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**Cognitive impairment, Activities of daily living, and  
Mortality among the Elderly in Rural South Korea:  
Kangwha Cohort Study**



**The Graduate School  
Yonsei University  
Department of Public Health**

**Cognitive impairment, Activities of daily living, and  
Mortality among the Elderly in Rural South Korea:  
Kangwha Cohort Study**

**A Dissertation**

**Submitted to the Department of Public Health  
and the Graduate School of Yonsei University  
in partial fulfillment of the  
requirements for the degree of  
Doctor of Philosophy**

**Jeong Ae Cho**

**December 2015**

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## ABSTRACT

### Cognitive impairment, activities of daily living, and mortality among the elderly in rural South Korea: Kangwha Cohort Study

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**Purpose:** Purpose: The purpose of this study is to examine the effects through the various combinations of cognitive impairment and ADL disability with mortality due to all-cause, vascular diseases, cancer, and senility, in a 14.5-year prospective cohort among community-dwelling elderly Koreans.

**Methods:** The cohort involved 2,501 participants ages 64 years and older starting from July 1994 to December 2008. Chi-squared tests and one-way analysis of variance (ANOVA) were performed to compare differences between the groups. Cox proportional hazards models were used to evaluate the associations among cognitive performance, ADL, and mortality.

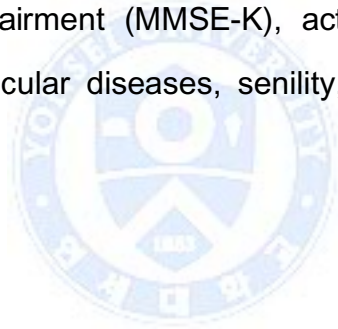
**Results:** There were 1,481 deaths during the follow-up. Mortality risks due to all-cause, vascular diseases, and senile were significantly associated with cognitive impairment and ADL disability. No association was found between cancer mortality and cognitive impairment or ADL disability. Domain-specific cognitive impairment or task-specific ADL disability was diversely related with cause-specific mortality. When cognitive impairment

and ADL disability were combined, the Synergy index increased due to interaction. The effects indicated all-cause (HR=2.72), vascular disease (HR=3.40), and senility (HR=1.58).

**Conclusion:** Cognitive impairment and ADL disability are important risk factors towards the increase of mortality due to all-cause, vascular disease, and senility, but cancer didn't suggest concrete correlation. Domain-specific cognitive function and task-specific ADL predicted the mortality risk. Combining cognitive impairment and ADL disability showed a higher risk for coexisting variables than for cognitive impairment or ADL disability alone.

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Key words: Cognitive impairment (MMSE-K), activities of daily living(ADL), all-cause, vascular diseases, senility, mortality



## Abbreviations:

ADL	activities of daily living
aHR	adjusted Hazard Ratio
BMI	body mass index
BP	blood pressure
CI	confidence interval
CVD	cardio vascular disease
IADL	instrumental activities of daily living
ICD-10	International Classification of Diseases 10th edition
MCI	mild cognitive impairment
MMSE-K	Mini-Mental State Examination Korean version
HR	hazard ratio
RERI	the relative excess risk due to interaction
S	synergy index
SPMSQ	short portable mental status questionnaire
SD	standard deviation



## I. INTRODUCTION

Functional capacity is a key indicator that measures the health status and independent living of the older adults. Older adults are under the effects of chronic diseases, complications, and may lose their mental and physical functions later in their life. Lack of functional capacity may cause increase in morbidity (Sands et al., 2002; Strauss et al., 2003; Dodge et al., 2005; Fauth et al., 2012; Robertson et al., 2013), mortality (Stuck et al., 1999; Ramos et al., 2001; Millán-Caleti et al., 2010; O'Donnell et al., 2012; Santabárbara et al., 2014), and most likely healthcare costs (Alzheimer's Disease International, 2015).

According to the reports, while the population of older adults has grown 17.4%, older adults with dementia grew 28.5%, and the prevalence of dementia increased from 8.4% in 2008 to 9.18% in 2012. The rate of the prevalence of dementia indicates 15.5% for severe, 25.7% for moderate, 41.4% for mild, and 17.4% for minimal of cognitive impairments (Ministry of Health & Welfare 2008 & 2013; Clinical Research center for Dementia 2014). Approximately 10-15% of Mild Cognitive Impairment (MCI) is converted to dementia every year (Ha et al., 2014). As a result, cost of dementia treatment and dependent care expenses enlarged by 87% from 30.6 billion (Korean won) in 2008 to 57.2 billion in 2013. This cost includes the financial contributions of both the central government and the local and regional government, excluding personal expenses (National Assembly Budget Office, 2014). Furthermore, due to rapid aging of the population, the number of dementia patients would presumably double in every 20 years (Ministry of Health and Welfare, 2011). According to the

diagnoses of Korean National Statistical of the mortality data, around 5,000 people die from dementia in Korea with the mortality rate of 12 out of one hundred thousand people (Statistics Korea, 2015).

The mini-mental state examination (MMSE) has contributed to detecting cognitive impairment with dementia (Magni et al., 1996; Fabrigoule et al., 2003; Pezzotti et al., 2008). Several studies have publicized the relationship between the cognitive impairment and correspondent with higher mortality rate after adjusting the confounding variables (Dewey et al., 2001; Jacobs et al., 2011; O'Donnell et al., 2012; Park et al., 2014; Santabárbara et al., 2014). Cognitive function domains, which are based on MMSE-K, include 'orientation to time', 'orientation to place', 'registration', 'attention and calculation', 'recall', 'naming and repetition', 'three-stage command', 'copying', and 'comprehension' (Park et al., 1990). Cognitive impairment in the community-based studies is associated with disabilities of Activities of Daily Living (ADL) (Dodge et al., 2005; Ishizaki et al., 2006; Ayalon et al., 2008; Park et al., 2014). However, whether the cognitive impairment or ADL disability has the association with cause-specific mortality after adjusting for confounding variables is yet debatable (Altieri. 2002; Nguyen et al., 2003; Anstery et al., 2006; Benito-León et al., 2014; Katsoulis et al., 2014; Paddick et al., 2015).

ADL disability is calculated based on essential activities of everyday (World Health Organization, 2001). Physical ADL modified from Katz index includes 'bathing', 'dressing', 'toileting', transferring ('moving in the bed'; and 'moving around the house'), 'eating', and 'continence' (Katz et al., 1976). Physical ADL reflects rudimentary functions for independent living of the older adults. ADL disability is often followed by frailty status (Takata et

al., 2013), tends to remain substantially until the end of dementia (Ha et al., 2014), and predicts mortality in older adults (Matsubayashi et al., 1999; Ramos et al., 2002; Cesari et al., 2008; Millán-Calenti et al., 2010; Nakazawa et al., 2012). Particularly, functional capacity is wheeled by cognitive function and ADL; because geriatric studies focus on mental and physical health, cognitive impairment and ADL disability can predict mortality for older adults. Most functional disability studies have evaluated cognitive impairment and ADL disability by a single factor, or have divided them into two factors or more (Bassuk et al., 2000; Ishizaki et al., 2006; Johnson et al., 2007; Iwashyna et al., 2010; Santabábara et al., 2015). Only a small number of studies show the association between domain-specific cognitive impairment with mortality or task-specific ADL with mortality for the functional capacity with different indexes. Little is known about the relationship between cause-specific mortality and functional capacity by subdivisions of cognitive impairment or ADL disability. The association with cause-specific mortality in cognitive impairment as well as with ADL disability have not been carefully examined; however, it is important to investigate possible preventions of cognitive impairment and disability. For inclusive understanding of the overall effects, the comprehensive interaction should be known between full factors of functional capacity and mortality.

The study has three objectives. First, we wished to clarify the association between cognitive impairment with mortality and ADL disability with mortality due to all-cause, vascular disease, cancer, and senility. Second, we attempted to investigate the association between domain-specific cognitive impairments with cause-specific mortality and task-specific ADL with cause-specific mortality. Third, we tried to



summarize the combined effects by of task-specific ADL and cognitive impairment status with cause-specific mortality in a 14.5-year prospective cohort among community-dwelling elderly Koreans. We expected that mortality would be associated with an increased likelihood of cognitive impairment and ADL combined than a single individual functional status of either cognitive impairment or ADL disability.



## II. OBJECTIVES


The purpose of this study is to examine the effects through the various combinations of cognitive impairment and ADL disability with mortality due to all-cause, vascular diseases, cancer, and senility in a 14.5-year prospective cohort among community-dwelling elderly Koreans.

1. To assess cognitive impairment, ADL disability and their attributions to the cause-specific mortality due to all-cause, vascular diseases, cancer, and senility
2. To evaluate the association between task-specific ADL with cause-specific mortality and domain-specific cognitive performance with cause-specific mortality due to all-cause, vascular diseases, cancer, and senility by functional status of each criterion
3. To explore the combined effects of cognitive performance and ADL for cause-specific mortality due to all-cause, vascular diseases, cancer, and senility

### III. MATERIALS AND METHODS

#### A. Study participants

This study used data from the Kangwha Cohort Study (Yi et al., 2009; Sull et al., 2010). From July to August in 1994, 3,592 (85.2%) of 4,217 survivors (50 losses to follow-up and 2,105 deaths as of July, 1994) of the 6,372 who participated in the first survey in March 1985, participated in the second survey. After excluding those with missing cognitive function (n=1,068), activities of daily living (n=14), hypertension (n=3), or marriage (n=6), a final 2,501 participants (1,059 men, 1,442 women) were included in the analysis. The Institutional Review Board of Human Research of Yonsei University approved the study (approval no. 4-2007-0182).



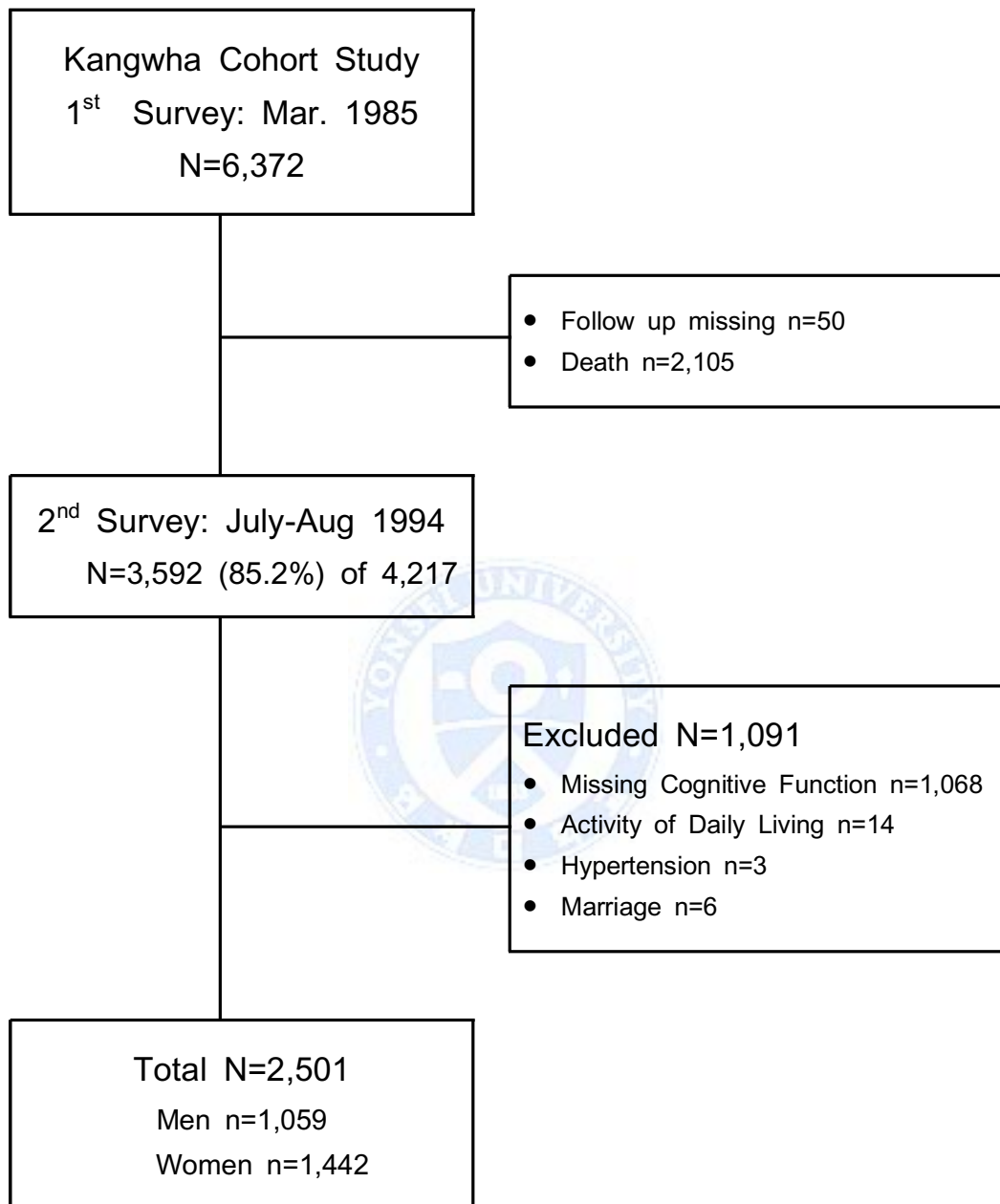


Figure 1. Flow chart describing study participants, Kangwha Cohort Study

## **B. Data collection**

The survey was conducted in July 1994. Trained researchers interviewed participants using a structured questionnaire to obtain demographic characteristics and health related information, including age at entry, gender, education, occupation, tobacco and alcohol consumption, chronic disease history, marital status, cognitive function and activities of daily living (Basic or Physical ADL) at the time of survey, and measured their blood pressure, height, and weight. More details of the data collection can be found elsewhere (Yi et al., 2009; Yi et al., 2010).

## **C. Cognitive testing**

Cognitive function was assessed through a survey in 1994 using the Korean Version of the Mini-Mental State Examination (MMSE-K) (Park and Kwon, 1990). The MMSE-K includes 7 domains (or 9 domains considering sub-domains in language) that measure orientation to time (5 points), orientation to place (5 points), registration (3 points), attention and calculation (5 points), recall (3 points), language (7 points; Naming and repetition [3 points], three-stage command [3 points], copying [1 point]), and comprehension and judgement (2 points). One point was added to scores of orientation to time, two to scores of attention and calculation, and one to scores of a language function (repetition) to non-educated individuals who did not make full score at each corresponding item, for the adjustment purpose due to a low educational status of Korean elderly (Park and Kwon, 1990). The MMSE-K ranges from 0 to 30-point, with a higher score indicating better cognitive function (O'Donnell et al., 2012;

Park and Kwon, 1990) Cognitive performance was categorized into 4 groups based on the median (no impairment [reference, 23-30 point], mild [19-22], moderate [14-18], severe [0-13]), 20 percentiles, and 5 percentiles of MMSE-K score, and into 3 groups (combining no and mild impairment, moderate, and severe). For a sensitivity analysis, it was also categorized into 3 groups (MMSE-K score; 25-30, 21-24, 0-20) suggested by the developers of MMSE-K (Park and Kwon, 1990), and 4 groups (23-30, 18-22, 13-17, 0-12) based on -2SD (standard deviation), -1SD, and mean scores. Cut-off points were generally lower in this study than in other studies that use MMSE or MMSE-K, since only 41% of participants had formal education.

#### **D. Measures of activities of daily living**

Basic ADL disability was evaluated by the following seven criteria modified from previous research (Katz et al., 1963): 'bathing', 'dressing', 'toileting', 'moving in the bed', 'moving around the house', 'eating', and 'continence'. They rated the task dependence when performing each activity except 'continence' as by self with ease (0), by self but with difficulty (1), with partial assistance from others (2), and unable to perform the activity without help (3). For the performance of the 'continence', they were asked to answer one of the four categories; controls urination and bowel movement completely by self (0), has occasional accidents (1), has frequent accidents (2), is incontinent or others help control (3). The ADL test ranges from 0 to 21, with a higher score indicating poorer performance. Participants were categorized into 3 groups; independence [0], partial dependence [1-2 point], dependence [3-21 point]).

## **E. Follow-up and outcome ascertainment**

Deaths among subjects from 1 July 1994 through 31 December 2008 were confirmed by the death records held at the National Statistical Office (Yi et al., 2009). Follow-up was performed through the record linkage at the national level and was complete. The main outcomes for this study were death from all-causes, cancers (C00-D58), vascular diseases (I00-I99), and senility (R54) as defined by the International Classification of Disease, Tenth Revision (ICD-10).

## **F. Statistical analysis**

Chi-squared tests and one-way analysis of variance (ANOVA) were performed to compare differences between the groups. Cox proportional hazards models were used to evaluate the association between cognitive performance with mortality and ADL with mortality. Analyses were adjusted for the following covariates where applicable; age at entry (continuous), gender, known hypertension (based on measured BP  $\geq 140/90$  mmHg or self-reported regular medication on hypertension; yes, no), smoking status (non-smoker, former smoker, current smoker), alcohol drinking status [(non-drinker, former drinker, current drinker) at least from March 1985], occupation (agriculture, other), education (none, elementary school, middle school or above), marital status (living with, without spouse), self-reported health (good or fair, poor), and body mass index (BMI,  $\text{kg}/\text{m}^2$ ;  $<18.5$ ,  $18.5-20.9$ ,  $21.0-24.9$ ,  $25.0-27.4$ ,  $\geq 27.5$ ).

A stratified analysis was performed according to the statuses of cognitive impairment (no or mild, moderate, and severe) or the levels of

ADL disability (independence, partial dependence, and dependence) to examine whether to confirm the association between cognitive performance and ADL each with cause-specific mortality. Combined effect of cognitive performance and ADL was also assessed via constructing a 9-level variable that combined 3 statuses of cognitive impairment with 3 levels of ADL disability. Additionally, analyses of the participants with follow-up until 2000, and analyses of survivors as from January 1, 2001 with follow-up until 2008, were done to evaluate whether the association differs by follow-up period. These various analyses served as a sensitivity analysis.

Two-sided p-values were calculated and the statistical significance level was set at 0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).





## IV. RESULTS

### A. General characteristics of the study participants

The total follow-up person-years numbered 28,225. During the 14.5 years of follow-up, all-cause mortality of 1,481 participants died of vascular diseases (345), cancer (232), and senility (428). The average (SD) age of the participants was 72.6 years at enrollment. Age, hypertension, poor self-rated health condition ( $p=0.2175$ ), and ADL dependency increased across the four categories of cognitive impairment statuses; no, mild, moderate, severe. The proportion of women was higher in groups of moderate-to-severe cognitive impairment than that of no-or-mild impairment (Table 1).

Table 1. Baseline characteristics of the study participants by cognitive impairment in Kangwha Cohort Study during 1994-2008

	Cognitive impairment status					p-value
	Total (N=2,501)	No (n=1,224)	Mild (n=686)	Moderate (n=441)	Severe (n=150)	
	mean±SD	mean±SD	mean±SD	mean±SD	mean±SD	
Age, year	72.6±6.0	71.1±5.1	73.0±5.7	75.0±6.7	76.3±6.8	<0.0001
BMI (kg/m <sup>2</sup> )	22.0±3.4	22.1±3.5	22.0±3.3	22.3±15.9	21.2±3.6	0.4455
	N (%)	N (%)	N (%)	N (%)	N (%)	
Gender						<0.0001
Men	1,059(42.3)	675(55.1)	240(35.0)	102(23.1)	42(28.0)	
Women	1,442(57.7)	549(44.9)	446(65.0)	339(76.9)	108(72.0)	
Smoking habits						<0.0001
Non smoker	1,427(57.0)	635(51.9)	409(59.6)	288(65.3)	93(62.0)	
Former smoker	248( 9.9)	148(12.1)	49( 7.1)	34( 7.7)	17(11.3)	
Current smoker	828(33.1)	441(36.0)	228(33.2)	119(27.0)	40(26.7)	
Alcohol drinking status						<0.0001
Non drinker	1,606(64.2)	696(56.9)	469(68.4)	334(75.7)	107(71.7)	
Former drinker	151( 6.0)	86( 7.0)	36( 5.3)	24( 5.4)	5( 3.3)	
Current drinker	744(29.8)	442(36.1)	181(26.4)	83(18.8)	38(25.3)	
Hypertension						0.0004
No	1,312(52.5)	693(56.6)	341(49.7)	212(48.1)	66(44.0)	
Yes	1,189(47.5)	531(43.4)	345(50.3)	229(51.9)	84(55.0)	
Self-rated Health						0.2175
Poor	1,008(40.3)	469(38.3)	285(41.5)	187(42.4)	67(44.7)	
Good or fair	1,493(59.7)	755(61.7)	401(58.5)	254(57.6)	83(55.3)	
BMI categories (kg/m <sup>2</sup> )						0.0007
<18.5	367(14.7)	163(13.3)	87(12.7)	77(17.5)	40(27.7)	
18.5-20.9	681(27.2)	310(25.3)	200(29.2)	130(29.5)	41(27.3)	
21-24.9	1,044(41.7)	539(44.0)	293(42.7)	166(37.6)	46(30.7)	
25-27.4	264(10.6)	138(11.3)	69(10.1)	44(10.0)	13( 8.7)	
≥27.5	145( 5.8)	74( 6.1)	37( 5.4)	24( 5.4)	10( 6.7)	

-Table continued-

	Cognitive impairment status					p-value
	Total (N=2,501)	No (n=1,224)	Mild (n=686)	Moderate (n=441)	Severe (n=150)	
Education						<0.0001
None	1,474(59.0)	607(49.6)	460(67.1)	315(71.4)	92(61.3)	
Elementary school or below	922(36.9)	535(43.7)	210(30.6)	120(27.2)	57(38.0)	
Middle school or above	105( 4.2)	82( 6.7)	16( 2.3)	6( 1.4)	1( 0.7)	
Occupation						0.8486
Non-agriculture	2,099(83.9)	1,019(83.2)	579(84.4)	372(84.3)	128(84.3)	
Agriculture	404(16.1)	205(16.8)	107(15.6)	69(15.7)	22(14.7)	
Marital status						<0.0001
Living with spouse	1,485(59.4)	847(69.2)	392(57.1)	181(41.0)	65(43.3)	
Living without spouse	1,016(40.6)	377(30.8)	294(42.9)	260(59.0)	85(56.7)	
ADL						<0.0001
Independence	1,737(69.4)	921(75.3)	456(66.5)	276(62.6)	84(56.0)	
Partial dependence	432(17.3)	206(16.8)	124(18.1)	78(17.7)	24(16.0)	
Dependence	332(13.3)	97( 7.9)	106(15.4)	87(19.7)	42(28.0)	

Values are presented as mean±SD or number(%); BMI, body mass index; ADL, Activity of Daily Living; Cognitive impairment was classified by MMSE-K scores. MMSE-K, Korean version of the Mini-Mental State examination.

## **B. Cause-specific mortality and cognitive impairment**

### **1. Cause-specific mortality with cognitive impairment**

Table 2 showed the association with the hazard ratios (HRs) for cause-specific mortality by cognitive impairment after adjusting for age and gender (Model 1). Model 2 was adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25.0-27.4;  $\geq 27.5$ ), self-rated health, hypertension, ADL disability (partial dependence and dependence), and cognitive impairment (moderate and severe). Model 3 comprised ADL (partial dependence and dependence) into Model 2. Regarding the cognitive status, mortality risks due to all-cause and senility increased significantly with a dose-response relationship in all Models. In contrast, cancer mortality was not associated with cognitive impairment status, and vascular disease mortality was the only risk increased in severe cognitive impairment status in Model 1.

The total follow-up per 100,000 person-years was 28,225 (vascular disease mortality 6,416; senile mortality 9,984; cancer mortality 3,335).

Table 2. Hazard ratios (95% CI) for cause-specific mortality with cognitive impairment status

Cognitive status	No. of deaths	total	PY	Model 1		Model 2		Model 3	
				HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
All-cause mortality	<b>1,481</b>	<b>2,501</b>	<b>28,225</b>						
No impairment	663	1,224	5,081	1.00		1.00		1.00	
Mild impairment	404	686	5,777	1.13(0.99-1.28)	0.0728	1.09(0.96-1.24)	0.1842	1.07(0.94-1.21)	0.3202
Moderate impairment	295	441	7,196	1.29(1.11-1.49)	0.0008	1.21(1.05-1.41)	0.0112	1.21(1.04-1.40)	0.0146
Severe impairment	119	150	10,171	1.79(1.46-2.19)	<0.0001	1.66(1.35-2.04)	<0.0001	1.61(1.31-1.98)	<0.0001
Vascular diseases mortality	<b>345</b>	<b>2,501</b>	<b>6,416</b>						
No impairment	165	1,224	1,265	1.00		1.00		1.00	
Mild impairment	82	686	1,173	0.90(0.69-1.19)	0.4654	0.87(0.66-1.14)	0.3064	0.83(0.63-1.09)	0.1725
Moderate impairment	72	441	1,756	1.26(0.94-1.70)	0.1226	1.22(0.91-1.65)	0.1899	1.19(0.91-1.65)	0.2679
Severe impairment	26	150	2,222	1.60(1.04-2.46)	0.0313	1.51(0.97-2.33)	0.0672	1.37(0.88-2.13)	0.1597
Senile mortality	<b>428</b>	<b>2,501</b>	<b>9,984</b>						
No impairment	132	1,224	1,012	1.00		1.00		1.00	
Mild impairment	129	686	1,845	1.55(1.20-1.98)	0.0006	1.45(1.13-1.87)	0.0039	1.42(1.10-1.83)	0.0069
Moderate impairment	117	441	2,854	1.81(1.38-2.37)	<0.0001	1.61(1.22-2.12)	0.0008	1.58(1.20-2.09)	0.0012
Severe impairment	50	150	4,274	2.53(1.79-3.59)	<0.0001	2.32(1.63-3.31)	<0.0001	2.23(1.57-3.19)	<0.0001
Cancer mortality	<b>232</b>	<b>2,501</b>	<b>3,335</b>						
No impairment	138	1,224	1,058	1.00		1.00		1.00	
Mild impairment	56	686	801	1.00(0.73-1.37)	0.9794	0.99(0.72-1.37)	0.9706	0.99(0.72-1.37)	0.9530
Moderate impairment	29	441	707	1.05(0.69-1.60)	0.8097	1.06(0.69-1.61)	0.8012	1.05(0.69-1.60)	0.8238
Severe impairment	9	150	769	1.15(0.58-2.27)	0.6960	1.11(0.56-2.22)	0.7599	1.10(0.55-2.19)	0.7966

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and ADL (partial dependence, dependence)

## 2. Distribution of domain-specific cognitive impairment

Table 3 summarized the prevalence of domain-specific cognitive impairment by cognitive impairment status. Most domains were increased in prevalence of cognitive impairment across all status.



Table 3. Distribution of domain-specific cognitive impairment at baseline by cognitive impairment status in Kangwha Cohort Study

Domain-specific cognitive impairment	Cognitive impairment status					p-value
	Total (N=2,501)	No (n=1,224)	Mild (n=686)	Moderate (n=441)	Severe (n=150)	
Orientation to time						<0.0001
No or mild impairment	1,926(77.0)	1,197(97.8)	536(78.1)	160(36.3)	33(22.0)	
Impairment	575(23.0)	27( 2.2)	150(21.9)	281(63.7)	117(78.0)	
Orientation to place						<0.0001
No or mild impairment	2,151(86.0)	1,207(98.6)	615(89.7)	282(64.0)	47(31.3)	
Impairment	350(14.0)	17( 1.4)	71(10.3)	159(36.0)	103(68.7)	
Registration						<0.0001
No or mild impairment	2,214(88.5)	1,198(97.9)	637(92.9)	339(76.7)	40(27.0)	
Impairment	287(11.5)	26( 2.1)	49( 7.1)	102(23.1)	110(73.0)	
Attention and Calculation						<0.0001
No or mild impairment	1,142(45.7)	912(74.5)	177(25.8)	48(10.9)	5( 3.3)	
Impairment	1,359(54.3)	312(25.5)	509(74.2)	393(89.1)	145(96.7)	
Recall						<0.0001
No or mild impairment	1,227(49.1)	832(68.0)	286(41.7)	101(22.9)	8( 5.3)	
Impairment	1,274(50.9)	392(32.0)	400(58.3)	340(77.1)	142(94.7)	
Naming and Repetition						<0.0001
No or mild impairment	2,398(95.9)	1,208(98.7)	663(96.6)	417(94.6)	110(73.3)	
Impairment	104( 4.1)	16( 1.3)	23( 3.4)	24( 5.4)	40(26.7)	
Three-stage Command						<0.0001
No or mild impairment	2,313(92.5)	1,208(98.7)	642(93.6)	380(86.2)	83(55.3)	
Impairment	188( 7.5)	16( 1.3)	44( 6.4)	61(13.8)	67(44.7)	
Copying						<0.0001
No or mild impairment	738(29.5)	586(47.9)	107(15.6)	35( 7.9)	10( 6.7)	
Impairment	1,763(70.5)	638(52.1)	579(84.4)	406(92.1)	140(93.3)	
Comprehension						<0.0001
No or mild impairment	1,890(75.6)	1,127(92.1)	508(74.0)	219(49.7)	36(24.0)	
Impairment	611(24.4)	97( 7.9)	178(26.0)	222(50.3)	114(76.0)	

Values denote numbers with percentages (%) in parentheses; Cognitive impairment was classified by MMSE-K scores, Korean version of the Mini-Mental State Examination.

### 3. Cause-specific mortality with domain-specific cognitive impairment

Table 4 showed that the all-cause mortality risk was strongly associated with domain-specific cognitive impairment status except 'naming and repetition' in age and gender adjusted to Model 1. In the Model 2, the risks were constantly significant with 'orientation to time', 'orientation to place', 'three-stage command', 'copying', and 'comprehension'.

Table 5 indicated that two domains ('orientation to place' and 'three-stage command') were significantly associated with the vascular disease mortality in model 1, and only 'orientation to place' domain reached the risk in Model 2 and 3.

The domain-specific cognitive impairments for senile mortality were significantly associated with most domains, except 'orientation to place' and 'naming and repetition'. Especially, 'copying' domain (HR=1.90; 95% CI, 1.41-2.55) presented higher risk score than any other cause-specific cognitive impairment domains in model 3 (Table 6).

Cancer mortality was not associated with any cognitive impairment domain (Appendix table 4).



Table 4. Hazard ratios (95% CI) for all-cause mortality with domain-specific cognitive impairment

Domain-specific Cognitive impairment		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>All-cause mortality (event=1,481)</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.23(1.09-1.39)	0.0007	1.17(1.04-1.33)	0.0104	1.16(1.03-1.32)	0.0167
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.27(1.10-1.47)	0.0012	1.20(1.04-1.39)	0.0131	1.22(1.05-1.41)	0.0087
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.25(1.07-1.45)	0.0041	1.14(0.98-1.33)	0.0847	1.14(0.98-1.33)	0.1029
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.12(1.00-1.24)	0.0469	1.11(0.99-1.24)	0.0650	1.09(0.98-1.22)	0.1072
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.11(1.00-1.24)	0.0433	1.11(1.00-1.24)	0.0467	1.10(0.99-1.22)	0.0912
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.15(0.89-1.47)	0.2842	1.13(0.88-1.45)	0.3435	1.13(0.88-1.46)	0.3325
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.25(1.04-1.50)	0.0173	1.20(1.00-1.45)	0.0470	1.18(0.99-1.42)	0.0713
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.28(1.13-1.44)	<0.0001	1.23(1.08-1.40)	0.0016	1.22(1.07-1.39)	0.0030
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.27(1.13-1.43)	<0.0001	1.23(1.09-1.39)	0.0008	1.22(1.08-1.38)	0.0011

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and ADL (partial dependence, dependence)

Table 5. Hazard ratios (95% CI) for vascular disease mortality with domain-specific cognitive impairment

Domain-specific Cognitive impairment		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Vascular disease mortality (event n=345)</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.20(0.93-1.55)	0.1517	1.23(0.95-1.58)	0.1182	1.20(0.93-1.55)	0.1665
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.43(1.07-1.91)	0.0153	1.39(1.04-1.86)	0.0265	1.40(1.04-1.87)	0.0244
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.25(0.91-1.71)	0.1734	1.15(0.84-1.59)	0.3913	1.13(0.82-1.56)	0.4541
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.91(0.73-1.13)	0.3907	0.86(0.69-1.08)	0.2024	0.84(0.67-1.05)	0.1254
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.03(0.83-1.28)	0.7876	1.05(0.85-1.31)	0.6372	1.03(0.83-1.28)	0.7995
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.89(0.50-1.59)	0.6978	0.89(0.50-1.59)	0.6886	0.86(0.48-1.54)	0.6159
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.49(1.05-2.12)	0.0258	1.41(0.99-2.00)	0.0581	1.33(0.93-1.89)	0.1138
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.09(0.85-1.40)	0.4902	1.10(0.84-1.43)	0.4973	1.05(0.80-1.37)	0.7313
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.24(0.97-1.58)	0.0941	1.22(0.95-1.57)	0.1191	1.21(0.94-1.55)	0.1387

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and ADL (partial dependence, dependence)

Table 6. Hazard ratios (95% CI) for senile mortality with domain-specific cognitive impairment

Domain-specific Cognitive impairment		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Senile mortality (n=428)</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.31(1.06-1.63)	0.0116	1.18(0.95-1.47)	0.1279	1.15(0.92-1.43)	0.2112
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.15(0.89-1.49)	0.2734	1.10(0.85-1.42)	0.4771	1.12(0.87-1.45)	0.3907
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.43(1.11-1.83)	0.0055	1.31(1.02-1.69)	0.0360	1.28(0.99-1.66)	0.0567
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.66(1.34-2.06)	<.0001	1.65(1.32-2.05)	<.0001	1.62(1.30-2.02)	<.0001
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.34(1.09-1.64)	0.0054	1.26(1.02-1.55)	0.0318	1.25(1.01-1.54)	0.0396
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.18(0.73-1.89)	0.5041	1.29(0.80-2.10)	0.2966	1.30(0.80-2.11)	0.2889
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.37(1.01-1.87)	0.0453	1.42(1.04-1.93)	0.0286	1.39(1.02-1.90)	0.0367
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	2.15(1.62-2.85)	<.0001	1.93(1.43-2.59)	<.0001	1.90(1.41-2.55)	<.0001
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.50(1.22-1.85)	0.0002	1.40(1.13-1.73)	0.0019	1.38(1.12-1.71)	0.0027

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and ADL (partial dependence, dependence)

## **C. Cause-specific mortality and ADL disability**

### **1. Cause-specific mortality with ADL disability**

Concerning ADL levels, mortality risks due to all-cause, vascular diseases, and senility were significantly associated with ADL dependency in Table 7. In contrast, no association was found between cancer mortality and ADL disability.



Table 7. Hazard ratios (95% CI) for cause-specific mortality with ADL disability levels

ADL levels	No. of deaths	total	PY	Model 1		Model 2		Model 3	
				HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
All-cause mortality	<b>1,481</b>	<b>2,501</b>	<b>21,346</b>						
Independence	960	1,737	5,191	1.00		1.00		1.00	
Partial dependence	271	432	6,417	1.17(1.02-1.34)	0.0224	1.12(0.98-1.29)	0.1043	1.14(0.99-1.31)	0.0686
Dependence	250	332	9,738	1.69(1.46-1.94)	<.0001	1.48(1.28-1.71)	<.0001	1.45(1.25-1.68)	<.0001
Vascular diseases mortality	<b>345</b>	<b>2,501</b>	<b>5,354</b>						
Independence	218	1,737	1,179	1.00		1.00		1.00	
Partial dependence	52	432	1,227	1.01(0.75-1.38)	0.9285	0.88(0.65-1.20)	0.4330	0.89(0.66-1.22)	0.4737
Dependence	75	332	2,949	2.36(1.80-3.09)	<.0001	1.90(1.44-2.52)	<0.0001	1.91(1.44-2.53)	<0.0001
Senile mortality	<b>428</b>	<b>2,501</b>	<b>7,625</b>						
Independence	257	1,737	1,498	1.00		1.00		1.00	
Partial dependence	81	432	2,170	1.06(0.82-1.37)	0.6587	1.06(0.82-1.37)	0.6597	1.08(0.84-1.40)	0.5392
Dependence	90	332	3,957	1.66(1.30-2.13)	<.0001	1.52(1.18-1.95)	0.0013	1.45(1.12-1.86)	0.0046
Cancer mortality	<b>232</b>	<b>2,501</b>	<b>2,486</b>						
Independence	181	1,737	979	1.00		1.00		1.00	
Partial dependence	31	432	731	0.89(0.61-1.31)	0.5576	0.87(0.59-1.28)	0.4768	0.87(0.59-1.29)	0.4872
Dependence	20	332	776	1.02(0.64-1.63)	0.9280	1.03(0.64-1.67)	0.8983	1.03(0.64-1.67)	0.9069

HR (95% CI), Hazard Ratios 95% confidence intervals;

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and cognitive impairment (mild, moderate, severe)

## 2. Distribution of task-specific ADL

Table 8 described the prevalence of task-specific ADL by cognitive impairment status. Prevalence of most tasks increased across growing severity in cognitive impairment. 'Bathing' task marked higher in prevalence at severe status than other tasks.



Table 8. Distribution of task-specific ADL at baseline by cognitive impairment status in Kangwha Cohort Study

Domain-specific ADL	Cognitive impairment status					p-value
	Total (N=2,501)	No (n=1,224)	Mild (n=686)	Moderate (n=441)	Severe (n=150)	
Bathing						<0.0001
Independence	2,131(85.2)	1,115(91.1)	577(84.1)	336(76.2)	103(68.7)	
Dependence	370(14.8)	109( 8.9)	109(15.9)	105(23.8)	47(31.3)	
Dressing						<0.0001
Independence	2,279(91.1)	1,163(95.0)	624(91.0)	376(85.3)	116(77.3)	
Dependence	222( 8.9)	61( 5.0)	62( 9.0)	65(14.7)	34(22.7)	
Toileting						<0.0001
Independence	2,327(93.0)	1,178(96.2)	641(93.4)	388(88.0)	121(80.0)	
Dependence	174( 7.0)	46( 3.8)	45( 6.6)	53(12.0)	31(20.4)	
Moving in Bed						0.0007
Independence	1,955(78.2)	999(81.6)	515(75.1)	327(74.2)	115(76.0)	
Dependence	546(21.8)	225(18.4)	171(24.9)	114(25.8)	37(24.0)	
Moving around the house						<0.0001
Independence	1,909(76.3)	983(80.3)	504(73.5)	315(71.4)	108(71.3)	
Dependence	592(23.7)	241(19.7)	182(26.5)	126(28.6)	45(28.7)	
Eating						<0.0001
Independence	2,413(96.5)	1,202(98.2)	664(96.8)	413(93.6)	135(89.3)	
Dependence	88( 3.5)	22( 1.8)	22( 3.2)	28( 6.4)	17(10.7)	
Continence						<0.0001
Independence	2,409(96.3)	1,205(98.4)	666(97.1)	409(92.7)	130(86.0)	
Dependence	92( 3.7)	19( 1.6)	20( 2.9)	32( 7.3)	22(14.5)	

Values denote numbers with percentages (%) in parentheses; ADL, Activity of Daily Living;

### 3. Cause-specific mortality with task-specific ADL

Table 9 showed that mortality due to all-cause risk was associated in robust relationship with full task-specific ADL in all Models. 'Eating' task (HR=2.16 in Model 1; HR=1.78 in Model 2; HR=1.68 in Model 3) had higher hazard ratio than any others.

The task-specific ADL for mortality due to vascular disease was found to be strongly associated with Model 1, 2 and 3, except 'moving in bed' task in Model 2 and Model 3. 'Eating' task (HR=3.57 in Model 1; HR=2.76 in Model 2; HR=2.67 in Model 3) marked the highest hazard ratio among other tasks whereas 'moving in bed' was not significant in Model 2 and 3 (Table 10).

Table 11 designated that HR for the mortality due to senile was significantly associated with three tasks ('bathing', 'dressing', and 'eating'), otherwise, 'toileting' task was significantly associated in Model 1 and 2, however 'toileting' task was not in Model 3. 'Moving in bed' and 'continence' were not related with senile mortality.

No relationship was found between Cancer mortality and task-specific ADL (Appendix table 5).



Table 9. Hazard ratios (95% CI) for All-cause mortality with task-specific ADL

Task-specific ADL		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>All-cause mortality (n=1,481)</b>							
Bathing	Independence	1.00		1.00		1.00	
	Dependence	1.76(1.54-2.01)	<.0001	1.55(1.35-1.77)	<.0001	1.50(1.31-1.73)	<.0001
Dressing	Independence	1.00		1.00			
	Dependence	1.83(1.55-2.14)	<.0001	1.59(1.35-1.87)	<.0001	1.55(1.31-1.82)	<.0001
Toileting	Independence	1.00		1.00			
	Dependence	1.68(1.41-2.01)	<.0001	1.54(1.29-1.84)	<.0001	1.47(1.22-1.76)	<.0001
Moving in Bed	Independence	1.00		1.00			
	Dependence	1.27(1.13-1.44)	<.0001	1.19(1.05-1.34)	0.0065	1.21(1.07-1.37)	0.0022
Moving around the house	Independence	1.00		1.00			
	Dependence	1.30(1.16-1.46)	<.0001	1.21(1.07-1.36)	0.0019	1.22(1.09-1.38)	0.0010
Eating	Independence	1.00		1.00			
	Dependence	2.13(1.68-2.69)	<.0001	1.78(1.40-2.26)	<.0001	1.68(1.32-2.14)	<.0001
Continence	Independence	1.00		1.00			
	Dependence	1.58(1.23-2.02)	0.0003	1.41(1.10-1.81)	0.0066	1.33(1.04-1.71)	0.0239

HR (95% CI), Hazard Ratios 95% confidence intervals;

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and cognitive impairment (mild, moderate, severe)

Table 10. Hazard ratios (95% CI) for Vascular disease mortality with task-specific ADL

Task-specific ADL		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Vascular disease mortality (n=345)</b>							
Bathing	Independence	1.00		1.00		1.00	
	Dependence	2.46(1.91-3.18)	<.0001	2.01(1.55-2.61)	<.0001	1.96(1.51-2.56)	<.0001
Dressing	Independence			1.00		1.00	
	Dependence	2.81(2.09-3.76)	<.0001	2.31(1.71-3.13)	<.0001	2.28(1.68-3.10)	<.0001
Toileting	Independence			1.00		1.00	
	Dependence	2.65(1.92-3.65)	<.0001	2.31(1.66-3.20)	<.0001	2.25(1.61-3.14)	<.0001
Moving in Bed	Independence			1.00		1.00	
	Dependence	1.37(1.07-1.75)	0.0123	1.16(0.90-1.50)	0.2420	1.20(0.93-1.55)	0.1563
Moving around the house	Independence			1.00		1.00	
	Dependence	1.50(1.18-1.89)	0.0008	1.30(1.02-1.66)	0.0324	1.33(1.05-1.70)	0.0207
Eating	Independence			1.00		1.00	
	Dependence	3.57(2.38-5.35)	<.0001	2.76(1.82-4.19)	<.0001	2.67(1.75-4.06)	<.0001
Continence	Independence			1.00		1.00	
	Dependence	2.07(1.31-3.27)	0.0018	1.69(1.07-2.69)	0.0253	1.62(1.01-2.58)	0.0434

HR (95% CI), Hazard Ratios 95% confidence intervals;

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and cognitive impairment (mild, moderate, severe)

Table 11. Hazard ratios (95% CI) for Senile mortality with task-specific ADL

Task-specific ADL		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Senile mortality (n=428)</b>							
Bathing	Independence	1.00		1.00		1.00	
	Dependence	1.73(1.37-2.18)	<.0001	1.58(1.25-2.00)	0.0001	1.51(1.19-1.91)	0.0007
Dressing	Independence	1.00		1.00		1.00	
	Dependence	1.72(1.31-2.27)	<.0001	1.58(1.19-2.09)	0.0013	1.49(1.13-1.97)	0.0052
Toileting	Independence	1.00		1.00		1.00	
	Dependence	1.39(1.02-1.90)	0.0358	1.37(1.00-1.88)	0.0498	1.23(0.90-1.70)	0.1942
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	1.19(0.96-1.48)	0.1085	1.16(0.93-1.45)	0.1962	1.20(0.96-1.51)	0.1044
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	1.27(1.03-1.56)	0.0278	1.22(0.98-1.51)	0.0718	1.24(1.00-1.53)	0.0523
Eating	Independence	1.00		1.00		1.00	
	Dependence	2.22(1.50-3.29)	<.0001	1.90(1.27-2.85)	0.0019	1.71(1.14-2.57)	0.0102
Continence	Independence	1.00		1.00		1.00	
	Dependence	1.46(0.97-2.20)	0.0722	1.38(0.91-2.09)	0.1297	1.24(0.81-1.88)	0.3230

HR (95% CI), Hazard Ratios 95% confidence intervals;

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and cognitive impairment (mild, moderate, severe)

## **D. Association of cause-specific mortality by cognitive impairment and ADL disability level**

### **1. ADL disability level for cause-specific mortality by cognitive impairment status**

Table 12 showed the adjusted Hazard Ratios (aHR) for cause-specific mortality by cognitive impairment status and ADL levels. The aHR for mortality due to all-cause, vascular disease, and senile significantly increased along with moderate to severe cognitive impairment. Mortality due to all-cause presented association even in partial dependency and dependency in ADL. No significant difference was observed in cancer mortality.

In moderate cognitive impairment, all-cause mortality risk increased with partial dependency (HR=1.44) and dependency (HR=1.98), and severe cognitive impairment risk increased with partial dependency (HR=2.37) and dependency (HR=2.08).

In moderate cognitive impairment, vascular disease mortality risk increased with dependency (HR=2.16), and severe cognitive impairment risk increased with partial dependency (HR=3.70 in borderline  $p=0.0581$ ) and dependency in ADL (HR=4.53).

In moderate cognitive impairment, senile mortality risk increased with dependency in ADL (HR=1.98), and severe cognitive impairment risk increased with partial dependency in ADL (HR=3.78). No significant difference was observed in cancer mortality.

Table 12. ADL levels for Cause-specific mortality by cognitive impairment status

ADL levels		Cognitive impairment					
		No or Mild* (n=686)		Moderate* (n=441)		Severe* (n=150)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
All-cause mortality	(event)	404		295		119	
	Independence	1.00		1.00		1.00	
	Partial dependence	1.08(0.83-1.40)	0.5856	1.44(1.05-1.97)	0.0246	2.37(1.32-4.25)	0.0040
	Dependence	1.17(0.89-1.54)	0.2604	1.98(1.47-2.65)	<.0001	2.08(1.26-3.45)	0.0043
Vascular disease mortality	(event)	82		72		26	
	Independence	1.00		1.00		1.00	
	Partial dependence	0.71(0.36-1.37)	0.3040	1.32(0.70-2.51)	0.3897	3.70(0.96-14.33)	0.0581
	Dependence	1.43(0.82-2.47)	0.2062	2.16(1.20-3.89)	0.0104	4.53(1.48-13.85)	0.0081
Senile mortality	(event)	129		117		50	
	Independence	1.00		1.00		1.00	
	Partial dependence	0.87(0.54-1.40)	0.5653	1.46(0.88-2.43)	0.1467	3.78(1.53-9.36)	0.0041
	Dependence	1.26(0.79-2.01)	0.3236	1.98(1.23-3.18)	0.0051	2.21(0.96-5.08)	0.0629
Cancer mortality	(event)	56		29		9	
	Independence	1.00		1.00		1.00	
	Partial dependence	1.13(0.56-2.25)	0.7379	0.24(0.03-1.81)	0.1664	-	-
	Dependence	0.99(0.40-2.45)	0.9869	1.25(0.44-3.51)	0.6780	5.22(0.20-135.95)	0.3208

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals;

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

## **2. Task-specific ADL for cause-specific mortality by cognitive impairment status**

Adjusted Hazard Ratios for mortality due to all-cause demonstrated that 'bathing' task was increased significantly across growing severity of cognitive impairment. Except 'bathing', other tasks were increased in moderate to severe cognitive function status (Table 13).

Adjusted Hazard Ratios for mortality due to vascular disease revealed that 'bathing', 'dressing' and 'toileting' were significantly increased in a robust dose-response relationship to the cognitive impairment status. On the other hand 'moving in bed', and 'moving around the house' were related to severe cognitive impairment status (Table 14).

Adjusted Hazard Ratios for mortality due to senile presented significant relationship between task-specific ADLs and moderate cognitive impairment status, while 'toileting', 'moving in bed', 'moving around the house', and 'continence' tasks were increased in a robust dose-response relationship (Table 15).

In the cancer mortality, only 'toileting' task was higher in risk (HR=3.02, 1.03-8.84) by the moderate cognitive impairment status (Appendix table 11).

Table 13. Task-specific ADL for all-cause mortality by cognitive impairment status

Task-specific ADL	ADL status	Cognitive impairment					
		No or Mild* (N=686)		Moderate* (N=441)		Severe* (N=150)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>All-cause mortality</b>	<b>event</b>	404		295		119	
Bathing	Independence	1.00		1.00		1.00	
	Dependence	1.53(1.19-1.99)	0.0012	1.71(1.31-2.24)	<.0001	1.58(1.01-2.48)	0.0476
Dressing	Independence	1.00		1.00		1.00	
	Dependence	1.23(0.88-1.71)	0.2230	2.14(1.57-2.93)	<.0001	1.63(1.01-2.62)	0.0451
Toileting	Independence	1.00		1.00		1.00	
	Dependence	0.99(0.68-1.45)	0.9616	1.87(1.33-2.63)	0.0003	1.57(0.97-2.56)	0.0688
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	1.00(0.80-1.26)	0.9937	1.66(1.27-2.17)	0.0002	2.49(1.57-3.95)	0.0001
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	1.07(0.86-1.33)	0.5639	1.70(1.31-2.20)	<.0001	2.07(1.32-3.25)	0.0016
Eating	Independence	1.00		1.00		1.00	
	Dependence	0.97(0.57-1.65)	0.9066	2.26(1.46--3.48)	0.0002	1.29(0.70-2.39)	0.4191
Continence	Independence	1.00		1.00		1.00	
	Dependence	0.53(0.27-1.05)	0.0701	2.29(1.53-3.43)	<.0001	1.77(1.01-3.13)	0.0481

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Table 14. Task-specific ADL for vascular disease mortality by cognitive impairment status

Task-specific ADL	ADL levels	Cognitive impairment					
		No or Mild*		Moderate*		Severe*	
		(N=686)		(N=441)		(N=150)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>Vascular disease mortality</b>	<b>event</b>	82		72		26	
Bathing	Independence	1.00		1.00		1.00	
	Dependence	1.86(1.10-3.16)	0.0215	2.15(1.27-3.64)	0.0043	2.76(1.05-7.26)	0.0390
Dressing	Independence	1.00		1.00		1.00	
	Dependence	1.73(0.92-3.25)	0.0904	2.59(1.41-4.77)	0.0022	3.81(1.44-10.04)	0.0069
Toileting	Independence	1.00		1.00		1.00	
	Dependence	1.34(0.62-2.88)	0.4577	2.34(1.20-4.55)	0.0124	2.90(1.09-7.72)	0.0335
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	0.84(0.50-1.40)	0.5015	1.48(0.86-2.55)	0.1547	4.83(1.73-13.51)	0.0027
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	1.10(0.68-1.79)	0.6936	1.59(0.95-2.67)	0.0799	3.85(1.36-10.90)	0.0111
Eating	Independence	1.00		1.00		1.00	
	Dependence	2.31(0.99-5.39)	0.0530	2.17(0.90-5.28)	0.0861	1.67(0.51-5.49)	0.4017
Continence	Independence	1.00		1.00		1.00	
	Dependence	0.86(0.26-2.85)	0.7997	2.15(0.94-4.92)	0.0700	2.60(0.94-7.20)	0.0651

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension



Table 15. Task-specific ADL for senile mortality by cognitive impairment status

Task-specific ADL	ADL levels	Cognitive impairment					
		No or Mild* (N=686)		Moderate* (N=441)		Severe* (N=150)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>Senile mortality</b>	event	129		117		50	
Bathing	Independence	1.00		1.00		1.00	
	Dependence	1.72(1.11-2.67)	0.0158	1.75(1.14-2.68)	0.0112	1.26(0.61-2.60)	0.5284
Dressing	Independence	1.00		1.00		1.00	
	Dependence	1.47(0.85-2.56)	0.1692	1.78(1.06-2.99)	0.0302	1.23(0.55-2.73)	0.6144
Toileting	Independence	1.00		1.00		1.00	
	Dependence	1.22(0.66-2.23)	0.5291	1.57(0.89-2.76)	0.1193	0.97(0.41-2.28)	0.9352
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	0.89(0.60-1.33)	0.5641	1.82(1.19-2.80)	0.0063	2.54(1.24-5.18)	0.0108
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	0.97(0.66-1.43)	0.8730	1.70(1.11-2.60)	0.0141	2.20(1.11-4.36)	0.0235
Eating	Independence	1.00		1.00		1.00	
	Dependence	0.61(0.20-1.85)	0.3770	2.45(1.24-4.86)	0.0104	1.64(0.65-4.10)	0.2944
Continence	Independence	1.00		1.00		1.00	
	Dependence	0.33(0.08-1.41)	0.1348	2.08(1.09-3.97)	0.0265	2.85(1.18-6.89)	0.0203

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

## **E. Combined effect of cognitive impairment and ADL disability**

### **1. Combined effects for cause-specific mortality**

The combined bar chart, Figure 2 (all-cause mortality), Figure 3 (vascular disease mortality), and Figure 4 (senile mortality) demonstrated the relationship between ADL disability level and cognitive impairment status after the adjustment of all the controlling confounders; age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4;  $\geq 27.5$ ), self-rated health, and hypertension. In place of separate analyses of cognitive impairment or ADL disability with mortality, hazard ratio was higher when cognitive impairment and ADL disability were combined. Both moderate and severe in cognitive impairment and dependence in ADL were associated with higher mortality.

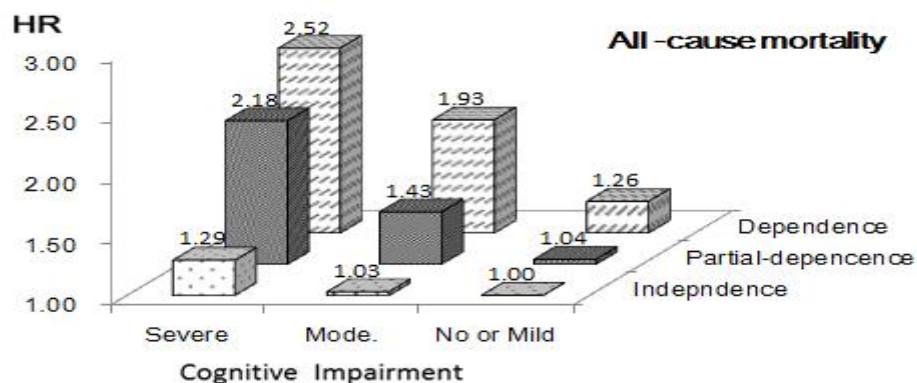


Figure 2. Combined effect of cognitive impairment status and ADL level for All-cause mortality.

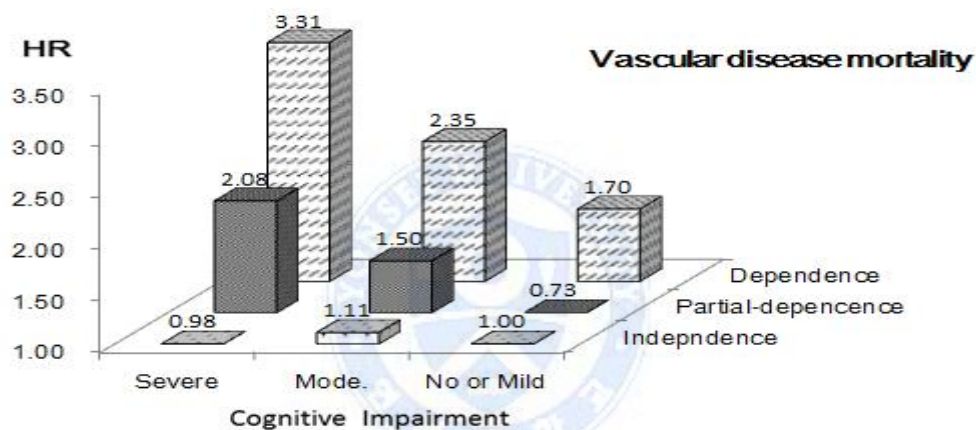


Figure 3. Combined effect of cognitive impairment status and ADL level for Vascular disease mortality.

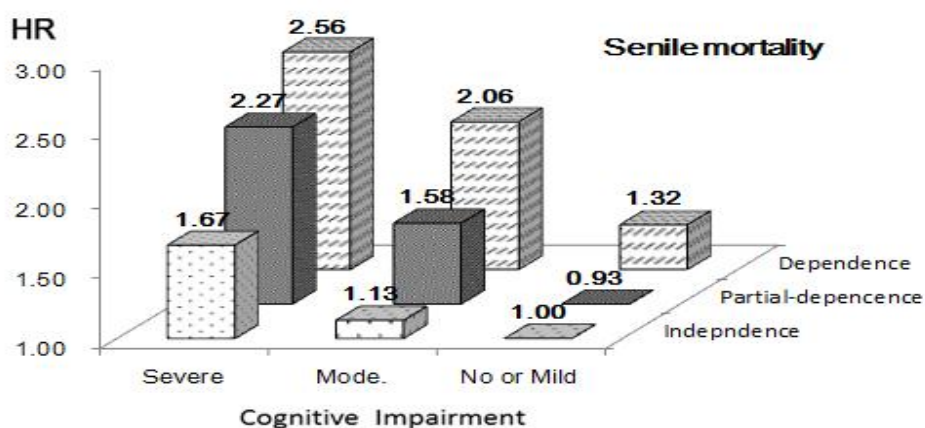


Figure 4. Combined effect of cognitive impairment status and ADL level for Senile mortality.

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

## 2. Calculating measures of biological interaction

We calculated the relative excess risk due to biological interaction by computerizing on the excel sheet after obtaining the adequate estimates from SAS program. The Relative Excess Risk due to biological Interaction (RERI) of vascular disease mortality was increased when cognitive impairment and ADL disability were combined. The effects indicated all-cause (HR=0.96, p=0.0031), vascular disease (HR=1.63, p=0.0545), and senility (HR=0.57, p=0.2703) in Figure 2, 3, and 4 adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; and  $\geq 27.5$ ), self-rated health, and hypertension.

The formula as below;

$$RERI = RR_{11} - RR_{10} - RR_{01} + 1 \quad (\text{Andersson et al., 2005})$$

Synergy Index (S) due to biological interaction of all-cause, vascular disease, senile mortality was increased when cognitive impairment and ADL disability were combined. The effects indicated all-cause (HR=2.72), vascular disease (HR=3.40), and senility (HR=1.58) in Figure 2, 3, and 4.

The formula as below;

$$S = \frac{(R_{11} - 1)}{(R_{10} - 1) + (R_{01} - 1)} \quad (\text{Andersson et al., 2005})$$

### 3. Biological interaction for cause-specific mortality

The following figures showed the interaction of cognitive impairment and ADL for each ADL task (7 ADL tasks). ADL was divided by bivariables (independence, dependence). Cognitive impairment status was divided by three groups within of MMSE-K score (no, or mild = more higher than 19, moderate = 14-18, severe = less than 13) adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; and  $\geq 27.5$ ), self-rated health, and hypertension.

Most of figures were observed as a higher positive interaction between cognitive impairment and ADL disability. Figure 5-1 and Figure 5-2 showed mortality due to all-cause; Figure 6-1 and Figure 6-2 showed mortality due to vascular disease; Figure 7-1 and Figure 7-2 showed mortality due to senile. Bar chart for cause-specific mortality presented different patterns. Cognitive function and ADL disability affected the mortality of the older adults.

a. All-cause mortality

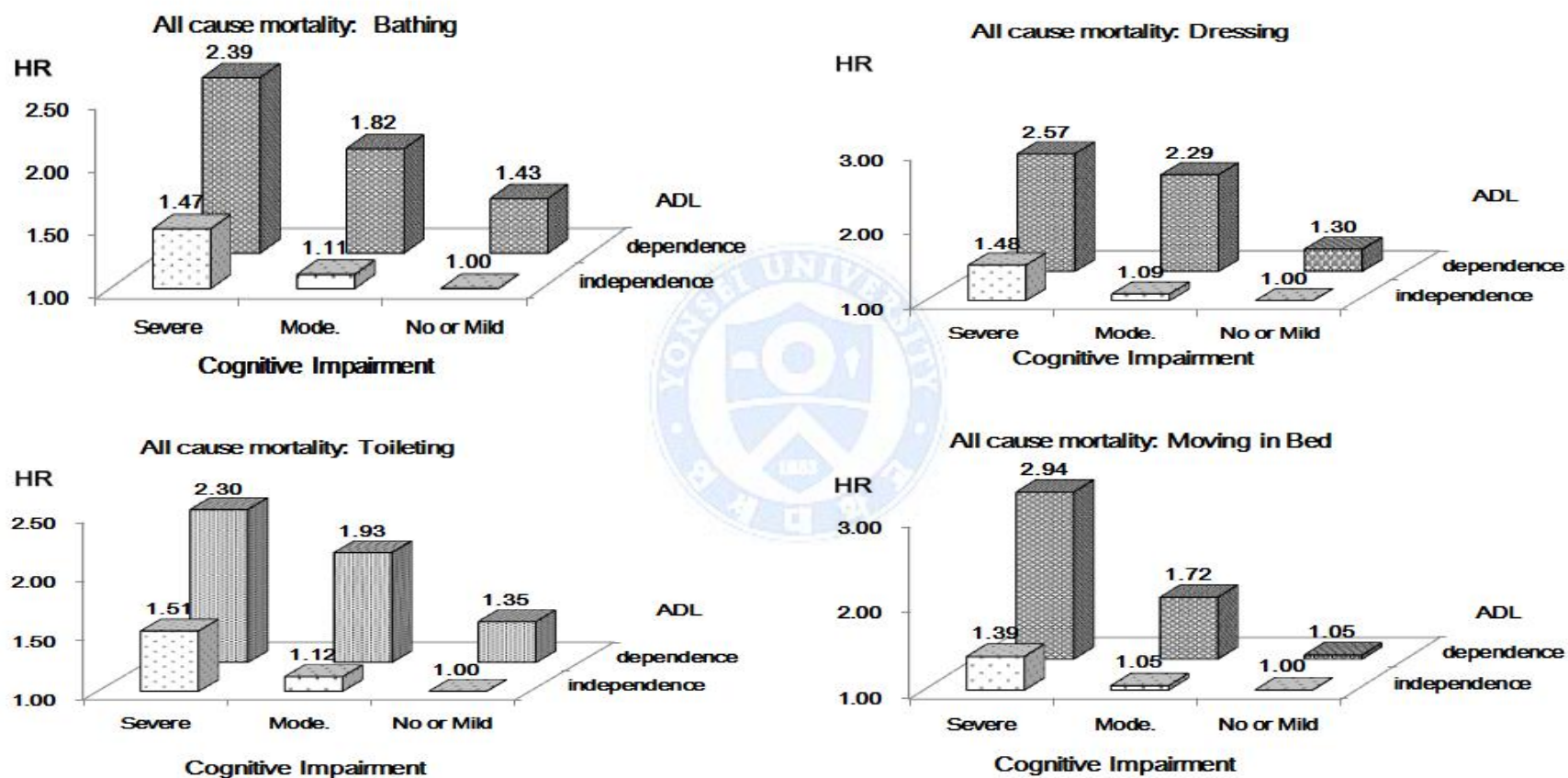


Figure 5-1. Combined effect of cognitive impairment status and ADL level for All-cause mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension



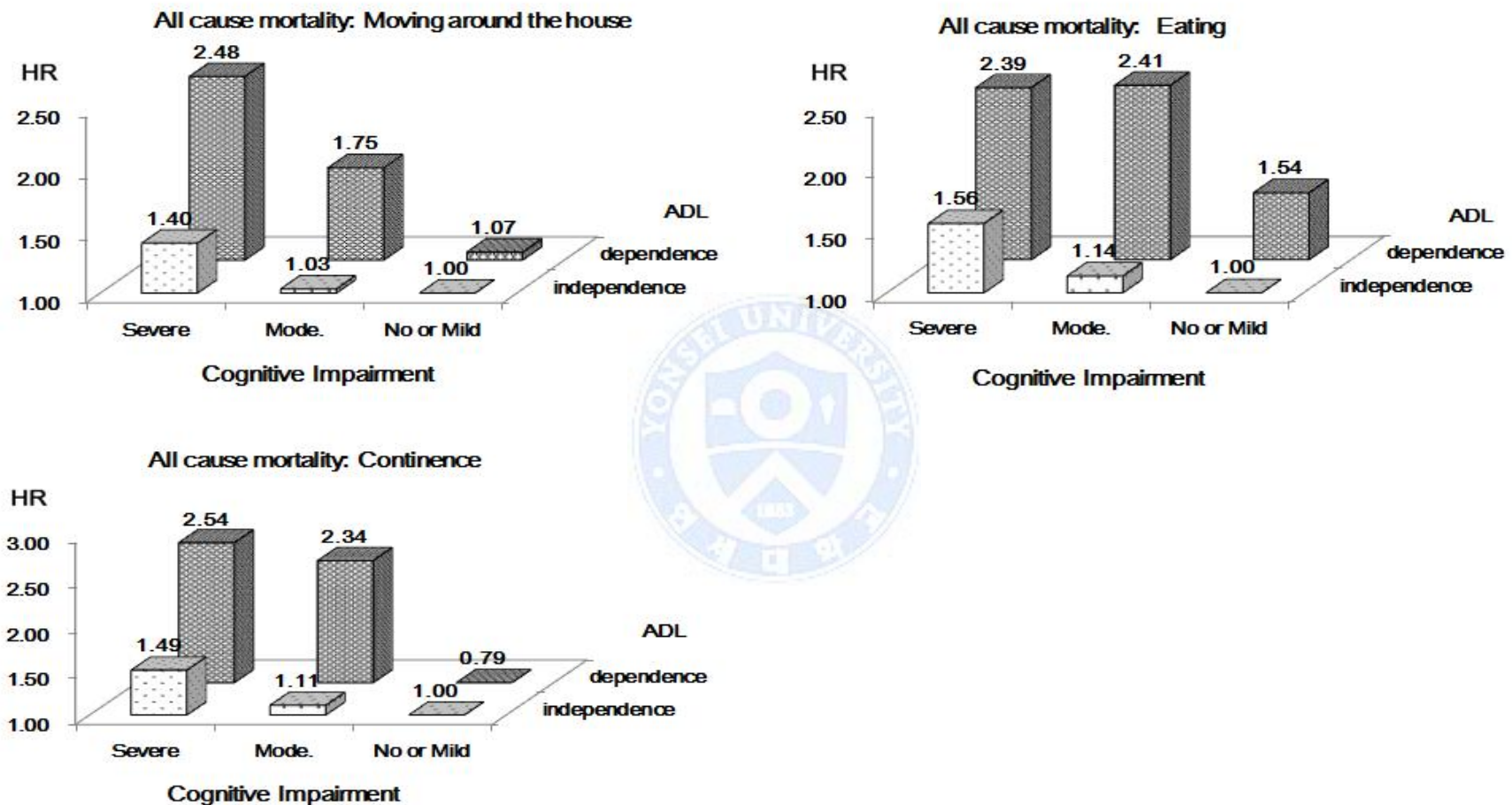


Figure 5-2. Combined effect of cognitive impairment status and ADL level for All-cause mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

## b. Vascular disease mortality

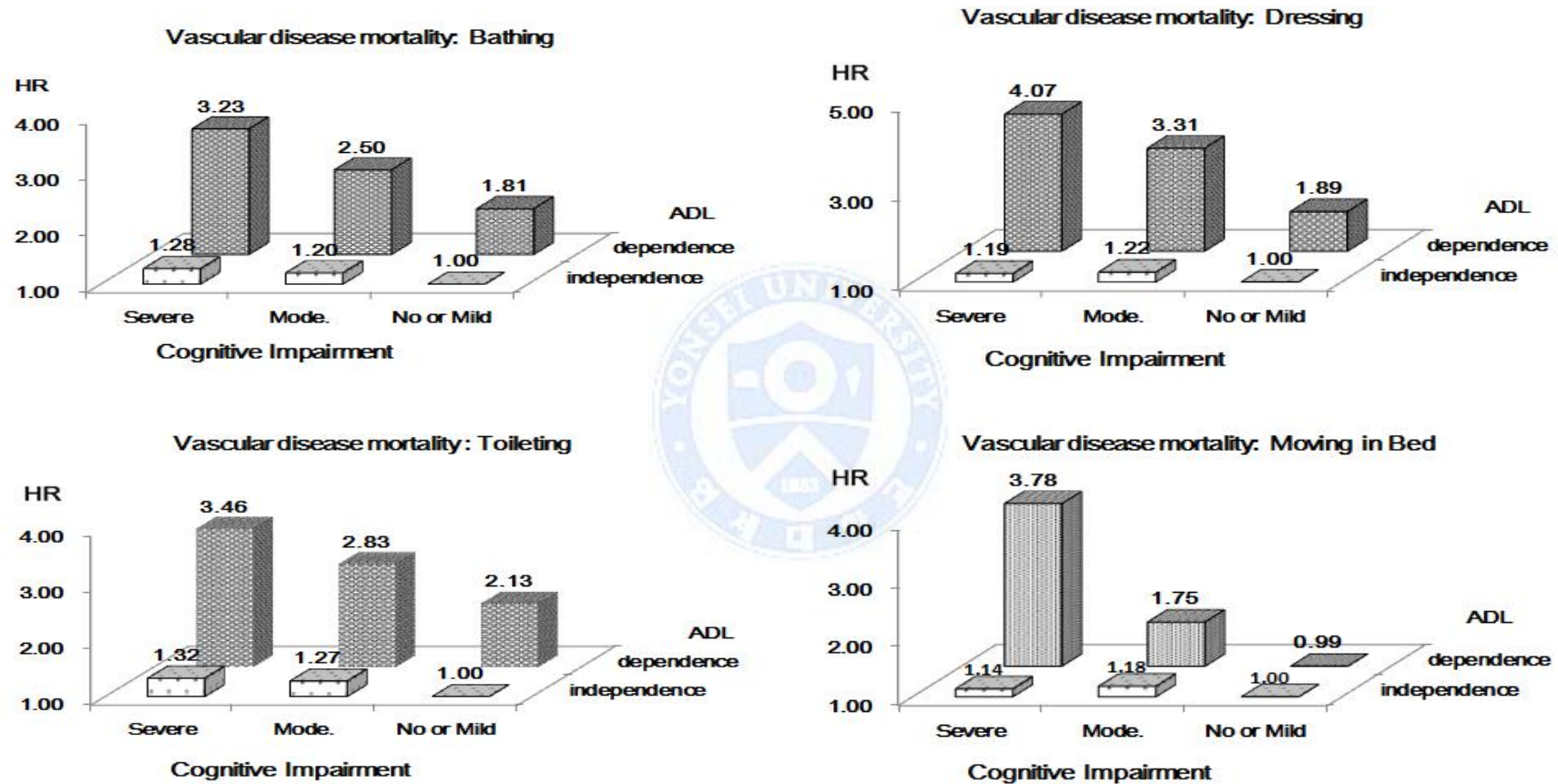


Figure 6-1. Combined effect of cognitive impairment status and ADL level for Vascular disease mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension



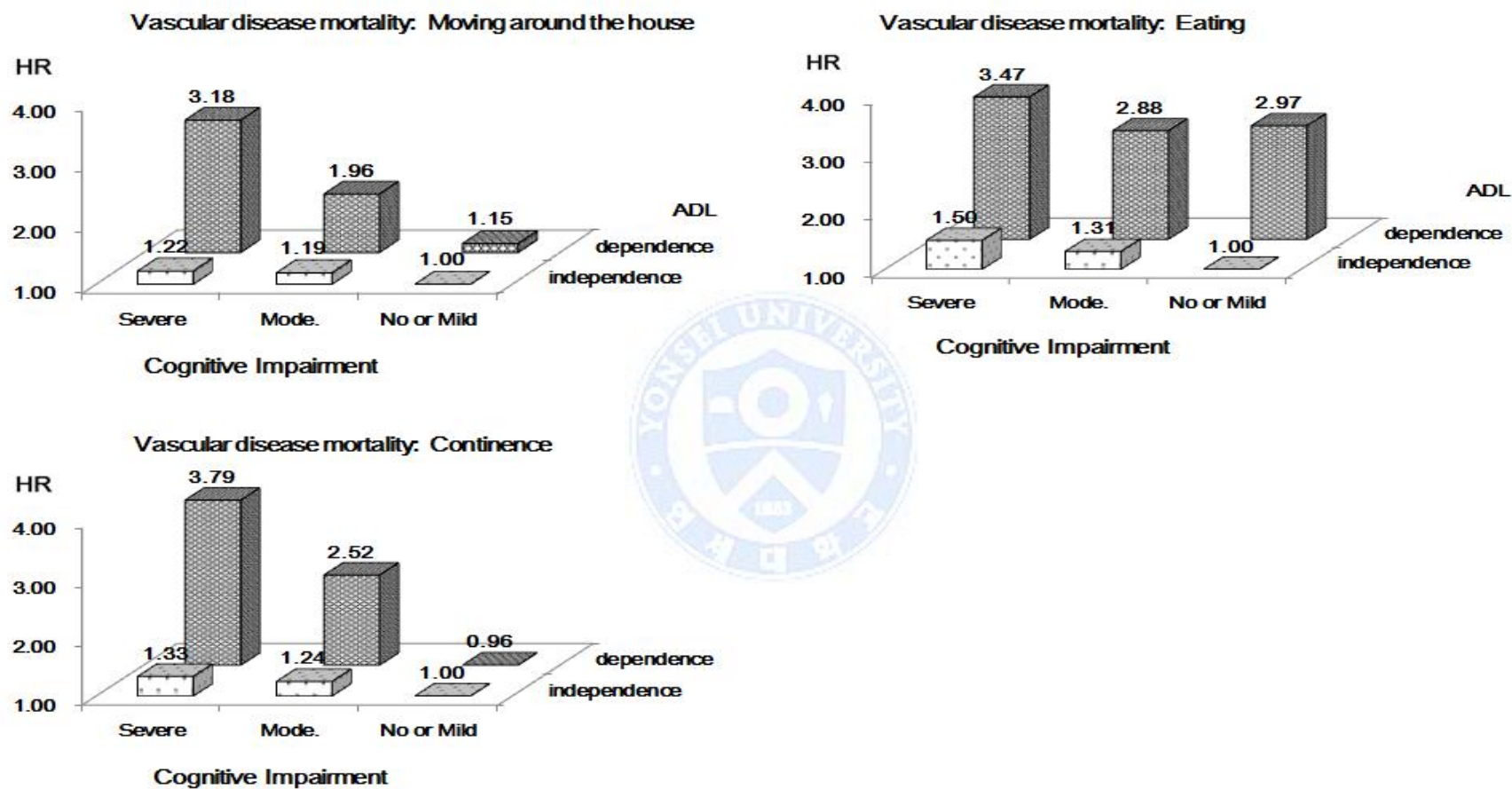


Figure 6-2. Combined effect of cognitive impairment status and ADL level for Vascular disease mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

### c. Senile mortality

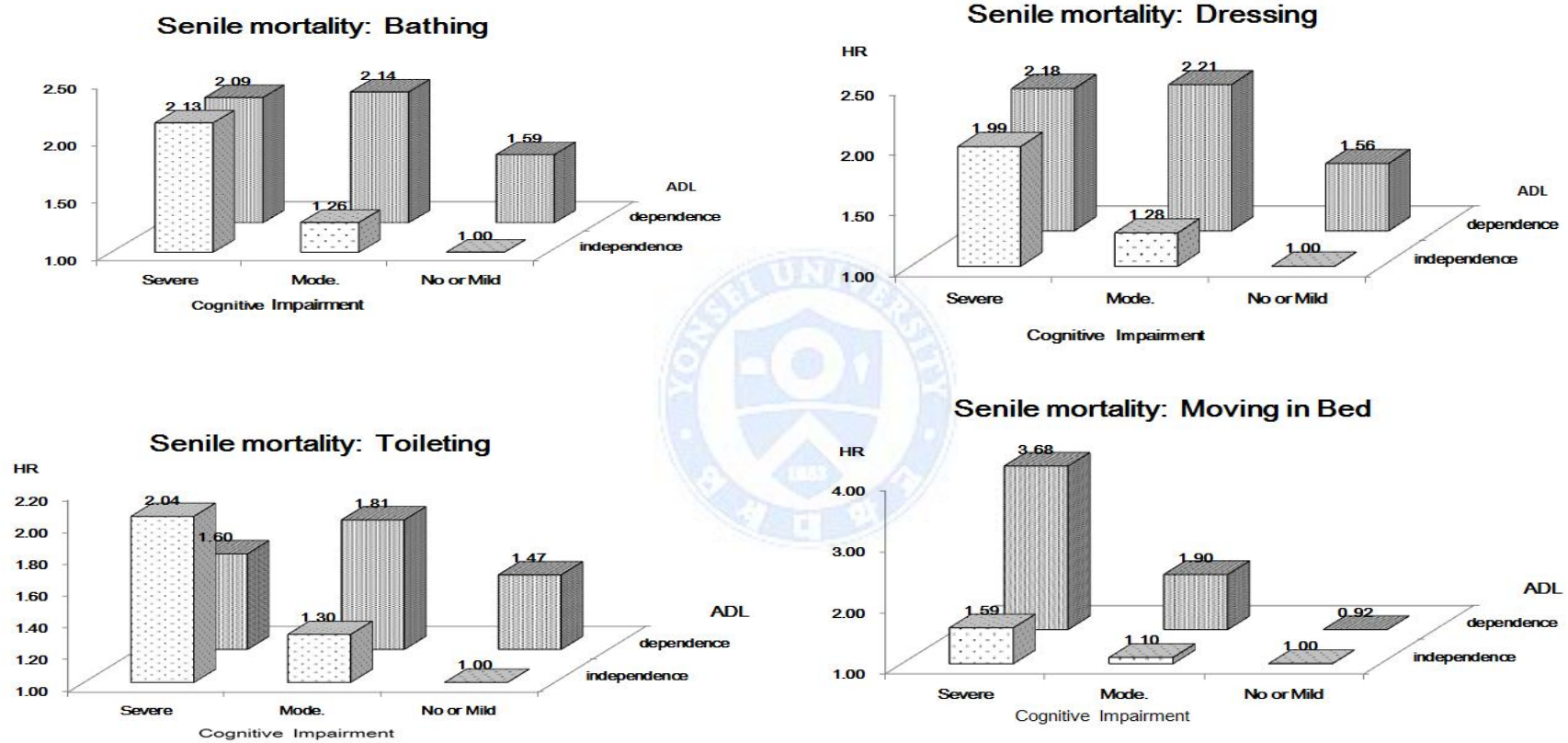


Figure 7-1. Combined effect of cognitive impairment status and ADL level for Senile mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

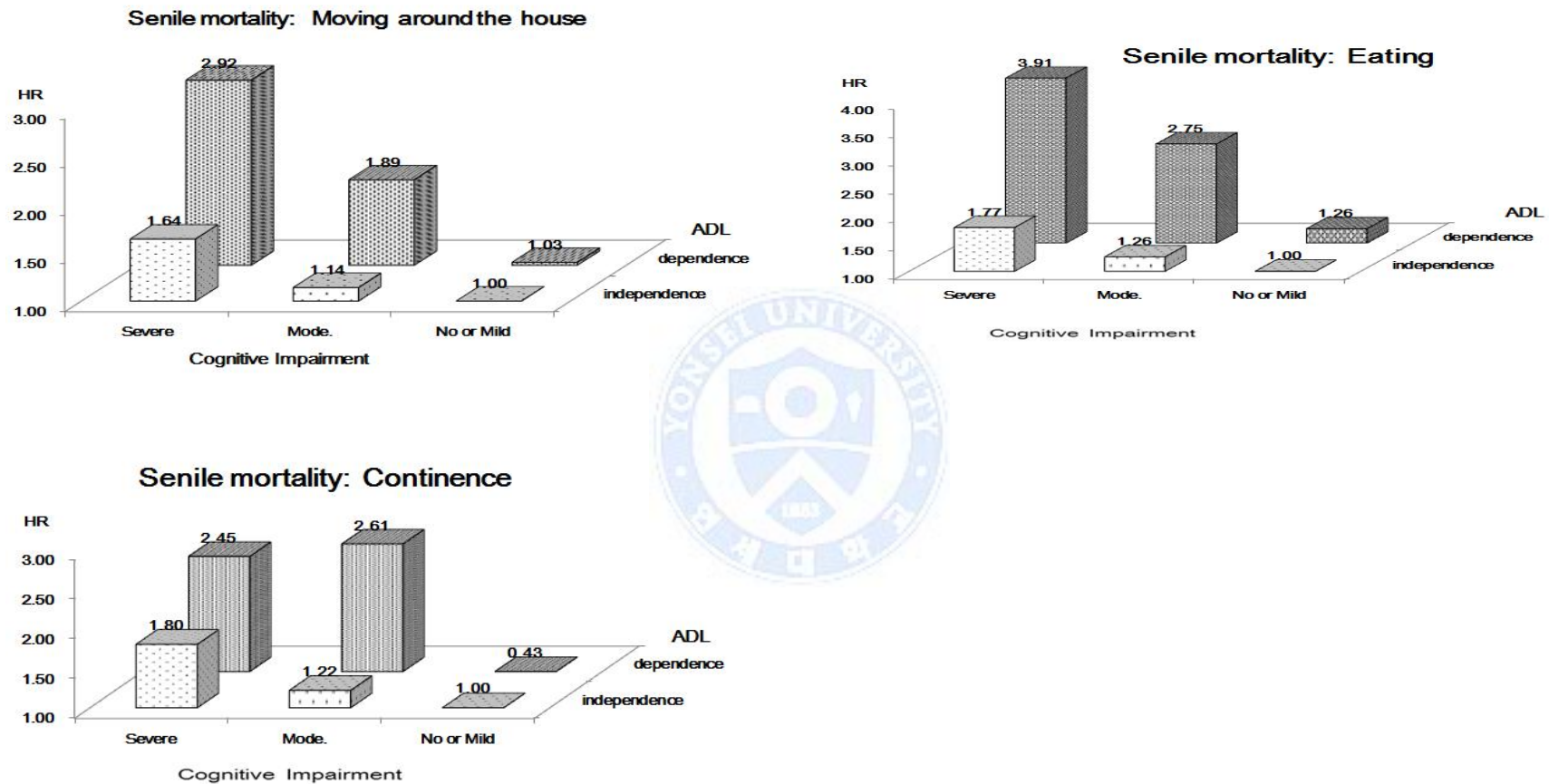


Figure 7-2. Combined effect of cognitive impairment status and ADL level for Senile mortality.

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

## V. DISCUSSION

In this study, we examined that cognitive impairment was significantly associated with increased mortality due to all-cause, vascular disease, and senility adjusted with confounding variables (age, gender, education, occupation, marriage, smoking status, drinking status, BMI categories, self-rated health, hypertension). And mild cognitive impairment (MCI) was associated with mortality due to all-cause and senility compared to no cognitive impairment. Some of domain-specific cognitive impairments were associated with increased mortality due to all-cause, vascular disease, and senility. Activities of daily living (ADL) were strongly related with increased mortality due to all-cause, vascular disease, and senility compared to ADL independency. Task-specific ADL had a striking effect on mortality due to all-cause, vascular, and senility. However, mortality due to cancer did not increase for cognitive domains and ADL tasks. Stratification by cognitive impairment gave a trend toward higher HR for mortality due to all-cause, vascular disease, and senility. Domain-specific cognitive function and task-specific ADL showed different results for cause-specific mortality.

Our findings are similar to the results of previous studies indicating an association between cognitive impairment and mortality due to all-cause (Schupf et al., 2005; Santabábara et al., 2014), vascular disease (Suh et al., 2005; Suh, 2006; Clarke et al., 2011; O'Donnell et al., 2012), and senility (NHS, 2010). However, no association is found between cognitive impairment and cancer mortality (Anstey et al., 2006). Cognitive impairment has shown remarkable effects on cause-specific mortality. In the meta-analysis after controlling the socio-demographic characteristics, comorbidity, and functional limitations, moderate and severe cognitive

impairment have known to be associated with higher mortality (Guehne et al., 2007).

Compared to ADL independency, ADL is closely related with increased mortality due to all-cause (Stineman et al., 2012), vascular disease (Suh 2006) and senility (Solfrizzi et al., 2012). However, no statistically significant difference is found between cancer mortality and ADL disability (Raji et al., 2004).

Combined effect measured by ADL disability and cognitive impairment showed higher risks for coexisting variables than for either cognitive impairment or ADL disability. We calculated the relative excess risk due to interaction by computerizing the account. When cognitive impairment and ADL disability were combined, the vascular disease mortality was increased with the relative excess risk due to interaction (RERI). The mortality due to all-cause, vascular disease, and senility was increased by the Synergy Index due to Interaction.

Our study suggests that older adults with coexisting ADL and cognitive impairment are more likely to have shorter lifespan than those without coexisting impairment.

### **All-cause mortality**

We reported the association between cognitive impairment and mortality due to all-cause showed in our study. The mortality risk increased equivalently to the status (HR=1.21, 1.04-1.40 in moderate; HR=1.61, 1.31-1.98 in severe) with potential confounding variables in our study. And there was a dose-response relationship between cognitive impairment and all-cause mortality. From a 17-year follow-up in a

community based Spanish study, cognitive impairment is associated with mortality due to all-cause adjusted for sociodemographical variables and medical variables (HR=1.29, 1.03-1.61 in moderate; HR=2.08, 1.42-3.04 in severe). The EPIC-Greece cohort study evaluated an increased risk that appears in all-cause mortality (MMSE score 10-20) (Katsoulis et al., 2014). Ramos et al. indicated that a MMSE score of  $\leq 18$  has mortality risk almost two times higher than those with a higher MMSE score (Ramos et al., 2001). In addition, other studies reported similarity to our results for the associations between cognitive impairment and mortality due to all-cause (Schupf et al., 2005; Santabárbara et al., 2014).

After controlling for covariates, some of domain-specific cognitive impairments were associated with increased mortality due to all-cause in this study. Especially 'orientation to time', 'orientation to place', 'recall', 'three-stage command', 'copying', 'comprehension', 'registration', and 'attention and calculation' domains were associated with increased risk in all-cause mortality. Like this study, Park et al. reported 'orientation to time' and 'attention and calculation' domains are independently associated with increased risk of mortality (Park et al., 2012). Iwasa et al. reported that mortality due to all-cause increases with cognitive impairment adjusted for 'orientation to time', 'orientation to place', 'attention and calculation', and 'recall' are significantly associated with mortality (Iwasa et al., 2013). Also Takata et al. reported that 'orientation to time', 'orientation to place', 'recall', 'naming and repetition', and 'listening and obeying' are associated with all-cause mortality (Takata et al., 2014).

Moderate (MMSE score 14-18) and severe (MMSE score 0-13) impairment in cognitive impairment are also independent predictors of all-cause mortality (Ramos et al., 2001; Katsoulis et al., 2014). These



results are similar to our study. The results of earlier studies, which reported that cognitive domains are associated with all-cause mortality, correspond with the results of the present study (Park et al., 2012; Iwasa et al., 2013; Takata et al., 2014).

The mortality risk is increased more in ADL dependency than in ADL independency (Stineman et al., 2012). A longitudinal study from Canada, ADL disability is statistically significant to mortality due to all-cause after adjusting for age, gender, education, and self-rated health (St John et al., 2002). After the trans-catheter aortic valve implantation cohort study, ADL disability is related with increased mortality due to all-cause (HR=3.36, 1.29-810.23) (Stortecky et al., 2012). The mortality due to all-cause was increased with ADL dependency in our study. Our results coincides with those of previous studies.

In this study, all task-specific ADLs had striking effects on mortality due to all-cause in every model. A study from Korea indicates that ADL of 'toileting', 'eating', 'dressing', 'bladder and bowel control', 'mobility' and 'bathing' are significant predictors of all-cause mortality (Suh. 2006). Moreover, according to a 2-year follow-up study in Brazil, 'continuance' task is associated with all-cause mortality (Ramos et al., 2001). An 1-year prospective study, Nakazawa et al. reported that ADL measured by the Barthel Index (basic activities of daily living) is associated with increased risk of 'feeding', 'transferring', 'toileting', 'bathing', 'dressing', and 'continent' tasks in nursing homes (Nakazawa et al., 2012). In the community-dwelling study from Japan, 'eating', 'dressing', 'bathing', 'toileting', and 'moving around the house' tasks measured by the HDS (Hasegawa Index) are associated minimal dependency (Dodge et al., 2005). ADL dependency has been presented to be a predictor of mortality in older adults (Ramos

et al., 2001; St John et al., 2002; Stineman et al., 2012). This association is proved in our study; ADL dependency has been investigated to be a predictor of mortality in older adults. This study demonstrated that most of ADL tasks exist with the risk for all-cause mortality (Dodge et al., 2005 and Nakazawa et al., 2012).

### **Vascular disease mortality**

Our study showed that mortality due to vascular disease was associated with severe cognitive impairment status after age and gender were adjusted. One of the short follow-up longitudinal cohort studies (Nguyen et al., 2003) presented that cognitive impairment in older adults is associated with mortality due to stroke after controlling the socio-demographic characteristics. The relationship between MMSE score and mortality due to vascular disease is strongly associated with increased risk as reported by the study conducted in Canada. Compared to the reference (MMSE score=30), mortality due to stroke, unstable or new angina, prior stroke or myocardial infarction, and congestive heart failure are associated with MMSE score <24 (HR=1.44, HR=1.12, HR=1.38, HR=1.43  $p<0.0001$ , respectively) (O'Donnell et al., 2012). The EPIC-Greece cohort study reported that CVD mortality increases the hazard ratio in MMSE score 10-20 (Katsoulis et al., 2014). Wu et al. also reported cognitive impairment measured by the SPMSQ (10-items cognitive index, short portable mental status questionnaire) is associated with an increased risk of mortality due to circulatory disease (Wu et al., 2014). Paddick et al. found that dementia and even mild cognitive impairment (MCI) are associated with excess risk mortality (Paddick et al., 2015).



However, a study conducted in Italy indicated that mortality due to ischemic stroke has no association with cognitive impairment (Altieri et al., 2002). Cano et al. reported stroke and heart attack are not associated with neither cognitive impairment nor mortality (Cano et al., 2012).

A study conducted in Canada by O'Donnell et al. reported that 'orientation to place', 'orientation to time', 'attention and calculation', 'recall', and 'copying' are increased categorized as domains of CV mortality; 'orientation to place', 'attention and calculation', and 'recall' are increased as domains of stroke; 'orientation to place', 'attention and calculation', and 'writing' are increased as domains of congestive heart failure. These domains predicted the mortality due to vascular events (O'Donnell et al., 2012). Our results were consistent with 'orientation to place' and 'three-stage command' for the mortality due to vascular disease.

Although results from early studies have various associations between cognitive impairment and vascular disease mortality (Altieri et al., 2002; O'Donnell et al., 2012; Cano et al., 2012; Katsoulis et al., 2014; Wu et al., 2014; Paddick et al., 2015), our study may provide clear answers that severe cognitive impairment increased the hazard ratio with long follow-up cohort study. 'Orientation to place' and 'three-stage command domains independently increased the hazard ratios in our participants.

We found an increase in mortality due to vascular disease (HR=1.91, 1.44-2.53) after adjusting for confounding variables with dependency in ADL. A study from Korea indicates that cerebrovascular disease has appeared to be a predictor of general mortality in older ages (Suh. 2006). Takata et al. found that mortality is increased with the patients who have cardiovascular disease patients aged 80 years or older, ADL disability is associated with increased risks of ADL-2 (almost-independence group,

HR=1.86, 1.05-3.15) and ADL-3 (dependent group, HR=0.97, 0.23-4.03) (Takata et al., 2013). Stineman et al. suggested that stroke and coronary artery disease are associated with mortality according to ADL stage from the big longitudinal study (Stineman et al., 2012). As cardiovascular and cerebral events occur after trans-catheter aortic valve implantation in 1-year prospective cohort study, ADL disability is related to increased mortality for patients aged 70 years and older (HR=3.63,  $p<0.01$ ) (Stortecky et al., 2012). ADL dependency has been presented to be a predictor of vascular disease mortality in older adults (Dodge et al., 2005; Suh, 2006; Stortecky et al., 2012; Stineman et al., 2012; Takata et al., 2013). This association is corroborated by our study.

Stroke has contributed to functional disability (Hayakawa et al., 2000; Lee et al., 2002; Chang et al., 2015). It has higher and the most persistent impact on every ADL task. Dodge et al. reported that stroke is associated with all of ADL tasks (Dodge et al., 2005). We found that all task-specific ADLs, 'bathing', 'dressing', 'toileting', 'moving in bed', 'moving around the house', 'eating', 'continence' and mortality due to vascular disease had a significant association. Other previous studies presented that 'dressing' task is a major domain affected by stroke (Blankevoort et al., 2010). 'Fecal and urinary incontinence' and stroke history are influenced by ADL disability (Ha et al., 2014). Also 'eating' task in stroke has the highest impact disability (Greiner et al., 1996; Dodge et al., 2005). This study demonstrated that most of ADL tasks exist with the mortality risk for vascular disease.

### **Senile mortality**

Our result showed that mortality due to senility was associated with the increased risk of developing MCI and moderate to severe cognitive impairment in community-dwelling older adults. In Taiwanese study, they confirmed a significant effect between frail status and cognitive impairment without dementia. Inferior cognitive impairment shows at the early stage of frailty (Wu et al., 2015). According to the British report, death due to dementia or senility appears on the top ten causes of deaths (The National End of Life Care Intelligence Network, 2010). Cano et al. reported that both senility and cognitive impairment increased mortality in older Mexican American (Cano et al., 2012). More over the Italian study, frail demented patients are higher risk of mortality (Solfrizzi et al., 2012). Our results have the same result as the previous study (HR=1.45, 1.63-3.31 in mild; HR=1.61, 1.63-3.31 in moderate; HR=2.32, 1.63-3.31 in severe) with senile mortality adjusted for age, gender, education, occupation, marriage, smoking status, drinking status, BMI, self-rated health, and hypertension. In this study, domain-specific cognitive impairments for senile mortality were significantly associated with most of the domains, 'orientation to time', 'registration', 'attention and calculation', 'recall', 'three-stage command', 'comprehension' and 'copying'. Especially, 'copying' (HR=1.90; 1.41-2.55) domain had higher risk score than any other domains.

Senility was associated with cognitive impairment even mild cognitive impairment and ADL disability in this study. Boyle et al. discovered that physical frailty is associated with an increased risk of developing MCI in the community-dwelling older adults. Frailty and cognitive impairment are separate clinical syndromes that share some features. They suggested that physical frailty and cognitive impairment share a common contributory pathogenesis (Boyle et al., 2007).

In this study, we indicated the analysis of mortality according to R54 (senility) in ICD-10 code which is mentioned on death certificates; however, support of our result for mortality due to R54 in ICD-10 was insufficient because other previous studies did not focused on R54, and they used frailty index with different definition. Senility/frailty brings a biological and physiological change with aging (Ma et al., 2009; Fried et al., 2001). Senility has no clear definition, so geriatricians has different views on operational definitions. Fried et al. defined potential definitions of senility as a synonym for disability, comorbidity, or advanced old age (Fried et al., 2001).

We found that mortality due to senility showed an association with ADL dependency. Fauth et al. reported that ADL carried an 83% higher risk of developing incident dementia compared to those without baseline ADL disability (Fauth et al., 2012). Senility is associated with increased risk of disability and comorbidity (Al Snih et al., 2009; Wong et al., 2010). In the Cardiovascular Health Study, it shows that frail participants are at high risk for reduced ADL (Fried et al., 2001). Snih et al. found pre-frail (HR=1.26; 1.05-1.52) and frail (HR=2.03; 1.40–2.94) in older Mexican Americans are associated with an increased risk of ADL disability over 10-year follow up (Snih et al., 2009). Another report, IADL impairment are more likely to be converted to dementia compared to those with MCI without reported IADL problems. Thus, it is clinically important to detect changes in ADL at an early stage (Jefferson et al., 2008; Goldberg et al., 2010; Ha et al., 2014). We indicated that the mortality due to senility was significantly increased in the risk for 'bathing', 'dressing', 'toileting', 'moving around the house', and 'eating'. Most tasks in ADL were not confirmed with other researches, because since they focused on different definitions.

A decline at ADL in particular accelerates in moderate dementia. Therefore, it is important to improve or stabilize the ability to perform ADL (Feldman et al., 2006; Ha et al., 2014).

## **Cancer mortality**

In this study, mortality due to cancer was not associated with cognitive impairment. Cancer mortality with cognitive impairment has rarely been reported. In the NEDICES study (Benito-León et al., 2014), faster cognitive decline without dementia measured by the 37-MMSE version is associated with the decreased risk of cancer mortality based on community-dwelling participants (unadjusted HR=0.75, 0.57-0.99). Otherwise, in the US study for Mexican Americans (Nguyen et al., 2003), cancer mortality is associated with decline cognitive function. Also the EPIC-Greece cohort study shows increasing risk in the relationship between cancer and low MMSE score (10-20) (Katsoulis et al., 2014). The meta-analysis cognitive function does not predict cancer mortality (Anstey et al., 2006). Our results, no statistically significant difference was found between cause-specific mortality and ADL disability.

## **Combined Effects**

We stratified cognitive impairment (no or mild, moderate, severe) and ADL disability (independence, partial dependence, dependence) by mortality due to all-cause, vascular disease, and senility. We found a strong association with mortality in cognitive impairment as well as with ADL disability due to all-cause, vascular disease, and senility. Combined effect

measured by ADL disability and cognitive impairment showed higher risks for coexisting variables than for cognitive impairment or ADL disability alone.

Mortality risk showed a greater likelihood when cognitive impairment and ADL disability were combined than when cognitive impairment or ADL disability was individually investigated. The highest impact on 'bathing' ADL disability by no or mild cognitive impairment led to increased hazard ratios in mortality due to all-cause (HR=1.53,  $p=0.0012$ ), vascular disease (HR=1.86,  $p=0.0215$ ), senility (HR=1.72,  $p=0.0158$ ) in this study. The result shows that mortality was increased with ADL disability in 'bathing' task even when cognitive impairment was absent or mild.

Mortality is lower when, 1) there is no ADL disability even in the presence of moderate cognitive impairment, or 2) cognitive impairment is below mild even though ADL indicates partial dependency. Therefore, mortality risk could be lowered when one of cognitive or ADL function functional capacity is maintained.

The Relative Excess Risk due to biological Interaction (RERI) of vascular disease mortality was increased when cognitive impairment and ADL disability were combined. The effects indicated all-cause (HR=0.96,  $p=0.0031$ ), vascular disease (HR=1.63,  $p=0.0545$ ), and senility (HR=0.57,  $p=0.2703$ ). Synergy Index (S) due to biological interaction (HR=2.72), vascular disease (HR=3.40), and senility (HR=1.58) were increased when cognitive impairment and ADL disability were combined. Functional capacity was a key predictor for surviving of older adults who have cognitive function and physical ability.

Our study suggests that older adults with coexisting ADL and cognitive impairment are more likely to have shorter lifespan than those

without coexisting impairments.

Some potential limitations. First, we were unable to measure cognitive decline because MMSE-K scores were measured only at the baseline of the study. Second, this study is its limited reliance on self-reporting of ADL and MMSE score. Third, It could not be able to confirmed the diagnose Alzheimer disease or dementia through imaging techniques before and after. Forth, It could not be ruled out of death due to senility with dementia or Alzheimer disease without doctor's diagnosis.

Our study has remarkable strengths. The prospective study design minimized recall bias. The big sample size, and long period (14.5-yrs follow-up) relatively long compared with other studies.



## VI. CONCLUSION

A simple screen of cognitive function and ADL provides important prognostic information of community-dwelling older adults. The cognitive impairment and ADL disability are important factors to increase the risk of mortality due to all-cause, vascular disease, and senility, but cancer didn't suggest concrete. Domain-specific cognitive function and task-specific ADL predicted mortality risk. Previous studies and our results indicated that the risk with evidence should consider the functional capacity for older adults. Thus, evidence based risk can be used to forecast service needs and develop intervention programs for older adults.





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## APPENDIX

Appendix table 1. Distribution of domain-specific cognitive impairment at baseline by cognitive impairment status in the Kangwha cohort study during 1994-2008

Domain-specific Cognitive impairment		Total (N=2,501)	None (n=1,910)	Mild (n=441)	Mod to Severe (n=150)	p-value
Time Orientation	No or mild	1,926(77.0)	1,733(90.7)	160(36.3)	33(22.0)	<0.0001
	Moderate & severe	575(23.0)	177( 9.3)	281(63.7)	117(78.0)	
Place Orientation	No or mild	2,151(86.0)	1,822(95.4)	282(64.0)	47(31.3)	<0.0001
	Moderate & severe	350(14.0)	88( 4.6)	159(36.0)	103(68.7)	
Registration	No or mild	2,214(88.5)	1,835(96.1)	339(76.9)	40(26.7)	<0.0001
	Moderate & severe	287(11.5)	75( 3.9)	102(23.1)	110(73.3)	
Attention and Calculation	No or mild	1,142(45.7)	1,089(57.0)	48(10.9)	5( 3.3)	<0.0001
	Moderate & severe	1,359(54.3)	821(43.0)	393(89.1)	145(96.7)	
Recall	No or mild	1,227(49.1)	1,118(58.5)	101(22.9)	8( 5.3)	<0.0001
	Moderate & severe	1,274(50.9)	792(41.5)	340(77.1)	142(94.7)	
Naming and Repetition	No or mild	2,398(95.9)	1,871(98.0)	417(45.6)	110(73.3)	<0.0001
	Moderate & severe	103(4.1)	39( 2.0)	24( 5.4)	42(26.7)	
Three-stage Command	No or mild	2,313(92.5)	1,850(96.9)	380(86.2)	83(55.3)	<0.0001
	Moderate & severe	188(7.5)	60( 3.1)	61(13.8)	72(44.7)	
Copying	No or mild	738(29.5)	693(36.3)	35( 8.0)	10( 6.7)	<0.0001
	Moderate & severe	1,763(70.5)	1,217(63.7)	406(92.0)	140(93.3)	
Comprehension	No or mild	1,890(75.6)	1,635(85.6)	219(49.7)	36(24.0)	<0.0001
	Moderate & severe	611(24.4)	275(14.4)	222(50.3)	114(76.0)	

Values are presented as number(%); MMSE-K, Korea Mini-Mental State formeramination

Appendix table 2. Distribution of domain-specific cognitive impairment at baseline by ADL levels in Kangwha Cohort Study

Domain-specific Cognitive impairment		total (n=2,501)	Activity of Daily Living Level			p-value
			Independence (n=1,737)	Partial dependence (n=432)	Dependence (n=332)	
Orientation to time	No or mild	1,926(77.01)	1,367(78.70)	338(78.24)	221(66.57)	<0.0001
	Moderate & severe	575(22.99)	370(21.30)	94(21.76)	112(33.43)	
Orientation to place	No or mild	2,151(86.01)	1,513(87.10)	377(87.27)	261(78.61)	0.0002
	Moderate & severe	350(13.99)	224(12.90)	55(12.73)	71(21.39)	
Registration	No or mild	2,214(88.52)	1,552(89.35)	390(90.28)	272(81.93)	0.0002
	Moderate & severe	287(11.48)	185(10.65)	42( 9.70)	60(18.07)	
Attention & Calculation	No or mild	1,142(45.66)	843(48.53)	189(43.75)	110(33.13)	<0.0001
	Moderate & severe	1,359(54.34)	894(51.47)	243(56.25)	222(66.97)	
Recall	No or mild	1,227(49.06)	924(53.20)	192(44.44)	111(33.43)	<0.0001
	Moderate & severe	1,274(50.94)	813(46.80)	240(55.56)	221(66.57)	
Naming & Repetition	No or mild	2,398(95.88)	1,667(95.97)	419(96.99)	312(93.98)	0.1090
	Moderate & severe	103( 4.12)	70( 4.03)	13( 3.01)	20( 6.02)	
Three-stage Command	No or mild	2,313(92.48)	1,626(93.61)	400(92.59)	287(86.45)	<0.0001
	Moderate & severe	188( 7.52)	111( 6.39)	32( 7.41)	45(13.55)	
Copying	No or mild	738(29.51)	564(32.47)	122(28.24)	52(15.66)	<0.0001
	Moderate & severe	1,763(70.49)	1,173(67.53)	310(71.76)	280(84.34)	
Comprehension	No or mild	1,890(75.57)	1,371(78.93)	306(70.83)	213(64.16)	<0.0001
	Moderate & severe	611(24.43)	366(21.07)	128(29.17)	119(35.84)	

HR (95% CI), Hazard Ratios 95% confidence intervals;

Appendix table 3. Distribution of task-specific ADL level at baseline by ADL level in Kangwha Cohort Study

Task-specific ADL	Activity of Daily Living Level				p-value
	Total (N=2,501)	Independence (N=1,737)	Partial dependence (N=432)	Dependence (N=332)	
Bathing					<0.0001
Independence	2,131(85.2)	1,737(100.0)	347(80.3)	47(14.2)	
Dependence	370(14.8)	0( 0.0)	85(16.7)	285(85.8)	<0.0001
Dressing					
Independence	2,279(91.1)	1,737(100.0)	427(98.8)	115(34.6)	<0.0001
Dependence	222( 8.9)	0( 0.0)	5( 1.2)	217(65.4)	
Toileting					<0.0001
Independence	2,327(93.0)	1,737(100.0)	431(99.8)	159(47.9)	
Dependence	174( 7.0)	0( 0.0)	45( 0.2)	173(52.1)	0.001
Moving in Bed					
Independence	1,955(78.2)	1,737(100.0)	182(42.1)	36(10.8)	<0.0001
Dependence	546(21.8)	0( 0.0)	250(57.9)	296(89.2)	
Moving around the house					<0.0001
Independence	1,909(76.3)	1,737(100.0)	148(34.3)	24( 7.2)	
Dependence	592(23.7)	0( 0.0)	284(65.7)	308(92.8)	<0.0001
Eating					
Independence	2,413(96.5)	1,737(100.0)	432(100.0)	244(73.5)	<0.0001
Dependence	89( 3.5)	0( 0.0)	0( 0.0)	88(26.5)	
Continence					<0.0001
Independence	2,409(96.3)	1,737(100.0)	666(90.7)	280(84.8)	
Dependence	92( 3.7)	0( 0.0)	40( 9.3)	52(15.7)	

Values denote mean±SD or numbers with percentages (%) in parentheses; ADL, Activity of Daily Living;



Appendix table 4. Hazard ratios (95% CI) for cancer mortality with domain-specific cognitive impairment

Domain-specific Cognitive impairment		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Cancer mortality (n=232)</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.13(0.80-1.59)	0.5016	1.11(0.78-1.58)	0.5465	1.11(0.78-1.57)	0.5771
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.02(0.65-1.62)	0.9209	0.99(0.62-1.56)	0.9504	0.97(0.61-1.54)	0.9089
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.08(0.69-1.70)	0.7402	1.06(0.67-1.67)	0.8182	1.05(0.66-1.66)	0.8455
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.96(0.73-1.25)	0.7484	0.98(0.75-1.29)	0.8979	0.98(0.74-1.29)	0.8741
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.81(0.62-1.05)	0.1109	0.81(0.62-1.06)	0.1177	0.81(0.62-1.06)	0.1189
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.09(0.59-1.99)	0.7882	1.05(0.57-1.95)	0.8747	1.05(0.57-1.95)	0.8757
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.55(0.27-1.12)	0.1013	0.53(0.26-1.07)	0.0746	0.52(0.26-1.06)	0.072
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.22(0.92-1.62)	0.1708	1.21(0.90-1.63)	0.2007	1.21(0.90-1.63)	0.2128
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.96(0.68-1.37)	0.8314	0.97(0.68-1.39)	0.8804	0.98(0.68-1.39)	0.888

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and ADL (partial dependence, dependence)

Appendix table 5. Hazard ratios (95% CI) for cancer mortality with task-specific ADL

Task-specific ADL		Model 1		Model 2		Model 3	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Cancer mortality (n=232)</b>							
Bathing	Independence	1.00		1.00		1.00	
	Dependence	0.92(0.57-1.48)	0.728	0.92(0.57-1.50)	0.74	0.91(0.56-1.49)	0.7192
Dressing	Independence	1.00		1.00		1.00	
	Dependence	0.95(0.52-1.76)	0.8802	0.96(0.52-1.79)	0.9085	0.96(0.52-1.79)	0.8994
Toileting	Independence	1.00		1.00		1.00	
	Dependence	1.62(0.94-2.81)	0.0841	1.71(0.98-2.98)	0.0605	1.70(0.97-2.97)	0.0635
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	1.17(0.84-1.63)	0.3569	1.17(0.84-1.65)	0.3535	1.18(0.84-1.66)	0.3398
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	1.12(0.81-1.55)	0.5123	1.10(0.79-1.53)	0.5908	1.10(0.79-1.53)	0.5769
Eating	Independence	1.00		1.00		1.00	
	Dependence	1.17(0.48-2.84)	0.7341	1.21(0.49-2.97)	0.679	1.20(0.49-2.96)	0.6918
Continence	Independence	1.00		1.00		1.00	
	Dependence	0.43(0.11-1.74)	0.2387	0.44(0.11-1.77)	0.2465	0.43(0.11-1.76)	0.2413

HR (95% CI), Hazard Ratios 95% confidence intervals

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Model 3: adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, hypertension, and cognitive impairment (mild, moderate, severe)

Appendix table 6. Cognitive impairment status for Cause-specific mortality by ADL level

Cause-specific mortality/ Cognitive impairment status		Independence ADL* (n=1,737)		Partial dependence ADL* (n=432)		Dependence ADL* (n=332)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
All-cause mortality	(event)	960		271		250	
No impairment		1.00		1.00		1.00	
Mild impairment		1.06(0.91-1.24)	0.4637	1.20(0.89-1.63)	0.2363	1.10(0.77-1.56)	0.6077
Moderate impairment		1.03(0.85-1.25)	0.7548	1.50(1.05-2.14)	0.0265	1.82(1.25-2.65)	0.0020
Severe impairment		1.30(0.97-1.73)	0.0773	2.55(1.51-4.30)	0.0004	2.21(1.43-3.40)	0.0003
Vascular Disease mortality	(event)	218		52		76	
No impairment		1.00		1.00		1.00	
Mild impairment		0.84(0.60-1.17)	0.3049	0.90(0.42-1.93)	0.7897	0.75(0.40-1.40)	0.3640
Moderate impairment		0.98(0.67-1.45)	0.9340	2.34(1.10-4.97)	0.0270	1.41(0.72-2.77)	0.3157
Severe impairment		0.85(0.42-1.70)	0.6413	4.27(1.35-13.53)	0.0136	1.97(0.93-4.16)	0.0776
Senile mortality	(event)	257		52		90	
No impairment		1.00		1.00		1.00	
Mild impairment		1.38(1.01-1.89)	0.0436	0.90(0.42-1.93)	0.7897	1.80(0.91-3.57)	0.0936
Moderate impairment		1.28(0.89-1.83)	0.1781	2.34(1.10-4.97)	0.0270	2.75(1.35-5.61)	0.0055
Severe impairment		1.88(1.16-3.05)	0.0110	4.27(1.35-13.53)	0.0136	3.22(1.45-7.17)	0.0042
Cancer mortality	(event)	181		31		20	
No impairment		1.00		1.00		1.00	
Mild impairment		0.95(0.65-1.37)	0.7654	1.29(0.59-2.86)	0.5235	0.53(0.16-1.69)	0.2801
Moderate impairment		1.12(0.70-1.80)	0.6283	0.24(0.03-1.94)	0.1828	0.92(0.24-3.49)	0.9051
Severe impairment		1.34(0.64-2.80)	0.4321	-	-	0.93(0.09-9.22)	0.9509

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals;

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (&lt;18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension, ADL (partial dependence, dependence).

Appendix table 7. Domain-specific cognitive impairment for all-cause mortality by ADL level

Domain-specific cognitive impairment	Cognitive status	Independence ADL* (n=960)		Partial dependence ADL* (n=271)		Dependence ADL* (n=250)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>All-cause mortality</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.08(0.92-1.27)	0.3227	1.36(1.01-1.83)	0.0454	1.35(1.01-1.79)	0.0400
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.04(0.85-1.26)	0.7221	1.32(0.91-1.90)	0.1400	1.79(1.32-2.43)	0.0002
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.04(0.85-1.27)	0.7009	1.29(0.87-1.90)	0.2035	1.48(1.07-2.05)	0.0188
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.11(0.97-1.27)	0.1421	1.04(0.79-1.36)	0.7981	1.13(0.86-1.50)	0.3768
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.03(0.91-1.18)	0.6270	1.09(0.84-1.42)	0.4961	1.34(1.01-1.77)	0.0433
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.99(0.72-1.35)	0.9315	1.03(0.48-2.24)	0.9347	1.76(1.05-2.95)	0.0335
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.99(0.77-1.29)	0.9648	1.36(0.90-2.06)	0.1492	1.60(1.12-2.30)	0.0103
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.15(0.99-1.35)	0.0744	1.33(0.98-1.81)	0.0676	1.36(0.91-2.03)	0.1364
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.13(0.96-1.32)	0.1335	1.28(0.98-1.67)	0.0759	1.51(1.14-2.00)	0.0043

ADL, Activity of daily living; HR (95% CI), HR (95% CI), Hazard Ratios 95% confidence intervals

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (&lt;18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Appendix table 8. Domain-specific cognitive impairment for vascular disease mortality by ADL level

Domain-specific cognitive impairment	Cognitive status	Independence ADL* (n=218)		Partial dependence ADL* (n=52)		Dependence ADL* (n=75)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
Vascular disease mortality							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.08(0.77-1.51)	0.6660	2.42(1.26-4.67)	0.0082	1.18(0.68-2.04)	0.5534
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.84(0.54-1.29)	0.4208	2.18(1.03-4.64)	0.0423	3.63(2.04-6.43)	<.0001
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.80(0.50-1.27)	0.3404	3.36(1.61-7.01)	0.0012	1.50(0.81-2.77)	0.1988
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.95(0.72-1.25)	0.6953	0.70(0.37-1.31)	0.2615	0.63(0.39-1.02)	0.0619
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.97(0.74-1.28)	0.8247	1.46(0.80-2.66)	0.2134	1.02(0.63-1.65)	0.9317
Naming & Repetition	No or mild	1.00		-		1.00	
	Moderate & severe	0.75(0.35-1.61)	0.4622	-		1.27(0.49-3.31)	0.6250
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.89(0.51-1.56)	0.6824	1.58(0.62-4.07)	0.3416	2.07(1.15-3.73)	0.0154
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.07(0.77-1.48)	0.6986	0.94(0.49-1.80)	0.8444	0.89(0.46-1.72)	0.7233
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.08(0.78-1.51)	0.642	1.31(0.71-2.44)	0.3904	1.62(0.96-2.74)	0.0699

ADL, Activity of daily living; HR (95% CI), HR (95% CI), Hazard Ratios 95% confidence intervals

\* Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Appendix table 9. Domain-specific cognitive impairment for senile mortality by ADL level

Domain-specific cognitive impairment	Cognitive status	Independence ADL* (n=257)		Partial dependence ADL* (n=81)		Dependence ADL* (n=90)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
Senile mortality							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.08(0.81-1.44)	0.5997	1.24(0.73-2.10)	0.4346	1.42(0.89-2.28)	0.1452
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.00(0.71-1.41)	0.9926	1.17(0.63-2.17)	0.6121	1.29(0.76-2.18)	0.3542
Registration	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.25(0.88-1.77)	0.2168	1.24(0.67-2.30)	0.5008	1.60(0.94-2.72)	0.0806
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.77(1.34-2.33)	<.0001	1.31(0.75-2.27)	0.3429	1.72(1.03-2.86)	0.0377
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.10(0.84-1.42)	0.4916	1.26(0.74-2.17)	0.3975	1.55(0.93-2.58)	0.0920
Naming & Repetition	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.89(0.45-1.76)	0.7358	2.90(0.85-9.87)	0.0878	2.28(0.94-5.49)	0.0670
Three-stage Command	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.32(0.85-2.03)	0.2152	1.47(0.74-2.92)	0.2714	1.80(0.94-3.47)	0.0778
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.69(1.18-2.41)	0.0043	2.31(1.14-4.68)	0.0201	2.67(1.14-6.25)	0.0238
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.42(1.08-1.87)	0.0126	1.40(0.86-2.29)	0.1732	1.30(0.81-2.10)	0.2739

ADL, Activity of daily living; HR (95% CI), Hazard Ratios 95% confidence intervals;

\* Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (&lt;18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Appendix table 10. Domain-specific cognitive impairment for cancer mortality by ADL level

Domain-specific cognitive impairment	Cognitive status	Independence ADL* (n=181)		Partial dependence ADL* (n=31)		Dependence ADL* (n=20)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>Cancer mortality</b>							
Orientation to time	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.06(0.71-1.60)	0.7727	1.22(0.43-3.45)	0.7116	2.34(0.74-7.33)	0.1464
Orientation to place	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.97(0.57-1.64)	0.9036	0.55(0.07-4.37)	0.5752	1.56(0.45-5.39)	0.4846
Registration	No or mild	1.00		-		1.00	
	Moderate & severe	1.24(0.77-2.02)	0.3795	-		0.99(0.20-4.80)	0.9867
Attention & Calculation	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.01(0.74-1.37)	0.9632	0.73(0.32-1.68)	0.4607	0.66(0.25-1.74)	0.3975
Recall	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.89(0.66-1.21)	0.4669	0.70(0.33-1.50)	0.3581	0.42(0.16-1.10)	0.0767
Naming & Repetition	No or mild	1.00		1.00		-	
	Moderate & severe	1.09(0.55-2.15)	0.8023	1.67(0.36-7.75)	0.5111	-	
Three-stage Command	No or mild	1.00		-		1.00	
	Moderate & severe	0.56(0.25-1.26)	0.1618	-		1.04(0.20-5.30)	0.967
Copying	No or mild	1.00		1.00		1.00	
	Moderate & severe	1.16(0.84-1.62)	0.3747	1.43(0.59-3.44)	0.4311	0.66(0.17-2.68)	0.5649
Comprehension	No or mild	1.00		1.00		1.00	
	Moderate & severe	0.93(0.61-1.43)	0.7516	0.85(0.33-2.17)	0.7299	0.89(0.31-2.56)	0.8258

ADL, Activity of daily living; HR (95% CI), HR (95% CI), Hazard Ratios 95% confidence intervals

\*Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (<18.5; 18.5-20.9; 25-27.4; ≥27.5), self-rated health, and hypertension

Appendix table 11. Task-specific ADL for senile mortality by cognitive impairment status

Task-specific ADL	ADL levels	Cognitive impairment					
		No or Mild* (N=686)		Moderate* (N=441)		Severe* (N=150)	
		aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
<b>Cancer mortality</b>	event	56		29		9	
Bathing	Independence	1.00		1.00		1.00	
	Dependence	0.87(0.34-2.27)	0.779	0.60(0.17-2.09)	0.4244	4.82(0.20-114.48)	0.3302
Dressing	Independence	1.00		1.00		1.00	
	Dependence	0.51(0.12-2.19)	0.3614	1.25(0.36-4.37)	0.7262	7.85(0.31-201.69)	0.2137
Toileting	Independence	1.00		1.00		1.00	
	Dependence	1.13(0.32-3.95)	0.8521	3.02(1.03-8.84)	0.0439	12.91(0.39-431.59)	0.1532
Moving in Bed	Independence	1.00		1.00		1.00	
	Dependence	1.38(0.73-2.60)	0.3255	0.89(0.33-2.46)	0.8267	15.98(0.52-489.55)	0.1124
Moving around the house	Independence	1.00		1.00		1.00	
	Dependence	1.40(0.76-2.56)	0.2767	1.02(0.40-2.62)	0.9655	8.18(0.32-210.44)	0.2046
Eating	Independence	-		1.00		1.00	
	Dependence	-		0.89(0.11-7.11)	0.9115	43.41(0.56-3350.56)	0.0891
Continence	Independence	-		1.00		-	
	Dependence	-		0.90(0.11-7.19)	0.9229	-	

ADL, Activity of daily living; HR (95% CI), HR (95% CI), HR (95% CI), Hazard Ratios 95% confidence intervals

Adjusted for age, gender, education, occupation, marriage, smoker (former, current), drinker (former, current), BMI (&lt;18.5; 18.5-20.9; 25-27.4; and ≥27.5), self-rated health, and hypertension



## Abstract in Korean

### 노인의 인지기능장애 및 일상생활활동장애와 사망과의 관련성 연구: 강화코호트 연구

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**목적:** 한국 노인들의 모든원인 사망, 혈관질환 사망, 암 사망, 노쇠로 기인한 사망을 인지능력 수행과 일상생활활동 수행능력을 통하여 복합적으로 예측하고 사망에 기여하는 요소들을 평가한다.

**방법:** 1985년 3월에 55세 이상 강화도에 거주하고 있는 6,372명을 대상으로 코호트를 구축하였다. 추가적으로 코호트 내의 대상자에게 한국판 간이 인지 기능검사(MMSE-K)와 일상생활활동(ADL) 수행능력을 1994년 7월부터 2008년 12월 31일까지 14년 5개월간 추적하였으며, 64세 이상 2,501명을 최종 분석대상으로 하였다. 분석은 카이검정 및 콕스비례위험모형을 사용하였다. MMSE-K 점수로 인지장애 정도를 분류하였고 각 영역(9가지) 인지기능과 사망과의 관련성 예측하였다. ADL도 점수에 따라 그룹을 분류하였으며, 직무(7가지)와 사망과의 관련성을 확인하였다. 또한 두요소를 결합하여 효과를 확인하였다.

**결과:** 첫째, 노인들의 인지장애 및 일상생활활동장애는 암사망을 제외하고 모든원인사망, 혈관질환사망, 노쇠사망과 높은 관련성이 있었다. 둘째, 인지

기능의 영역별 및 일상생활활동의 직무수행별 사망과의 관련성은 다양한 연관성을 보였으나 암사망과는 관련성이 없었다. 셋째, 인지장애와 일상생활활동장애를 합쳐서 보았을 때 위험비는 더 높아졌고, 시너지효과가 크게 증가되었다. 시너지효과는 모든원인사망에서 3.72 (HR), 혈관질환사망 3.40 (HR), 노쇠사망은 1.58 (HR)의 시너지 효과 위험비를 보였다.

**결론:** 인지기능장애와 일상생활활동장애는 노인들에게 있어서 사망률을 높이는 요인이다. 사망원인에 따라 각 영역별 인지기능장애와 직무별 일상생활활동장애의 위험요소가 다르므로 이에 따라 노인들의 기능장애 관련요인을 고려하면 노인들에게 적합한 보건의로 복지 서비스 개발을 하는데 있어서 전략적인 기틀을 마련할 수 있을 것이다.

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핵심 어휘: 인지기능장애, 일상생활활동장애, 모든원인사망, 혈관질환사망, 노쇠사망, 암 사망