

Quality of Oral Anticoagulation Control with Warfarin in Patients Followed at the Hematology Service of a Public Referral Hospital in Fortaleza, Ceará, Brazil: A Retrospective, Single-Center, Exploratory Study

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Abstract: Warfarin, a vitamin K antagonist, remains widely prescribed within resource-limited public health systems, but its narrow therapeutic index requires close monitoring through the International Normalized Ratio (INR) and the Time in Therapeutic Range (TTR). Real-world data on warfarin control within the Brazilian Unified Health System are scarce. We conducted a retrospective, single-center, exploratory observational study, reported following STROBE, to describe the quality of anticoagulation control in patients on chronic warfarin therapy at a public referral hematology service in Fortaleza, Brazil. Between August and September 2023, the longitudinal records of 34 adult patients (a convenience sample; about 12% of clinic warfarin users) were reviewed, comprising 879 PT/INR determinations analyzed against a target range of 2.0–3.0; TTR was estimated as the proportion of determinations within range. No sample-size calculation was performed, and analyses were descriptive. Approximately half of the determinations (456/879; 51.9%) were in range, and approximately one-third of patients (12/34; 35.3%) achieved a TTR above 60%, indicating predominantly suboptimal control. No thromboembolic events occurred during warfarin therapy; 28 patients (82.4%) self-reported adherence difficulties. These findings do not establish effectiveness but highlight the need to strengthen monitoring, adherence support, and multidisciplinary anticoagulation care. Results are hypothesis-generating.

Keywords: Warfarin; International Normalized Ratio; Anticoagulants; Drug Monitoring; Thromboembolism.

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1. Introduction

Oral anticoagulation is a cornerstone strategy for the prevention and treatment of thromboembolic disease, including venous thromboembolism, systemic embolism, and cardioembolic stroke. Despite the growing availability of direct oral anticoagulants (DOACs), the vitamin K antagonist warfarin remains extensively used worldwide and is frequently the first-line option in low- and middle-income settings because of its low cost and wide availability. Warfarin is nonetheless a demanding drug: it has a narrow therapeutic index, a highly variable dose–response relationship, and multiple food and drug interactions, so that keeping anticoagulation within the intended intensity is essential to preserve both efficacy and safety [1].

The intensity of warfarin anticoagulation is monitored through the prothrombin time, standardized as the INR. A single INR value reflects only the anticoagulation status on the day of collection and does not capture the quality of control over time. The accepted metric for longitudinal control is the TTR, which estimates the proportion of time a patient's INR remains within the intended range. A TTR above approximately 65–70% is associated with a substantially lower risk of both thromboembolic and hemorrhagic events, whereas values below 60% denote poor control and are associated with adverse outcomes [1–3].

Although the determinants and consequences of anticoagulation quality are well characterized in high-income health systems, real-world data on the quality of warfarin control within the Brazilian Unified Health System (SUS), and specifically in specialized public coagulopathy services, remain limited. Characterizing the quality of control actually achieved in this context is a prerequisite for designing interventions, such as structured anticoagulation clinics, pharmacist-led services, point-of-care INR testing, patient education, or selective transition to DOACs, that could improve outcomes for a population with restricted access to newer therapies.

Accordingly, the aim of this study was not to establish the clinical effectiveness of warfarin, which its design cannot support, but to describe the quality of oral anticoagulation control, expressed as the proportion of INR determinations within range and as the TTR, among patients on chronic warfarin therapy followed at the coagulopathy outpatient clinic of a public referral hematology service in Fortaleza, Ceará, Brazil.

2. Materials and Methods

2.1 Study design

This was a retrospective, single-center, exploratory observational study that combined a retrospective review of longitudinal PT/INR laboratory records with a cross-sectional structured patient interview. It is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement. Because the sample was a small convenience sample without an a priori sample-size calculation, and because there was no internal comparison group, the study is best regarded as exploratory and hypothesis-generating rather than as an analytical cohort study.

2.2 Setting

The study was carried out at the Coagulopathies Outpatient Clinic of the Hematology and Hemotherapy Center of Ceará (HEMOCE), a national referral center for coagulopathies and hemoglobinopathies. Patients followed at this clinic are patients of the Hospital Universitário Walter Cantídio and are seen at weekly, biweekly, or monthly intervals according to clinical status. Data collection, record extraction and interviews, was performed during a two-month window, from August to September 2023; the INR records reviewed for each patient spanned that patient's entire warfarin treatment history, which extended back up to 26 years.

2.3 Participants, inclusion and exclusion criteria

Eligible participants were adults of both sexes, aged 18–74 years, on chronic oral anticoagulation with warfarin and under active follow-up at the Coagulopathies Outpatient Clinic. The indication for anticoagulation and the underlying thrombotic or thromboembolic diagnosis had been confirmed by the responsible physician on the basis of prior imaging (for example, Doppler ultrasonography) and/or laboratory investigation. Indications were clinically heterogeneous, as is typical of a referral coagulopathy service. A single target INR range of 2.0–3.0 was applied for the analysis of anticoagulation control. Patients not under follow-up at the clinic, or with incomplete records, were excluded.

2.4 Source population, sampling, and study size

The Coagulopathies Outpatient Clinic follows approximately 300 patients, of whom 282 were using warfarin. A convenience sample of 34 patients, corresponding to about 12% of the warfarin users, was analyzed; for these 34 patients, 879 PT/INR determinations were available. No formal a priori sample-size or power calculation was performed; the sampling fraction was pragmatic rather than statistically derived. This is acknowledged as a limitation and is the principal reason the study is presented as exploratory.

2.5 Variables and operational definitions

The primary outcomes were the quality-of-control metrics: the proportion of INR determinations within the target range of 2.0–3.0, and the per-patient TTR. Secondary outcomes were the occurrence of thromboembolic events during warfarin therapy and self-reported adherence. Each INR determination was classified as within range (2.0–3.0), below range (<2.0), or above range (>3.0).

2.6 Data sources and measurement

PT/INR results and clinical data were obtained from patients' medical and laboratory records. Thromboembolic events were ascertained from medical-record review, including imaging confirmation, by the responsible physician. A structured questionnaire was additionally administered by the researcher, under the supervision of the collaborating physician, covering sociodemographic data, clinical diagnosis, date and duration of anticoagulant use, dietary habits, and concomitant medications. Adherence was assessed during this interview and was therefore self-reported; it was not corroborated by pill counts or pharmacy-refill data, a limitation addressed below.

2.7 Time in Therapeutic Range

For each patient, TTR was estimated as the percentage of INR determinations that fell within the target range of 2.0–3.0, a measurement-based estimate obtained by the proportion-of-determinations method. This approach was adopted because the available records comprised discrete INR measurements without the inter-visit interpolation required by the Rosendaal linear-interpolation method [4], which is the international reference standard. The Rosendaal method was not used. Because the measurement-based estimate does not weight the time elapsed between successive determinations, the resulting values may differ from interpolation-based TTR; this limits direct comparability with studies that used the Rosendaal method and is acknowledged as a limitation.

2.8 Bias

Several sources of bias were anticipated. Because only patients still under active follow-up and still receiving warfarin were sampled, the study is susceptible to selection and survivor bias, which tends to over-represent patients who tolerated and remained stable on warfarin. The retrospective ascertainment of events over long and heterogeneous treatment periods introduces the potential for immortal-time bias when interpreting the absence of on-treatment events. Self-reported adherence is subject to recall and social-desirability bias. These issues are considered in the Discussion and Limitations.

2.9 Statistical analysis

Data was tabulated in Microsoft Excel® and analyzed in GraphPad Prism 8.0. Continuous variables are summarized as means or as medians with interquartile ranges, and categorical variables as counts and percentages. The distribution of INR determinations across the three predefined categories (within, below, and above range) is presented descriptively; because these categories are mutually exclusive subsets defined a priori by INR thresholds, no inferential comparison between them was performed, as such a

comparison would be tautological. Descriptive analysis was considered appropriate to the exploratory objectives of the study.

3. Results

3.1 Anticoagulation control

For the 34 patients analyzed, 879 PT/INR determinations were available. The duration of warfarin therapy ranged from 1 to 26 years (mean, 9.5 years). Of the 879 determinations, 456 (51.9%) were within the target range of 2.0–3.0, 295 (33.6%) were below 2.0, and 128 (14.6%) were above 3.0; thus 423 determinations (48.1%) fell outside the target range (Table 1). The wide spread of values below and above the range reflects the well-recognized intra- and inter-individual variability of warfarin response.

Table 1. Quality of warfarin anticoagulation control (INR determinations and TTR).

Parameter	Value
Patients analyzed, n	34
PT/INR determinations, n	879
Duration of warfarin therapy (years), range	1–26
Mean duration of warfarin therapy (years)	9.5
INR determinations within target range (2.0–3.0), n (%)	456 (51.9)
INR determinations below range (<2.0), n (%)	295 (33.6)
INR determinations above range (>3.0), n (%)	128 (14.6)
INR determinations outside target range, n (%)	423 (48.1)
Patients with TTR >60% (adequate control), n (%)	12 (35.3)
Patients with TTR ≤60% (suboptimal control), n (%)	22 (64.7)

PT, prothrombin time; INR, International Normalized Ratio; TTR, Time in Therapeutic Range (measurement-based estimate). Percentages for INR determinations are calculated over 879 determinations; percentages for TTR categories are calculated over 34 patients.

3.2 Time in Therapeutic Range

Twelve of the 34 patients (35.3%), approximately one-third, achieved a TTR above 60%, whereas the remaining 22 patients (64.7%) had a TTR of 60% or below. At the population level, therefore, anticoagulation control was predominantly suboptimal, with the majority of patients below the 60% threshold. The distribution of patients across TTR bands is shown in Figure 1.

3.3 Thromboembolic events

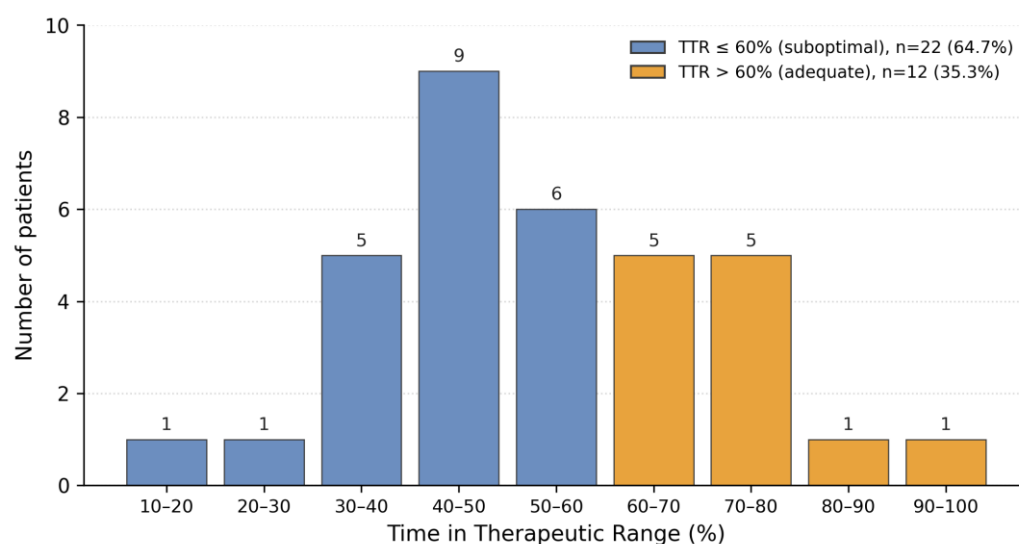
No thromboembolic events were recorded in any of the 34 patients during warfarin therapy within the observation period. According to medical-record review, five patients (14.7%) had experienced thromboembolic events during earlier anticoagulant therapy, before warfarin was started. As discussed below, the absence of on-treatment events must be interpreted cautiously in light of the sampling strategy and the small sample size, and does not by itself indicate therapeutic effectiveness.

3.4 Self-reported adherence

Of the 34 patients, 28 (82.4%) reported difficulties with adherence during the interview, attributing these to regimen complexity, dietary restrictions, financial constraints,

and drug interactions. Because adherence was self-reported and not corroborated by objective measures, these figures should be interpreted as indicative rather than definitive.

Figure 1. Distribution of patients according to Time in Therapeutic Range (TTR; measurement-based estimate). Bars show the number of patients within each 10% TTR band (n = 34). Patients with a TTR of 60% or below (blue) were classified as having suboptimal control and represented the majority of the sample (22/34; 64.7%); those with a TTR above 60% (orange) represented 12/34 (35.3%).



4. Discussion

The principal finding of this exploratory study is that the quality of warfarin anticoagulation control in this public referral service was predominantly suboptimal: approximately half of all INR determinations fell within the target range, and approximately one-third of patients achieved a TTR above 60%. This pattern is inconsistent with a narrative of therapeutic effectiveness and instead identifies anticoagulation quality as the key target for improvement.

These results align closely with contemporary real-world data. In a 2025 retrospective study of a primary-care warfarin clinic, the mean TTR was only 46.7% and just 30.1% of patients reached a TTR above 60% [7], figures very similar to our own and obtained in a well-resourced setting, which suggests that suboptimal control is a pervasive challenge of vitamin K antagonist therapy rather than a phenomenon confined to low-resource services. Randomized and observational data consistently show that clinical benefit depends on the quality of control, with better outcomes at higher TTR and more thromboembolic and hemorrhagic events when TTR falls below 60–65% [2–4]. Our finding that most patients did not reach a TTR of 60% therefore signals a meaningful gap between the intended and the achieved intensity of anticoagulation.

Maintaining a therapeutic INR is intrinsically difficult with warfarin. The drug has a narrow therapeutic index and a dose–response modulated by pharmacogenetic variation, dietary vitamin K intake, intercurrent illness, and numerous drug–drug interactions [1]. In a population reporting frequent adherence difficulties together with dietary and financial constraints, these factors compound one another and make stable control hard to sustain, as reflected in the high proportion of out-of-range determinations. Frequent, structured INR monitoring is the main tool available to counteract this variability: closer monitoring allows earlier dose adjustment, shortens the time spent out of range, and, when embedded in a systematic service, has been shown to improve TTR.

These considerations are particularly salient for the Brazilian public health system. Warfarin will remain a first-line agent in many SUS services because of its low acquisi-

tion cost and wide availability relative to DOACs; however, the true cost of warfarin includes the resources required for safe monitoring and the clinical cost of poor control. Socioeconomic factors, limited health literacy, transport and appointment barriers, food insecurity affecting dietary vitamin K intake, and the cost of concomitant medications, directly undermine adherence and INR stability in this population and are unlikely to be resolved by pharmacological measures alone.

The evidence therefore supports investment in structured, multidisciplinary anticoagulation management. Pharmacist-led anticoagulation services have improved control even in resource-constrained settings; in a 2024 quasi-experimental study at a tertiary hospital in Ethiopia, a pharmacist-led service was associated with better anticoagulation quality than usual medical care [6], illustrating a model directly transferable to the SUS. Dedicated anticoagulation clinics, point-of-care INR testing, and structured patient education are complementary components. For selected patients with persistently poor control despite such measures, and where clinically appropriate, transition to a DOAC may be considered, recognizing that DOACs are not suitable for all indications, vitamin K antagonists remain preferred for mechanical heart valves and for thrombotic antiphospholipid syndrome, and evidence in advanced kidney disease is still evolving [5].

The absence of on-treatment thromboembolic events in our sample should be interpreted with considerable caution and does not, by itself, demonstrate effectiveness. The sample was small; patients were included only if they remained under active follow-up and still on warfarin, which favors the inclusion of “survivors” who tolerated and responded to therapy; and the retrospective ascertainment over long, heterogeneous periods is prone to immortal-time bias. With few expected events and no comparison group, the study is not designed to detect differences in clinical outcomes, and the emphasis of interpretation should remain on the quality-of-control metrics.

At the level of public policy, these results argue for routine, service-level auditing of anticoagulation quality (for example, periodic TTR monitoring as a performance indicator) and for equitable protocols that match anticoagulant choice and monitoring intensity to patient needs across the network of specialized outpatient clinics.

5. Limitations

This study has important limitations. First, the small convenience sample ($n = 34$), selected without a priori power calculation, limits precision and external validity and exposes the analysis to type II error; the study should be read as exploratory and hypothesis-generating. Second, selection and survivor bias, together with the potential for immortal-time bias, constrain any inference about clinical effectiveness. Third, treatment durations were long and heterogeneous (1–26 years), and data were extracted within a two-month cross-sectional window. Fourth, TTR was estimated by the measurement-based proportion-of-determinations method rather than by the Rosendaal linear-interpolation method, limiting direct comparability with some international studies.

Fifth, a single target INR range of 2.0–3.0 was applied to all patients, whereas some indications (for example, mechanical heart valves) may warrant different target ranges; if the sample included such indications, the in-range and TTR estimates could be affected. Sixth, adherence was self-reported and uncorroborated by objective measures. Seventh, detailed baseline clinical and demographic characterization of the sample was not available for reporting, which limits assessment of generalizability; future studies should include a full baseline characteristics table. These limitations should be addressed through larger, adequately powered, and ideally multicenter studies with prospectively defined outcomes and appropriate comparison groups.

6. Conclusion

In this small, single-center, exploratory sample of patients on chronic warfarin therapy within the Brazilian public health system, the quality of anticoagulation control was predominantly suboptimal: approximately half of INR determinations were within

the target range, and approximately one-third of patients achieved a TTR above 60%. The absence of on-treatment thromboembolic events cannot, given the design and the potential for selection and survivor bias, be interpreted as evidence of therapeutic effectiveness. Rather, the findings highlight a clear opportunity to improve warfarin control through more structured and multidisciplinary anticoagulation care, including closer INR monitoring, adherence support, and, where appropriate, reassessment of anticoagulant choice. Larger, adequately powered, and comparative studies are needed to confirm these observations and to guide service-level improvement.

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Research Ethics Committee Approval: The study was approved by the Research Ethics Committee (CEP) of the Hospital Universitário Walter Cantídio and of the Fametro University Center (UNI-FAMETRO) under approval No. 5.769.727, in accordance with Resolution No. 466/2012 of the Brazilian National Health Council, which safeguards the confidentiality, privacy, and dignity of participants. Because the study included structured interviews with patients, written informed consent was obtained from each participant, and a data-custodian agreement was signed by the responsible depositary.

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Supplementary Materials: None.

References

1. 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-e88S. doi: 10.1378/chest.11-2292.
2. Szummer K, Gasparini A, Eliasson S, Ärnlov J, Qureshi AR, Bárány P, Evans M, Friberg L, Carrero JJ. Time in therapeutic range and outcomes after warfarin initiation in newly diagnosed atrial fibrillation patients with renal dysfunction. *J Am Heart Assoc*. 2017;6(3):e004925. doi: 10.1161/JAHA.116.004925.
3. White HD, Gruber L, Cannon CP, Sabatine MS. Comparison of outcomes among patients randomized to warfarin therapy according to anticoagulant control: results from SPORTIF III and V. *Arch Intern Med*. 2007;167(3):239-245. doi: 10.1001/archinte.167.3.239.
4. Rosendaal FR, Cannegieter SC, van der Meer FJM, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost*. 1993;69(3):236-239.
5. Hsu CC, Chen CC, Chou CY, Chen KH, Wang SF, Chang SL, Chang YL. Effectiveness and safety of direct oral anticoagulants versus warfarin in patients with atrial fibrillation and advanced kidney disease. *J Thromb Thrombolysis*. 2023;56(4):518-528. doi: 10.1007/s11239-023-02859-x.
6. Tadesse TA, Gebremedhin A, Yadeta D, Chelkeba L, Fenta TG. Comparison of anticoagulation control and outcomes between usual medical care and pharmacist-led anticoagulation service in ambulatory patients taking warfarin at a tertiary hospital in Ethiopia: a quasi-experimental study. *J Pharm Health Care Sci*. 2024;10(1):32. doi: 10.1186/s40780-024-00355-9.
7. Viswanathan D, Sivanandam A, De Silva P. Assessment of Time in Therapeutic Range (TTR) in a primary care warfarin clinic. *Cureus*. 2025;17(6):e85653. doi: 10.7759/cureus.85653.