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

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Introduction

- Atrial fibrillation (AF) has become more prevalent in an aging US population, and this trend is expected to increase exponentially in the coming decades.[1]
- Oral anticoagulants (OACs) reduce stroke risk in AF patients.[2,3]
- Little is known about the patterns of OAC prescription and outcomes in AF patients among different age groups.

Objective

- The goal of this analysis was to examine the association of age with likelihood of OAC prescription and with 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-month continuous health plan enrollment with medical and pharmacy benefits after the index date (see 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/Systemic embolism (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.
- Major Bleeding (MB)
  - 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
  - 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 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:

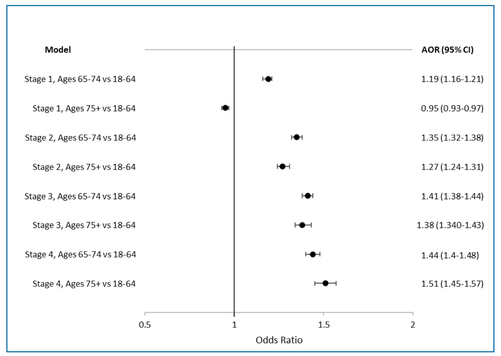
- A total of 244,507 AF patients were identified, of whom 99,390 (40.6%) were prescribed an OAC versus 145,117 (59.4%) who did not have a claim for an OAC prescription during the study identification period.
- For the final sample, 114,648 (47%) were patients aged 18-64, 62,544 (26%) were patients aged 65-74 and 67,315 (27%) were patients aged 75+.

Clinical Outcomes

Figure 2:

- Patients aged 65-74 (odds ratio [OR] 1.44; 95% confidence interval [CI] [1.40, 1.48]) and 75+ (OR 1.51 [95% CI 1.45, 1.57]) had higher likelihoods of receiving an OAC prescription compared to patients aged 18-64 after adjusting for potential confounders.

Figure 2. Association of Age Groups with OAC Prescription



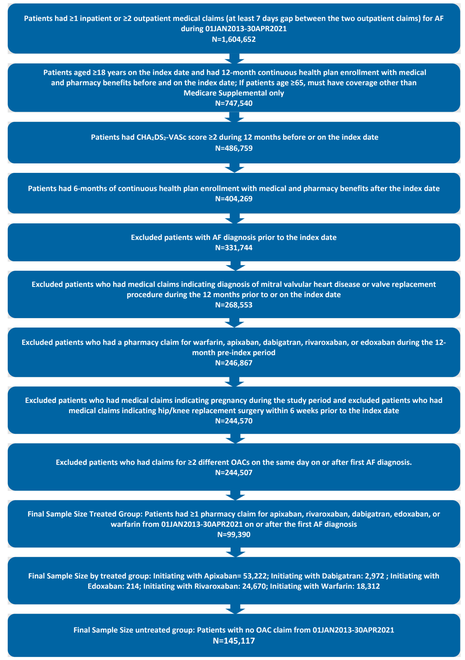
AOR: adjusted odds ratio; CI: confidence interval; OAC: oral anticoagulant
Age group 18-64 is reference group.

Stage 1 is adjusted for sex, 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 3:

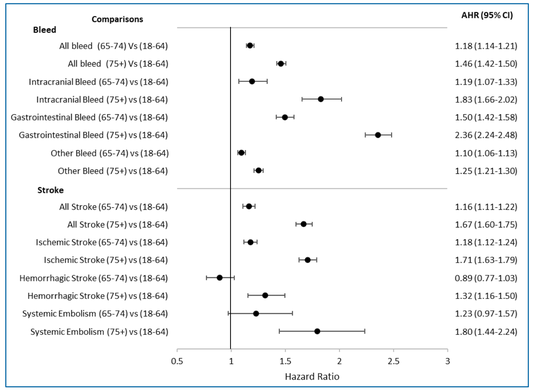
- Patients aged 65-74 had an 18% higher adjusted risk of MB (odds ratio [OR] 1.18; (95% CI [1.14, 1.21]) and 75+ had a 46% higher adjusted risk of MB (OR 1.46 (95% CI [1.42, 1.50]).
- Older ages were also significantly associated with a 50% (OR 1.50 (95% CI [1.42, 1.58]) and 136% higher adjusted risk (OR 2.36 (95% CI [2.24, 2.48]) of GI bleeds in ages 64-75 and 75+, respectively. Results for intracranial and other bleeds were similar.
- Patients aged 65-74 also had a 16% higher adjusted risk (OR 1.16 (95% CI [1.11, 1.22]), and 75+ had a 67% higher adjusted risk (OR 1.67 (95% CI [1.60, 1.75]), of any stroke outcome.
- Age 75+ was also associated with a 32% higher adjusted risk (OR 1.32 (95% CI [1.16, 1.50]) of hemorrhagic stroke. Results for ischemic stroke and SE were similar.

Figure 1. Patient Selection Criteria



AF: atrial fibrillation; OAC: oral anticoagulant

Figure 3. Association of Age Groups with Clinical Outcomes



AHR: adjusted hazard ratio; CI: confidence interval; OAC: oral anticoagulant
Age group 18-64 is reference group.
Model controls for sex, 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.

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.
- PharMetrics plus is a commercial claims database in which patients aged 65+ are under-represented. This age-adjusted analysis may have underestimated treatment rates in older patients
- 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 association of age groups with likelihood of OAC prescription and with risk of major bleeding (MB), stroke and systemic embolism (SE) among newly diagnosed AF patients with elevated stroke risk (CHA_2DS_2-VASc score≥2). Leveraging data from IQVIA PharMetrics Plus Health Plan claims databases, this study reports key findings:
- (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) Older patients (65-74) and (75+) were more likely to be prescribed an OAC than younger patients (18-64).
- (3) Older patients (65-74) and (75+) were at a higher risk of adverse clinical outcomes than the younger patients (18-64).

Main Findings:

- Older patients are more likely to be prescribed an appropriate OAC for AF treatment, but are at a higher likelihood of suffering a MB, stroke, or SE.

Conclusion

- **After adjusting for demographics, comorbidities and medication use, older AF patients had higher likelihoods of receiving an OAC prescription and were at significantly higher risk for adverse outcomes compared to younger AF patients.**
- **Clinical implications of this study include older patients are more likely to be prescribed an appropriate OAC, but with a higher likelihood of MB, stroke, or SE after adjusting for demographics, comorbidities, and medication use.**

References

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Disclosures

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