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Anticoagulant Use in High Stroke-Risk Patients With Nonvalvular Atrial Fibrillation

Hannah K. Nguyen, Douglas Humber, Harvey Checkoway, Daniel Blanchard, Jonathan H. Watanabe

BACKGROUND: Oral anticoagulants (OACs) are recommended for nonvalvular atrial fibrillation (NVAF) patients with moderate- to high-stroke risk.

OBJECTIVE: To examine nationally reflective OAC usage in incident NVAF patients longitudinally.

DESIGN: Three-year retrospective cohort analysis.

SETTING: Medicare Part D recipients in the contiguous United States.

PARTICIPANTS: 52,465 Medicare beneficiaries with incident NVAF in 2010 with two or more atrial fibrillation diagnoses seven or more days apart.

MAIN OUTCOME MEASURE: Stroke risk via congestive heart failure, hypertension, age greater than or equal to 75, diabetes, stroke, vascular disease, age 65-74, sex category (CHA_2DS_2-VASc) score. Primary outcome was proportion of patients receiving one or more OACs post-NVAF diagnoses.

RESULTS: Of 48,980 high-risk patients, 32.7% received one or more OAC within 60 days of diagnosis. By close of 2011, 48% had one or more OAC. OAC use increased to 52.9% by close of 2012.

CONCLUSIONS: Fewer than 33% of high-risk NVAF patients received OACs within 60 days of diagnosis in 2010. Despite increased use over time, oral anticoagulation was below 53% at study end. Use of OACs declined with CHA_2DS_2-VASc greater than 6. Expanded efforts are warranted to augment OAC use in high stroke-risk patients.

KEY WORDS: Anticoagulation, Atrial fibrillation, CHA_2DS_2-VASc, Stroke.

ABBREVIATIONS: AF = Atrial fibrillation, CHA_2DS_2-VASc = Congestive heart failure, hypertension, age equal to or greater than 75, diabetes, stroke, vascular disease, age 65-74, sex category, CHF = Congestive heart failure, DOACs = Direct oral anticoagulants, ESLD = End-stage liver disease, FDA = Food & Drug Administration, HAS-BLED = Hypertension, abnormal renal/liver function, stroke, bleeding history/predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly, NVAF = Nonvalvular atrial fibrillation, OACs = Oral anticoagulants, TE = Thromboembolism.

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Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia most frequent in older adults and is considered the primary etiologic factor in as many as 23.5% of strokes in persons between the ages of 80 and 89 years.[1,2] Prevalence of AF increases significantly with age, ranging from 1.2% to 2.8% in patients aged 60 to 69 years of age and 7.3% to 13.7% in patients 80 years of age and older.[1-5] In comparison with those without AF, patients with AF face higher rates of cardiovascular and all-cause mortality with significantly increased financial burden, validating early management approaches to minimize stroke risk. Total direct costs for treatment of AF in the United States have been estimated to be $6.65 billion annually.[6]

Nonvalvular atrial fibrillation (NVAF) is associated with a five-fold increase in the risk of stroke and accounts for approximately 15% of all strokes nationwide.[7,8] Per consensus guidelines for management of patients with AF, oral anticoagulants (OACs) are indicated for stroke prevention in patients classified as high-risk based on a score of two or greater using the validated congestive heart failure (CHF), hypertension, age equal to or greater than 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category (CHA_2DS_2-VASc) risk score.[8-10] Previous studies have reported limited rates of OAC use among patients with NVAF indicated for oral anticoagulants per guideline, ranging from 42.1% to 61.8%.[11-14] However, these studies are limited by estimates at a single time point. This analysis addresses this weakness by examining the use of OACs, in a nationally representative cohort of patients, particularly the elderly Medicare beneficiaries, over multiple years measured at three time points. Our goal was to quantify potential underuse of OACs in older adults to motivate increased monitoring by senior care pharmacists of NVAF patients and to augment appropriate OAC use per CHA_2DS_2-VASc risk score.

Methods

Data Source

Claims data were analyzed from the Truven Health MarketScan Medicare Supplemental Database, a nationally reflective and validated database of Medicare enrollees, for years 2010 through 2012. Outpatient files contained physician visits and diagnoses, as well as demographic characteristics and program eligibility and enrollment status. Drug files contained prescription drug claims and drug coverage. Inpatient files contained date of hospital admission, inpatient diagnosis, and length of stay. All files contained cross-linked unique beneficiary identifiers. This study project was issued institutional review board exemption from the University of California, San Diego, Human Research Protections Program.

Study Design

We conducted a retrospective cohort study among Medicare recipients with incident NVAF diagnosed in 2010, as identified using outpatient claims obtained from Truven Health MarketScan Medicare Supplemental Database. Incident cases of NVAF were defined as no diagnosis of AF (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 427.31) six months prior to the first AF (index) date in 2010, with no diagnoses for mitral valve disease (i.e., mitral stenosis [ICD-9-CM 394.0, 394.2, 396.0, 396.1, 396.8] or unspecified mitral valve diseases [ICD-9-CM 394.9]); presence of mitral valve replacement (ICD-9-CM 35, 35.2, 35.9, 35.24); or prosthetic heart valve (ICD-9-CM V42.2, V43.3).[8-10,15,16] To establish a diagnosis of persistent AF, patients were required to have at least two outpatient diagnoses of AF a minimum of seven days apart. From the first diagnosis date in 2010, study subjects were followed until close of December 31, 2012. Complete insurance plan enrollment for the study period since the index date in 2010 through 2012 was required for inclusion. Medical history was collected at the index date and by the end of each calendar year. Patients with absolute contraindications to warfarin, dabigatran, or rivaroxaban were identified based on diagnosis of intracranial hemorrhage (ICD-9-CM 430, 431, 432.x), intracranial mass (ICD-9-CM 191.x, 225.x, 239.6, 198.3), or end-stage liver disease (ESLD), based on an algorithm developed by Goldberg et al.[17-19]

Of 386,051 qualifying diagnoses of AF, 104,048 (27.0%) were incident cases of AF among patients with full enrollment in the index year of 2010 (Figure 1). Within this patient population, 3,253 (3.1%) were diagnosed with valvular AF (i.e., mitral valve diseases including mitral stenosis with or without insufficiency, presence of mitral valve replacement, or prosthetic heart valve), and 22,823 (21.9%) were diagnosed with paroxysmal NVAF lasting less than seven days.[8-10,15-16] In addition, 24,188 (23.2%) patients were excluded because of discontinuous enrollment in the year 2011 or 2012. Patients who developed valvular conditions (n = 2,073 [2.0%]) or had absolute contraindications to oral anticoagulants (n = 431 [0.4 %]) were also excluded from the study because they were not candidates for DOACs or warfarin. The remaining patients (n = 52,465) were deemed fully enrolled and eligible to receive OAC therapy (Figure 1).

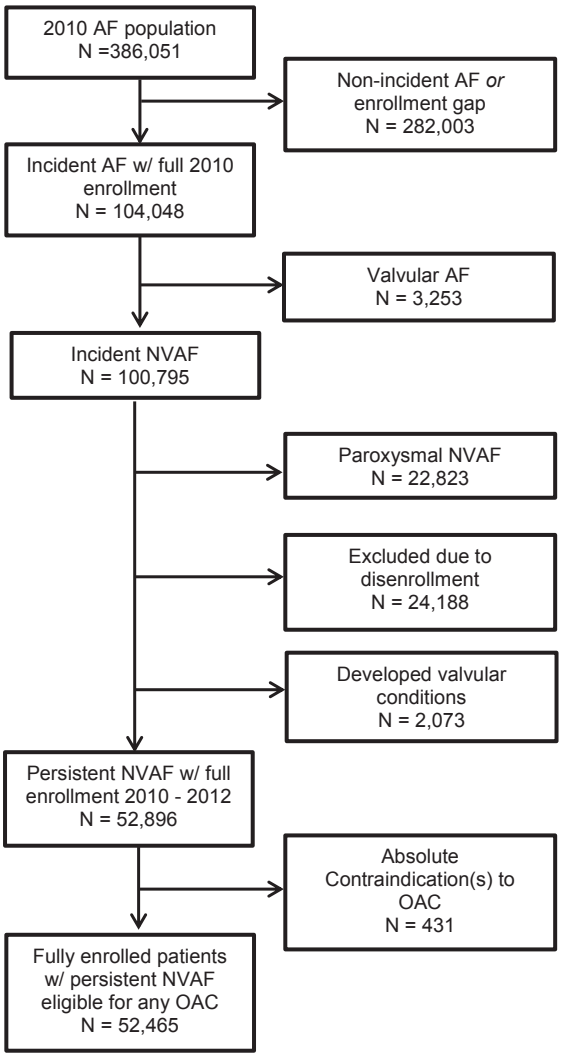
Study Outcomes

The primary outcome of this study was the proportion of patients who received at least one OAC prescription for warfarin ("coumadin" or "jantoven" or "warfarin sodium"), dabigatran ("pradaxa" or "dabigratan"), or rivaroxaban ("xarelto" or "rivaroxaban") postdiagnosis of incident NVAF, as found in the outpatient drug claims obtained from the Truven Health MarketScan Medicare Supplemental Database. Apixaban and edoxaban were not approved by the Food & Drug Administration (FDA) during the study period and were not included in this data analysis.

Statistical Analysis

The congestive heart failure, hypertension, age greater than or equal to 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category (CHA_2DS_2-VASc) score was used for stroke assessment. The CHA_2DS_2-VASc system has been validated to identify patient scenarios where anticoagulation is not recommended because of low risk of thromboembolic event (CHA_2DS_2-VASc

Figure 1. Cohort Selection



Abbreviations: AF = Atrial fibrillation, NVAF = Non-valvular atrial fibrillation, OAC = Oral anticoagulant.

equal to zero).[20] Statistical differences in the continuous variables (CHA_2DS_2-VASc score, age) were analyzed using ANOVA and expressed as mean ± standard deviation. Categorical variables were expressed as percentage and differences in categorial variables (use of OACs, comorbidities, categorical age, contraindications to OACs) were assessed via chi-squared test. The α level was set at 0.05 for all comparisons. All analyses were conducted using SAS 9.4 (Cary, NC).

Role of the Funding Source

The University of California San Diego, provided institutional support. Supporting organizations did not have any role in the design, methods, analysis, or preparation of this manuscript.

Results

The final study cohort included 52,465 patients. Women represented 46.6% of the study groups, and 99.2% were 65 years of age or older. Medical history taken at index date demonstrated that 2,715 (5.2%) patients had previous stroke(s), 13,052 (24.9%) had diabetes, 8,397 (16.0%) had CHF, 29,061 (55.4%) had hypertension, 9,134 (17.4%) had vascular disease, and the mean CHA_2DS_2-VASc was 3.35 ± 1.3. Among the cohort, 93.4% (n = 48,980) were classified as high risk at baseline, with CHA_2DS_2-VASc greater than or equal to 2 (Table 1).

By the close of 2011, 6,184 (11.8%) patients from the cohort had a previous stroke, 16,907 (32.2%) had diabetes, 16,851 (32.1%) had CHF, 41,563 (79.2%) had hypertension, 17,742 (33.8%) had vascular disease. The mean CHA_2DS_2-VASc score was 4.20 ± 1.5. The prevalence of their comorbidities continued to rise over the study period. By the close of 2012, 8,310 (15.8%) had previous stroke(s), 18,554 (35.4%) had diabetes, 20,553 (39.2%) had CHF, 45,292 (86.3%) had hypertension, 21,997 (41.9%) had vascular disease, and the mean CHA_2DS_2-VASc score significantly increased to 4.53 ± 1.6 ($P < 0.01$) (Table 1).

Among the high-risk patients with CHA_2DS_2-VASc of two or greater, 16,000 (32.7%) received an OAC prescription within 60 days of index date. By the end of the year 2011 and 2012, 48.0% (n = 24,607) and 52.9%

Table 1. Characteristics of Nonvalvular Atrial Fibrillation Cohort (N = 52,465)

	Index	2010	2011	2012	*P*-Value
Average Age ± SD	77.8 ± 7.5	77.8 ± 7.5	78.8 ± 7.5	79.8 ± 7.5	< 0.01
Age, n (%)					
< 65 years	431 (0.8)	431 (0.8)	329 (0.6)	268 (0.5)	< 0.01
65-74 years	17,992 (34.3)	17,992 (34.3)	15,924 (30.4)	13,984 (26.7)	
> 75 years	34,042 (64.9)	34,042 (64.9)	36,212 (69.0)	38,213 (72.8)	
Women, n (%)	24,454 (46.6)	24,454 (46.6)	24,454 (46.6)	24,454 (46.6)	n/a
Comorbidities, n (%)					
Previous Stroke or TIA	2,715 (5.2)	3,912 (7.5)	6,184 (11.8)	8,310 (15.8)	< 0.01
Diabetes Mellitus	13,052 (24.9)	14,524 (27.7)	16,907 (32.2)	18,554 (35.4)	< 0.01
Congestive Heart Failure	8,397 (16.0)	11,692 (22.3)	16,851 (32.1)	20,553 (39.2)	< 0.01
Hypertension	29,061 (55.4)	34,355 (65.5)	41,563 (79.2)	45,292 (86.3)	< 0.01
Vascular Disease	9,134 (17.4)	12,291 (23.4)	17,742 (33.8)	21,997 (41.9)	< 0.01
Contraindicated to OAC, n (%)	0 (0.0)	221 (0.4)	744 (1.4)	1,313 (2.5)	< 0.01
Intracranial Hemorrhage	0 (0.0)	165 (0.3)	577 (1.1)	992 (1.9)	< 0.01
Intracranial Mass	0 (0.0)	34 (0.06)	125 (0.2)	233 (0.4)	< 0.01
ESLD*	0 (0.0)	23 (0.04)	54 (0.1)	119 (0.2)	< 0.01
Average CHA_2DS_2-VASc ± SD	3.35 ± 1.3	3.64 ± 1.4	4.20 ± 1.5	4.53 ± 1.6	< 0.01
CHA_2DS_2-VASc, n (%)					
< 2	3,485 (6.6)	2,504 (4.8)	1,163 (2.2)	791 (1.5)	< 0.01
≥ 2	48,980 (93.4)	49,961 (95.2)	51,302 (97.8)	51,674 (98.5)	< 0.01

Note: Medicare patients with AF are in poorer health than those without a diagnosis of AF (higher prevalence of comorbidities: diabetes, hypertension, etc.). Of those diagnosed with incident NVAF, 24,188 were excluded because of disenrollment. 133 died in 2010. 1,068 died in 2011. 844 died in 2012. For those who died, last-observation-carried-forward method was applied.

Abbreviations: AF = Atrial fibrillation, CHA_2DS_2-VASc = Congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category, NVAF = Nonvalvular atrial fibrillation, OAC = Oral anticoagulant, SD = Standard deviation, TIA = Transient ischemic attack.

(n = 26,744), respectively, of the study cohort had one or more prescription drug claims for OAC. Warfarin was the most prescribed OAC among all subgroups (high-risk, n = 15,603/48,980 [31.9%]; low- to moderate-risk, n = 1,161/3,485 [33.3%]) (Table 2). Patients at low risk for stroke, based on CHA_2DS_2-VASc of zero, were anticoagulated at a rate of 39% within 60 days of the index date (Table 3).

Discussion

During the bulk of the follow-up period, the majority of high-risk patients with NVAF did not receive thromboembolic prevention, with as few as 32.7% receiving any OAC within 60 days of initial diagnosis (Table 2). The slow progression in OAC use reflects a delay in OAC initiation (Figure 2B). Of the 52,465 patients included in the cohort, 3,485 had CHA_2DS_2-VASc of 1 or less at index date. By close of

Table 2. Anticoagulant Use Among Cohort Population in 2010-2012 (N = 52,465)

Index			
Anticoagulant	**CHA_2DS_2-VASc < 2**	**CHA_2DS_2-VASc ≥ 2**	***P*-Value**
n (%)	**(n = 3,485)**	**(n = 48,980)**	
Warfarin	1,161 (33.3)	15,603 (31.9)	0.0744
Dabigatran	44 (1.3)	521 (1.1)	0.2718
Rivaroxaban	0 (0.0)	0 (0.0)	—
Any OAC	**1,196 (34.3)**	**16,000 (32.7)**	**0.0447***
2010			
Anticoagulant	**CHA_2DS_2-VASc < 2**	**CHA_2DS_2-VASc ≥ 2**	***P*-Value**
n (%)	**(n = 2,504)**	**(n = 49,961)**	
Warfarin	935 (37.3)	18,250 (36.5)	0.4105
Dabigatran	47 (1.9)	744 (1.5)	0.1202
Rivaroxaban	0 (0.0)	0 (0.0)	—
Any OAC	**963 (38.5)**	**18,637 (37.3)**	**0.2435**
2011			
Anticoagulant	**CHA_2DS_2-VASc < 2**	**CHA_2DS_2-VASc ≥ 2**	***P*-Value**
n (%)	**(n = 1,163)**	**(n = 51,302)**	
Warfarin	524 (45.1)	23,201 (45.2)	0.9091
Dabigatran	113 (9.7)	4,199 (8.2)	0.0601
Rivaroxaban	0 (0.0)	30 (0.06)	0.4094
Any OAC	**559 (48.1)**	**24,607 (48.0)**	**0.9460**
2012			
Anticoagulant	**CHA_2DS_2-VASc < 2**	**CHA_2DS_2-VASc ≥ 2**	***P*-Value**
n (%)	**(n = 791)**	**(n = 51,674)**	
Warfarin	351 (44.4)	25,572 (49.5)	0.0043
Dabigatran	86 (10.9)	5,023 (9.7)	0.2782
Rivaroxaban	19 (2.4)	976 (1.9)	0.2936
Any OAC	**391 (49.4)**	**26,744 (52.9)**	**0.0039***

Note: Totals of anticoagulant subgroups by type may exceed the number of patients receiving any OAC because of individual patients receiving multiple types of anticoagulants. Patients counted as "Any OAC" were those with at least one claim for warfarin, dabigatran, or rivaroxaban.

Abbreviations: CHA_2DS_2-VASc = Congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category, OAC = Oral anticoagulant.

2011, the number of these low-risk subjects had dropped to 1,163, indicating that 2,322 patients developed a CHA_2DS_2-VASc score of 2 or greater. Assuming that all 2,322 patients who progressed to CHA_2DS_2-VASc of 2 or greater in 2011 initiated anticoagulants per their risk level, the proportion of OAC use among high-risk patients was expected to increase to 35.7% [(16,000 ± 2,322) / (48,980 ± 2,322)]. However, the percent of OAC use among high stroke-risk patients increased to 48.0% by end of 2011, a 12.3%-greater OAC use frequency than expected if only those newly indicated began OACs. Hence, the additional increase in OAC use over time is attributable to OAC initiation in high stroke-risk patients who qualified for stroke prevention, but did not receive

Table 3. Percent of Patients Receiving OAC Prescription(s), Stratified Based on CHA_2DS_2-VASc Score

	CHA_2DS_2-VASc	0	1	2	3	4	5	6	7	8	9
% of	**Baseline**	38.96	34.21	34.54	33.58	31.97	29.61	30.84	30.52	27.11	16.67
Patients	**2010**	42.59	38.37	39.13	38.57	37.30	35.31	34.14	35.03	28.33	26.32
Receiving	**2011**	36.84	48.25	47.68	48.34	48.45	48.17	47.35	46.81	45.02	42.29
OACs	**2012**	37.50	47.77	50.58	52.00	53.35	53.67	53.19	53.28	51.20	50.55

Note: Totals of anticoagulant subgroups by type may exceed the number of patients receiving any OAC because of individual patients receiving multiple types of anticoagulants. Patients counted as "Any OAC" were those with at least one claim for warfarin, dabigatran, or rivaroxaban.

Abbreviations: CHA_2DS_2-VASc = Congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category, OACs = Oral anticoagulants.

anticoagulation at diagnosis. A similar pattern was witnessed in 2012 and accounts for the disproportionate increase in OAC use among high stroke-risk patients by study conclusion.

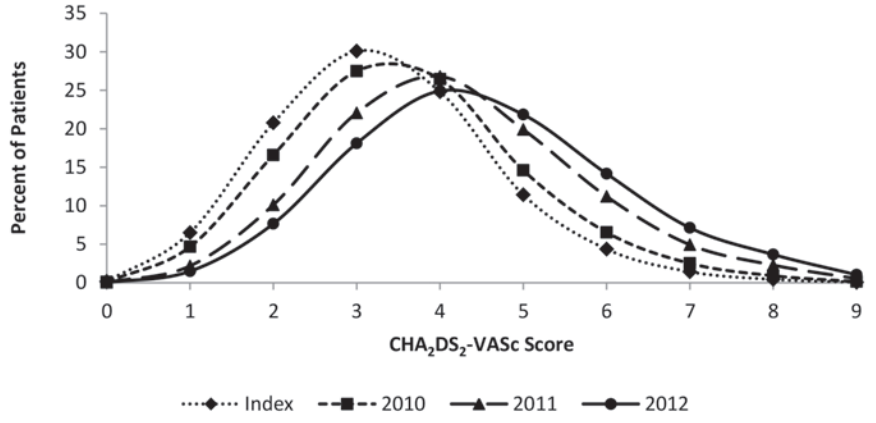
Despite the increase, only 52.9% of high stroke-risk patients were anticoagulated by the close of the study, suggesting opportunities for improvement in care. According to Olesen et al., the 10-year follow-up event rate of hospital admission and death from thromboembolism (TE) in high stroke-risk patients (CHA_2DS_2-VASc of 2 or greater) was estimated to be 5.72 per 100 person-years (95% confidence interval 5.60-5.84), and reached as high as 15.89 per 100 person-years in those with a CHA_2DS_2-VASc equal to 9.[20] Furthermore, the underuse of OACs has been perceived as one of the major causes of ischemic stroke in patients with NVAF.[21] Thus, it is imperative that patients with NVAF receive anticoagulant therapy for prevention of TE-related hospitalization and death, in accordance with evidence-based guidelines.

As depicted in Figure 2, the CHA_2DS_2-VASc score of the cohort population increased with time, ranging from 3.35 ± 1.3 at baseline to 4.53 ± 1.6 by the end of 2012. This is consistent with the development of age-related comorbidities such as hypertension and diabetes, all of which contribute to worsened stroke risk. To ensure appropriate continuum of care, patients with NVAF should be reviewed for CHA_2DS_2-VASc score periodically and initiated on OAC, unless contraindications prevail.

The general increase in CHA_2DS_2-VASc score was accompanied by an increase in OAC use over time (Figure 2). By the close of the study period in 2012, 52.9% of patients received OAC prescriptions, compared with 32.7% within 60 days of index date. The failure to initially treat with OAC may be partially explained by the reluctance of prescribers to initiate OAC therapy in patients with higher perceived bleed risk, fall risk, frailty, and diminished renal function.[22,23] The decreasing rates of OAC prescription use among patients with CHA_2DS_2-VASc of 6 or greater may reflect a clinician's hesitation in OAC initiation in patients who, at baseline, have increased complications and overall frailty (Figure 2).[22-25]

Pharmacists are critical members of the interdisciplinary care team with an outsized role in assuring appropriate anticoagulation is achieved. Studies conducted by Virdee et al. and Bajorek et al. demonstrate the importance of pharmacists in optimizing anticoagulation therapy in patients with AF.[26,27] Pharmacist-led interventions culminated in increased antithrombotic use and realignment of oral anticoagulation therapy to the most current evidence-based guidelines.[26,27] Pharmacists in long-term care have a fundamental role in detection, management, and prevention of stroke-related risks in patients with AF. At admission to a long-term care facility, the pharmacist should obtain and review the complete medical record and medication profile to perform robust medication reconciliation. For long-stay patients, the pharmacist

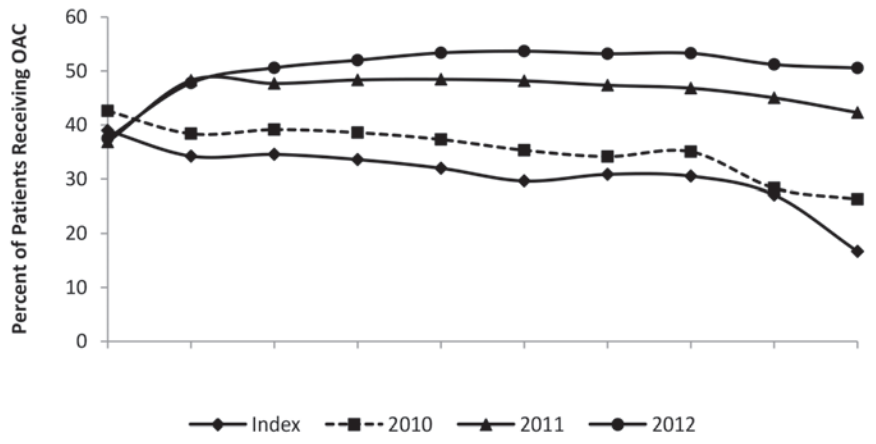
Figure 2A. CHA_2DS_2-VASc Score of Cohort Over Time*



*Index = Initial date of diagnosis of NVAF.
Note: To ensure incident diagnosis, patients must not have prior diagnosis of AF within six months of the initial AF diagnosis in 2010. Anticoagulant use was analyzed using outpatient drug claims from 2010-2012. CHA_2DS_2-VASc score was obtained at baseline and at the end of each calendar year.

Abbreviations: AF = Atrial fibrillation, CHA_2DS_2-VASc = Congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex, OAC = Oral anticoagulant.

Figure 2B. Percent of Patients Receiving OAC Prescription(s), Stratified by CHA_2DS_2-VASc Score



Note: To ensure incident diagnosis, patients must not have prior diagnosis of AF within six months of the initial AF diagnosis in 2010. Anticoagulant use was analyzed using outpatient drug claims from 2010-2012. CHA_2DS_2-VASc score was obtained at baseline and at the end of each calendar year.

Abbreviations: AF = Atrial fibrillation, CHA_2DS_2-VASc = Congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex, OAC = Oral anticoagulant.

should periodically review for history of bleeds and updated CHA_2DS_2-VASc score, with active surveillance for new diagnoses of CHF, hypertension, diabetes, stroke, or vascular diseases. For high-risk patients not already anticoagulated, the pharmacist should engage with the prescriber to initiate OAC, unless prevailing contraindications surface. Prescribers must also work closely with pharmacists to identify high-risk patients who may benefit from anticoagulation.

While limited rates of OAC use have been previously reported, ranging from 56.0% to 61.8%, no prior published study has examined OAC use over time in a nationally representative cohort of older adults with incident NVAF.[11-13] Our findings demonstrate not only the low rates of OAC use among high-risk patients over multiple years of follow-up, but also a delay in anticoagulation initiation among those indicated.

This analysis utilized the more recent CHF, hypertension, age greater than or equal to 75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category (CHA_2DS_2-VASc) scoring system, rather than the earlier $CHADS_2$ stratification system, as

the stroke assessment measure because of improved predictive values.[20] The study period from 2010 to 2012 aligns with the transition period for adoption of $CHADS_2$ to CHA_2DS_2-VASc scoring system by clinicians. However, application of the older $CHADS_2$ alone cannot explain the limited use of OAC rates observed. The difference between the risk score schemes hinges on stratification of low- to moderate-risk patients with $CHADS_2$ score equal to 0 or 1. Patients classified as low-risk using $CHADS_2$ (score equal to 0) could qualify either as a low- or intermediate-risk using CHA_2DS_2-VASc (score equal to 0 or 1).[20] By way of comparison, a patient classified as high-risk using $CHADS_2$ with a score of 2 has a 10-year risk of 5.40 for hospitalization and TE-related death per hundred person-years, corresponding roughly to a CHA_2DS_2-VASc score of 4 with a 10-year risk of 6.46 for hospitalization and TE-related death per hundred person-years. In patients with CHA_2DS_2-VASc of 4 or greater, the stroke risks are elevated to the extent that the $CHADS_2$ system would produce the identical recommendation for anticoagulation. Data analysis showed that even among patients with CHA_2DS_2-VASc of 4 or greater, the rates of OAC use did not exceed 53.67% (Table 3).

Limitations

The analysis database lacked the complete variable list to calculate the hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly (HAS-BLED) score for one-year risk of major bleeds for patients with AF.[28] Elevated HAS-BLED score necessitates consideration of modifications to reduce bleed risk and potential consideration of alternatives to anticoagulation, but does not automatically preclude oral anticoagulation.[29] Physicians, however, appear to generally overestimate bleed risk and underestimate stroke risk, and thereby prescribe OACs conservatively.[30] In published studies, patients with NVAF and an elevated HAS-BLED score have demonstrated a net clinical benefit from oral anticoagulation when balancing ischemic stroke against intracranial bleeds.[31-33] High bleeding-risk patients (HAS-BLED scores of 3 or more) are also at higher risk for ischemic stroke, and the absolute reduction in stroke risk with OAC use has been shown to outweigh the small absolute increase in intracranial hemorrhage.[33] Moreover, prior studies estimated the prevalence of bleed risk in NVAF patients at a maximum of 29%. This is well below the roughly 50% of patients without anticoagulation in this analysis.[31,34,35]

An additional limitation is a study period that concluded in 2012, prior to the widespread use of DOACs. However, our findings are consistent with cross-sectional analyses performed in more recent data.[12,14,36] Because rivaroxaban was FDA-approved in 2011 for stroke prevention in NVAF patients, usage was not detected in the index year. By the end of 2012, user count had increased to 995, equal to 1.9% of the original cohort. The DOACs apixaban and edoxaban entered the market after this study period and were therefore not measured. As DOACs continue to integrate into clinical practice, future studies of OAC use should be performed.

Conclusions

In this nationally representative analysis of Medicare beneficiaries, fewer than 55% of high stroke-risk patients were anticoagulated at any point of the three-year study, with fewer than 33% of high-risk patients receiving an OAC prescription within 60 days of index date. Contrary to guidelines, prevalence of OAC prescriptions declined with increasing CHA_2DS_2-VASc score greater than 6. Given the increased risk of thromboembolic events, expanded efforts are warranted to augment the use of OACs in this patient population. For senior care pharmacists, these findings underscore the importance of vigilant review of the patient profile and concordant OAC initiation in patients identified at high risk for stroke.

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References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991;22:983-8.

2. Heeringa J, van der Kuip DAM, Hofman A et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006;27:949-53.

3. Lake FR, Cullen KJ, de Klerk NH et al. Atrial fibrillation and mortality in an elderly population. Aust N Z J Med 1989;19:321-6.

4. Phillips SJ, Whisnant JP, O'Fallon WM et al. Prevalence of cardiovascular disease and diabetes mellitus in residents of Rochester, Minnesota. Mayo Clin Proc 1990;65:344-59.

5. Furberg CD, Psaty BM, Manolio TA et al. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). Am J Cardiol 1994;74:236-41.

6. Coyne KS, Paramore C, Grandy S et al. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. Value Health J Int Soc Pharmacoeconomics Outcomes Res 2006;9:348-56.

7. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomized controlled trials. Arch Intern Med 1994;154:1449.

8. January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary. Circulation 2014;130:2071.

9. January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation 2014;130:e199-267.

10. Nishimura RA, Otto CM, Bonow RO et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017;135:e1159-95.

11. Piccini JP, Mi X, DeWald TA et al. Pharmacotherapy in Medicare beneficiaries with atrial fibrillation. Heart Rhythm 2012;9:1403-8.

12. Hsu JC, Maddox TM, Kennedy K et al. Aspirin instead of oral anticoagulant prescription in atrial fibrillation patients at risk for stroke. J Am Coll Cardiol 2016;67:2913-23.

13. Zimetbaum PJ, Thosani A, Yu H-T et al. Are atrial fibrillation patients receiving warfarin in accordance with stroke risk? Am J Med 2010;123:446-53.

14. Averlant L, Ficheur G, Ferret L et al. Underuse of oral anticoagulants and inappropriate prescription of antiplatelet therapy in older inpatients with atrial fibrillation. Drugs Aging 2017;34:701-10.

15. Barnett AS, Lewis WR, Field ME et al. Quality of evidence underlying the American Heart Association/American College of Cardiology/Heart Rhythm Society Guidelines on the Management of Atrial Fibrillation. JAMA Cardiol 2017;2:319.

16. Di Biase L. Use of direct oral anticoagulants in patients with atrial fibrillation and valvular heart lesions. J Am Heart Assoc 2016;5:e002776.

17. Goldberg D, Lewis J, Halpern S et al. Validation of three coding algorithms to identify patients with end-stage liver disease in an administrative database. Pharmacoepidemiol Drug Saf 2012;21:765-9.

18. Steinberg BA, Greiner MA, Hammill BG et al. Contraindications to anticoagulation therapy and eligibility for novel anticoagulants in older patients with atrial fibrillation. Cardiovasc Ther 2015;33:177-83.

19. Connolly SJ, Ezekowitz MD, Yusuf S et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-51.

20. Olesen JB, Lip GYH, Hansen ML et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:d124.

21. Nakamura A, Kuroda J, Ago T et al. Causes of ischemic stroke in patients with non-valvular atrial fibrillation. Cerebrovasc Dis 2016;42:196-204.

22. Sen S, Dahlberg KW. Physician's fear of anticoagulant therapy in nonvalvular atrial fibrillation. Am J Med Sci 2014;348:513-21.

23. Flaker G, Turagam MK, Velagapudi P. Stroke prevention in the elderly atrial fibrillation patient with comorbid conditions: focus on non-vitamin K antagonist oral anticoagulants. Clin Interv Aging 2015:1431.

24. Berger J, Balfour DC, Biskupiak JE et al. Research to real-world application: experts weigh in on the underuse of anticoagulants. Am J Manag Care 2014;20:s312-8.

25. Biteker M, Başaran Ö, Doğan V et al. Real-world clinical characteristics and treatment patterns of individuals aged 80 and older with nonvalvular atrial fibrillation: results from the ReAl-life Multicenter Survey Evaluating Stroke Study. J Am Geriatr Soc 2017;65:1684-90.

26. Bajorek BV, Krass I, Ogle SJ et al. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: a pharmacist-led multidisciplinary intervention: Pharmacists Optimizing Antithrombotic Use in Atrial Fibrillation. J Am Geriatr Soc 2005;53:1912-20.

27. Virdee MS, Stewart D. Optimizing the use of oral anticoagulant therapy for atrial fibrilation in primary care: a pharmacist-led intervention. Int J Clin Pharm 2017;39:173-80.

28. Pisters R, Lane DA, Nieuwlaat R et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation. CHEST 2010;138:1093–100.

29. Camm AJ, Lip GYH, De Caterina R et al. 2012 focused update of the ESC Guidelines for the Management of Atrial Fibrillation: an update of the 2010 ESC Guidelines for the Management of Atrial Fibrillation -- developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012;33:2719-47.

30. Riva N, Smith DE, Lip GYH et al. Advancing age and bleeding risk are the strongest barriers to anticoagulant prescription in atrial fibrillation. Age Ageing 2011;40:653-5.

31. Olesen JB, Lip GYH, Lindhardsen J et al. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with atrial fibrillation: a net clinical benefit analysis using a 'real world' nationwide cohort study. Thromb Haemost 2011;106:739-49.

32. Friberg L, Rosenqvist M, Lip GYH. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish Atrial Fibrillation Cohort Study. Circulation 2012;125:2298-307.

33. Banerjee A, Lane DA, Torp-Pedersen C et al. Net clinical benefit of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus no treatment in a 'real world' atrial fibrillation population: a modelling analysis based on a nationwide cohort study. Thromb Haemost 2012;107:584-9.

34. Apostolakis S, Lane DA, Buller H et al. Comparison of the CHADS2, CHA2DS2-VASc and HAS-BLED scores for the prediction of clinically relevant bleeding in anticoagulated patients with atrial fibrillation: the AMADEUS Trial. Thromb Haemost 2013;110:1074-9.

35. Lefebvre M-CD, St-Onge M, Glazer-Cavanagh M et al. The effect of bleeding risk and frailty status on anticoagulation patterns in octogenarians with atrial fibrillation: the FRAIL-AF Study. Can J Cardiol 2016;32:169-76.

36. Brown JD, Shewale AR, Dherange P et al. A comparison of oral anticoagulant use for atrial fibrillation in the pre- and post-DOAC eras. Drugs Aging 2016;33:427-36.