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Original Research

A descriptive study of antithrombotic medication patterns in adult patients with recent venous thromboembolism

Fady ALLAHWERDY, Steven PAN, Michael FEEHAN, Aubrey E. JONES, Mark A. MUNGER, Daniel M. WITT.

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Abstract

Objectives: The objective of this study is to describe the most common self-reported antithrombotic therapy utilization patterns in a national cohort of patients with recent venous thromboembolism (VTE).

Methods: Extant data from a national online survey administered to 907 patients 18 years of age or older with VTE in the last two years were analyzed. Patients' self-reported antithrombotic usage patterns used during three phases of treatment for the most recent VTE episode were summarized using descriptive statistics.

Results: The following overall antithrombotic usage patterns were identified: warfarin (38.7%), direct oral anticoagulants (DOACs) (26.1%), switching between warfarin and DOACs (13.3%), aspirin only (8.7%), switching between different DOACs (4.5%), injectable anticoagulants only (3.9%), and no treatment (4.7%). Extended antithrombotic therapy beyond 90 days was reported by 65.7% of patients. Aspirin coadministration with anticoagulant therapy occurred for 33.7%.

Conclusions: In this national sample of recent VTE sufferers warfarin therapy remains the most used anticoagulant followed closely by DOAC therapy. Switching between warfarin and DOACs and between different DOACs was common which could indicate adverse events or affordability issues. Aspirin coadministration with anticoagulant therapy was present in 1 of 3 patients and is a potential medication safety intervention for anticoagulation providers.

Keywords

Anticoagulants; Thrombolytic Therapy; Venous Thromboembolism; Drug Utilization; Practice Patterns, Physicians'; Cohort Studies; Utah

INTRODUCTION

Venous thromboembolism (VTE) is a medical condition where a blood clot originates in the veins and is potentially life threating when clots embolize to the lungs.[1] The estimated average annual incidence rate of overall VTE ranges from 104 to 183 per 100,000 person-years.[2] These statistics and the relatively high cost of treating VTE underscore the importance of understanding VTE treatment strategies and their impact on the care of patients with VTE.[3]

VTE treatment generally consists of using anticoagulants.[4] Since its introduction in 1954, warfarin has been the mainstay of VTE treatment but is prone to drug and diet interactions and requires frequent dosing titration using the international normalized ratio (INR).[5] Due to recognized difficulties with warfarin, the direct oral anticoagulants (DOACs) are becoming increasing prescribed for VTE management. Recent randomized clinical trials show that DOACs are safer and either more effective or non-inferior to warfarin in the treatment of VTE.[4] Additionally, evidence-based guidelines now recommend DOACs as the drugs of first choice for VTE treatment over warfarin.[4]

Studies have analyzed prescribing trends of warfarin and DOACs for stroke prevention in atrial fibrillation and show an increasing utilization of DOACs.[6] General prescribing trends for oral anticoagulants in the treatment of VTE have recently been published, but anticoagulant utilization data for VTE treatment during different stages of therapy (initial, long-term and extended) are not available.[7] Furthermore, most data regarding prescribing trends is derived from electronic pharmacy claims data which have known limitations, including discrepancies between drug prescribing and actual drug taking behavior, and missing data.[8] Further, electronic pharmacy claims data is often limited to a particular healthcare system or insurance type (e.g., Medicare, Medicaid). Information on injectable anticoagulants such as heparin, low-molecular-weight heparin and fondaparinux, and concomitant aspirin use as well as information regarding patients who switch between anticoagulant types during VTE treatment is also needed to better characterize the realities of anticoagulant utilization during various phases of VTE therapy. Previous studies have provided evidence that self-reported medication use

Fady ALLAHWERDY. PharmD. Department of Pharmacotherapy, College of Pharmacy, University of Utah. Salt Lake City, UT (United States). fady.allahwerdy@pharm.utah.edu
Steven PAN. PharmD. Department of Pharmacotherapy, College of Pharmacy, University of Utah. Salt Lake City, UT (United States). steven.pan@pharm.utah.edu
Michael FEEHAN. PhD. Kantar LLC, San Francisco, CA (United States). michael.feehan@kantar.com
Aubrey E. JONES, PharmD. Thrombosis Service, University of Utah Health; & Department of Pharmacotherapy, College of Pharmacy, University of Utah. Salt Lake City, UT (United States). aubrey.e.jones@pharm.utah.edu
Mark A. MUNGER. PharmD, FCCP, FACC, FHFSA. Department of Pharmacotherapy, College of Pharmacy; & Department of Internal Medicine, School of Medicine, University of Utah. Salt Lake City, UT (United States). mark.munger@hsc.utah.edu
Daniel M. WITT. PharmD, FCCP, BCPS. Thrombosis Service, University of Utah Health; & Department of Pharmacotherapy, College of Pharmacy, University of Utah. Salt Lake City, UT (United States). dan.witt@pharm.utah.edu

reports may provide a more complete picture of individuals' current medication profiles than do electronic pharmacy claims data.[9,10] Thus, for the purpose of collecting medication information to ascertain what medications individuals are actually taking at a particular time self-reported data may be better than electronic claims data. Therefore, the purpose of this study was to describe the most common self-reported anticoagulant therapy utilization patterns during three phases of VTE treatment including injectable anticoagulants, concomitant aspirin use, and switching between anticoagulants in a large, national cohort of patients with recent VTE who completed a comprehensive online survey regarding their VTE experiences.

METHODS

Sample and procedure

The study was approved by the University of Utah's Institutional Review Board (IRB) before initiating data collection. All participants provided informed consent prior to commencing the survey. The survey sample was comprised of participants recruited by an independent contract research agency (Hall & Partners, New York, NY) from a nationally representative panel of consumers who pre-enrolled to participate in research studies (Research Now®, Research Now Group, Inc., New York, NY). Between May and July 2016 eligible patients accessed and completed an online survey, through a link in an invitation e-mail. Patients eligible to complete the survey were those aged 18 years or older who experienced at least one VTE event in the past 2 years. Patients diagnosed with cancer within the past 2 years were excluded. A sample size of approximately 1,000 patients was targeted to provide sufficiently accurate estimates for meaningful subgroups of interest, such as antithrombotic therapy usage patterns during the various phases of VTE treatment.

Survey

Patients indicated the number of VTE events they had experienced in their lifetimes, types of VTE experienced whether deep vein thrombosis (DVT) and/or pulmonary embolism (PE), and the type and timing of their most recent VTE event (within the past month, between 1 to 3 months ago, 3 to 12 months ago, and more than 12 months ago). The survey asked a comprehensive array of questions related to VTE treatment as described in detail previously.[11-13] However, the primary outcome for this study related to antithrombotic treatment pathways used during three phases of treatment for the most recent VTE episode. Antithrombotic medication use was categorized in the initial phase (days 0-7 since VTE diagnosis), long-term phase (days 8-90) and extended phase (90+ days). Patients indicated which oral and/or injectable antithrombotic medications they had been prescribed for their most recent VTE event in each of these time periods. Patients selected single or multiple agents from the following choices: injectable anticoagulants (unfractionated heparin, low-molecular-weight heparin, and fondaparinux); warfarin; DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban); and aspirin. Patients could also report if no antithrombotic medications were prescribed.

Table 1. Baseline characteristics of cohort of patients with recent VTE (N=907)

Characteristics	Result
Age (years), Mean (SD)	52.4 (14.4)
Female (%)	514 (56.7)
Race (%)	
Caucasian	804 (88.6)
African American	62 (6.8)
Asian/ Pacific Islander	28 (3.1)
Native American/ Alaskan Native	16 (1.8)
Other	20 (2.2)
Comorbidities (%)[a]	
Anxiety	242 (26.7)
Depression	258 (28.4)
Diabetes	156 (17.2)
Heart disease	249 (27.5)
High blood pressure	414 (45.6)
High cholesterol	347 (38.3)
Stroke or TIA	77 (8.5)
PE	306 (33.7)
DVT	769 (84.8)
Most recent VTE Type	
PE	164 (18.1)
DVT	579 (63.8)
PE + DVT	164 (18.1)
Number of VTE in lifetime, median (IQR)	2.0 (3.0)
Number of VTE in past 2 years, median (IQR)	2.0 (1.0)
VTE within past month (%)	77 (8.5)
Insurance	
Through employer	319 (35.2)
Medicare	308 (34.0)
Medicaid	128 (14.1)
Uninsured	24 (2.6)
Other	128 (14.1)
Household income, annual <$50,000 (%)	337 (37.2)

[a]Patients could select more than one comorbidity
SD-standard deviation, TIA-transient ischemic attack, PE-pulmonary embolism, DVT-distal venous thromboembolism, VTE-Venous thromboembolism, IQR-interquartile range.

Analysis

The proportions of patients corresponding to the various treatment pathways in each treatment phase were calculated by dividing the number of patients in each pathway by the total number of patients. Overall anticoagulant pathways were also assigned to each patient considering only anticoagulants used during days 8 to 90+. The proportions of patients who used injectable anticoagulants and/or aspirin in addition to other anticoagulants in each treatment phase were also calculated. Data was summarized using basic descriptive statistics, for example proportions for categorical variables and means and standard deviation (SD) or median and interquartile range (IQR) for continuous variables.

RESULTS

A total of 4,092 patients had access to the online survey. The data set included 971 who completed the survey and 64 patients were removed from the data set for reasons that included no VTE within past two years, choosing none of the medication options during most recent VTE treatment, and completing the survey in an unrealistically short amount of time (less than 6 minutes). A total of 907 patients were included in the final analysis (Table 1). The mean (SD) age of patients was 52.4 (14.4) years and 56.7

Table 2. Prevalence of self-reported anticoagulation use during various treatment phases

Anticoagulation medication pathway	Initial phase (First 7 days since diagnosis) (%)	Long-term phase (8 to 90 Days since diagnosis) (%)	Extended phase (90+ days since diagnosis) (%)	Overall (%)
Injectable anticoagulants only	355 (39.1)	47 (5.2)	14 (1.5)	35 (3.9)
Warfarin	244 (26.9)	349 (38.5)	239 (26.4)	351 (38.7)
DOAC	147 (16.2)	242 (26.7)	187 (20.6)	237 (26.1)
Switched between different DOACs	23 (2.5)	33 (3.6)	8 (0.88)	41 (4.5)
Switched between warfarin and DOACs	52 (5.7)	72 (7.9)	20 (2.2)	121 (13.3)
Aspirin only	46 (5.1)	80 (8.8)	128 (14.1)	79 (8.7)
No treatment	34 (3.7)	84 (9.3)	311 (34.3)	43 (4.7)

DOAC-direct oral anticoagulant

percent were women. In the overall population, the most common comorbidities were hypertension (45.6%), hyperlipidemia (38.3%), depression (28.4%), heart disease (27.5%), anxiety (26.7%), and diabetes (17.2%). The most recent VTE episode was deep vein thrombosis (DVT) in 63.8 percent, pulmonary embolism (PE) in 18.1 percent, or both DVT and PE in 18.1 percent of patients.

We identified the following antithrombotic usage patterns: injectable anticoagulants only, aspirin therapy only, warfarin, DOACs, patients who switched between warfarin and DOACs, patients who switched between different DOACs, and no treatment (Table 2). Overall, 38.7% of patients received warfarin-based treatment, 26.1% DOACs, 8.7% aspirin monotherapy and 3.9% injectable therapy only. 13.3% of patients switched between warfarin and DOACs, 4.5% switched between different types of DOACs, and 4.7% reported not receiving any of these treatments.

During the initial treatment phase, some responses were deemed implausible (e.g., respondent selected all types of anticoagulant therapy) and were excluded from the analysis for that phase. The proportion of patients receiving injectable anticoagulant monotherapy, mainly low-molecular-weight heparin, during the first 7 days of treatment was 39.1% declining to 5.2% and 1.5% during days 8-90 and 90+, respectively. During the first 7 days of treatment 48.4% of warfarin patients also received injectable anticoagulants, compared to 38.1% of DOAC patients (Table 3). 82.6% and 67.3% of patients who switched between different DOACs and between warfarin and DOACs also received injectable anticoagulants during the first 7 days of therapy, respectively. Concurrent injectable use dropped sharply after the first 7 days of therapy, but was still more common in patients who switched between warfarin and DOACs or between different DOACs. The proportion of patients receiving extended anticoagulant therapy beyond 90 days was 65.7%. Aspirin coadministration with anticoagulant therapy

Table 3. Prevalence of self-reported concurrent injectable anticoagulant and aspirin use during various treatment phases

	Injectable (%)	Aspirin (%)
Initial Phase (First 7 days since diagnosis)		
Injectable only (N= 355)	NA	59 (16.6)
Warfarin (N= 244)	118 (48.4)	75 (30.7)
DOAC (N= 147)	56 (38.1)	41 (27.9)
Switched between different DOACs (N= 23)	19 (82.6)	13 (56.5)
Switched between warfarin and DOAC (N= 52)	35 (67.3)	28 (53.8)
Aspirin only (N=46)	0	NA
No treatment (N=34)	0	0
Long-Term Phase (8 to 90 days since diagnosis)		
Injectable only (N= 47)	NA	9 (19.1)
Warfarin (N= 349)	49 (14.0)	80 (22.9)
DOAC (N= 242)	16 (6.6)	58 (24.0)
Switched between different DOACs (N= 33)	9 (27.3)	12 (36.4)
Switched between warfarin and DOAC (N= 72)	15 (20.8)	37 (51.4)
Aspirin only (N= 80)	0	NA
No treatment (N= 84)	0	0
Extended Phase (90+ days since diagnosis)		
Injectable only (N= 14)	NA	6 (42.9)
Warfarin (N= 239)	8 (3.4)	68 (28.5)
DOAC (N= 187)	4 (2.1)	56 (29.9)
Switched between different DOACs (N= 8)	1 (12.5)	3 (37.5)
Switched between warfarin and DOAC (N= 20)	5 (25.0)	8 (40.0)
Aspirin only (N= 128)	0	NA
No treatment (N= 311)	0	0
Overall		
Injectable only (N= 35)	NA	15 (42.9)
Warfarin (N= 351)	62 (17.7)	133 (37.9)
DOAC (N= 237)	17 (7.2)	84 (35.4)
Switched between different DOACs (N= 41)	9 (22)	14 (34.1)
Switched between warfarin and DOAC (N= 121)	22 (18.2)	60 (49.6)
Aspirin only (N= 79)	0	NA
No treatment (N= 43)	0	0

DOAC-direct oral anticoagulant

occurred in 33.7% of patients ranging from 34.1% (patients switching between different DOACs) to 49.6% (patients switching between warfarin and DOACs).

DISCUSSION

In this study, we identified self-reported antithrombotic utilization patterns during various VTE treatment periods (0-7, 8-90 and 90+days) in a large national sample of recent VTE patients who completed an online survey. We were able to discern seven distinct antithrombotic utilization patterns. The results revealed that warfarin-based therapy was the most prevalent overall anticoagulant used to treat VTE, followed by DOACs. These results differ from those reported in a retrospective cohort analysis of 12,390 commercially insured adults treated with oral anticoagulants for VTE diagnosed between 2010 and 2016.[7] The percentage of patients treated with warfarin decreased from 99.9% to 34.0% while the use of DOACs increased from <0.1% to 66.0%. Possible explanations for why DOACs had not overtaken warfarin in our study population include the fact that only a third of patients who took the survey indicated that they were commercially insured. Further approximately a third of our patient population reported an annual household income over USD50,000. Thus, affordability issues may have resulted in a greater proportion of patients in our study opting for warfarin as the less expense anticoagulant option. This may also explain why some patients switched between anticoagulants during the various VTE treatment phases.

Switching between anticoagulant types was common; both between warfarin and DOACs and between different types of DOACs. We were not able to discern the specific sequencing of anticoagulants nor the reasons for switching. We speculate that possible reasons for switching between anticoagulants could include cost, adverse events, health plan formulary considerations, and patient and/or provider preferences. Further study is needed to determine the specific reasons why patients switch between anticoagulants.

We also described the concurrent use of injectable anticoagulants during various phases of VTE treatment. The use of injectables in addition to oral anticoagulant therapy was most common during the first 7 days of treatment. The use of injectable anticoagulants is common with initiation of warfarin therapy. However, less than half of patients who reported taking warfarin during the first 7 days of therapy also reported receiving injectable anticoagulants while a high number of patients reported receiving only injectable anticoagulants during the initial 7 days of therapy. The reasons behind this finding are unknown but could be related to some patients receiving initial therapy in the hospital where it may not have been clear which anticoagulants were being administered. Injectable anticoagulant use was common in the initial 7 days even in patients who received DOAC therapy, a finding which requires further study as a potential advantage of DOACs (apixaban and rivaroxaban) over warfarin is no need for injectable anticoagulation. Injectable anticoagulant use decreased during days 8-90 and 90+ as would be expected. The use of injectable anticoagulants was higher in patients who switched between warfarin and DOACs and between different DOAC types in all phases of treatment. Reasons underlying this observation are unknown but could include the management of recurrent VTE or the use of bridge therapy during anticoagulant therapy transitions, especially from DOACs to warfarin. DOAC prescribing information suggests use of parenteral anticoagulants as one approach that can be used during transitions from DOACs to warfarin.[14-16]

We observed a high prevalence of combined anticoagulant and aspirin use that is similar to that reported in other observational studies.[17,18] Combined use of anticoagulants and aspirin has been associated with increased risk for major bleeding without concomitant benefit in terms of thromboembolic event prevention.[17] Anticoagulant providers should carefully watch for unnecessary aspirin use during the treatment of VTE and discontinue aspirin in patients without a valid indication for combined therapy.

This study was unique in the use of anticoagulant utilization data derived from patient self-reports instead of pharmacy claim data. Self-reported anticoagulant use may provide a more realistic snapshot of actual anticoagulant use than pharmacy claims data where whether the patient actually took the prescribed medication may not always be clear.[9,10] However, self-reported data is also subject to recall bias, by both over and under reporting of actual anticoagulant use. We were unable to determine the specific sequencing of switches between warfarin and DOACs and between specific DOACs and the rationale for switching between agents. We were also unable to determine the specific reasons why patients were receiving concurrent aspirin therapy or reported receiving no therapy. We included data from a large national sample of recent VTE sufferers which increase the generalizability of results. However, this study required access to an online survey which might introduce some selection bias where participation was limited to a population who had access to computers.

CONCLUSIONS

Overall, anticoagulant utilization in patients with recent VTE remained predominated by warfarin followed closely by DOACs. Given that DOACs are now recommended over warfarin by evidence-based guidelines, our results indicate that some patients and prescribers continue to prefer warfarin and that anticoagulant prescribing for VTE treatment needs to evolve to be more consistent with contemporary guideline recommendations. Switching between warfarin and DOACs and between different types of DOACs was common early in therapy which could indicate adverse events or affordability issues. Reasons for switching between anticoagulant therapies during VTE treatment requires additional study. Concurrent injectable anticoagulant use was common during the first 7 days of therapy even among patients prescribed DOACs which indicates prescribers may not be taking full advantage of the rapid onset of effect associated with DOAC therapy. Aspirin therapy was frequently coprescribed with all anticoagulant therapy types and is a potential target for medication safety interventions by anticoagulation providers as updated consensus guidelines no longer recommend indefinite aspirin following percutaneous coronary intervention and use of combined therapy of

aspirin with oral anticoagulant therapy has been shown to increase the risk of bleeding without providing additional protection against thromboembolic complications.[17,19]

CONFLICT OF INTEREST

Dr. Feehan has consulted to Pfizer previously. All other authors have no conflicts of interest to report.

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References

1. Thaler J, Pabinger I, Ay C. Anticoagulant treatment of deep vein thrombosis and pulmonary embolism: the present state of the art. Front Cardiovasc Med. 2015;2:30. https://doi.org/10.3389/fcvm.2015.00030
2. Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. J Thromb Thrombolysis. 2016;41(1):3-14. https://doi.org/10.1007/s11239-015-1311-6
3. Casciano JP, Dotiwala Z, Kemp R, Li C, Cai J, Preblick R. Economic burden of recurrent venous thromboembolism: analysis from a U.S. hospital perspective. Am J Health Syst Pharm. 2015;72(4):291-300. https://doi.org/10.2146/ajhp140204
4. Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, Stevens SM, Vintch JRE, Wells P, Woller SC, Moores L. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. 2016;149(2):315-352. https://doi.org/10.1016/j.chest.2015.11.026
5. Witt DM, Clark NP, Kaatz S, Schnurr T, Ansell JE. Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. J Thromb Thrombolysis. 2016;41(1):187-205. https://doi.org/10.1007/s11239-015-1319-y
6. Alalwan AA, Voils SA, Hartzema AG. Trends in utilization of warfarin and direct oral anticoagulants in older adult patients with atrial fibrillation. Am J Health Syst Pharm. 2017;74(16):1237-1244. https://doi.org/10.2146/ajhp160756
7. Nathan A, Geng Z, Raman S, Dayoub E, Adusumalli S, Geller B, Kobayashi T, Giri J, Groeneveld P. Trends in oral anticoagulant use for the treatment of venous thromboembolism in the United States, 2010-2016. Paper presented at: ACC.19: The American College of Cardiology 68th Annual Scientific Sessions; New Orleans, LA, March 16-18, 2019. https://doi.org/10.1016/S0735-1097(19)32716-0
8. Garber MC, Nau DP, Erickson SR, Aikens JE, Lawrence JB. The concordance of self-report with other measures of medication adherence: a summary of the literature. Med Care. 2004;42(7):649-652. https://doi.org/10.1097/01.mlr.0000129496.05898.02
9. Caskie GI, Willis SL, Warner Schaie K, Zanjani FA. Congruence of medication information from a brown bag data collection and pharmacy records: findings from the Seattle longitudinal study. Exp Aging Res. 2006;32(1):79-103. https://doi.org/10.1080/03610730500326341
10. Caskie GI, Willis SL. Congruence of self-reported medications with pharmacy prescription records in low-income older adults. Gerontologist. 2004;44(2):176-185. https://doi.org/10.1093/geront/44.2.176
11. Feehan M, Walsh M, Van Duker H, Godin J, Munger MA, Fleming R, Johnson SA, Morrison MA, DeAngelis MM, Witt DM. Prevalence and correlates of bleeding and emotional harms in a national US sample of patients with venous thromboembolism: A cross-sectional structural equation model. Thromb Res. 2018;172:181-187. https://doi.org/10.1016/j.thromres.2018.05.025
12. Jones AE, Feehan M, Fleming R, Johnson SA, Witt DM. Outcomes associated with a change in clinical practice to alleviate emotional harm related to venous thromboembolism. Thromb Res. 2019;180:29-31. https://doi.org/10.1016/j.thromres.2019.05.022
13. Pulleyn T, Kim K, Witt DM, Feehan M, Munger MA. Understanding patients' care barriers in the treatment of venous thromboembolism. J Thromb Thrombolysis. 2019;48(1):35-41. https://doi.org/10.1007/s11239-019-01880-3
14. Bristol Myers Squibb C. Eliquis Prescribing Information. http://packageinserts.bms.com/pi/pi_eliquis.pdf (accessed Aug 3, 2019).
15. Daiichi Sankyo I. Savaysa Prescribing Information. http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true (accessed Aug 3, 2019).
16. Janssen Pharmaceuticals I. Xarelto Prescribing Information. https://www.xareltohcp.com/shared/product/xarelto/prescribing-information.pdf (accessed Aug 3, 2019).
17. Johnson SG, Rogers K, Delate T, Witt DM. Outcomes associated with combined antiplatelet and anticoagulant therapy. Chest. 2008;133(4):948-954. https://doi.org/10.1378/chest.07-2627
18. Johnson SG, Witt DM, Eddy TR, Delate T. Warfarin and antiplatelet combination use among commercially insured patients enrolled in an anticoagulation management service. Chest. 2007;131(5):1500-1507. https://doi.org/10.1378/chest.06-2374
19. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, Ellinor PT, Ezekowitz MD, Field ME, Furie KL, Heidenreich PA, Murray KT, Shea JB, Tracy CM, Yancy CW. 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. J Am Coll Cardiol. 2019;74(1):104-132. https://doi.org/10.1016/j.jacc.2019.01.011