Effect of Angiotensin II Receptor Blockers on Alzheimer's Disease Progression: A Population-Based Cohort Study

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INTRODUCTION

Alzheimer's Disease (AD)

- Cognitive or behavioral impairment severe enough to affect behavior, feelings, and relationships and interfere with daily activities.
- The most common cause of dementia, accounting for 60~80% of all cases.

Renin-Angiotensin System (RAS) and Neurodegeneration

- RAS in central nervous system (CNS) is known to involve in oxidative stress, neuroinflammation, and apoptosis of the brain.
- Angiotensin II receptor blockers (ARBs) show neuroprotective potential for attenuating cognitive decline in individuals with AD.

OBJECTIVES

- To assess the effect of ARBs on the progression of AD
- To compare the difference in effect between new users and previous users

METHODS

Study Design and Data Source

- 1:1 propensity score (PS) matched retrospective cohort design (Figure 1)
- Korean Health Insurance Review & Assessment (HIRA) data (M20220622004) covering 2009 to 2021

Study Population and Exposure Assessment

- Patients aged 60 to 79 newly diagnosed with AD in 2010
- The index date was defined as the first use of AD treatment medication.
- Patients were classified as either ARB users or non-users.
- ARB users were further classified as new or previous users based on ARB prescription records from 1 year before the index date.
- Exposure to ARB was assessed for 3 years from the index date.

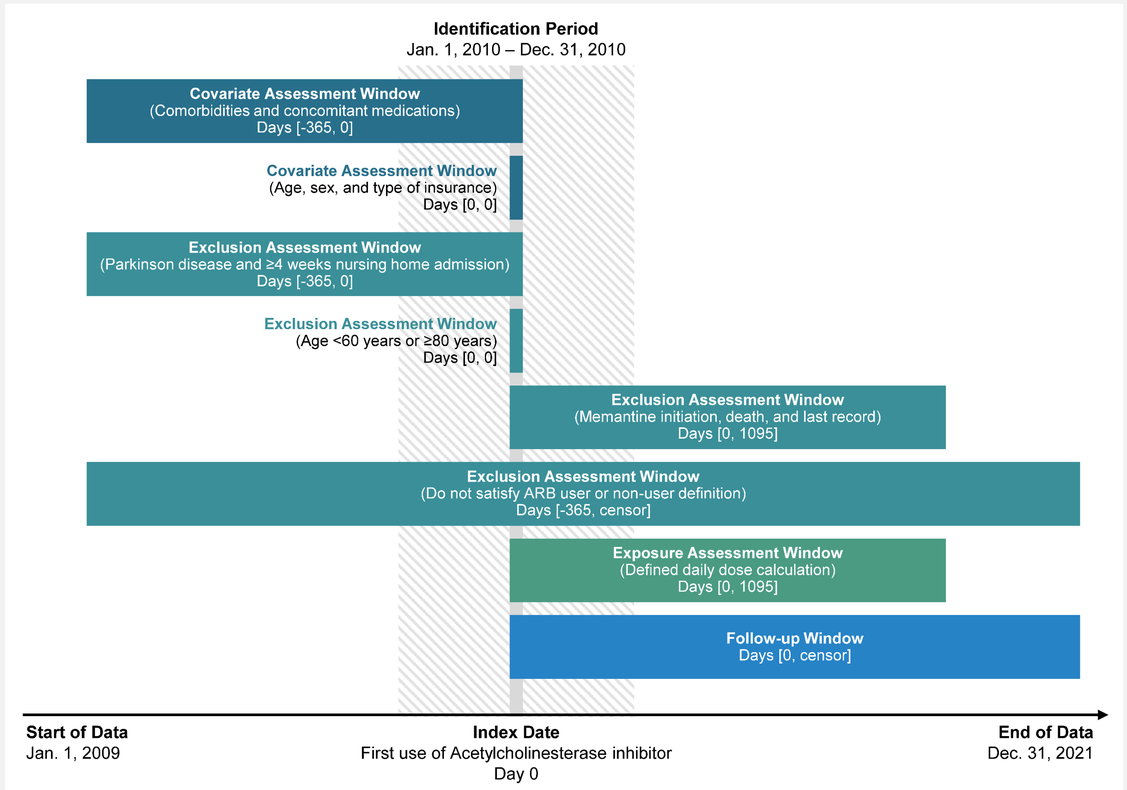


Figure 1. Study design and study population.

Key Exclusion Criteria

- More than 4 weeks of nursing home admission at baseline
- Record of Parkinson disease diagnosis at baseline

Statistical Analyses

- PS matching was performed based on confounding factors for AD progression, including age, sex, insurance type, baseline comorbidities, and baseline concomitant medications.
- Effect of ARBs on AD progression (mortality and memantine initiation) was assessed using a multivariable Cox proportional hazards regression model.
- A comparison of new and previous ARB users was graphically shown using Kaplan-Meier curves.

RESULTS

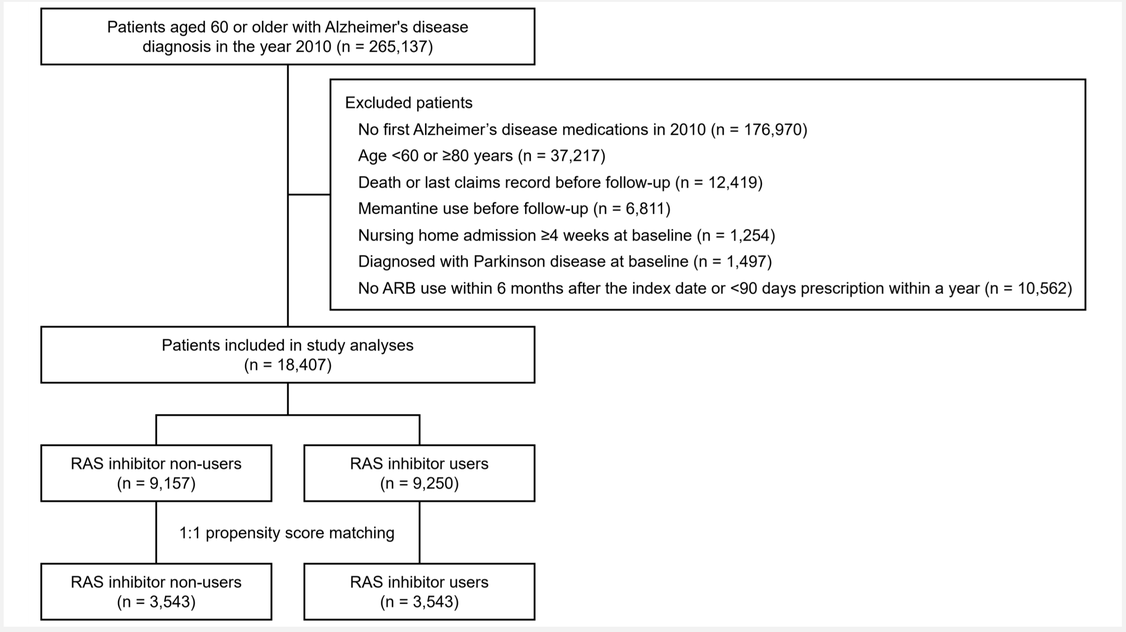


Figure 2. Flow chart of study population inclusion.

Effect of ARBs on the Risk of AD Progression

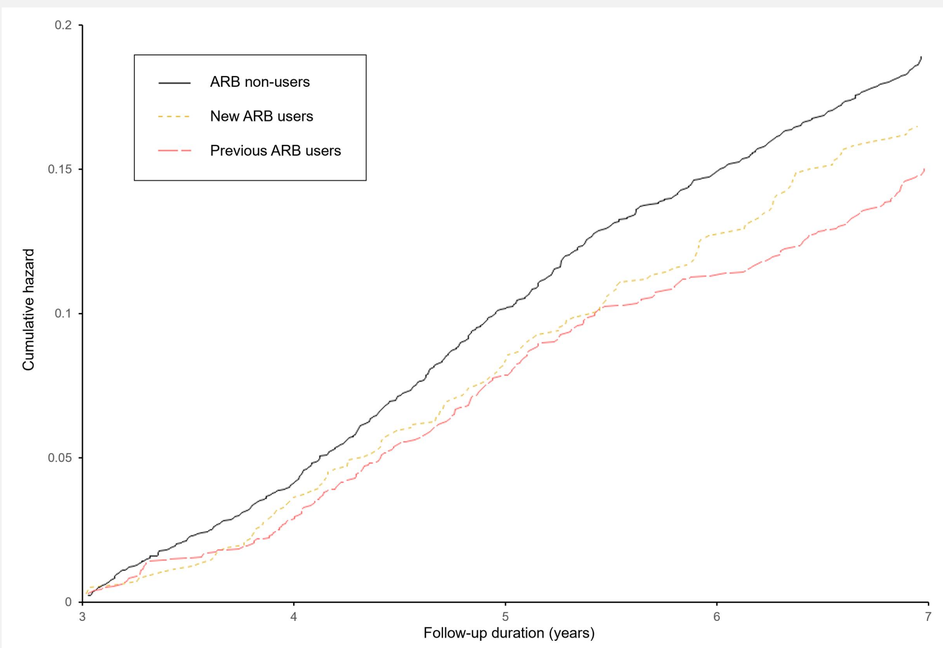
- Among 7,086 matched individuals, a total of 1,019 memantine initiation and 2,448 deaths were observed.
- ARB use significantly reduced the risk of memantine initiation (HR, 0.79; 95% CI, 0.70–0.89) and mortality (HR, 0.83; 95% CI, 0.76–0.89).

Table 1. Risk of AD progression with ARB use.

		Memantine initiation		Death	
Classification	**Subjects**	**Events**	**HRs (95% CI)**	**Events**	**HRs (95% CI)**
ARB non-users	3,543	547	Reference	1,271	Reference
ARB users	3,543	472	0.79 (0.70–0.89)	1,177	0.83 (0.76–0.89)

Effect of New vs. Previous ARB Use on the Risk of AD Progression

- Previous ARB users showed a significant reduction in the risk of memantine initiation (HR, 0.77; 95% CI, 0.66–0.89), whereas new users did not.
- No difference was observed between new and previous ARB users in terms of mortality risk.



Classification	No. of subjects	No. of events	HRs (95% CI)
ARB non-users	3,543	547	Reference
New ARB users	969	139	0.85 (0.71–1.02)
Previous ARB users	1,890	247	0.77 (0.66–0.89)

Figure 3. New vs. previous ARB use on the risk of memantine initiation.

CONCLUSIONS

- This study underscores the potential of ARBs as a disease-modifying treatment option to slow the progression of Alzheimer's disease.

References

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