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Treatment Stability of Warfarin and Acenocoumarol in Patients With Mechanical Heart Valves and Atrial Fibrillation: A One-Year Cohort Study

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Abstract

Objective. This study aimed to investigate which of the two vitamin K antagonists, warfarin or acenocoumarol, provides more stable anticoagulation control in patients with mechanical heart valves and atrial fibrillation. **Patients and Methods.** This was a prospective, one-year clinical cohort study. In total, 73 outpatients with mechanical heart valves and atrial fibrillation who were already treated with warfarin or acenocoumarol were recruited from the Blood Transfusion Institute of the Federation of Bosnia and Herzegovina. The prothrombin time target values, expressed as the international normalized ratio (INR), were 2.0–3.0/4.0. Numerical data between the treatment groups were summarized descriptively. **Results.** Patients in the warfarin (N=35) and acenocoumarol (N=38) treatment groups were similar in terms of sex, age, body mass index, body surface area, and number of concomitant drugs known to interact with vitamin K antagonists. The number of INR measurements per patient, number of INR measurements within the therapeutic range per patient, mean time interval between successive INR measurements, and mean INR values across consecutive measurements were similar in both groups. However, compared to acenocoumarol, warfarin treatment seemed to be associated with more stable anticoagulation, i.e., with a higher mean time in the therapeutic range (TTR) (76.1±24.2 vs. 69.1±21.5%) and a smaller proportion of patients below all predefined TTR thresholds (<60%, <65%, and <70%). **Conclusion.** Our unadjusted descriptive results suggested that warfarin, compared to acenocoumarol, may provide more stable and therefore safer anticoagulation control in patients with mechanical heart valves and atrial fibrillation. To confirm this, larger prospective clinical studies are needed in patients with mechanical heart valves with or without atrial fibrillation.

Key Words: Mechanical Heart Valves ▪ Atrial Fibrillation ▪ Warfarin ▪ Acenocoumarol ▪ INR ▪ Treatment Stability.

Introduction

Although new oral anticoagulants are available, the vitamin K antagonists (VKAs) warfarin and acenocoumarol remain irreplaceable for lifelong prevention and treatment of thromboembolic complications in patients with mechanical heart valves (1, 2). Given the narrow therapeutic index of VKA therapy, which presents risks of thromboembolic complications on one hand and bleeding on the other, the physician's primary goal is to maintain it within optimal and stable anticoagulation control. To achieve and maintain optimal anticoagulation treatment, the American College of Cardiology (ACC) recommends targeting international normalized ratio (INR) values of 2.0–3.0 for patients with low-risk aortic valve replacement (AVR) and INR values of 2.5–3.5 for patients with high-risk AVR and mitral valve replacement (1). According to the European Society of Cardiology (ESC) and the European Association

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for Cardio-Thoracic Surgery (EACTS) the target INR should be adapted to each patient's prosthesis thrombogenicity and individual risk factors, i.e. for valves with low thrombogenicity the target INR is 2.5 (without risk factors) or 3.0 (with ≥1 risk factor), for medium thrombogenicity INR is 3.0 or 3.5, and for high thrombogenicity, INR is 3.5 or 4.0 (3).

A time in therapeutic range (TTR) of ≥65% is commonly accepted as the definition of INR stability (4). For patients with stable INR values, previous recommendations suggested monitoring every four to eight weeks, and current guidelines allow extending this interval up to twelve weeks (4, 5).

Due to the differences in pharmacokinetics (PK), i.e., the longer elimination half-life attributed to warfarin (20–60 vs. 8–10 hours), warfarin anticoagulation treatment is considered more stable compared to acenocoumarol (6). In addition to PK, patient age and body weight, and regardless of indication, genetic factors largely determine the anticoagulant effect and, therefore, the dose of VKAs in patients with mechanical heart valve replacement (7). Gene polymorphisms are important factors responsible for variability in warfarin dose requirements (8). According to a recent study, one-third of all variations in response to warfarin are the result of mutations in two genes: a gene for cytochrome P450 (CYP2C9) and a vitamin K-epoxide reductase gene (VKORC1) (9). The PK and pharmacodynamics of warfarin are also influenced by environmental factors such as diet, drug interactions, critical illness, etc. (4). Daily fluctuations in vitamin K-dependent factor VII levels, which were assumed to lead to the difference in stability of warfarin and acenocoumarol treatment, have been shown to occur with both drugs (10).

Unlike in our country, Bosnia and Herzegovina, where both drugs are available and prescribed, only one VKA is commonly available in most regions (11). Warfarin is the drug of choice in the United States, Scandinavia, and the UK, and is predominantly used in Italy. Acenocoumarol is commonly used in Spain, the Netherlands, and Poland. Phenprocoumon is primarily used in Germany, and fluindione in France (12). This may be the reason why data from post-marketing studies comparing the stability of warfarin and acenocoumarol treatments are still lacking.

Therefore, this study aimed to investigate which of the two VKAs, warfarin or acenocoumarol, leads to more stable anticoagulation control in patients with mechanical heart valves and atrial fibrillation.

Material and Methods

Study Design and Patients

This was a prospective, one-year clinical cohort study. Patient recruitment and data collection were performed at the Blood Transfusion Institute of the Federation of Bosnia and Herzegovina (FB&H). The enrolment period was from May 2014 to May 2015.

Surgical implantation of a mechanical heart valve in our community is performed at the Clinical Center of Sarajevo University. Following implantation, an internist or cardiologist from the same department prescribes the initial lifelong anticoagulation therapy. After hospital discharge, the anticoagulation therapy of most of these patients is followed up and managed at the Institute under the care of transfusion specialists, and the remaining patients are followed up under the care of internists, cardiologists, or general practitioners at different healthcare institutions. Due to the lack of a centralized registry for these patients at the time of the study, this study included only patients who were followed up with anticoagulation therapy and managed at the Institute under the care of transfusiologists.

Patients were identified by accessing the electronic medical records of the Institute. The study inclusion criteria were age 15–80 years, a confirmed diagnosis of atrial fibrillation, at least eight months of warfarin/acenocoumarol treatment, regular monthly INR check-ups prior to study enrolment, no presence of acute thromboembolic event, and no planned surgery or diagnostic procedures requiring discontinuation of anticoagulation

treatment in the planned one-year study period. Eligible patients were then followed prospectively for one year with regular INR monitoring.

The minimum period of eight months of warfarin/acenocoumarol treatment was chosen to ensure that patients had completed the initial phase of dose titration and INR stabilization, which typically occurs within the first few months of therapy. This duration allows for a more reliable assessment of anticoagulation control and reduces the impact of early fluctuations that are common immediately after therapy initiation. Although there is no universally established minimum period defined in the literature, this approach is consistent with previous studies evaluating anticoagulation stability in patients with mechanical heart valves (13–15), where the inclusion of patients with at least several months of stable therapy is common practice.

Data Collection

Patient demographic and clinical data (sex, age, height, weight, body mass index (BMI), body surface area (BSA), medical and surgical history, list of concomitant drugs with the potential to affect INR values, and position of the mechanical heart valve) were collected from patients' electronic records and through medical interviews and were recorded in the case report form. Information on INR measurements (dates, INR values, drug doses, and dosing regimens) was collected from the patient's anticoagulant therapy card.

INR Measurement

Plasma was obtained from blood samples collected by venipuncture of the cubital vein into 1.8 ml test tubes containing 3.2% sodium citrate (Vacutainer, Becton Dickinson, United Kingdom). The blood samples were centrifuged (Laboratory centrifuge CENTRIC 322A, Slovenia) at room temperature at 3000 rpm for 15 minutes. Prothrombin time (PT) was measured using a hemostatic automated analyzer (ACL Elite Pro, Italy) with a commercial liquid calcium recombinant human tissue factor – thromboplastin reagent (RecombiPlasTin, ISI 1.03). The INR is calculated automatically according to the formula $INR=(PT\ ratio)^{ISI}$ (International Sensitivity Index) (16). Measurements and calculations were performed in the laboratory of the Department for Detection of Coagulation Disorders at the Blood Transfusion Institute of the FB&H. Based on the AHA/ACC and ESC/EACTS guidelines (1, 3), the target INR value (2.0–3.0/4.0) was determined for each patient depending on the mechanical heart valve position, prosthesis thrombogenicity, and risk factors.

Ethics Statement

The study protocol was approved by the Review Board of the University of Sarajevo Pharmaceutical Faculty (Approval No. 0101-1833/15). All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee, as well as the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Informed consent was obtained from all patients prior to their enrollment in the study.

Statistical Analyses

The data were analyzed descriptively. The number of INR measurements per patient per year, the number of INR measurements within the therapeutic range per patient, the time interval between successive INR measurements, and the INR values across 12 consecutive measurements were assessed for patients treated with warfarin and acenocoumarol. The stability of anticoagulation treatment was assessed using the TTR and the proportion of patients below predefined TTR thresholds (<60%, <65%, and <70%). The time in therapeutic range was calculated using Rosendaal's daily linear interpolation between consecutive INR measurements method over a predefined one-year observation period that assumes linear changes in INR between successive measurements to estimate the proportion of time spent within the target range (17). Continuous numerical variables were tested for the normality of their distribution. Normally distributed data are reported

as mean±standard deviation (SD) and not normally distributed data as median and interquartile range (IQR, Q25–Q75). Categorical variables are reported as numbers and percentages. Data analyses were performed using MS Excel.

Results

Of the 201 patients with mechanical heart valves identified in the community, 90 were excluded because their clinical data were not accessible, and 111 patients were identified by accessing the Institute's electronic medical records. Of these, 73 patients, mostly women, met the inclusion criteria, with 35 patients treated with warfarin and 38 with acenocoumarol. The remaining 38 patients were excluded due to the absence of a confirmed diagnosis of atrial fibrillation, duration of VKA treatment shorter than 8 months, or planned surgery or diagnostic procedures requiring discontinuation of anticoagulation treatment in the planned one-year study period (Figure 1).

The demographic and clinical characteristics and valve positions of patients in the warfarin and acenocoumarol groups are shown in Table 1.

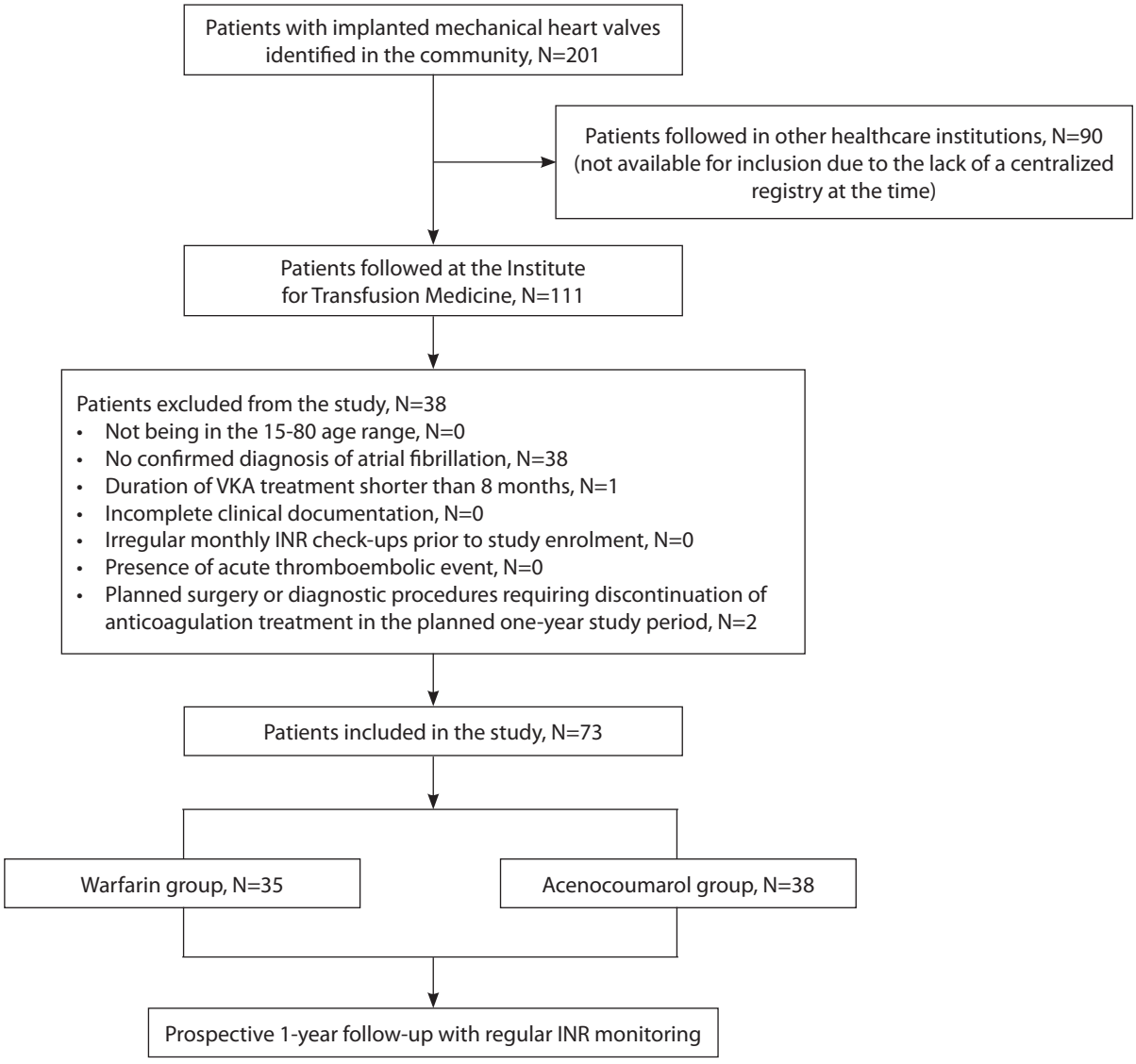

Figure 1. Flow diagram.

Table 1. Demographic and Clinical Characteristics of Patients in the Warfarin and Acenocoumarol Treatment Groups

Variable	Warfarin (N=35)	Acenocoumarol (N=38)
Sex (M/F)	12/23	15/23
Age (years)	63.71±9.60	58.71±11.97
BMI (kg/m^2)	26.89±3.61	26.07±3.53
BSA (m^2)	1.87±0.18	1.90±0.22
Mechanical valve position		
Aortic valve (N; %)	9 (25.7)	3 (7.9)
Mitral valve (N; %)	19 (54.3)	33 (86.8)
Both valves (N; %)	7 (20.0)	1 (2.6)
Unknown position (N; %)	-	1 (2.6)

M=Men; F=Women; BMI=Body mass index; BSA=Body surface area.

The patients in both groups were taking up to three concomitant drugs. The medications with the potential to increase INR values used in both treatment groups were amiodarone, digoxin (methyldigoxin), statins (simvastatin and atorvastatin), verapamil, allopurinol, propranolol, levothyroxine, acetylsalicylic acid, diclofenac, and vitamin E. The medications with the potential to decrease INR values used in both treatment groups were carbamazepine and spironolactone.

The mean number of INR measurements per patient per year was 11.05±1.87 in the warfarin group and 11.71±2.22 in the acenocoumarol group. The mean number of INR measurements within the therapeutic range per patient was 8.05±2.08 in the warfarin group and 7.21±2.17 in the acenocoumarol group. The mean time interval between successive INR measurements was 37.54±6.33 days in the warfarin group and 34.89±7.90 days in the acenocoumarol group.

All monthly median INR values across 12 consecutive measurements for warfarin (2.20–2.67) and acenocoumarol (2.14–2.68) were within the therapeutic range (Figure 2).

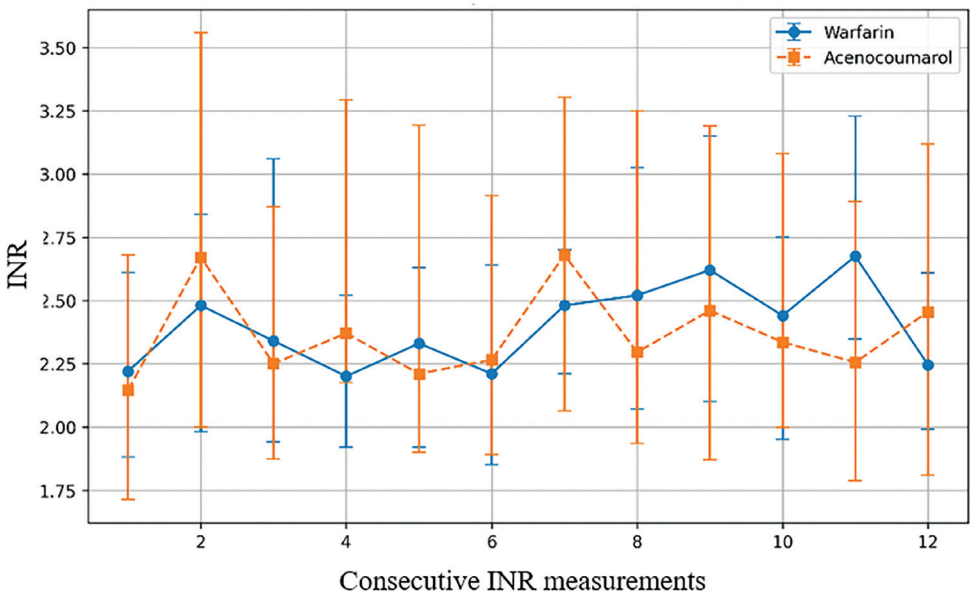

Figure 2. The monthly median with interquartile range (Q25–Q75) INR values for warfarin and acenocoumarol treatments across 12 consecutive measurements during a one-year observation period.

Table 2. Treatment Stability in the Warfarin and Acenocoumarol Treatment Groups

Variable	Warfarin (N=35)	Acenocoumarol (N=38)
TTR %, mean±SD	76.1±24.2	69.1±21.5
TTR <60	22.9	39.5
TTR <65	28.6	42.1
TTR <70	28.6	47.4

TTR=Time in therapeutic range; SD=Standard deviation.

The mean TTR was higher in patients treated with warfarin than in those treated with acenocoumarol, with better-quality anticoagulation being consistently more frequent in the warfarin group across all predefined TTR thresholds (Table 2).

Discussion

Our crude and descriptive results in patients with mechanical heart valves and atrial fibrillation, similar in sex, age, BMI, BSA, the number of used concomitant drugs known to interact with vitamin K antagonists, the number of INR measurements per patient, the number of INR measurements within the therapeutic range per patient, the mean time interval between successive INR measurements, and the mean INR values across consecutive measurements, showed that compared to acenocoumarol, warfarin treatment might have been associated with more stable anticoagulation i.e. with a higher mean time in the therapeutic range and a smaller proportion of patients being below all predefined TTR thresholds (<60%, <65%, and <70%).

Considering that a TTR of ≥65% is commonly accepted as a marker of INR stability, warfarin therapy demonstrated greater anticoagulation stability compared with acenocoumarol, as reflected by higher mean and TTR values and a lower proportion of patients with suboptimal TTR levels. Nevertheless, the overall mean TTR in the acenocoumarol group also exceeded the 65% threshold, indicating that satisfactory anticoagulation control was achieved with both VKAs in this cohort. Similar findings have been reported in other studies (6, 18, 19). When comparing TTR values across studies, it is important to acknowledge that different methodological approaches were used. While some of the cited publications applied Rosendaal's linear interpolation method, most commonly recommended given that it directly incorporates time (17, 18), others assessed anticoagulation quality using alternative approaches, i.e. using the Last Check in File method based on the last INR measurement of each month (10), or using the percentage of INR values within the therapeutic range (proportion-in-range method) without applying linear interpolation (6, 19, 20).

The recent Italian nationwide PLECTRUM study compared the quality of warfarin and acenocoumarol treatments in 2111 patients with mechanical prosthetic heart valves, of whom 1716 (81.3%) were treated with warfarin and 395 (18.7%) with acenocoumarol. Consistent with our results, the results of this study also showed better anticoagulation quality, i.e., longer mean TTR in patients treated with warfarin compared to those treated with acenocoumarol (61.6±19.4% vs. 56.1±19.2%) (18). This suggests that our observations align with findings reported in larger populations. The PLECTRUM study also showed a lower TTR on acenocoumarol in all subgroups of patients analyzed according to sex, hypertension, diabetes, age, valve site, atrial fibrillation, and INR range.

Although studies comparing the stability of warfarin and acenocoumarol treatment in patients with mechanical heart valves are lacking, similar studies investigating the stability of these drugs in patients with non-valvular atrial fibrillation or other indications have also suggested the advantage of warfarin over acenocoumarol (6, 19). To this end, an Italian retrospective case-control study documented both the percentage of INR values within the therapeutic range (72% vs. 67%, P<0.001) and the percentage of patients with ≥75% of measurements of INR in the therapeutic range (50.7% vs. 34.5%, P<0.05), which were significantly higher in patients treated with warfarin than in those treated with acenocoumarol (6). In addition, Olivia et al. showed that INR values were more frequently in the therapeutic range in patients treated with warfarin than with acenocoumarol (65.5% vs. 63.4%) (19). These findings are consistent with our

results in patients with mechanical heart valves and atrial fibrillation, as we also observed higher TTR values and a lower proportion of patients below the predefined TTR thresholds in the warfarin group than in the acenocoumarol group.

Samsa et al. (21) showed that, compared to primary health care, the therapeutic value of INR is more often achieved in specialized institutions (55–60% vs. 34–47%). Despite the satisfactory overall median TTR in our study, a considerable proportion of patients with mechanical heart valves and atrial fibrillation, particularly in the acenocoumarol group, remained below the 65% threshold, indicating that consistently stable INR control can still be challenging, even in specialized care settings. As mentioned above, patients with stable INR values should be monitored every four to eight or even twelve weeks (4, 5).

The mean time interval between the two successive INR measurements in our study was approximately 5 weeks, 37.54 days in the warfarin group and 34.89 days in the acenocoumarol group. In the study by Kulo et al. (20), the time between the two measurements in patients with non-valvular atrial fibrillation recruited from the same institution was 27.17 days. In contrast to our study, some studies did not confirm the advantage of warfarin (10, 20, 22). Barcellona et al. showed that warfarin did not appear to be better than acenocoumarol in terms of PTs within the therapeutic range per patient (10). Moreover, Kulo et al. showed better stability of acenocoumarol compared to warfarin treatment in a one-year observational clinical study in patients with non-valvular atrial fibrillation (37.6% vs. 35.7%) (20). In the same study, the proportion of INR values in the therapeutic range was higher in patients treated with acenocoumarol than in those treated with warfarin (53.62% vs. 51.77%).

The clinical relevance of our results is that they can help clinicians determine which of the two available VKAs may be more suitable for patients with mechanical heart valves and atrial fibrillation. Greater stability of anticoagulation predicts better safety, improved quality of life, as fewer INR controls are needed, and reduced healthcare costs.

Strengths and Limitations of the Study

Our study is the first to compare two VKAs, warfarin and acenocoumarol, in patients with mechanical heart valves to whom both treatments are equally accessible and prescribed. As, according to established guidelines, VKA therapy remains the standard and only anticoagulant option for these patients, with treatment patterns based on INR-guided monitoring and dose adjustments remaining the same over the past decade, our study population and findings may be of clinical relevance. However, this study has several limitations. First, a small sample size resulting from the lack of a centralized registry of patients with mechanical heart valves in our community; therefore, patients whose anticoagulation treatment was followed in other healthcare institutions were not available for inclusion, which may limit the generalizability of our findings. Second, as no standardized predefined criteria/clinical scoring system/laboratory parameter is used to systematically guide the initial internists' or cardiologists' decisions on the assignment of a specific patient to warfarin or acenocoumarol, the treatment decision is made largely based on their preference/prescribing habits, comorbidities, concomitant drugs, availability of each drug through insurance reimbursement or market supply, and the patient's ability to access the drug. However, we did not collect information on those factors that might have predicted assignment to one VKA over the other or the stability of anticoagulation control. As these factors could theoretically function as confounders, we missed the opportunity to adjust the model for confounding, and residual confounding cannot be excluded. Therefore, based on crude and unadjusted analyses, the reported results are rather descriptive and hypothesis-generating than causal and may be partially or entirely explained by factors not accounted for in the analyses.

Conclusion

In this prospective, single-center, one-year clinical cohort study, based on crude and descriptive results, better anticoagulation stability, with a higher

mean time in the therapeutic range and a smaller proportion of patients below the predefined TTR thresholds, was suggested in warfarin- compared with acenocoumarol-treated patients with mechanical heart valves and atrial fibrillation. However, these unadjusted findings only represent a population description and should be interpreted cautiously. To confirm and expand our findings, additional larger prospective clinical studies are needed in patients with mechanical heart valves, with or without atrial fibrillation.

What Is Already Known on This Topic:

The prevention of thromboembolic events in patients with mechanical heart valves requires lifelong oral anticoagulants. Although new oral anticoagulants are available, vitamin K antagonists (VKAs) remain irreplaceable in these patients. Maintaining optimal anticoagulation with VKAs is difficult due to their narrow therapeutic index, i.e., the need to achieve therapeutic INR values while balancing thrombosis and bleeding. Although dose-dependent, their effectiveness also shows significant individual variation over time. Maintaining stable anticoagulation depends not only on numerous clinical factors, including age, body weight, diet, comedications, comorbidities, and patient compliance, but also on genetic variations. Unlike in Bosnia and Herzegovina, where both drugs are equally available and prescribed, only one of the VKAs is commonly available in most other regions. This may be the reason why data from post-marketing studies comparing the stability of warfarin and acenocoumarol treatments are still lacking.

What This Study Adds:

The descriptive findings of this study support the hypothesis that compared with acenocoumarol, warfarin may provide more stable anticoagulation control in patients with mechanical heart valves and atrial fibrillation.

Authors' Contributions: Conception and design: ŠHT and AKĆ; Acquisition, analysis and interpretation of data: ŠHT, AM and AKĆ; Drafting the article: ŠHT and AM. Revising it critically for important intellectual content: ŠHT and AKĆ. Approved final version of the manuscript: AKĆ.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021;143(5):e35-e71. doi: 10.1161/CIR.0000000000000932. Erratum in: Circulation. 2021 Feb 2;143(5):e228. doi: 10.1161/CIR.0000000000000960. Erratum in: Circulation. 2021 Mar 9;143(10):e784. doi: 10.1161/CIR.0000000000000966.
2. Mandefro BT, Sundara SV, Lu X, Busmail H, Weerakoon S, Avula S, et al. Effectiveness and Safety of Direct Oral Anticoagulants Versus Warfarin in Patients With Mechanical Heart Valves: A Systematic Review. Cureus. 2025;17(8):e89736. doi: 10.7759/cureus.89736.
3. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017;38(36):2739-91. doi: 10.1093/eurheartj/ehx391.
4. Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S. doi: 10.1378/chest.11-2292.
5. Holbrook A, Schulman S, Witt DM, Vandvik PO, Fish J, Kovacs MJ, et al. Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e152S-84S. doi: 10.1378/chest.11-2295.
6. Pattacini C, Manotti C, Pini M, Quintavalla R, Dettori AG. A comparative study on the quality of oral anticoagulant therapy (warfarin versus acenocoumarol). Thromb Haemost. 1994;71(2):188-91. PMID: 8191397
7. Kaur A, Khan F, Agrawal SS, Kapoor A, Agarwal SK, Phadke SR. Cytochrome P450 (CYP2C9*2,*3) and vitamin K epoxide reductase complex (VKORC1-1639G<A) gene polymorphisms and their effect on acenocoumarol dose in patients with mechanical heart valve replacement. Indian J Med Res. 2013;137(1):203-9. PMID: 23481074.
8. Aquilante CL, Langaee TY, Lopez LM, Yarandi HN, Tromberg JS, Mohuczy D, et al. Influence of coagulation factor, vitamin K epoxide reductase complex subunit 1, and cytochrome P450 2C9 gene polymorphisms on warfarin dose requirements. Clin Pharmacol Ther. 2006;79(4):291-302. doi: 10.1016/j.clpt.2005.11.011.
9. Lee MT, Klein TE. Pharmacogenetics of warfarin: challenges and opportunities. J Hum Genet. 2013;58(6):334-8. doi: 10.1038/jhg.2013.40.
10. Barcellona D, Vannini ML, Fenu L, Balestrieri C, Marongiu F. Warfarin or acenocoumarol: which is better in the management of oral anticoagulants? Thromb Haemost. 1998;80(6):899-902. doi: 10.1055/s-0037-1615385.
11. Gadisseur AP, van der Meer FJ, Adriaansen HJ, Fihn SD, Rosendaal FR. Therapeutic quality control of oral anticoagulant therapy comparing the short-acting acenocoumarol and the long-acting phenprocoumon.

Br J Haematol. 2002;117(4):940-6. doi: 10.1046/j.1365-2141.2002.03493.x.

12. Le Heuzey JY, Ammentorp B, Darius H, De Caterina R, Schilling RJ, Schmitt J, et al. Differences among Western European countries in anticoagulation management of atrial fibrillation: data from the PREFER IN AF registry. Thromb Haemost. 2014;111(5):833-41. doi: 10.1160/TH13-12-1007.
13. Dalmau LMR, Aguilar MC, Carrasco-Querol N, Hernández RZ, Forcadell DE, Rodríguez CD, et al. Anticoagulation Control with Acenocoumarol or Warfarin in Non-Valvular Atrial Fibrillation in Primary Care (Fantas-TIC Study). Int J Environ Res Public Health. 2021;18(11):5700. doi: 10.3390/ijerph18115700.
14. Zhu X, Xiao X, Wang S, Chen X, Lu G, Li X. Rosendaal linear interpolation method appraising of time in therapeutic range in patients with 12-week follow-up interval after mechanical heart valve replacement. Front Cardiovasc Med. 2022;9:925571. doi: 10.3389/fcvm.2022.925571.
15. Farsad B, Abbasinazari M, Dabagh A, Bakshandeh H. Evaluation of Time in Therapeutic Range (TTR) in Patients with Non-Valvular Atrial Fibrillation Receiving Treatment with Warfarin in Tehran, Iran: A Cross-Sectional Study. J Clin of Diagn Res. 2016;10(9):FC04-06. doi: 10.7860/JCDR/2016/21955.8457.
16. Olson JD, Brandt JT, Chandler WL, Van Cot EM, Cunningham MT, Hayes TE, et al. Laboratory reporting of the international normalized ratio: progress and problems. Arch Pathol Lab Med. 2007;131(11):1641-7. doi:10.5858/2007-131-1641-LROTIN.
17. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost. 1993;69(3):236-9. PMID: 8470047.
18. Menichelli D, Poli D, Antonucci E, Cammisotto V, Testa S, Pignatelli P, et al. Comparison of anticoagulation quality between acenocoumarol and warfarin in patients with mechanical prosthetic heart valves: insights from the nationwide PLECTRUM study. Molecules. 2021;26(5):1425. doi: 10.3390/molecules26051425.
19. Oliva BE, Galán AP, Pacheco OAM. Comparison of quality and hemorrhagic risk of oral therapy using acenocoumarol versus warfarin. Med Clin (Barc). 2008;131(3):96-7. doi: 10.1157/13124012.
20. Kulo A, Kusturica J, Kapić E, Bečić F, Rakanović-Todić M, Burnazović-Ristić L, et al. Better stability of acenocoumarol compared to warfarin treatment in a one-year observational clinical study in patients with non-valvular atrial fibrillation. Med Glas (Zenica). 2011;8(1):9-14. PMID: 21263388.
21. Samsa GP, Matchar DB, Goldstein LB, Bonito AJ, Lux LJ, Witter DM, et al. Quality of anticoagulation management among patients with atrial fibrillation: results from a review of medical records from two communities. Arch Intern Med. 2000;160(7):967-73. doi: 10.1001/archinte.160.7.967.
22. Kulo A, Mulabegović N, Kusturica J, Hadžić H, Burnazović-Ristić L, Rakanović-Todić M, et al. Outpatient management of oral anticoagulation therapy in patients with nonvalvular atrial fibrillation. Bosn J Basic Med Sci. 2009;9(4):313-9. doi: 10.17305/bjbms.2009.2787.