KJFM

Korean Journal of Family Medicine

■ **Original Article**

Survival Analysis of Patients with Alzheimer's Disease: A Study Based on Data from the Korean National Health Insurance Services' Senior Cohort Database

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Background: Korea's rapidly aging population has experienced a sharp rise in the prevalence of dementia. Patients with Alzheimer's disease (AD), which is estimated to be about three-quarters of all patients with dementia, tend to have higher mortality rates compared with patients without Alzheimer's disease. In this study, a survival analysis of patients with AD was conducted in order to provide knowledge to those who provide medical care to these patients.

Methods: Data on individuals over 65 years old in 2004 were extracted from the Korean National Health Insurance Services' Senior Cohort database (2002–2013). The subjects were 209,254 patients, including 2,695 who were first diagnosed with AD (the AD group) and 206,559 that had not been diagnosed with the disease (non-AD group). To investigate the independent effect of AD on survival, the Cox proportional-hazards model, hazard ratios (confidence interval of 95%), and the Kaplan-Meier method were used.

Results: Mean survival time in the AD group was 5.3±3.3 years, which was about 2.5 years shorter than that in the non-AD group (7.8±2.4 years). The mortality rate in the AD group (66.3%) was higher than that in the non-AD group (26.3%). The adjusted hazard ratio in the AD group was 2.5 and, therefore, it was found that the AD group had a 2.5-fold higher risk of death than the non-AD group.

Conclusion: Overall, AD has a large, independent impact on survival. Survival time was shorter, and the mortality rate and risk were generally higher in the AD group, compared with the non-AD group.

Keywords: Alzheimer Disease; Database; Survival Analysis; Mortality

INTRODUCTION

As indicated in "Towards a dementia plan: a WHO guide" published by the World Health Organization in 2018,[1] there are about 50 million patients with dementia around the world and dementia is the seventh leading cause of death globally. However, Alzheimer's disease (AD) is still incurable.[2-4] Korea was officially declared an aged society in 2017, and the country's rapidly aging population is experiencing a sharp rise in the prevalence of dementia.[5,6] According to the Korean Dementia Observatory 2017, the number of patients with dementia is about 660,000 which is high enough to accounts for approximately 9.8% of the total Korean population over 65 years of age.[7] Patients with AD are estimated to make up three-quarters of the total patients with dementia. Among the 17.9% of the total dementia deaths, patients with AD account for the largest percentage at 9.4%.[7] Therefore, management of the population with AD has become more important than ever. Concern about dementia is greater than ever in Korea, and the ratio of treatment and management has increased. However, there is still a lack of support services, and it is imperative to be strengthened policies for dementia care.[8,9] Moreover, there have been few related Korean studies, and those Korean studies that currently exist have limitations such as small sample sizes or short follow-up durations. In this study, a survival analysis of patients with AD was conducted using data from the National Health Insurance Services' Senior Cohort database (2002–2013), a database representative of the elderly population of Korea that can provide more generalizable results.

METHODS

1. Subjects

Data on individuals aged 65 years or older in 2004 were extracted from the Korean National Health Insurance Services' Senior Cohort database (2002–2013). The subjects were 209,254 individuals, including 2,695 with a first diagnoses of AD during the year 2004 (the AD group) and 206,559 without AD (the non-AD group) (Figure 1). In order to select the population diagnosed with AD (International Classification of Diseases, 10th revision [ICD-10] codes F00, F000–F002, F009, F03, G30, G300–G301, G308, and G309) for the first time in life, in 2004, all patients formerly diagnosed with AD were excluded. We also excluded patients with cerebral vascular accident (CVA; ICD-10 codes I60–I69 and G46), cardiovascular disease (CVD; ICD-10 codes I20–I25), and cancer (ICD-10 codes C00–C97 and D01–D09), which have significant impact on death, from 2002 to 2004. In addition, during the same period, all deceased patients were excluded. Additionally, all patients newly diagnosed with AD during the observation period (2005–2013) were excluded from the non-AD (control) group.

2. Observation Period

The length of the observation period was 9 years (from January 1, 2005 to December 31, 2013). In the case of death within the period, the survival time to the day of death was converted to the number of years. For further analysis, from the date of the first AD diagnosis in 2004 to the date of death, the survival days were also converted into years.

3. Covariates and Statistical Analysis

To investigate the independent effect of AD on mortality risk, factors associated with survival, such as gender, age, income level, and the three most common major chronic diseases (i.e., hypertension, diabetes, and dyslipidemia) were used as adjustment variables. In addition, the Cox proportional-hazard model was used to find correlation among the factors, and hazard ratio (HR) and 95% confidence interval (CI) were calculated. In addition, stratification analysis was conducted for each variable to examine the effect of AD on survival in more detail. Mortality rates were analyzed by gender and age during the study period, and the Kaplan-Meier method was used to compare the survival times and the survival rates. Statistical significance level was set at $P<0.05$, and all analyses were performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC, USA). The protocol of this study was approved by the Institutional Review Board of Hallym University Dongtan Sacred Heart Hospital (IRB approval no., 2018-05-007), and the requirement for informed consent from individual patients was omitted because of the retrospective design of this study.
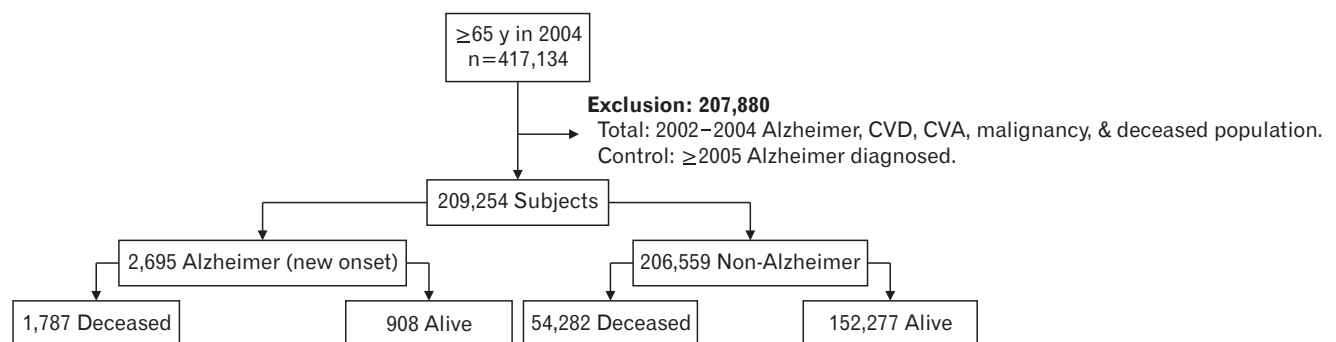
Figure 1. Flowchart of subjects from the Korean National Health Insurance Services' Senior Cohort database (2002–2013). To compare the survival of the AD group and the non-AD group during the observation period, those who died before the study period were excluded. The total number of included subjects was 209,254, including 2,695 who were first diagnosed with AD during the year 2004 and 206,559 non-AD subjects. The numbers of deaths were 1,787 and 54,282 in the non-AD group, respectively. AD, Alzheimer's disease; CVD, cardiovascular disease; CVA, cerebral vascular accident.

RESULTS

1. Demographic and Baseline Characteristics

Out of the entire sample of 209,504 individuals, there were 2,695 (1.3%) in the AD group, and 206,559 (98.7%) in the non-AD group. Mean age in the AD and non-AD groups were 76.4±6.8 years and 71.5±5.9 years, respectively, and the mean age of the AD group was 4.9 years older. In terms of sex, 40.9% of the subjects were male and 59.1% were female. Among subjects in the AD group, 30.3% were male and 69.7% were female, and among subjects in the non-AD group, 41.0% were male and 59.0% were female. Thus, it was found that the proportion of women in the AD group was higher (Table 1). In the analysis by age, subjects were classified into one of the following four age groups: 65–69 years old, 70–74 years old, 75–79 years old, and over 80 years old. The age

Table 1. Basaline characteristics and mortalities of the cohort

Characteristic	Total	AD		Non-AD		P-value
		Subtotal	Mortality	Subtotal	Mortality	
Total	209,254	2,695 (1.3)	1,787 (66.3)	206,559 (98.7)	54,282 (26.3)	<0.0001
Age (y)	71.59±6.0	76.4±6.8		71.5±5.9		<0.0001
Gender						<0.0001
Male	85,710 (40.9)	816 (30.3)	619 (75.9)	84,786 (41.0)	27,453 (32.4)	
Female	123,980 (59.1)	1,879 (69.7)	1,168 (62.2)	121,773 (59.0)	26,829 (22.0)	
Age range (y)						<0.0001
65–69	97,997 (46.8)	473 (17.6)	202 (42.7)	97,524 (47.2)	13,551 (13.9)	
70–74	56,522 (27.0)	662 (24.6)	353 (53.3)	55,860 (27.0)	12,818 (22.9)	
75–79	30,113 (14.4)	675 (25.0)	465 (68.9)	29,438 (14.3)	11,598 (39.4)	
≥80	24,622 (11.8)	885 (32.8)	767 (86.7)	23,737 (11.5)	16,315 (68.7)	
Hypertension						<0.0001
Yes	80,479 (38.5)	1,160 (43.0)	758 (65.3)	79,319 (38.4)	22,072 (27.8)	
No	128,775 (61.5)	1,535 (57.0)	1,029 (67.0)	127,240 (61.6)	32,210 (25.3)	
Diabetes mellitus						0.035
Yes	32,130 (15.3)	453 (16.8)	298 (65.8)	31,677 (15.3)	9,705 (30.6)	
No	177,124 (84.7)	2,242 (83.2)	1,489 (66.4)	174,882 (84.7)	44,577 (25.5)	
Dyslipidemia						0.0022
Yes	12,612 (6.0)	200 (7.4)	102 (51.0)	12,412 (6.0)	2,068 (16.7)	
No	196,642 (94.0)	2,495 (92.6)	1,685 (67.5)	194,147 (94.0)	52,214 (26.9)	
Income level*						0.0003
Very low	2,498 (1.2)	44 (1.6)	38 (86.4)	2,454 (1.2)	866 (35.3)	
Low	23,625 (11.3)	247 (9.2)	167 (67.6)	23,378 (11.3)	6,622 (28.3)	
Mid to high	183,131 (87.5)	2,404 (89.2)	1,582 (65.8)	180,727 (87.5)	46,794 (25.9)	

Values are presented as number (%) or mean±standard deviation.

AD, Alzheimer's disease.

*Devided into following three categories: very low (income decile=0), low (income decile=1), and mid to high (income decile ≥2).

Table 2. Causes of death

Variable	AD			Non-AD		
	Total	Male	Female	Total	Male	Female
Dementia (F00–F03, G30)	374 (20.9)	112 (18.1)	262 (22.4)	-	-	-
CVA (I60–69, G46)	269 (15.1)	103 (16.6)	166 (14.2)	6,697 (12.3)	3,054 (11.1)	3,643 (13.6)
Senescence (R54)	238 (13.3)	60 (9.7)	178 (15.2)	7,272 (13.4)	2,546 (9.3)	4,726 (17.6)
Cancer (C00–C97)	113 (6.3)	56 (9.0)	57 (4.9)	14,938 (27.5)	9,203 (33.5)	5,731 (21.4)
Lung (C33, C34)	22 (1.2)	14 (2.3)	8 (0.7)	4,087 (7.5)	3,021 (11.0)	1,066 (4.0)
Stomach (C16)	17 (1.0)	8 (1.3)	9 (0.8)	2,207 (4.1)	1,396 (5.1)	811 (3.0)
Colon (C18–C21)	14 (0.8)	6 (1.0)	8 (0.7)	1,600 (2.9)	834 (3.0)	766 (2.9)
Liver (C22)	12 (0.7)	7 (1.1)	5 (0.4)	1,660 (3.1)	1,030 (3.8)	630 (2.3)
Pneumonia (J12–J18, J69)	101 (5.7)	41 (6.6)	60 (5.1)	1,941 (3.6)	1,006 (3.7)	935 (3.5)
Diabetes (E10–14)	91 (5.1)	24 (3.9)	67 (5.7)	2,543 (4.7)	1,145 (4.2)	1,398 (5.2)
CVD (I20–I25)	85 (4.8)	24 (3.9)	61 (5.2)	2,850 (5.3)	1,252 (4.6)	1,598 (6.0)
Missing	29 (1.6)	6 (1.0)	23 (2.0)	623 (1.1)	238 (0.9)	385 (1.4)
Total	1,787 (100.0)	619 (100.0)	1,168 (100.0)	54,282 (100.0)	27,453 (100.0)	26,829 (100.0)

Values are presented as number (%).

AD, Alzheimer's disease; CVA, cerebrovascular accident; CVD, cardiovascluar disease.

composition ratios were 46.8%, 27.0%, 14.4%, 11.8% in the entire sample; 17.6%, 24.6%, 25.0%, and 32.8%, in the AD group; and 47.2%, 27.0%, 14.3%, and 11.5% in the non-AD group. Therefore, unlike in the non-AD group, it was found that the composition ratio of individuals in the AD group increased with age. In the analysis of the three most common chronic diseases (hypertension, diabetes, and dyslipidemia), all prevalence rates in the AD group were relatively higher than those

in the non-AD group. In the income analysis, composition ratios of the non-AD group and the total sample were similar, whereas the AD group showed slight differences from the non-AD group and the entire sample: 1.6% of subjects were in the very low-income bracket (income decile=0, medical aid), 9.2% were in the low-income bracket (income decile=1), and 89.2% were in the mid- to high-income bracket (income decile 2). These findings indicate that the proportion of subjects in the
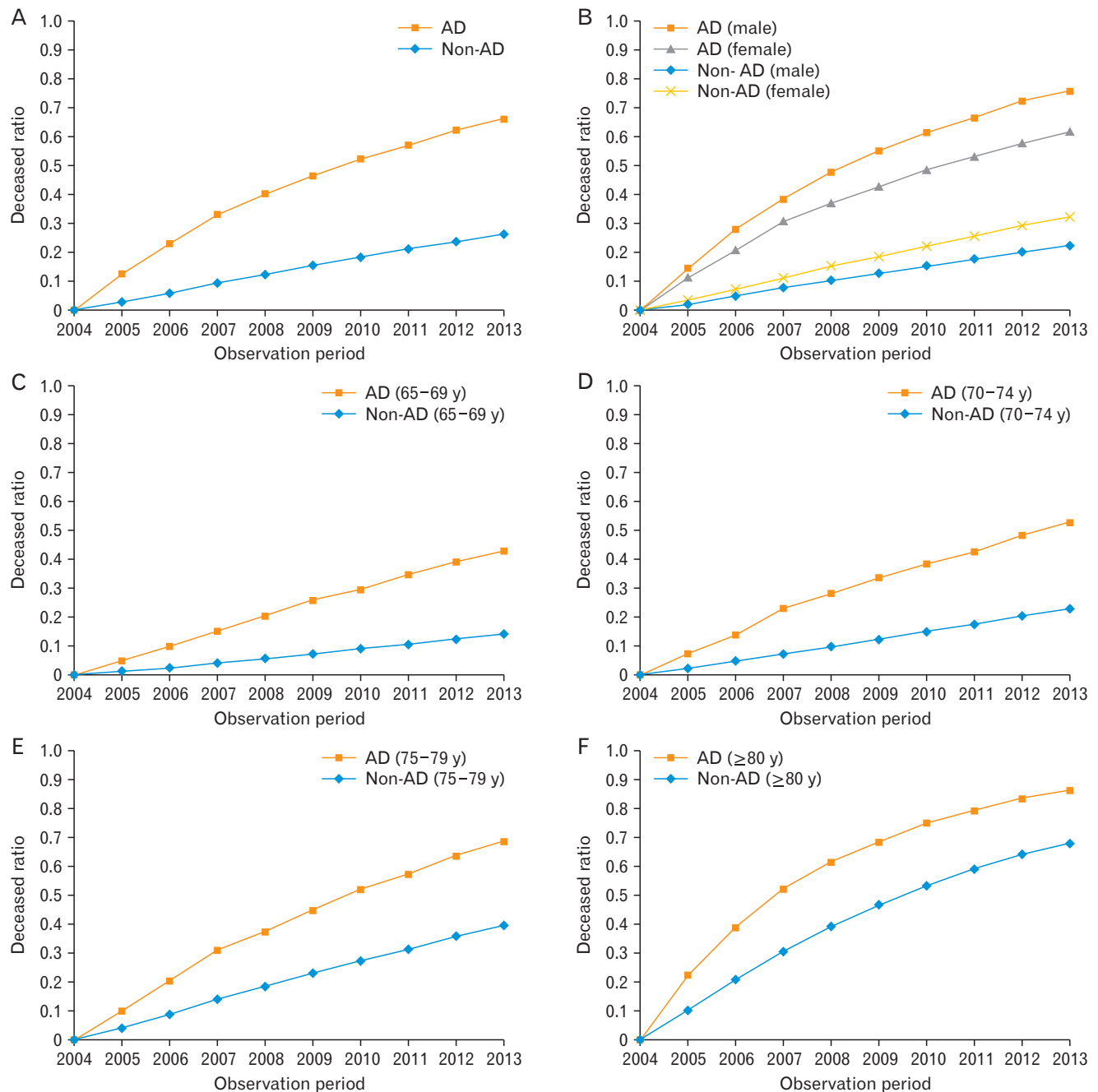
Figure 2. Differences in survival time between the AD and the non-AD groups, as determined using the Kaplan-Meier method. In the graphs, the x-axis represents the number of survival times converted into years, and the y-axis represents the number of deaths corresponding to each survival period. (A) Graph A shows the results of the comparison of deaths between the AD and the non-AD groups. (A) Graph A compares the survival times of the AD group with those of the non-AD group. (B) Graph B compares survival time by gender, and the remaining graphs (C–F) show the comparison of age-specific survivals. Each statistical significance level was P<0.0001. AD, Alzheimer's disease.

very low-income bracket in the AD group was higher than that of the non-AD group.

2. Deaths among the Study Population

The total number of deaths in the study period was 56,069. The mortality rate in the AD group was 66.3% (1,787 out of 2,695) and the mortality rate in the non-AD group was 26.3% (54,282 out of 206,559). Results of the analysis by sex indicated that the mortality rate of male subjects (AD group 75.9%, non-AD group 32.4%) was higher than that of female subjects (AD group 62.2%, non-AD group 22.0%) in both groups. The results of the age-specific analysis indicated that in both groups, mortality increased with age. Overall, in the analyses of gender and age, mortality rates in the AD group, were generally higher than those in the non-AD group (Table 1). In the analysis of the three most common accompanying chronic diseases, it was found that subjects with hypertension, diabetes, and dyslipidemia in the AD group were less likely to die than subjects with the same diseases in the non-AD group. On the other hand, except for dyslipidemia, in the non-AD group, the mortality rates were higher in subjects with hypertension and diabetes. In the income analysis, the mortality rates of subjects in the very low-income bracket (AD 86.4%, non-AD 35.3%) were higher than those of subjects in the other two income brackets in both groups, and the difference in the mortality rates, between subjects receiving medical aid (very low-income bracket) and those with health insurance (low or mid- to high-income bracket) was greater in the AD group.

3. Causes of Death

In the comparison of the causes of death other than dementia, CVA was found to be the most frequent cause other than dementia (15.1%) in the AD group, followed by senescence (13.3%), malignant neoplasm (6.3%), pneumonia (5.7%), diabetes (5.1%), and CVD (4.8%) (Table 2). In the non-AD group, the most frequent causes of death other than dementia were malignant neoplasm 27.5%, followed by senescence (13.4%), CVA (12.3%), CVD (5.3%), diabetes (4.7%), and pneumonia (3.6%).

When the malignant neoplasms were analyzed in detail, lung cancer (AD group 1.2%, non-AD group 7.5%) was found to be the most frequent type of neoplasm among the causes of death other than dementia, and stomach cancer (AD group 1.0%, non-AD group 4.1%) was found to be the second most frequent type. In the analysis of the causes of death by gender and age, the mortality rates in the AD group were generally higher than those in the non-AD group (Table 2).

4. Survival Rates

Results of the comparison of survival curves using the Kaplan-Meier method, suggested that deaths in the AD group were generally higher than those in the non-AD group. The proportion of deceased females in the AD group was even higher than the proportion of deceased males in the non-AD group (Figure 2).

During the observation period (2005–2013), the mean survival interval of the AD group was 5.3±3.3 years, which was about 2.4 years shorter than that of the non-AD group, which was 7.8±2.4 years. In addition, in the analysis by sex, the mean survival intervals of males (AD group 4.7±3.2 years, non-AD group 7.5±2.6 years) were shorter than those of females (AD group 5.6±3.3 years, non-AD group 8.0±2.3 years), in both groups. More precisely, the difference in the survival interval between males and females in the AD group was approximately

Table 3. Survival interval, during observation period (from the initial diagnosis, year)

Variable	AD				Non-AD		P-value
	During observation period		From the initial diagnosis		Median	Average±SD	
	Median	Average±SD	Median	Average±SD			
Total	5.5	5.3±3.3	6.1	5.9±3.3	9.0	7.8±2.4	<0.0001
Gender							<0.0001
Male	4.2	4.7±3.2	4.9	5.3±3.2	9.0	7.5±2.6	
Female	6.3	5.6±3.3	7.0	6.2±3.3	9.0	8.0±2.3	
Age (y)							<0.0001
65–69	9.0	7.0±2.9	9.2	7.6±2.9	9.0	8.4±1.7	
70–74	8.3	6.3±3.2	8.9	6.9±3.1	9.0	8.0±2.2	
75–79	5.5	5.4±3.2	6.2	6.0±3.2	9.0	7.2±2.8	
≥80	2.8	3.7±3.0	3.4	4.3±3.1	5.4	5.4±3.2	
Comorbidity*							
Diabetes	4.6	5.0±3.3	5.3	5.6±3.3	9.0	7.5±2.6	<0.0001
Hypertension	5.8	5.4±3.3	6.5	6.0±3.4	9.0	7.7±2.5	<0.0001
Dyslipidemia	9.0	6.9±2.8	9.1	7.5±2.9	9.0	8.4±1.7	0.0002
Income level†							
Very low	3.2	4.0±3.1	4.0	4.6±3.1	9.0	7.2±2.8	<0.0001
Low	4.6	4.9±3.4	5.2	5.5±3.4	9.0	7.7±2.5	<0.0001
Mid to high	5.6	5.4±3.3	6.2	6.0±3.3	9.0	7.8±2.4	<0.0001

AD, Alzheimer's disease; SD, standard deviation.
*Frequent accompanying three disease (hypertension, diabetes, and dyslipidemia). †Devided into following three categories: very low (income decile=0), low (income decile=1), and mid to high (income decile ≥2).

0.9 years, greater than in the non-AD group (Table 3).

In the age-group analysis, survival time significantly decreased with age, and survival time in the over-80-year-old group was shorter than that of the 65- to 69-year-old group, by 3.3 years in the AD group and 3.1 years in the non-AD group. In the analysis of the three most frequent major chronic diseases, the survival times of the patients with diabetes were the shortest (AD group 5.0±3.3 years, non-AD group 7.5±2.6 years) in both groups. In contrast, the survival times of the patients with dyslipidemia were the longest (AD group 6.9±2.8 years, non-AD group 8.4±1.7 years).

In the income analysis, the survival times of the subjects in the very low-income bracket were shorter than those of subjects in the other income brackets in both groups, but the difference between survival times of the subjects in the very low-income bracket and the mid- to high-income bracket in the AD group was about 1.4 years, which was greater than that of subjects in these two income brackets in the non-AD group.

In the AD group, when the survival was separately calculated from the date of being first diagnosed with AD, the mean survival interval was 5.9±3.3 years, and the male survival interval was 5.3±3.3 years, about 0.9 years shorter than that (6.2±3.3) of females (Table 3).

5. Covariates

Results of the mortality risk analysis using the Cox proportional-hazard model (HR, 95% CI), indicated that subjects in the AD group had a HR of 3.7 (95% CI, 3.53–3.88,) and after adjustment with variables (i.e., gender, age, income level, and the three most common major chronic diseases), it was 2.5 (95% CI, 2.38–2.62). Therefore, it was found that the AD group had a 2.5-fold higher risk of death than the non-AD group. The analysis of stratification using gender, age, income level, and three most common major chronic diseases (i.e., hypertension, diabetes, and dyslipidemia) showed similar results. In sum, the analysis of stratification showed that the risk of death in the AD group was higher than in the non-AD group (Table 4).

DISCUSSION

1. Survival Analysis

This study was based on the National Health Insurance Services' Senior Cohort database (2002–2013), and compared the survival of subjects in the AD group with that of subjects in the non-AD group. In particular, our study examined the independent impact of AD itself on mortality risk. With regard to mortality risk, patients with AD had an HR of 2.5 (adjusted) in this study, which was slightly higher than the HR of 1.82 found in a recent Korean study on patients with all types of dementia.[10] However, the results (HR, 1.7–2.9) of foreign studies analyzing AD groups showed similar findings to both.[11-14] In the present study, stratification analyses were conducted for each variable to examine the effect of AD on survival in more detail. It was found that the overall risks of death in the AD group were higher than in the non-AD group.

Table 4. Cox propotional hazard ratio by multivariable and stratification

Variable	Category	Hazard ratio (95% condfidence interval)	P-value
Unadjusted	AD	3.7 (3.53–3.88)	<0.0001
	Non-AD	1.0	
Adjusted	AD	2.5 (2.38–2.62)	<0.0001
	Non-AD	1.0	
Gender*			
Male	AD	2.7 (2.51–2.95)	<0.0001
	Non-AD	1.0	
Female	AD	2.3 (2.19–2.46)	<0.0001
	Non-AD	1.0	
Age (y)†			
≥80	AD	1.9 (1.79–2.07)	<0.0001
	Non-AD	1.0	
75–79	AD	2.6 (2.33–2.81)	<0.0001
	Non-AD	1.0	
70–74	AD	3.2 (2.92–3.60)	<0.0001
	NonAD	1.0	
65–69	AD	4.1 (3.56–4.71)	<0.0001
	Non-AD	1.0	
Comorbidity‡			
Diabetes	AD	2.3 (1.89–2.85)	<0.0001
	Non-AD	1.0	
Hypertenion	AD	2.4 (2.23–2.66)	<0.0001
	Non-AD	1.0	
Dyslipidemia	AD	2.6 (1.67–3.94)	<0.0001
	Non-AD	1.0	
Income level§,‖			
Very low	AD	2.5 (2.35–2.60)	<0.0001
	Non-AD	1.0	
Low	AD	2.7 (2.28–3.10)	<0.0001
	Non-AD	1.0	
Mid to high	AD	3.3 (2.33–4.54)	<0.0001
	Non-AD	1.0	

AD, Alzheimer's disease.
*Variables for stratification adjustment: age, income level and frequent accompanying diseases such as hypertension, diabetes, and dyslipidemia. †Variables for stratification adjustment: gender, income level and frequent accompanying diseases such as hypertension, diabetes, and dyslipidemia. ‡Variables for stratification adjustment: gender age and income level. §Variables for stratification adjustment: gender, age and frequent accompanying diseases such as hypertension, diabetes, and dyslipidemia. ‖Divided into three categories: very low (income decile=0), low (income decile=1), and mid to high (income decile ≥2).

During the observation period (2005–2013), the survival intervals of the AD and non-AD groups were compared, and the survival interval of the AD group was about 2.4 years shorter. However, when only the survival interval after being first diagnosed with AD was calculated, the overall average was 5.9 years, and the survival interval in males was on average 0.9 years shorter than that in females. This suggested that the survival interval after being diagnosed with AD was shorter than the average of 9.7 years reported in a previous domestic study.[15] However, the finding was similar to those of foreign studies (Ganguli et al.[12] 6.39 years, Fitzpatrick et al.[16] 7.1 years) under similar conditions. A possible explanation for the different findings may the age of the subjects. Unlike the previous Korean studies that included subjects with early onset dementia, subjects in the present study were 65 years of age or old-

er. Therefore, there was a difference in population composition. The mean age of the subjects was 76.4 years, which was higher than in the previous studies. In addition, the percentage of the population over 80 years old, who had many complex factors to consider (such as, comorbidity, functional impairments, and severity of dementia) was as high as 32.8%.

When comparing the causes of death other than dementia between the AD group and the non-AD group, in general, CVA was the most frequent cause (15.1%) in the AD group, and malignant neoplasm was the most frequent (27.5%) in the non-AD group. Interestingly, there was a significant difference in malignancies between the AD and non-AD groups. It could be derived from the difference in age composition. The higher mean age in the AD group was likely to be survived from the malignancies and may indicate survival effects. In the AD group, dementia was the most common cause of death at 20.9%, but this rate was less than the 36% reported in the previous Korean study (Table 2). In addition, senescence (10.4%), the second most common cause of death in the previous study, accounted for 13.3% in the present study, which was lower than that of CVA (15.1%) in the AD group.[15] This could be the result of differences in population composition, as described above, and also because of the proportion of women (69.7%), who had a longer survival and lower mortality risk in the present study. In foreign studies, CVD (Fitzpatrick et al.[16] 19%, Ganguli et al.[12] 47.5%) was the most common cause of death, but in the present study, it was 4.8%. It was also 6.1% in the domestic study. The incongruencies may be due to cultural differences.[17]

The present study also found that the age at diagnosis of AD was the most important factor affecting the increase in mortality and the shortening of the survival interval.[18] However, we also found that in both groups, mortality increased sharply with age. This finding may be due to the effects of multimorbidity on the survival of elderly patients as age increases.[19-23] Survival time and mortality rates were significantly better in the patients with dyslipidemia. This finding may be due to the relationship between malnutrition and death, or body mass index and survival, but further research is needed.[24-27]

2. Limitations and Strengths
The limitations of this study are as follows: First, this study excluded the deceased population from the baseline year 2004, which included some individuals diagnosed with AD. In this case, the population could have had greater mortality risk and shorter survival periods. Therefore, there is a possibility that some bias may have occurred. Second, as mentioned above, the higher mean age in the AD group, like other studies, may indicate survival from diseases with high risk of death, so this could also indicate survival-effect bias. Third, further research on the comorbid factors with various diseases and on the lifestyles of the patients with AD, which were not investigated in this study, are needed.

However, this study has several strengths. First, it was based on the National Health Insurance Services' Senior Cohort database (2002–2013), which is a good representation of the Korean general popula-

tion. Second, this study covered a larger population than in previous studies. Third, the accuracy of the study was high because there were few missing values in the cohort data. Finally, there have been few previous Korean studies that have directly compared the survival of AD and non-AD groups, and have analyzed survival from the onset of AD.

3. Conclusion
Overall, AD has a large, independent impact on survival, and can shorten life expectancy. The prevalence of AD in Korea is rapidly rising, and it is necessary to have proper awareness of the clinician and to respond accordingly. More diverse research on AD and a more comprehensive understanding of the disease can promote healthy aging and better quality of life in the elderly.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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