Meta-Analysis of Androgen Deprivation Therapy's Impact on Cognitive Disorders in Prostate Cancer Patients: Evidence from Korean Real-World Data

Jiwoo Yun[1,], Subin Lee[1], Hankil Lee[1, 2, *]

[1] Department of Biohealth Regulatory Science, Graduate School of Ajou University, South Korea;
[2] College of Pharmacy, Ajou University, South Korea;
(Presenting: jiwooyun@ajou.ac.kr; Corresponding author: hankil@ajou.ac.kr)

SA86

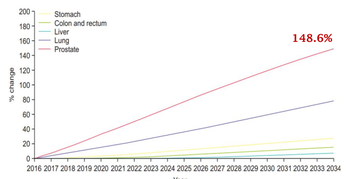
KEYWORDS: Prostate cancer; Androgen deprivation therapy; Cognitive Disorders; Meta-analysis;

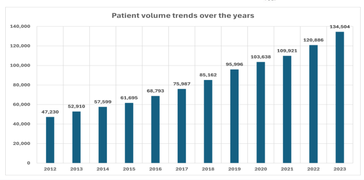
BACKGROUND

South Korea Incidence

73.1 Per 1000

5.6%





Treatment

- Androgen deprivation therapy (ADT) is a standard treatment for prostate cancer.

ADT
- LHRH agonist
- 1st antiandrogen
- LHRH antagonist

Cognitive Disorders

- Of particular concern is cognitive dysfunction, as reduced testosterone diminishes neuroprotection, impacting memory-related regions like the hippocampus. This can lead to significant cognitive issues, including memory loss and decreased attention.

OBJECTIVES

*This study aims to quantitively synthesize the **safety** of androgen deprivation therapy (**ADT**) to increase the risk of **Cognitive Disorders** in patients with prostate cancer in a Korean real-world setting through a systematic review and meta-analysis.*

METHODS

Key question

P	Prostate cancer
I	Androgen deprivation therapy
C	- (Not limited)
O	adverse event (Cognitive Disorders)
S	cohort study in korea

Search

- *Date:* June 2023

PubMed, Google Scholar

Outcome

- ✓ Dementia
- ✓ Alzheimer's disease
- ✓ Vascular disease
- ✓ Parkinson's disease

Statistical

- Recalculated SEs using the inverse-variance method on log HR.

Meta-analysis

- meta
- metafor

Analysis

Literature Review

- Total selected literature 5

First author	Tae (2019)	Shim (2020)	Kang (2020)	Kim (2022)	KIDS (2023)
Data source	NHIS database	NHIS database, Hospital cohort	NHIS database	HIRA database	HIRA database
Study population	- Total patients | n=37,549 - Full Cohort | age 71.2±8.2 - propensity score-matched | age 71.2±8.2	- Total patients | n=7,324 | 684 - Full Cohort | age 72.8±8.5 - propensity score-matched cohort | age 72.8±8.5	- Total patients | n=51,251 - all population | age 67.8±9.0 - screening cohort | age 67.2±8.5	- Total patients | n=22,427 - before matching | age 72.72±7.87 - after exact matching | age 71.16±7.38	Total patients | n=24,456 - before matching | age 67.78±7.15 - after exact matching | age 67.27±6.60
Exposure (Type of ADT)	- LHRH agonist - LHRH antagonist - anti-androgen	Defined as patients with first use of GnRHa from 1 July 2012 to 31 December 2012 and at least 1 year of exposure- GnRH agonist (+anti-androgen)	- ADT - ADT+Surgery - ADT+RT	- Patients who have received at least 1 dose of agonist or antagoinst since PC diagnosis - GnRH agonist - GnRH antagonist - anti-androgen	- LHRH agonist - LHRH antagonist - anti-androgen
Study design	propensity score matching	propensity score matching	cohort study	cohort study	cohort study
Analysis methods	cox-proportional hazard regression model	cox-proportional hazard regression model	cox-proportional hazard regression model	cox-proportional hazard regression model	- cox-proportional hazard regression model
Outcome (AE)	**Cognitive Dysfunction**	**Dementia Parkinson's Disease**	**Dementia**	**Dementia**	**Dementia, Alzheimer's disease, Vascular dementia, Other Dementia, Parkinson's disease**
Results	- Cognitive disorders: 1.169 (1.077-1.270)	<NHIS Cohort> - Dementia: 0.912 (0.759–1.097) - Parkinson's diseases: 1.495 (0.846–1.985) <Hospital cohort> - Dementia: 1.203 (1.021–1.859), - Parkinson's diseases: 1.226 (0.847–1.554)	- Dementia: 1.13 (1.09-1.18) - Alzheimer's disease: 1.12 (1.07-1.18)	- Dementia: 1.070 (1.009-1.134) - Alzheimer's disease: 1.086 (1.018-1.160) - Vascular dementia: 0.990 (0.870-1.126)	- Dementia: 1.07 (0.97-1.18) - Alzheimer's disease: 1.36 (1.18-1.56) - Vascular dementia: 1.12 (0.69-1.82) - Other Dementia 0.91 (0.80-1.03) - Parkinson's disease 1.00 (0.75-1.34)

Data used for analysis

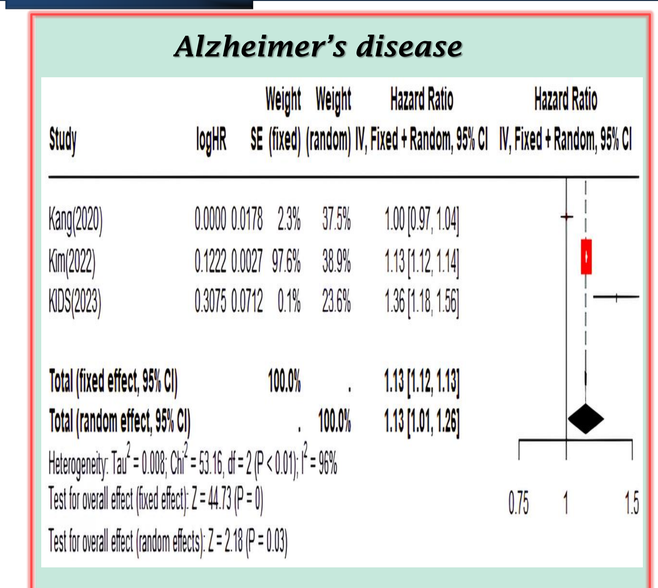
- HRs and 95% CIs collected from each article used in the meta-analysis from the literature review

	Tae(2019)	Shim(2020)	Kang(2020)	Kim(2022)	KIDS(2023)
Dementia	1.169 (1.077-1.270) Cognitive Disorders	0.957 (0.798-1.085)	1 (0.97-1.03)	1.122 (1.117-1.127)	1.07 (0.97-1.18)
Alzheimer's disease	-	-	1 (0.97-1.04)	1.130 (1.124-1.136)	1.36 (1.18-1.56)
Vascular dementia	-	-	0.89 (0.82-0.98)	1.089 (1.079-1.100)	1.12 (0.69-1.82)
Other Dementia	-	-	-	-	0.91 (0.80-1.03)
Parkinson's disease	-	1.195 (0.958-1.518)	-	-	1.00 (0.75-1.34)

Extracted hazard ratios (HRs) and 95% confidence intervals (CIs) from Cox proportional hazards models for each study.

RESULTS

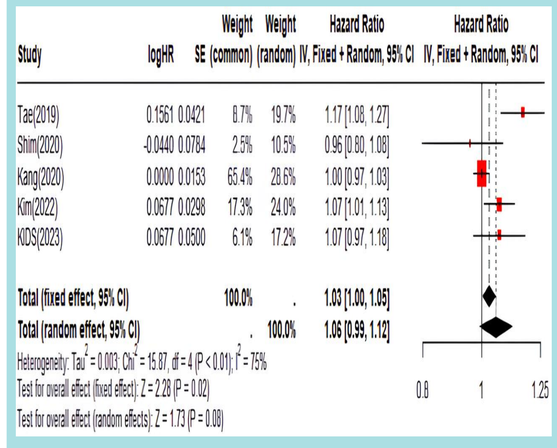
Alzheimer's disease



HR 1.13 (95% CI 1.01-1.26), I^2=96%, P<0.01

Model	HR	95% CI Lower	95% CI Upper	p-value	Q(df)	I^2
Fixed	1.13	1.12	1.13	0	53.16(2)	96
Random	1.13	1.01	1.26	0.292		

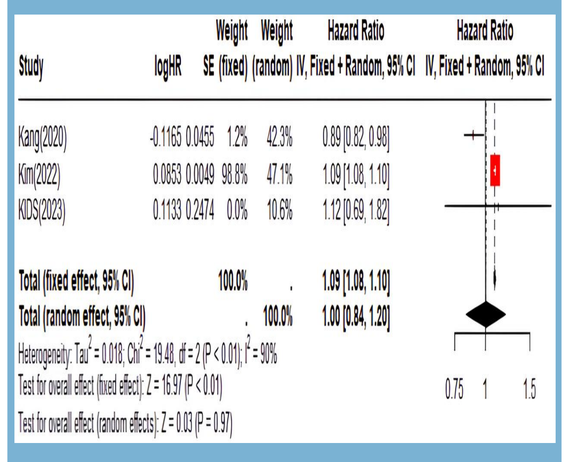
Dementia



HR 1.13 (95% CI 1.01-1.26), I^2=96%, P<0.01

Model	HR	95% CI Lower	95% CI Upper	p-value	Q(df)	I^2
Fixed	1.03	1.00	1.05	0.0224	15.87(4)	75
Random	1.06	0.99	1.12	0.0917		

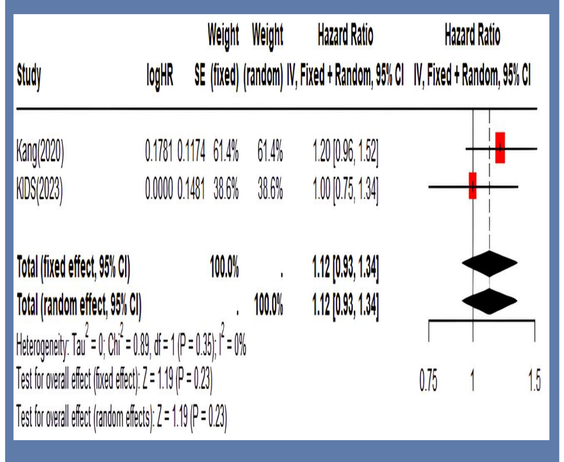
Vascular dementia



HR 1.13 (95% CI 1.01-1.26), I^2=96%, P<0.01

Model	HR	95% CI Lower	95% CI Upper	p-value	Q(df)	I^2
Fixed	1.09	1.08	1.10	<0.001	19.48(2)	90
Random	1.00	0.84	1.20	0.9744		

Parkinson's disease



HR 1.13 (95% CI 1.01-1.26), I^2=96%, P<0.01

Model	HR	95% CI Lower	95% CI Upper	p-value	Q(df)	I^2
Fixed	1.12	0.93	0.34	0.2346	0.89(1)	0
Random	1.12	0.93	0.34	0.2346		

DISCUSSION

- Significant heterogeneity was observed in the meta-analysis results of this study. This may be attributed to differences in study design, characteristics of the study populations, and data collection methods, necessitating careful interpretation of the results. Such heterogeneity may pose limitations in drawing consistent conclusions, highlighting the need for further research to enhance the accuracy and reliability of findings.

CONCLUSION

- The use of ADT in men with prostate cancer may increase the risk of developing Alzheimer's disease, but has not been shown to have a significant effect on the risk of overall dementia, vascular dementia, or Parkinson's disease.
- Monitoring for Alzheimer's disease is recommended for patients receiving ADT as part of their prostate cancer treatment.

CONFLICT OF INTEREST

- All authors declare that they have no conflicts of interest.

ACKNOWLEDGEMENTS

- This study was supported by a grant from the Korea Institute of Drug Safety and Risk Management in 2023
- This research was supported by a grant (21153MFDS602) from the Ministry of Food and Drug Safety.
- This work was supported by the GRRC program of Gyeonggi province (GRRCAjou2023-B02)