

Original Research

Incidence and pattern of anticoagulation in patients with atrial fibrillation and atrial flutter at tertiary hospital in Oman

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Abstract

Background: Atrial fibrillation (AF) and atrial flutter (AFL) are the two most common cardiac arrhythmias encountered in clinical practice. Anticoagulants are the cornerstone in cerebrovascular accident prevention in these patients. Despite their role in reducing stroke risk, emergency room visits, and overall treatment costs, studies have shown that oral anticoagulants (OAC) are underutilized, even in high-risk patients. **Objective:** The aim of this study is to explore the appropriateness and pattern of anticoagulant prescriptions in patients with AF and/or AFL in a tertiary hospital as recommended by the international guidelines. **Method:** This retrospective observational study was conducted by reviewing the electronic medical records of 389 adult patients with either AF or AFL in Sultan Qaboos University Hospital (SQUH) between July 2018 and July 2020. The appropriateness of oral anticoagulation was assessed according to international guidelines, namely, 2020 Canadian Cardiology Society (CCS), 2020 European Society of Cardiology (ESC), and 2019 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS). Analysis was performed using univariate statistics (Chi-square and percentages) to report categorical data. Results: Oral anticoagulants were prescribed appropriately in 91% of the patients according to CCS guidelines, and 92% and 96% according to ESC and (AHA/ACC/HRS) class Ia and IIa recommendations, respectively. Among non-anticoagulated patients (28 patients, 9%) had proper justification. On the other hand, 38 patients (9.8%) out of the whole cohort (389) had a CHADS-65 score of zero but received OAC mostly due to cardioversion, rheumatic heart disease, or mechanical heart valve prosthesis. Novel oral anticoagulants (NOACs) were the most commonly used OAC 251/336 (75%), with rivaroxaban being the main drug used 234/250 (92%) of all NOAC prescriptions. 75% of patients with eGFR<50 ml/min received the proper dose of rivaroxaban. Bleeding was the most frequently reported side effect of OAC in 52 (13.4%) of the entire cohort. **Conclusion:** Nearly 91% of patients with AF/AFL followed at SQUH were prescribed an appropriate anticoagulant as per international guidelines. The decisions to anticoagulate a patient with AF/AFL and the type of anticoagulant used were appropriate

Keywords: anticoagulation; atrial fibrillation; atrial flutter

INTRODUCTION

Atrial fibrillation (AF) and atrial flutter (AFL) are the two most common cardiac arrhythmias encountered in clinical practice, with atrial fibrillation taking the lead.¹ AF is a heart condition that causes an irregular and often abnormal chaotic rhythm pattern.² AFL, on the other hand, is a supraventricular arrhythmia characterized by rapid, regular atrial depolarization.³ Moreover, both conditions are associated with significant impairments in functional capacity and health-related quality of life (HRQOL) and increased morbidity and mortality.^{2,3}

Despite the scarcity of studies on the prevalence of AF and AFL in the Middle East, the few available data show important epidemiological characteristics of Middle Eastern AF populations. In particular, the AF population is younger and has more co-morbidities than patients with the same diagnosis

in the West.⁴ Additionally, the Gulf Survey of Atrial Fibrillation Events (Gulf SAFE) concluded that the most common type of AF encountered in the Arabian Gulf patients was first attack AF, which occurred in 37%, whereas 19% of patients had lone AF. The most common concomitant medical condition was hypertension, present in (52%), followed by diabetes in 30% of the study population.⁵

The main strategies of AF/AFL management are symptom control, achieved by either rate or rhythm control, and stroke prevention.⁶ Patients with AF particularly have a 3- to 5-fold increased risk of stroke if they are not anticoagulated.⁷ The thromboembolic risk of patients with AF are stratified based on the CHADS-65 or CHA2DS2-VASc scores. Patients with a CHADS-65 score of ≥ 1 or a CHA2DS2-VASc score of ≥ 2 for men and ≥ 3 for women should be started on oral anticoagulants. Furthermore, most patients should receive a direct-acting oral anticoagulant (DOAC) in preference to warfarin when oral anticoagulant (OAC) therapy is indicated, except in patients with moderate to severe mitral stenosis or a mechanical heart valve.⁶

There have been several reports on the OAC prescription pattern in patients with AF/AFL. For example, the Japanese J-RHYTHM registry and AVAIL (the Adherence eValuation After Ischemic Stroke Longitudinal) registry indicate that warfarin underutilization in patients at high stroke risk reached 34.7%, as well as overuse of warfarin in patients at low risk reached 49.1%.^{8,9} Furthermore, Akash R et al. and Schaffer et al. studies

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showed that OAC in patients with atrial arrhythmias is severely underused at (83.8%) and (51%) respectively, even among high-risk individuals.^{10,11} On the other hand, the ORBIT-AF study (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation) reported that 76% of eligible patients received OAC.¹² Moreover, the General Registry Pilot program EORP-AF (EurObservational Research Programme-Atrial Fibrillation) in 2013 showed improved uptake of OACs by European cardiologists, with OACs prescribed for 80% of patients with AF.^{13,14}

Several researchers studied the use of NOAC in patients with AF. O'Neal et al., Kattoor et al., and GLORIA-AF (Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation) concluded that overall DOAC use was higher than that of VKA, reaching 65%.¹⁵⁻¹⁷ This preference was explained by the SPRINT-AF trial (Stroke Prevention and Rhythm Intervention in Atrial Fibrillation) by improved side effect profile (as perceived by the patient) and improved efficacy (as perceived by the physician) of NOACs.¹⁸ On the other hand, the Japanese J-RHYTHM registry reported that warfarin was prescribed appropriately in (99.3%) of AF patients with mitral stenosis and mechanical valve replacement.⁸

Despite the importance of anticoagulation in the management of AF/AFL, many patients are not anticoagulated appropriately. Furthermore, prescribing OAC for AF/AFL patients' needs to be better studied in the Middle East. Therefore, this study aims to explore the pattern of anticoagulant prescription in patients with AF/AFL as recommended by the international guidelines in a tertiary care hospital that represents a snapshot of the practice in Oman. It also aims to describe the appropriateness of the OAC type used.

METHODS

Setting and design

This retrospective observational study was conducted in 2021 at Sultan Qaboos University Hospital (SQUH), Oman's tertiary care academic institution. The study included all patients diagnosed with AF or AFL between July 2018 and July 2020, followed at SQUH aged 16 years and over. Ethical approval was obtained from the Medical Research Ethics Committee at Sultan Qaboos University, Muscat, Oman.

Data collection

The data were collected from SQUH Electronic Patient Records (EPR). Patient demographics and clinical characteristics, such as age, sex, height, weight, comorbidities, arrhythmia type, CHADS-65 score, CHADS-VAC score, and OAC used, were collected.

OAC agents

The available OAC drugs at SQUH include warfarin, rivaroxaban, apixaban, and dabigatran. The appropriateness of anticoagulant use was assessed according to the Canadian Cardiovascular Society (CCS), European Society of Cardiology (ESC), and American Heart Association/ American College of

Cardiology/Heart Rhythm (AHA/ACC/HRS) protocols. The need for anticoagulation was based on the specific stroke risk factors, namely CHADS-65 score and CHADS-VAC score 17,18,19. The anticoagulant prescription was deemed appropriate if it met any previously mentioned anticoagulation protocols in patients with AF/AFL.

Statistical analysis

Descriptive statistics were used to describe the data. For categorical variables, frequencies and percentages were reported. Differences between groups were analyzed using the chi-square test. For continuous variables, mean and standard deviation (medians and interquartile range when normally distributed) were used to summarize the data. A *priori* two-tailed level of significance was set at 0.05. Statistical analyses were performed using STATA version 13.1 (STATA Corporation, College Station, TX, USA).

RESULTS

A total of 389 eligible patients' data was analyzed. Around 51% (n=197) were female, the mean age of the patients was 66.77 ±13.9 years (range: 23- 96 years), 93% had AF, 4% had AFL, and 3% had both diagnoses. Furthermore, 69% of the cohort had hypertension, 42% had diabetes mellitus, and 38.8% had coronary artery disease, as shown in Table 1.

Table 1. Patient's demographics and clinical characteristics

Characteristic, n (%) unless specified otherwise	Results	N
Age, mean ± SD, years	67 ± 14	389
Female gender	197 (51%)	389
Body mass index, mean ± SD, kg/m ²	30 ± 8.5	247
Creatinine, mean ± SD, µmol/L	102 ± 84	384
eGFR, mean ± SD, ml/min	68 ± 22	373
INR, mean ± SD	2.2 ± 6.2	353
Hemoglobin, mean ± SD, g/dL	12 ± 2.2	381
Atrial fibrillation	374, (93%)	389
Atrial flutter	27, (4%)	389
Both	12, (3%)	389
Hypertension	272, (69%)	389
Diabetes mellitus	165, (42%)	389
Peripheral vascular disease	12, (3.1%)	389
Cerebrovascular disease	75, (19.3%)	389
Coronary artery disease	151, (38.8%)	389
Congestive heart failure	68, (17.5%)	389
COPD	16, (4.1%)	389
Dyslipidemia	112, (28.8%)	389
Valvular disease	77, (19.8%)	389
Mitral valve replacement	23, (5.9%)	389

SD: Standard deviation, eGFR: Estimated glomerular filtration rate, INR: International normalization ratio, COPD: Chronic obstructive pulmonary disease



The study cohort of 389 patients was stratified based on both CHADS₂-65 and CHA₂DS₂-VASc scores. 326 patients were eligible for oral anticoagulation according to the CCS guideline, as shown in Figure 1, of whom 298 patients (91%) were appropriately anticoagulated, compared to 275 (92%) out of 299 patients were eligible for OAC according to class Ia of the ESC and AHA guidelines, and 315 (96%) out of 329 patients according to class IIa of the same guidelines, as shown in Figure 1.

Most of the anticoagulated patients (N=336) received a DOAC (N=251, 75%). Around 85 patients (25%) were on warfarin, among which 14 patients (4.2%) were on aspirin as well. Moreover, 24 patients were on aspirin alone, as shown in Table 2. Rivaroxaban was the main DOAC prescribed at (92%) compared to apixaban (2.8%) and dabigatran (4.6%) which was rarely used. In addition, all the patients with moderate to severe mitral stenosis and mechanical heart valves were appropriately anticoagulated with warfarin, as shown in Figure 2.

Drug used	Percent	Total
NOAC, n (%)	251, 75%	336
Warfarin, n (%)	85, 25%	336
OAC and aspirin	14, 4.2%	336
Aspirin, n (%)	24, 6.2%	389
None, n (%)	30, 7.7%	389

NOAC: Novel oral anticoagulant, OAC: oral anticoagulant

DISCUSSION

Stroke prevention is the cornerstone of AF/AFL management. OAC reduces devastating cerebrovascular complications and emergency room visits and, therefore, healthcare costs. However, the pattern of use of anticoagulants in the Middle East has yet to be explored. In this study, we examined the prescription pattern of anticoagulants in patients with AF/AFL

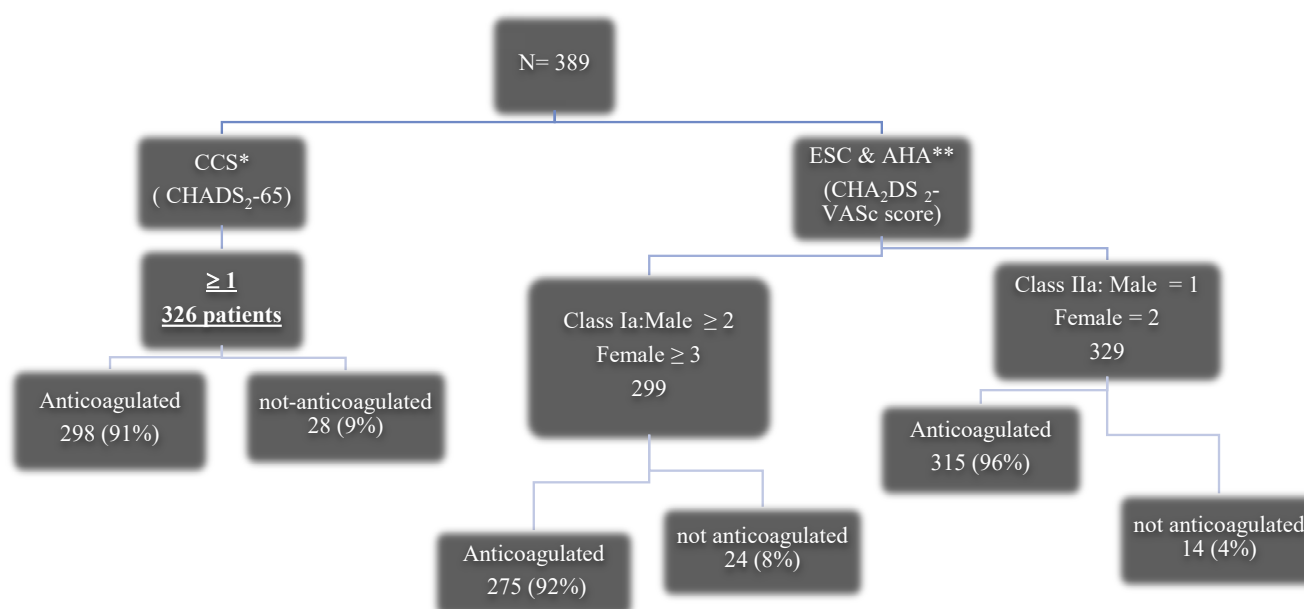


Figure 1. Anticoagulation of AF/AFL patients according to the CCS, ESC, and AHA guidelines

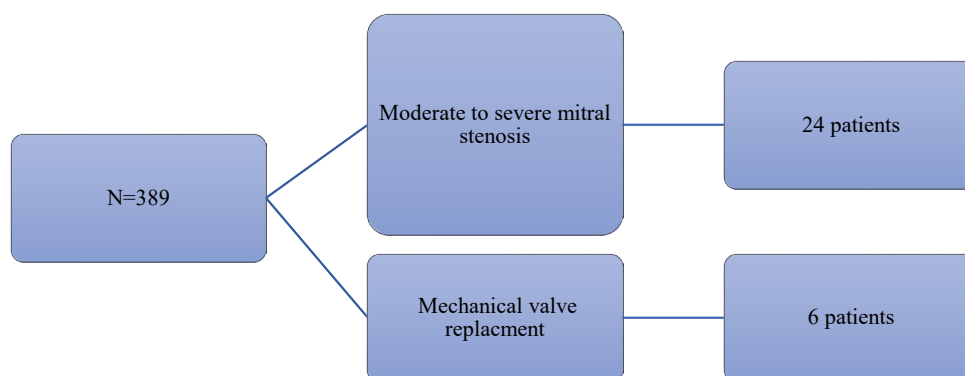


Figure 2. Use of warfarin in patients with moderate to severe mitral stenosis and mechanical heart valves

in a tertiary hospital in Oman.

Most of our cohort population had more than one comorbidity, mainly hypertension (69%), followed by diabetes (42%). These findings are consistent with those of previous studies in this region.⁵

389 patients during the study period had AF/AFL. Patients with CHADS₂-65 of ≥ 1 were 326. The vast majority (N=298, 91%) of eligible patients for anticoagulation, according to the CCS guidelines, were actually anticoagulated. 92% and 96% of eligible patients, according to ESC & AHA guidelines, class Ia and class IIa, respectively, were indeed anticoagulated. Only 28 patients (9%) were not on OAC; this result shows the high quality of SQUH practice, as previous studies from the literature have shown that OAC in such patient population is severely underused between 50% to 85%, even among high-risk individuals.^{10,19-21} Our findings are comparable to the results of ORBIT-AF and EORP-AF studies.^{12,13} Similarly, our study is in agreement with JoFib (Jordan Atrial Fibrillation) study,²² where 76% of eligible patients received OAC.

Among non-anticoagulated patients (28 patients, 9%), seven patients (2.3%) had severe bleeding-related complications, and two patients (0.6%) had eGFR less than 15 ml/min. In fact, patients with severe renal dysfunction and patients on hemodialysis are at an increased risk of bleeding. Thus, some physicians justify withholding OAC due to the increased risk of bleeding regardless of the potential net benefit of OAC. Although withholding OAC in those at high risk for bleeding may seem intuitive, several potential downfalls exist to such an approach. Primarily, stroke risk and bleeding risk are highly correlated. Patients at high risk of bleeding are often at the highest risk of stroke. Furthermore, a clear positive correlation exists between stroke risk and the absolute benefit derived from OAC.^{23,24} Although it would seem logical to withhold OAC from patients with AF at high bleeding risk, current data suggest that most patients with high bleeding or stroke scores derive clinical benefit from OAC through reduced stroke risk.^{25,26} Furthermore, Current evidence suggests that patients with AF/AFL who have CKD with an eGFR above 15 mL/ min/1.73 m² should be treated with an OAC if they have at least an intermediate risk of thromboembolism as assessed with the CHADS₂-65 or CHA2DS₂-VASc score. For patients with advanced CKD (eGFR from 15 to 29 mL/ min/1.73 m²), however, this recommendation is based only on registry studies. For dialysis patients with AF/AFL, decisions on whether to give OAC drugs should be taken on an individual basis, in view of the elevated risk of bleeding and the unclear efficacy of such drugs in these patients.²⁷ In addition, 19 patients (6.4%) had undocumented justifications for lack of OAC therapy.

As CHADS₂-65 and CHA2DS₂-VASc score is used only in nonvalvular AF/AFL, we can justify the use of OAC in 38 patients (9.8%) out of the whole cohort (389) who had CHADS-65 score of zero but received OAC. Among this group, 14 patients (3.6%) had cardioversion either electrically or chemically and therefore required peri-procedural OAC. Additionally, eight patients (2%) had rheumatic heart disease, six patients (1.5%) had mechanical heart valve prosthesis, one patient (0.3%) had

hypertrophic cardiomyopathy, and one patient (0.3%) had thyrotoxicosis, which are all indications for OAC. Moreover, eight patients (2%) had no documented justification for OAC use.

Many reasons may account for the higher rates of OAC in the current study. Earlier studies documenting lower rates of anticoagulation enrolled patients in the 1990s, shortly after the publication of trials supporting its efficacy,^{24,28} and before widespread adoption of anticoagulation into clinical practice. It is also possible that OAC use has improved as a result of quality control measures.²⁹ Furthermore, the introduction of DOAC made utilization of OAC easier in comparison to warfarin. With DOAC, no regular monitoring is required, and no interaction with food and drugs is encountered. More recent studies focusing on outpatients with AF have documented higher rates of anticoagulation. For example, a study from the AFFECTS (Atrial Fibrillation: Focus on Effective Clinical Treatment Strategies) Registry, enrolling patients from 2005 to 2007, documented that 64% of eligible patients received warfarin and 83% received warfarin or aspirin.³⁰ Furthermore, most of the patients in this study were treated by specialists. Previous studies have shown lower rates of OAC among patients who are not followed by a cardiologist.^{31,32} Thus, it is possible that high rates of justified OAC use reflect providers who are more aware of guideline recommendations and quality measures. Furthermore, the majority of the study cohort was on DOAC (75%), which is consistent with previous studies.¹⁵⁻¹⁷

Moreover, warfarin was reserved for patients with moderate to severe mitral stenosis, patients with mechanical heart valves, and for some patients with end-stage renal disease. Furthermore, 24 patients had the above indications for warfarin and were placed appropriately on it. Rivaroxaban was the most commonly used DOAC (92%) among all DOAC prescriptions, followed by dabigatran (4.6%), and finally, apixaban (2.8%) was the least frequently seen OAC in SQUH. This pattern of use can be explained by the availability of rivaroxaban at SQUH pharmacy. Physician preference indeed affects the choice of OAC as it depends on individual clinical features, patterns of risk factors, and comorbidities, although physicians also consider OAC, which tends to increase patients' compliance.³⁴

CONCLUSION

At SQUH, OAC is used for as high as 91% of AF/AFL patients. Furthermore, 32% of non-anticoagulated patients have rational justification for lack of OAC, and 68% have undocumented justification. Moreover, 100% of the low-risk patients who received OAC had rational explanations. DOAC was the most commonly used type of OAC, namely rivaroxaban.

CONFLICTS OF INTEREST STATEMENT

All authors declare that they have no conflicts of interest.

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References

1. Carlos AM, Amitava B, Pablo P, David W, Xavier J. Atrial fibrillation: the current epidemic. *J Geriatr Cardiol.* 2017;14(3):195-203. <https://doi.org/10.11909/j.issn.1671-5411.2017.03.011>
2. Leonard. Uptodate.2020. [Online]. Available: <https://www.uptodate.com/contents/epidemiology-of-and-risk-factors-for-atrialfibrillation> [Accessed 12 December 2020].
3. Riles SM. Classification and mechanisms of atrial flutter. *ESC CardioMed.* 2018. [Online]. Available: <https://oxfordmedicine.com/view/10.1093/med/9780198784906.001.0001/med9780198784906> chapter-517. [Accessed 5 December 2020].
4. Salam A. Atrial fibrillation in Middle Eastern Arabs and South Asians: Summary of published articles in the Arabian Gulf. *Heart Failure Rev.*2019;20(4):158. https://doi.org/10.4103/heartviews.heartviews_116_19
5. Jakub G, Magdalena D, Marco P, Yan GL, Nidal A, Wafa R, et al. Gulf Survey of Atrial Fibrillation Events (Gulf SAFE). *J Am Heart Assoc.* 2020;9(5):1286. <https://doi.org/10.1161/circoutcomes.110.959700>
6. Jason GA, Martin A, Clare A, Alan B, John AC, Christopher C, et al. Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive, 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation. *Can J Cardiol.* 2020;36(12):1847-1948. <https://doi.org/10.1016/j.cjca.2020.09.001>
7. Paul D, Werner J, David N, Miney P, Kathryn W, Gregory MA, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. *J Am Coll Cardiol.* 2000;36(4):1303-9. [https://doi.org/10.1016/s0735-1097\(00\)00886-x](https://doi.org/10.1016/s0735-1097(00)00886-x)
8. Hirotsugu A, Hiroshi I, Ken O, Takeshi Y, Naoko K, Hideki O. Present status of anticoagulation treatment in Japanese patients with atrial fibrillation: a report from the J-RHYTHM Registry. *Circ Res.* 2011;75(6):1328-33. <https://doi.org/10.1253/circj.cj-10-1119>
9. Brett D, Jose AJ, Alberto JL, Hadar LT. Treatments to prevent primary venous ulceration after deep venous thrombosis. *J Vasc Surg Venous Lymphat Disord.* 2019;7(2):260-71. <https://doi.org/10.1016/j.jvsv.2018.12.009>
10. Akash R, Kenneth YK, Shawn DS, Dipayon R, Youning Z, Jonathan N, et al. Anticoagulation Patterns in Patients with Atrial Fibrillation Following Percutaneous Coronary Intervention in an Academic Center. *J Innov Card Rhythm Manag.* 2019;10(8):3785-9. <https://doi.org/10.19102/icrm.2019.100802>
11. Andrea LS, Michael OF, David B, Louisa RJ, Andrew W, Melanie H, et al. Evidence-Practice Gaps in Postdischarge Initiation with Oral Anticoagulants in Patients with Atrial Fibrillation. *J Am Heart Assoc.* 2019;8(24):e014287. <https://doi.org/10.1161/jaha.119.014287>
12. Michael WC, Sunghie K, Jonathan PP, Jack EA, Gerg CF, Elaine MH, et al. Risks and Benefits of Anticoagulation in Atrial Fibrillation. *Circulation.* 2013;6:461-9
13. Gregory YH, Cécile L, Gheorghe AD, Massimo S, Zbigniew K, Lars HR, et al. Real-world antithrombotic treatment in atrial fibrillation: the EURObservational Research Programme Atrial Fibrillation General Pilot survey. *Am J Med.* 2014;127(6):519-29.
14. Robby N, Alessandro C, Gregory YH, Bertil SO, Martin H, Fred HN, et al. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. *Eur Heart J.* 2006;27(5):3018-26.
15. Wesley TO, J'Neka SC, Pratik BS, Richard FM, Lin YC, Lindsay GB, et al. Provider Specialty, Anticoagulation Prescription Patterns, and Stroke Risk in Atrial Fibrillation. *J Am Heart Assoc.* 2018;7(16):1913-22.
16. Ajoe JK, Naga VP, Akshay G, Mahanazuddin S, Shorabuddin S, Hakan P, et al. (2019). Prescription Patterns and Outcomes of Patients with Atrial Fibrillation Treated With Direct Oral Anticoagulants and Warfarin: A Real-World Analysis. *J. Cardiovasc. Pharmacol. Ther.* 2019;24(5):428-34. <https://doi.org/10.1177/1074248419841634>
17. Menno VH, Kenneth JR, Miney P, Christine T, Hans CD, Sergio JD, et al. Antithrombotic Treatment Patterns in Patients with Newly Diagnosed Nonvalvular Atrial Fibrillation: The GLORIA-AF Registry, Phase II. *Am. J. Med.* 2015;128(12):1306-13. <https://doi.org/10.1016/j.amjmed.2015.07.013>
18. Andrew CH, Narendra S, Jafna LC, John M, Paul D, Carl FM, et al. Oral Anticoagulation for Stroke Prevention in Canadian Practice: Stroke Prevention and Rhythm Interventions in Atrial Fibrillation (SPRINT-AF) Registry. *Can J Cardiol.* 2016;32(2):204-10. <https://doi.org/10.1016/j.cjca.2015.04.028>
19. Xiaomeng Y, Zixiao L, Xingquan Z, Chunjuan W, Liping L, Chaunxue W, et al. Use of Warfarin at Discharge Among Acute



- Ischemic Stroke Patients with Nonvalvular Atrial Fibrillation in China. *Stroke*. 2015;47(2):464-70. <https://doi.org/10.1161/strokeaha.115.011833>
20. Chunjuan W, Zhonghua Y, Chunxue W, Yilong W, Xingquan Z, Liping L, et al. Significant Underuse of Warfarin in Patients with Nonvalvular Atrial Fibrillation: Results from the China National Stroke Registry. *J Stroke Cerebrovasc Dis*. 2014;23(5):1157-63. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.10.006>
 21. Noritomo N, Ken O, Takahiko K, Joko M, Katsuko T, Reiko T, et al. Trends in Prevalence of Non-Valvular Atrial Fibrillation and Anticoagulation Therapy in a Japanese Region—Analysis Using the National Health Insurance Database. *Circ J*. 2020;84(5):706-13. <https://doi.org/10.1253/circj.cj-18-0989>
 22. Hammoudeh AJ, Khader Y, Kadri N, Al-Mousa E, Badaine Y, Hababbeh L, et al. Adherence to the 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline on the Use of Oral Anticoagulant Agents in Middle Eastern Patients with Atrial Fibrillation: The Jordan Atrial Fibrillation (JoFib) Study. *Int. J. Vasc. Med*. 2021;4(2):1-9. <https://doi.org/10.1155/2021/5515089>
 23. Alan SG, Elaine MH, Yuchiao C, Kathleen AP, Lori EH, Angela MC, et al. Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *JAMA*. 2003;290(20):2685-92. <https://doi.org/10.1001/jama.290.20.2685>
 24. Medi C, Hankey GJ, Freedman SB. Stroke Risk and Antithrombotic Strategies in Atrial Fibrillation. *J Am. Heart Assoc*. 2010;41:2705-13. <https://doi.org/10.1161/strokeaha.110.589218>
 25. Daniel ES, Yuchiao C, Margaret CF, Leila HB, Niela KP, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. *Ann Intern Med*. 2009;151(5):297-305. <https://doi.org/10.7326/0003-4819-152-4-201002160-00017>
 26. Maneesha M, Julia DB, Alan CF, Roger MM. Impact of relative contraindications on the use, benefits, and risks of anticoagulant prophylaxis in atrial fibrillation: analysis of a claims database. *Open J. Intern. Med*. 2011;1(1):60-7.
 27. Gunnar HH, Vincent B, Stephan HS. Oral Anticoagulation in Chronic Kidney Disease and Atrial Fibrillation. *Dtsch Arztebl Int*. 2018;115(17):287-94. <https://doi.org/10.3238/arztebl.2018.0287>
 28. Michael DE, Samuel LB, Kenneth EJ, Nathan HC, Cindy LC, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med*. 1992;327:1406-12. <https://doi.org/10.1056/nejm199211123272002>
 29. Estes MN, Halperin JL, Calkins H, Ezekowitz MD, Gitman P, Go AS, et al. ACC/AHA/Physician Consortium 2008 Clinical Performance Measures for Adults with Nonvalvular Atrial Fibrillation or Atrial Flutter. *J Am Coll Cardiol*. 2008;51(8):865-84. <https://doi.org/10.1161/circulationaha.107.187192>
 30. Peter RK, James AR, Robert M, Gerald VN, Douglas LP, Craig MP, et al. AFFECTS Scientific Advisory Committee and Investigators. Warfarin and aspirin use in atrial fibrillation among practicing cardiologists (from the AFFECTS Registry). *Am J Cardiol*. 2010;105(8):1130-4. <https://doi.org/10.1016/j.amjcard.2009.11.047>
 31. Rowan SB, Bailey DN, Bubnitz CE, Anderson RJ. Trends in anticoagulation for atrial fibrillation in the U.S.: an analysis of the national ambulatory medical care survey database. *J Am Coll Cardiol*. 2007;49(14):1561-5. <https://doi.org/10.1016/j.jacc.2006.11.045>
 32. Turakhia MP, Hoang DD, Xu X, Frayne S, Schmitt S, Yang F, et al. Differences and trends in stroke prevention anticoagulation in primary care vs cardiology specialty management of new atrial fibrillation: the Retrospective Evaluation and Assessment of Therapies in AF (TREAT-AF) study. *Am Heart J*. 2013;165 (8):93-101. <https://doi.org/10.1016/j.ahj.2012.10.010>
 33. Kodani E, Atarashi H, Inoue H, Okumura K, Yamashita T, J-RHYTHM Registry Investigators. Target Intensity of Anticoagulation with Warfarin in Japanese Patients with Valvular Atrial Fibrillation. *Circulation*. 2015;79(2):325-330. <https://doi.org/10.1253/circj.cj-14-1057>
 34. Wilke T, Bauer S, Muller S, Kohlmann T, Bauersachs R. Patient Preferences for Oral Anticoagulation Therapy in Atrial Fibrillation: A Systematic Literature Review. *Patient Exp J*. 2016;10(1):17-37. <https://doi.org/10.1007/s40271-016-0185-9>