MedCrave
Step into the World of Research

Pharmacy & Pharmacology International Journal

Research Article

Open Access

CrossMark

# Evaluation of a pharmacist-managed warfarin dosing service in a community hospital

## Abstract

**Objective:** Warfarin is used as the mainstay of oral anticoagulant therapy for the prevention and treatment of various thromboembolic disorders. Effective methods of managing anticoagulation are available, but underemployed. Standardized dosing protocols (nomograms) and anticoagulation management services are some ways to manage warfarin use. The primary objective of this study was to evaluate a difference in time in therapeutic range (TTR) of international normalized ratio (INR) level in physician-managed groups versus pharmacist-managed warfarin groups.

**Methods:** The institutional review board approved this single center, retrospective study which was conducted in a small community hospital. Men and women ages 44-97 who were previously on or began warfarin therapy during hospitalization were evaluated for selection. A total of 38 patients were randomly selected for the review during August-December 2017. The primary outcome of TTR in physician- versus pharmacist-managed warfarin groups was calculated. A two proportion Z-test was utilized for statistical analysis. Secondary outcomes included time with subtherapeutic INR, time with supratherapeutic INR, safety outcomes (bleeding, transfusion), and the need for bridge therapy.

**Results:** Thirty-four total patients were included for the final review, and four were excluded as they switched from one group to another during the review period. The primary outcome, TTR, was higher in the pharmacist-managed group compared to the physician-managed group (p=0.03). Secondary outcomes were similar in both groups per descriptive statistics.

**Conclusions:** Pharmacist consults for warfarin management or auto consults for all orders should be considered more often. The clinical significance of TTR when warfarin is managed by pharmacists must be determined in larger, randomized clinical trials.

**Keywords:** warfarin, pharmacists, hospitals, community, international normalized ratio, anticoagulants, thromboembolism

Volume 9 Issue 2 - 2021

Essie Samuel,[1] Sonia Thomas,[2] Kinjal Shah,[3] Jonas Arthur[4]

[1]Assistant Professor, Pharmacy Practice, PCOM Georgia, USA
[2]Associate Professor, Pharmacy Practice, PCOM Georgia, USA
[3]Doctor of Pharmacy Class of 2021 Candidate, PCOM Georgia, USA
[4]PharmD, PCOM Georgia, USA

**Correspondence:** Essie Samuel, PharmD, BCPS, Assistant Professor, Pharmacy Practice, PCOM Georgia, 625 Old Peachtree Rd NW, Suwanee, GA 30024, Email essiesa@pcom.edu

**Received:** February 26, 2021 | **Published:** March 23, 2021

## Introduction

For many decades, warfarin has been the mainstay of oral anticoagulant therapy for the prevention and treatment of various thromboembolic disorders. Warfarin is a high-risk medication due to its narrow therapeutic window and risk of hemorrhage or thrombosis. Its use in clinical practice is challenging due to its complex pharmacokinetics and pharmacodynamics, variability in dose response among patients, numerous interactions with drugs and diet, narrow range between therapeutic and toxic doses, effects of comorbid illnesses on dosing, and frequent laboratory monitoring. Due to these concerns, meticulous dosing and frequent clinical monitoring is required.[1,2] When managing the dosing of a medication, knowledge of its pharmacokinetics and pharmacodynamics is important for better outcomes. Warfarin dosing management is, therefore, an ideal area for pharmacists to become involved as it makes use of many of the facets of a pharmacist's training including the pharmacokinetics and pharmacodynamics of warfarin.[3] Prothrombin time (PT) is a blood test used to measure the time it takes for clot to form. International normalized ratio (INR) is a standardized way of expressing PT. A therapeutic INR is recommended between 2 to 3, except for cases in patients with mechanical or biological valves, anti-phospholipid syndrome, post myocardial infarction and high-risk thrombosis patient, INR of 2.5 to 3.5 is recommended.

Studies have shown that among patients starting warfarin or already on warfarin at the hospital, daily pharmacy consult decreases the length of stay at the hospital and the number of patients who receive excess amount of doses.[4] Overall, these findings have shown reduction in cost for patients and also improvement in the quality of care. Effective methods of managing anticoagulation are available, but underemployed. An assessment of antithrombotic practice in 38 academic and community hospitals in the United States reported that many patients failed to receive appropriate treatment despite the benefit of anticoagulation therapy.[5] Standardized dosing protocols (nomograms) and anticoagulation management services are some ways to manage warfarin use.[4] The primary outcome of the study was the duration of time in therapeutic range (TTR) of international normalized ratio (INR) in physician versus pharmacist managed group. Secondary outcomes included percent of time INR was subtherapeutic and the need for bridge therapy, percent of time INR was supratherapeutic, percent of time INR was supratherapeutic in patients who were subtherapeutic or therapeutic at baseline, and the outcomes associated with supratherapeutic INR including bleeding and requirement for blood transfusions.

## Methods

A single-center retrospective chart review was conducted at _____, a 202 bed community hospital, evaluating warfarin patients managed by pharmacists compared to physicians. Patients aged 18 years or above who received warfarin between August and December 2017 were included in the study. Data collected utilizing a paper data collection form (Table 1) included patient demographics,

indication for warfarin use, warfarin home regimen and inpatient dosing regimen, vitamin K utilization and/or blood transfusions, and daily laboratory values [(INR, complete blood count (CBC)] when available. Collected data was transferred to an excel sheet for evaluation of outcomes.

**Table 1** Data collection sheet

Patient Demographics:

| | |
|---|---|
| Account number | Age |
| Attending physician | Sex |
| Admission date | Height (inches) |
| Discharge date | Weight (kg) |
| Length of Stay | |

Indication for warfarin (Goal):

Labs:

| |
|---|
| Date |
| INR |
| Warfarin Dose |
| Hgb |
| Hct |

| |
|---|
| Date |
| INR |
| Warfarin Dose |
| Hgb |
| Hct |

Dosed by: Physician ☐ Pharmacist ☐

Warfarin initial dose:
Bridging Yes ☐ No ☐

Warfarin prior to admission: Yes ☐ No ☐
With:

Baseline INR drawn: Yes ☐ No ☐

Interacting medications:

- Amiodarone
- Sulfamethoxazole/trimethoprim
- Metronidazole
- Fluconazole
- Erythromycin
- Rifampin
- Levaquin

Other interventions:

Bleeding:

- Vitamin K: Yes ☐ No ☐ If yes, how much?
- Transfusion: Yes ☐ No ☐ If yes, how many units?

A total of 38 patients met the inclusion criteria. Four of these patients were excluded because they switched from one group to the other during their inpatient stay leaving a total of 34 patients (17 patients each in the pharmacist- and physician-managed groups). This study was approved by the institutional review board. Percent of time patients' INR results were in the therapeutic range, subtherapeutic range, as well as in the supratherapeutic range was calculated from the data collected. A two proportion Z-test was used to determine statistical significance of the difference between TTR in both groups.

## Results

Thirty-eight participants were selected for this study and baseline characteristics were similar among the two groups based on descriptive statistics (Table 2). Patient ages ranged from 44 to 97. The primary outcome (Table 3, Figure 1) was higher in the pharmacist-managed group with TTR being 64% compared to 45% in the physician-managed group (p=0.03). Secondary outcomes (Table 4, Figure 2) are listed below:

a. Percent of time patients were with subtherapeutic INR in the pharmacist-managed group was 31 compared to 52 in the physician-managed group (p=0.01).

b. Seven patients (41%) in the pharmacist-managed group were bridged with a parenteral anticoagulant compared to 10 patients (59%) in the physician-managed group.

c. A higher number of patients had supratherapeutic INR in the pharmacist-managed group at 13% compared to 3% in the physician-managed group. However, time with supratherapeutic INR in patients who were therapeutic or subtherapeutic at baseline was 4.4% in the pharmacist-managed group versus 2.7% in the physician-managed group (p=0.5).

d. No patients experienced bleeding events in either group. One patient in the physician-managed group did receive a transfusion due to low hemoglobin/hematocrit.

**Table 2** Baseline characteristics

| Variable | Pharmacist-managed group (n=17) | Physician-managed group (n=17) |
|---|---|---|
| Age, mean (years) | 78 (range 44-97) | 76 (range 46-91) |
| Male, No (%) | 9 (53) | 12 (71) |
| Service, No (%) | | |
| · Hospitalists | 15 (88) | 15 (88) |
| · Specialists | 2 (12) | 2 (12) |
| Warfarin use prior to admission, No (%) | 14 (82) | 11 (65) |
| Baseline INR drawn, No (%) | 16 (94) | 16 (94) |
| Venous thromboembolism, No (%) | 5 (29) | 8 (47) |
| Atrial fibrillation, No (%) | 8 (47) | 4 (24) |
| Cerebrovascular accident, No (%) | 1 (6) | 3 (18) |
| Mechanical valve, No (%) | 2 (12) | 2 (12) |
| Others, No (%) | 1 (6) | 0 (0) |

**Citation:** Samuel E, Thomas S, Shah K, et al. Evaluation of a pharmacist-managed warfarin dosing service in a community hospital. *Pharm Pharmacol Int J.* 2021;9(2):34–37. DOI: 10.15406/ppij.2021.09.00324

**Table 3** Primary outcome

| Outcome | Pharmacist-managed group (n=17) | Physician-managed group (n=17) |
|---|---|---|
| Time in therapeutic range (mean, %) | 64 | 45 |

**Table 4** Secondary outcomes

| Outcome | Pharmacist-managed group (n=17) | Physician managed group (n=17) |
|---|---|---|
| Time with subtherapeutic INR (%) | 31 | 52 |
| Time with supratherapeutic INR (%) | 13 | 3 |
| Bleeding (No, %) | 0 | 0 |
| Transfusion (No, %) | 0 | 1 (6) |
| Drug interactions, (No, %) | 5 (29) | 5 (29) |
| · Amiodarone (No, %) | 5 (29) | 3 (18) |
| · Levofloxacin (No, %) | 0 | 1 (6) |
| · Sulfamethoxazole/trimethoprim (No, %) | 0 | 1 (6) |
| Bridge therapy (No, %) | 7 (41) | 10 (59) |

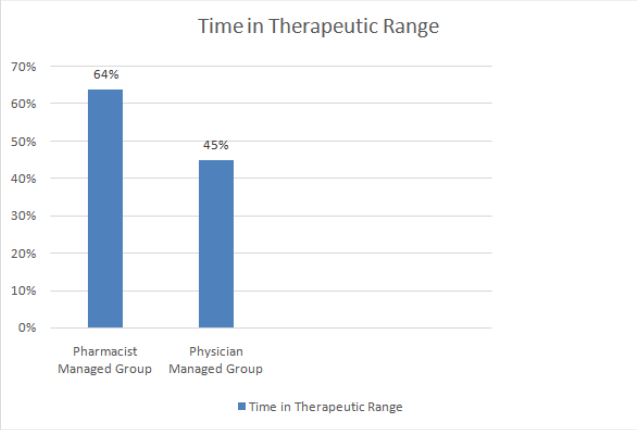


**Figure 1** Primary outcomes.

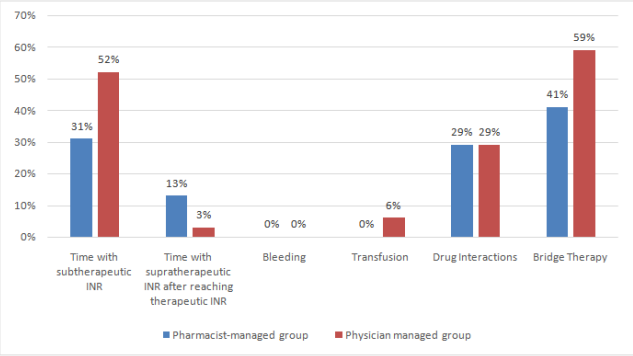


**Figure 2** Secondary outcomes.

In addition, five patients (29%) in each group were identified to be on medications with major drug interactions with warfarin which could potentially have had significant implications on their INR results. All five warfarin patients in the pharmacist-managed group were on amiodarone concurrently while three patients were on amiodarone, one patient on levofloxacin, and one patient on sulfamethoxazole/trimethoprim in the physician-managed group.

## Discussion

A total of 38 patients were randomly selected for this retrospective review during August-December 2017. Thirty-four of these patients were included for the final review and four were excluded as they switched from one group to another during the review period. The primary outcome, TTR, was significantly higher in the pharmacist-managed group compared to the physician-managed group (p=0.03). Time with subtherapeutic INR was also significantly lower in the pharmacist-managed group (p=0.01) while patients who required bridging in either group were not significantly different. Time with supratherapeutic INR was higher in the pharmacist-managed group. However, most of these patients were supratherapeutic at admission. Among the patients who were therapeutic or subtherapeutic at admission, there was not a difference in time with supratherapeutic INR between physician- or pharmacist-managed groups (p=0.5). Same number of patients experienced significant drug interactions in both groups. None of the patients experienced bleeding during the review period, however, one patient did have to receive transfusion due to low hemoglobin/hematocrit in the physician-managed group. Limitations found with this study include retrospective analysis, small sample size, inconsistencies resulting from warfarin management in both groups by multiple pharmacists and physicians. In addition, pharmacists at the hospital who follow and make recommendations even when not consulted could skew the physician-managed group results.

Similar to other studies, this study also found that pharmacist-managed warfarin dosing in an inpatient setting is superior to physician-managed warfarin dosing. A meta-analysis of 26 studies showed that pharmacist led anticoagulation management in the inpatient setting results in better outcomes compared to physician managed or usual management protocol.[6] Another study at Mayo Clinic hospitals in Rochester, Minnesota used a pharmacist-managed warfarin protocol (PMWP) for managing warfarin dosing by inpatient pharmacists with support from computerized algorithms. The PMWP resulted in improved INR for inpatient warfarin recipients and to less near-term bleeding among higher risk, surgical patients.[7] Pharmacist consultation and management of patients on warfarin therapy has

shown to improve INR and reduce adverse events compared to physician-managed groups.

Another finding of the study was lack of consistent baseline INR reporting in all patients. Baseline INR should be drawn prior to warfarin initiation so that the response to warfarin therapy can be monitored appropriately. In those institutions with computerized prescription order entry (CPOE), steps should be taken to prevent verification of warfarin prescriptions without an active INR level on the patient's profile. For those institutions unable to implement such measures or those without CPOE, steps to educate prescribers, nurses, and pharmacists should be undertaken on a regular basis to prevent inappropriate ordering of warfarin without an INR level.

## Conclusion

Since this study was conducted, pharmacist-managed warfarin groups have consistently displayed better management of INR results in the therapeutic range. This has now led to auto consultation of pharmacists for all warfarin orders at the hospital. Pharmacist consults for warfarin management or auto consults for all warfarin orders should be considered more often at inpatient facilities. The clinical significance of TTR when warfarin is managed by pharmacists in an inpatient setting must be determined in larger, prospective clinical trials.

## Funding statement

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Acknowledgments

None.

## Conflicts of interest

Authors declare that there is no conflict of interest.

## References

1. Ageno W, Gallus AS, Wittkowsky A, et al. 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–e88S.
2. Witt DM, Clark NP, Vazquez SR. Venous Thromboembolism. In: DiPiro JT, Talbert RL, Yee GC, et al. eds. *Pharmacotherapy: A Pathophysiologic Approach*. 10th ed. New York, NY: McGraw-Hill; 2017.
3. Boddy C. Pharmacist involvement with warfarin dosing for inpatients. *Pharm World Sci*. 2001;23(1):31–35.
4. Donovan JL, Drake JA, Whittaker P, et al. Pharmacy-managed anticoagulation: assessment of in-hospital efficacy and evaluation of financial impact and community acceptance. *J Thromb Thrombolysis*. 2006;22(1):23–30.
5. Tapson VF, Hyers TM, Waldo AL, et al. Antithrombotic therapy practices in US hospitals in an era of practice guidelines. *Arch Intern Med*. 2005;165(13):1458–1464.
6. Daniels PR, Manning DM, Moriarty JP, et al. Improving inpatient warfarin therapy safety using a pharmacist-managed protocol. *BMJ Open Qual*. 2018;7(2):e000290.
7. Lee T, Davis E, Kielly J. Clinical impact of a pharmacist-led inpatient anticoagulation service: a review of the literature. *Integr Pharm Res Pract*. 2016;5:53–63.