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Original Article

Modifiable risk factors for early- and late-onset dementia using the Korean national health insurance service database

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ABSTRACT

Background: Early-onset dementia (EOD) and late-onset dementia (LOD) may have distinct modifiable risk-factor profiles.

Objective: To identify and compare factors associated with EOD and LOD using a nationwide cohort database.

Design: Nationwide two nested case-control studies.

Setting: We used the National Health Insurance Service-National Sample Cohort database (2004–2019).

Participants: The initial sample size was 514,866; 5157 EOD and 39,326 LOD cases were matched 1:1 with controls based on age, sex, and the Charlson Comorbidity Index.

Measurements: Socioeconomic status, residential area, body mass index, alcohol consumption, smoking status, physical activity, blood pressure, and laboratory findings were analyzed. Multivariable logistic regression models were used to identify the risk factors.

Results: Higher socioeconomic status and increased frequency of physical activity were associated with a lower risk of both EOD and LOD. Rural residence, heavy alcohol consumption, and higher fasting blood sugar levels were associated with an increased risk of LOD, although there was no significant association with EOD. Overall, these factors impacted LOD more strongly than EOD. Demographic and lifestyle factors had a greater effect on LOD than blood pressure and relevant laboratory findings.

Conclusion: Modifiable risk factors were associated with LOD and EOD. The influence of some modifiable risk factors was more pronounced in the LOD group than in the EOD group. Identifying modifiable risk factors associated with dementia can aid in the development of preventive strategies, underscoring the clinical importance of our findings.

1. Introduction

Dementia is characterized by a decline in cognitive function (e.g., memory, language, problem-solving, and other thinking skills), which ultimately impacts an individual's ability to perform daily activities [1]. It poses a substantial global health challenge and burden, with a rapidly growing prevalence owing to an aging population [2]. Dementia is classified based on the age of onset, with early-onset dementia (EOD) occurring before 65 years of age and late-onset dementia (LOD) occurring at or after 65 years [3]. Although EOD and LOD share similar clinical manifestations, their underlying etiologies and risk factor profiles may differ [4].

Numerous studies have attempted to identify risk factors for dementia, aiming to develop effective prevention and intervention strategies [5]. These risk factors can be broadly categorized as nonmodifiable (e.g., age and genetics) or modifiable (e.g., lifestyle and environmental factors). Modifiable risk factors are of particular interest, as they offer potential targets for interventions to delay or prevent dementia onset. The association between dementia and various modifiable factors, including socioeconomic status (SES), lifestyle choices (e.g., physical activity, alcohol consumption, and smoking), and metabolic health indicators, has been extensively explored [6,7].

Despite considerable progress in the understanding of dementia risk factors, certain knowledge gaps, particularly regarding EOD, are yet to

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be addressed [8]. Although LOD has been extensively studied, research on modifiable risk factors for EOD remains relatively limited, owing to its lower prevalence and distinct characteristics. Moreover, few studies have directly compared the risk factors for EOD and LOD, leaving uncertainties regarding the similarities and differences in their modifiable risk profiles.

In the current study, we investigated the impact of modifiable risk factors on EOD and LOD using a nationwide cohort database. We aimed to identify and compare modifiable risk factors associated with both types of dementia and to identify differences in the magnitude and direction of associations between these factors and EOD versus LOD. By addressing these objectives, we aimed to deepen our understanding of the modifiable risk factors contributing to EOD and LOD, ultimately leading to the development of targeted prevention and intervention strategies.

2. Materials and methods

2.1. Data source

We used a large population-based national sample cohort from the National Health Insurance Service of South Korea (NHIS-Sample Cohort Database 2.2) [9]. This sample database contains approximately half a million research subjects, representing 1 % of the total population, extracted by stratified sampling according to age, sex, location, insurance premium, and subscription type. It includes qualifications, medical treatment, health screening, and clinical and long-term care data from 2002 to 2019.

This study was reviewed and approved by the Institutional Review Board of the National Health Insurance Service, Ilsan Hospital (approval number: 2024-03-001). The need for informed consent was waived owing to the retrospective nature of the study design and the lack of identifiable individual information in the database. This study was conducted in compliance with the principles of the Declaration of Helsinki.

2.2. Study design and outcomes

We performed two nested case-control studies: the EOD group and its corresponding control group and the LOD group and its corresponding control group. We defined 2002 and 2003 as the pre-enrollment periods to exclude previously claimed dementia diagnosis codes. Lifestyle factors can change after the onset of dementia. In addition, the primary focus of the study was to analyze modifiable risk factors prior to disease onset; hence, we excluded patients who had already been diagnosed with dementia. The data on baseline characteristics was from 2004, and the occurrence of dementia was observed until December 2019. Supplementary Figure 1 presents a flowchart of the participants included in this study. During this period, 54,289 individuals from among the initial sample of 514,866 were identified as having dementia based on the International Classification of Disease-10 codes; the remaining 460,577 individuals were classified as controls. Exclusion criteria were as follows: 1) the presence of a Parkinson's disease accompanied by a dementia-related diagnosis code without a prescription for dementia-related medications (donepezil, galantamine, rivastigmine, and memantine); 2) dementia diagnosis during the pre-enrollment period; 3) missing demographic information; and 4) propensity score matching failure. Among individuals diagnosed with dementia, those diagnosed before the age of 65 were classified into the EOD group, whereas those diagnosed at ≥ 65 were classified into the LOD group. The types of dementia according to EOD and LOD are presented in Supplementary Table 1.

2.3. Variable definitions

Herein, covariates were defined as described by Omura et al. [10]. Age was calculated as of January 1, 2004. Given that the Charlson Comorbidity Index (CCI) needs to be defined based on comorbidities within

a specific period, we calculated the comorbidity score based on outpatient and inpatient diagnoses at hospitals between 2002 and 2005 [11]. Because mandatory health screenings are conducted biannually in Korea, we used the health examination information closest to January 1, 2004, to establish baseline characteristics. Information on patients diagnosed with dementia before 2004 was removed; however, this was not applicable to participants in this study.

We used the SES and residential areas identified in the qualification data as demographic factors. SES was defined as low, middle, or high by distinguishing an individual's insurance premium quintile. The qualification data specify the medical aid and national health insurance groups and are presented in 10 quintiles with the national health insurance group according to the insurance premium. We defined the Medical Aid group and insurance premium quintiles 1–3 as low SES, 4–7 as middle SES, and 8–10 as high SES. Residential areas were defined as urban if the participant lived in Seoul, other metropolitan cities, or Sejong (a self-governing city); otherwise, they were defined as rural areas.

Body mass index (BMI), alcohol consumption, smoking, and physical activity were considered lifestyle factors. The health screening data included self-reported information on alcohol consumption, smoking, and physical activity, as well as measured BMI data, which were defined as lifestyle variables. BMI was categorized as underweight ($< 18.5 \text{ kg/m}^2$), normal ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 23 \text{ kg/m}^2$), overweight ($23 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), and obese ($\geq 25 \text{ kg/m}^2$) using the Asian-specific BMI category. Alcohol consumption was classified as non-drinker, social drinker (1–4 times per week), or heavy drinker (≥ 5 times per week). Smoking was defined as a non-smoker, quitter, or current smoker, as reported by the participant during health screening. The frequency of physical activity was defined as the number of days per week during which the subject reported engaging in at least 30 min of mild-to-moderate physical activity.

In addition to demographic and lifestyle factors, we considered systolic/diastolic blood pressure and laboratory findings as potential covariates. We obtained information regarding blood pressure measurements and laboratory test results (urine protein, hemoglobin, fasting blood sugar, total cholesterol, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase) from the health screening data of the NHIS-Sample Cohort Database.

2.4. Statistical analysis

This nested case-control study applied propensity score matching to match cases and controls. Propensity score matching was conducted in a 1:1 ratio, and variables such as age, sex, and CCI, excluding dementia, were utilized. While matching with multiple controls can increase statistical power, the gains may diminish with increasing numbers of controls, especially in large cohorts [12]. Considering the expected dementia incidence in the Korean population and desired statistical power, we determined that a 1:1 matching would not substantially reduce power. In SAS, we utilized 'PROC PSMATCH' with the following options: METHOD = GREEDY ($K = 1$); caliper = 0.5; and exact for age, sex, and CCI (excluding dementia). Given the abundance of controls compared with available cases, we were able to achieve a 1:1 match with groups that were exactly matched on the covariates, not based on propensity scores. We then analyzed the matched data using conditional logistic regression in 'PROC LOGISTIC' with strata for the matching ID to identify risk factors for EOD and LOD. Each lifestyle factor of interest was independently applied in a separate model. Continuous variables are expressed as mean \pm standard deviation, with variables compared between groups using the paired *t*-test. Categorical variables are described as frequency (proportion), with the McNemar test used to compare the groups. Each model was adjusted for age, sex, and CCI score, excluding dementia, blood pressure, and laboratory findings, with adjusted odds ratio (aOR) calculated for each variable. We performed a complete case analysis, and the numbers of patients with each variable are provided

Table 1
Baseline characteristics of patients with early-onset dementia and the respective control group.

Variables ^a	Early-onset dementia (n = 5157)	Control (n = 5157)	p-value
Age, years	51.49 ± 5.39	51.49 ± 5.39	>0.999
Male, n (%)	2324 (45.07)	2324 (45.07)	>0.999
Charlson comorbidity index [†]	1.36 ± 1.28	1.36 ± 1.28	>0.999
Body mass index, kg/m ²	23.99 ± 3.02	24.15 ± 2.95	0.004
Socioeconomic status, n (%)			<0.001
Low	1154 (22.38)	1028 (19.93)	
Middle	1859 (36.05)	1772 (34.36)	
High	2144 (41.58)	2357 (45.71)	
Residential area, n (%)			0.133
Urban	2746 (53.25)	2670 (51.77)	
Rural	2411 (46.75)	2487 (48.23)	
Alcohol consumption [‡] , n (%)			0.006
None	3074 (59.66)	2973 (57.66)	
Social	1868 (36.25)	2009 (38.96)	
Heavy	211 (4.10)	174 (3.38)	
Smoking, n (%)			0.015
None	3707 (71.88)	3637 (70.53)	
Quitter	376 (7.29)	398 (7.72)	
Current	1074 (20.83)	1122 (21.76)	
Physical activity frequency [§] , n/week	4.08 ± 2.61	4.26 ± 2.54	0.001
Systolic blood pressure, mmHg	125.18 ± 18.11	125.50 ± 17.64	0.349
Diastolic blood pressure, mmHg	78.91 ± 11.89	79.16 ± 11.73	0.264
Urine protein, positives	1.07 ± 0.39	1.06 ± 0.36	0.524
Hemoglobin, g/d	13.78 ± 1.52	13.82 ± 1.52	0.155
Fasting blood sugar, mg/d	98.46 ± 36.58	98.14 ± 35.21	0.646
Total cholesterol, mg/dL	200.56 ± 39.37	201.08 ± 38.68	0.488
Aspartate aminotransferase, U/L	27.22 ± 16.84	26.10 ± 15.92	<0.001
Alanine aminotransferase, U/L	26.30 ± 21.60	25.77 ± 19.85	0.171
Gamma-glutamyl transferase, U/L	40.68 ± 69.45	36.70 ± 53.58	<0.001

^a Continuous variables are expressed as mean ± standard deviation and categorical variables are described as frequency (proportion). The variables used for matching were age, gender, and Charlson comorbidity index.

[†] Comorbidities excluding dementia.

[‡] Classified as non-consumer, social (1–4 times per week), or heavy (≥ 5 times per week). (self-report).

[§] Days per week engaged in at least 30 min of mild-to-moderate physical activity (self-report): 1 (no exercise), 2 (1–2 times/week), 3 (3–4 times/week), 4 (5–6 times/week), and 5 (more than 6 times/week). || 1 (negative), 2 (trace), 3 (positive +1), 4 (positive +2), 5 (positive +3), 6 (positive +4).

in Supplementary Table 2. Data analyses were performed using the SAS Enterprise Guide (version 7.15; SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Baseline characteristics

The final sample included 5157 EOD cases and 39,326 LOD cases. Dementia diagnosis codes and patient distributions are presented in Supplementary Table 1. Most identified cases of LOD were associated with AD, while EOD was relatively heterogeneous in terms of the dementia type.

Table 1 presents the characteristics of the EOD and control groups. The EOD group had a significantly lower mean BMI ($p = 0.004$) and a higher proportion of individuals in lower SES categories than the control group ($p < 0.001$). Additionally, the EOD group had significantly higher proportions of both non-drinkers and heavy drinkers than the control group ($p = 0.006$). The mean physical activity frequency was significantly lower in the EOD group than in the control group ($p = 0.001$).

Table 2 shows the characteristics of the LOD and control groups. The BMI did not differ significantly between the two groups. However, similar to the EOD group, the LOD group had a higher proportion of individuals in the lower SES category than the control group ($p < 0.001$). The LOD group also had a slightly higher proportion of urban residents ($p < 0.001$) and heavy drinkers ($p < 0.001$). The mean frequency of physical activity was significantly lower in the LOD group than in the control group ($p < 0.001$). The LOD group had significantly lower systolic blood pressure ($p = 0.023$) and higher fasting blood sugar levels than the control group ($p < 0.001$).

3.2. Risk factor analysis

Table 3 presents modifiable risk factors associated with EOD. The group with the highest BMI had a significantly lower risk of EOD (aOR, 0.875; 95 % confidence interval [CI], 0.797–0.961; $p < 0.001$). The high SES group had a significantly lower risk of EOD (aOR, 0.805; 95 % CI, 0.725–0.893; $p < 0.001$), and the social drinker group had a lower risk of EOD than other alcohol habit groups (aOR, 0.879; 95 % CI, 0.802–0.964; $p = 0.002$). Meanwhile, the higher the physical activity frequency, the lower the risk of EOD (aOR, 0.969; 95 % CI, 0.951–0.988; $p = 0.001$).

Table 4 presents modifiable risk factors associated with the occurrence of LOD. Considering BMI, the underweight (aOR, 0.880; 95 % CI, 0.817–0.949; $p < 0.001$), overweight (aOR, 0.959; 95 % CI, 0.924–0.994; $p = 0.023$), and obese (aOR, 0.967; 95 % CI, 0.935–1.000; $p = 0.049$) groups had a lower risk of LOD than the normal weight group. Similar to EOD, the high SES group had a significantly lower risk of LOD (aOR, 0.936; 95 % CI, 0.904–0.968; $p < 0.001$). Meanwhile, urban residence was associated with a significantly reduced risk of LOD (aOR, 0.878; 95 % CI, 0.852–0.904; $p < 0.001$). Heavy alcohol consumption was associated with a significantly elevated risk of LOD (aOR, 1.130; 95 % CI, 1.058–1.208; $p < 0.001$). Similar to EOD, a higher frequency of physical activity was associated with a lower risk of LOD (aOR, 0.947; 95 % CI, 0.938–0.956; $p < 0.001$). Finally, higher fasting blood sugar level was associated with a higher risk of LOD (aOR, 1.001; 95 % CI, 1.000–1.001; $p < 0.001$).

Fig. 1 presents a forest plot summarizing the modifiable risk factors, confirming the degree to which these factors influence the development of EOD and LOD. Overall, modifiable risk factors strongly impacted LOD.

Table 2
Baseline characteristics of patients with late-onset dementia and the respective control group.

Variables*	Late-onset dementia (n = 39,326)	Control (n = 39,326)	p-value
Age, years	67.77 ± 6.41	67.77 ± 6.41	>0.999
Male, n (%)	14,977 (38.08)	14,977 (38.08)	>0.999
Charlson comorbidity index [†]	1.53 ± 1.32	1.53 ± 1.32	>0.999
Body mass index, kg/m ²	23.91 ± 3.19	23.92 ± 3.20	0.552
Socioeconomic status, n (%)			<0.001
Low	11,577 (29.44)	11,304 (28.74)	
Middle	12,480 (31.74)	12,095 (30.76)	
High	15,269 (38.83)	15,927 (40.50)	
Residential area, n (%)			<0.001
Urban	26,072 (66.30)	24,921 (63.37)	
Rural	13,254 (33.70)	14,405 (36.63)	
Alcohol consumption [‡] , n (%)			<0.001
None	28,774 (73.38)	28,725 (73.30)	
Social	8214 (20.95)	8493 (21.67)	
Heavy	2227 (5.68)	1971 (5.03)	
Smoking, n (%)			0.385
None	30,994 (78.81)	30,903 (78.58)	
Quitter	2455 (6.24)	2558 (6.51)	
Current	5877 (14.94)	5865 (14.91)	
Physical activity frequency [§] , n/week	3.45 ± 2.80	3.91 ± 2.76	<0.001
Systolic blood pressure, mmHg	133.09 ± 19.63	133.40 ± 19.62	0.023
Diastolic blood pressure, mmHg	80.75 ± 11.86	80.92 ± 11.90	0.050
Urine protein	1.08 ± 0.41	1.09 ± 0.44	0.013
Hemoglobin, g/dL	13.49 ± 1.38	13.50 ± 1.39	0.082
Fasting blood sugar, mg/dL	103.56 ± 40.71	102.30 ± 39.45	<0.001
Total cholesterol, mg/dL	203.93 ± 40.22	204.21 ± 40.23	0.307
Aspartate aminotransferase, U/L	27.68 ± 18.19	27.57 ± 18.48	0.427
Alanine aminotransferase, U/L	23.91 ± 18.86	23.80 ± 18.64	0.412
Gamma-glutamyl transferase, U/L	33.08 ± 53.62	32.63 ± 50.97	0.223

* Continuous variables are expressed as mean ± standard deviation and categorical variables are described as frequency (proportion). The variables used for matching were age, gender, and Charlson comorbidity Index.

[†] Comorbidities excluding dementia.

[‡] Classified as non-consumer, social (1–4 times per week), or heavy (≥ 5 times per week). (self-report).

[§] Days per week engaged in at least 30 min of mild-to-moderate physical activity (self-report): 1 (no exercise), 2 (1–2 times/week), 3 (3–4 times/week), 4 (5–6 times/week), and 5 (more than 6 times/week).

^{||} 1 (negative), 2 (trace), 3 (positive +1), 4 (positive +2), 5 (positive +3), 6 (positive +4).

Table 3
Association between modifiable risk factors and the incidence of early-onset dementia.

Variables	aOR*	95 % CI	p-value
Body mass index, kg/m ²			
Normal weight	Reference		
Underweight	1.284	0.966–1.708	0.085
Overweight	0.985	0.892–1.088	0.391
Obesity	0.875	0.797–0.961	<0.001
Socioeconomic status			
Low	Reference		
Middle	0.933	0.838–1.039	0.357
High	0.805	0.725–0.893	<0.001
Urban residence	0.942	0.872–1.018	0.133
Alcohol intake			
None	Reference		
Social	0.879	0.802–0.964	0.002
Heavy	1.149	0.928–1.422	0.055
Smoking			
None	Reference		
Quitter	0.895	0.762–1.051	0.421
Current	0.906	0.806–1.020	0.477
Physical activity frequency, n/week	0.969	0.951–0.988	0.001
Systolic blood pressure, mmHg	0.999	0.997–1.001	0.349
Diastolic blood pressure, mmHg	0.998	0.995–1.001	0.264
Hemoglobin, g/dL	0.976	0.944–1.009	0.156
Fasting blood sugar, mg/dL	1.000	0.999–1.001	0.646
Total cholesterol, mg/dL	1.000	0.999–1.001	0.488

* Adjusted for age, sex, and Charlson comorbidity index. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

Table 4
Association between modifiable risk factors and the incidence of late-onset dementia.

Variables	aOR*	95 % CI	p-value
Body mass index, kg/m ²			
Normal weight	Reference		
Underweight	0.880	0.817–0.949	<0.001
Overweight	0.959	0.924–0.994	0.023
Obesity	0.967	0.935–1.000	0.049
Socioeconomic status			
Low	Reference		
Middle	1.008	0.972–1.045	0.112
High	0.936	0.904–0.968	<0.001
Urban residence	0.878	0.852–0.904	<0.001
Alcohol intake			
None	Reference		
Social	0.967	0.931–1.004	0.445
Heavy	1.130	1.058–1.208	<0.001
Smoking			
None	Reference		
Quitter	0.948	0.891–1.008	0.108
Current	0.992	0.949–1.037	0.444
Physical activity frequency, n/week	0.947	0.938–0.956	<0.001
Systolic blood pressure, mmHg	0.999	0.998–1.000	0.023
Diastolic blood pressure, mmHg	0.999	0.998–1.000	0.050
Hemoglobin, g/dL	0.989	0.978–1.001	0.082
Fasting blood sugar, mg/dL	1.001	1.000–1.001	<0.001
Total cholesterol, mg/dL	1.000	0.999–1.000	0.307

* Adjusted for age, sex, and Charlson Comorbidity Index. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

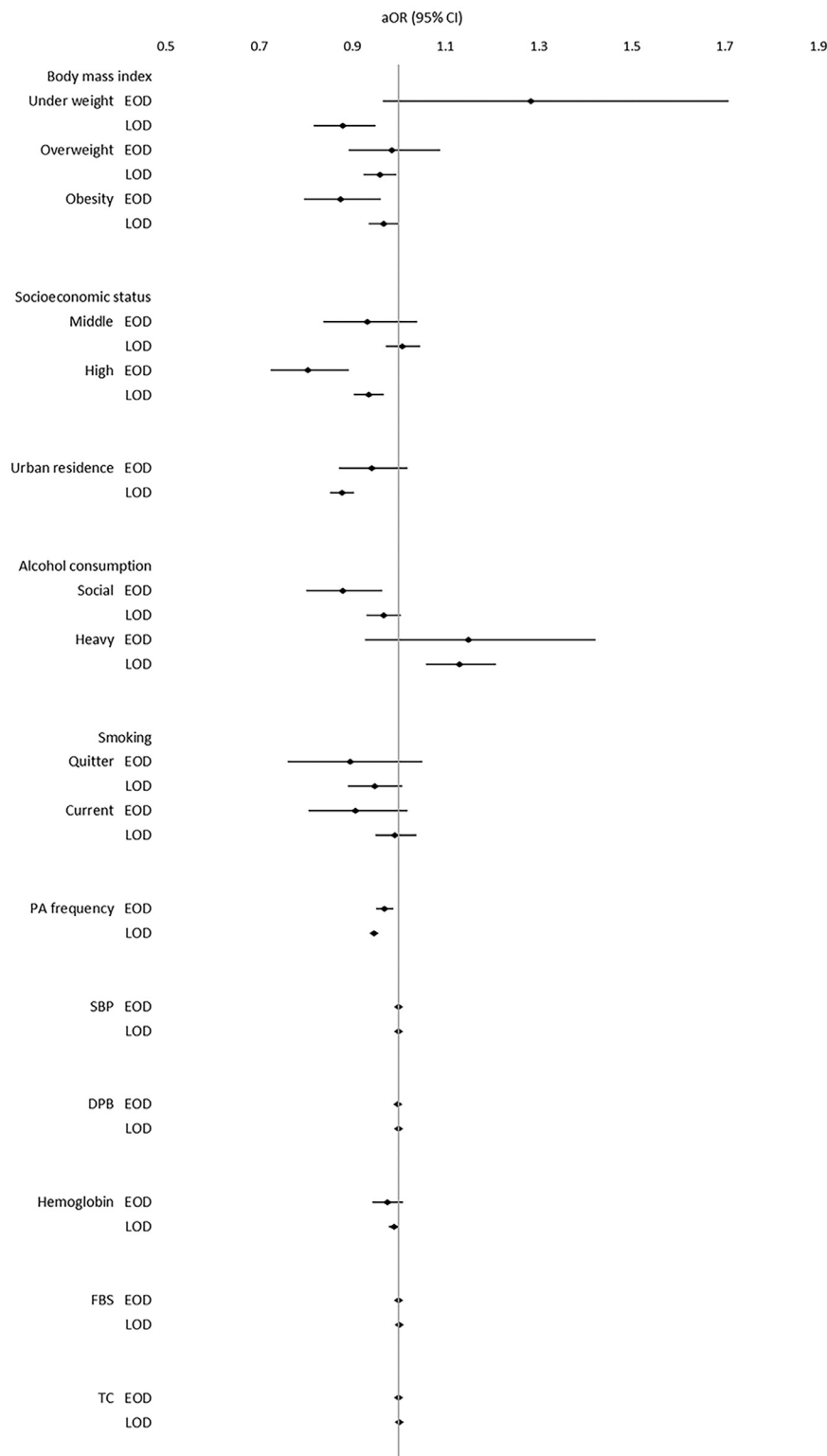


Fig. 1. A forest plot summarizing the risk of environmental and lifestyle factors on the occurrence of early- and late-onset dementia. Models were adjusted for age, sex, and Charlson comorbidity index. The modifiable risk factors are less strongly related to early-onset dementia than late-onset dementia.

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; EOD, early onset dementia; FBS, fasting blood sugar; LOD, late-onset dementia; PA, physical activity; SBP, systolic blood pressure; TC, total cholesterol.

Moreover, demographic and lifestyle factors had a greater effect on LOD than blood pressure and relevant laboratory findings.

4. Discussion

In this study, we investigated the effects of modifiable risk factors on the development of EOD and LOD. Our results demonstrated that various demographic and lifestyle factors were associated with both

EOD and LOD, with LOD showing a stronger association with these factors than EOD. Higher SES and increased frequency of physical activity were consistently associated with a lower risk of both EOD and LOD.

Our study utilized a population-based sample database from Korea, which facilitated a prolonged observation period and reliable information on each variable through qualification and health screening data. The use of a nationwide database enabled the analysis of a relatively

larger number of EOD and LOD cases when compared with previous studies, enhancing the value of our findings, especially considering the scarcity of large-scale studies on EOD.

Typically, low SES, physical inactivity, increased alcohol consumption and smoking, high blood pressure, and metabolic diseases (e.g., diabetes and dyslipidemia) have been identified as risk factors for dementia [10,13]. Our results are broadly consistent with these findings, confirming that higher SES and increased frequency of physical activity can decrease the risk of both EOD and LOD. In addition, rural residence, heavy alcohol consumption, and elevated fasting blood sugar levels were associated with an increased risk of LOD. Lifestyle factors have been recognized as risk factors for EOD, metabolic diseases, and alcohol consumption [14]. Although the results of the LOD group were relatively consistent with those of previous studies, we observed that these factors had a lower impact on EOD than on LOD. This difference may be attributed to the characteristics of EOD; it is relatively heterogeneous, and the etiologies are more closely linked to pathophysiological changes caused by genetic or organic factors [15,16]. In contrast, LOD, a late-onset disease, is exposed to demographic- and lifestyle-related factors for a longer duration, which may explain our results. However, our findings partially contradict those of Li et al. [17], who recently reported a greater magnitude of risk factors, such as low SES and an unhealthy lifestyle, in EOD than in LOD in a large-scale study using the UK Biobank database. This discrepancy stems from differences in variable definitions and ethnicities owing to the distinct databases employed. Furthermore, while the UK Biobank study analyzed 502 EOD and 5768 LOD cases, our study analyzed approximately six times more cases in each group, which may have contributed to the differing results. Future efforts, including multi-ethnic studies, are required to address this knowledge gap.

In Korea, the risk factors for dementia have been previously explored. Using nationwide Korean cohort data for individuals over 65 years of age, Hwangbo et al. [18] reported physical inactivity, diabetes, and hypertension as the top modifiable risk factors for dementia. However, the authors only analyzed the LOD and found no significant association with obesity, SES, residential area, or alcohol consumption. These inconsistencies may be due to the use of the NHIS-Sample Cohort Database, which contains more detailed information on lifestyle and demographic factors than their database. Chun et al. [19] also conducted a related study using data from the Korean National Health Insurance Database. The authors simultaneously analyzed the incidence and mortality risks of both EOD and LOD, reporting that diabetes, osteoporosis, hypertension, and atrial fibrillation were associated with EOD and LOD, whereas dyslipidemia exerted protective effects. However, their study focused primarily on medical factors and did not extensively explore the roles of demographic and lifestyle factors, which is a key difference from our research. To our knowledge, our study focused more on the impact of modifiable risk factors on the development of EOD and LOD than previous Korean studies.

This study had several limitations that need to be addressed. First, as this was a retrospective study using a sample cohort, we could not establish causality between modifiable risk factors and dementia. Second, while our study included more patients with EOD than previous studies, the sample size imbalance between the EOD and LOD groups may have influenced our results. Third, the nature of the database limits the availability of detailed clinical information, resulting in a lack of variable diversity and hindering the consideration of detailed clinical contexts. Additionally, owing to the limitations of the database, we were unable to analyze factors such as air pollution and educational level [20,21], which were found to be highly relevant in previous studies. Nevertheless, it is essential to note that we conducted long-term follow-up observations and reliably obtained information such as SES and residential areas by utilizing the strengths of the National Health Insurance Service database. Finally, our study did not differentiate between EOD and LOD subtypes.

5. Conclusions

This study analyzed modifiable risk factors influencing the incidence of EOD and LOD. Higher SES and increased frequency of physical activity were found to lower the risk of both EOD and LOD. Rural residence, heavy alcohol consumption, and higher fasting blood sugar were associated with an increased risk of LOD but not EOD. Accordingly, modifiable risk factors appear to exert a greater influence on LOD than on EOD. One strength of this study was the utilization of a large-scale population database. The identification of modifiable risk factors associated with dementia can contribute to the development of preventive strategies, which highlights the clinical importance of our findings. Finally, future research, such as multi-ethnic studies, is needed to address the knowledge gaps regarding dementia risk factors.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.tjpad.2024.100032](https://doi.org/10.1016/j.tjpad.2024.100032).

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