Statin Initiation Time After Graves' Disease Diagnosis and the Risk of Graves' Orbitopathy: A One-Year Landmark Analysis

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Minsung Kim[1,2], Hae Sun Suh[1,2,3]*

[1] *Department of Regulatory Science, Graduate School, Kyung Hee University, Seoul, Republic of Korea*
[2] *Institute of Regulatory Innovation through Science, Kyung Hee University, Seoul, Republic of Korea*
[3] *College of Pharmacy, Kyung Hee University, Seoul, Republic of Korea*
Corresponding author

Pharmaceutical Economics
Big Data Analysis and Policy Lab

Introduction

- Although previous studies have suggested that statin use is associated with a reduced risk of Graves' orbitopathy(GO), whether the timing of statin initiation after GD diagnosis is associated with subsequent GO risk remains unclear.
- **Objectives:** This study aimed to evaluate whether early statin initiation after newly diagnosed GD was associated with subsequent GO risk.

Methods

Study design : Retrospective cohort study

Data source

- The Health Insurance Review and Assessment database representative of the whole Korean population from January 1, 2018 ,to June 30, 2024

Study Population

- We included patients with newly diagnosed GD between January 1, 2019 and June 30, 2023 (*Figure 1*).
  - Newly diagnosed GD was defined as ≥ 2 claims with ICD-10 code E05 recorded in any diagnosis field, together with cumulative antithyroid d f and ≥ 180 days of antithyroid drug use
  - Patients with thyroid cancer (ICD-10 code: C73) before cohort entry were excluded

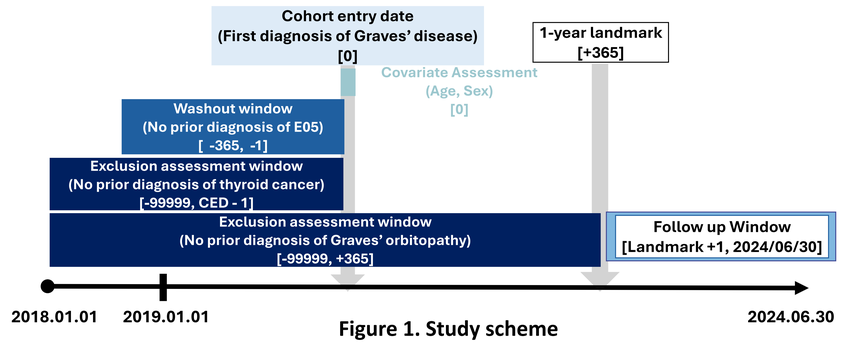

Figure 1. Study scheme

Exposure

- Patients were classified into an early initiation group and a late initiation group according to timing of the first statin prescription after GD diagnosis.
  - **Early initiation**: first statin prescription within 1 year following GD diagnosis
  - **Late initiation**: first statin prescription after 1 year following GD diagnosis

Landmark and Outcome

- The landmark was defined as 365 days after GD diagnosis.
  - Patients with GO before or at the landmark were excluded.
- GO was defined as at least one claim with ICD-10 code H06.2. Follow-up began at the landmark and continued until GO occurrence or the end of the study period.

Results

Baseline characteristics

- Among 33,853 patients who initiated statins after GD diagnosis, 22,623 (66.8%) initiated statins within 1 year, and 11,230 (33.2%) initiated statins after 1 year (*Table 1)*.
- The early statin initiation group was older on average than the late initiation group, while sex distribution was similar between groups.

Table 1. Baseline characteristics

	Total (n= 33,853)	Early initiation (n= 22,623)	Late initiation (n = 11,230)	P-value
Age, mean (SD)	59.19 (11.86)	60.38 (11.65)	56.78 (11.92)	<0.001
Age group, n (%)				
< 30	353 (1.04)	192 (0.85)	161 (1.43)	
30-39	1,353 (4.00)	700 (3.09)	653 (5.81)	
40-49	4,667 (13.79)	2,717 (12.01)	1,950 (17.36)	
50-59	10,792 (31.88)	6,881 (30.42)	3,911 (34.83)	
60-69	10,421 (27.30)	7,335 (32.51)	3,066 (27.30)	
≥ 70	6,267 (18.51)	4,778 (21.12)	1,489 (13.26)	
Sex, n (%)				0.195
Male	10,647 (31.45)	7,063 (31.2)	3,584 (31.9)	
Female	23,206 (68.55)	15,560 (68.8)	7,646 (68.1)	
Insurance type, n (%)				<0.001
National Health Insurance	31,951 (94.38)	21,253 (93.94)	10,698 (95.26)	
Medical Aid (I, II)	1,871 (5.53)	1,345 (5.95)	526 (4.68)	
Other (Veterans Affairs etc.)	31 (0.09)	25 (0.11)	6 (0.05)	

Cox Proportional Hazards Model

- Early statin initiation was associated with a significantly lower subsequent risk of GO compared with late initiation after adjustment for age and sex (adjusted HR 0.71, 95% CI 0.59-0.85, p<0.001) (*Table 2*).

Table 2. Hazard ratios for Graves' orbitopathy

Model	HR	95% CI	P-value
Crude	0.66	0.54-0.79	<0.001
Adjusted (age, sex)	0.71	0.59-0.86	<0.001

Graves' orbitopathy occurrence

- During follow-up after the 1-year landmark, GO occurred in 233 patients (0.99%) in the early initiation group and 200 patients (1.78%) in the late initiation group (*Table 3*).

Table 3. GO occurrence during the follow up period

Outcome	Early initiation (n= 22,623)	Late initiation (n = 11,230)	Total (n= 33,853)
GO event, n (%)	233 (0.99)	200 (1.78)	423 (1.25)
No GO event, n (%)	22,400 (99.01)	11,030 (98.22)	33,430 (98.75)

Discussion

Summary

- Early statin initiation was associated with a lower subsequent risk of GO among patients who initiated statins after GD diagnosis.
- This finding is consistent with prior research suggesting the potential relevance of statin initiation timing.

Limitations

- Clinical information, including smoking status, thyroid function, and GO severity, was unavailable in claims data.
- Residual confounding and potential bias related to statin initiation timing may remain.

Study implications

- Statin initiation timing may be considered when evaluating subsequent GO risk among patients with newly diagnosed GD.
- Further studies incorporating time-varying statin exposure and clinical disease severity are needed to confirm these findings.

Conclusions

- Early statin initiation within 1 year after GD diagnosis was associated with a lower subsequent risk of GO compared with late initiation among statin initiators.
- These findings suggest that statin initiation timing may be relevant in evaluating GO risk among patients with GD.

Acknowledgment

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minsung.kim @ khu.ac.kr