

Factors Associated with Caregiver Burden in Patients with Alzheimer's Disease

Hyo Shin Kang^{1*}, Woojae Myung^{2*}, Duk L. Na³, Seong Yoon Kim⁴, Jae-Hong Lee⁵, Seol-Heui Han⁶, Seong Hye Choi⁷, SangYun Kim⁸, Seonwoo Kim⁹, and Doh Kwan Kim^{1,2}✉

¹Center for Clinical Research, Samsung Biomedical Research Institute, Seoul, Republic of Korea

²Department of Psychiatry, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

³Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

⁴Department of Psychiatry, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

⁵Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

⁶Department of Neurology, Konkuk University School of Medicine, Seoul, Republic of Korea

⁷Department of Neurology, Inha University School of Medicine, Incheon, Republic of Korea

⁸Department of Neurology, Seoul National University College of Medicine, Seoul, Republic of Korea

⁹Biostatistics Unit, Samsung Biomedical Research Institute, Seoul, Republic of Korea

Objective Caregivers for patients with Alzheimer's disease (AD) suffer from psychological and financial burdens. However, the results of the relationship between burden and cognitive function, performance of activities of daily living, and depressive symptoms have remained inconsistent. Therefore, the aim of this study was to examine which factors are more significant predictors of heightened burden, cognitive impairment or functional decline, besides neuropsychiatric symptoms.

Methods A cross-sectional study was conducted in a sample comprised of 1,164 pairs of patients with AD and caregivers from the Clinical Research of Dementia of South Korea study cohorts. The cognitive function of each sub-domain, functional impairments, depressive symptoms, and caregiver burden were assessed using the dementia version of Seoul Neuropsychological Screening Battery (SNSB-D), Barthel Index for Daily Living Activities (ADL), Seoul-Instrumental Activities of Daily Living (S-IADL), the Clinical Dementia Rating Sum of Box (CDR-SB), the Global Deterioration Scale (GDS), the Korean version of the Neuropsychiatric Inventory (K-NPI), and the 15-item Geriatric Depression Scale.

Results We found that higher severity (higher CDR-SB and GDS scores) and more functional impairment (lower ADL and higher S-IADL scores) were significantly associated with higher caregiver burden. In addition, depressive symptoms of patients (higher Geriatric Depression Scale scores) were associated with higher caregiver burden.

Conclusion Therefore, interventions to help maintain activities of daily living in patients with AD may alleviate caregiver burden and improve caregiver well-being.

Psychiatry Investig 2014;11(2):152-159

Key Words Caregiver, Alzheimer's disease, Cognition, Activities of daily living.

INTRODUCTION

Alzheimer's disease (AD) is a progressive and degenerative disease of the brain that causes multiple cognitive areas to be-

come seriously impaired and results in a decline in functional abilities and behavioral changes. The prevalence of AD among persons aged >65 years is 2.7–11.2%, and the annual costs for AD are \$20 to \$100 billion in the United States.^{1,2} As the prevalence and costs of AD grow rapidly, the burden to family, society, and the nation increases.

In particular, primary caregivers frequently suffer from enormous psychological and financial stress. This stress makes caregivers choose to institutionalize patients with AD earlier and, consequently, the burden on social and health services increases.^{3,4} Thus, it is important to focus on caregiver burden, because it increases social costs and the individual burden of dementia.

Received: April 25, 2013 Revised: July 30, 2013

Accepted: August 7, 2013 Available online: April 11, 2014

✉ Correspondence: Doh Kwan Kim, MD, PhD

Department of Psychiatry, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 135-710, Republic of Korea

Tel: +82-2-3410-3582, Fax: +82-2-3410-0941, E-mail: paulkim@skku.edu

*These individuals contributed equally to this article as co-first authors.

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Several studies have been conducted with the aim of identifying factors related to caregiver burden. Mohamed et al.³ found that severity of psychiatric symptoms, behavioral disturbances, and patient quality of life have a stronger association with caregiver-experienced burden. Kim et al.⁵ reported that caregiver-related factors, such as gender, history of home care, and education level are correlated with caregiver burden. Additionally, patient-related factors such as performance of activities of daily living (ADLs) have been related to burden.

Although many studies have tried to show the factors associated with caregiver burden, there is a lack of comprehensive studies that have investigated which factor is the most significant predictor of caregiver burden. Many studies have focused on caregiver or patient-related sociodemographic characteristics,⁴⁻⁶ but few studies have conducted comprehensive neuropsychological testing and examined cognitive function sub-domains to identify the association between patient cognitive function and caregiver burden.

We designed this study to explore specific factors that are associated with caregiver burden and to integrate current findings. In this study, we examined whether cognitive dysfunction or functional impairment is more related to caregiver burden. In addition, we examined the association among caregiver burden and demographic variables of patients and caregivers, patient depressive symptoms, insight, and underlying medical conditions using multivariate analysis in a large cohort of multicenter patients.

METHODS

Subjects and study design

The Clinical Research of Dementia of South Korea (CREDOS) study is a 9-year longitudinal, nationwide, hospital-based study that has been carried out in 56 hospitals. This study had a cross-sectional design. The sample comprised 1,164 patients diagnosed with incident AD and 1,164 caregivers. This study was based on baseline data derived from the CREDOS study from February 2005 to February 2011. All patients were diagnosed with AD or probable AD using the criteria of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA).⁷

Patients were excluded if they had any neurodegenerative disease other than AD (dementia with Lewy bodies, Parkinson's disease, Huntington's disease, etc.). Patients with mild cognitive impairment were also excluded. Subjects with a severe medical condition (e.g., uncontrolled diabetes mellitus, severe liver failure, severe arrhythmia, and end-stage renal disease) were excluded due to safety issues. Additionally, we excluded subjects with significant hearing or visual impairments

that rendered interviews difficult. Each caregiver met the following inclusion criteria: 1) was a relative of the patient; 2) was familiar with the patient's daily activities; and 3) agreed to be interviewed.

This study protocol was approved by the Institutional Review Boards of all participating hospitals (#2005-02-008). Signed informed consent was obtained from both caregivers and patients.

Dementia assessment

The clinical workup included complete medical histories, physical and neurological evaluations, routine laboratory tests, including complete blood counts, blood chemistry profiles, vitamin B₁₂/folate levels, syphilis serology, thyroid function tests, and a brain magnetic resonance imaging (MRI) evaluation. Genotyping for the APOE polymorphism was undertaken in 733 subjects. Brain MRI scans included transaxial T2, T1-weighted scans, and fluid-attenuated inversion recovery slices. CREDOS rating scales were employed to assess white matter changes.⁸ Patients were classified into three groups (mild, moderate, and severe) based on their white matter changes around the lateral ventricles or in deep white matter.

All patients underwent a standardized neuropsychological battery (the dementia version of Seoul Neuropsychological Screening Battery, SNSB-D) (Table 1).⁹ The SNSB-D consists of sub-domains that assess attention (score of 0-17), language and related function (score of 0-27), visuospatial function (score of 0-36), memory (score of 0-150) and frontal/executive function (score of 0-70). Higher scores indicate intact function in all sub-domains. The Barthel Index for Daily Living Activities (rating 0-20, higher scores indicate more independence) was used to evaluate basic ADLs.¹⁰ We used the Seoul-Instrumental Activities of Daily Living (S-IADL) for the instrumental ADL tasks.^{11,12} The S-IADL was developed to assess patient ability to perform social and instrumental ADLs. All items were scored on a 4-point scale ranging from 0 to 3, and the possible score ranged from 0 to 24. A lower score indicates better functioning. The Korean version of the Neuropsychiatric Inventory (K-NPI) was administered to the caregivers of the subjects.¹³ The K-NPI evaluates 12 domains of common behavioral and psychological symptoms, including delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, sleep/nighttime disturbances, and appetite/eating abnormalities. The caregivers were asked about symptoms that had occurred within the preceding 4 weeks. After the questions were answered, the caregivers were asked about symptom frequency (scale of 1 to 4, higher scores indicate more frequent) as well as severity (scale of 1 to 3, higher

scores indicate more severe). The composite score (rating, 0–12) for each domain was calculated by multiplying frequency by severity. A total score (range, 0–144) was calculated by adding the 12 composite scores. Depressed mood was assessed using the 15-item Geriatric Depression Scale,¹⁴ and the Korean version of the Mini-Mental State Examination (K-MMSE) was used to assess cognitive impairment.^{15,16} Global severity of disease was assessed using the Clinical Dementia Rating Sum of Box (CDR-SB)¹⁷ and the Global Deterioration Scale (GDS).¹⁸

Caregiver assessment

Caregiver burden was evaluated using the Neuropsychiatric Inventory Caregiver Distress Scale (NPI-D).¹⁹ The NPI-D was developed to provide a quantitative measure of distress experienced by caregivers in relation to the individual symptom domains assessed by the K-NPI. After rating each symptom item of the K-NPI, caregivers were asked to rate their distress (range, 0–5, higher score indicates more distress). The NPI-D has a moderate correlation ($r=0.51$, $p<0.01$) with the Zarit Caregiver Burden Inventory (ZBI), which is a widely used assessment scale for measuring caregiver perceived burden as reported by caregivers.^{20,21}

Table 1. Construction of the SNSB-D

Domains	Scores	Subtests
Attention	17	Digit span forward
		Digit span backward
Language and related function	27	Short form of K-BNT (A form)
		Calculation
Visuospatial function	36	RCFT copy
Memory	150	Orientation
		SVLT free/delayed recalls
		SVLT recognition
		RCFT immediate/delayed recalls
Frontal/Executive function	70	RCFT recognition
		Motor impersistence
		Contrasting program
		Go-no-go test
		Fist-edge-palm
		Luria loop
		Category word generation (animal)
Phonemic word generation (□)		
GCF score	300	Stroop test-color reading

SNSB-D: Seoul Neuropsychological Screening Battery-Dementia Version, K-BNT: Korean-Boston Naming Test, RCFT: Rey-Complex Figure Test, SVLT: Seoul Verbal Learning Test, GCF: global cognitive function

Data analysis

Continuous variables that were not normally distributed are presented as medians and interquartile ranges. Non-parametric methods were applied to analyze these variables. We employed the Wilcoxon rank-sums test or the Kruskal-Wallis test to compare groups of continuous variables. Spearman’s rank correlation test was used to test correlations between continuous variables. Median regression was employed to test the multivariate association between NPI-D and the dependent variables. We examined potential collinearity by using Variance inflation factor (VIF) scores, and we did not detect any variables with collinearity ($VIF>5$). Results were considered significant at $p<0.05$. p -values were corrected using Bonferroni’s correction if necessary.

RESULTS

Subject characteristics

The clinical and demographic characteristics of the patients are shown in Table 2. The median age of the patients was 74 years (interquartile range, 68–79 years). We recruited 445 (38.1%) male patients and 719 (62.8%) female patients (male:female, 1:1.62). Almost all of the patients were educated more than 6 years (median, 7 years; interquartile range, 6–12 years).

Table 2. Clinical and demographic characteristics of the subjects

	Patients (N=1164)	Caregiver (N=1164)
Age (years)	74 (68–79)	51 (42–66)
Gender (% male)	445 (38.1)	402 (34.5)
Education (years)	7 (6–12)	
ADL	20 (20–20)	
S-IADL	15 (10–23)	
K-NPI	7 (2–18)	
K-MMSE	20 (17–23)	
CDR-SB	4.5 (3–6)	
GDS	4 (4–5)	
NPI-D		4 (1–12)
Relationship (N, %)		
Spouse		388 (33.3)
Son		240 (20.6)
Daughter		332 (28.5)
Others		204 (17.5)
Living with patients (%)		58.9

Continuous variables that were not normally distributed are presented as medians and interquartile ranges. ADL: activities of daily living, S-IADL: Seoul-Instrumental Activities of Daily Living, K-NPI: Korean Neuropsychiatric Inventory, K-MMSE: Korean Mini Mental State Examination, CDR-SB: Clinical Dementia Rating Sum of Boxes, GDS: Global Deterioration Scale, NPI-D: Neuropsychiatric Inventory-caregiver Distress Scale

Table 3. Correlations among clinical and demographic characteristics of patients, caregivers, and caregiver burden (NPI-D)

Variables	NPI-D	Statistics	p
Patients			
Demographic			
Age (years)*		rho=-0.01	0.82
Gender (male/female)†	4 (1,12)/4 (1,12)	Z=-0.28	0.78
Education (years)*		rho=-0.05	0.11
Current alcohol drinking (drinker/non-drinker)†	4 (1,12)/4 (1,12)	Z=-0.67	0.50
Smoking history (smoker/non-smoker)†	4 (1,12)/4 (0,11)	Z=-1.80	0.08
Clinical			
CDR-SB*		rho=0.37	<0.0001
ADL*		rho=-0.25	<0.0001
S-IADL*		rho=0.42	<0.0001
K-MMSE*		rho=-0.14	<0.0001
GDS*		rho=0.30	<0.0001
Geriatric Depression Scale*		rho=0.12	<0.0001
Illness duration*		rho=-0.03	0.39
Onset type (acute/insidious)†	4 (1,10)/4 (1,12)	Z=-1.09	0.27
Insight (impaired/partial/intact)‡	7 (2,15)/4 (0,10)/5 (1,12)	X ² ₂ =17.64	<0.001
Genetic and Imaging			
APOE genotype (0/1/2, number of E4 allele)‡	4 (1,12)/5 (1,11)/6 (1,14)	X ² ₂ =1.19	0.55
Brain Ischemic change			
Deep brain white matter change (mild/moderate/severe)‡	4 (1,12)/5 (0,12)/4 (1,10)	X ² ₂ =0.03	0.98
Periventricular white matter change (mild/moderate/severe)‡	4 (1,12)/4 (1,11)/4 (1,12)	X ² ₂ =0.26	0.88
Neurologic Exam (with/without)			
Motor weakness†	7 (1.5,16)/4 (1,12)	Z=-1.31	0.19
Sensory loss†	12 (0,16)/4 (1,12)	Z=-0.24	0.81
Parkinsonian feature†	4 (1.5,13)/4 (1,11)	Z=-1.15	0.25
Neuropsychological test (SNSB-D score)			
Attention*		rho=-0.07	0.02
Language*		rho=-0.10	0.001
Visuospatial*		rho=-0.07	0.01
Memory*		rho=-0.14	<0.0001
Frontal and Executive*		rho=-0.16	<0.0001
Underlying Medical History (with/without)			
DM†	4 (1,13)/4 (1,11)	Z=-1.16	0.25
HTN†	4 (1,12)/4 (1,12)	Z=-0.33	0.74
Hyperlipidemia†	6 (1,12)/4 (1,11)	Z=-1.80	0.07
Heart disease†	6 (1,14)/4 (1,11)	Z=-2.26	0.02
Stroke†	6 (2,14)/4 (1,11)	Z=-1.63	0.10
Head trauma†	6.5 (2,15)/4 (1,12)	Z=-1.28	0.20
CO poisoning†	5 (2,10)/4 (1,12)	Z=-0.48	0.63
Brain surgery†	3.5 (2,7)/4 (1,12)	Z=0.56	0.57
Syphilis†	20 (8,24.5)/4 (1,12)	Z=-1.39	0.16
Thyroid disease†	4 (1,10)/4 (1,12)	Z=0.06	0.96
Liver disease†	15 (2,15)/4 (1,12)	Z=-0.97	0.33

Table 3. Continued

Variables	NPI-D	Statistics	p
Renal disease [†]	9 (3,19)/4 (1,11)	Z=-5.56	<0.0001
Lung disease [†]	8 (3,17)/4 (1,11)	Z=-2.57	0.01
Cancer [†]	6 (1,13)/4 (1,11)	Z=-2.18	0.03
Epilepsy [†]	13 (9.5,22)/4 (1,12)	Z=-2.23	0.03
Caregiver			
Age (year)*		rho=-0.12	<0.0001
Gender (male/female) [†]	8 (3,19)/6 (2,16)	Z=3.40	<0.001
Relationship (spouse/son/daughter/others) [‡]	6 (1,17)/6 (2,17)/8 (3,21)/10 (4,20.5)	X ² ₃ =20.97	<0.001
Living (with/without) [†]	7 (2,18)/7 (3,17)	Z=-0.59	0.56

Continuous variables that were not normally distributed are presented as medians and interquartile ranges. *Spearman's rank correlation test, [†]Wilcoxon rank-sum test, [‡]Kruskal-Wallis test. NPI-D: Neuropsychiatric Inventory-caregiver Distress Scale, CDR-SB: Clinical Dementia Rating Sum of Boxes, ADL: activities of daily living, S-IADL: Seoul-Instrumental Activities of Daily Living, K-MMSE: Korean Mini Mental State Examination, GDS: Global Deterioration Scale, APOE genotype: apolipoprotein E genotype, SNSB-D: Seoul Neuropsychological Screening Battery-Dementia version

The median K-NPI and K-MMSE scores were 7 (interquartile range, 2–18) and 20 (interquartile range, 17–23), respectively. The median GDS score was 4 (interquartile range, 4–5), comparable with moderate cognitive decline. The median age of the caregivers was 51 years (interquartile range, 42–66 years), and they consisted of 402 males (34.5%) and 762 females (65.5%). The median NPI-D score was 4 (interquartile range, 1–12). In total, 33% of patient caregivers were spouses, 20.6% were sons, 28.5% were daughters, and 17.5% were others.

Univariate analysis for the factors associated with caregiver burden

No notable association with caregiver burden was found for patient age, patient gender, patient education level, or current alcohol drinking/smoking in patients (Table 3).

The patient's ability to perform ADLs was highly associated with caregiver burden. The caregivers of more dependent patients had higher NPI-D scores. The scales for dementia severity (CDR-SB and GDS) were correlated with higher caregiver burden. The Geriatric Depression Scale showed a positive correlation with NPI-D. In addition, patient insight for their disease was associated with caregiver burden. The impaired insight of patients was associated with higher caregiver burden (impaired insight group vs. partial insight group: corrected $p=1.45 \times 10^{-4}$; impaired insight group vs. intact insight group: corrected $p=0.02$). No significant difference was observed for the NPI-D score between the partial insight and intact insight groups (corrected $p=0.11$). Patient cognitive function was associated with caregiver burden. In the SNSB-D test, memory function and frontal and executive function were more significantly associated with caregiver burden than the other sub-domain scores. Among the underlying medical histories of patients, heart disease, renal disease, lung disease,

cancer, and epilepsy were associated with caregiver burden (Table 3).

Among the caregiver-related variables, age, gender and the relationship with the patient were significantly associated with NPI-D score. However, we did not find a significant association between living with the caregiver and NPI-D score in this analysis.

Neither apolipoprotein E genotype nor brain ischemic changes were significantly associated with NPI-D score. Additionally, we did not find an association between neurological deficit (motor weakness, sensory loss, or parkinsonian features) and caregiver burden (Table 3).

Median regression analysis for factors associated with caregiver burden

We tested a multivariable model that included cognitive variables (SNSB-D sub-domains) and functional variables (ADL and S-IADL) as representative variables of cognitive parts and functional parts of dementia severity, respectively. In this test we adjusted for demographic characteristics, the Geriatric Depression Scale score, insight of patients, and underlying medical history, which were significant in the univariate analysis.

The results of the multivariate analysis are shown in Table 4. The more dependent patients (patients with lower ADL scores or higher S-IADL scores) had higher caregiver burden. In contrast with the result of the functional part of dementia severity, cognitive impairment in patients was not significantly associated with caregiver burden. None of the SNSB-D sub-domains were significantly associated with caregiver burden.

A higher Geriatric Depression Scale score was significantly associated with higher caregiver burden in both models. Among underlying medical conditions, renal disease was sig-

Table 4. Median regression analysis for the factors associated with caregiver burden (NPI-D)

	Coefficient	S.E.	t	p	95% CI, lower	95% CI, upper
Demographic						
Patient's age	-0.04	0.03	-1.10	0.27	-0.11	0.03
Patient's gender, male	0.22	0.56	0.39	0.70	-0.88	1.31
Patients education year	-0.05	0.05	-1.04	0.30	-0.16	0.05
Caregiver						
Caregiver's age	-0.06	0.03	-2.01	0.04	-0.11	-0.001
Caregiver's gender, male	-0.86	0.76	-1.14	0.25	-2.34	0.62
Caregiver's Relationship (spouse vs. son)	-0.35	1.10	-0.32	0.75	-2.50	1.80
Caregiver's Relationship (spouse vs. daughter)	-0.16	1.00	-0.17	0.87	-2.12	1.79
Caregiver's Relationship (spouse vs. others)	-0.25	1.04	-0.24	0.81	-2.29	1.79
Clinical						
ADL	-0.90	0.12	-7.63	<0.0001	-1.13	-0.67
S-IADL	0.29	0.03	10.74	<0.0001	0.23	0.34
Geriatric Depression Scale	0.17	0.05	3.34	<0.0001	0.07	0.26
Insight	0.38	0.31	1.22	0.22	-0.23	0.98
Neuropsychological test						
Attention	0.08	0.12	0.68	0.50	-0.15	0.32
Language	-0.03	0.06	-0.50	0.62	-0.15	0.09
Visuospatial	0.03	0.03	1.20	0.23	-0.02	0.08
Memory	0.005	0.02	0.28	0.78	-0.03	0.04
Frontal and Executive	0.002	0.03	0.08	0.94	-0.05	0.06
Underlying Medical History						
Heart disease	0.57	0.62	0.92	0.36	-0.64	1.77
Renal disease	2.47	0.61	4.03	<0.0001	1.27	3.67
Lung disease	0.81	0.99	0.82	0.41	-1.13	2.75
Cancer	0.44	0.51	0.86	0.39	-0.57	1.45
Epilepsy	2.99	2.37	1.26	0.21	-1.67	7.64

NPI-D: Neuropsychiatric Inventory-caregiver Distress Scale, ADL: activities of daily living, S-IADL: Seoul-Instrumental activities of daily living

nificantly associated with a higher NPI-D score. Caregiver age was significantly associated with caregiver burden. Patient insight was not significantly associated with caregiver burden.

DISCUSSION

This study examined which factors were more significant predictors of heightened burden, cognitive impairment, and functional decline. The results indicated that caregiver burden had a stronger association with functional impairment than that of cognitive functioning. In the correlation analysis, both ADLs and cognitive function were associated with caregiver burden. However, only functional ability was related to caregiver burden after controlling for other variables. In previous studies, the correlation between caregiver burden and patient ADLs and cognitive function has been controversial. For example, Mohamed et al.³ found only limited relationships

among cognitive function, ADLs, and caregiver burden. Additionally, Coen et al.²² reported that neither cognitive function nor functional impairment in patients with AD predicts caregiver burden, whereas Huang et al.²³ found that poorer cognitive function and instrumental ADLs and ADL performance are associated with higher caregiver burden. Therefore, we controlled for other variables that could significantly impact caregiver burden to identify the association between functional ability and cognitive function. Our findings support that functional impairment of patients with AD was more related to caregiver burden.

Christofolletti et al.²⁴ also suggested that caregivers of physically active patients with AD exhibit reduced burden. They noted that patients with dementia require increasing supervision and personal care depending on their functional ability, and that this results in negative effects on caregiver health. Therefore, interventions to help maintain ADLs in patients

with AD can decrease caregiver burden compared to those that focus on cognitive decline. For example, Rolland et al.²⁵ suggested that a collective exercise program leads to improved ability to perform ADLs, and that this could reduce caregiver burden.

In the present study, depressive symptoms of patients were highly associated with increased caregiver burden. This finding is similar to those of previous studies.³ Many studies have suggested that depressive symptoms are common in patients with dementia.^{26,27} Karttunen et al.²⁸ evaluated 240 patients with AD and showed that 32.1% of patients with very mild and 39.6% of patients with mild AD have depressive symptoms. Enache et al.²⁹ reported that 20–30% of patients with AD have depression.

Diagnosing depression in patients with dementia is important for adequate patient management, and depression of patients is significantly related to caregiver burden. However, diagnosing depression correctly may be complicated due to overlap of symptoms between dementia and depression.²⁹ Therefore, clinicians should take more notice of depressive symptoms in patients with dementia.

The results of the present study indicate that dementia patient and caregiver demographic factors did not significantly impact caregiver burden except the caregiver age was related to caregiver burden, indicating that the younger the caregiver, the greater the burden. This result is inconsistent with findings from some studies. Lim et al.³⁰ reported that older caregivers have much more caregiver burden, because older caregivers have more stress from multiple roles than that of young caregivers. In contrast, the results of Hope et al.³¹ were consistent with ours. They found that younger caregivers are less committed to care because they may have jobs or greater demands from other family members. Additionally, Fitting et al.³² reported that younger caregivers are lonelier and more resentful of their role. In particular, Koreans have more sense of responsibility to care for elderly family members due to the influence of filial piety. Thus, our findings suggest that less emotional and social support in younger caregivers leads to a greater burden.

We tested the association between caregiver burden and patient underlying medical history. The results showed that renal disease was associated with high caregiver burden in patients with AD. Renal disease is a representative chronic physical illness and caregivers of patients with chronic mental or physical illnesses experience significant distress and psychological burden.³³ Our results indicate that the co-morbidity of medical illness in patients with AD could place additional burden on caregivers. The non-significant results of other medical history may be due to the limitation of our data, because we were unable to consider the severity, specific diag-

nosis, or clinical stage of underlying medical conditions.

Several limitations should be noted in this study. It was a cross-sectional study, not a longitudinal study; thus, we could not draw conclusions regarding causality. A longitudinal study may have been more appropriate for an accurate assessment of predictors related to caregiver burden. Another limitation is that the majority of the patients were early stage AD. Therefore, the findings may not be generalizable to more severely demented patients. In addition, we used the NPI-D to evaluate caregiver burden. This is an adjunct scale to the NPI for assessing the impact of neuropsychiatric symptoms on caregiver burden. However, this scale has a moderate correlation with the ZBI, which is the most widely used instrument for assessing caregiver distress.²⁰ Despite these limitations, we think our findings are quite reliable, because we examined patients with AD in a large multicenter cohort, which was assessed comprehensively including neuropsychological testing, brain MRI, and diverse underlying medical history.

In conclusion, caregiver burden had a stronger association with functional impairment than that of cognitive functioning. Therefore, interventions to help maintain ADLs in patients with AD may alleviate caregiver burden and improve caregiver well-being.

Acknowledgments

D.K.K was supported by grants from the Korean Health Technology R & D Project, Ministry of Health & Welfare, Republic of Korea (HI10C2020), and Eisai Korea Inc. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author Contributions

Doh Kwan Kim, Hyo Shin Kang, and Woojae Myung were involved in study planning and writing of the manuscript; Doh Kwan Kim, Duk L. Na, Seong Yoon Kim, Jae-Hong Lee, Seol-Heui Han, Seong Hye Choi, and SangYun Kim were involved in CRCD study planning and conducted the clinical aspects of the study. Seonwoo Kim and Woojae Myung performed the statistical analyses.

Accession Numbers

The study is registered (NCT01198093) in ClinicalTrials.gov.

REFERENCES

- Ernst RL, Hay JW. Economic research on Alzheimer disease: a review of the literature. *Alzheimer Dis Assoc Disord* 1997;11(Suppl 6):135-145.
- Trabucchi M. An economic perspective on Alzheimer's disease. *J Geriatr Psychiatry Neurol* 1999;12:29-38.
- Mohamed S, Rosenheck R, Lyketsos CG, Schneider LS. Caregiver burden in Alzheimer disease: cross-sectional and longitudinal patient correlates. *Am J Geriatr Psychiatry* 2010;18:917-927.
- Tew CW, Tan LF, Luo N, Ng WY, Yap P. Why family caregivers choose to institutionalize a loved one with dementia: a Singapore perspective. *Dement Geriatr Cogn Disord* 2010;30:509-516.
- Kim MD, Hong SC, Lee CI, Kim SY, Kang IO, Lee SY. Caregiver burden among caregivers of Koreans with dementia. *Gerontology* 2009;55:106-113.

6. Kim JM, Shin IS, Jeong SJ, Gormley N, Yoon JS. Predictors of institutionalization in patients with dementia in Korea. *Int J Geriatr Psychiatry* 2002;17:101-106.
7. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34:939-944.
8. Moon SY, Na DL, Seo SW, Lee JY, Ku BD, Kim SY, et al. Impact of white matter changes on activities of daily living in mild to moderate dementia. *Eur Neurol* 2011;65:223-230.
9. Ahn HJ, Chin J, Park A, Lee BH, Suh MK, Seo SW, et al. Seoul Neuropsychological Screening Battery-dementia version (SNSB-D): a useful tool for assessing and monitoring cognitive impairments in dementia patients. *J Korean Med Sci* 2010;25:1071-1076.
10. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud* 1988;10:61-63.
11. Ahn IS, Kim JH, Kim S, Chung JW, Kim H, Kang HS, et al. Impairment of instrumental activities of daily living in patients with mild cognitive impairment. *Psychiatry Investig* 2009;6:180-184.
12. Ku HM, Kim JH, Kwon EJ, Kim SH, Lee HS, Ko HJ, et al. A study on the reliability and validity of Seoul-Instrumental Activities of Daily Living (S-IADL). *J Korean Neuropsychiatr Assoc* 2004;43:189-199.
13. Choi SH, Na DL, Kwon HM, Yoon SJ, Jeong JH, Ha CK. The Korean version of the neuropsychiatric inventory: a scoring tool for neuropsychiatric disturbance in dementia patients. *J Korean Med Sci* 2000;15:609-615.
14. Bae JN, Cho MJ. Development of the Korean version of the Geriatric Depression Scale and its short form among elderly psychiatric patients. *J Psychosom Res* 2004;57:297-305.
15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-198.
16. Kang Y, Na DL, Hahn S. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. *J Korean Neurol Assoc* 1997;15:300-308.
17. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 1993;43:2412-2414.
18. Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Psychiatry* 1982;139:1136-1139.
19. Kaufer DI, Cummings JL, Christine D, Bray T, Castellon S, Masterman D, et al. Assessing the impact of neuropsychiatric symptoms in Alzheimer's disease: the Neuropsychiatric Inventory Caregiver Distress Scale. *J Am Geriatr Soc* 1998;46:210-215.
20. Zarit SH, Reeve KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist* 1980;20:649-655.
21. Huang SS, Lee MC, Liao YC, Wang WF, Lai TJ. Caregiver burden associated with behavioral and psychological symptoms of dementia (BPSD) in Taiwanese elderly. *Arch Gerontol Geriatr* 2012;55:55-59.
22. Coen RF, Swanwick GR, O'boyle CA, Coakley D. Behaviour disturbance and other predictors of carer burden in Alzheimer's disease. *Int J Geriatr Psychiatry* 1997;12:331-336.
23. Huang SS, Lee MC, Liao YC, Wang WF, Lai TJ. Caregiver burden associated with behavioral and psychological symptoms of dementia (BPSD) in Taiwanese elderly. *Arch Gerontol Geriatr* 2012;55:55-59.
24. Christoforetti G, Oliani MM, Bucken-Gobbi LT, Gobbi S, Beinotti F, Stella F. Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. *Clinics (Sao Paulo)* 2011;66:613-618.
25. Rolland Y, Pillard F, Klapouszczak A, Reynish E, Thomas D, Andrieu S, et al. Exercise program for nursing home residents with Alzheimer's disease: a 1-year randomized, controlled trial. *J Am Geriatr Soc* 2007;55:158-165.
26. Castilla-Puentes RC, Habeych ME. Subtypes of depression among patients with Alzheimer's disease and other dementias. *Alzheimers Dement* 2010;6:63-69.
27. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA* 2002;288:1475-1483.
28. Karttunen K, Karppi P, Hiltunen A, Vanhanen M, Välimäki T, Martikainen J, et al. Neuropsychiatric symptoms and quality of life in patients with very mild and mild Alzheimer's disease. *Int J Geriatr Psychiatry* 2011;26:473-482.
29. Enache D, Winblad B, Aarsland D. Depression in dementia: epidemiology, mechanisms, and treatment. *Curr Opin Psychiatry* 2011;24:461-472.
30. Lim YM, Son GR, Song JA, Beattie E. Factors affecting burden of family caregivers of community-dwelling ambulatory elders with dementia in Korea. *Arch Psychiatr Nurs* 2008;22:226-234.
31. Hope T, Keene J, Gedling K, Fairburn CG, Jacoby R. Predictors of institutionalization for people with dementia living at home with a carer. *Int J Geriatr Psychiatry* 1998;13:682-690.
32. Fitting M, Rabins P, Lucas MJ, Eastham J. Caregivers for dementia patients: a comparison of husbands and wives. *Gerontologist* 1986;26:248-252.
33. Given CW, Given B, Stommel M, Collins C, King S, Franklin S. The caregiver reaction assessment (CRA) for caregivers to persons with chronic physical and mental impairments. *Res Nurs Health* 1992;15:271-283.