

Indications and Quality of Care of Warfarin at King Abdulaziz Hospital, Al Ahsa

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Abstract

INTRODUCTION: The anticoagulation effect of warfarin is monitored through two laboratory tests: PT and INR. The quality of warfarin control in patients is assessed by calculating the TTR using INR values. However, there are only a few studies in Saudi Arabia that have investigated INR control in patients receiving warfarin.

METHODS: Demographical data, indications for anticoagulation, and INR values were extracted from electronic medical records of patients on warfarin therapy between November 1, 2020, and October 31, 2021. The TTR for each patient was calculated using the Rosendaal method.

RESULTS: A total of 88 patients were included in this study, comprising 29 males and 59 females. The indications for anticoagulation were categorised into four groups: 'Mechanical Valve' (28 patients), 'Atrial Fibrillation' (14 patients), 'Mechanical Valve + Atrial Fibrillation' (12 patients), and 'Other Indications' including haematological disorders (34 patients). The overall median TTR for the cohort was 58.73%. Patients with 'Mechanical Valves' had a median TTR of 62.50%, those with 'Atrial Fibrillation' had a median TTR of 50.18%, patients with 'Mechanical Valve + Atrial Fibrillation' had a median TTR of 54.61%, and patients with 'Other Indications' had a median TTR of 55.11%. The differences in TTR between these groups were not statistically significant ($p = 0.101$).

CONCLUSION: The INR control for patients taking warfarin was suboptimal, with a median TTR below the recommended threshold of 60%. This underscores the need for further studies to explore and improve the management of warfarin in patients.

LIST OF ABBREVIATIONS: PT: Prothrombin Time, INT: International Normalised Ratio, TTR: Time in Therapeutic Range, WHO: World Health Organisation, & DOAC: Direct Oral Anticoagulant

Introduction

Warfarin is an anticoagulant widely employed in the prevention and management of venous thromboembolism, myocardial infarction, and atrial fibrillation ¹. It achieves its effect by inhibiting the synthesis of vitamin K-dependent clotting factors, thereby diminishing the blood's ability to form clots ¹.

The anticoagulant effect of warfarin is monitored using two laboratory tests: PT and the INR ². PT quantifies the time, measured in seconds, required for plasma to clot after the addition of thromboplastin to the patient's plasma sample ³. The INR, standardised by the WHO, represents the ratio of the patient's prothrombin time to a control prothrombin time, adjusted using an international reference thromboplastin reagent ³. In most clinical scenarios, the target INR range

is set between 2 and 3, although specific circumstances may necessitate alternative target ranges ².

The quality of anticoagulation control in patients on warfarin therapy is assessed using the INR values to calculate the TTR ⁴. TTR refers to the proportion of time during which a patient's INR remains within the target range, typically between 2 and 3, as previously noted ². According to the 2017 Thrombosis Canada Guidelines, adequate INR control is generally defined as a TTR exceeding 60% ⁵. Suboptimal TTR has been associated with an increased risk of both thromboembolic events and major bleeding, highlighting the critical importance of maintaining effective anticoagulation control ⁵.

Limited studies in Saudi Arabia have evaluated the quality of warfarin therapy among patients receiving the medication for various indications ^{6, 7, 8, 9, 10}. One such study reported that

patients spent less than half of their TTR within the target INR range. This suboptimal TTR underscores the necessity to enhance service quality and address factors influencing TTR outcomes 6.

This study aimed to optimise the management of warfarin therapy in patients treated for various indications at King Abdul-Aziz Hospital in Al Ahsa, Saudi Arabia. The primary objective was to identify the indications for warfarin use among adult patients aged 18 years and older over the past 12 months. The secondary objective was to evaluate the quality of warfarin control in this population by calculating the TTR for each patient.

King Abdul-Aziz Hospital, located in Al Ahsa, Saudi Arabia, is a tertiary care centre. This study aims to contribute valuable data on the quality of anticoagulation control in patients prescribed warfarin for various indications, providing insights that could benefit Saudi Arabia, the Middle East, and the global medical community.

Materials and Methods

STUDY DESIGN, PARTICIPANTS & STUDY ETHICS

This study was a retrospective review of all adult patients receiving warfarin therapy at King Abdul-Aziz Hospital from November 1, 2020, to October 31, 2021. It specifically focused on adult patients aged 18 years and older at the time of treatment, who were treated with warfarin at the hospital in Al Ahsa, Saudi Arabia.

The medical record numbers of eligible patients were retrieved from the anticoagulation clinic's electronically maintained database at the hospital.

Ethical approval for the study was obtained from the Institutional Review Board at King Abdul-Aziz Hospital on October 25, 2021, under registration number H-01-R-005.

STUDY MEASURES, PROCEDURES & DATA ANALYSIS

The electronic medical records of all eligible patients were reviewed to extract data on patient characteristics, including age, age at the start of warfarin therapy, and sex, as well as the indications for warfarin use and the quality of warfarin control, as measured by INR. The indications for warfarin use were classified into four groups: (1) patients receiving warfarin due to mechanical valve replacement, (2) patients receiving warfarin due to atrial fibrillation, (3) patients receiving warfarin due to a combination of mechanical valve replacement and atrial fibrillation, and (4) patients receiving warfarin for indications other than mechanical valve replacement or atrial fibrillation.

The TTR was calculated using the Rosendaal method, which considers the time interval between consecutive INR measurements and the variations in INR values 11.

The data were analysed using the Kruskal-Wallis test to compare the TTR across the different indications for warfarin. Data analysis was performed using IBM SPSS Statistics software, version 28.0.1.1. Statistical significance was assessed with a threshold p-value of less than 0.05.

Results

DEMOGRAPHICAL INFORMATION

Among the 88 patients receiving warfarin at our institution, the median age at the start of warfarin therapy was 43 years (range: 19–80), with a predominantly female cohort, comprising 67% of the total population, as illustrated in Figure 1. Male patients had a median age of 49 years, while female patients had a median age of 41 years. However, the age range for female patients was broader, spanning from 19 to 80 years, compared to 20 to 75 years for male patients. The age distribution of the cohort at the start of warfarin therapy is summarised in Table 1.

Table 1 Age Distribution at Start of Warfarin Therapy

	Number of Patients	Median Age	Minimum Age	Maximum Age	Standard Deviation (Age)
Male	29	49	20	75	14.7
Female	59	41	19	80	13.4
All Patients	88	43	19	80	14.0

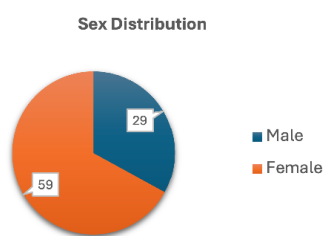


Figure 1

TTR FINDINGS

Among the patients included in this study, 28 were receiving warfarin due to mechanical valve replacement, 14 were treated with warfarin for atrial fibrillation, 12 were treated with warfarin for both mechanical valve replacement and atrial fibrillation, and the remaining 34 were prescribed warfarin for indications other than mechanical valve replacement and atrial fibrillation such as haematological disorders including Protein S

deficiency, Protein C deficiency, Systemic Lupus Erythematosus, and others. The distribution of warfarin indications is summarised in Figure 2.

Table 2 presents the TTR values for patients receiving warfarin based on their indication group. The minimum TTR across all groups was 20.69%, while the maximum TTR reached 86.84%. The mean TTR was highest in patients with mechanical valves (58.93%) and lowest in those with atrial fibrillation (52.36%). Similarly, the median TTR was also highest among patients with mechanical valves (62.50%) and lowest for those with atrial fibrillation (50.18%). For the total cohort, the mean TTR was 55.79%, and the median TTR was 58.73%.

STATISTICAL ANALYSIS

The Kruskal-Wallis test, used to compare the TTR across all four groups, yielded a p-value of 0.101, indicating no statistically significant differences among the groups.

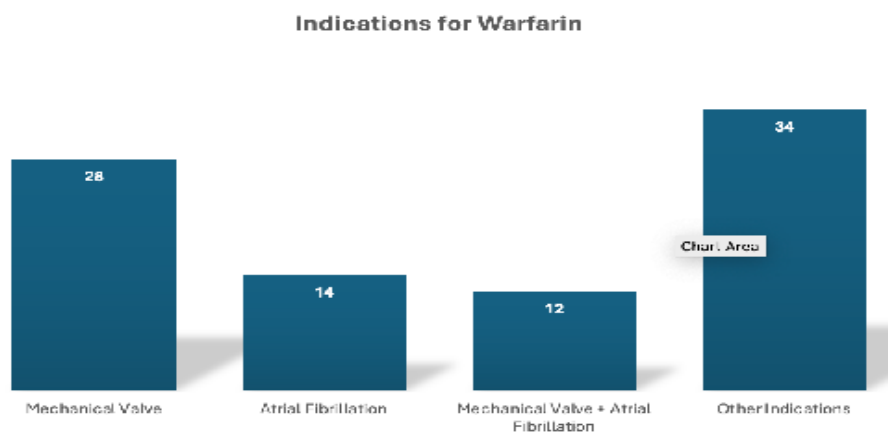


Figure 2

Table 2 TTR for Patients Receiving Warfarin

	Minimum TTR	Maximum TTR	Mean TTR	Median TTR
Mechanical Valve	20.69%	79.05%	58.93%	62.50%
Atrial Fibrillation	39.29%	66.44%	52.36%	50.18%
Mechanical Valve + Atrial Fibrillation	34.53%	78.74%	54.58%	54.61%
Other Indications	30.95%	86.84%	55.05%	55.11%
Total	20.69%	86.84%	55.79%	58.73%

Discussion

This study offers valuable insights into the indications for and quality of warfarin control at King Abdulaziz Hospital, categorising patients by indication into four distinct groups: mechanical valve replacement, atrial fibrillation, mechanical valve replacement combined with atrial fibrillation, and other indications.

The TTR has become the most widely accepted and validated method for assessing anticoagulation control and predicting adverse events ¹². The overall median TTR for the cohort was 58.73%, falling short of the recommended threshold of 60% for adequate anticoagulation control ⁵. Among the groups, patients with mechanical valves demonstrated the highest median TTR at 62.50%, surpassing the threshold, whereas the atrial fibrillation group had the lowest median TTR at 50.18%.

The findings highlight variability in TTR control based on the indication for warfarin use, with patients treated for mechanical valves achieving relatively better outcomes. This may be due to structured follow-up care often associated with mechanical valve management. However, the median TTR for all groups, except mechanical valves, remained below the recommended threshold, indicating suboptimal anticoagulation control. The group with atrial fibrillation had particularly low TTR values, potentially reflecting challenges such as irregular follow-up, adherence issues, or the inherent difficulty in managing anticoagulation in this population.

The Kruskal-Wallis test, used to compare the TTR across all four groups, yielded a p-value of 0.101, indicating no statistically significant differences among the groups. However, the overall median TTR for the cohort (58.73%) was more favourable than a similar study conducted in Saudi Arabia, which reported a median TTR of 52% ⁶. This suggests that while anticoagulation control at King Abdul-Aziz Hospital is suboptimal, it compares relatively well to other regional findings, reflecting potential differences in patient care approaches or population characteristics.

Improving anticoagulation control in this setting requires multifaceted interventions, including improved patient education, regular INR monitoring, and leveraging alternative therapies such as DOACs for eligible non-mechanical valve replacement patients. Additionally, ensuring access to anticoagulation clinics and structured follow-up programs may help address the observed disparities.

A key strength of this study is its comprehensive analysis conducted over an extended period. However, there are some

limitations. First, as a single-centre retrospective study, the findings should be validated in an independent prospective cohort. Second, while this study suggests satisfactory INR control at King Abdul-Aziz Hospital, further stratification is needed for patients with indications other than mechanical valve replacement and atrial fibrillation.

Conclusion

The median TTR among patients on warfarin at King Abdul-Aziz Hospital was suboptimal at 58.73% during this limited time, with only patients in the mechanical valve group achieving a median TTR exceeding 60%. These findings underscore the need for targeted interventions to enhance anticoagulation management. Key strategies include improving patient education, increasing access to INR monitoring services, and considering alternative therapies such as DOACs when appropriate. Further studies are necessary to explore the barriers to achieving optimal TTR and to develop tailored solutions for improving warfarin management in this population.

References

1. Patel S, Singh R, Preuss CV, et al. Warfarin. [Updated 2024 Oct 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470313/>
2. Hirsh J, Fuster V, Ansell J, et al. Warfarin: Beyond the Basics. In: UpToDate [Internet]. Waltham (MA): UpToDate; [cited 2024 Dec 19]. Available from: <https://www.uptodate.com/contents/warfarin-beyond-the-basics>
3. Yang R, Zubair M, Moosavi L. Prothrombin time. [Updated 2024 Jan 23]. In: Treasure Island (FL): StatPearls Publishing. 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544269/>
4. Farsad BF, Abbasinazari M, Dabagh A, et al. 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 Diagn Res*. 2016 Sep;10(9):FC04-FC06. doi: 10.7860/JCDR/2016/21955.8457.
5. Thrombosis Canada. Clinical Guides [Internet]. Toronto: Thrombosis Canada; [cited 2024 Dec 19]. Available from: https://thrombosiscanada.ca/hcp/practice/clinical_guides
6. Albabtain MA, Alharthi MM, Dagriri K, et al. Assessment of the quality of anticoagulation management with warfarin in a tertiary care center. *Saudi Med J*. 2020 Nov;41(11):1245-1251. doi: 10.15537/smj.2020.11.25456.
7. Alghadeer S, Alzahrani AA, Alalayet WY, et al. Anticoagulation Control of Warfarin in Pharmacist-Led Clinics Versus Physician-Led Clinics: A Prospective Observational Study. *Risk Manag Healthc Policy*. 2020 Aug 17;13:1175-1179. doi: 10.2147/RMHP.S248222.
8. Mayet AY. Patient adherence to warfarin therapy and its impact on anticoagulation control. *Saudi Pharm J*. 2016 Jan;24(1):29-34. doi: 10.1016/j.jsps.2015.02.005.
9. Alyousif SM, Alsaileek AA. Quality of anticoagulation control among patients with atrial fibrillation: An experience of a tertiary care center in Saudi Arabia. *J Saudi Heart Assoc*. 2016 Oct;28(4):239-43. doi: 10.1016/j.jsha.2016.02.001.
10. Balkhi B, Al-Rasheedi M, Elbur AI, et al. Association between satisfaction with and adherence to warfarin therapy on the control of International Normalized Ratio: A hospital-based study in Saudi Arabia. *Saudi Pharmaceutical Journal*. 2018 Jan;26(1):145–9. doi: 10.1016/j.jsps.2017.11.010.
11. Rosendaal FR, Cannegieter SC, van der Meer et al. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost*. 1993 Mar 1;69(3):236-9.
12. Siddiqui S, DeRemer CE, Waller JL, et al. Variability in the Calculation of Time in Therapeutic Range for the Quality Control Measurement of Warfarin. *J Innov Card Rhythm Manag*. 2018 Dec 15;9(12):3428-3434. doi: 10.19102/icrm.2018.091203.