

Risk of Seizures Among Patients with Cerebral Amyloid Angiopathy – a Nationwide Retrospective Cohort Study in the United States

Neal S. Parikh¹; Jie (Sophie) Zhang¹; Anup Abraham¹; Lynn Farrugia¹; Varun Kumar¹; Julia Shirvan¹; Michelle P. Lin²

¹Alnylam Pharmaceuticals, Inc., Cambridge, MA, USA; ²Mayo Clinic, Jacksonville, FL, USA



For US HCPs Only
Scan to View Congress
Material Presented

Key Points

- Patients with cerebral amyloid angiopathy (CAA) were approximately 9 and 11 times more likely to experience seizures and status epilepticus, respectively, than matched controls without CAA in this large retrospective cohort study (Figure 1).
- Increased risk is observed after accounting for medical history, including prior intracerebral hemorrhage (ICH), and when stratifying by prior seizure history.
- These findings suggest that seizure may be an underappreciated clinical manifestation of CAA, beyond its cardinal clinical presentations.

Background and Objective

Background

- CAA is a progressive neurovascular disease caused by amyloid-beta deposition in the cerebral vasculature.
- Emerging evidence suggests that its clinical spectrum extends beyond hemorrhagic stroke to include cognitive and functional decline, as well as seizures.
- Risk of seizures in patients with CAA remains poorly characterized.¹

Objective

- To estimate the risk of seizure in patients with CAA versus age- and sex-matched CAA-free controls, and to identify risk factors associated with seizure in CAA.

Methods

Study Design

- Retrospective cohort study using data from an administrative claims database of US Medicare Advantage and commercial insurance beneficiaries.
 - Patients with CAA : >50 years old; ≥1 physician encounter with ICD-10 code I68.0 from 2017 to 2024; 12 months of continuous enrollment.
 - Controls: age- and sex-matched, CAA-free, 1:4 ratio.

Study Outcomes

- Primary: seizure, ascertained using a set of validated ICD-10 codes for seizure from inpatient or emergency department encounter.
- Secondary: hospitalization with status epilepticus.

Data Analysis

- Descriptive statistics of patient characteristics.
- Poisson regression for incidence rates with 95% confidence intervals (CIs).
- Crude and adjusted* Cox proportional hazard regression with 95% CIs to assess association between CAA and seizure risk compared with controls, stratified by history of seizure (based on diagnoses and medication use data).

*Adjusted for ICH (which included non-cortical hemorrhagic stroke), kidney disease, and liver disease, chosen on the basis of known strong association with the outcome of seizure.

Results

Demographics and Clinical History (Table 1)

- 7294 patients with CAA and 29 176 matched controls were identified.
- Median age was 77 years (Q1: 72, Q3: 82) and median follow-up was 29.4 months (Q1: 12.3, Q3: 56.8).
- Patients with CAA had higher prevalence of prior ICH (32.4% vs 0.5%) and seizure (18.7% vs 1.8%) versus matched controls.

Table 1. Distribution of Baseline Demographic and Clinical Characteristics

| Baseline Characteristics | Patients with CAA | Matched Controls |
|--|-------------------|------------------|
| Patients, n | 7294 | 29 176 |
| Age on index date, years, n (%) | | |
| 50–59 | 112 (1.5) | 448 (1.5) |
| 60–69 | 931 (12.8) | 3724 (12.8) |
| 70–79 | 3327 (45.6) | 13 308 (45.6) |
| 80+ | 2924 (40.1) | 11 696 (40.1) |
| Female, n (%) | 3914 (53.7) | 15 656 (53.7) |
| Insurance type, n (%) | | |
| Commercial | 399 (5.5) | 4641 (15.9) |
| Medicare | 6889 (94.4) | 24 488 (83.9) |
| Both | 6 (0.1) | 47 (0.2) |
| Medical history of, n (%) | | |
| ICH | 2364 (32.4) | 143 (0.5) |
| Seizure | 1361 (18.7) | 538 (1.8) |
| Seizure treatment | | |
| Medications | 1388 (19.0) | 923 (3.2) |
| Neuromodulation | 64 (0.9) | 244 (0.8) |
| Diabetes | 2105 (28.9) | 7826 (26.8) |
| Hypertension | 6169 (84.6) | 21 659 (74.2) |
| Dementia | 2839 (38.9) | 1970 (6.8) |
| Liver disease | 400 (5.5) | 977 (3.3) |
| Kidney disease | 297 (4.1) | 795 (2.7) |

CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage.

Seizure Incidence (Table 2)

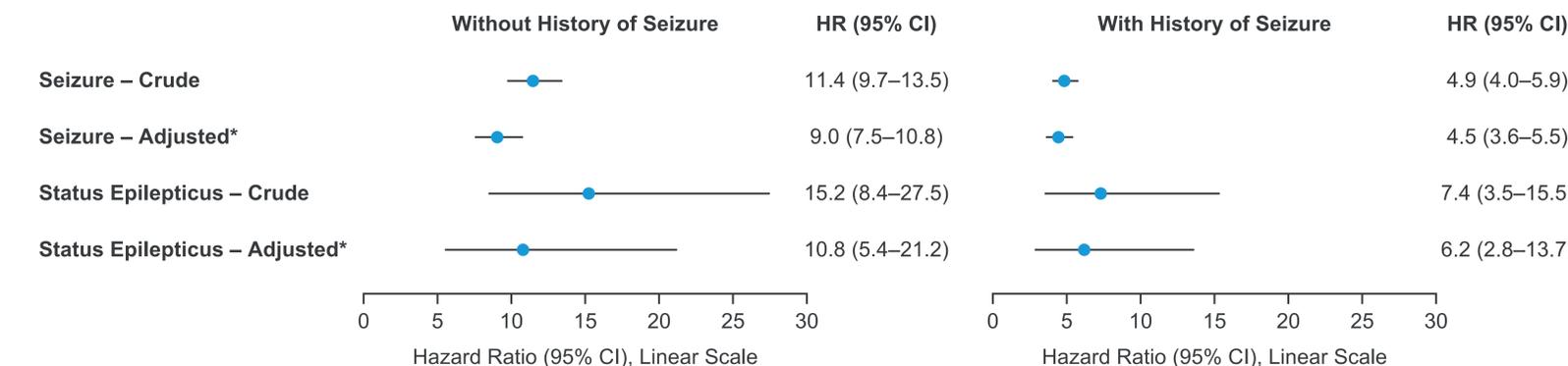
- Incidence of seizure in patients without history of seizure/epilepsy was 4.0 and 0.3 per 100 person-years in patients with CAA and in matched controls, respectively.
- Increased risk was observed when stratified by history of ICH; the incidence rate ratios were 7 and 14 comparing patients with CAA with controls, among those with and without ICH history, respectively.

Table 2. Incidence Rate and Incidence Rate Ratio of Seizure in Patients with CAA and Matched Controls

| | Patients with CAA | | | Matched Controls | | | Incidence Rate Ratio |
|---------------------------|-------------------|--------------------|------------------------------------|------------------|--------------------|------------------------------------|----------------------|
| | Patients, n | Seizure Events, n* | Incidence Rate per 100 PY (95% CI) | Controls, n | Seizure Events, n* | Incidence Rate per 100 PY (95% CI) | |
| Overall | 7294 | 987 | 8.1 (7.6–8.6) | 29 176 | 406 | 0.4 (0.4–0.5) | 19 |
| Age group, years | | | | | | | |
| 50–59 | 112 | 17 | 10.5 (6.5–16.9) | 448 | 0 | – | – |
| 60–69 | 931 | 170 | 11.1 (9.6–12.9) | 3724 | 31 | 0.3 (0.2–0.4) | 38 |
| 70–79 | 3327 | 470 | 8.0 (7.3–8.8) | 13 308 | 198 | 0.4 (0.3–0.5) | 20 |
| 80+ | 2924 | 330 | 7.1 (6.4–7.9) | 11 696 | 177 | 0.5 (0.5–0.6) | 14 |
| History of seizure | | | | | | | |
| Yes | 1361 | 559 | 34.9 (32.1–37.9) | 538 | 110 | 8.2 (6.8–9.9) | 4 |
| No | 5933 | 428 | 4.0 (3.7–4.4) | 28 638 | 296 | 0.3 (0.3–0.4) | 13 |
| History of ICH | | | | | | | |
| Yes | 2364 | 500 | 13.6 (12.5–14.8) | 143 | 7 | 2.0 (1.0–4.2) | 7 |
| No | 4930 | 487 | 5.7 (5.2–6.3) | 29 033 | 399 | 0.4 (0.4–0.5) | 14 |

*Seizure event is defined as emergency department or inpatient encounter with a seizure diagnosis. CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; PY, person-years.

Figure 1. Hazard Ratio of Seizure and Status Epilepticus Comparing Patients with CAA with Matched Controls



*Adjusting for ICH, kidney disease, and liver disease, matched on age and sex. CAA, cerebral amyloid angiopathy; HR, hazard ratio; ICH, intracerebral hemorrhage.

REFERENCE

1. Freund BE et al. *Neural Clin Pract* 2025;15:e200454.

DISCLOSURES

NSP, JZ, AA, LF, VK, and JS are employees of and shareholders in Alnylam Pharmaceuticals. ML has no conflicts to report.

Funding

This study was funded by Alnylam Pharmaceuticals.

Acknowledgments

Editorial support provided by PharmaGenesis Cardiff, Cardiff, UK, was funded by Alnylam Pharmaceuticals in accordance with Good Publication Practice guidelines.