한국임상약학회지 제34권 제2호
Korean J Clin Pharm, Vol. 34, No. 2, pp. 118-125, 2024
Original Article

Korean Journal of Clinical Pharmacy
Official Journal of
Korean College of Clinical Pharmacy
pISSN 1226-6051 eISSN 2508-786X
https://doi.org/10.24304/kjcp.2024.34.2.118

Patterns of Depressive Symptoms on Cognitive Function Decline: An Investigation in Middle-Aged Koreans Based on the Korean Longitudinal Study of Aging (KLoSA)

Seungyeon Kim*
College of Pharmacy, Dankook University, Cheonan 31116, Republic of Korea

ABSTRACT

Background: Numerous studies have consistently demonstrated that depression can be associated with cognitive function decline, primarily focusing on older adults due to the neurodegenerative characteristics of dementia. With persistent depression frequently reported in patients with early-onset or young-onset dementia, this study aimed to assess the impact of depression, specifically the changes in depressive symptoms over time, on the risk of cognitive function decline in middle-aged adults in Korea. **Methods:** This retrospective study utilized data from the first four waves (2006-2012) of the Korean Longitudinal Study of Aging (KLoSA), focusing on middle-aged adults with normal cognitive function at baseline. Changes in depressive symptoms were categorized into four groups based on the CES-D score, and their association with cognitive function decline was evaluated using a multivariate logistic regression model. **Results:** Of the initial 10,254 participants, 3,400 were included in the analysis. Depressive status, particularly newly onset (adjusted odds ratio [aOR] 1.96; 95% confidence interval [CI] 1.32-2.93) and persistent depression groups (aOR 5.59; 95% CI 2.90-10.78), were significantly associated with cognitive function decline. In contrast, recovery from depressive symptoms was not significantly associated with cognitive function decline (p=0.809). **Conclusions:** Our study showed a significant association between changes in depressive symptoms and cognitive function decline in middle-aged Korean adults. This suggests that management of depressive symptoms could be crucial for the prevention of cognitive function decline in this population.

KEYWORDS: Cognitive function decline, depressive symptoms, Korean longitudinal study of aging, middle-aged adults

With the increasing global prevalence and disease burden of depression, as well as in Korea,[1-3] various chronic conditions and diseases have been observed to be linked to depressive symptoms and depression. Depression is known to be associated with multimorbidity, including cardiovascular disease (CVD),[4] cognitive impairment,[5] and other psychiatric disorders.[6] Numerous explanations have been proposed for the association between depression and multimorbidity, encompassing factors such as disability, poor quality of life, and low adherence to disease management.[6] Furthermore, biological explanations have been reported regarding the role of depression as a risk factor in cardiovascular disease and other chronic conditions.[7,8] Particularly, the impact of depression on changes or declines in cognitive function has been consistently observed and reported.[9,10] As Korean society has transitioned into an 'aged society', with the aging population now representing over 14%,[11] concerns about dementia and cognitive impairment have notably increased. Consequently, the development of preventive strategies for cognitive function decline by identifying and controlling the modifiable risk factors has become increasingly significant.

Numerous studies have consistently shown that the onset, remission, or persistence of depression can be associated with cognitive function decline,[12-16] highlighting the negative impact of depression on cognitive functions. Notably, depressive symp-

*Correspondence to: Seungyeon Kim, College of Pharmacy, Dankook University, 119 Dandae-ro, Dongnam-gu, Cheonan, 31116, Republic of Korea
Tel: +82-41-550-1437, Fax: +82-41-559-7899, E-mail: gsy927@dankook.ac.kr

Received 3 May, 2024; Revised 2 June, 2024; Accepted 4 June, 2024

toms, including persistent depression, have been frequently reported in patients with early-onset or young-onset dementia,[17,18] suggesting a crucial link between depressive states and cognitive function across various age groups. Recent health insurance claims data analysis[19] indicates a trend of shifting high prevalence of depression from the elderly to young and middle-aged adults in Korea. Considering that most studies have focused on older adults due to the neurodegenerative characteristics of dementia, it is crucial to extend research efforts beyond this study population.

This study aimed to assess the impact of depression, specifically the patterns of symptoms, on the risk of cognitive function decline in middle-aged adults, using data from the Korean Longitudinal Study of Aging (KLoSA) panel survey database.

Materials and Methods

Data source and study population

This retrospective study was conducted using the longitudinal data derived from the 1st (2006) to the 4th (2012) rounds of the KLoSA. The KLoSA is a longitudinal panel survey data of a nationally representative sample of individuals aged 45 years or older (born before 1961). The survey participants were interviewed biennially based on the computer-assisted personal interview, and the survey included detailed questions asking about household background, demographic characteristics, health status, employment, income and medical service usage.[20,21] Detailed descriptions of the study design and methods of KLoSA have been presented elsewhere.[22] This study was approved by the Institutional Review Board (IRB) of SNU-SMG Boramae Medical Center (IRB No. 07-2019-30), which waived the requirement for informed consent due to the use of anonymized clinical data.

This study focused on middle-aged adults, who were under 65 years of age at the time of the initial survey, demonstrated normal cognitive function with a score of 24 or above on the K-MMSE (the Korean version of the Mini-Mental State Examination), and had completed all four surveys. Participants were excluded if they had a baseline depression, indicated by a CES-D (the Korean version of the Center for Epidemiologic Studies Depression Scale) score of 4 or above, or a history of depression. Exclusion criteria also included non-responses to CES-D score or history of depression questions (C141) in all survey rounds, non-response to K-MMSE score in the 4th round survey, or if the participants had deceased during the course of the survey.

Data collection

To determine changes in the depression status of the study population, data on responses regarding depression status, as indicated by CES-D scores or questions about the history of depression, were collected during the 2nd and 3rd waves of the survey. Participants were categorized as 'depressed' if they reported a CES-D score of 4 or above, or answered 'yes' to having a history of depression, and as 'non-depressed' if they met neither of these criteria. In the study, participants who were not depressed in both the second and third waves of the survey were categorized as the ‘Never depressed’ group. Those who were not depressed in the second wave but were depressed in the third wave were defined as the ‘Newly onset’ group. Participants who were depressed in the 2nd wave but not in the third wave were categorized as the ‘Recovered’ group, and those who continued to report depression in the third wave were defined as the ‘Persistent depression’ group.

Comprehensive data on the potential confounders, including baseline characteristics, as well as risk factors associated with cognitive function, were collected. Variables such as sex, age, baseline BMI, income level, education level, marital status, type of health insurance, residential area, smoking and alcohol consumption, activities of daily living (ADL), regular physical activity (defined as more than once per week), employment status, baseline K-MMSE score, and the comorbidities including hypertension, diabetes mellitus, heart disease, cerebrovascular disease, psychiatric disease were collected. These factors were all assessed based on the 1st wave of survey. Baseline BMI was categorized into four groups: underweight (BMI<18.5), normal weight (18.5≤BMI<23), overweight (23≤BMI<25), and obese (BMI≥25).[21] Residential areas were classified into urban and rural areas. ADL were divided into two categories: those requiring assistance in at least one activity area (score of 1 or more) and those requiring no assistance (score of 0). Income levels were classified into five groups based on total income in 2005. Regarding smoking and alcohol consumption, participants were categorized into current smokers and drinkers, past smokers and drinkers, and those who had never smoked or drunk. Educational levels were classified into four groups: less than elementary school, middle school graduates, high school graduates, and college graduates or higher.

Outcome measures

The study outcome was defined as the occurrence of cognitive function decline, which was categorized into two groups based on the K-MMSE scores from the 4th wave of the survey. Mild Cognitive Impairment (MCI) was defined as a K-MMSE score of 18 or above but less than 24, and Severe Cognitive Impairment (SCI) was defined as a K-MMSE score of less than 17.[21)]

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the study population. The comparison of categorical variables including sex, income level, educational level, marital status, type of insurance, residential area, smoking and alcohol consumption, presence of comorbidities, regular physical activity, ADL, and employment status among depression status groups were conducted using the Pearson chi-squared test, whereas continuous variables such as age, baseline BMI, and baseline K-MMSE score were compared using analysis of variance (ANOVA). To evaluate the correlation between depression status change and cognitive function, univariable and multivariable logistic regression analyses were performed. The multivariable logistic models were adjusted for all baseline characteristics and the results were presented as odds ratio (ORs) and corresponding 95% confidence intervals (CIs). Additionally, we incorporated a Sankey diagram[23)] to graphically delineate the transitions within our study population based on changes in depression status. It illustrates the progression from each status to various cognitive functions, thereby facilitating an understanding of the dynamic relationship between depression status and cognitive function decline in this study.

All statistical analyses were conducted using SAS statistical software (version 9.4; SAS Institute, Cary, NC, United States), and $p<0.05$ was considered statistically significant.

Results

In the initial 2006 survey (N=10,254), we excluded participants aged 65 and above, those with missing baseline depression status or K-MMSE scores, those who reported baseline depression, or with K-MMSE scores below 24. From the remaining 4,809 participants, we further excluded those who died at each wave of the survey, as well as those who did not respond to the depression status questions or the K-MMSE score items. Consequently, a total of 3,400 participants were included in the study (Fig. 1).

Table 1 presents the baseline characteristics of the study population categorized by depression status. With the exception of baseline BMI, type of health insurance, and smoking status, significant differences were observed across all variables for differ-

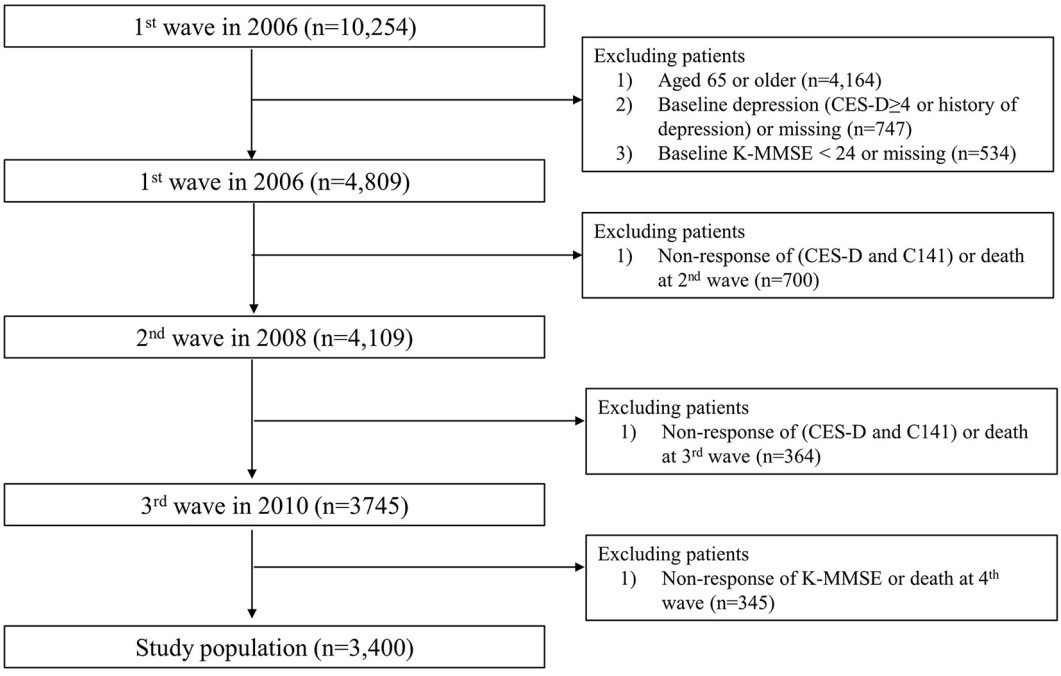

Fig. 1. Flow chart of study population selection process

Table 1. Demographic characteristics of study population (n=3,400)[a]

	Depression Status				
	Never depressed	Recovered	Newly onset	Persistent depression	*p*-value
Number of people	3,028	148	179	45	
Age (years), mean (SD)	53.7 (5.7)	55.5 (5.9)	55.1 (5.9)	57.9 (5.7)	<0.001
40s (45-49)	896 (29.6)	29 (19.6)	40 (22.4)	7 (15.6)	
50s (50-59)	1,516 (50.1)	70 (47.3)	86 (48.0)	16 (35.5)	<0.001
60s (60-64)	616 (20.3)	49 (33.1)	53 (29.6)	22 (48.9)	
Sex, Male (%)	1,448 (47.8)	51 (34.5)	71 (39.7)	21 (46.7)	0.003
Baseline BMI (kg/m^2), mean (SD)[b]	23.5 (2.5)	23.4 (2.7)	23.4 (2.9)	24.2 (3.4)	0.285
Underweight	41 (1.35)	3 (2.0)	3 (1.7)	1 (2.2)	
Normal	1,264 (41.7)	58 (39.2)	74 (41.3)	14 (31.1)	0.881
Overweight	978 (32.3)	46 (27.0)	65 (36.3)	18 (40.0)	
Obese	734 (24.2)	40 (0.7)	37 (20.7)	12 (26.7)	
Household income quintile[c]					
1st (lowest)	458 (19.6)	33 (30.0)	39 (27.1)	7 (21.2)	
2nd	439 (18.8)	29 (25.4)	31 (21.5)	15 (45.5)	
3rd	452 (19.4)	21 (18.4)	41 (28.5)	9 (27.3)	<0.001
4th	471 (20.2)	16 (14.0)	24 (16.7)	2 (6.0)	
5th (highest)	513 (22.0)	15 (13.2)	9 (6.2)	0 (0.0)	
Education[d]					
Elementary	700 (23.1)	50 (33.8)	69 (38.6)	24 (53.3)	
Middle school	638 (21.1)	41 (27.7)	48 (26.8)	12 (26.7)	<0.001
High school	1,243 (41.1)	42 (28.4)	53 (29.6)	7 (15.6)	
College or higher	446 (14.7)	15 (10.1)	9 (5.0)	2 (4.4)	
Marital status					
Married	2,804 (92.6)	121 (81.8)	158 (88.3)	40 (88.9)	
Separated	204 (3.7)	2 (16.2)	15 (8.4)	4 (8.9)	<0.001
Never married	20 (0.7)	3 (2.0)	6 (3.3)	1 (2.2)	
Health Insurance					
National health insurance	2,957 (97.7)	146 (98.7)	172 (96.1)	42 (93.3)	0.123
Medicaid	71 (2.3)	2 (1.3)	7 (3.9)	3 (6.7)	
Residential area					
Urban	1,418 (46.8)	56 (37.8)	67 (37.4)	14 (31.1)	0.003
Rural	1,610 (53.2)	92 (62.2)	112 (62.6)	31 (68.9)	
Smoking status					
Never smoker	2,103 (69.5)	107 (72.3)	130 (72.6)	27 (60.0)	
Past smoker	261 (8.6)	12 (8.1)	13 (7.3)	3 (6.7)	0.564
Current smoker	664 (2.9)	29 (19.6)	36 (20.1)	15 (33.3)	
Alcohol drinking status					
Never drinker	1,432 (47.3)	52 (35.1)	67 (37.4)	14 (31.1)	
Past drinker	111 (3.7)	9 (6.1)	6 (3.4)	2 (4.4)	0.003
Current drinker	1,485 (49.0)	87 (58.8)	106 (59.2)	29 (64.5)	
Regular physical activity, yes	1,393 (46.0)	59 (39.9)	64 (35.8)	17 (37.8)	0.021
Activities of daily living					
0 (normal)	3,017 (99.6)	147 (99.3)	178 (99.4)	43 (95.6)	0.001
1+	11 (0.4)	1 (0.7)	1 (0.6)	2 (4.4)	
Baseline K-MMSE, mean (SD)	28.4 (1.7)	28.1 (1.8)	27.6 (1.9)	27.0 (1.9)	<0.001
Employment status					
Employed	1,774 (58.6)	64 (43.2)	84 (46.9)	17 (37.8)	<0.001
Unemployed	1,254 (41.4)	84 (56.8)	95 (53.1)	28 (62.2)	
Baseline comorbidities					
Psychiatric disease	7 (0.2)	2 (1.4)	2 (1.1)	3 (6.7)	<0.001
Hypertension	525 (17.3)	38 (25.7)	38 (21.2)	20 (44.4)	<0.001
Diabetes mellitus	229 (7.6)	23 (15.5)	15 (8.4)	10 (22.2)	<0.001
Heart disease	84 (2.8)	5 (3.4)	7 (3.9)	4 (8.9)	0.094
Cerebrovascular disease	30 (1.0)	3 (2.0)	1 (0.6)	5 (11.1)	<0.001

[a]Pearson's Chi-squared and ANOVA were used for comparing the categorical and continuous variables between depression status categories, respectively. Continuous variables in this table were the mean age, baseline BMI, and baseline K-MMSE.
[b]Baseline BMI data is missing for 11 participants.
[c]Household income data is missing for 776 participants.
[d]Education level data is missing for 1 participant.
Abbreviation: BMI- body mass index, K-MMSE – the Korean version of the Mini-mental state examination, SD-standard deviation

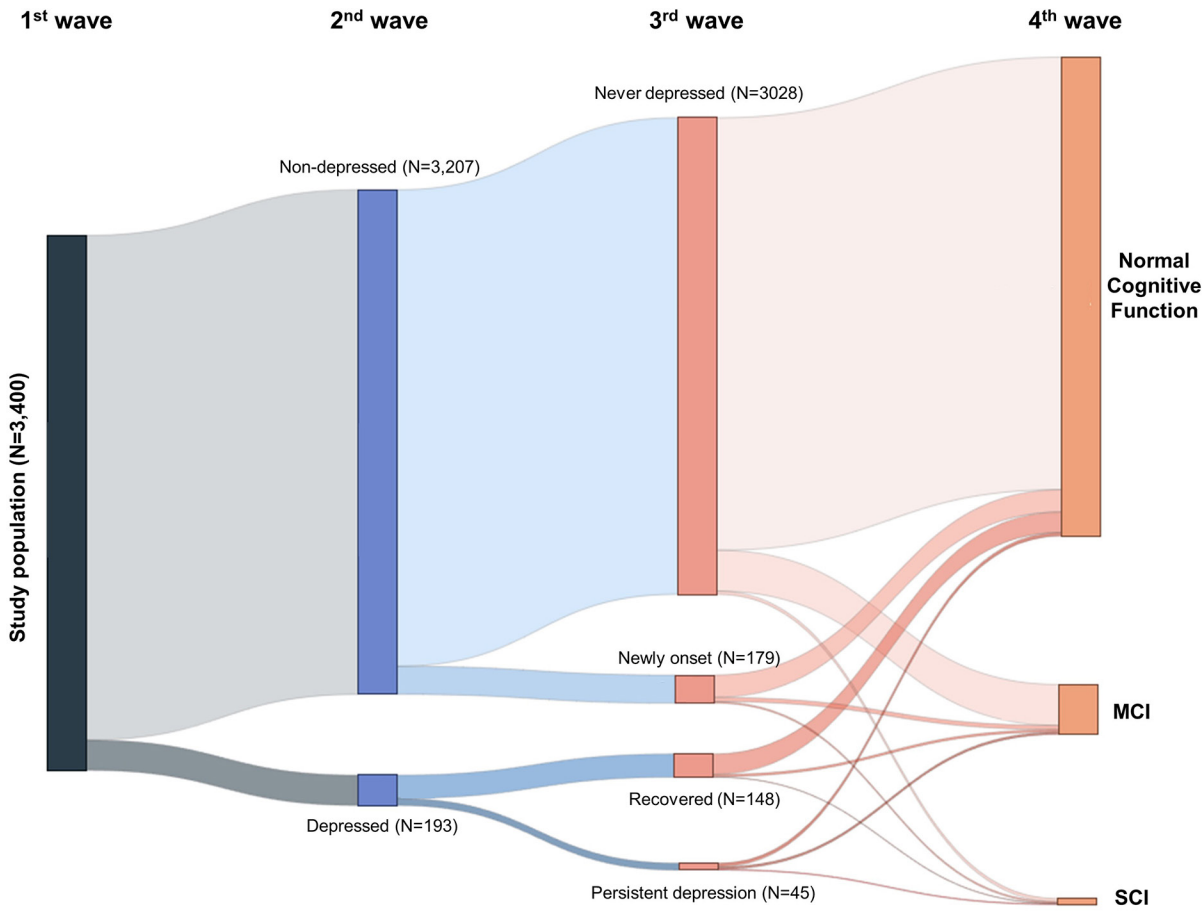

Fig. 2. Sankey plot illustrating the progression of cognitive function decline by depressive symptom status

ent depression statuses. The persistent depression group showed a higher mean age and a greater proportion of participants in their sixties compared to other groups (p<0.001). Additionally, this group showed the highest percentages of lower income and lower education levels. Compared to the never depressed group, those who had experienced depression at least once (recovered, newly onset, persistent depression) showed a higher rate of living in rural areas (p=0.003) and a higher rate of current drinkers (p=0.003). Conversely, the rates of regular physical activity and employment, and mean baseline K-MMSE scores were all lower in the groups that had experienced depression compared to the never depressed group.

Sankey plots (Fig. 2) depict the flows of changing depression status and the incidence of cognitive function decline. From the study population, 193 participants were classified as depressed in the 2nd wave of the survey, among whom 45 were categorized into the persistent depression group in the 3rd wave. Of the 3,207 participants classified as non-depressed in the 2nd wave, 179 were classified into the newly onset group in the 3rd wave. Most participants belonged to the never depressed group; the newly onset and recovered groups had comparable numbers, while the persistent depression group was notably smaller, constituting less than 2%. The rate of cognitive function decline into MCI or SCI was highest in the persistent depression group (48.9%). Notably, the incidence of progressing to MCI or SCI was higher in the newly onset group compared to the recovered group (20.7% vs. 12.2%). After adjusting for confounding factors, logistic regression models showed that the recovered group was not significantly associated with the risk of cognitive function decline (p=0.809), whereas both the newly onset and persistent depression groups showed statistically significant risks of MCI or SCI, compared to the never depressed group (adjusted aOR [aOR] 1.96; 95% CI 1.32-2.93 for the newly onset group, aOR 5.59; 95% CI 2.90-10.78 for the persistent depression group) (Table 2) Additionally, regarding the baseline comorbidities, cerebrovascular disease was associated with a higher risk of MCI or SCI (p=0.045).

Table 2. The effect of depression status on declined cognitive functiona

	MCI or SCI		SCI	
Depression Status	aORs (95% CI)	*p*-value	aORs (95% CI)	*p*-value
Never depressed	Ref		Ref	
Recovered	0.94 (0.55-1.60)	0.809	2.03 (0.55-7.57)	0.290
Newly onset	1.96 (1.32-2.93)	0.001	7.08 (2.99-16.74)	<0.001
Persistent depression	5.59 (2.90-10.78)	<0.001	10.35 (3.18-33.71)	<0.001

[a]Adjusted ORs (95% confidence intervals) were calculated with a multivariate logistic regression model for cognitive decline with all baseline characteristics in Table 1.
aOR, adjusted odds ratio; CI, confidence interval; MCI, mild cognitive impairment; Ref, reference; SCI, severe cognitive impairment.

Discussion

The study evaluated the extent of changes in the onset, recovery, and persistence of depressive states among middle-aged adults in Korea, and the association with cognitive function decline using nationally representative longitudinal panel data. Our study found that persistent depression had the most detrimental effect, and the newly onset depressive symptoms were also significantly associated with cognitive function decline. Notably, there was no significant association with cognitive function decline in patients who had recovered from depressive symptoms, akin to those who had never experienced depressive symptoms. This underscores the importance of not only preventing depressive symptoms in middle age but also effectively managing and controlling these symptoms to maintain cognitive function. The K-MMSE scores used in this study, known to be influenced by factors such as age, gender, and education level,[21] were adjusted for these various confounding factors. In addition to existing evidence, these findings are expected to offer valuable insights in preparing for a super-aging society.

Cognitive impairment and dementia have been widely reported as being associated with depressive disorders in many recent studies.[14,16,17] Similarly, the results of this study also show the risk of depressive symptoms on the occurrence of cognitive function decline. Specifically, our findings suggest a higher risk of cognitive function decline with persistent depression status, aligning with other studies.[10,16] Regarding the group recovered from depressive symptoms, our results indicated no significant risk of cognitive function decline compared to the never depressed group. However, this finding diverges from the results of other studies.[10] Such discrepancy might be attributed to differences in measuring cognitive function decline. According to a study by Kim *et al*.,[10] the recovered group was found to be associated with declines in cognitive function scores compared to the normal group. However, in our study, the recovered group did not show an increased risk of MCI or SCI. This suggests that while cognitive function scores may change significantly as depressive symptoms ameliorate, these score changes may not necessarily lead to SCI or MCI status, which are clinically significant. Further research is needed on cognitive function in patients who have recovered from depressive symptoms.

It is widely acknowledged that dementia is a progressive disease for which no curative medications are currently available. Therefore, preventing cognitive function decline is considered crucial for managing dementia, with various lifestyle factors and diseases identified as both risk and modifiable factors.[24-26] Specifically, this study considered the effects of patients' comorbidities—including cardiovascular, cerebrovascular, and psychiatric diseases—which can trigger cognitive impairment. By adjusting for these baseline comorbidities in the logistic model, the study found a significant risk associated with cerebrovascular disease and depression status in the decline of cognitive function. In the case of depression, growing evidence, including our results, suggests that it can be targeted for the prevention of dementia.[9] Notably, our results indicated that recovery from depressive symptoms was not significantly associated with the risk of developing MCI. Surprisingly, both animal and human studies[9] have suggested that antidepressants may play a significant role in preventing cognitive function decline through various mechanisms, including the promotion of neurogenesis, inhibition of pathologies related to amyloid-beta and tau proteins, and regulation of inflammatory responses. Indeed, a retrospective study[27] suggested that that chronic users of antidepressants were associated with a lower rate of dementia than short-term users. Furthermore, favorable effects on cognitive functions of SSRIs in MCI patients have been reported in randomized, controlled trials.[28] This suggests that, beyond their application in treating depression, antidepressants could be considered as part

of the treatment strategies for the prevention of cognitive function decline.

From a large-scale study[2] based on a nationally representative sample of the Korean population, it was found that the prevalence of depression, still underestimated, has steadily increased over a decade. Along with this, a considerable rate of non-adherence to depression treatment was reported among elderly patients with major depressive disorder (MDD) in Korea.[29] Poor adherence to antidepressants, resulting in negative outcomes in patients with MDD, is not uncommon.[30-32] Thus, adherence to antidepressant medications in the management of depression can be critical for the prevention of cognitive function decline. Evidence from systematic reviews and meta-analyses[33] suggests that pharmacist-led interventions have been effective in enhancing adherence to antidepressant medications. As South Korea, an aging society, currently faces an increasing disease burden due to dementia, the healthcare professionals, particularly pharmacists who are positioned to counsel patients, should focus on improving adherence to antidepressants to facilitate optimal medication outcomes, including the prevention of cognitive function decline.

Several limitations should be noted. First, this study used data from the KLoSA spanning for 2006 to 2012, which may be considered outdated. However, the K-MMSE scores, used to evaluate cognitive function in the study, were not available beyond the 7th wave of the survey. The sample size in later waves was also reduced due to participant dropout, leading us to rely on data from the first four waves. Second, because this study used panel survey data, potential biases due to the self-reported nature of the survey can be considered. The accuracy of information such as weight, height, income level, education, physical activity, smoking, and drinking included in our analysis cannot be assured. Moreover, as depressive symptoms and cognitive function decline were assessed based on self-reported scores such as CES-D and K-MMSE, respectively, the validity of depressive status and cognitive function decline might not be fully reliable. The K-MMSE, a tool frequently used in clinical settings and research since the 1970s, has limitations in presenting and measuring comprehensive cognitive function, and a newer version of K-MMSE has been released. Furthermore, given that the CES-D and K-MMSE scores were recorded biennially in the KLoSA survey, depressive symptoms or cognitive function decline may be transient. Therefore, our findings should be carefully interpreted. Third, there is a potential for selection bias in the study population. The subjects of this study were adults aged under 65 years with normal cognitive functions at the first survey who completed up to the fourth survey. This selection could lead to bias due to mortality, loss to follow-up, or missing information, which may limit the generalizability of our results.

Conclusion

This study evaluated the impact of depressive symptom status on the risk of cognitive function decline in the middle-aged population, aged 45 to under 65, using data from the KLoSA panel survey database. The analysis revealed that the newly onset or persistent depressive symptoms was associated with an increased risk of cognitive function decline, while recovery from depressive symptoms showed no significant association with cognitive function decline. These findings suggest that depressive symptoms could be promising for the prevention of cognitive function decline, underscoring the importance for healthcare professionals to focus on the management of depressive symptoms.

Acknowledgment

The present research was supported by the research fund of Dankook University in 2022.

Conflict of Interest

The author has no conflicts of interest to declare with regards to the contents of this study.

References

1. Hong JW, Noh JH Kim DJ. The prevalence of and factors associated with depressive symptoms in the korean adults: The 2014 and 2016 korea national health and nutrition examination survey. Soc Psychiatry Psychiatr Epidemiol 2021;56(4):659-70.
2. Kim GE, Jo MW, Shin YW. Increased prevalence of depression in south korea from 2002 to 2013. Sci Rep 2020;10(1):16979.
3. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. Lancet 2006;367(9524):1747-57.
4. Jang HY, Song YK, Kim JH, *et al.* Impact of depression on change in coronary heart disease risk status: The korean genome and epidemiology study (koges). Ther Clin Risk Manag 2018;14:121-8.
5. Baek SU, Yoon JH. Depressive symptomatology as a predictor of cognitive impairment: Evidence from the korean longitudinal study of aging (klosa), 2006-2020. Biomedicines 2023;11(10):2713.
6. Read JR, Sharpe L, Modini M, Dear BF. Multimorbidity and depression: A systematic review and meta-analysis. J Affect Disord

2017;221:36-46.
7. Mast BT, MacNeill SE, Lichtenberg PA. Post-stroke and clinically-defined vascular depression in geriatric rehabilitation patients. Am J Geriatr Psychiatry 2004;12(1):84-92.
8. Pariante CM, Lightman SL. The hpa axis in major depression: Classical theories and new developments. Trends Neurosci 2008;31(9):464-8.
9. Dafsari FS, Jessen F. Depression-an underrecognized target for prevention of dementia in alzheimer's disease. Transl Psychiatry 2020;10(1):160.
10. Kim JH, Kim Y, Kwon J, Park EC. Association between changes in depressive state and cognitive function. Int J Environ Res Public Health 2019;16(24):4944.
11. OCED. Elderly Population (Indicator) 2023. Available from https://doi.org/10.1787/8d805ea1-en. Accessed August 16, 2023.
12. Bora E, Harrison BJ, Yücel M, Pantelis C. Cognitive impairment in euthymic major depressive disorder: A meta-analysis. Psychol Med 2013;43(10):2017-26.
13. Semkovska M, Quinlivan L, O'Grady T, *et al.* Cognitive function following a major depressive episode: A systematic review and meta-analysis. Lancet Psychiatry 2019;6(10):851-61.
14. Snyder HR. Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review. Psychol Bull 2013;139(1):81-132.
15. Rock PL, Roiser JP, Riedel WJ, Blackwell AD. Cognitive impairment in depression: A systematic review and meta-analysis. Psychol Med 2014;44(10):2029-40.
16. Kim D. Effects of depression on changes in cognitive function in older adults: A fixed-effects model analysis using the korean longitudinal study of aging (klosa). Alzheimer Dis Assoc Disord 2022;36(4):319-26.
17. Rosness TA, Barca ML, Engedal K. Occurrence of depression and its correlates in early onset dementia patients. Int J Geriatr Psychiatry 2010;25(7):704-11.
18. Fatima K, Mehendale AM, Reddy H. Young-onset dementia and neurodegenerative disorders of the young with an emphasis on clinical manifestations. Cureus 2022;14(10):e30025.
19. Health Insurance Review & Assessment Service. Analysis of treatment status for depression and anxiety disorders over the last five years (2017-2021) 2022. Available from https://www.hira.or.kr/bbsDummy.do?pgmid=HIRAA020041000100&brdScnBltNo=4&brdBltNo=10627&pageIndex=1. Accessed September 20, 2023.
20. Kim S, Kim Y, Park SM. Body mass index and decline of cognitive function. PLoS One 2016;11(2):e0148908.
21. Kim S, Shin S, Yoo H, *et al.* Impact of weight change on decline of cognitive function among korean adults. Korean J Clin Pharm 2019;29(4):238-46.
22. Jang SN, Kawachi I, Chang J, *et al.* Marital status, gender, and depression: Analysis of the baseline survey of the korean longitudinal study of ageing (klosa). Soc Sci Med 2009;69(11):1608-15.
23. Otto E, Culakova E, Meng S, *et al.* Overview of sankey flow diagrams: Focusing on symptom trajectories in older adults with advanced cancer. J Geriatr Oncol 2022;13(5):742-6.
24. Coley N, Giulioli C, Aisen PS, Vellas B, Andrieu S. Randomised controlled trials for the prevention of cognitive decline or dementia: A systematic review. Ageing Res Rev 2022;82:101777.
25. Zhang Y, Chen SD, Deng YT, *et al.* Identifying modifiable factors and their joint effect on dementia risk in the uk biobank. Nat Hum Behav 2023;7(7):1185-95.
26. Yu JT, Xu W, Tan CC, *et al.* Evidence-based prevention of alzheimer's disease: Systematic review and meta-analysis of 243 observational prospective studies and 153 randomised controlled trials. J Neurol Neurosurg Psychiatry 2020;91(11):1201-9.
27. Kessing LV, Søndergård L, Forman JL, Andersen PK. Antidepressants and dementia. J Affect Disord 2009;117(1-2):24-9.
28. Mowla A, Mosavinasab M, Pani A. Does fluoxetine have any effect on the cognition of patients with mild cognitive impairment? A double-blind, placebo-controlled, clinical trial. J Clin Psychopharmacol 2007;27(1):67-70.
29. Lee KJ, Lee YJ. Adherence to antidepressants in Korean elderly patients with major depressive disorder. Korean J Clin Pharm 2023;33(1):62-9.
30. Keyloun KR, Hansen RN, Hepp Z, Gillard P, Thase ME, Devine EB. Adherence and persistence across antidepressant therapeutic classes: A retrospective claims analysis among insured us patients with major depressive disorder (mdd). CNS Drugs 2017;31(5):421-32.
31. Sawada N, Uchida H, Suzuki T, *et al.* Persistence and compliance to antidepressant treatment in patients with depression: A chart review. BMC Psychiatry 2009;9:38.
32. Prukkanone B, Vos T, Burgess P, Chaiyakunapruk N, Bertram M. Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in thailand. BMC Psychiatry 2010;10:64.
33. Readdean KC, Heuer AJ, Scott Parrott J. Effect of pharmacist intervention on improving antidepressant medication adherence and depression symptomology: A systematic review and meta-analysis. Res Social Adm Pharm 2018;14(4):321-31.