HSD49

Diagnosis and Treatment Journey of Patients With Atrial Fibrillation Prior to Stroke Occurrence

Amiee Kang,[1,*] Ellen O'Brien,[2] Dimitra Lambrelli,[3] Sandy Maumus-Robert,[3] Achim Wolf,[3] Alyshah Abdul Sultan,[4] Ricardo Garcia-Sanchez,[1] Gregory Lip[5]

[1]Bristol Myers Squibb, Princeton, NJ, USA; [2]Johnson & Johnson, Horsham, PA, USA; [3]Evidera, London, UK; [4]Johnson & Johnson, Raritan, NJ, USA; [5]Liverpool Heart and Chest Hospital, Liverpool, UK.

*Presenting author.

BACKGROUND

- The prevalence of atrial fibrillation (AF) is estimated at approximately 60 million cases worldwide,[1] with 1.4 million cases in the United Kingdom alone,[2] and it continues to increase with the aging population[3]
- The risk of ischemic stroke is increased 4- to 5-fold by AF compared with individuals without AF[4]
  - Guidelines recommend oral anticoagulants (OACs) to reduce this risk[5-7]; however, some patients are not diagnosed prior to the stroke event or are not treated according to the guideline recommendations
- A recent systematic literature review exploring the burden of undertreatment and nontreatment with OACs among patients with AF concluded that rates of undertreatment and nontreatment are high and associated with preventable cardiovascular events and death[8]
- A report from the global prospective GARFIELD-AF Registry explored discontinuation of OACs among newly diagnosed patients with AF. Of the >23,000 patients who were prescribed OACs, 13% discontinued for ≥7 days. Discontinuation was associated with significantly higher all-cause mortality, stroke/systemic embolism (SE), and myocardial infarction[9]

OBJECTIVES

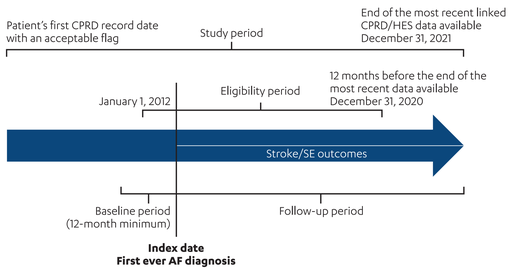
- The current study describes the characteristics, treatment patterns, and outcomes of a subpopulation of patients with AF who have experienced a stoke/SE
- Instead of the traditional approach of exploring real-world evidence from all available patients with AF, this retrospective observational study focused specifically on patients with AF who had a stroke/SE and the diagnosis and treatment decisions that occurred before their stroke/SE

METHODS

Patients, Data Source, and Study Design

- This was a retrospective observational study of patients in the United Kingdom that utilized data from the Clinical Practice Research Datalink (CPRD) Aurum database that is linked to Hospital Episode Statistics Admitted Patient Care data and the Office for National Statistics' data on death
- The patient index date was defined as the first record of an AF diagnosis received within the eligibility period, which ended 12 months before the end of the study period (ie, January 1, 2012, to December 31, 2020; **Figure 1**)
- The follow-up period lasted from the day after the index date until the first occurrence of death, disenrollment from the CPRD Aurum database, or the end of the study
- Eligible patients included adults ≥18 years of age on the index date who had a stroke/SE, were diagnosed with AF, and had 12 months of continuous registration before the index date
  - Patients were categorized by the timing of their AF diagnosis relative to their stroke/SE (ie, stroke/SE during the 90 days before or on/after their AF diagnosis index date) and OAC treatment pattern (ie, continued or discontinued treatment)

Figure 1. Study design.



AF, atrial fibrillation; CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics; SE, systemic embolism.

Assessments

- Patient characteristics, including demographics, clinical characteristics, and prevalence of baseline comorbidities, were evaluated during the 12-month baseline period
- Treatment patterns and the duration of time to treatment initiation, time from AF diagnosis to treatment discontinuation, time from treatment discontinuation to first occurrence of stroke/SE, and time from AF diagnosis to first stroke/SE were evaluated

Statistical Analysis

- Descriptive statistics were calculated for categorical and continuous variables

CONCLUSIONS

- **Despite available OAC therapies, a subset of UK patients with AF who experienced a stroke/SE received no OAC treatment or discontinued treatment**
- **Regardless of similar overall risk scores (ie, CHA_2DS_2-VASc and HAS-BLED) and similarities across the different treatment groups, patients who were not treated with OACs had the highest prevalence of hemorrhagic stroke and prior bleeding at baseline and the shortest time from AF diagnosis to a stroke/SE**

References

1. Li H, et al. *BMC Public Health*. 2022;22(1):2450.
2. Stroke Association. Atrial fibrillation. Accessed March 21, 2024. https://www.stroke.org.uk/stroke/managing-risk/atrial-fibrillation
3. Linz D, et al. *Lancet Reg Health Eur*. 2024;37:100786.
4. Virani SS, et al. *Circulation*. 2021;143(8):e254-e743.
5. Joglar JA, et al. *Circulation*. 2024;149(1):e1-e156.
6. Van Gelder IC, et al. *Eur Heart J*. 2024;45(36):3314-3414.
7. National Institute for Health and Care Excellence. Atrial fibrillation: diagnosis and management – NICE guideline NG196. Accessed April 1, 2025. https://www.nice.org.uk/guidance/NG196
8. Sussman M, et al. *Curr Med Res Opin*. 2022;38(1):7-18.
9. Cools F, et al. *J Thromb Haemost*. 2021;19(9):2322-2334.

Acknowledgments

This study was sponsored by Bristol Myers Squibb and Johnson & Johnson. Medical writing support was provided by Kim Caldwell, PhD, of Lumanity Communications Inc., and was funded by Bristol Myers Squibb and Johnson & Johnson.

Disclosures

AK and **RG-S** are employees and shareholders of Bristol Myers Squibb. **EO** is an employee of and may hold stock in Johnson & Johnson. **DL** and **AW** are employees of Evidera. **SM-R** was an employee of Evidera at the time of the study. **AAS** was an employee of Johnson & Johnson at the time of the study. **GL** received research support from Bristol Myers Squibb and Johnson & Johnson.

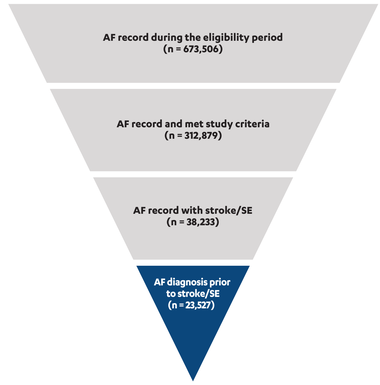
POSTER PRESENTED AT THE PROFESSIONAL SOCIETY FOR HEALTH ECONOMICS AND OUTCOMES RESEARCH (ISPOR) CONFERENCE; MAY 13-16, 2025; MONTRÉAL, QC, CANADA

RESULTS

Patients

- A total of 312,879 patients with AF who met the study criteria were identified in the CPRD database, of whom 38,233 (12.2%) experienced a stroke/SE; of those, 23,527 (61.5%) received an AF diagnosis prior to the stroke/SE (**Figure 2**)

Figure 2. Identification of eligible patients with AF who experienced a stroke/SE.



AF, atrial fibrillation; SE, systemic embolism.

- Of patients who were diagnosed with AF before the stroke/SE event (n = 23,527), half (50.1%) were female, the mean age was 77.7 years, and the mean CHA_2DS_2-VASc and HAS-BLED scores were 4.0 and 3.4, respectively; 28.2% of these patients had stage ≥3 chronic kidney disease and 40.1% had a history of bleeding (**Table 1**)

Table 1. Baseline Demographic and Clinical Characteristics of Patients With Stroke/SE After the AF Diagnosis Index Date*

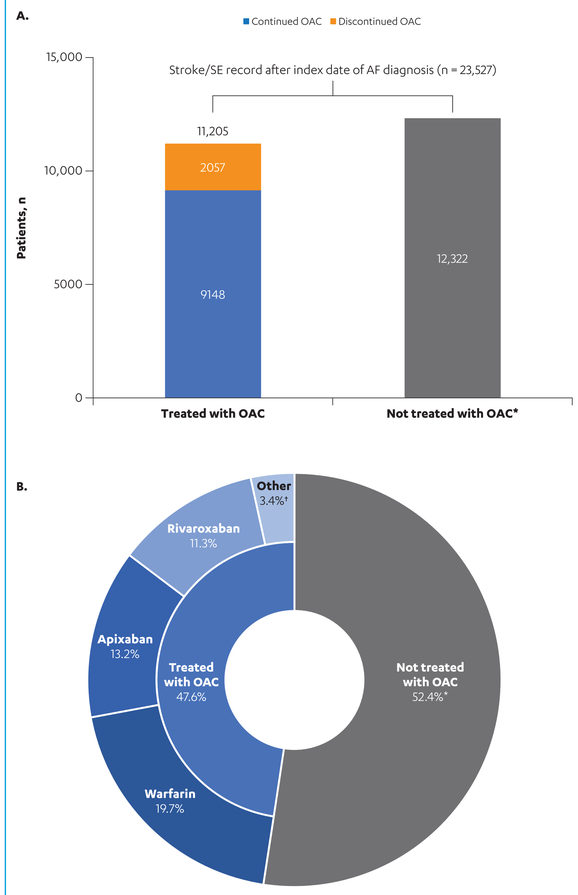
	Not treated with OAC (n = 12,322)	Treated with OAC (n = 11,205)	Continued OAC use† (n = 9148)	Discontinued OAC use‡ (n = 2057)	Total (N = 23,527)
Female, n (%)	6401 (51.9)	5380 (48.0)	4347 (47.5)	1033 (50.2)	11,781 (50.1)
Mean (SD) age at index, years	78.3 (11.2)	77.0 (9.6)	76.9 (9.5)	77.7 (10.3)	77.7 (10.5)
Age group, n (%)					
18-54 years	442 (3.6)	289 (2.6)	224 (2.4)	65 (3.2)	731 (3.1)
55-64 years	1028 (8.3)	852 (7.6)	688 (7.5)	164 (8.0)	1880 (8.0)
65-74 years	2464 (20.0)	2762 (24.6)	2345 (25.6)	417 (20.3)	5226 (22.2)
75-79 years	2033 (16.5)	2336 (20.8)	1953 (21.3)	383 (18.6)	4369 (18.6)
≥80 years	6355 (51.6)	4966 (44.3)	3938 (43.0)	1028 (50.0)	11,321 (48.1)
Race, White, n (%)	11,522 (93.5)	10,651 (95.1)	8693 (95.0)	1958 (95.2)	22,173 (94.2)
Mean (SD) CCI score	2.0 (1.9)	1.7 (1.7)	1.6 (1.7)	1.7 (1.8)	1.8 (1.9)
Comorbidities not in CCI, n (%)					
Hypertension	10,267 (83.3)	9523 (85.0)	7824 (85.5)	1699 (82.6)	19,790 (84.1)
SE§	209 (1.7)	166 (1.5)	134 (1.5)	32 (1.6)	375 (1.6)
IS§	2032 (16.5)	1828 (16.3)	1593 (17.4)	235 (11.4)	3860 (16.4)
Hemorrhagic stroke	386 (3.1)	183 (1.6)	157 (1.7)	26 (1.3)	569 (2.4)
Prior major bleeding¶	5236 (42.5)	4203 (37.5)	3427 (37.5)	776 (37.7)	9439 (40.1)
CKD stage ≥3	3672 (29.8)	2958 (26.4)	2383 (26.0)	575 (28.0)	6630 (28.2)
Mean (SD) CHA_2DS_2-VASc score	4.0 (1.7)	3.9 (1.6)	3.9 (1.6)	3.8 (1.6)	4.0 (1.6)
Mean (SD) HAS-BLED score#	3.4 (1.5)	3.4 (1.4)	3.4 (1.4)	3.3 (1.4)	3.4 (1.4)
Selected comorbidities in HAS-BLED, n (%)					
Renal disease	4112 (33.4)	3320 (29.6)	2681 (29.3)	639 (31.1)	7432 (31.6)
Liver disease	529 (4.3)	377 (3.4)	307 (3.4)	70 (3.4)	906 (3.9)
Medication use, n (%)					
ACE inhibitors and ARBs	5502 (44.7)	5682 (50.7)	4753 (52.0)	929 (45.2)	11,184 (47.5)
Amiodarone	38 (0.3)	28 (0.2)	25 (0.3)	3 (0.1)	66 (0.3)
Antiplatelets	5364 (43.5)	5045 (45.0)	4199 (45.9)	846 (41.1)	10,409 (44.2)
Beta blockers	3745 (30.4)	3541 (31.6)	2889 (31.6)	652 (31.7)	7286 (31.0)
H2-receptor antagonists	490 (4.0)	381 (3.4)	304 (3.3)	77 (3.7)	871 (3.7)
NSAIDs	665 (5.4)	706 (6.3)	563 (6.2)	143 (7.0)	1371 (5.8)
Proton pump inhibitors	4513 (36.6)	4008 (35.8)	3294 (36.0)	714 (34.7)	8521 (36.2)
Statins	5825 (47.3)	5796 (51.7)	4845 (53.0)	951 (46.2)	11,621 (49.4)

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; INR, international normalized ratio; IS, ischemic stroke; NSAID, nonsteroidal anti-inflammatory drug; OAC, oral anticoagulant; SE, systemic embolism.
*Baseline comorbidities all used the entire baseline period (ie, no date restrictions).
†Includes patients who initiated any anticoagulant and did not have complete discontinuation.
‡Includes patients who initiated any anticoagulant and had complete discontinuation (ie, end of a continuous treatment episode with no further dispensing of any anticoagulants during all available follow-up).
§Prior to the index date.
¶Major bleeding (ie, intracranial, gastrointestinal, and other).
#Modified HAS-BLED score was calculated as the sum of all conditions (ie, hypertension, renal disease, liver disease, history of stroke, prior major bleeding or predisposition to bleeding, >65 years of age, and medication usage predisposing to bleeding) except INR because Medicare data do not contain INR levels.

Treatment Patterns and Stroke/SE Events

- Of the 23,527 patients diagnosed with AF prior to their stroke/SE, 47.6% were treated with an anticoagulant while 52.4% were not; the most common OACs were warfarin (19.7%), apixaban (13.2%), and rivaroxaban (11.3%; **Figure 3**)

Figure 3. Treatment (A) disposition and (B) pattern of patients with an AF diagnosis who had a stroke/SE.



AF, atrial fibrillation; OAC, oral anticoagulant; SE, systemic embolism.
*The not treated with OAC group includes patients who were not given any anticoagulants between the index date of AF diagnosis (inclusive) and the first stroke/SE after the index date.
†The other treatment group includes dabigatran (2.0%) and edoxaban (1.4%).

- Of the 11,205 patients who received an OAC, the median time from the AF diagnosis to the first treatment and to discontinuation was 21 days and 305 days, respectively (**Table 2**)
- The time from the first AF diagnosis to the first stroke/SE was 823 days in treated patients (822 and 830 days for those who continued and discontinued an OAC, respectively) and 304 days in untreated patients (ie, no anticoagulants between the AF diagnosis index date and the first stroke/SE after the index date; **Table 2**)
  - For patients who received an OAC and discontinued treatment, the median time from discontinuation to a stroke/SE was 248 days

Table 2. Median Duration of Time to Treatment Initiation, Discontinuation, and Stroke/SE

Median (IQR) time to event, days	Not treated with OAC (n = 12,322)	Treated with OAC (n = 11,205)	Continued OAC use* (n = 9148)	Discontinued OAC use† (n = 2057)
Time from first AF diagnosis to first stroke/SE	304.0 (50.0-867.0)	823.0 (353.0-1472.0)	822.0 (338.5-1478.0)	830.0 (419.0-1442.0)
Time to OAC initiation	–	21.0 (6.0-77.0)	21.0 (6.0-75.0)	22.0 (7.0-89.0)
Time from first AF diagnosis to OAC discontinuation	–	305.0 (120.0-747.0)	–	305.0 (120.0-747.0)
Time from OAC discontinuation to first stroke/SE	–	248.0 (54.0-674.0)	–	248.0 (54.0-674.0)

AF, atrial fibrillation; IQR, interquartile range; OAC, oral anticoagulant; SE, systemic embolism.
*Includes patients who initiated any anticoagulant and did not have complete discontinuation.
†Includes patients who initiated any anticoagulant and had complete discontinuation (ie, end of a continuous treatment episode with no further dispensing of any anticoagulants during all available follow-up).

Limitations

- Not all underlying reasons for health care providers' and patients' decisions related to anticoagulants can be ascertained in electronic health records
- The study objectives did not include the analysis of possible observable reasons for not initiating or discontinuing anticoagulants, such as bleeding events, contraindications, or left atrial appendage closure devices
- This study focused on the subpopulation of patients with AF who have had a stroke/SE and the findings may not be generalizable to patients with AF who do not have a recorded stroke/SE
- The study period introduced an arbitrary cutoff for the observation of stroke/SE events that might have occurred after the end of the study period; therefore, time-to-event analyses may be limited