Anticoagulant Prescriptions Provided in US Ambulatory Practice, 2014 to 2016

J Gen Intern Med 37(13):3515–7
DOI: 10.1007/s11606-022-07536-y

INTRODUCTION

The introduction of direct oral anticoagulants (DOACs) has revolutionized treatment for patients requiring anticoagulation. The DOACs, including dabigatran, rivaroxaban, apixaban, and edoxaban, were approved by the US Food and Drug Administration between 2010 and 2015. Advantages of DOACs compared to warfarin include less frequent need for blood monitoring and dose adjustments. As a result, DOACs are now recommended as first-line treatment for nonvalvular atrial fibrillation and venous thromboembolism.[1,2] As DOACs are less rapidly reversible than older anticoagulants, we examined their use for any indication among high-risk groups. Specifically, we examined women of childbearing age, who may experience menstrual difficulties and require contraceptive counseling given the teratogenicity of some anticoagulants, and the elderly, who are at greater risk of falls, drug-drug interactions, and altered drug metabolism due to renal insufficiency.

METHODS

Data from the 2014, 2015, and 2016 National Ambulatory Medical Care Survey (NAMCS), a nationally representative population-based survey, were combined and evaluated in a series of cross-sectional analyses.[3] NAMCS data is extracted from the electronic medical record of patients seen during participating physicians' pre-selected reporting weeks. In our study, 56,040 ambulatory visits to US physicians by patients 18 years and older were identified with 2777 visits involving an anticoagulation prescription. We examined use of DOACs, warfarin, and heparin-based products by US region, patient age, and gender. In women less than 50 years old, we assessed concurrent contraception use. Data was analyzed using SAS Analytics Software.

Received December 8, 2021
Accepted March 29, 2022
Published online April 11, 2022

RESULTS

Between 2014 and 2016, 8.7% (95% CI 8.0–9.5%) of US ambulatory visits involved a patient prescribed anticoagulation. Visits involving anticoagulation more frequently occurred in the South (30.1% [95% CI 24.6–35.7%]) than in the West (19.3% [95% CI 14.9–23.8%]), with similar rates in the Midwest (28.3% [95% CI 23.4–33.2%]) and Northeast (22.3% [95% CI 16.5–28.1%]). Most (77.7% [95% CI 74.2–81.3%]) visits involving anticoagulation were made by patients over the age of 65 years; 30.7% [95% CI 27.0–34.6%] were made by patients over 80 years.

Most visits with anticoagulation (63.7% [95% CI 59.9–67.7%]) involved warfarin; fewer involved DOACs (31.1% [95% CI 27.4–34.9%]) or heparin-based products (5.1% [95% CI 3.4–6.9%]). Visits involving DOACs were most common in patients aged 66–80 (45.5% [95% CI 39.2–51.8%]). As shown in Table 1, the proportion of visits with DOACs was highest in the Northeast (35.1% [95% CI 25.2–45.0%]) and lowest in the Midwest (24.8% [95% CI 19.4–30.1%]).

Table 2 highlights gender differences in rates of any anticoagulation, which is notable for variation by patient age. Among those over 80 years, women were more frequently prescribed anticoagulation than men: (59.6% [95% CI 52.5–66.7%] vs 40.4% [95% CI 33.3–47.6%]). Of 193 visits involving anticoagulation of women 18 to 49 years, only 1.9% ($N = 6$) documented concurrent contraception with four women prescribed combined oral contraceptives and two women progesterone-only pills.

DISCUSSION

In this population-representative cross-sectional study of US ambulatory practice, warfarin remains the most common anticoagulant prescribed for any indication in the USA, which follows the pattern previously described for anticoagulant use in atrial fibrillation.[4] The majority of anticoagulants are prescribed to patients over 65 years. Our finding of regional variation in DOAC use warrants attention for dissemination of best practice guidelines, and consideration of the role insurance formularies may play in limiting access. Our finding that DOAC prescriptions were more common among elderly women than men is consistent with prior observational studies of anticoagulation use in atrial fibrillation.[5,6]

In addition, our finding that very few women of childbearing age receiving anticoagulation had concurrent

Table 1 Anticoagulants Prescribed in US Ambulatory Visits by Age, Gender, and Region, 2014–2016

	Warfarin	DOACs	Heparin based
	Row % (CI)	Row % (CI)	Row % (CI)
Age			
18–50 years *N* = 193	53.6 (38.7, 68.5)	26.1 (12.8, 39.4)	20.3 (9.6, 31.0)
50–65 years *N* = 501	55.9 (46.0, 65.8)	34.5 (25.2, 43.7)	9.7 (5.2, 14.2)
66–79 years *N* = 1246	65.5 (60.6, 70.5)	30.1 (25.4, 35.0)	4.3 (2.0, 6.6)
≥ 80 years *N* = 837	67.3 (59.9, 74.6)	31.5 (24.1, 38.9)	1.2 (0.02, 2.4)*
Gender			
Female *N* = 1297	59.8 (54.6, 65.0)	34.8 (29.6, 39.9)	5.5 (2.8, 8.2)
Male *N* = 1480	67.3 (62.1, 72.5)	28.0 (22.9, 33.0)	4.8 (2.5, 7.1)
Region			
Northeast *N* = 405	61.1 (51.5, 70.7)	35.1 (25.2, 45.0)	3.8 (1.5, 6.1)*
Midwest *N* = 938	69.4 (63.7, 78.2)	24.8 (19.4, 30.1)	5.8 (2.5, 9.1)
South *N* = 780	62.1 (54.8, 69.4)	33.3 (26.6, 40.0)	4.6 (1.5, 7.8)
West *N* = 654	61.3 (52.5, 70.1)	32.3 (22.5, 42.1)	6.4 (1.2, 11.7)*

*Counted Visits Had at Least One Medication Documented in Visit Records. Reported Percentages Are Weighted. *Interpret These Estimates with Caution Due To Small Sample Size*

documentation of contraception is concerning, as warfarin is a known teratogen and the safety of DOAC use during pregnancy is unknown. Although NAMCS collects data on a range of contraceptives including hormonal intrauterine devices (IUDs), contraceptive rings, and injectables, anticoagulated patients were only found to be prescribed oral contraceptives. Limitations of this analysis include possible variation in documentation of long-acting contraception and the lack of inclusion of sterilization procedures, contraceptive implants, and copper IUDs; this may lead to underestimating the proportion of women with concurrent use of anticoagulation and contraception. Nonetheless, this study shows that warfarin remains commonly prescribed (despite recommendations that DOACs are first line) and that young women are often prescribed anticoagulation without concurrent contraception, which may lead to unnecessary risks.

Table 2 Gender Differences in Anticoagulant Use by Patient Age. Anticoagulants Included Warfarin, Direct Oral Anticoagulants, and Heparin-Based Products. Counted Visits Had at Least One Medication Documented in Visit Records. Reported Percentages Are Weighted

Age (years)	Female	Male
	Row % (CI)	Row % (CI)
18–49 *N* = 193	52.2 (38.2, 66.2)	47.8 (33.8, 61.8)
50–64 *N* = 501	35.4 (27.3, 43.6)	64.6 (56.4, 72.7)
65–79 *N* = 1246	40.8 (35.6, 46.0)	59.2 (54.0, 64.4)
≥ 80 *N* = 837	59.6 (52.5, 66.7)	40.4 (33.3, 47.5)

Tali Azenkot, MD[1]
Brittany Chatterton, MD[1,2]
Eleanor Bimla Schwarz, MD, MS[3]

[1]Department of Internal Medicine, University of California Davis School of Medicine, Sacramento, CA, USA
[2]Center for Healthcare Policy and Research, University of California, Davis, Sacramento, CA, USA
[3]Division of General Internal Medicine, Department of Internal Medicine, University of California San Francisco, San Francisco, CA, USA

Corresponding Author: *Tali Azenkot, MD; Department of Internal Medicine, University of California Davis School of Medicine, Sacramento, CA, USA (e-mail: tazenkot@ucdavis.edu).*

Declarations:

Conflict of Interest: *The authors have no conflicts of interest to report.*

REFERENCES

1. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, et al. 2019 AHA/ACC/HRS Focused Update of the 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 Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration with the Society of Thoracic Surgeons. Circulation [Internet]. 2019 Jul 9 [cited 2021 Aug 25];140(2). Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000665
2. Stevens SM, Woller SC, Kreuziger LB, Bounameaux H, Doerschug K, Geersing G-J, et al. Antithrombotic Therapy for VTE Disease: Second

Update of the CHEST Guideline and Expert Panel Report. Chest. 2021 Aug 2;S0012-3692(21)01506-3.
3. Centers for Disease Control and Prevention. Ambulatory Health Care Data [Internet]. 2021 Dec. Available from: https://www.cdc.gov/nchs/ahcd/index.htm
4. Essien UR, Magnani JW, Chen N, Gellad WF, Fine MJ, Hernandez I. Race/ethnicity and sex-related differences in direct oral anticoagulant initiation in newly diagnosed atrial fibrillation: a retrospective study of Medicare data. J Natl Med Assoc. 2020;112(1):103–8.
5. Zhu J, Alexander GC, Nazarian S, Segal JB, Wu AW. Trends and variation in oral anticoagulant choice in patients with atrial fibrillation, 2010-2017. Pharmacotherapy. 2018;38(9):907–20.
6. Pagès A, Sabatier R, Sallerin B. Factors associated with the choice of oral anticoagulant class in the older patients: an observational study. J Cardiovasc Pharmacol Ther. 2020;25(4):332–7.