ISSN: 2634 - 6796

Journal of Cardiology Research Reviews & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Time in the Therapeutic Range for Patients with Atrial Fibrillation and Taking Warfarin in Gaza (TTR- AF Gaza)

Mohammed Habib

Department of Cardiology And Cardiac Catheterization, Al-Shifa Hospital, Gaza, Palestine

ABSTRACT

Background: Anticoagulation control with warfarin, as assessed by the international normalized ratio (INR), Poor quality of warfarin control by low INR or low time in therapeutic range (TTR) can lead to increased risk of adverse events. The objective of this study was to examine the overall quality of (INR) control and the association of TTR among patients in Gaza Strip.

Method: A prospective study was conducted among patients on warfarin for NVAF who attended the Cardiology Outpatient Clinic of Alshifa Hospital between June 2021 to October 2022. Patients' TTR was calculated by using Traditional method.

Results: A total of 231 patients were included with mean age 59.15±12.6 years. The mean TTR score was 50.93±16.37%, the total 1155 INR measurements were calculated. Of the sample patients, 47.6 % were in the good control category (TTR ≥ 60%), and 52.4% were in the poor control category (TTR<60%).

Conclusion: Our study demonstrates more than half of patients have poor anticoagulation control and we urgent need to improve oral anticoagulation care for most patient segments in the Gaza Strip.

***Corresponding author**
Mohammed Habib, Department Of Cardiology And Cardiac Catheterization, Al-Shifa Hospital, Gaza, Palestine.
E-mail: Cardiomohammad@yahoo.com

Received: November 28, 2022; **Accepted:** December 15, 2022; **Published:** December 28, 2025

Introduction

Time in therapeutic range (TTR) is interpreted to reflect the overall quality of anticoagulation achieved on warfarin in clinical practice, the international normalized ratio (INR) is a standard test used by providers for patients who are on anticoagulation therapy and allows for a provider to evaluate the immediate control of warfarin dosage. TTR, account multiple INR values from contiguous visits, is used to reflect anticoagulation control over time [1].

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the world and increases the risk of ischemic stroke ~ 5-fold, and these strokes confer a 30-day mortality of 24% [2,3]. The vitamin K antagonist warfarin greatly reduces the risk of ischemic stroke and is the most commonly used therapy to prevent stroke and stroke recurrence in patients with AF [4-6]. Because of its variable dose-response relationship, drug drug, drug food interactions and narrow therapeutic window, warfarin requires frequent monitoring of its anticoagulant effect as reflected by the international normalized ratio (INR). Percent of time in the therapeutic range has been shown to correlate with ischemic stroke, major hemorrhage, and mortality [7-8].

There are three commonly accepted methods for calculating TTR:

1. Rosendaal method assumes a linear progression of change in INR between a patient's visits; in other words, it assumes that the INR changes the same amount each day.
2. The traditional and cross-sectional methods do not treat INR as a dynamic value that changes over time. Instead, these methods consider each individual INR value to be static and binary, either in or out of range. The traditional method calculates TTR as the proportion of in-range INR values to the total number of INR values
3. The cross-sectional method takes into account only the INR from the last visit before an arbitrarily chosen date.

In our study we use the traditional method calculates TTR as the proportion of in-range INR values to the total number of INR values. Traditional = (no. of in-range visits/ total no. of visits)

Method

Study Design and Data Collection

We conducted a prospective study for patients with non valvular atrial fibrillation (NVAF) on warfarin who attended the Cardiology Outpatient Clinic of Alshifa Hospital between June 2021 to October 2022.

All patients included were aged 18 years and above, and have been receiving warfarin for at least past six months and The first INR of patients were collected during their referral then monthly INR was measurement and every patient had at least 5 INR measurements taken in total. Patients were excluded from the study if they had less than 5 INR record, valvular heart disease or mechanical heart valves. We obtained written informed consent from all the participants.

The patients' INR readings over the past six months were recorded. Their TTR was calculated by using Traditional method. we used the outpatient 5 INRs values in months 1– 6 after the initial prescription to classify patients as having 'good control' (TTR ≥ 60 %) or suboptimal control (TTR <60%).

Inclusion criteria:
1. Patients must be at least 18 years old and nonvalvular atrial fibrillation
2. The CHADS-VASc score 2 or more for male and 3 or more for female.
3. The INRs of patients were collected in cardiology outpatient clinic during their referral to the clinic where every patient had at least 5 INR measurements taken in total for 6 months.

Exclusion criteria:
Patients were excluded if they had valvular lesions (any prosthetic valves or moderate to severe mitral stenosis)
Patients had less than 5 INRs measurements taken in total for 6 months.

Calculation of TTR
In our study we use the traditional method calculates TTR as the proportion of in-range INR values to the total number of INR values. Traditional = (no. of in-range visits/ total no. of visits)

The Primary Outcome
The total TTR score for at least 5 continues recorded monthly INR

Statistical analysis
Results of continuous data such age , TTR score and INR level are reported as mean ± SD. Data were analyzed using the Statistical Package for the Social Sciences version 20 (SPSS- 20), and p-values less than 0.05 were considered statistically significant.

Results
A total of 231 patients were included with mean age 59.15±12.6 years. A 113 female (49%) and 118 male (51%). The youngest patient included in this study was 19 years old and the oldest patient was 82 years old. The mean TTR score was 50.93±16.37%, The CHADS-VASc score

The primary outcome: The optimal TTR ≥ 60% was seen in 110 patients 47.6 % (62 male and 48 female) and Suboptimal TTR 60% was seen in 121 patients 52.4% (56 male and 65 female) Table: 1. There were no significant differences in TTR between male and females (p = 0.15), patients <75 years, those >75 years (p = 0.49), and patients with and without heart failure (p = 0.52). Table: 2

Table 1: TTR according non valvular atrial fibrillation in our trial

TTR	Male	Female
20%	15	25
40%	41	40
60%	35	25
80%	25	20
100%	2	3
Total	118	113

Table 2: Factors affected TTR score

	TTR >60%	TTR<60%	P value
Male /female	62/48	56/65	0.15
Age >75 /< 75years	14/56	13/48	0.49
CHF	12	15	0.52
CHADS-VASc score	3.5	3.1	0.19

Discussion
In the present study, only 47.6% of patients had good TTR score. In recent major clinical trials, the numbers have been higher, with mean and median values often in the mid to high 60% range. In the case of the four recent NOAC versus warfarin trials in AF, the respective mean and median TTR values were 62.2% and 66.6% in ARISTOTLE; 64.9% and 68.4% in ENGAGE AF; 55% and 58% in ROCKET AF; and a mean of 64% in RE-LY with no median reported [9-12].

Melamed et al. studied TTR in 906 patients diagnosed with atrial fibrillation in the United States who were treated with warfarin for at least 6 months. They concluded that poor control (TTR < 60% in their study) was significantly associated with females, advanced age (>75 years), and heart failure [13]. However, in our study, there were no significant differences in TTR between male and females (p = 0.15), patients <75 years, those >75 years (p = 0.49), and patients with and without heart failure (p = 0.52).

Conclusion
We found a mean TTR score was 50.93±16.37% in the Palestinian patients diagnosed with non-valvular atrial fibrillation who were receiving warfarin therapy. And only 47.6% of the patients have TTR score ≥ 60%.we urgent need to improve oral anticoagulation care for most patient segments in the Gaza Strip.

References

1. SAFIA SIDDIQUI, CHRISTINA E DEREMER, JENNIFER L WALLER, JASPAL S. GUJRAL (2018) Variability in the Calculation of Time in Therapeutic Range for the Quality Control Measurement of Warfarin. J Innov Cardiac Rhythm Manage 9: 3428-3434.
2. Hylek EM, Go AS, Chang Y, Jensvold NG, Henault LE, et al. (2003) Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. N Engl J Med 349: 1019-1026.
3. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, et al. (1998) Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 98: 946-952.
4. Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, et al. (1996) Stroke severity in atrial fibrillation: the Framingham study. Stroke 27: 1760-1764.
5. Connolly SJ, Pogue J, Eikelboom J, Flaker G, Commerford P, et al. (2008) ACTIVE W Investigators. Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control achieved by centers and countries as measured by time in therapeutic range. Circulation 118: 2029-2037.
6. Wysowski DK, Nourjah P, Swartz L (2007) Bleeding complications with warfarin use: a prevalent adverse effect resulting in regulatory action. Arch Intern Med 167: 1414-1419.
7. White HD, Gruber M, Feyzi J, Kaatz S, Tse HF, et al. (2007) Comparison of outcomes among patients randomized to warfarin therapy according to anticoagulant control: results

from SPORTIF III and V. Arch Intern Med 167: 239-245.
8. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, et al. (2008) American College of Chest Physicians. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 133:160S-198S.
9. Granger CB, Alexander JH, McMurray JIJV, Lopes RD, Hylek EM, et al. (2011) Apixaban versus warfarin inpatients with atrial fibrillation. New Engl J Med 365: 981-992.
10. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, et al. (2013) Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med 369: 2093-2104.
11. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, et al. (2009) Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 361: 1139-1151.
12. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, et al. (2011) Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 365: 883-891
13. Melamed OC, Horowitz G, Elhayany A, Vinker S (2011) Quality of anticoagulation [19] control among patients with atrial fibrillation. Am J Manag Care 17: 232-37.