founding factors and without consideration of the sex difference in adiponectin level.[23] Sex is an important confounding factor for evaluating adiponectin concentration, and the clinical importance of smoking habit in evaluating adiponectin concentration has not been fully elucidated. In the present study, we examined whether smoking habit is associated with a lower adiponectin level. First, we performed a cross-sectional study using a large number of subjects, including only males, to examine the chronic effect of smoking. Second, we performed an acute smoking exposure test in never-smokers and evaluated the effect for 12 hours. Finally, we demonstrated an inhibitory effect of H_2O_2 and nicotine on the expression and secretion of adiponectin in vitro.

Methods

Epidemiological Study (Chronic Effect of Smoking)

A total of 331 male subjects were selected from patients who were admitted and underwent medical investigation including a general check-up at Osaka University Hospital, Japan. All subjects enrolled in this study were Japanese. The study protocol was approved by the ethical committee of Osaka University, and all subjects gave written informed consent to participate in the study. All procedures followed were in accordance with the institutional guidelines of Osaka University. Smoking status was determined by interview on the day of measuring clinical parameters, and the subjects were divided into 3 groups according to smoking habit: never-smokers, past smokers (who had a history of habitual smoking but had quit), and current smokers. As a result, the numbers of never-smokers, past smokers, and current smokers were 79, 136, and 116, respectively. Hypertension was defined as systolic blood pressure (BP) of ≥140 mm Hg or diastolic BP of ≥90 mm Hg on repeated measurements, or receiving antihypertensive treatment. Diabetes mellitus was defined according to World Health Organization criteria.[24] Hyperlipidemia was defined as total cholesterol (T-chol) of >6.22 mmol/L, triglyceride (TG) of >2.26 mmol/L, or HDL cholesterol (HDL-chol) of <0.91 mmol/L. Ischemic heart disease was defined as a ≥75% organic stenosis of ≥1 major coronary artery as confirmed by coronary angiography or a history of myocardial infarction or percutaneous transluminal coronary angioplasty. Renal failure was defined as fasting serum creatinine (Cr) concentration >176.8 μmol/L. Subjects with ischemic heart disease, chronic renal failure, nephrotic syndrome, overt congestive heart failure, valvular heart disease, secondary hypertension, or atrial fibrillation were excluded. Furthermore, no subjects receiving steroid therapy were included in this study.

Each subject was studied on the day after admission, in the morning after having abstained from alcohol, caffeine, and smoking, as well as food for 8 hours before the study. BP was measured by well-trained physicians, and venous blood was drawn from all subjects. Height and body weight were measured and body mass index (BMI) calculated. Plasma samples for subsequent assay were stored at −80°C. Insulin sensitivity was estimated using the homeostatic model assessment (HOMA) index (ie, plasma glucose level×(plasma insulin level/22.5). Brinkman index was calculated using the formula: number of cigarettes smoked per day×number of years of smoking. Plasma concentration of adiponectin was determined using a sandwich ELISA system (Adiponectin ELISA kit; Otsuka Pharmaceutical Co. Ltd.), as reported previously.[12] The parameters T-chol, TG, HDL-chol, and Cr levels were also determined. Urine samples were collected for 24 hours to evaluate Cr clearance (Ccr).

Acute Smoking Exposure Test

To examine the acute effect of smoking on adiponectin concentration, we measured plasma adiponectin level in 5 healthy volunteers who had never smoked (age 33 to 46 years; BMI 24.0±1.0 kg/m^2). All subjects were male and were coauthors included in this study, and the exclusion criteria of this study were the same as those described previously. After completion of the baseline study, all participants were asked to smoke a cigarette (1.1 mg nicotine; 14 mg tar) and were instructed to inhale. Before and 3, 6, and 12 hours after smoking, venous blood was drawn.

Effect of H_2O_2 and Nicotine on Expression and Secretion of Adiponectin In Vitro

3T3-L1 mouse preadipocytes were grown to confluence and induced to differentiate into adipocytes, as described previously.[25] Seven days after the initiation of differentiation (assessed by this criterion), 85% to 90% of the cells were judged to be differentiated. On day 7, the indicated concentrations of H_2O_2 with/without *N*-acetyl-L-cysteine (NAC) or nicotine (Sigma) were added to the media for 24 hours.

An aliquot of the media after 24 hours of stimulation was subjected to ELISA (Adiponectin ELISA kit; Otsuka Pharmaceutical Co. Ltd.) to detect the amount of adiponectin secreted.

Loss of 3T3-L1 adipocyte integrity was evaluated spectrophotometrically by measurement of lactate dehydrogenase (LDH) activity in the supernatant using a standard kit (LDH-Cyotoxic Test; Wako).

3T3-L1 adipocyte cellular protein samples were isolated using ISOGEN (Nippon Gene) according to manufacturer protocol. Adipocyte protein concentration was determined by colorimetric protein assay (detergent solubilization) using DC Protein Assay (Bio-Rad) according to manufacturer protocol. The relative secretion of adiponectin into the media was normalized to the amount of cellular protein in the same sample.

Total RNA from adipocytes was isolated using ISOGEN, treated with DNAse to prevent contamination with genomic DNA, and finally resuspended in diethylpyrocarbonate-treated MilliQ. Expression levels of adiponectin and 18S mRNA were quantified by real-time quantitative RT-PCR using an ABI Prism 7900 HT Sequence Detection System (Applied Biosystems, Inc.) according to manufacturer instructions. TaqMan probes and primers for adiponectin and 18S were Assay-on-Demand Gene Expression products (Applied Biosystems, Inc.). We used amplification of 18S ribosomal RNA in each of the stimulated conditions for sample normalization. The relative expression of adiponectin mRNA was normalized to the amount of 18S in the same mRNA sample using the standard curve method described by the manufacturer.

Statistical Analysis

Means or proportions of clinical characteristics and cardiovascular risk factors were computed for each smoking pattern. Continuous variables were expressed as mean±SEM. Differences between smoking status groups for variables including adiponectin concentration were analyzed by 1-way ANOVA and post hoc comparison (Dunnet's procedure). Unpaired *t* test was used to examine the differences in adiponectin between 2 groups. Pearson's correlation coefficients were used to assess the relationships between adiponectin and all other variables. Multiple regression models were used to assess the relationship between adiponectin concentration and smoking status after adjustment for potential confounding factors. The significance of differences in adiponectin levels before and after smoking was evaluated using repeated-measures ANOVA. In the in vitro study, differences were analyzed by unpaired *t* test. All *P* values were 2-sided, and those <0.05 were considered statistically significant. All calculations were performed using a standard statistical package (JMP 4.0; SAS Institute).

Results

Association of Plasma Adiponectin Concentration With Smoking Habit in Humans

The clinical and biochemical characteristics of the study subjects divided into 3 groups according to smoking habit are shown in Table 1. We first examined the association between smoking habit and adiponectin concentration. The concentra-

TABLE 1. Clinical Characteristics of Study Subjects

Variables	Never-Smokers	Past Smokers	Current Smokers
n	79	136	116
Brinkman index	0±0	792±53	742±58
Age, years	58.0±1.2	62.2±0.9*	57.5±1.0
BMI	23.6±0.3	23.7±0.3	23.2±0.3
Adiponectin, μg/mL	6.5±0.4	5.7±0.3	5.3±0.3*
Systolic BP, mm Hg	130±2	134±1	133±2
Diastolic BP, mm Hg	80±1	81±1	85±1*
Hypertension, %	66.7	71.0	73.9
Diabetes, %	10.3	15.9	20.0
Hyperlipidemia, %	27.9	30.0	38.0
T-chol, mmol/L	4.99±0.09	5.18±0.08	5.26±0.10*
TG, mmol/L	1.48±0.12	1.78±0.09	1.64±0.11
HDL-chol, mmol/L	1.48±0.05	1.45±0.04	1.41±0.04
HOMA index	1.7±0.3	2.0±0.3	2.1±0.4
Cr, μmol/L	82.0±2.5	80.6±1.8	76.3±2.2
Ccr, mL/min	85.7±3.7	82.4±2.6	83.5±3.2

Values are given as mean±SEM.
*$P<0.05$ compared with never-smokers for each parameter.

TABLE 2. Clinical Characteristics of Subgroups Without Medication and Diabetes

Variables	Never-Smokers	Past Smokers	Current Smokers
n	27	41	30
Brinkman index	0±0	850±94	554±74
Age, years	58.8±2.5	62.0±2.1	60.1±2.5
BMI	22.6±0.5	22.3±0.4	21.8±0.3
Adiponectin, μg/mL	8.3±0.8	7.1±0.6	6.1±0.7*
Systolic BP, mm Hg	117±4	125±3	128±4
Diastolic BP, mm Hg	74±3	76±2	79±3
Hypertension, %	14.8	17.1	16.1
Hyperlipidemia, %	31.8	29.4	34.8
T-chol, mmol/L	4.99±0.15	5.14±0.15	4.90±0.16
TG, mmol/L	1.49±0.20	1.48±0.18	1.64±0.22
HDL-chol, mmol/L	1.55±0.10	1.53±0.09	1.62±0.11
HOMA index	1.1±0.4	1.4±0.3	1.5±0.7
Cr, μmol/L	72.9±6.7	75.4±4.7	76.6±7.8
Ccr, mL/min	84.0±5.4	80.8±4.1	83.0±5.4

Values are given as mean±SEM.
*$P<0.05$ compared with never-smokers for each parameter.

tion of adiponectin was significantly lower in current smokers than in never-smokers ($P=0.01$). Furthermore, the concentration of adiponectin showed a tendency to be lower in past smokers than in never-smokers ($P=0.06$). Diastolic BP and T-chol in current smokers and age in past smokers were significantly higher than those in never-smokers ($P<0.05$). In addition, the kinds of drugs that influence adiponectin concentration, such as angiotensin II receptor blockers, angiotensin-converting enzyme (ACE) inhibitors, and peroxisome proliferator-activated receptor-γ (PPAR-γ) ligands, were not significantly different among the smoking status.

In the total subjects, adiponectin level was significantly associated with age ($r=-0.38$; $P<0.01$), BMI ($r=-0.33$; $P<0.01$), and Ccr ($r=-0.36$; $P<0.01$). Furthermore, adiponectin level was significantly lower in patients with hypertension (5.1±0.2 versus 7.3±0.3 μg/mL; $P<0.01$), diabetes (5.0±0.2 versus 6.2±0.3 μg/mL; $P<0.01$), and hyperlipidemia (4.5±0.3 versus 5.8±0.2 μg/mL; $P<0.01$). We next performed multiple regression analysis including age, BMI, hypertension, diabetes, hyperlipidemia, and Ccr and revealed that adiponectin concentration in never-smokers was ≈1.25× higher than that in current smokers (never-smokers 6.5±0.4 μg/mL; past smokers 5.6±0.3 μg/mL; current smokers 5.2±0.4 μg/mL; $F=4.52$; $P=0.01$).

To exclude the effect of diabetes and drugs on adiponectin concentration, we next examined the effect of smoking habit on adiponectin concentration after excluding subjects with diabetes and subjects receiving any medication. The clinical and biochemical characteristics of these study subjects are shown in Table 2. Adiponectin concentration significantly increased with age ($r=0.41$; $P<0.01$) and HDL-chol ($r=0.43$; $P<0.01$) and decreased with BMI ($r=-0.50$; $P<0.01$), systolic BP ($r=-0.35$; $P<0.01$), diastolic BP ($r=-0.36$; $P<0.01$), TG ($r=-0.30$; $P<0.05$), HOMA ($r=-0.29$; $P<0.05$), and Ccr ($r=-0.41$; $P<0.01$). On the other hand, there was no significant association between adiponectin and T-chol ($r=-0.04$). Although clinical variables other than adiponectin concentration were not significantly different, adiponectin concentration was significantly lower in current smokers than in never-smokers ($P=0.04$).

Brinkman index was not associated with adiponectin concentration in the total subjects ($r=-0.05$) or in subjects without medication or diabetes ($r=-0.19$). However, in current smokers (n=116), the number of cigarettes smoked per day was inversely associated with adiponectin concentration ($r=-0.21$; $P<0.04$).

Effect of Acute Smoking Exposure on Plasma Adiponectin Concentration

The mean adiponectin level before smoking was 7.0±1.5 μg/mL. Percent changes in plasma concentration of adiponectin in response to smoking are shown in Figure 1. Acute smoking exposure produced a significant decrease in plasma level of adiponectin at 3 hours (−9.2±0.7%) and 6 hours (−13.1±1.2%), and the maximum decrease was observed at 12 hours after smoking (−14.5±0.6%; $F=17.3$; $P<0.01$).

Inhibitory Effects of H_2O_2 and Nicotine on Expression and Secretion of Adiponectin in 3T3-L1 Adipocytes

We investigated the effect of H_2O_2 and nicotine on the regulation of adiponectin secretion and gene expression in 3T3-L1 adipocytes. Incubation with H_2O_2 or nicotine reduced adiponectin mRNA expression and adiponectin secretion into the media in a dose-dependent manner (Figures 2 and 3). The effects of H_2O_2 to reduce adiponectin mRNA expression and secretion into the media were antagonized by coincubation with NAC (Figure 2). Secretion of adiponectin into the media was significantly reduced compared with control by nicotine

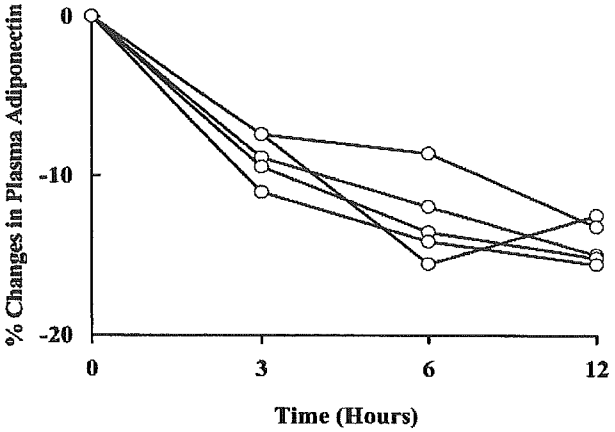

Figure 1. Percent changes in plasma adiponectin levels before and after smoking. Individual changes in adiponectin level were plotted. Adiponectin levels were expressed as percent change from initial values (n=5).

at concentrations $\geq 10^{-8}$ mol/L. We next studied the adipocyte protein concentration; the amount of adiponectin in the media was adjusted by each of the amount of cellular protein. As shown in Figures 2B and 3B, even after adjustment for protein amount, adiponectin secretion was significantly reduced by incubation with H_2O_2 or nicotine in a dose-dependent manner.

Cytotoxicity was also assessed by LDH leakage from adipocytes into the media. As shown in Figure 2C, H_2O_2 (100 μmol/L) significantly increased LDH release from adipocytes. When cultured in the presence of NAC (10^{-2} M), this increase was significantly attenuated. On the other hand, as shown in Figure 3C, treatment with nicotine also significantly increased leakage of LDH from adipocytes at concentrations $\geq 10^{-7}$ mol/L.

Discussion

The present study demonstrated that the plasma adiponectin concentration was significantly lower in male subjects who were current smokers than in never-smokers, and the association was observed even in subjects without diabetes and medication. Furthermore, multiple regression analysis including age, BMI, hypertension, diabetes, hyperlipidemia, and Ccr showed that adiponectin concentration was significantly lower in current smokers. Acute smoking exposure reduced adiponectin concentration significantly at 12 hours after smoking in never-smokers. In cultured 3T3-L1 adipocytes, oxidative stress and nicotine reduced the secretion and expression of adiponectin. These results suggest that smoking may decrease plasma adiponectin concentration in men.

In this study, even in subjects without diabetes and medication, the association between adiponectin concentration and clinical variables was in accordance with previous reports that adiponectin concentration was significantly associated with age,[18,26] BMI,[12] TG,[13] HDL-chol,[27] BP,[18] and insulin resistance indicated by HOMA.[14]

Although adiponectin concentration is decreased in several diseases,[12–14,16,18] the mechanisms that regulate plasma adiponectin concentration have not been fully elucidated. It has been reported that weight reduction[13] and certain drugs such as PPAR-γ ligands,[25] ACE inhibitors, and angiotensin II receptor blockers[28] increased the adiponectin concentration, a cytokine, tumor necrosis factor-α (TNF-α), reduced the expression of adiponectin in adipocytes,[25] and some human mutations of adiponectin affect plasma adiponectin concentration.[18,29] In this study, we demonstrated that smoking habit is also associated with adiponectin concentration. Furthermore, our finding of lower adiponectin levels in chronic smokers is in line with the fact that chronic smokers are insulin resistant.[30] Thus, our results may support investigation of the mechanisms of several disorders induced by smoking.

Smoking is known to be associated with increased oxidative stress. Reactive oxygen species such as H_2O_2 are also normally produced during cellular oxidation reduction processes. Although our results showed significant cytotoxicity in adipocytes incubated with H_2O_2 at a concentration of 100 μmol/L, this cytotoxicity was significantly attenuated when they were cultured with NAC. Furthermore, H_2O_2 decreased the expression and secretion of adiponectin from adipocytes in a dose-dependent manner. Previous reports have shown that oxidative stress disrupts activation of phosphatidylinositol 3-kinase (PI3K),[31,32] which is a key molecule in the secretion of adiponectin in 3T3-L1 adipocytes.[33] Thus, we propose the idea that oxidative stress induced by tobacco smoke decreases the secretion and expression of plasma adiponectin via inhibition of activation of PI3K in adipocytes.

Nicotine activates nicotinic acetylcholine (nACh) receptors, which belong to the family of ionotropic receptors consisting of 5 transmembrane subunits building up ion channels. nACh receptors are widely distributed throughout the central and peripheral nervous system and are involved in signal transmission at the skeletal neuromuscular junction, in autonomic ganglia, and in the brain.[34,35] Functional nACh receptors are expressed in adipocytes in mice,[36] and nicotine exerts direct stimulation of lipolysis via nACh receptors in human adipose tissue.[7] Thus, nicotine has the possibility of regulating adiponectin concentration directly. In our experiments, nicotine had a significant inhibitory effect at concentrations $\geq 10^{-7}$ mol/L, which can be found in the plasma of smokers.[37] Furthermore, our results also showed significant cytotoxicity in adipocytes incubated with nicotine at a concentration of 10^{-6} mol/L. These results could also be in accordance with previous reports that nicotine itself induces lipolysis by activating local nicotinic cholinergic receptors in adipose tissue.[7] Thus, our results indicate that nicotine in tobacco smoke decreases plasma adiponectin via inhibition of the secretion and expression of adiponectin in adipocytes.

Apart from nicotine and oxidative stress, there are several other possible mechanisms by which smoking habit may affect adiponectin concentration. It has been reported that smoking itself and tissue hypoxia elevate TNF-α,[38,39] a powerful proinflammatory cytokine and a mediator of inflammation, which is known to decrease adiponectin concentration.[25] These findings also support the idea that persistent production of TNF-α induced by chronic exposure to cigarette smoke may promote the development of hypoadiponectinemia. Furthermore, nicotine elicits release of the catecholamines epinephrine and norepinephrine,[40] and

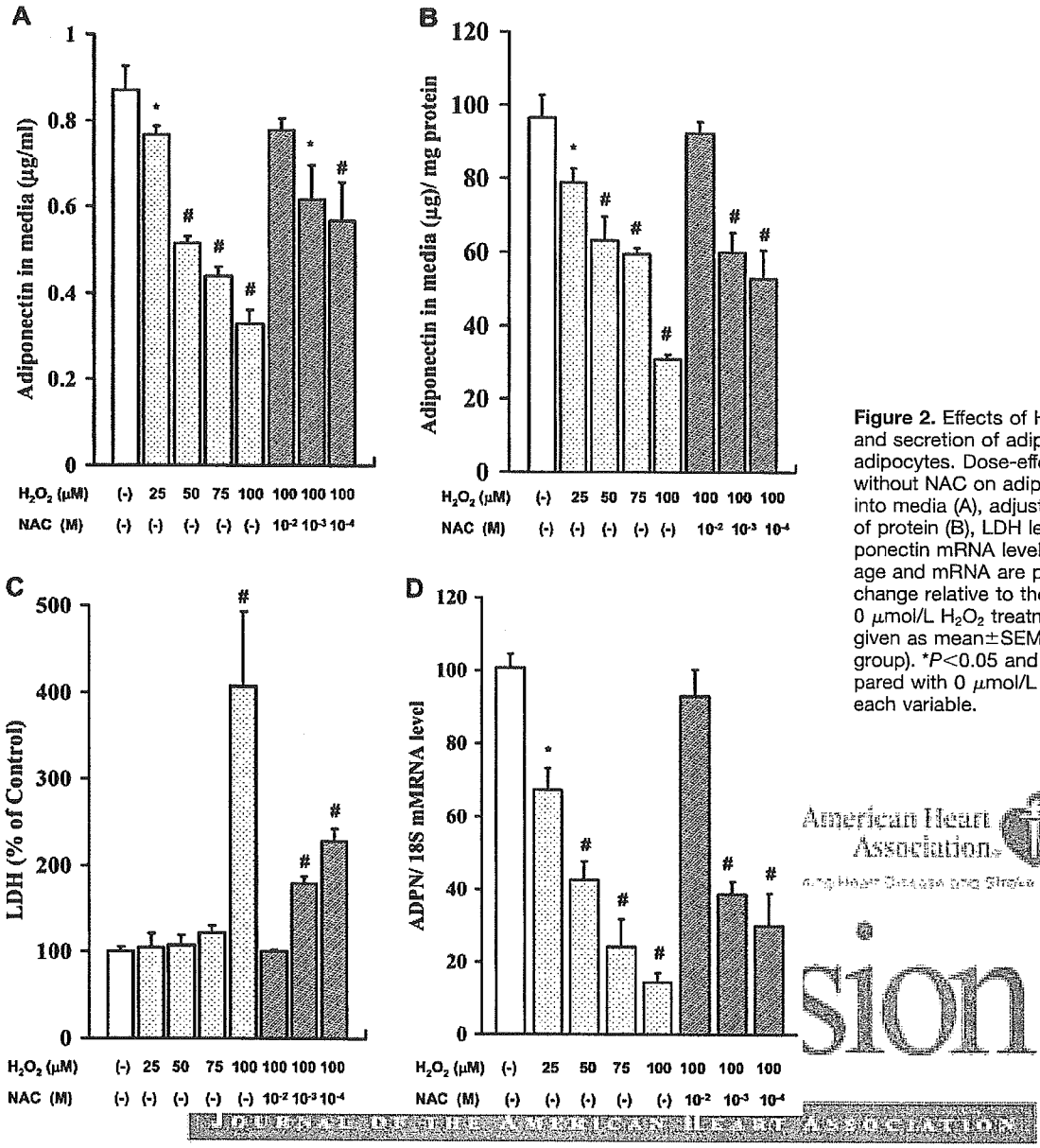

Figure 2. Effects of H_2O_2 on expression and secretion of adiponectin in 3T3-L1 adipocytes. Dose-effect of H_2O_2 with/without NAC on adiponectin secreted into media (A), adjusted by the amount of protein (B), LDH leakage (C), and adiponectin mRNA level (D). All LDH leakage and mRNA are plotted as percent change relative to the level with 0 μmol/L H_2O_2 treatment. Values are given as mean±SEM (n=12 in each group). *P<0.05 and #P<0.01 compared with 0 μmol/L H_2O_2 treatment for each variable.

β-adrenergic stimulation suppresses adiponectin gene expression.[41]

With respect to cessation of habitual smoking, in this study, adiponectin level was between those of nonsmokers and current smokers, even after adjustment for confounding factors. These results suggest that the decreasing effect of smoking on adiponectin concentration might remain even after smoking cessation. Another reason is that even after smoking cessation, smoking-related damage persisted, such as endothelial dysfunction and continuing low-grade inflammation indicated by C-reactive protein,[42] which is known to affect adiponectin concentration.[19,43] To clearly confirm whether smoking cessation affects adiponectin concentration, a cohort study is required.

Because tobacco smoke consists of >4000 chemical constituents, it is impossible to predict the effect of nicotine and oxidative stress within this complex mixture of components. Although we showed that nicotine and oxidative stress have a potent inhibitory effect on adiponectin secretion, there are several other molecules in cigarette smoke that may be toxic to adipocytes (eg, cadmium, cotinine, and thiocyanate).[44] The net effect of cigarette smoke on the function of adiponectin may be quite different from that of nicotine or H_2O_2 alone. Another limitation is that this study was designed as a cross-sectional study rather than a randomized clinical trial or observational study. Furthermore, several important determinants of adiponectin level, such as body fat content and waist circumference, were not measured in our study. Instead of these measurements, we included HOMA and BMI in the analysis of this study. Previous reports have shown that body fat content, especially intra-abdominal fat, is a determinant of adiponectin level.[26] On the other hand, the different localization of fat mass itself influences cardiovascular risk factors such as T-chol, TG, and HDL-chol.[45] In our study, except for T-chol, the clinical characteristics were not significantly different among subjects (Table 1). Furthermore, the subjects

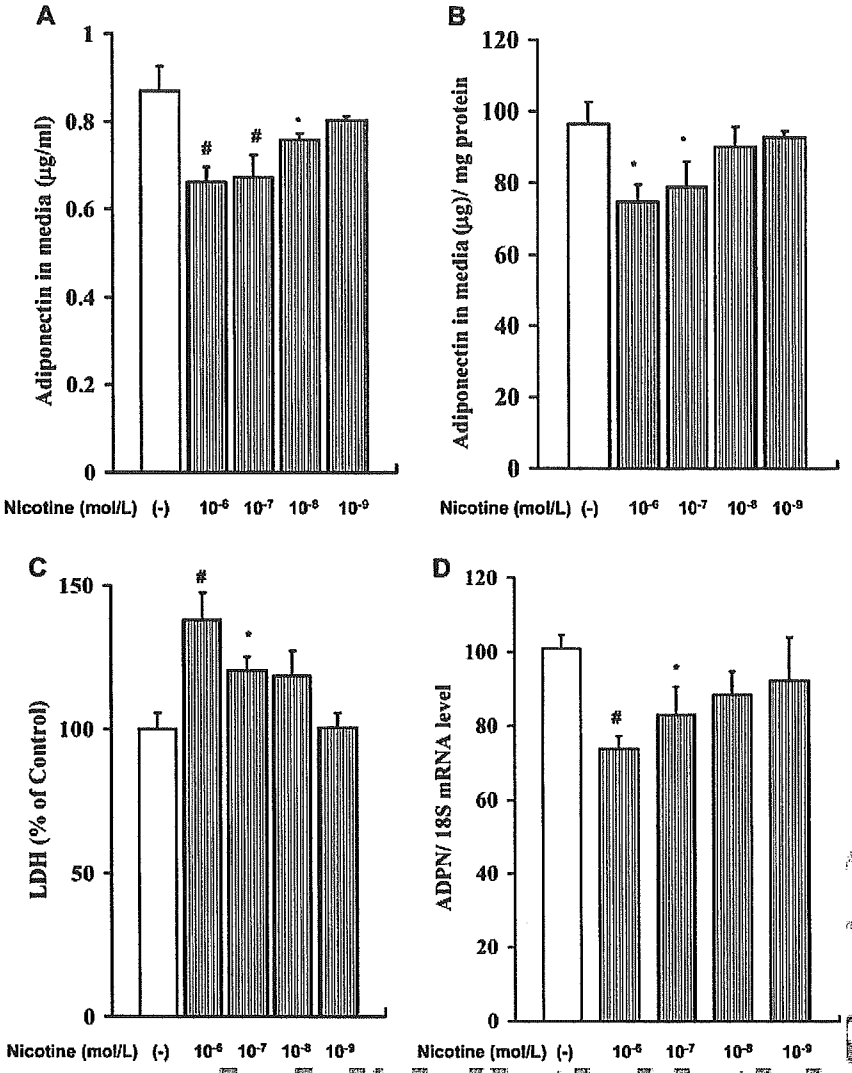

Figure 3. Effects of nicotine on expression and secretion of adiponectin in 3T3-L1 adipocytes. Dose-effect of nicotine on adiponectin secreted into media (A), adiponectin adjusted by the amount of protein (B), LDH leakage (C), and adiponectin mRNA level (D). All LDH leakage and mRNA are plotted as percent change relative to the level with 0 mol/L nicotine treatment. Values are given as mean±SEM (n=12 in each group). *$P<0.05$ and #$P<0.01$ compared with 0 mol/L nicotine treatment for each variable.

included in this study were relatively lean, and obesity (BMI ≥30 kg/m^2) was present in only 2.5% of the total subjects. Thus, the effect of different fat distributions on adiponectin concentration among the groups may be relatively small in this study. On the other hand, our study could not provide a conclusion on the influence of "passive smoking" on adiponectin concentration. Further investigation is required to examine these effects.

In conclusion, our results demonstrated that smoking habit is associated with a lower adiponectin concentration in men. This reduction may be induced through a direct effect of oxidative stress and nicotine on adipocytes.

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ORIGINAL ARTICLE

Usefulness of measuring serum markers in addition to comprehensive geriatric assessment for cognitive impairment and depressive mood in the elderly

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Background: To determine the utility of various serum markers for assessment of cognitive and mental functions in the elderly, we performed a Comprehensive Geriatric Assessment (CGA) in the out-patient clinic in Kyoto University Hospital.

Methods: We measured serum levels of dehydroepiandrosterone (DHEA), DHEA-S, malondialdehyde low-density lipoproteins (MDA-LDL), and high-sensitivity C-reactive protein (hs-CRP) in 145 patients to find the association of these markers with activities of daily living (ADL), cognitive impairment and depressive symptoms.

Results: We found that the levels of hs-CRP were significantly higher in patients with lower scores in Mini-Mental State Examination (MMSE) and Kohs block design test, and higher scores in the button test, indicating that hs-CRP may be associated with the cognitive function in elderly patients. We also found that the levels of DHEA-S were lower in patients with higher scores (9 or over) on the Geriatric Depression Scale-15 (GDS), indicating that DHEA-S may be associated with depressive mode in elderly patients. Total cholesterol, high-density cholesterol (HDL-C), or albumin were not statistically different in each group studied.

Conclusions: Thus, our data indicate that measuring hs-CRP and DHEA-S would be helpful to assess the cognitive function and depressive symptoms in elderly patients.

Keywords: Comprehensive Geriatric Assessment (CGA), cognitive function, C-reactive protein (CRP), depression, dehydroepiandrosterone (DHEA).

Introduction

The Comprehensive Geriatric Assessment (CGA) emerged during the 1980s as an important strategy to improve care for elderly patients with complex, medical, psychosocial and functional problems.[1,2] Earlier studies showed that CGA in inpatient units dramatically improved survival and functional status.[3,4] Therefore, if

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we utilize CGA more intensively for the care of elderly patients in our hospitals, CGA will have a more beneficial effect on outcomes.[5] Although CGA for inpatients is very important to improve the outcomes of elderly patients, the focus of recent investigations has been shifted to outpatient CGA due to high cost of inpatient care in the United States.[6] One study showed that outpatient CGA helps maintain functioning and the ability to perform daily activities.[7] However, its benefits are not consistently demonstrated or recognized.

Although survival is one of the most commonly reported outcomes in clinical studies, Stuck *et al.* reported in a meta-analysis that outpatient CGA did not improve survival compared to usual care despite the fact that significant survival benefits were observed in inpatients and home-based CGA.[8] Two of the four trials of outpatient CGA in the meta-analysis were, however, criticized because the subjects were relatively healthy and not at high risk. Additional studies of outpatient CGA were therefore conducted with greater attention to targeting frail subjects, resulting in improved outcomes in elderly patients including mental health[9–11] and functional status.[6,7] Although outpatient CGA has, so far, no demonstrable benefit for the survival of older, frail patients compared to usual care, outpatient CGA should be a good way to assess elderly patients, to diagnose patients with mild cognitive impairment or depressive symptoms, and to eventually prevent functional decline. However, additional measurement might be required to improve the survival.

Cognitive impairment in elderly patients is sometimes hard to diagnose in the outpatient clinic. Therefore, screening elderly patients by Mini-Mental State Examination (MMSE) is useful to diagnose the initial phase of dementia or mild cognitive impairment, although it takes time to screen all the patients with MMSE. Screening depression is also helpful for the care of elderly patients and a 15-item Geriatric Depression Scale (GDS-15) is commonly used for that purpose. This test also takes time in the outpatient clinic. Finding a marker for early diagnosis of cognitive impairment or depressive mood therefore would be important to select high-risk patients.

Chronic brain inflammation characterizes Alzheimer's disease (AD), the most of common neurodegenerative disease associated with progressive cognitive decline. Certain cytokines, such as interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, are shown to influence a number of different mechanisms that can induce or accelerate the development of neurodegeneration, indicating a correlation of inflammation with cognition.[12,13] Because high-sensitivity C-reactive protein (hs-CRP) can reflect the presence of inflammation and can be induced by these cytokines, we chose hs-CRP as a candidate marker for screening patients with cognitive impairment.

Androstenedione and dehydroepiandrosterone (DHEA) are produced in the biosynthetic pathway of androgen and estrogen. The sulfate ester of DHEA is DHEA-S. The decline of DHEA has been pursued as a major factor in the development of age-associated disorders.[14] Among the studies investigating the effect of DHEA-S on mood in the elderly, some studies show that DHEA-S improves mood[15,16] while others do not.[17,18] Therefore, the effect of these steroids on neurodegenerative diseases remains inconclusive. Malondialdehyde-low density lipoproteins (MDA-LDL) are associated with oxidatively-modified products of LDL and can be associated with atherosclerotic disease.[19] Therefore, if MDA-LDL is associated with cognitive impairment or depressive mood, controlling risk factors for atherosclerotic disease might be important.

From these findings we assessed the activities of daily living (ADL), cognitive functions and depressive symptoms in elderly patients who visited our outpatient clinic for the first time and examined the correlation with various serum markers listed above. We also used 'Get up and go', 'Button scores' and 'Functional reach' to assess neurobehavioral functions in these patients. By these measurements, we should be able to select high-risk patients for cognitive and functional decline and eventually would be able to use outpatient CGA to improve survival of elderly patients.

Methods

Subjects

All elderly (basically 65 years or older) patients who came to Kyoto University Hospital for the first time or had not been seen for the past 6 months in this hospital were asked to attend for health problem screening. We started outpatient CGA in May 2001. One hundred and forty-five consecutive patients aged 62 and older (mean age ± SD: 75.6 ± 0.56) who visited the outpatient clinic from May 2001 through March 2004 were enrolled for this study after written informed consent was taken from each patient or his/her family member. The study protocol was approved by the Ethical Committee of Kyoto University School of Medicine.

Measurements

Comprehensive Geriatric Assessment (CGA) was done on the day of patient visit by experienced speech therapists after history taking and physical examination were done. The CGA included height, body weight, blood pressure, basic activities of daily living (BADL), which was measured with the Barthel Index. For higher-level functional capacity, each subject's independence was rated by the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of competence.[20] This

assessment consists of a 13-item index including three sublevels of competence: (i) instrumental self-maintenance; (ii) intellectual activities; and (iii) social role. MMSE was used to assess cognitive functions. Neurobehavioral functions were assessed by the Kohs block design (KBD) test,[21] 'Get up and go' and 'Button scores'. A cutoff point of 12 for KBD test was used as described.[21] Functional reach was also determined as described.[22] Briefly, each subject was positioned next to the wall with one arm raised 90° with fingers extended, and a yardstick was mounted on the wall at shoulder height. The distance in centimeters that a subject was able to reach forward from an initial upright posture to the maximal anterior leaning posture without moving or lifting the feet was measured by visual observation of the third finger tip against the mounted yardstick. The distances of two trials were averaged as the functional reach score, with a greater distance indicating better balance ability.

We screened depressive symptoms using the Japanese version of GDS-15.[23] Higher scores of GDS-15 indicate a greater degree of depressive mood. In this study we used a cutoff point of 9. Therefore, we defined depression as a GDS-15 score of 9 or more.

'Get up and go'

This test of balance is commonly used to examine functional mobility in elderly subjects.[24] The test requires the subject to stand up, walk 3 m (10 ft), turn, walk back and sit down. The time to complete the test is strongly correlated with functional mobility. Elderly people who can complete the test in less than 20 s are independent in transfer tasks, which are normal activities in daily living.

'Button scores'

'Button scores' evaluate manual dexterity using a panel with combinations of 10 hooks, 10 big buttons and five small buttons. There were three discrete measurements of time recorded for each participant (10 hook-ons, 10 big button-on-and-offs, and five small button-on-and-offs). Total manual dexterity time in seconds, defined as the Button Score, was calculated by adding the average times for one hook-on and one big or small button-on-and-off.[25,26] A cutoff point of 17 was used for the analysis.

Serum marker measurement

Serum levels of DHEA, DHEA-S, MDA-LDL and hs-CRP were measured by SRL (Tokyo, Japan). DHEA and DHEA-S were measured by radioimmunoassay. MDA-LDL was measured by enzyme-linked immunosorbent assay (ELISA). Hs-CRP was measured with CardioPhase kit (Dade Behring, Tokyo, Japan).

Statistical analysis

Differences in continuous variables among the disease groups were determined by one-way analysis of variance (ANOVA). A *P*-value of less than 0.05 was considered significant. Multiple regression analysis was used to assess the involvement of age and sex.

Results

Table 1 summarizes the patient characteristics in the study population. The mean age in this study group was 75.6 years and the percentage of males was 40%. There was no statistical difference in age between males and females. The ADL of the patients was relatively well preserved. The mean Barthel index (0–100) was 98.3 and was not statistically different between males and females. Instrumental ADL was assessed by the Tokyo Metropolitan Institute of Gerontology Index (TMIG Index) (0–13). The mean value was 10.3 and was not statistically significant between males and females either. We assessed depression by GDS-15 and found that the mean score was 5.23. The GDS scores were slightly higher in females than in males, but the difference was not statistically significant. The mean score was almost comparable to that of community-dwelling elderly people in Japan.[27]

We then determined the cognitive function by MMSE and found that the mean scores were 25.2 (Table 2). We also determined the KBD test to assess spatial recognition and found that the mean score was 22.3. 'Get up and go' and 'Button scores' were assessed and the mean time to be required was 14.9 and 12.1 s, respectively. The mean length of functional reach in these patients

Table 1 Mean age, Barthel index, Tokyo Metropolitan Institute of Gerontology (TMIG) index and Geriatric Depression Scale (GDS) scores in males and females

	n	Age	Barthal index	TMIG index	GDS
Total	145	75.6 ± 0.56	98.3 ± 0.61	10.3 ± 0.25	5.23 ± 0.31
Male	58	74.8 ± 0.90	99.5 ± 0.38	10.5 ± 0.37	4.51 ± 0.45
Female	87	75.9 ± 0.72	98.3 ± 0.98	10.1 ± 0.33	5.70 ± 0.41

Data are expressed as mean ± SEM.

Table 2 Mean MMSE, KBS, button scores, Get up and go, and functional reach in males and females in this population

	MMSE	KBS	Button score	'Get up and go'	Functional reach
n	142	133	134	131	125
Total	25.2 ± 0.46	22.3 ± 1.13	12.1 ± 0.45	14.9 ± 0.46	23.4 ± 0.66
Male	25.7 ± 0.77	24.0 ± 1.88	12.8 ± 0.62	14.1 ± 0.74	26.2 ± 0.84*
Female	25.0 ± 0.56	21.0 ± 1.39	11.6 ± 0.62	15.5 ± 0.57	21.3 ± 0.66*

Data are expressed as mean ± SEM. *$P < 0.01$. *n*, number of patients studied.

Table 3 Mean levels of dehydroepiandrosterone (DHEA), DHEA-S, malondialdehyde-low density lipoproteins (MDA-LDL) and high-sensitivity C-reactive protein (hs-CRP). Difference in male and female patients

	DHEA (ng/ml)	DHEA-S (ng/ml)	MDA-LDL (U/L)	hs-CRP (ig/ml)
Total	2.08 ± 0.10	777 ± 49.3	147 ± 5.84	4.98 ± 1.56
Male	2.02 ± 0.15	995 ± 93.8*	128 ± 8.31**	3.42 ± 1.66
Female	2.12 ± 0.13	625 ± 45.3*	158 ± 7.62**	5.79 ± 2.22

Data are expressed as mean ± SEM. *$p < 0.01$, **$p < 0.01$, male vs female.

was 23.4 cm. These values were also comparable to the data of community-dwelling elderly in Japan.[28]

We next measured the serum levels of DHEA, DHEA-S, MDA-LDL and hs-CRP in this population. The mean value of DHEA, DHEA-S, MDA-LDL and hs-CRP were 2.08 ng/mL, 777 ng/mL, 147 U/L and 4.98 μg/mL, respectively (Table 3). DHEA-S was higher and MDA-LDL was lower in males than in females. However, there was no statistical difference in DHEA or hs-CRP in males and females. Figure 1 A shows the age-dependent decrease of DHEA-S in this population. DHEA-S and age were negatively correlated (the coefficient was −0.4). DHEA also showed an age-dependent decline in this population, but the coefficient was −0.2 (Fig. 1b). MDA-LDL and hs-CRP did not show age-dependent changes in this population (data not shown).

To determine the association of hs-CRP with the cognitive function in the elderly, we examined the correlation to MMSE, KBD and 'Button scores'. We divided the patients into two groups according to the points of MMSE (cutoff; 24), KBD (cutoff; 12), and Button scores (cutoff; 17). We found that the level of hs-CRP was significantly higher in the patients with lower MMSE and KBD, and higher button scores (Fig. 2a). These differences were significant by multiple regression analysis after adjusting for age and sex. These results indicate the association of hs-CRP with cognitive and functional impairment. However, the level of total cholesterol, high-density cholesterol (HDL-C) or albumin was not statistically different between each group studied (data not shown). Although the level of hs-CRP was also higher in the patients who took longer time to complete 'Get up and go', the difference was not statistically significant. The levels of DHEA, DHEA-S or MDA-LDL

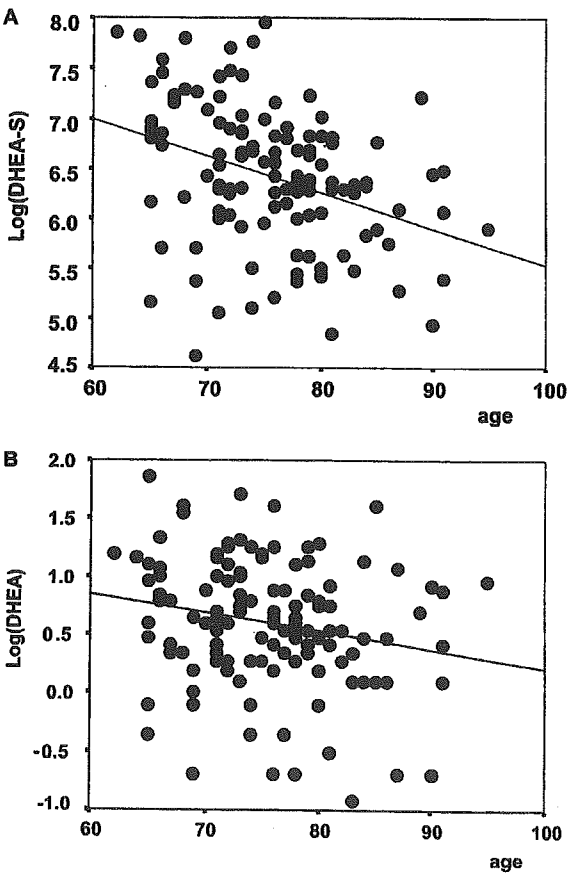

Figure 1 Age-dependent decrease of dehydroepiandrosterone (DHEA)-S and DHEA in elderly patients. Relationship between age and serum levels of (A) DHEA-S or (B) DHEA in the study patients is shown. The Y-axis is shown as natural log of (A) DHEA-S or (B) DHEA.

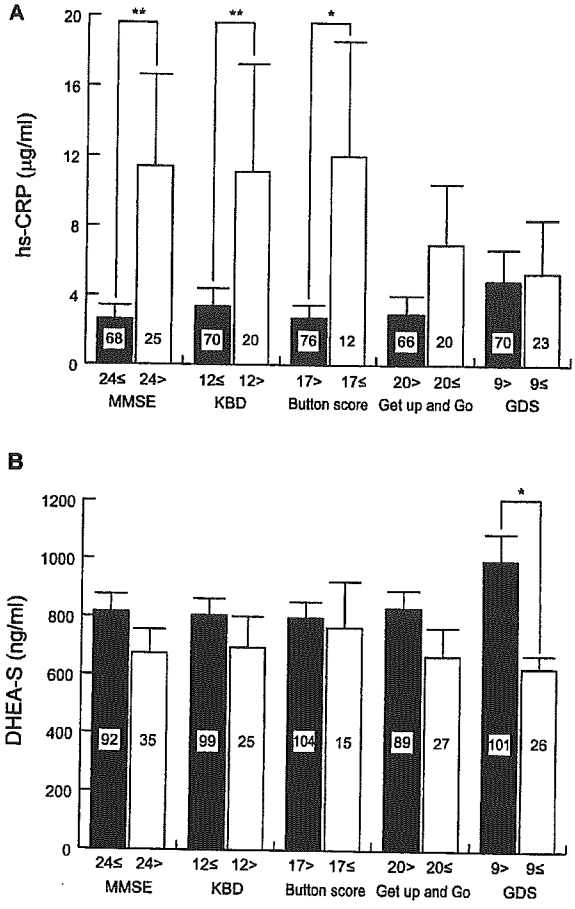

Figure 2 Levels of high-sensitivity C-reactive protein (hs-CRP) and DHEA-S in study patients. (A) Hs-CRP and (B) DHEA-S were measured in patients at the first visit to Kyoto University hospital after informed consent was taken. Patients were divided into two groups according to the level of each test. Patients were divided into two groups according to the score of Mini-Mental State Examination (MMSE); 24 and more, and less than 24, time for Kohs block design (KBD); less than 12 and 12 and more, 'Button scores'; less than 17 and 17 and more, the time required for 'Get up and go'; less than 20 and 20 and more, Geriatric Depression Scale (GDS); less than 9 and 9 and more. Values are the mean ± SEM. Number of the patients in each group is shown in each column. $*P < 0.05$, $**P < 0.01$.

were, however, not associated with these tests (Table 4, Fig. 2b).

In contrast, the levels of DHEA-S were significantly lower in the patients with higher GDS scores (9 or over). These differences were also significant by multiple regression analysis after adjusting for age and sex ($P < 0.05$). In contrast, the other markers, including hs-CRP, were not associated with GDS scores (Fig. 2b).

Among the patients with lower MMSE (less than 24), 52.6% had dementia while only 4.1% had dementia among the patients with normal MMSE (24 or over). As

Table 4 Mean dehydroepiandrosterone (DHEA) and malondialdehyde-low density lipoproteins (MDA-LDL) levels in each group of patients

	MMSE		KBD		'Button score'		'Get up and go'		GDS	
	≤ 24	> 24	≤ 12	> 12	≥ 17	< 17	> 20	≤ 20	> 9	≤ 9
DHEA (ng/ml)	2.07 ± 0.11	2.11 ± 0.22	2.11 ± 0.11	2.12 ± 0.23	2.08 ± 0.10	1.98 ± 0.16	2.14 ± 0.11	1.78 ± 0.18	2.10 ± 0.11	2.04 ± 0.21
MDA-LDL (U/L)	146 ± 6.67	150 ± 12.0	151 ± 7.00	134 ± 11.3	150 ± 6.54	145 ± 17.2	152 ± 7.38	141 ± 12.0	147 ± 6.56	145 ± 13.1

Data are expressed as mean ± SEM. MMSE, Mini-Mental State Examination; KBD, Kohs block design; GDS, Geriatric Depression Scale.

a risk factors for stroke, hypertension was found in 26.3% of the patients with lower MMSE, while 32.0% of the patients with normal MMSE had hypertension. Other risk factors, such as diabetes mellitus and hyperlipidemia were found in less than 5% of the patients in both groups. In terms of GDS scores, 37.9% of the patients with high scores (nine or over) were diagnosed with depression, while only 5.4% of the patients with low scores (less than 9) were diagnosed with depression. The incidence of dementia was 20.7% and 15.2% in each group, respectively.

Discussion

In this study we demonstrate that hs-CRP could be a marker to predict the cognitive impairment in elderly patients in outpatient clinic. Our study also indicates that DHEA-S is lower in patients with depressive mood in the elderly. Thus, measuring these markers in the outpatient clinic might be very useful to assess cognitive and functional impairment as well as depressive mood in elderly patients in addition to the assessment by CGA.

Comprehensive Geriatric Assessment is a very effective way to assess cognitive and functional impairment in the elderly and to find geriatric problems to improve their quality of life (QOL). However, most of hospitals have not utilized this assessment at their outpatient clinics because it is time consuming and unprofitable. Therefore, most geriatricians assess inpatients with CGA, which is getting more and more popular in Japan. Studies with outpatient CGA have not been successful in terms of survival so far. Therefore, by utilizing outpatient CGA and serum markers we would be able to select patients with potential risk for the future decline of cognitive functions and to eventually improve survival of frail elderly patients, although Bradly *et al.* indicated that the improvement of mental health may be an appropriate and realistic goal for outpatient CGA.[29]

Findings from epidemiological studies and some small clinical trials that non-steroidal anti-inflammatory drug (NSAID) users have a lower risk of AD, with indications of dose effects, has drawn much interest in inflammatory mechanisms in AD.[30,31] As our data show that the patients with cognitive impairment or potential decline have higher levels of hs-CRP, we might be able to select those patients to treat with NSAID to prevent the progression of cognitive impairment. To rationalize this treatment, we need a larger scale of study to prove whether or not the decline in cognitive function is faster in patients with higher hs-CRP levels.

Plasma DHEA shows a progressive age-related decline in men and women. DHEA and androstenedione have been shown to inhibit IL-6 secretion from human mononuclear cells *in vitro*,[32] suggesting a connection between aging of endocrine and immune systems. DHEA has also been shown to suppress IL-4, IFN-γ and astrocytic TNF-α and IL-6 production.[33,34] Despite its interesting inverse association with IL-6 levels and beneficial effects on senescence and cognition, a recent Cochrane Systematic Review found only limited evidence of an improved sense of well-being with DHEA supplementation.[35] Clinical benefit of DHEA supplementation should wait for other ongoing trials.

Association between DHEA-S levels and degenerative disorders of the nervous system, such as dementia and cognitive decline, have been controversial.[17,36–38] Some reports did not show the association of low serum DHEA-S levels with AD and other forms of cognitive dysfunction,[39,40] while others suggest a role of DHEA-S in depression, dementia and impaired cognitive performances in the elderly.[41,42] Although our study did not show the association of DHEA or DHEA-S with MMSE, KBD, 'Get up and go' or functional reach, a significant association of low DHEA-S with depressive mood was shown in our patient group. Our study is a cross-sectional study and the number of the patients is relatively small. Therefore, a longitudinal study will be necessary to determine whether or not the patients with low DHEA-S have a higher risk for the development of depression and whether or not treatment of those patients with DHEA-S can prevent the development of depression. Since the levels of DHEA-S declined according to age, the age-related increase of depression might be explained by a decrease of sex hormone, such as DHEA-S. In this study, we used 8/9 as cutoff for GDS. We used this cutoff point because it was appropriate in terms of sensitivity and specificity (Wada *et al.* unpubl. data). When we used 5/6 as cutoff for GDS, we found a lower level of DHEA-S in patients with GDS scores of 6 or over, but could not find a statistical significance.

Our data indicate higher incidence of dementia in patients with low MMSE and higher hs-CRP. We also demonstrated higher incidence of depression in patients with higher GDS scores and lower DHEA-S levels in elderly patients with relatively preserved ADL. Risk factors for stroke such as hypertension did not seem to be involved in these markers. With these cross-sectional data in hand, we think that it is important to follow these patients to determine whether or not high levels of hs-CRP results in a decrease in cognitive and functional impairment and whether or not low levels of DHEA-S predicts future depression. If low levels of DHEA-S are associated with the development of depression in the elderly, supplementation of DHEA might be beneficial to improve their QOL. It is also important to determine the cutoff point of these markers to select patients with high risk for cognitive decline or depression. A larger scale of study is necessary to address this issue.

In summary, our study indicates that measuring serum markers such as hs-CRP and DHEA-S would be useful to assess elderly patients along with CGA.

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原著論文

一般高齢者がもつアルツハイマー型認知症についての知識量と関連要因の検討

杉原百合子*1，山田裕子*2，武地　一*3

抄録

本研究では，一般高齢者がもつアルツハイマー型認知症(Dementia of Alzheimer's type；DAT)についての知識量および認知症のイメージや自分自身が認知症になる不安感と，それらに関連する要因について検討することを目的に，京都府下の生涯学習センターの受講生188人を対象として調査を実施した．その結果，5割以上の人がDATの周辺症状や治療薬について誤った認識をもっており，高年齢になるほど知識が低くなることが示された．また，認知症に対して「病気ではない」というイメージをもつ人が7割を超えていた．自分自身が認知症になる不安感は8割の人が，わずかあるいはそれ以上あるとしていた．今後，正しい知識や情報を提供し，認知症の正しい理解をうながし不安感を軽減させていく必要がある．認知症専門外来も啓発活動の重要な担い手となるべきであるが，認知症専門外来そのものの認知率は約3割であり，周知に向けた努力が必要であろうと考える．

Key Words：アルツハイマー型認知症，知識，イメージ，不安感，認知症専門外来

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緒　言

現在，わが国にはおよそ160万人以上の認知症患者がいるといわれているが，さらに増加の一途をたどることは確実であり，多くの人々にとって自分自身あるいは家族が認知症になるということが，身近な問題になってきている．今日，アルツハイマー型認知症(Dementia of Alzheimer's type；DAT)については，医学・医療的見地から発症のメカニズムの解明や治療薬および早期診断技術の開発が，また福祉的見地から介護方法や介護サービス等の整備が，さらには社会的見地から認知症高齢者に対する見方等についての研究など，多方面から研究や対策が急速に進んでいる．しかし，それらの知見が一般の人々に周知されているかといえばそうとも限らない現状がある．さらに，TVや書籍等のメディアにより散発的に伝えられる情報は必ずしも正しい理解につながっているとはいえず，かえって不安感を助長している可能性もある．

一方，現在認知症を本人に告知するか否かが大きな課題となりつつある．認知症の告知に対する一般の人々や介護者の態度についての研究もいくつかなされているが，その是非や理由についてたずねたものがほとんどである[1-3]．認知症の告知について検討する際，告知を受ける側である患者やその家族になる可能性をもっている一般高齢者が，認知症はどのような病気であると認識し，認知症になった際にどのような力が残され，どういった状態になると考えているのかという点について把握しておくことは，より差し迫った事態になったとき，どのような反応を生じるかを予測するうえで重要であると考える．

海外においては介護専門職や家族介護者および一般大衆の認知症に対する知識を評価する重要性

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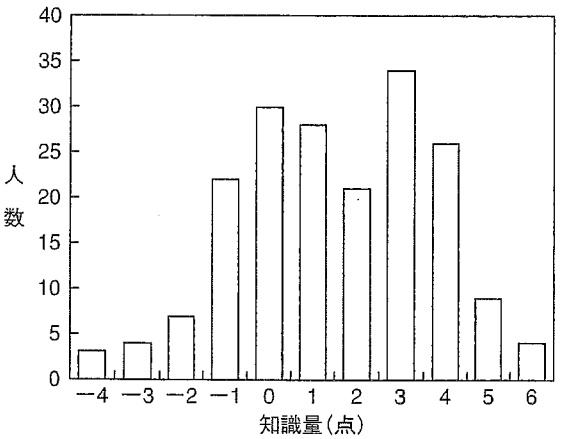
表1　調査対象者の基本属性

		対象者数(%)
性　別	男性	126(67)
	女性	62(33)
年齢別	69歳以下	120(63.8)
	70歳以上	68(36.2)
結　婚	未婚	2(1.1)
	既婚	160(85.1)
	離別・死別	26(13.8)
家族形態	独居	19(10.1)
	夫婦のみ	98(52.1)
	2・3世代同居	69(36.7)
	その他	2(1.1)
認知症介護経験	あり	31(16.5)
	なし	157(83.5)

調査対象者188人の基本属性について示す.



アルツハイマー型認知症についての知識量を点数で表しその人数を示す(n=188)

図1　アルツハイマー型認知症についての知識量

でも選択できることとした.

統計学的処理にはSPSS10.0Jを用い，2群間の検定にはt検定，χ^2検定を行った.

Ⅱ. 結　果

調査対象者の基本属性を表1に示す.

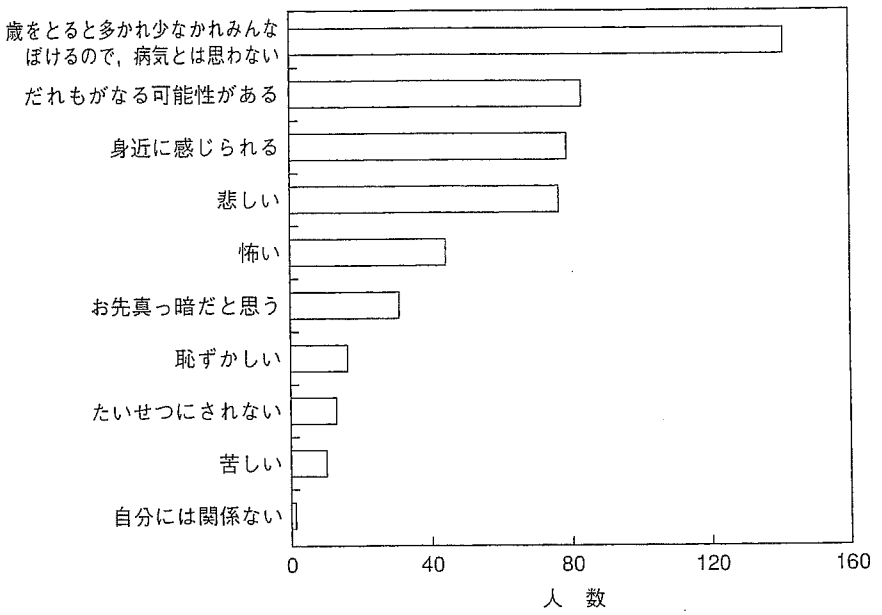
DATの知識量では7問が正解であるため，理論上の最高点は7点となり，最低点は−11点となる.結果は図1に示したように，最高6点，最低−4点であり，平均1.52点(SD=2.20)であった.設問に丸印をつけた数は1人当たり平均7.38個(SD=2.50，範囲2〜13)であった.

各設問の積極的回答の正誤については，表2に示す.DATの一般的知識について，認知症の原因疾患，発症年代，原因の解明についての正解率はそれぞれ77.7%，70.7%，52.7%で，原因の解明がどの程度進んでいるのかについての認識にはばらつきがみられた.一方，老化との関連について，DATが脳の老化によりだれもがなると誤答していたのは14.4%であった.

DATの症状のなかで，中核症状についての知識では，失見当識，判断力の低下についての正解率はそれぞれ67.0%，79.8%であった.一方，DATでみられる障害が記憶障害のみであると誤答しているのは4.3%とわずかであり，早期から人格が崩壊する，同じことを何度も聞くようになると重症であると誤答していたのはそれぞれ20.2%，38.8%であった.周辺症状の知識では，もの盗られ妄想がでてくることもよくあると正解したのは48.4%であり，徘徊行動がでる場合が多いと誤答していたのは62.2%と6割を超えていた.早期の段階の行動能力についての知識では，身の回りのことがほとんどできなくなる，金銭管理は不可能，独居は不可能と誤答していた人は，それぞれ14.4%，23.4%，38.3%であった.

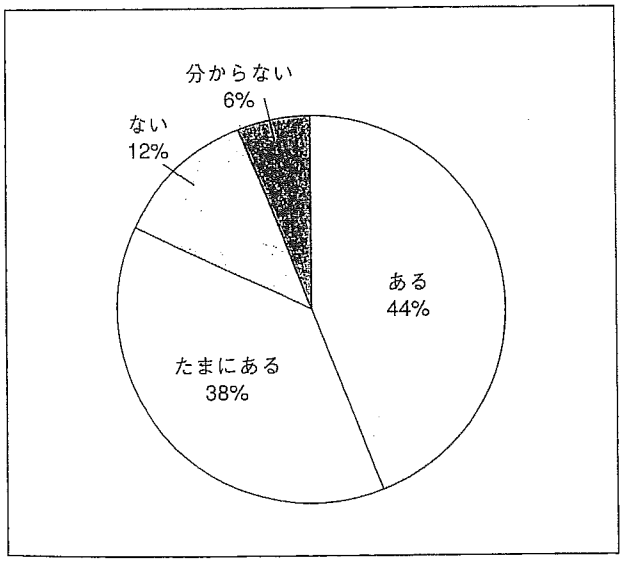
DATの治療についての知識では，治療薬の有無についての正解率は48.4%であったが，17.6%の人が現在治療法はまったくないと誤答していた.早期治療は効果がない，周囲の対応によっても問題行動は軽減しないと誤答しているのはそれぞれ20.2%，17.0%であった.

性別でDATについての知識量の差をみると，男性の平均1.4点(SD=2.30)，女性の平均1.74点(SD=1.97)であり，有意な差はみられなかった.設問ごとにみてみると，認知症の原因疾患についての設問では，女性の正解率90.3%，男性71.5%と女性の正解率が有意に高かった($p<0.01$).一方，早期治療は効果がないと認識している人は男性15.9%，女性29%と女性に多かった($p<0.05$).



認知症に対するイメージの各項目に丸印をつけた人数を示す．回答は複数回答可(n=188)

図 2　認知症に対するイメージ



自分自身が認知症になることへの不安感について“ある”“たまにある”“ない”“分からない”と答えた割合を示す．

図 3　自分自身が認知症になることへの不安感

は33.0%であった．性別，年齢で認知に有意な差はみられなかった．

Ⅲ．考　　察

今回の研究では，DATが自分自身あるいは家族にとって差し迫った問題となるであろう一般高齢者が，DATについてどんな認識やイメージをもっているかを把握することを目的とした．認知症に対するイメージのなかで，「自分には関係ない」と答えた人が188人中1人のみであったことからも，ほとんどの人が自分自身のこととしてとらえていることがうかがえる．

調査の結果，周辺症状についての知識が低いことが示された．周辺症状の1つとしてもの盗られ妄想がよくあることへの認識が低かったことは，実際にもの盗られ妄想の症状に直面した介護者が，それを認知症の症状とは結びつけることができず，介護者に対する悪意と誤解したり，さらには攻撃とまで受け取ってしまうという現象例の1つの原因とも考えられる．また，徘徊行動が頻発すると認識している人が多いことについては，DATの症状のなかで徘徊行動が一般の人々の目にも触れやすい症状であることや，マスメディア等の情報において徘徊行動を強調するようなものも見受けられるため，そのような認識をもつ人が多かった可能性が考えられる．さらに，中核症状の知識でも，早期の段階から人格が崩壊すると誤って答えた人は2割にとどまったが，「同じことを何度も聞くのは重症」と誤って考えている人

あった．本間の調査では若年層を多く含むことから，あまり差し迫った問題とは考えておらず，自分自身が認知症になる不安が4割程度にとどまったものと思われる．さらに，今回の調査では本間のものより知識の正答率が高いことから，知識が増えたことにより，イメージや不安感に影響を及ぼした可能性も考えられる．この関連性の分析は今後の研究に期したい．

今後，正しい知識や，治療および対応方法についての情報を提供し，認知症の正しい理解をうながし不安感を軽減させていく必要があると思われる．これらの啓発活動を多方面から行う必要があるが，認知症専門外来も重要な担い手の1つとなるべきであろう．しかし認知症専門外来そのものの認知も浸透しているとは言い難く，今後周知に向けた努力が必要であろうと考える．

次に介護経験の有無による影響については，Wernerが行った調査によると，アルツハイマー病についての知識の低さ，とくに病気の原因や症状についての知識が低かったことが指摘されている[6]が，介護者のみを対象にしており，介護していない人との比較におけるものではない．今回の調査では認知症の介護経験の有無で知識量に差はみられず，介護経験により必ずしも知識量は増えていないと考えられる．ただし，今回の調査では調査対象者である一般高齢者を，本人の申告による認知症介護経験の有無で分別したものであったので，現在あるいは過去に痴呆専門外来に通院している患者の主介護者といったような，より明確な形での認知症介護経験者への追調査が望まれる．いずれにしても，いかに介護者に必要な知識を提供していくかは重要な課題であり，そのことに患者や介護者と接する診療機関としての認知症専門外来等がどのようにかかわるかも問われるであろう．認知症についての知識水準が高い介護者ほど，うつの傾向は低いが不安感が高い傾向にあるというGrahamらの報告[7]もあり，どの領域の知識がうつや不安につながるのかといった調査や，さらにはGrahamらも述べているように，うつも不安も最小限にとどめ得る教育のあり方の開発が望まれる．

今回の研究では，一般高齢者がDATについてどんな認識をもっているかを把握することを目的としたが，測定方法にはさらなる検討が必要である．Dieckmannらや Gilleardらのスケールは，いずれも生物学的な内容の設問が多く，専門的で複雑なものであり，一般高齢者を対象に認知症についての知識を計るスケールとしてはやや不適切であると思われたので，本研究では本間の調査の設問を参考にし，DATについて重要と思われる内容の設問を加え調査を行った．しかし，今回の設問も必要十分とはいえず，改善の余地があると思われる．また設問によっては，有無のみをたずね明確に答えが出るものもあれば，その程度を含んだ設問であるため答えにあいまいさが残るものもあった．さらに，徘徊の定義や，早期の段階の独居をどの程度で不可能とみなすかによって，設問の正誤が変わる可能性もある．今後さらに検討を加えたい．

今回の調査では認知症の告知についての希望も合わせて調査したが，これらについては別稿で述べることとしたい．

認知症を患った人やその家族が病気を適切に受け止めたり，地域社会のなかで認知症の人のノーマライゼーションがはかられるためには，このような研究結果が参考にされ，より正確な知識が普及することを期待したい．

なお，本研究は日本興亜福祉財団ジェロントロジー研究助成を受け，「痴呆症の病名および予後の告知に関する研究」の一端として行った．調査にご協力いただいた，岡本民夫教授（同志社大学文学研究科社会福祉学専攻）ならびにアンケートの回答者の皆さまに深く感謝申し上げる．

【文　献】

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はじめに

センター方式が認知症の人のためのケアマネジメントツールとして本格的に使用されることになったが，認知症という病気を診療する立場から認知症ケアの新たな進歩を喜ぶと同時にセンター方式が医療との連携を今まで以上に深めるツールになることを期待している。

センター方式の評価と今後の課題
—医療の立場から—

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私は同僚らと介護保険開始の1年前，老年内科に物忘れ外来を開設し，認知症の早期発見，早期介入に取り組んできた[1]。また，院内の地域ネットワーク医療部という地域の医療・福祉施設との連携を深め患者の立場を支援するソーシャルワーク部門の立ち上げに参加した。そして，認知症の知識を一般市民に周知するため市民講座や保健所講座を行ったり，介護実務者講習の講師を務めたりしてきた。その関係から，平成16年度，京都市がセンター方式のモデル事業に全国16地域の一つとして参加する際，地域検討委員としてこの事業に参加させていただいた。地域でのセンター方式学習会や事例検討，地域および中央での報告会などを通じてその成果を見ることができた。これらの経緯を踏まえて，医療の立場からセンター方式の位置づけや可能性，課題について論じたい。

KEY WORDS
◆認知症の障害
◆認知症ケアの方法論
◆介護と医療の連携
◆早期からの導入
◆本人・家族の参加

間だけでその人の状態を把握することは困難な場合が多い。C-1-1「心身の情報」，D-1「できること・できないこと」，D-2「わかること・わからないこと」，D-3「生活リズム・パターン」，D-4「24時間生活変化」などの情報があれば，主治医も全体を把握した上で検査や処方を適切に行うことが可能であろう。例えば「興奮や易怒性が目立つのでどうにかなりませんか」と介護者が強く訴えてきた場合でもD-4シートで穏やかな時間も多いことを確認して投薬による対処を控えたり，D-3シートで睡眠や排泄など体調面での問題が浮き彫りになれば，その点の改善に集中することができるであろう。これらはほんの一例でありセンター方式の情報が医療者の判断に役立つ場面は多いであろう。従来，介護の現場から医療への情報発信が積極的に行われることは少なかったが，今後はセンター方式というツールを媒介に連携が強化されることを期待したい。

次に，医師・看護師・薬剤師の方から多くの役立つ情報をケアスタッフに提供することも可能であろう。A-3「私の療養シート」ではその人の持つ病気や飲み薬などについて詳しい情報があればケアの現場での援助は円滑になるだろう。D-1「できること・できないこと」，D-2「わかること・わからないこと」などのシートで，神経の障害の側面から「できること・できないこと」「わかること・わからないこと」がなぜそうなのか，それは神経の障害により不可避なものなのか，今後関わりによって変化する可能性があるのかなどを検討することができるであろう。D-3シートにおいても心臓や腎臓の機能との関係で水分や食事・排泄について相談が可能であろうし，睡眠の状態や睡眠薬などの副作用としてのふらつき・転倒の有無と睡眠薬・安定剤・抗うつ剤の使用の適否について相談が可能であろう。

ただ，これらの連携において，ケアスタッフとセンター方式シートについて議論するためにはセンター方式や新しいケアの進め方に関する医療関係者への研修も必要であろう。講習の参加により認知症ケア連携医などの資格を与える制度を創設し実質的な連携が行えるような工夫が望まれる。

2．早期からの導入と本人・家族の参加について

医療機関は多くの認知症患者と家族が最初に訪れるところであり，今後，早期発見の機運が高まればその傾向はさらに顕著になるであろう。そして，この時，患者自身も自分がどのように生きてきて，今後どのように生きたいのか，自分で判断する力を持っている場合は多い。また，家族も認知症患者への対応に疲れ切ってしまった状態ではなく，むしろ，肯定的に支えてあげたいという気持ちを持っていることも多い。モデル事業におけるセンター方式の大きな成果の一つとして「家族とスタッフの対話の増加」や「家族の認知症ケアへの理解向上」が見られたが，多くの家族や本人は介護保険サービスを利用するまでにいろいろと悩んでいる。特に，施設での介護に委ねるときは大きな決断を迫られている。ローリー・ホワイトとベス・スペンサーの「高齢者のお引っ越しガイド」[8]は家族に対してその心理的プロセスの援助者として優しく語りかけているが，家族としてももっと早い時期にセンター方式などを通じて認知症ケアを学んでいたらもっと上手く過ごせたのにと思うことがあるだろう。

このように考えると，認知症のどの段階からセンター方式を利用していくべきだろうか。医療機関でセンター方式を応用していくためにはどのようにすれば良いであろうか。早期診断を受けた直後からは介護保険サービスを利用しない場合も多いが，センター方式の持つ家族教育機能なども含めてこの時点からセンター方式を利用する意味はあると思われる。しかし，誰がどのようにセンター方式を運用するべきだろうか。介護保険サービスを使わない状態でもケアマネジャーが主治医と連携してセンター方式を通じた介入を開始できるような制度的改革を行うのが理想的かもしれない。

また，大きな問題点として本人への告知の問題も