Association of Sex with Oral Anticoagulant Prescription and Outcomes in Patients with Atrial Fibrillation: Insights from a United States Commercial Claims Database

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Introduction

- Oral anticoagulants (OACs) reduce stroke risk in atrial fibrillation (AF) patients.
- Despite the effectiveness of OACs against stroke in AF patients, OACs continue to be underutilized.
- Past research has shown that females are more likely to suffer a stroke outcome than males.[1-3]
- There is limited research that observes the differences between males and females and with AF and likelihood of receiving an OAC prescription, and this study aims to add to this knowledge.

Objective

- The goal of this analysis was to examine the association of sex with likelihood of OAC prescription and risk of major bleeding (MB), stroke and systemic embolism (SE) among newly diagnosed AF patients.

Methods

Data Source

- This study was conducted using IQVIA's PharMetrics Plus Health Plan claims database which includes claims for medical (provider and institutional) and pharmacy services in the United States. The population aged >65 years consists of enrollees in managed care plans for seniors, the working elderly, and others in commercial plans; BHI Medicare Advantage members are not included.

Study Sample

- Adult patients with ≥1 inpatient claim or ≥2 outpatient claims for AF (≥ 7 days apart and in any diagnosis position) between January 1, 2013 and April 30, 2021 were selected. The patient index date was the first AF diagnosis claim date during this study identification period.
- Patients had 12 months of continuous health plan enrollment with medical and pharmacy benefits prior to the index date (baseline period), with a CHA_2DS_2-VASc score ≥ 2.
- Patients had 6 months of continuous health plan enrollment with medical and pharmacy benefits after the index date (see Figure 1).
- Patients were further stratified by sex (male versus female).
- Full inclusion and exclusion criteria are shown in Figure 1.

Cohorts

- Patients were assigned to the following cohorts based on the use of OACs.
  - *Treated:* Initiated with apixaban, dabigatran, edoxaban, rivaroxaban, or warfarin from 01JAN2013-30APR2021.
  - *Untreated:* Patients with no OAC claim from 01JAN2013-30APR2021.

Study Outcomes

- Stroke/SE
  - Stroke/SE included all stroke, ischemic stroke, hemorrhagic stroke, and systemic embolism; Identified using International Classification of Disease, 9th/10th Revision, Clinical Modification (ICD-9/10-CM) diagnosis codes for stroke/SE.
- Major bleeding
  - MB included all bleeds, gastrointestinal hemorrhage, intracranial hemorrhage, and other bleeds. Identified using International Classification of Disease, 9th/10th Revision, Clinical Modification (ICD-9/10-CM) diagnosis codes for MB.
- OAC prescription prevalence
  - All OAC including apixaban, dabigatran, edoxaban, rivaroxaban and warfarin were included. OAC prescription was identified using National Drug Code (NDC).

Statistical Analysis

- Multivariable staged logistic regression was used to estimate odds ratios (OR) for OAC prescription.
- Multivariable Cox models were used to estimate hazard ratios of MB and stroke/SE.
- Models were adjusted for demographics, comorbidities, and medication use.

Results

Patient Population

Figure 1:

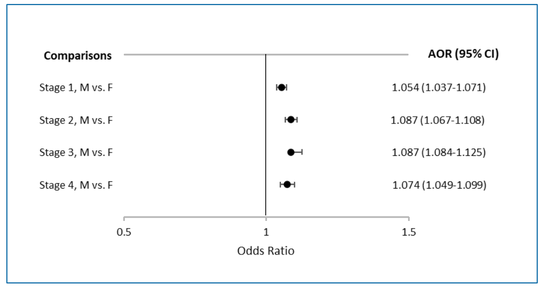
- A total of 244,507 AF patients were identified, of whom 99,390 (40.6%) were prescribed an OAC versus 145,117 (59.4%) who did not have a claim for an OAC prescription during the study identification period.
- For the final sample, 133,317 (55%) males were identified compared to 111,190 (45%) females.

Outcomes

Figure 2:

- Males had a slightly higher likelihood of receiving an OAC prescription compared to females (OR 1.07; 95% confidence interval [CI] [1.05-1.10]).

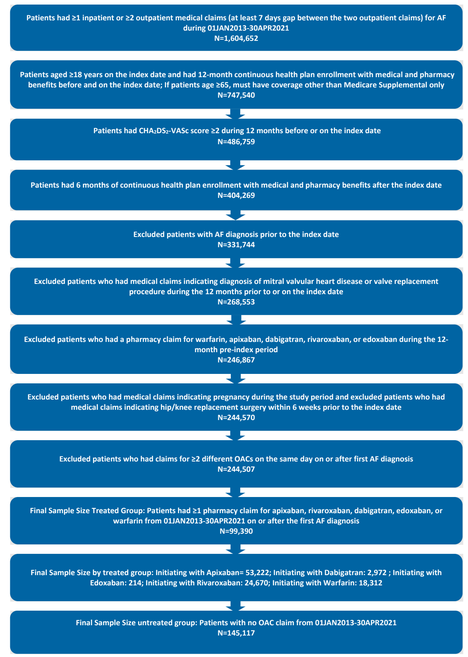
Figure 2. Odds of OAC Prescription by Sex



AOR: adjusted odds ratio; CI: confidence interval; OAC: oral anticoagulant
Females are reference group.

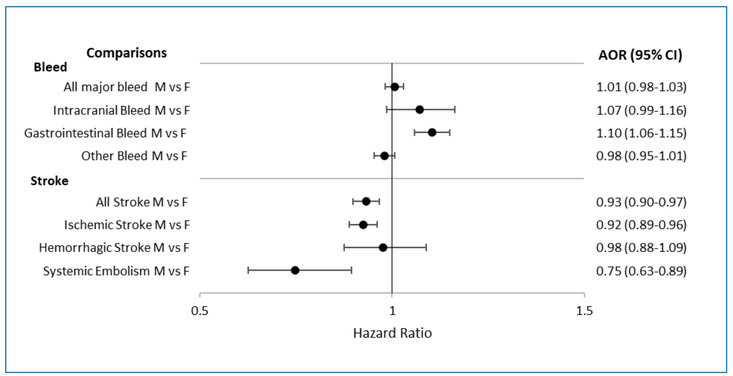
Stage 1 is adjusted for age, region.
Stage 2 is adjusted for Stage 1 + comorbidities (CHA_2DS_2-VASc score, Charlson Comorbidity Index, obesity, falls, chronic obstructive pulmonary disease, congestive heart failure, congenital heart defects, peripheral vascular disease, dyspepsia or stomach discomfort, diabetes, prior bleed, prior stroke, renal disease, hypertension, liver disease).
Stage 3 is adjusted for Stage 2 + prior bleed and prior stroke.
Stage 4 is adjusted for Stage 3 + medications (warfarin inducers, warfarin inhibitors, antidepressants, statins, non-steroidal anti-inflammatory drugs, antiplatelets, anti-hypertensives, anti-gastrointestinals, anti-diabetics).

Figure 1. Patient Selection Criteria



AF: atrial fibrillation; OAC: oral anticoagulant

Figure 3. Risk of Study Outcomes by Sex



AHR: adjusted hazard ratio; CI: confidence interval; OAC: oral anticoagulant
Females are reference group
Model controls for age, region, time-dependent OAC, comorbidities (CHA_2DS_2-VASc score, CCI score, obesity, falls, chronic obstructive pulmonary disease, congestive heart failure, congenital heart defects, peripheral vascular disease, dyspepsia or stomach discomfort, diabetes, prior bleed, prior stroke) and medications.

Figure 3:

- There was not a statistically significant difference in overall MB, intracranial, or other bleed risk between males and females, but males had a 10% higher risk (OR 1.10 (95% CI [1.06-1.15]) of gastrointestinal (GI) bleeding compared to females.
- Males had a 7% lower risk (OR 0.93) (95% [CI 0.90-0.97]) of all stroke outcomes, 8% lower risk (OR 0.92 (95% CI (0.89-0.96)) of ischemic stroke, and 25% lower risk (OR 0.75 (95% CI [0.63-0.89]) of SE as compared to females.
- There was not a statistically significant difference in the risk of hemorrhagic stroke between males and females.

Limitations

- OAC utilization was based on observation of a claim for filled therapy. We don't know to what extent patients were prescribed OAC but did not have it filled.
- This is a retrospective observational study and can only demonstrate association and not causation.
- The results may not be generalizable to the entire US AF population since only commercially insured patients are evaluated.

Discussion

- This study provides evidence of an association of female versus male sex with likelihood of OAC prescription and with risk of MB and stroke/SE among newly diagnosed AF patients with elevated stroke risk (CHA_2DS_2-VASc score ≥2). This study reports several key findings which include: 1) the prevalence of OAC prescription remained low, with 60% of the eligible population not receiving an OAC prescription in the follow-up period. 2) males had a slightly higher likelihood of receiving an OAC prescription, and 3) males were also at a slightly higher risk of GI bleeding than females with AF, but were at lower risk of stroke and SE.

Main Findings:

- Males are more likely to be prescribed an OAC, and to experience a lower risk of adverse events such as MB and stroke compared to females after adjusting for demographics, comorbidities, and medication use.

Conclusion

After adjusting for demographics, comorbidities and medication use, males with AF had a slightly higher likelihood of receiving an OAC prescription, and were also at a slightly higher risk of GI bleeding than females with AF, but were at lower risk of stroke and SE.

References

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Disclosures

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