diagnosis of dementia is generally made based on the Diagnostic and Statistical Manual of Mental Disorders III revised criteria in patients with or without DM.[20] The disturbance in memory impairment with at least one of the following is required for the diagnosis of dementia: abstract thinking, judgement, higher cortical function and personality changes interferes with work or social activities. The leading cause of dementia in diabetic patients is AD, as is those without DM. DM patients often have cerebrovascular disease, and clinical-pathological studies support the notion that vascular lesions aggravate the deleterious effects of AD pathology by reducing the threshold for cognitive impairment.[21]

Pathogenesis of diabetes-associated cognitive dysfunction

The precise mechanisms underlying T2DM-related cognitive dysfunction or the development of dementia, especially AD-type dementia, remain to be elucidated; however, several hypothetical mechanisms have been proposed (Fig. 1). To develop pharmacological and non-pharmacological strategies for treating the diabetic elderly with cognitive impairment, elucidating the pathogenesis of this complication might be essential.

High glucose concentration, a major pathological characteristic of diabetes, might have toxic effects on neurons in the brain through osmotic insults and oxidative stress, and the maintenance of chronic high glucose also leads to the enhanced formation of advanced glycation end-products (AGE).[22] AGE couple with free radicals and create oxidative damage, which in turn leads to neuronal injury,[23] and they also reactivate microglia, the resident innate immune cells in the brain. A wealth of evidence shows that activated microglia can become deleterious and damage neurons.[24]

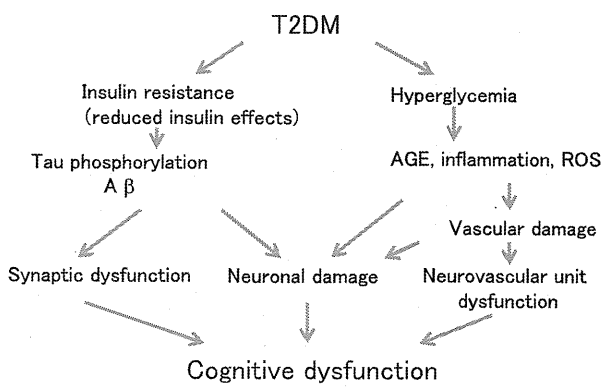

Figure 1 Pathogenesis of type 2 diabetes mellitus (T2DM)-associated cognitive dysfunction. Cognitive dysfunction in T2DM is induced by multiple pathways. Insulin resistance might be associated with Alzheimer's disease pathology, and hyperglycemia induces advanced glycation end-products (AGE) formation, inflammation and reactive oxygen species (ROS) production, which might lead to neuronal damage and neurovascular dysfunction.

T2DM, especially in conjunction with obesity, is characterized by insulin resistance and/or hyperinsulinemia. Insulin degrading enzyme (IDE) catabolizes insulin in the liver, kidneys and muscles.[25,26]

It is generally agreed that insulin located within the brain is mostly of pancreatic origin, having passed through the blood–brain barrier, although there is debate about the amount of insulin that is produced de novo within the central nervous system.[27] Major known actions of insulin in the brain include control of food intake (through insulin receptors located in the olfactory bulb and thalamus) and effects on cognitive functions, including memory.[28,29] Insulin also regulates acetylcholine transferase expression, which is an enzyme responsible for acetylcholine (ACh) synthesis. ACh is a critical neurotransmitter in cognitive function, and it might be relevant to neurocognitive disorders in diabetics.[30] Recent basic research showed that insulin signaling in the central nervous system prevents the pathological binding of amyloid beta (Aβ) oligomers.[31] Aβ oligomers are soluble molecules that attach with specificity to particular synapses, acting as pathogenic ligands.[32]

Insulin has multiple important functions in the brain, as aforementioned. These functions are disrupted in insulin-resistant states. The transport of insulin into the brain across the blood–brain barrier is reduced in insulin-resistance-associated hyperinsulinemia, and insulin levels in the brain are subsequently lowered.[33,34] Intranasal insulin showed some benefits in early AD patients.[35] With intranasal administration, insulin bypasses the periphery and the blood–brain barrier, reaching the brain and cerebrospinal fluid within minutes through extracellular bulk flow transport along olfactory and trigeminal perivascular channels, as well as through more traditional axonal transport pathways.[36,37]

Some basic research suggests that insulin signaling is involved in AD-related pathology through its effects on the Aβ metabolism and tau phosphorylation.[38] Insulin signaling activates PI3K/Akt pathway, which leads to inactivation of glycogen synthase kinase-3β (GSK-3β). GSK-3β regulates tau phosphorylation, one of the main pathological components in AD. Less insulin signaling might also induce increased activity of GSK-3β, which leads to the enhanced phosphorylation of tau protein and the formation of neurofibrillary tangles.[39] Decreased insulin signaling reduces the synthesis of several proteins, including IDE. IDE degrades Aβ as well as insulin, and reduced amounts of IDE might result in greater amyloid deposition. The results of pathological assessments in AD with or without DM, however, are highly controversial.[40,41] More research would be warranted to elucidate the relevance of insulin and insulin resistance in the underlying mechanism of T2DM-assocaiated cognitive dysfunction.

Diabetic patients often have ischemic brain lesions.[42] Even asymptomatic cerebral infarctions have affects on the cognition in elderly diabetic patients.[18,43] On cerebral magnetic resonance imaging, white matter hyperintensities and lacunae, both of which are frequently observed in the elderly, are generally viewed as evidence of small vessel disease in the brain (white matter lesions and lacunae). Small vessel diseases affect cognitive function in older diabetics.[18,44] DM also affects the function of microvascular endothelial cells. The deterioration of the endothelial cell function leads to the disruption of blood–brain barrier function, which might induce neuroinflammatory reactions and neurodegeneration.[45] The endothelial cells play a critical role in the control of hemodynamic coupling among neuronal, glial and vascular components; that is, "neurovascular units". Dysfunction of "neurovascular units" might have some impact on cognition in diabetic patients.[46]

Treatment of vascular risk factors including T2DM was reportedly associated with a lower conversion rate from mild cognitive impairment to AD[47] or slower cognitive decline in AD patients.[48] Comprehensive management in DM patients should be warranted.

Treatment and management of diabetic patients with cognitive impairment

T2DM is associated with cognitive dysfunction; however, it has not yet been made clear whether glycemic control leads to the preservation or improvement of cognitive function. Several prospective studies[19,49,50] have shown that higher glycated hemoglobin (HbA1c) levels at baseline are associated with cognitive decline. A recent prospective study by Christman *et al.*, however, showed that HbA1c levels at baseline had no effects on cognitive function.[51] A large cohort study, the Action to Control Cardiovascular Risk in Diabetes–Memory in Diabetes (ACCORD-MIND) trial, has found that HbA1c levels were cross-sectionally associated with worse performance on several cognitive functional tests.[52] However, the results of the interventional study were rather disappointing.[53] Although total brain volume in the intensive glycemic control group was significantly greater than in the standard treatment group after 40 months, there was no significant difference in cognitive assessment. The results of the study, however, should be interpreted cautiously because of the early drop-outs in the intervention group.

In the ACCORD-MIND study, the intensive control group achieved a HbA1c level of 6.6% compared with 7.5% in the standard treatment group. Several smaller studies involving less intensive glycemic treatment, however, indicated that modest cognitive decrements in patients with T2DM are partially reversible with the improvement of glycemic control,[54–59] although not invariably.[60] Postprandial hyperglycemia is associated

with atherosclerosis and diabetic complications,[61] and a control of postprandial hyperglycemia might prevent cognitive decline in older diabetic individuals.[59] These studies suggested that metabolic control might have beneficial effects in terms of cognitive function; however, the appropriate levels of blood glucose control remain unclear. In contrast, a recent report has suggested that a history of severe hypoglycemic episodes is associated with a greater risk of dementia.[62] The diabetic control in this population should be balanced between the merits of treatment and the risk of hypoglycemia.

Another issue related to the treatment that pertains to cognitive dysfunction is the selection and combination of antidiabetic medicines. The Rotterdam Study reported that insulin use increased the incidence of dementia.[3] However, many confounding factors must be considered when interpreting the results of that study. The patients who used insulin might have had worse diabetic control, a longer history and more complications, and these factors might have some impact on the incidence of dementia. Greater insulin resistance means that a greater amount of insulin is required to control the blood glucose level. The association of the use of an excessive amount of insulin with insulin resistance status might be undesirable, the appropriate prescription of insulin for maintaining a desirable blood glucose level has not yet been determined for individuals with insulin resistance. A small study reported that pioglitazone, an insulin sensitizer, has some beneficial effects on cognition in AD.[63] Comprehensive management in combination with insulin use would be necessary to achieve appropriate glycemic control, and efforts to reduce insulin resistance would be warranted.

Recently, a new class of diabetic pharmacological treatments known as incretin-related medicines has emerged. Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP), whose activity is reduced in insulin resistance, have been implicated in central nervous system function, including cognition, synaptic plasticity and neurogenesis.[64] An animal study showed that GLP-1 prevented the neurodegenerative developments in AD model mice.[65] Further clinical investigation from the perspective of brain protection is warranted.

Many studies suggested that exercise has the potential to protect brain function. A systematic review of the Cochran database by Angevaren *et al.* reported the effects in elderly individuals without known cognitive impairment, and another systematic review of a prospective cohort study by Hamer *et al.* reported that exercise reduces the risk of incidence of dementia by 28% and of AD by 45%.[66,67]

Exercise also has effects on patients with mild cognitive impairment and dementia.[68] Although existing evidence does not indicate the effects of exercise on the protection of brain function exclusively in the diabetic population, exercise has multiple established effects on diabetic patients, including the improvement of insulin resistance. Studies to investigate the effects of exercise on diabetic cognitive dysfunction are warranted.

Cognitive dysfunction is associated with poor ability of self-care in elderly diabetics, and the use of both health and social services.[69] In addition, physical function is often more compromised in those with cognitive impairment. Individuals with DM with cognitive impairment might have difficulty carrying out the daily tasks of DM self-care effectively,[70] which might result in worse glycemic control than in individuals without cognitive impairment. A study reported that cognitively impaired DM patients were at increased risk of mortality and functional disability.[71] The relationship between cognition and self-management ability might be bidirectional. While it could be that poor self-management practices lead to poorer metabolic control and therefore brain dysfunction, cognitive deterioration would lead to changes in self-management ability.

A depressive mood is often comorbid with dementia,[72] especially in diabetics.[73] Depressed mood might also be associated with cognitive impairment and might interfere with effective self-management.[74–77]

People with dementia often experience behavioral and psychological symptoms of dementia (BPSD) during the course of their illness. The management of dementia is complicated by BPSD, such as psychosis, depression, agitation, aggression and disinhibition. BPSD also disrupts the daily diabetes care routine, with "denial" of having diabetes or memory loss (anosognosia) being the most disruptive.[78] Caregivers often report that caring for both diabetes and dementia is highly burdensome, that they feel overwhelmed by BPSD, and that they want more support from family and from the patients' healthcare providers.

To control BPSD, antipsychotic medication is sometimes prescribed. Antipsychotic drugs, especially second-generation drugs including olanzapine and quetiapine, have the potential to induce weight gain and elevate plasma glucose levels.[79] The use of these drugs in demented diabetic patients should be avoided.

Conclusion

Cognitive dysfunction might be a novel class of diabetic complication in the elderly. The management of diabetic patients with this complication is challenging and presents many unresolved problems. Considering the progressive aging of the worldwide population, it will be important to carry out investigations to improve our understanding of the association between T2DM and cognitive dysfunction, and to determine the best way to manage these populations.

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Disclosure statement

Nothing to declare.

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ORIGINAL ARTICLE: BEHAVIORAL AND SOCIAL SCIENCES

Day-care service use is a risk factor for long-term care placement in community-dwelling dependent elderly

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Aims: To identify predictors of long-term care placement and to examine the effect of day-care service use on long-term care placement over a 36-month follow-up period among community-dwelling dependent elderly.

Methods: This study was a prospective cohort analysis of 1739 community-dwelling elderly and 1442 caregivers registered in the Nagoya Longitudinal Study for Frail Elderly. Data included the clients' demographic characteristics, basic activities of daily living, comorbidities, and use of home care services, including the day-care, visiting nurse, and home-help services, as well as caregivers' demographic characteristics and care burden. Analysis of long-term care placement over 36 month was conducted using Kaplan–Meier curves and multivariate Cox proportional hazards models.

Results: Among the 1739 participants, 217 were institutionalized at long-term care facilities during the 36-month follow-up. Multivariate Cox regression models, adjusted for potential confounders, showed that day-care service use was significantly associated with an elevated risk for long-term care placement within the 36-month follow-up period. Participants using a day-care service two or more times/week had significantly higher relative hazard ratios than participants not using such a service.

Conclusion: The results highlight the need for effective measures to reduce the long-term care placement of day-care service users. Policy makers and practitioners must consider implementing multidimensional support programs to reduce the caregivers' willingness to consider long-term care placement. **Geriatr Gerontol Int 2012; 12: 322–329.**

Keywords: community, day-care service, elderly, long-term care placement, nursing home.

Introduction

Japan introduced a universal-coverage long-term care insurance (LTCI) program in April 2000.[1,2] This program brought a radical change from traditional, family-based care toward elderly care involving socialization and the integration of medical care and welfare

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services. There are two types of services covered by LTCI: community-based services and institutional services. Community-based services include various programs such as the home-help service, visiting bathing service, visiting rehabilitation, day care (rehabilitation), visiting nurse service, assistive device leasing, short stays (temporary stays at nursing facilities), in-home medical care, and care management services, care services provided by for-profit private homes, and allowance for the purchase of assistive devices and home renovation. In theory, the applicant can choose any certified providers and listed services.

In practice, a major role is played by a "care manager," a licensed professional who has passed an examination and undergone brief training, who draws up a care plan and a weekly schedule of service provision for individual seniors. It is essential that the care plan must be approved by the client or the client's family, and new care managers can be requested at any time if care plans prove inadequate. The maximum amount of reimbursement in the LTCI system is capped according to the care level.[3,4] Elderly beneficiaries pay a 10% co-payment for services received.

The aims of LTCI home care programs are to reduce the care burden of caregivers, maintain and improve the functional abilities and well-being of elderly people, and decrease the use of institutional care services and mortality. However, there is little evidence of how community-based services affect care recipients' outcomes, the subjective burden of caregivers or reduce the use of institutional care services.

The Nagoya Longitudinal Study for Frail Elderly (NLS-FE) compares outcomes of the use of different care services provided by the LTCI program; it was designed to provide a structured comparison of services and a comprehensive standardized assessment instrument.[5,6] Day-care service, which includes "day care" and "day rehabilitation," is provided in designated centers and is one of the major LTCI community-based services. Day-care service is a facility-based daytime program of nursing care, rehabilitation therapies, supervision and socialization that enables frail, older people, who are in poor overall health and have multiple comorbidities and varying physical or mental impairments, to remain active in the community. The individual visits the facility once or several times a week and then returns to his or her own home.

Although one of the aims of day-care service is to minimize or delay the possibility of institutionalization and maximize the potential for care recipients to maintain an independent life in the community, only a limited number of studies have examined the impact of day-care service on long-term care (LTC) placement among community-dwelling older adults. Moreover, most of these studies have targeted patients with dementia. Previous studies targeting dementia have demonstrated that day-care use is associated with nursing home placement in persons with Alzheimer's disease.[7,8] However, the effect of using day-care service on the LTC placement of community-dwelling, frail elderly with various chronic diseases remains unknown, although it has been reported that day-care services reduce caregiving time and provide respite to caregivers.[9,10]

In the present prospective cohort study using the NLS-FE cohort, we examined whether day-care service use among community-dwelling older people using various community-based services under LTCI in Japan influenced LTC placement during a 36-month follow-up period. Analysis of LTC placement over the 36-month was conducted using Kaplan–Meier curves and multivariate Cox proportional hazards models.

Methods

Subjects

The present study employed baseline data of the participants in the NLS-FE and data on the mortality of these patients during the 36-month follow-up. Details of participants and the NLS-FE have been published elsewhere.[5,6] The study population initially consisted of 1875 community-dwelling dependent elderly (632 men and 1243 women, age 65 years or older) who were eligible for LTCI, lived in Nagoya City and received various home care services from the Nagoya City Health Care Service Foundation for Older People, which has 17 visiting nursing stations associated with care-managing centers. These NLS-FE participants, who were enrolled between 1 December 2003 and 31 January 2004, were scheduled to undergo comprehensive in-home assessments by trained nurses at the baseline and at 6, 12, 24, and 36 months. At 3-month intervals, data were collected about any events participants experienced, including admission to the hospital, LTC admission and mortality. Per the procedures approved by the institutional review board of Nagoya University Graduate School of Medicine, participants provided written informed consent and, for those with substantial cognitive impairment, a surrogate (usually the closest relative or legal guardian) or family caregivers provided it.

Data collection

Data were collected from standardized interviews with patients or surrogates and caregivers conducted at clients' homes and from care-managing center records by trained nurses. The data included clients' demographic information, depressive symptoms as assessed by the short version of the Geriatric Depression Scale (GDS-15),[11] and a rating for the seven basic activities of daily living (ADL) (feeding, bathing, grooming, dressing, using the toilet, walking, and transferring) using

summary scores ranging from 0 (total disability) to 20 (no disability).[12] The interview with participants also included questions about using care services, including day-care service, which includes day care and day rehabilitation, visiting nurse service, and home-help service programs, as well as medical services. In addition, the weekly frequency with which clients used these services was obtained.

Information obtained from care-managing center records included data on the following physician-diagnosed chronic conditions: ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, dementia, cancer, and other diseases comprising the Charlson comorbidity index,[13] which represents the sum of a weighted index that takes into account the number and seriousness of preexisting comorbid conditions.

Data were also obtained from caregivers concerning their own personal demographic characteristics and their subjective burden as assessed by the Japanese version of the Zarit Burden Interview (ZBI),[14] which is a 22-item self-report inventory that examines the burden associated with functional behavioral impairments in the home care situation.

For the analysis, 136 of the original 1875 participants were excluded because of missing data regarding service use or confounding/intermediary variables, leaving 1739 in the analysis. Of these 1739 participants, 412 could not complete the GDS-15 because of severe cognitive impairment or communication impairment. Also, among the 1739 older participants, 1442 participants had primary caregivers. Of these 1442 caregivers, 289 could not or refused to complete the ZBI.

We defined three types of care facilities providing LTCI as LTC facilities: nursing homes, care health facilities for the elderly, and group homes for elders with dementia. We assessed LTC placement over 36 months using event reports at 3-month intervals. LTC placement was confirmed by visiting nurses or care-managing center records. Placement time was defined as the number of months (3-month intervals) between the baseline interview and the event report of LTC placement. We censored participants living at home after 36 months of follow-up ($n = 773$), at death ($n = 401$), or at dropout ($n = 248$).

Statistic analysis

The Student's t-test and χ^2 test were used to compare differences at baseline between users and nonusers of day-care service. To create ideal model, we first evaluated the association between each covariate and LTC placement using univariate Cox proportional hazards model. LTC placement over 36 months was estimated for each group (day-care service use once or multiple times per week, and nonusers) using the Kaplan–Meier method. We then evaluated the impact of day-care service use and weekly frequency of service use on the overall model with a series of Cox proportional hazards models, which included gender, age, ADL status, presence or absence of dementia, and caregiver's sex, age and ZBI score. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95%CI. All analyses were performed using the SPSS v. 11 (Chicago, IL, USA). $P \leq 0.05$ was considered significant.

Results

When the baseline characteristics were compared between day-care service users and nonusers, older age, a higher Charlson comorbidity index, and a lower GDS-15 score were observed in day-care service users than in nonusers (Table 1). Higher prevalence rates of cerebrovascular disease and dementia were also observed in day-care service users. The rates of nursing service use, home-help service use and living alone among day-care service users were lower than those of nonusers. Among caregivers' variables, the rate of male caregivers was significantly lower for day-care service users than nonusers. Higher ZBI score was detected in users' caregivers.

Among the 1739 participants, 217 participants were institutionalized at LTC facilities during the 36-month follow-up period. A higher rate of LTC placement was observed in day-care service users than in nonusers ($n = 143$, 18.5% vs. $n = 74$, 7.7%, $P < 0.001$) (Table 1). Among the 1327 participants who could complete the GDS-15, 150 participants were institutionalized at LTC facilities during the 36-month follow-up period. Of the 412 who could not perform the GDS-15, 67 were institutionalized at LTC facilities during the 36-month follow-up period. A higher LTC placement rate was observed in the participants who could not complete GDS-15 test than in those who could (16.3% vs. 11.3%, $P = 0.008$). There were no significant differences in LTC placement rate between participants living alone and those living with others (12.8% vs. 12.4%, $P = 0.802$). Furthermore, there was no significant difference in the LTC placement rate between participants living with caregivers who completed the ZBI and those who did not (13.0% vs. 11.1%, $P = 0.375$).

Cox hazard regression and Kaplan–Meier models

Table 2 shows the results of the unadjusted univariate Cox hazard regression analysis, which suggested that LTC placement within the 36-month follow-up period was associated with older age, a lower function of basic ADL, day-care service use, and the presence of dementia (Table 2). Among caregivers' variables, only higher care burden was associated with LTC placement. Figure 1A shows Kaplan–Meier curves exploring the

Table 1 Baseline characteristics of the 1739 care recipients and the 1442 caregivers

	Day-care service		*P*-value
	User	Nonuser	
Care recipients (n = 1739)			
Men/women (% of men/total)	256/518 (33.1)	319/646 (33.1)	0.994
Age, years (mean, SD)†	81.4 (7.7)	80.2 (7.5)	0.002
Basic ADL, range: 0–20 (mean, SD)†	13.0 (5.9)	13.5 (6.7)	0.099
Charlson comorbidity index, range: 0–35 (mean, SD)†	2.2 (1.5)	1.8 (1.6)	<0.001
GDS-15 (range: 0–15), mean (SD)†‡	6.1 (3.6)	6.8 (3.7)	0.002
Chronic diseases (% of total)			
Ischemic heart disease	12.4	12.0	0.809
Congestive heart failure	8.7	8.4	0.845
Cerebrovascular disease	42.8	27.6	<0.001
Diabetes mellitus	12.4	11.7	0.659
Dementia	44.2	22.6	<0.001
Cancer	8.0	10.1	0.142
Visiting nurse service use (% of total)	38.1	54.0	<0.001
Home-help service use (% of total)	42.4	50.5	0.001
Regular medical checkups (% of total)	55.3	60.7	0.023
Living alone (% of total)	17.3	28.1	<0.001
Hospitalization during 36-month follow-up (% of total)	42.5	41.0	0.537
Long-term care placement during 36-month follow-up (% of total)	18.5	7.7	<0.001
Caregiver variables (n = 1442)			
Men/women (% of men/total)	137/553 (19.9)	217/535 (28.9)	<0.001
Age (years), mean (SD)†	63.4 (12.3)	64.3 (12.4)	0.177
Relationship to care recipient (% of total)			
Spouse	35.4	42.8	
Child	35.8	37.1	<0.001
Daughter-in-law	25.7	15.4	
Others	3.2	4.7	
ZBI score, range: 0–88 (mean, SD)†§	30.1 (16.8)	26.8 (17.0)	0.001

†Student's t-test, others were analyzed by χ^2 test (user vs.nonuser). ‡GDS-15, geriatric depression scale, n = 1327. §ZBI, the Zarit Burden Interview. n = 1153.

association between weekly frequency of day-care service use and time to LTC placement (3-month intervals). The risk of LTC placement was higher for participants who used day-care service more frequently than those who used it less frequently.

Table 3 shows the results of the series of Cox proportional hazards models that examine the HR of day-care service use to LTC placement during the 36-month follow-up period. The sequential adjustment had minor influences on the association between day-care service use and LTC placement during the 36-month follow-up period. The HR for the fully adjusted models was 2.34 (95%CI = 1.60–3.41).

In the Cox regression model adjusted for potential confounders, participants with more frequent use of day-care service had a significantly higher relative HR than participants with less frequent use of the service (Fig. 1B). Although there was no significant association between using day-care service once per week and the risk of LTC placement, participants using a day-care service two or more times per week had a significantly higher relative HR than participants not using the service.

Discussion

In the present study we demonstrated that day-care service use was associated with LTC placement during the 36-month study period among community-dwelling frail elderly using various community-based services under the LTCI program in Japan. Many previous studies have examined predictors of LTC placement in study samples, but these have been limited to people with dementia and there have been fewer evaluations of risk factors for LTC placement in community samples.[15–19] Few studies have comprehensively investigated how both caregiver and recipient characteristics influence LTC placement.[19] Previous observations

Table 2 Univariate Cox proportional hazards model to identify predictors of long-term care placement over 36 months

Variable	Univariate HR†	95% CI	*P*-value
Care recipients (n = 1739)			
Men (vs. women)	0.75	0.56–1.02	0.067
Age (continuous)	1.04	1.03–1.06	<0.001
Living with someone (vs. living alone)	1.02	0.74–1.39	0.920
Basic ADL (range: 0–20) (continuous)	0.97	0.95–0.99	0.001
Regular medical checkups per month (no regular checkup)	1.19	0.90–1.56	0.214
Formal care use (vs. nonuse)			
Visiting nurse	1.15	0.88–1.51	0.295
Day-care service	2.42	1.83–3.21	<0.001
Home helper	0.71	0.81–1.37	0.714
Charlson comorbidity index (continuous)	1.04	0.95–1.13	0.375
GDS-15 (continuous)†	1.01	0.96–1.05	0.762
Presence of chronic diseases (vs. absence)			
Ischemic heart disease	1.02	0.68–1.53	0.926
Congestive heart failure	1.16	0.73–1.84	0.523
Cerebrovascular disease	1.00	0.76–1.32	0.986
Diabetes mellitus	0.78	0.50–1.22	0.272
Dementia	3.00	2.29–3.92	<0.001
Cancer	0.84	0.49–1.44	0.520
Hospitalization during 36-month follow-up (vs. never admitted)	1.08	0.82–1.42	0.576
Caregiver variables (n = 1442)			
Men (vs. women)	0.95	0.67–1.33	0.752
Age (continuous)	1.01	1.00–1.02	0.059
Character of caregiver (vs. child)			
Spouse	0.90	0.64–1.28	0.555
Daughter-in-law	1.29	0.88–1.88	0.189
Others	1.21	0.60–2.43	0.596
ZBI score(continuous)‡	1.03	1.02–1.04	<0.001

†GDS-15, geriatric depression scale, n = 1327. ‡ZBI, the Zarit Burden Interview. n = 1153. HR, hazard ratio.

demonstrated that common risk factors of LTC placement of community-dwelling elderly were older age, presence of dementia, and caregiver's burden.[16,18,19]

Although one of the aims of day-care service is to minimize or delay the possibility of institutionalization and maximize the potential for care recipients to maintain an independent life in the community, only a limited number of studies have examined the impact of day-care service on LTC placement among community-dwelling older adults – and most of these have targeted demented patients. Previous studies targeting dementia have demonstrated that day-care use is associated with nursing home placement in persons with Alzheimer's disease.[7,8] We expanded the target group and demonstrated a striking association between day-care service use and the risk of LTC placement for community-dwelling dependent elderly patients with various chronic diseases, even after adjusting for the presence of dementia and caregiver's burden. We clearly showed, after adjusting for potential confounders, that the frequency of day-care service use had a negative impact on LTC admission with the 36-month follow-up period. The use of day-care service two or more times per week negatively affected LTC placement, but there was no significant association between institutionalization and the use of day-care service once a week. It is possible that participants with more comorbidities and a more depressive mood use day-care service more frequently; thus, participants using a day-care service two or more times per week were more likely to be placed in LTC facilities. However, even if comorbidity index score and GDS-15 score were included in the analysis, the association between LTC placement and the use of day-care service two or more times per week persisted (data not shown). This contrasts with our recent report that the risk of 21-month mortality among community-dwelling elderly was reduced significantly with frequent use of day-care service.[6] The complex decision to place older

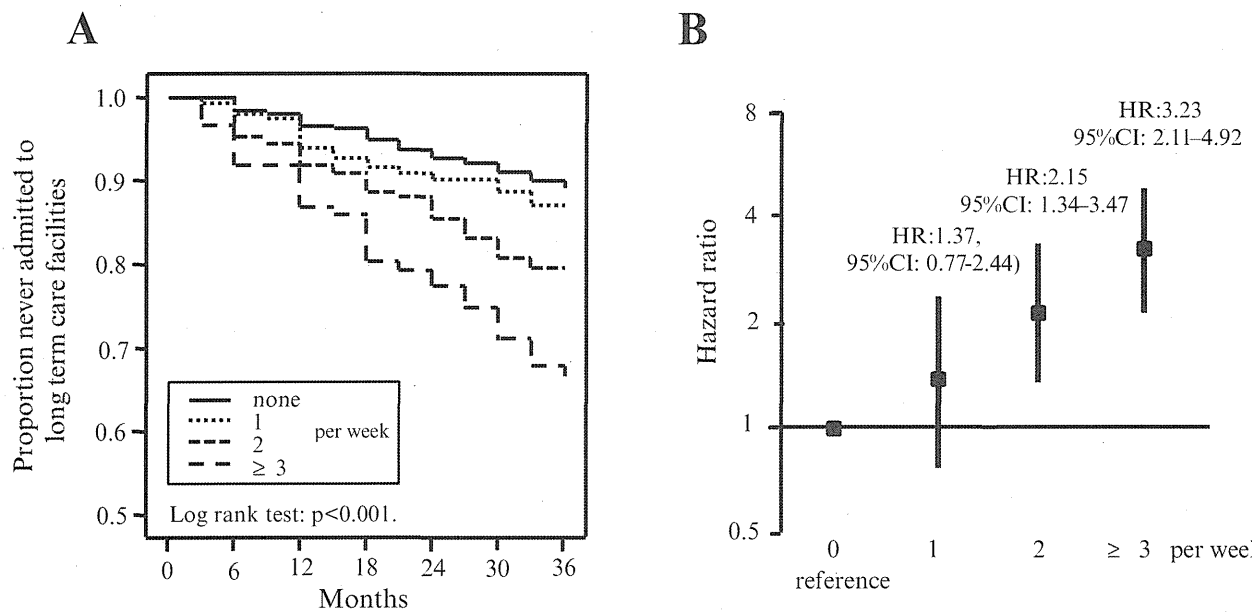

Figure 1 (A) Kaplan–Meier estimates of long-term care (LTC) placement over 36 months according to the frequency of day-care service use (times per week). The log-rank test: $P < 0.001$. (B) Risk of LTC placement based on the frequency of day-care service use (times per week), adjusting for potential confounders (recipient's gender, age, ADL status, presence or absence of dementia, caregiver's gender, age, and Zarit Burden Interview score). The y-axis is the adjusted hazard ratios (HR) on a log scale. Black squares are point estimates from a Cox proportional hazards model adjusting for potential confounders. The error bars represent 95%CI. A simple black square without confidence intervals represented the referent group, nonusers.

Table 3 Hazard ratios for long-term care placement associated with day-care service use (multivariate models)

Models	Hazard ratio	95% CI	*P*-value
Model 1 ($n = 1739$)	2.32	1.75–3.08	<0.001
Model 2 ($n = 1739$)	1.96	1.47–2.62	<0.001
Model 3 ($n = 1150$)	2.34	1.60–3.41	<0.001

Model 1 includes recipient gender and age. Model 2 includes recipient gender, age, ADL score, and presence or absence of dementia. Model 3 includes variables used in model 2 and caregiver's gender, age and Zarit Burden Interview score.

people in LTC is based on care recipient and caregiver characteristics and the sociocultural context of the recipient and caregiver. We do not know the exact reason for this negative effect of day-care service on LTC placement. There are conflicting findings in regard to the effect of day-care service on caregivers' stress, depression, subjective or objective burden, and physical and emotional well-being,[20] although a recent relatively large study demonstrated that day-care service had a beneficial effect on restricting caregiving time and providing respite to caregivers.[9,10] It is possible that day-care service alone cannot satisfy the complex needs of caregivers and care recipients sufficiently to enable continued home care, and it is unlikely to change the caregiver's preference for institutional placement.[21] Although we still do not know whether the characteristics of caregivers and recipients, or day-care service use itself, increase the risk of LTC placement, the relief and improved mental and physical well-being of caregivers following day-care service use may enhance the willingness of caregivers to consider LTC placement. Caregivers who use day-care service or other respite services may become more aware of their level of stress and more willing to consider LTC placement as an acceptable option, especially if the service experience is positive or if the caregiver receives encouragement to institutionalize from professionals or other caregivers.[22]

This study has important limitations. First, the study was not a randomized intervention trial. Japan has introduced the LTCI program, which provides various services, including day-care services, according to clients' preferences. Therefore, we could not randomize the use

of this service. Because of the observational design of the present study, differences in unmeasured factors including the severity of patients' chronic diseases, caregivers' health conditions, and quality of services may account in part for the findings. Those who use formal services may have greater need for caregiving than those who do not use formal services. The unmeasured needs that contribute to day-care service use may be stronger than the positive effects of service. Other aspects of the present study should also be considered. In the analysis, baseline data of service use was included, but changes in service use during the follow-up period were not considered. Our results may not be representative of the Japanese frail elderly in the community as a whole because the subjects in this study represented an urban population. In addition, these findings may not be generalizable to other populations given that local health practices, a variety of social and economic factors, ethnic attitudes about caring for very old people, and cost/access to day-care centers may have influenced these results.

In the present study, we showed that day-care service does not achieve the LTCI program aim of reducing the use of institutional care services of elderly people to enable them to maintain their lives at home. It may be possible that the respite for caregivers provided by day-care service is not enough to continue caregiving at home. As is true for any observational study, we cannot firmly establish a cause-and-effect relationship between day-care service use and LTC placement. In addition, the present study could not evaluate the exact reasons for the unfavorable effect of this service on LTC placement. Further studies are needed to determine why caregiving families decide to use day-care services, reasons for LTC placement, and whether day-care services meet the needs of families and care recipients throughout the caregiving career. In addition, future research should assess the quality of day-care programs and examine whether the quality of day-care services affects the LTC placement of clients. Health-care providers and care managers should recognize that day-care service use may augment LTC placement in dependent older people. Policy makers and practitioners should consider implementing a multidimensional support program to reduce caregivers' willingness to consider LTC placement.

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Disclosure statement

The authors have no conflicts of interest with any of the manufacturers of medications evaluated in this paper.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Cognitive impairments and functional declines in older adults at high risk for care needs

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Aim: Functional status of those who have very mild cognitive impairment have not been sufficiently investigated. In the current study, we analyzed the characteristics of functional awareness in older adults who had cognitive impairment and were at high risk of requiring support/care (termed as specified elderly at high risk for care needs in the long-term care insurance scheme).

Methods: The answers of a health check, which is provided by the local municipal government for those aged 75 years or older who have not been certified as eligible for care services, were analyzed. The differences of the variables between the two groups regarding yes/no answers to each of three cognition-related questions were analyzed. Then, a multiple logistic analysis was carried out to investigate the association of yes/no answers of the three cognition-related questions and the awareness of functional decline.

Results: The participants who had cognitive impairment had greater awareness of functional declines. Multiple logistic regression analysis showed that subjective memory impairment and disorientation were significantly associated with a wider range of awareness of functional decline.

Conclusions: Subjective cognitive impairment was associated with a wide range of awareness of functional decline in older adults at high risk for care need. **Geriatr Gerontol Int 2013; 13: 77–82.**

Keywords: depressive mood, dysphagia, instrumental activities of daily life, memory impairment, physical activity, vitality.

Introduction

Screening for cognitive impairment is essential for better health outcomes. Early identification and intervention holds the promise of improving overall care for affected persons through the use of chronic disease management strategies. In general, the existing literature does not support screening of unselected older adults for cognitive impairment;[1] however, screening in a high-risk population might be valid.

Several factors are closely associated with mild cognitive impairment (MCI) and very early dementia. Depressive mood might be a risk factor or an early manifestation of dementia.[2–4] Subtle impairments of instrumental activities of daily living (IADL) might also be very early manifestations.[5,6]

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In Japan, the public long-term care insurance system provides services to older adults who have been certified as requiring support (level 1 and 2) or care (levels ranging from 1 to 5 depending on their care needs). Uncertified, but not quite healthy, older adults who are considered at high risk of requiring support/care are categorized as specified elderly at high risk of care needs (specified elderly are provided with preventive care services by the municipalities in which they reside). The specified elderly are community-dwelling and have neither basic activities of daily living (B-ADL) impairments nor dementia. The specified elderly, however, is supposed to be the transitional stage to requiring care. Elucidating the characteristics of this group and developing some adequate intervention on this population to prevent the transition to requiring care are warranted. The local governments provide a health check of the uncertified elderly annually, in which all examined subjects complete a basic yes/no questionnaire that consists of simple assessments of their instrumental activities of daily living (7 items), memory problems (3 items), walking status (5 items), dysphagia (3 items), nutritional

status (2 items) and depressive mood (5 items).[7] Subjective memory complaint might be an easy method to screen cognitive impairment, and a report showed that subjective memory complaint was associated with depressive mood and difficulties of activities of daily living (ADL).[8] In this assessment, subjective cognitive dysfunction was evaluated by three questions, and in the same assessment awareness of functional declines were also evaluated.

However, the functional characteristics of those who have subjective cognitive impairment by this assessment in the specified elderly at high need for requiring care have been unclear. Elucidating the characteristics of this population might lead to the development of intervention for the prevention of the transition to dementia and/or the status of requiring care.

In order to portray the characteristics of awareness of functional decline in those who are considered to have subjective cognitive impairment by this assessment, we examined the associations between non-cognitive items and cognitive items of the questionnaire in older adults at high risk of requiring support/care.

Methods

Measurements

To screen the elderly at high risk for care, a health check is provided by the local municipal government for those elderly aged 75 years or older who have not been certified as eligible for care services.

The health check includes a yes/no questionnaire that consists of simple assessments of their IADL (7 items), subjective cognitive problems (3 items), walking status (5 items), dysphagia (3 items), nutritional status (2 items) and depressive mood (5 items). In the current study, we calculated the scores for each of these six domains, with higher scores indicating worse functioning. The data for 1163 men and 2651 women who were determined to be specified elderly were obtained from annual health checks implemented in one of the urban municipalities in central Japan during October and November in 2009.

Continuous variables (age, blood pressure, hemoglobin, serum albumin and body mass index) were compared by Student's *t*-test, and others were compared by χ^2 analysis.

The questionnaire was as follows;

1) IADL

1. Do you go out alone using transportation? 2. Do you shop for daily necessaries by yourself? 3. Do you manage your bank account on your own? 4. Do you visit your friends alone? 5. Are you consulted by your family or friends?

2) Waking status

6. Do you climb up the stairs without holding onto handrails or walls? 7. Do you stand up without assistance? 8. Can you walk for more than 15 min without rest? 9. Have you fallen within a year? 10. Are you anxious about falls?

3) Nutrition

11. Have you lost more than 2–3 kg in weight in the recent 6 months? 12. BMI < 18.5 kg/m^2

4) Dysphagia

13. Do you have difficulty in eating hard food? 14. Do you choke with liquid? 15. Do you care about dry mouth?

5) Vitality

16. Do you go out more than once a week? 17. Do you go out less frequently than last year?

6) Cognition

18. Are you told that you repeatedly ask the same things? 19. Do you look up the numbers, dial and make phone calls without help? 20. Do you sometimes forget the date?

7) Depressive mood

21. Do you feel unfulfilled with daily life? 22. I do not enjoy my life as I used to (recent 2 weeks). 23. I feel more bothered to do everyday things than before (recent 2 weeks). 24. I do not feel that I am useful (recent 2 weeks). 25. I feel tired for no reason (recent 2 weeks).

The differences of the variables between the two groups regarding yes/no answers to each of the three cognition-related questions (Are you told that you always ask the same things? [memory]; Do you look up numbers, dial and make calls without help? [telephone]; Do you sometime forget what day it is? [orientation]) were analyzed. In the analysis, answers for related questions were scored as follows: IADL, 0–5; walking status, 0–5; depressive mood, 0–5; dysphagia, 0–3; vitality, 0–2; and nutritional status, 0–2. The difference of the distribution was analyzed by Student's *t*-test, Mann–Whitney *U*-test, or χ^2 analysis. Then, a multiple logistic analysis was carried out to investigate the association of yes/no answers of these three cognition-related questions and the awareness of functional decline.

Results

The characteristics of the participants are shown in Table 1.

IADL, walking status, depressive mood, vitality, and nutrition were all associated with subjective memory impairment and disorientation in univariate analysis (Tables 2 and 4). IADL, walking status, depressive mood and vitality were associated with an inability to call by themselves, but dysphagia and nutritional status were not significantly associated (Table 3).

Multiple logistic regression analysis showed that vitality was not associated with each of the three

cognition-related items (Table 5), although it was associated in univariate analysis (Tables 2–4). Nutritional status was not associated with subjective memory impairment and disorientation by multiple logistic regression analysis either (Table 5).

Discussion

The present study showed that self-claiming memory impairment was associated with a wide range of awareness of functional decline. The results also showed that depressive mood was significantly associated with subjective cognitive impairment. Community studies in normally-aging populations suggest that depression is associated with cognitive decline.[9–18] Older adults with depression often present with signs and symptoms indicative of functional or cognitive impairment. These somatic symptoms make evaluating and treating depression in older adults more complex. Depression in late life is more frequently associated with cognitive changes. Cognitive impairment in late-life depression might be a result of a depressive disorder or an underlying dementing condition. Memory complaints are also common in older adults with depression. There is a wide range of cognitive impairment in late-life depression, including decreased central processing speed, executive dysfunction and impaired short-term memory. The etiology of cognitive impairment might include cerebrovascular disease, which likely interrupts key pathways between frontal white matter and subcortical structures important in mood regulation and structural changes, such as hippocampal atrophy.[19] Depressive symptoms often coexist with dementia or MCI.[4] In the current survey, the questionnaire asked for subjective answers regarding cognitive function. Hence, one cannot deny the possibility that depressive mood might have interfered with the self-assessment of one's own cognition.

Memory impairment and disorientation was associated with lower walking status. The association of physical activity and memory is well recognized.[20,21] Also, an association between physical frailty and cognitive dysfunction has been reported.[22,23] Physical frailty is associated with the risk of MCI and a rapid rate of cognitive decline in aging.[24] A lower level of fitness was associated with hippocampal atrophy,[25] and exercise training increased the hippocampal volume.[26] The current results were in agreement with these previous findings.

Table 1 Participants' backgrounds

n	3814
Age (years)	75.1 (6.2)
Sex (male/female)	1163/2651
Body mass index	22.5 (4.5)
Systolic BP (mmHg)	134.0 (17.8)
Diastolic BP (mmHg)	74.4 (11.0)
Hemoglobin (g/dL)	12.8 (1.4)
Albumin (g/dL)	4.2 (0.3)

Mean (SD). BP, blood pressure.

Table 2 Differences between participants with or without memory impairment

	No memory impairment	Memory impairment	*P*-value
n	2654	1160	
Age (years)	74.6 ± 6.0	76.2 ± 6.4	<0.01
Male (% of male)	799 (30.1)	364 (31.4)	0.45
Body mass index(kg/m^2)	22.6 ± 4.7	22.4 ± 4.1	0.10
Systolic BP (mmHg)	134.2 ± 18.0	133.6 ± 17.4	0.33
Diastolic BP (mmHg)	74.5 ± 11.0	73.9 ± 10.9	0.12
Hemoglobin (g/dl)	12.8 ± 1.4	12.7 ± 1.4	<0.01
Albumin (g/dl)	4.3 ± 0.3	4.2 ± 0.3	0.02
IADL (0–7)	5.8 ± 1.5	5.1 ± 1.8	<0.01
Walking status (0–5)	2.8 ± 1.4	2.5 ± 1.3	<0.01
Depressive mood (0–5)	1.3 ± 1.5	2.3 ± 1.7	<0.01
Dysphagia (0–3)	1.5 ± 1.0	1.8 ± 1.0	<0.01
Vitality (0–2)	1.6 ± 0.6	1.3 ± 0.7	<0.01
Nutrition (0–2)	16 ± 0.6	1.5 ± 0.6	0.01

Mean ± SD. Age, body mass index, systolic and diastolic blood pressure (BP), hemoglobin and albumin were analyzed by Student's *t*-test. Sex was analyzed by χ^2-test. Instrumental activities of daily living (IADL), walking status, depressive mood, dysphagia, vitality and nutrition were analyzed by Mann–Whitney *U*-test.

Table 3 Differences between participants with or without impairment in telephone function

	No impairment	Impairment	*P*-value
n	3350	464	
Age (years)	74.9 ± 6.0	76.5 ± 7.2	<0.01
Male (% of male)	981 (29.3)	182 (39.2)	<0.01
Body mass index (kg/m^2)	22.5 ± 4.5	22.6 ± 4.8	0.88
Systolic BP (mmHg)	133.8 ± 17.8	135.7 ± 17.9	0.03
Diastolic BP (mmHg)	74.2 ± 10.9	75.21 ± 1.0	0.07
Hemoglobin (g/dL)	12.8 ± 1.4	12.9 ± 1.5	0.23
Albumin (g/dL)	4.2 ± 0.3	4.3 ± 0.4	0.85
IADL (0–7)	5.8 ± 1.4	4.1 ± 2.0	<0.01
Walking status (0–5)	2.8 ± 1.4	2.4 ± 1.4	<0.01
Depressive mood (0–5)	1.6 ± 1.6	2.2 ± 1.8	<0.01
Dysphagia (0–3)	1.6 ± 1.0	16 ± 1.0	0.73
Vitality (0–2)	1.5 ± 0.6	13 ± 0.7	<0.01
Nutrition (0–2)	1.6 ± 0.6	1.6 ± 0.6	0.72

Mean ± SD. Age, body mass index, systolic and diastolic blood pressure (BP), hemoglobin and albumin were analyzed by Student's *t*-test. Sex was analyzed by χ^2-test. Instrumental activities of daily living (IADL), walking status, depressive mood, dysphagia, vitality and nutrition were analyzed by Mann–Whitney *U*-test.

Table 4 Differences between participants with or without disorientation

	No impairment	Impairment	*P*-value
n	2550	1264	
Age (years)	74.7 ± 5.9	76.0 ± 6.7	<0.01
Male (% of male)	743 (29.1)	420 (33.2)	0.01
Body mass index (kg/m^2)	22.7 ± 4.7	22.3 ± 4.1	0.01
Systolic BP (mmHg)	134.2 ± 17.7	133.7 ± 18.0	0.49
Diastolic BP (mmHg)	74.6 ± 10.7	73.9 ± 11.4	0.09
Hemoglobin (g/dL)	12.8 ± 1.4	12.8 ± 1.4	0.84
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	0.02
IADL (0–7)	5.8 ± 1.5	5.1 ± 18	<0.01
Walking status (0–5)	2.8 ± 1.4	2.6 ± 1.4	<0.01
Depressive mood (0–5)	1.3 ± 1.5	2.3 ± 1.7	<0.01
Dysphagia (0–3)	1.5 ± 1.0	1.8 ± 1.0	<0.01
Vitality (0–2)	1.5 ± 0.6	1.3 ± 0.7	<0.01
Nutrition (0–2)	1.6 ± 0.6	1.5 ± 0.6	0.02

Mean ± SD. Age, body mass index, systolic and diastolic blood pressure (BP), hemoglobin and albumin were analyzed by Student's *t*-test. Sex was analyzed by χ^2-test. Instrumental activities of daily living (IADL), walking status, depressive mood, dysphagia, vitality and nutrition were analyzed by Mann–Whitney *U*-test.

Awareness of lower IADL was significantly associated with subjective cognitive impairment. This finding is conceivable, given that IADL requires complex cognitive function, and becomes vulnerable in early stages of cognitive decline.[27–29]

Univariate analysis showed that vitality was associated with awareness of subjective cognitive declines; however, multiple logistic analysis did not show a significant association with subjective cognitive dysfunction in the current study. The exclusion of depressive mood from the multiple regression analysis models made both vitality and nutrition significantly associated with cognition-related items (data not shown). The association of vitality with subjective cognitive declines might be at least partly through depressive mood. Toba *et al.* reported that vitality was impaired in the elderly with cognitive impairment.[30] That study involved more severely