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ORIGINAL RESEARCH

Cognitive impairment risk in patients with rheumatoid arthritis: a population-based cohort study

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To cite: Kwon OC, Lee HS, Yang HJ, *et al*. Cognitive impairment risk in patients with rheumatoid arthritis: a population-based cohort study. *RMD Open* 2026;**12**:e006685. doi:10.1136/rmdopen-2025-006685

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/rmdopen-2025-006685).

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Received 31 December 2025
Accepted 29 March 2026

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ABSTRACT

Background This study aimed to evaluate the incidence rate and incident cognitive impairment risk in patients with rheumatoid arthritis (RA) compared with matched controls.

Methods This population-based matched cohort study enrolled patients newly diagnosed with RA (n=26 437) between 2011 and 2014 and 1:1 age-, sex- and index-year-matched controls (n=26 437) from a Korean nationwide claims database. Follow-up spanned the index date to the earliest occurrence of incident cognitive impairment or December 2022. Cognitive impairment was defined using the International Classification of Diseases, 10th Revision, codes (F00-F03, F31.82, F06.7, G30 and G31.00). Incidence rates were calculated as events per 1000 person-years. Multivariable stratified competing risks regression analyses estimated adjusted subdistribution HRs (SHRs) with 95% CIs for incident cognitive impairment, treating death as a competing risk.

Results During the mean respective follow-up of 9.410±2.271 and 9.508±2.217 years, 2952 (11.17%) and 2388 (9.03%) patients with RA and controls developed incident cognitive impairment, respectively. The cognitive impairment incidence rates in patients with RA and controls were 11.493 (95% CI 7.648 to 15.338) and 9.219 (95% CI 5.386 to 13.052) per 1000 person-years, respectively. Compared with the control individuals, patients with RA had a significantly higher risk of developing cognitive impairment (adjusted SHR, 1.222 (95% CI 1.171 to 1.275)).

Conclusions These findings suggest that cognitive impairment may represent an important comorbidity in patients with RA that merits clinical awareness and longitudinal monitoring.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous epidemiological studies examining the association between rheumatoid arthritis (RA) and cognitive impairment have yielded inconsistent results, with limited evidence from large-scale population-based studies.

WHAT THIS STUDY ADDS

⇒ Using a nationwide, population-based matched cohort, we showed that the incidence of cognitive impairment was higher in patients with RA than in matched controls, at 11.493 (95% CI 7.648 to 15.338) versus 9.219 (95% CI 5.386 to 13.052) per 1000 person-years, respectively.

⇒ The adjusted risk of cognitive impairment was significantly higher in patients with RA than in the matched controls, as estimated based on stratified competing risks regression analyses (adjusted subdistribution HR (SHR), 1.222 (95% CI 1.171 to 1.275)).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Given the significantly higher adjusted subdistribution SHR obtained for patients with RA compared with controls, cognitive impairment may represent a clinically relevant comorbidity that merits risk stratification and longitudinal patient management.

⇒ Future research should investigate the mechanisms underlying cognitive impairment, including the role of systemic inflammation and disease activity, and assess preventive or therapeutic strategies.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by joint synovium inflammation, which leads to progressive joint destruction.[1] Owing to the chronic nature of RA, a substantial proportion of patients develop various comorbidities that adversely affect their long-term outcomes.[2 3] Depression is among the most common comorbidities, affecting 15%–32% of patients,[2 3] with cognitive impairment being recognised as a further important comorbidity that has emerged as a growing concern in patients with RA. This impairment encompasses a spectrum of cognitive decline, ranging from mild cognitive impairment to clinically diagnosed dementia, including Alzheimer's disease and vascular dementia.[4–6] Even when mild, cognitive impairment is closely associated with less frequent treatment compliance and reduced functional capacity, as well as a diminished quality of life in patients with RA.[4 7 8] Cognitive impairment adversely affects medication adherence,

potentially leading to less favourable outcomes.[9] Therefore, it is important to accurately assess the burden of cognitive impairment, including its incidence and risk, in patients with RA.

Despite the clear clinical relevance of cognitive impairment in RA, the epidemiological evidence linking them remains inconsistent. Previous cohort, cross-sectional and case-control studies investigating the epidemiology of cognitive impairment in patients with RA have reported conflicting findings. Some studies have suggested a potential association, whereas others have reported no significant relationship between RA and cognitive impairment.[10–12] Therefore, uncertainty persists regarding whether patients with RA truly have an increased risk of cognitive impairment compared with the general population, highlighting the need for large-scale population-based studies to clarify the incidence and risk of cognitive impairment in patients with RA.

In this study, we aimed to investigate the incidence rate and risk of cognitive impairment in patients with RA compared with those of matched controls using a nationwide population-based cohort.

METHODS

Database

Data were extracted from the Korean National Health Insurance Service (NHIS) claims database, which covers approximately 97% of the South Korean population. A detailed profile of this database has been described previously.[13] The NHIS claims database contains comprehensive information on demographics, socioeconomic status, medical treatments and procedures, and disease diagnoses, which are recorded using the Korean Standard Classification of Diseases, a diagnostic coding system based on the International Classification of Diseases, 10th Revision (ICD-10).

Study design

From the NHIS database, patients with new RA claims (ICD codes M05 or M06, excluding M06.1: adult-onset Still's disease and M06.4: inflammatory polyarthropathy) between 2009 and 2014 (n=691 747), identified from both outpatient and inpatient claims, and their 1:3 age- and sex-matched controls without any RA claims (n=2 074 581) were extracted. Among patients with new RA claims between 2009 and 2014, the following operational definition was applied to more accurately identify legitimate RA: ≥2 RA ICD-10 claims accompanied by ≥1 prescription for disease-modifying antirheumatic drugs (DMARDs), which has been established to have a positive predictive value of approximately 86%–89% in previous validation studies.[14 15] Based on this definition, 58 181 patients were diagnosed with RA between 2011 and 2014. A 2-year washout period (2009–2010) was applied, and 43 925 patients newly diagnosed with RA between 2011 and 2014 were identified. Among these, participants who received a diagnosis of cognitive impairment prior to that of RA (n=980), those diagnosed with cognitive impairment within 1 year of the RA diagnosis (n=499), and those diagnosed with depression (ICD codes F32–F33) or anxiety (ICD codes F40–F41) prior to the index date (n=7646) were excluded. The remaining patients constituted the RA group (n=34 800). In the 1:3 matched controls, the following exclusion criteria were applied: (1) RA diagnosis before 2011 (n=0), (2) cognitive impairment diagnosis before 2011 (n=25 487), (3) RA diagnosis during follow-up (n=0), (4) no medical records before the earliest cognitive impairment diagnosis date or medical records available only within 1 year before the earliest cognitive impairment diagnosis date (n=57 143) and (5) depression or anxiety prior to the index date (n=5133), yielding 1 986 818 eligible controls. Next, the RA and control groups were matched for age, sex and index year in a 1:1 ratio. Participants for whom adequate matches were unavailable were excluded from the matched analytical cohort. Finally, 26 437 patients with RA and 26 437 age-, sex- and index year-matched controls were included in the analysis (figure 1).

The follow-up period extended from the index date to the occurrence of incident cognitive impairment or December 2022, whichever occurred first. In the RA group, the index date was defined as the RA diagnosis date. For the control group, the index date was assigned by matching it to the corresponding patient with RA to ensure a common reference time point.

This study was approved by the Institutional Review Board (IRB) of Gangnam Severance Hospital (IRB No: 3–2024-0204). Informed consent was waived owing to the study's retrospective design.

Participant characteristics and outcomes

The baseline characteristics of patients included periodontal disease, fibromyalgia, insomnia, hypertension, type 2 diabetes mellitus (T2DM), dyslipidaemia, ischaemic heart disease (IHD), atherosclerosis, stroke, asthma, chronic obstructive pulmonary disease (COPD) and the Charlson Comorbidity Index (CCI) at the index date. The definitions of the assessed characteristics were as follows: periodontal disease, ICD-10 code K05; fibromyalgia, ICD-10 code M79.7; insomnia, ICD-10 codes G47.0 and F51.0; hypertension, ICD-10 codes I10–I13; T2DM, ICD-10 codes E11–E14; dyslipidaemia, ICD-10 code E78; IHD, ICD-10 codes I20–I25; atherosclerosis, ICD-10 code I70; stroke, ICD-10 codes I60–I64; asthma, ICD-10 codes J45–J46; COPD, ICD-10 code J44; the CCI was calculated as the sum of weighted scores assigned to 17 comorbidities according to their relative risk of 1-year mortality.[16–18] Details of the items and ICD codes for CCI are presented in online supplemental table 1.

The outcome of interest was the occurrence of incident cognitive impairment, defined as new claims with ICD-10 codes corresponding to the following categories: Alzheimer's dementia (F00 and G30), vascular dementia

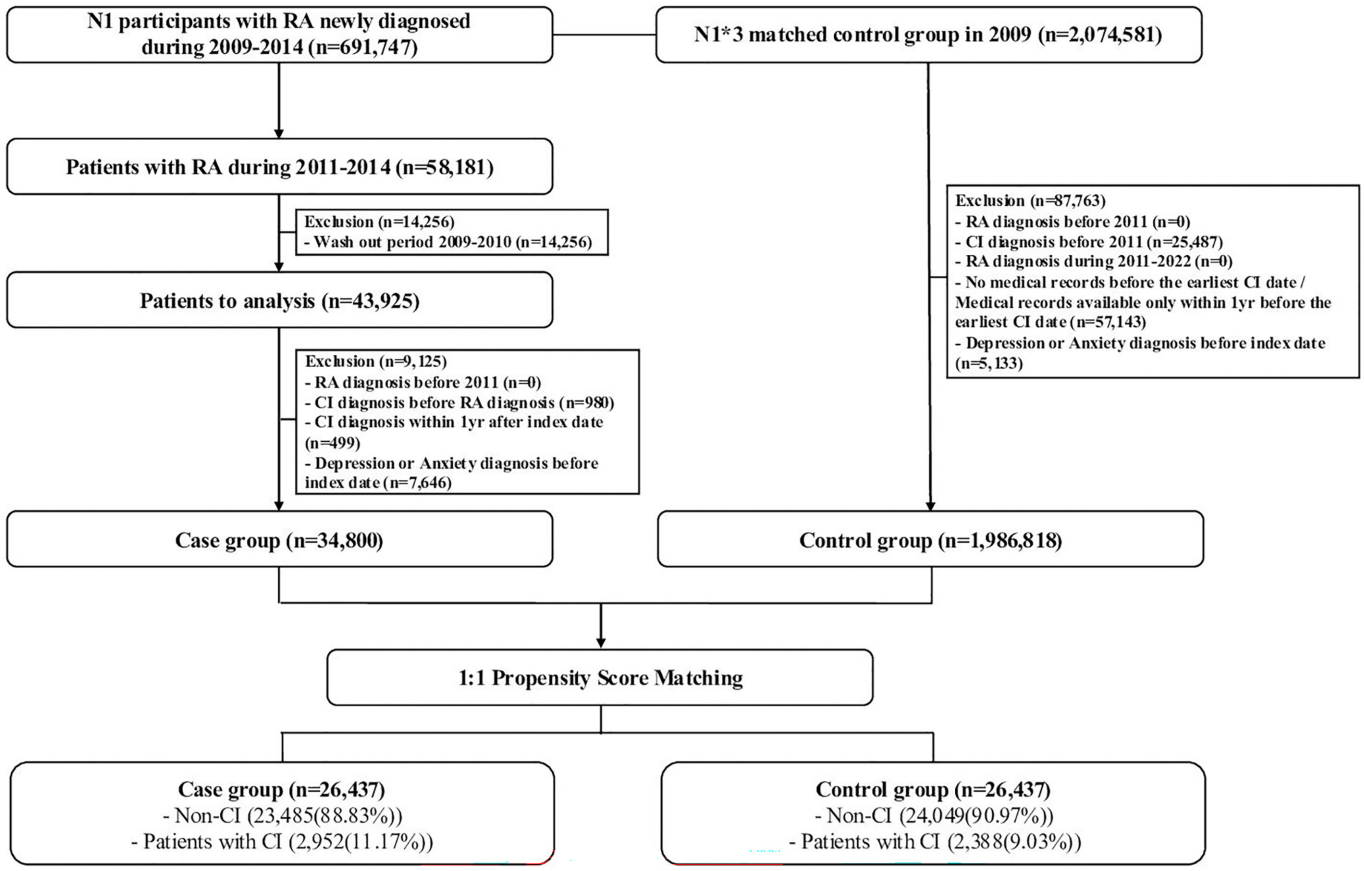

Figure 1 Study flowchart. CI, cognitive impairment; RA, rheumatoid arthritis.

(F01) and other cognitive impairment (F02, F03, G31.00, F31.82 and F06.7).[19] Similar to other studies that have used administrative claims data, this study was conducted based on the assumption that diagnostic coding practices remained reasonably consistent over the follow-up period.[16–19]

Statistical analysis

Continuous and categorical variables are summarised as means (±SD) and numbers (%), respectively. To compare the characteristics between patients with RA and age-, sex- and index-year-matched controls, the paired t-test and McNemar's test were used for continuous and categorical variables, respectively. The incidence rate of cognitive impairment was calculated as the number of events per 1000 person-years in patients with RA and matched controls. Cumulative incidence curves were constructed with death treated as a competing event, and between-group differences were assessed using the Fine–Gray test. Follow-up time was truncated at the point where the number at risk fell below 100. To account for the potential effects of differential mortality, we performed stratified competing risks regression analyses based on the Fine–Gray subdistribution hazard model (stratified by age, sex and index year), treating death as a competing risk, to assess the risk of incident cognitive impairment in patients with RA compared with matched controls. For both univariable and multivariable analyses, we calculated subdistribution HRs (SHRs) with 95% CIs. In multivariable analyses, we adjusted for covariates considered to be associated with cognitive impairment, including income level and comorbidities,[20–23] with periodontal disease being included as a potential confounder, given its association with both RA and cognitive impairment.[23–25] To minimise potential correlations among the comorbidity variables, periodontal disease, insomnia, fibromyalgia and CCI were included in the model. An additional model including individual vascular risk factors that were statistically significant in the univariable analysis (T2DM, dyslipidaemia, IHD, atherosclerosis and stroke) was constructed to further evaluate the association between vascular risk factors and cognitive impairment and to avoid potential overlap with the CCI. SHRs and 95% CIs for incident cognitive impairment risk were estimated. All p-values were two-sided and values<0.05 were considered statistically significant. All statistical analyses were performed using SAS V.9.4 (SAS Institute, Cary, NC, USA).

To test the robustness of our findings, we conducted a sensitivity analysis using an alternative definition of cognitive impairment. This stricter definition required ≥2 claims for the ICD-10 codes for cognitive impairment to exclude potential false-positive cases. Using this outcome definition, we also performed the Fine–Gray test and stratified competing risks regression analyses.

Table 1 Characteristics of patients with RA and 1:1 propensity score-matched controls

	Patients with RA (n=26 437)	Controls (n=26 437)	P value	Absolute standardised difference
Matched variables				
Age	51.290±14.071	51.290±14.071		0
Sex				
Male	7268 (27.49)	7268 (27.49)		0
Female	19 169 (72.51)	19 169 (72.51)		
Index year				
2011	7647 (28.93)	7647 (28.93)		0
2012	7276 (27.52)	7276 (27.52)		0
2013	6513 (24.64)	6513 (24.64)		0
2014	5001 (18.92)	5001 (18.92)		0
Characteristics				
Income			0.319	
First quartile (lowest)	5949 (22.64)	5774 (21.99)		
Second quartile	5155 (19.62)	5113 (19.47)		
Third quartile	6494 (24.71)	6518 (24.82)		
Fourth quartile (highest)	8680 (33.03)	8852 (33.71)		
Fibromyalgia	619 (2.34)	180 (0.68)	<0.001	
Insomnia	1284 (4.86)	842 (3.18)	<0.001	
Periodontal disease	601 (2.27)	506 (1.91)	0.004	
Hypertension	7106 (26.88)	6797 (25.71)	0.001	
T2DM	3694 (13.97)	3212 (12.15)	<0.001	
Dyslipidaemia	6612 (25.01)	5216 (19.73)	<0.001	
IHD	1824 (6.90)	1361 (5.15)	<0.001	
Atherosclerosis	565 (2.14)	462 (1.75)	0.001	
Stroke	658 (2.49)	644 (2.44)	0.691	
Asthma	4972 (18.81)	3729 (14.11)	<0.001	
COPD	843 (3.19)	507 (1.92)	<0.001	
CCI	1.526±1.512	1.184±1.387	<0.001	
Outcome				
Occurrence of cognitive impairment	2952 (11.17)	2388 (9.03)	<0.001	
Alzheimer's dementia	860 (29.13)	773 (32.37)		
Vascular dementia	100 (3.39)	116 (4.86)		
Other cognitive impairment	1982 (67.48)	1499 (62.77)		

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; RA, rheumatoid arthritis; T2DM, type 2 diabetes mellitus.

RESULTS

Comparison of characteristics between patients with RA and controls

The characteristics of 26 437 patients with RA and their 1:1 age-, sex- and index-year-matched controls are summarised in table 1. Age, sex and index year were well matched between the two groups, with an absolute standardised difference of 0. The mean age was 51.290±14.071 years in both groups, and 72.51% were women. Patients with RA more commonly had hypertension (26.88% vs 25.71%, p=0.001), T2DM (13.97% vs 12.15%, p<0.001), dyslipidaemia (25.01% vs 19.73%, p<0.001), IHD (6.90% vs 5.15%, p<0.001), atherosclerosis (2.14% vs 1.75%, p=0.001) and asthma (18.81% vs 14.11%, p<0.001), as well as a higher CCI (1.526±1.512 vs. 1.184±1.387, p<0.001), compared with the controls. In the RA group, 17 849 (67.52%) and 8588 (32.48%) patients were seropositive and seronegative, respectively.

Continuous and categorical variables are expressed as the mean±SD and numbers (%), respectively.

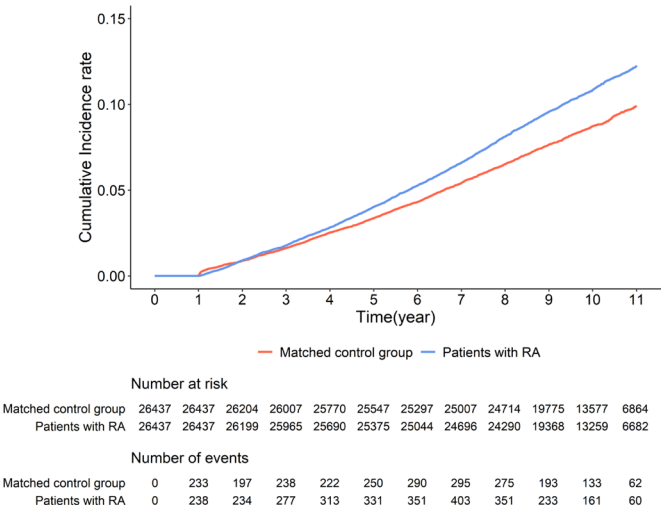

Figure 2 Cumulative incidence of cognitive impairment in patients with RA and controls. RA, rheumatoid arthritis.

Information regarding income was missing for 339 participants. Percentages for Alzheimer's dementia (F00 and G30), vascular dementia (F01) and other cognitive impairments (F02, F03, G31.00, F31.82 and F06.7) were calculated using the total number of incident cognitive impairment events as the denominator.

Cognitive impairment incidence rate

During the mean follow-up duration of 9.410±2.271 and 9.508±2.217 years, respectively, cognitive impairment occurred in 2952 patients with RA (11.17%) and in 2388 controls (9.03%). Among the overall cognitive impairment, Alzheimer's dementia (RA patients, 29.13%; controls, 32.37%) was more common than vascular dementia (RA patients, 3.39%; controls, 4.86%) in both groups. The rates of incidence of cognitive impairment in patients with RA and controls were 11.493 (95% CI 7.648 to 15.338) and 9.219 (95% CI 5.386 to 13.052) per 1000 person-years, respectively. As the number at risk fell below 100 at 12 years of follow-up, the cumulative incidence curves were truncated at 11 years. After truncation, the cumulative cognitive impairment incidence rate during follow-up was significantly higher in patients with RA compared with the controls (figure 2, p<0.001).

Risk of cognitive impairment in patients with RA compared with controls

In the univariable stratified competing risk regression analysis, patients with RA demonstrated a higher risk of incident cognitive impairment compared with the controls (unadjusted SHR, 1.261 (95% CI 1.210 to 1.313), p<0.001). This association remained statistically significant in the multivariable analysis (adjusted SHR, 1.222 (95% CI 1.171 to 1.275), p<0.001), indicating a higher incident cognitive impairment risk in patients with RA (table 2). This association remained statistically significant in multivariable analysis after excluding the CCI and adjusting for individual vascular risk factors (adjusted SHR, 1.243 (95% CI 1.191 to 1.296), p<0.001) (online supplemental table 2).

SHRs were estimated using the entire 1:1 propensity score-matched cohort (patients with RA and matched controls). Stratified competing risks regression analyses were conducted, stratified by age, sex and index year, with death treated as a competing risk. Multivariable models included RA status as the primary exposure and were adjusted for income level, periodontal disease, fibromyalgia, insomnia and the CCI.

Sensitivity analysis

In the sensitivity analysis conducted using stricter outcome definitions, the results were similar to those of the main analysis. As the number at risk fell below 100 at 12 years of follow-up, the cumulative incidence curves were truncated at 11 years. After truncation, the cumulative cognitive impairment incidence rate during follow-up was significantly higher in patients with RA than in the controls (figure 3; p<0.001). Furthermore, in the multivariable stratified competing risks regression analysis, patients with RA exhibited a significantly higher risk of incident cognitive impairment compared with the

Table 2 Stratified competing risks regression analysis for incident cognitive impairment

	Univariable analysis		Multivariable analysis	
	Unadjusted SHR (95% CI)	P value	Adjusted SHR (95% CI)	P value
RA (vs controls)	1.261 (1.210 to 1.313)	<0.001	1.222 (1.171 to 1.275)	<0.001
Income (vs first quartile)				
Second quartile	0.807 (0.735 to 0.885)	<0.001	0.812 (0.739 to 0.893)	<0.001
Third quartile	0.785 (0.719 to 0.856)	<0.001	0.778 (0.712 to 0.850)	<0.001
Fourth quartile	0.887 (0.821 to 0.958)	0.002	0.890 (0.822 to 0.963)	0.004
Periodontal disease	1.393 (1.199 to 1.619)	<0.001	1.334 (1.140 to 1.560)	<0.001
Fibromyalgia	1.650 (1.306 to 2.084)	<0.001	1.467 (1.156 to 1.862)	0.002
Insomnia	1.471 (1.306 to 1.656)	<0.001	1.385 (1.224 to 1.567)	<0.001
CCI	1.083 (1.063 to 1.103)	<0.001	1.060 (1.040 to 1.080)	<0.001

CCI, Charlson Comorbidity Index; RA, rheumatoid arthritis; SHR, subdistribution HR.

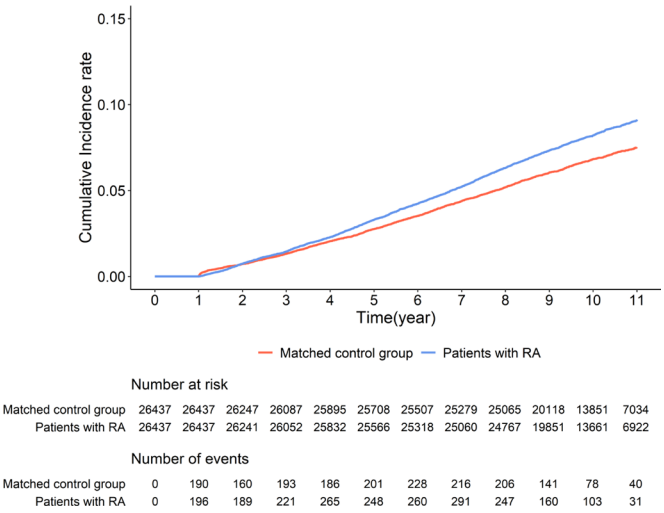

Figure 3 Sensitivity analysis: cumulative incidence of cognitive impairment using different definitions. RA, rheumatoid arthritis.

controls (adjusted SHR, 1.2 (95% CI 1.143 to 1.259), p<0.001; table 3).

SHRs were estimated using the entire 1:1 propensity score-matched cohort (patients with RA and matched controls). Stratified competing risks regression analyses were conducted, stratified by age, sex and index year, treating death as a competing risk. Multivariable models included RA status as the primary exposure and were adjusted for income level, periodontal disease, fibromyalgia, insomnia and the CCI.

DISCUSSION

In this large, nationwide, population-based, matched cohort study, we demonstrated that patients with RA experienced a significantly higher incidence and risk of cognitive impairment compared with age-, sex- and index year-matched controls. Specifically, the rate of cognitive impairment incidence was 11.493 per 1000 person-years in patients with RA, which was higher than that observed in matched controls (9.219 per 1000 person-years). Furthermore, after adjusting for various comorbidities that can affect cognitive impairment, patients with RA exhibited an approximately 22% higher risk of developing cognitive impairment compared with controls. These findings offer robust epidemiological evidence supporting the association between RA and cognitive impairment incidence.

Over a mean follow-up of 9.410±2.271 years—a sufficiently long duration to capture clinically meaningful incident events—the incidence rate of cognitive impairment in patients with RA was 11.493 per 1000 person-years. This incidence rate is lower than that of depression, which is the most common comorbidity with RA, with an incidence rate of approximately 40 per 1000 person-years.[26] Nonetheless, when compared with cardiovascular events, which are significant RA comorbidities associated with excess mortality,[27–29] the cognitive impairment incidence rate observed herein was higher than that of cardiovascular events (5–8 per 1000 person-years).[30 31] This comparison demonstrated that the burden of cognitive impairment in patients with RA is substantial. Therefore, cognitive impairment should be considered a comorbidity that warrants careful clinical attention.

The importance of cognitive impairment as a comorbidity becomes even more robust when compared directly with matched controls. In the multivariable stratified competing risks regression analysis, patients with RA exhibited an approximately 22% higher risk of developing cognitive impairment (adjusted SHR, 1.222). Given the substantial burden posed by cognitive impairment on the general population,[32] a 22% relative increase in risk represents a clinically meaningful elevation. This magnitude of excess risk suggests that cognitive impairment may represent a comorbidity in patients with RA, rather than a marginal or incidental finding, that warrants clinical awareness and monitoring over the disease course.

In studies using a claims database, an inherent concern regarding the accuracy of disease definitions exists,

Table 3 Sensitivity analysis: risk of incident cognitive impairment using different definitions

	Univariable analysis		Multivariable analysis	
	Unadjusted SHR (95% CI)	P value	Adjusted SHR (95% CI)	P value
RA (vs controls)	1.231 (1.175 to 1.290)	<0.001	1.200 (1.143 to 1.259)	<0.001
Income (vs first quartile)				
Second quartile	0.795 (0.716 to 0.884)	<0.001	0.802 (0.720 to 0.893)	<0.001
Third quartile	0.785 (0.711 to 0.866)	<0.001	0.785 (0.710 to 0.868)	<0.001
Fourth quartile	0.851 (0.780 to 0.928)	<0.001	0.855 (0.782 to 0.935)	<0.001
Periodontal disease	1.558 (1.313 to 1.848)	<0.001	1.503 (1.259 to 1.793)	<0.001
Fibromyalgia	1.283 (0.993 to 1.657)	0.056	1.155 (0.889 to 1.499)	0.281
Insomnia	1.479 (1.294 to 1.690)	<0.001	1.384 (1.205 to 1.589)	<0.001
CCI	1.075 (1.054 to 1.098)	<0.001	1.054 (1.032 to 1.077)	<0.001

CCI, Charlson Comorbidity Index; RA, rheumatoid arthritis; SHR, subdistribution HR.

particularly for conditions such as cognitive impairment that lack a single confirmatory diagnostic test. To address this issue, we performed a sensitivity analysis using a stricter definition that required at least two diagnostic claims, thereby reducing the likelihood of false positives or provisional diagnoses. The results of the sensitivity analysis were consistent with those of the main analysis, demonstrating a similar effect of RA (adjusted SHR, 1.2) on incident cognitive impairment, thereby supporting the validity of the main analysis and suggesting that the association observed in our study is less likely to be driven by diagnostic misclassification. Although claims-based definitions cannot completely replace detailed neuropsychological assessments, the reproducibility of our findings across alternative definitions adds confidence to the robustness of our results.

An important consideration when interpreting the association between RA and incident cognitive impairment is the potential influence of RA medications. As the comparison was made between patients with RA and non-RA controls, it was difficult to precisely determine whether the increased risk of cognitive impairment was attributable to RA itself or to the DMARDs used for RA treatment. A previous case-control study reported that a tumour necrosis factor inhibitor (TNFi), a widely used biological DMARD for RA treatment, mitigated the risk of cognitive impairment in patients with RA.[33] Another cohort study observed no significant difference in the risk of cognitive impairment between patients treated with conventional synthetic DMARDs (csDMARDs) and those treated with TNFi.[34] Therefore, RA medications, including csDMARDs and TNFi, do not increase cognitive impairment risk and may even tend to mitigate it. Thus, in a comparison between RA and non-RA controls, RA medications would be expected to bias the results toward the null hypothesis (ie, no significant difference in the risk of incident cognitive impairment between RA and controls) rather than produce a spurious risk increase. Therefore, the observed increase in the risk of cognitive impairment in RA is more likely attributable to RA itself rather than to the effects of RA medications. Indeed, a growing body of evidence suggests that systemic inflammation disrupts the blood–brain barrier and induces neuroinflammation, contributing to cognitive impairment.[35] Given this evolving understanding, it is biologically plausible that chronic systemic inflammation in RA promotes neuroinflammatory processes, thereby increasing cognitive impairment risk.

This study had certain limitations. First, as it was based on a claims database, information on RA disease activity was unavailable. Consequently, it was not possible to determine whether the effect size differed by disease activity severity. Second, although we adjusted for multiple comorbidities that may influence cognitive impairment, residual confounding factors cannot be fully excluded, owing to the retrospective design, and factors such as frailty, lifestyle and educational level may have influenced the results. Furthermore, as this was a retrospective observational epidemiological study, the mechanisms underlying the elevated risk of cognitive impairment in RA could not be elucidated. Third, as the cohort consisted exclusively of Koreans, extrapolation of these findings to other ethnic groups should be approached with caution. Future multiethnic studies and mechanistic investigations are warranted to clarify these associations.

In conclusion, this large nationwide cohort study demonstrated that patients with RA exhibit a significantly higher incidence and risk of cognitive impairment compared with matched controls. The consistent findings across the main and sensitivity analyses reinforced the robustness of this association. Given the substantial functional impact of cognitive impairment and its implications on treatment adherence and long-term outcomes, clinicians should integrate cognitive health assessments into the routine care of patients with RA. Future studies are warranted to clarify these mechanistic pathways and explore potential therapeutic strategies to mitigate cognitive impairment in RA.

Contributors Conceptualisation was performed by OCK, HSL and WB. Methodology was developed by OCK, HSL, HJY and WB. Formal analysis and data curation were carried out by HSL and HJY. Validation was conducted by HSL and HJY. Visualisation was prepared by OCK, HSL and HJY. The original draft of the manuscript was written by OCK, HSL and WB, and the manuscript was reviewed and edited by OCK, HSL and WB. Supervision was provided by WB. Funding acquisition was performed by WB. All authors read and approved the final manuscript. OCK and HSL contributed equally, and WB is the guarantor.

Funding This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean Government (MSIT) (No. RS-2024-00350086). The funder had no role in the study design; collection, analysis and interpretation of data; writing of the manuscript or decision to submit the manuscript for publication.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Institutional Review Board (IRB) of Gangnam Severance Hospital (IRB No: 3-2024-0204). Informed consent was waived owing to the retrospective design of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The data used in this study were provided by the National Health Insurance Service (NHIS) in Korea. The authors do not have the authority to share the data publicly. Access to these data is restricted to researchers who have received approval from the NHIS Institutional Review Board. Further information regarding data access and application procedures can be found at the NHIS website (https://nhiss.nhis.or.kr).

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