Research Article

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Effects of Warfarin Nomogram in Initial Phase Warfarin Patients at Charoenkrung Pracharak Hospital

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Abstract: Most physicians initiate and adjust warfarin dose based on International Normalized Ratio (INR) and their clinical judgment. This study was conducted to investigate the effects of using warfarin nomograms in patients-initiated warfarin at Charoenkrung Pracharak Hospital. This randomized controlled trial involved patients who began warfarin therapy during hospitalization at Charoenkrung Pracharak Hospital between August and November 2023. The sample size was calculated using G*Power 3.1.9, employing the Chi-square test to test the research hypothesis. The total sample size was 116 participants. The experimental group's warfarin initiation and dosage adjustments were guided by warfarin nomograms, whereas the control group's regimen was based on physician's clinical judgment. The study analyzed the proportion of patients achieving an INR between 2.0 and 3.0 within 14 days of initiating warfarin; differences between groups were compared using either the Chi-square test or Fisher's Exact test. A total of 98 patients were randomized into experimental (n=49) and control (n=49) groups. Apart from gender, the baseline characteristics of both groups showed no significant differences. The research findings indicated a statistically significant difference between the experimental and control groups regarding the proportion of patients with INR values within the range of 2.0 to 3.0 within 14 days after receiving warfarin (44.9% and 24.5%, respectively, p=0.034). Implementing warfarin nomograms for initiating and adjusting dosages allows patients to achieve their target INR range more effectively than starting and adjusting doses solely based on physician judgment. Additionally, the safety of using warfarin nomograms did not show significant from initiating and adjusting doses solely based on physician judgment.

Keywords: Warfarin, Warfarin nomogram, Effectiveness, Dose initiation

INTRODUCTION

Warfarin is an oral anticoagulant used for various conditions to prevent or treat blood clotting disorders. INR measurement is the standard method for evaluating the efficacy and safety of warfarin. The target INR value for warfarin to be effective in preventing or treating thromboembolism is in the range of 2.0 to 3.0 (1).

The Thai Heart Association recommends an initial warfarin dosage of 3-5 mg/day, considering factors like age, ethnicity, weight, comorbidities, drug interactions, and liver and kidney function that may influence warfarin's efficacy (2). However, the anticoagulant effect of warfarin depends on the reduction of vitamin K-dependent

coagulation factors including factors 2, 7, 9, and 10. Therefore, proper monitoring of INR and appropriate dosage adjustments after initiating warfarin are crucial factors in achieving treatment goals (1).

Initiation of warfarin therapy for patients at Charoenkrung Pracharak Hospital is typically guided by physicians based on clinical indications. However, from data collected from patients who had started warfarin therapy at the hospital from January 1, 2018 to December 31, 2020, totaling 763 cases, it was observed that the average time for reaching the therapeutic INR range after starting warfarin was approximately 105 days. Therefore, patients initiating warfarin therapy at Charoenkrung Pracharak Hospital might require a longer duration to reach the therapeutic INR range, which may hinder the maximum benefits of the medication. This delay might prolong hospital stays and increase the risk of adverse drug reactions (3).

Literature reviews indicated that warfarin nomograms for dosage initiation and adjustment offer effectiveness and safety comparable to conventional physician initiated dosing methods. However, most studies are single-center and often tailored to specific units or populations with specific indications for warfarin, excluding a broader scope of patients (4-6). Additionally, some studies set lower INR targets for preventing DVT compared to the guidelines (7). Warfarin nomogram are mostly created from overseas studies, and ethnic factors affect warfarin response (8). Hence, researchers aimed to study the effectiveness of warfarin nomograms for initiating and adjusting dosages in Thai patients using warfarin at Chareonkrung Pracharak Hospital.

MATERIALS AND METHODS

This research was a randomized controlled trial conducted in hospitalized patients who started using warfarin while hospitalized at Charoenkrung Pracharak Hospital between August and November 2023. The sample size was calculated using G*Power 3.1.9 (9, 10), utilizing the Chi-square test to test the research hypothesis. The effect size was set at 0.3, with a confidence level (α) of 95% and a power of 80%. This calculation yielded a total required sample size of 88 participants. Anticipating a 20% dropout rate, we adjusted the total sample size to 116 participants. The randomization employed a block of four randomizations, dividing them equally into an experimental group of 58 and a control group of 58.

The inclusion criteria involved Thai patients who aged 20 years and older, hospitalized at Charoenkrung Pracharak Hospital, diagnosed with Deep Vein Thrombosis (I80.2), Pulmonary Embolism (I26), Atrial Fibrillation (I48), arterial thrombosis (I74) or venous thrombosis (I82), and consent to participate. Exclusion criteria included (1) patients with an allergy to warfarin, (2) active bleeding, (3) severe thrombocytopenia (<50 platelets/μL), (4) prosthetic mitral heart valves, (5) pregnancy, those unable to communicate in Thai and (6) those previously treated with warfarin during screening.

This research was ethically reviewed and approved by the Institutional Review Board, Chulalongkorn University, under project number COA No. 168/66.

Instrument

The experimental tool used was the warfarin nomogram, or the warfarin initiation and dose adjustment table. The research team, comprised of one cardiologist, clinical pharmacist, and one researcher, collaborated to design a modified warfarin dose adjustment table based on medical guidelines from "Pharmacotherapy: A Pathophysiologic Approach, 11th edition" (11) and a review of literature related to warfarin dosing in the initial phase. Factors influencing warfarin response were considered (2, 8, 12-38). The presented table outlines the initial warfarin dosing, considering factors that might affect the drug response rate. It incorporates INR monitoring as per medical guidelines and adjusts warfarin doses based on INR response by setting weekly dose modifications as a percentage of the total weekly dose (as shown in Figure 1).

Warfarin nomogram

☐ **High risk patients** : start warfarin ≤2.5 mg/day

☐ **Low risk patients** : start warfarin 3–5 mg/day

The high risk patient is one of the following Age>70 years, impaired nutritional status or low BMI, decompensated heart failure, chronic liver disease (Child-Pugh B/C), chronic kidney disease (eGFR≤30 ml/min/1.73 m^2), hyperthyroidism, hypoalbuminemia (<2.5 g/dl), taking medications known to increase warfarin activity or increase bleeding risk or taking with amiodarone, recent major surgery or high risk of bleeding

Warfarin initial dosing nomogram

Day Measure INR	INR (Target 2.0 – 3.0)	Action
Day 1		Start warfarin as risk profile
Day 3–4	≤1.3 1.4–1.9 2.0–2.9 ≥3.0	Increase dose 10–50% No change or Increase 10–25% Decrease dose 10–50% May-be hold warfarin and repeat INR next 1–2 days if INR ~ 2 then decrease dose ≥ 50%
Day 5–7	≤1.5 1.6–1.9 2.0–3.0 >3.0	Increase dose 10–50% Increase dose 0–35% Decrease dose 0–25% May-be hold warfarin and repeat INR next 1–2 days if INR ~ 2 then decrease dose ≥ 25%

Note: Adjust the dose by percentage of total weekly dose.

INR monitoring after Initiation of Warfarin

Check INR	
Every 2–3 days	Until INR within the therapeutic range on 2 consecutive days
Then every 1–2 weeks	When dose is stable, check monthly

Figure 1. Warfarin nomogram

The content validity was conducted by three qualified healthcare professional who were not involved in this research project (39). They included one cardiologist and two pharmacists specializing in cardiovascular diseases. The criterion for accepting the warfarin nomogram tool was an Item Objective Congruence (IOC) value of at least 0.5, indicating its suitability for use. The evaluation results for the IOC for the warfarin nomogram yielded a value of 0.93, signifying a high level of agreement among the experts regarding its content validity.

Data collection

In the experimental group, patients received their initial warfarin dosages and subsequent adjustments as directed by medical intern who adhered to the guidelines provided by the warfarin nomogram. Conversely, the control group's warfarin dosages, both initial and adjustments, were determined by medical intern based on their clinical judgment. Both groups of physicians are skill-enhancing doctors who work to care for patients at Charoenkrung Pracharak Hospital. Throughout the study, a researcher closely monitored and ensured the proper implementation of warfarin administration and INR monitoring for both groups, strictly following the procedures outlined in the research protocol (Figure 2).

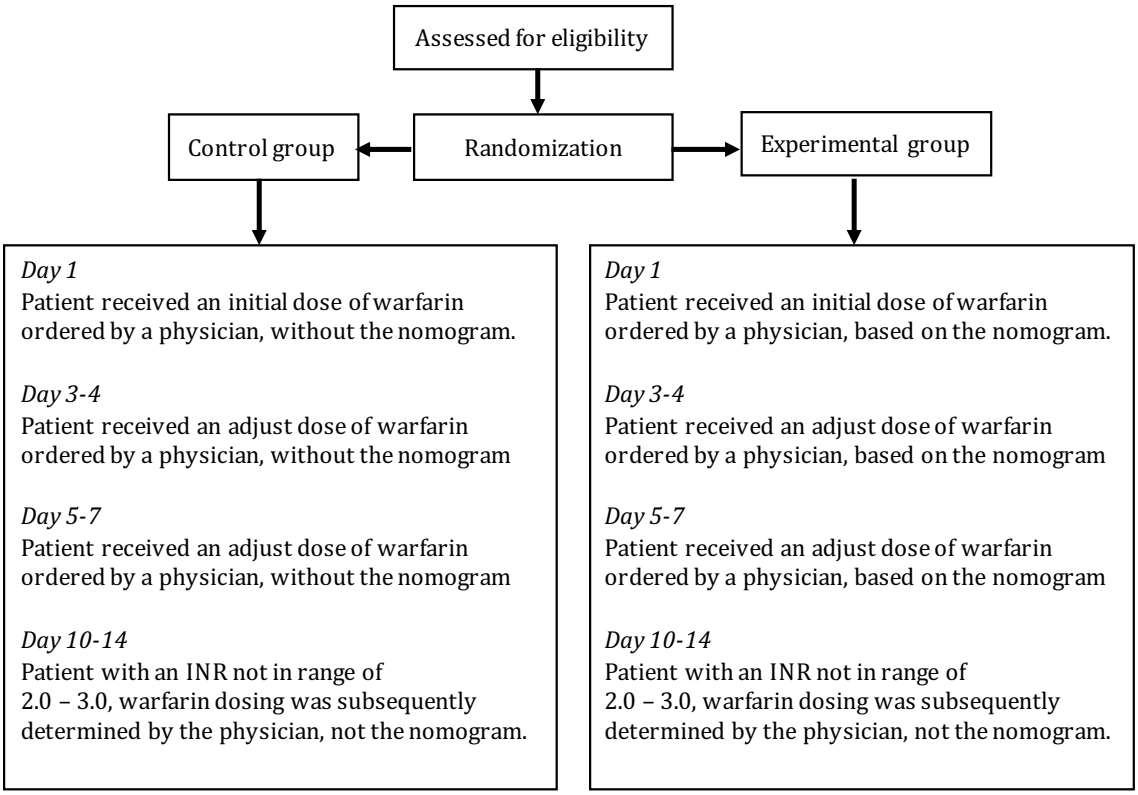

Figure 2. Research protocol

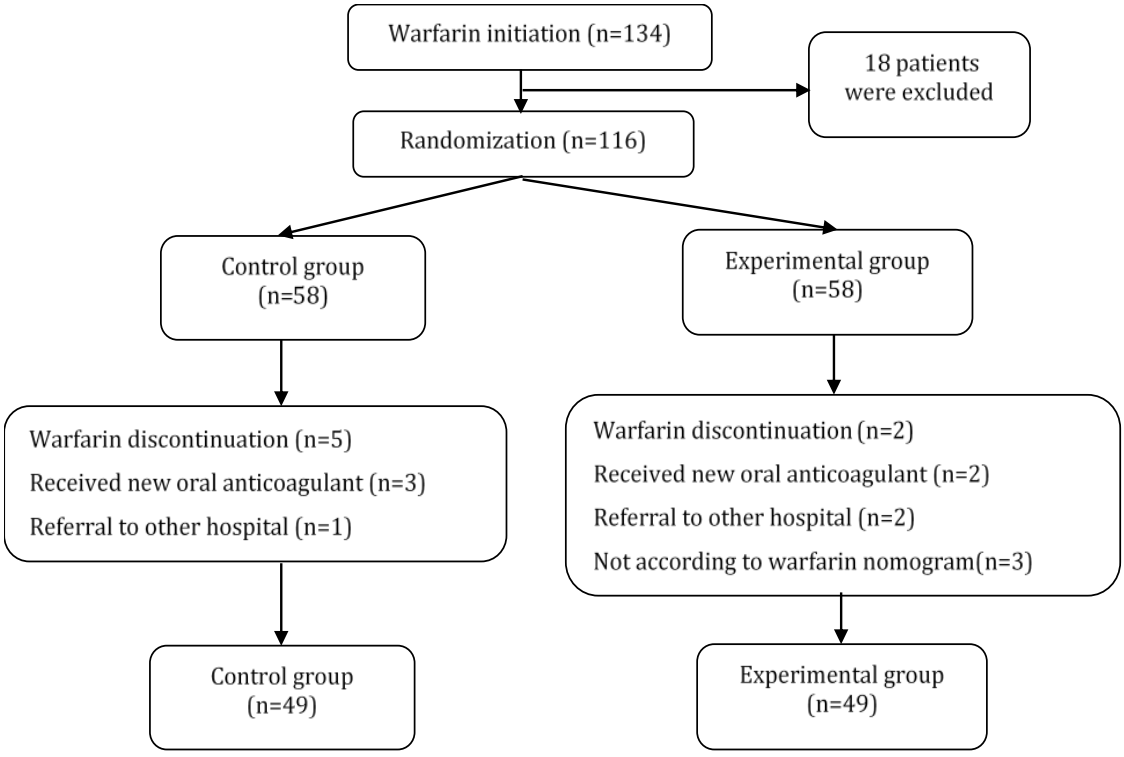

Figure 3. Sample screening

Data analysis

The characteristics of the patients were analyzed, presenting the data as frequencies, percentages, means, standard deviations, medians, and quartiles. To compare differences in proportions for qualitative data, the Chi-square test or Fisher's Exact test was employed. For quantitative data with a normal distribution, differences were assessed using the independent T-test. In cases where data did not follow a normal distribution, differences were evaluated using the Mann-Whitney U test.

In analyzing the proportion of patients with INR value within the range of 2.0 to 3.0 within 14 days, differences between groups were compared using either the Chi-square test or Fisher's Exact test, depending on the data type. For instances of participant withdrawals from the study groups, a per-protocol (PP) analysis approach was utilized to ensure the integrity of the data analysis.

RESULTS

The sample group that received warfarin while admitted to Charoenkrung Pracharak Hospital between August and November 2023, totaling 116 patients (58 in the experimental group and 58 in the control group). In the experimental group, 9 individuals withdrew, accounting for 15.5% (3 due to mismatched drug dosage according to the warfarin nomogram, 2 receiving alternative anticoagulant medication, 2 transferring to another hospital, and 2 discontinuing warfarin). In the control group, 9 individuals withdrew as well, also accounting for 15.5% (5 discontinued warfarin, 3 received alternative anticoagulant medication, and 1 transferred to another hospital). This resulted in a remaining sample of 98 individuals, split into 49 in both the experimental and control groups. The baseline characteristics between the control and experimental groups were not significantly different ($p>0.05$) except for the gender. It was observed that in the control group, the majority were males, accounting for 57.1%, while in the experimental group, the majority were females, accounting for 65.3%. This difference in gender distribution was statistically significant ($p=0.026$) as shown in Table 1.

It was found that the proportion of patients whose INR was within the target range (INR 2.0–3.0) within 14 days after receiving warfarin was significantly higher in the experimental group (44.9%) compared to the control group (24.5%), ($p=0.034$). The proportion of patients with an INR lower than the target (INR<2.0) within 14 days in the experimental group and the control group, was 40.8% vs 51.0%, respectively. The proportion of patients with an INR higher than the target (INR > 3.0) within 14 days in the experimental group and in the control group was 14.3% vs 24.5%, respectively. Although the experimental group had a lower proportion of patients with INR≥5.0 within 14 days (4.1% vs. 6.1%), the difference was not statistically significant ($p>0.05$).

DISCUSSION

Currently, there's an effort to develop warfarin nomograms for initiation and dosage adjustments, aiming for accuracy, clarity in guidelines, and a reduction in the time for reaching the therapeutic INR range. Asnis PD et al. and Anderson DR et al. explored the effectiveness and safety of using warfarin nomograms for initiation and dosage adjustments. They found that using warfarin nomograms in patients undergoing knee or hip replacement surgery showed no difference in effectiveness compared to initiation and dosage adjustments by physicians (4, 5).

Regarding the safety of using warfarin nomograms, Chamoun et al. found that using nomograms in patients initiating warfarin showed no safety differences compared to initiation and dosage adjustments by physicians (40). In Thailand, Ratchnee Hotarawareekarn found that using warfarin nomograms in patients undergoing heart valve replacement surgery helped patients reach the therapeutic INR range faster than initiation and dosage adjustments by physicians (6).

Table 1. Baseline characteristics

Characteristics	Frequencies (percentage or Mean±S.D)		p-value
	Control (n=49)	Experimental (n=49)	
Sex Male Female	 28 (57.1) 21 (42.9)	 17 (34.7) 32 (65.3)	0.026[a]
Age (year)	65.2±17.62	64.1±18.69	0.765[t]
Weight (kg)	63.8±16.58	62.7±16.31	0.745[t]
BMI (kg/m^2)	24.3±5.28	25.3±6.02	0.392[t]
Smoking	3 (6.1)	3 (6.1)	1.000[f]
Alcohol consumption	4 (8.2)	1 (2.0)	0.362[f]
Indication • Atrial fibrillation • Deep vein thrombosis • Pulmonary embolism • Prevention of systemic embolism • Prophylaxis of venous thrombosis	 19 (38.9) 2 (4.1) 11 (22.4) 16 (32.6) 1 (2.0)	 26 (53.0) 3 (6.1) 9 (18.4) 7 (14.3) 4 (8.2)	0.146[a]
CHA_2DS_2-VASc score	3.7±1.56	3.9±1.87	0.726[t]
HAS-BLED score	1.9±1.07	2.0±1.38	0.744[t]
Baseline INR	1.1±0.13	1.1±0.16	0.281[t]
eGFR (ml/min/1.73 m^2)	69.6±30.15	69.3±36.94	0.482[t]
Comorbidity • Heart failure • Hyperthyroid	 8 (16.3) 2 (4.1)	 10 (20.4) 0	 0.602[a] 0.495[f]
Drug interactions • Amiodarone • Aspirin • Ciprofloxacin • Clarithromycin • Fluorouracil • Simvastatin • Sulfamethoxazole	 8 (16.3) 13 (26.5) 0 1 (2.0) 1 (2.0) 6(12.2) 0	 7 (14.3) 9 (18.4) 1 (2.0) 0 0 6 (12.2) 1 (2.0)	 0.779[a] 0.333[a] 1.000[f] 1.000[f] 1.000[f] 1.000[a] 1.000[f]
Other medication • Heparin or enoxaparin	 27 (55.1)	 34 (69.4)	 0.145[a]

[a] Chi-square test, [f] Fisher's Exact test, [t] Independent t-test

Analysis of the data comparing general population characteristics between the control and experimental groups revealed no significant differences, except in gender distribution. The control group predominantly consisted of males, while females were more common in the experimental group, marking a statistically significant variance (p=0.026). This observation prompts consideration of gender's impact on warfarin dosing, as explored by Khoury G. et al., who investigated how gender affects the achievement of INR values within the 2.0–3.0 range. Their findings indicated no significant difference in the average warfarin dosages needed to reach these INR values between males (39.44±14.211) and females (36.15±15.433, p=0.281) (41), in alignment with research conducted by Mueanjanjaem K., which found that gender was not correlate with the warfarin dosage required to achieve the target INR range (r=0.017, p=0.759) (26). This consistency indicated that gender does not significantly affect the outcomes of warfarin therapy in this research.

The research findings revealed that a greater proportion of individuals achieved INR values within the 2.0–3.0 range within 14 days of treatment initiation in the nomogram group compared to the physician-directed group (44.9% and 24.5%, p=0.034), which aligns with the findings by Yoo SH. et al. Similarly, Anderson DR. et al. (60.5% and 57.7%, p=0.02) (4) and Freter S. et al. (77.0% and 53.0%, p<0.0001) (42) reported higher proportions of patients achieving INR values within the 1.8–2.5 range using warfarin nomograms, suggesting an advantage over traditional physician adjustments.

In contrast to these findings, Asnis PD. et al. found no difference in the proportion of patients with INR values in the 1.8–2.5 range between those initiating and adjusting medication using a warfarin nomogram and those initiated and adjusted by a physician (47.1% and 26.3%, respectively) (5). It could be due to the high initial warfarin dosages set by the warfarin nomogram in that study, which did not consider factors that might influence individual responses to warfarin, resulting in some patients receiving higher initial dosages.

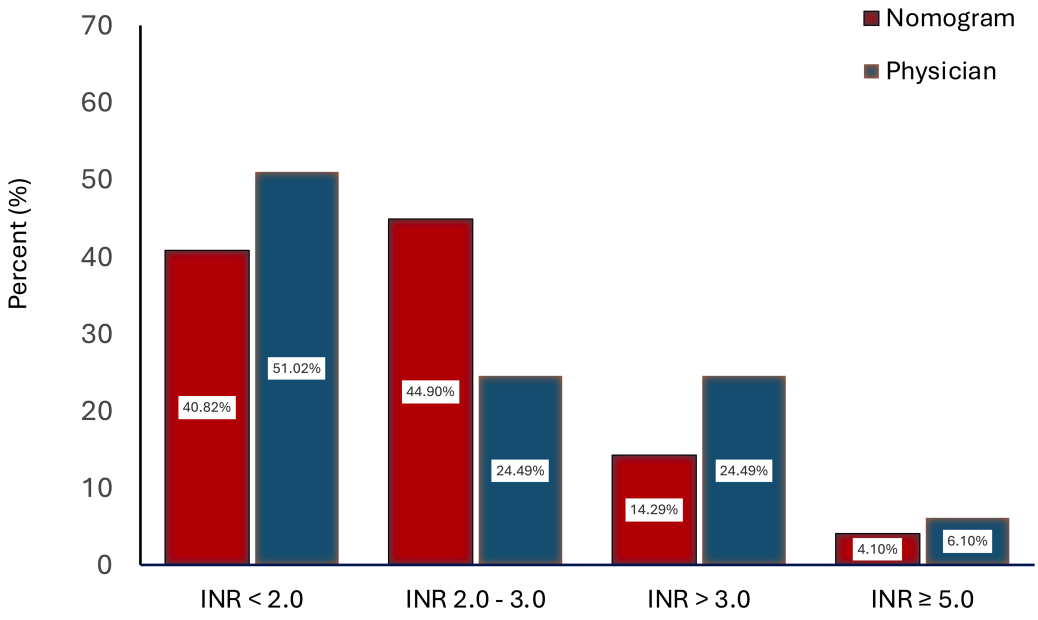

Figure 4. The proportion of patients with an INR value in 14 days

There was no statistically significant difference (p>0.05) in the proportion of patients with INR>3.0 or ≥5.0 between those who initiated and adjusted medication using a warfarin nomogram and those initiated and adjusted by a physician, aligning with Anderson DR. et al.'s study (4). Additionally, Yoo SH. et al. found no difference in the proportion of patients with INR > 3.5 between patients using a warfarin nomogram and those initiated and adjusted by a physician (0% and 2.1%, p=0.23) (43). However, Chamoun N. et al. found a significant lower proportion of patients with INR>4.0 in the warfarin nomogram group than in the physician-initiated group (0.7% and 1.0%, p=0.025) (40). It is possible that the warfarin nomogram employed in the study enabled more frequent INR monitoring. This facilitates the rapid identification of trends in a patient's response to warfarin compared to checking the INR every few days. Consequently, physicians can utilize this information as a reference when considering adjustments of warfarin dosage if the INR falls outside the target range.

Although the study did not find a statistically significant difference in the proportion of patients with an INR below 2.0, the results indicated that the group using a warfarin nomogram for medication initiation and adjustment had a higher number of patients with an INR value within the range of 2.0 to 3.0 compared to those with an INR below 2.0. Conversely, the group receiving initiation and dose adjustment by a physician had a lower number of patients with an INR value within the range of 2.0 to 3.0 compared to those with an INR below 2.0, as illustrated in Figure 4. Therefore, the use of a warfarin nomogram appears to be effective in bringing a patient's INR value within the target range. This study had limitations as it was conducted in a single institution and mainly comprised Thai participants. Dang MT. et al.'s study found that ethnicity influenced the warfarin dosage that achieved the target INR (8), suggesting further studies involving other ethnic groups in the future. Additionally, the warfarin nomogram used in this study might not be suitable for patients undergoing cardiac valve replacement surgery, as the target INR in that study was higher than in this research.

CONCLUSION

The use of warfarin nomograms for initiation and dose adjustment leads to patients achieving their target INR levels more effectively compared to physician-initiated and adjusted dosing. Furthermore, the safety of using warfarin nomograms is not significantly different from physician-initiated and adjusted dosing.

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REFERENCES

1. Hirsh J, Fuster V, Ansell J, Halperin JL. American Heart Association/American College of Cardiology Foundation guide to warfarin therapy. Circulation. 2003;107(12):1692-711. https://doi.org/10.1161/01.CIR.0000063575.17904.4E
2. The Heart Association of Thailand under the Royal Patronage of H.M. Warfarin guideline. n.p.:2010.
3. Godoy LC, Tomlinson G, Abumuamar AM, Farkouh ME, Rudolph M, Billia F, et al. Association between time to therapeutic INR and length of stay following mechanical heart valve surgery. J Card Surg. 2022;37(1):62-9. https://doi.org/10.1111/jocs.16083
4. Anderson DR, Wilson SJ-A, Blundell J, Petrie D, Leighton R, Stanish W, et al. Comparison of a nomogram and physician-adjusted dosage of warfarin for prophylaxis against deep-vein thrombosis after arthroplasty. J Bone Joint Surg Am. 2002;84(11):1992-7.
5. Asnis PD, Gardner MJ, Ranawat A, Leitzes AH, Peterson MG, Bass AR. The effectiveness of warfarin dosing from a nomogram compared with house staff dosing. J Arthroplasty. 2007;22(2):213-8. https://doi.org/10.1016/j.arth.2006.03.006

6. Hotarawareekarn R. New dosage regimen for starting warfarin in patients with mechanical prostheticheart valve replacement at Rajavithi Hospital [Thesis]. Grad - E-Theses: Chulalongkorn University; 1997.
7. Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C, et al. Guidelines on oral anticoagulation with warfarin - fourth edition. Br J Haematol. 2011;154(3):311-24. https://doi.org/10.1111/j.1365-2141.2011.08753.x
8. Dang M-TN, Hambleton J, Kayser SR. The influence of ethnicity on warfarin dosage requirement. Ann Pharmacother. 2005;39(6):1008-12. https://doi.org/10.1345/aph.1E566
9. Cohen J. CHAPTER 7 - Chi-Square tests for goodness of fit and contingency tables. In: Cohen J, editor. Statistical Power Analysis for the Behavioral Sciences: Academic Press; 1977. p. 215-71.
10. Kang H. Sample size determination and power analysis using the G*Power software. J Educ Eval Health Prof. 2021;18:17. https://doi.org/10.3352/jeehp.2021.18.17
11. Witt DM, Clark NP, Vazquez SR. Venous thromboembolism. In: DiPiro JT, Yee GC, Posey LM, Haines ST, Nolin TD, Ellingrod V, editors. Pharmacotherapy: A Pathophysiologic Approach, 11e. New York, NY: McGraw-Hill Education; 2020.
12. Blann AD, Fitzmaurice DA, Lip GY. Anticoagulation in hospitals and general practice. BMJ. 2003;326(7381):153-6. https://doi.org/10.1136/bmj.326.7381.153
13. del Campo M, Roberts G. Changes in warfarin sensitivity during decompensated heart failure and chronic obstructive pulmonary disease. Ann Pharmacother. 2015;49(9):962-8. https://doi.org/10.1177/1060028015590438
14. Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child–Pugh versus MELD. J Hepatol. 2005;42(1, Supplement):S100-S7. https://doi.org/10.1016/j.jhep.2004.11.015
15. Efird LM, Mishkin DS, Berlowitz DR, Ash AS, Hylek EM, Ozonoff A, et al. Stratifying the risks of oral anticoagulation in patients with liver disease. Circ: Cardiovasc Qual Outcomes. 2014;7(3):461-7. https://doi.org/10.1161/CIRCOUTCOMES.113.000817
16. Gage BF, Fihn SD, White RH. Management and dosing of warfarin therapy. Am J Med. 2000;109(6):481-8. https://doi.org/10.1016/S0002-9343(00)00545-3
17. Gatta A, Verardo A, Bolognesi M. Hypoalbuminemia. Intern Emerg Med. 2012;7(3):193-9.
18. Hirsh J, Dalen J, Anderson DR, Poller L, Bussey H, Ansell J, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest. 2001;119(1 Suppl):8s-21s. https://doi.org/10.1378/chest.119.1_suppl.8S
19. Howard-Thompson A, Luckey A, George C, Choby BA, Self TH. Graves' disease and treatment effects on warfarin anticoagulation. Case Rep Med. 2014;2014:1-6. https://doi.org/10.1155/2014/292468
20. Jantara S, Pattarawimonchai O, Juntaranimi P. Clinical factors associated with low, medium and high warfarin dose requirements in adult and older adult patients at Loei hospital. Srinagarind Med J. 2023;38(3):291-302. https://li01.tci-thaijo.org/index.php/SRIMEDJ/article/view/258157
21. Kawai M, Harada M, Motoike Y, Koshikawa M, Ichikawa T, Watanabe E, et al. Impact of serum albumin levels on supratherapeutic PT-INR control and bleeding risk in atrial fibrillation patients on warfarin: A prospective cohort study. Int J Cardiol Heart Vasc. 2019;22:111-6.
22. Kellett HA, Sawers JSA, Boulton FE, Cholerton S, Park BK, Toft AD. Problems of anticoagulation with warfarin in hyperthyroidism. Q J Med. 1986;58(1):43-51.
23. Lee VW, You JH, Lee KK, Chau TS, Waye MM, Cheng G. Factors affecting the maintenance stable warfarin dosage in Hong Kong Chinese patients. J Thromb Thrombolysis. 2005;20(1):33-8. https://doi.org/10.1007/s11239-005-3121-8
24. Limdi NA, Limdi MA, Cavallari L, Anderson AM, Crowley MR, Baird MF, et al. Warfarin dosing in patients with impaired kidney function. Am J Kidney Dis. 2010;56(5):823-31.
25. Merative™ Micromedex® Drug Interaction Checking (warfarin).Merative, Ann Arbor, Michigan, USA.2023 Oct 15 [cited 2023 Oct 15]. Available from: https://www.micromedexsolutions.com/
26. Mueanjanjaem K. Optimum and clinical factors affecting the stable maintenance dose of warfarin at Ratchaburi Hospital. Hua Hin Med J. 2020;5(1):18-29. https://he01.tci-

thaijo.org/index.php/hhsk/article/view/240517
27. Nakornchai W, Rojnuckarin P. Bleeding risk of warfarin therapy among cirrhotic patients. J Hematol Transfus Med. 2019;29:205-13.
28. Panompong K, Tonhongsa P. Factors predicting of warfarin dosage and Factors Related to International Normalized Ratio (INR) of the patients , Nong Phok hospital, Roi Et Province. J Res Health Innov Dev. 2021;2(3):109-20.
29. Rivey MP, Wood RD, Allington DR, Stratton TP, Erickson CC, Stenson TA. Pharmacy-managed protocol for warfarin use in orthopedic surgery patients. Am J Health Syst Pharm. 1995;52(12):1310-6. https://doi.org/10.1093/ajhp/52.12.1310
30. Stephens MA, Self TH, Lancaster D, Nash T. Hypothyroidism: effect on warfarin anticoagulation. South Med J. 1989;82(12):1585-6.
31. Suwanawiboon B, Kongtim P, Chinthammitr Y, Ruchutrakool T, Wanachiwanawin W. The efficacy of 3-mg warfarin initiating dose in adult Thai patients, who required long-term anticoagulant therapy. J Med Assoc Thai. 2011;94 Suppl 1:S225-31.
32. Suwanawiboon B, Rotchanapanya W, Mahaprom K, Thongnoppakhun W, Lalerd Y, Limwongse C, et al. The efficacy of low-dose warfarin initiation (3 mg versus 5 mg) in newly diagnosed venous thromboembolism patients among a population with a high prevalence of warfarin-sensitive haplotype of the VKORC1 gene: a randomized controlled trial. Hematology. 2022;27(1):95-104. https://doi.org/10.1080/16078454.2021.2019891
33. Tincani E, Mazzali F, Morini L. Hypoalbuminemia as a risk factor for over-anticoagulation. Am J Med. 2002;112(3):247-8. https://doi.org/10.1016/S0002-9343(01)00957-3
34. Tyson K, Hutchinson N, Williams S, Scutt G. Identification of clinical factors predicting warfarin sensitivity after cardiac surgery. Ther Adv Drug Saf. 2018;9(8):415-24. https://doi.org/10.1177/2042098618776541
35. Wallace JL, Reaves AB, Tolley EA, Oliphant CS, Hutchison L, Alabdan NA, et al. Comparison of initial warfarin response in obese patients versus non-obese patients. J Thromb Thrombolysis. 2013;36(1):96-101. https://doi.org/10.1007/s11239-012-0811-x
36. Wattanasombat S. Anticoagulant :Warfarin. TPHSJ. 2010;5:87-98.
37. Witt DM, Delate T, Clark NP, Martell C, Tran T, Crowther MA, et al. Outcomes and predictors of very stable INR control during chronic anticoagulation therapy. Blood. 2009;114(5):952-6. https://doi.org/10.1111/j.1538-7836.2010.03756.x
38. Witt DM, Delate T, Clark NP, Martell C, Tran T, Crowther MA, et al. Twelve-month outcomes and predictors of very stable INR control in prevalent warfarin users. J Thromb Haemost. 2010;8(4):744-9. https://doi.org/10.1111/j.1538-7836.2010.03756.x
39. Rovinelli RJ, Hambleton RK. On the use of content specialists in the assessment of criterion-referenced test item validity. Tijdschrift voor Onderwijsresearch. 1977;2(2):49-60.
40. Chamoun N, Macías CG, Donovan JL, Klugman R, Gore J, Salameh P, et al. Implications of an inpatient warfarin dosing nomogram on safety outcomes post-discharge. J Thromb Thrombolysis. 2017;43(4):454-62. https://doi.org/10.1007/s11239-016-1462-0
41. Khoury G, Sheikh-Taha M. Effect of age and sex on warfarin dosing. Clin Pharmacol. 2014;6:103-6. https://doi.org/10.2147/CPAA.S66776
42. Freter S, Bowles SK. Comparison of a frail-friendly nomogram with physician-adjusted warfarin dosage for prophylaxis after orthopaedic surgery on a geriatric rehabilitation unit. Can J Aging. 2005;24(4):443-7.
43. Yoo SH, Kwon SU, Jo MW, Kang DW, Kim JS. Age- and weight-adjusted warfarin initiation nomogram for ischaemic stroke patients. Eur J Neurol. 2012;19(12):1547-53. https://doi.org/10.1111/j.1468-1331.2012.03772.x