Discrepancy Among Self-Reported Adherence, Prescription Refills, and Actual Anticoagulant Control

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ABSTRACT

Background: Patients must adhere to their prescribed warfarin regimens and regularly monitor the anticoagulation effect to maintain therapeutic levels. The ability to evaluate regimen adherence accurately is crucial to the success of patient coaching. However, prevention of thromboembolic events is challenging when the association between medication adherence and the actual amount of anticoagulant agent taken cannot be determined.

Purpose: This study used self-reported medication taken and prescription refills to (a) verify warfarin medication adherence and (b) assist clinicians to determine the discrepancy between medication adherence and anticoagulant control efficacy.

Methods: This study was conducted at a national-university-affiliated hospital in Yilan County, Taiwan. Structured questionnaires and medical record reviews were adopted. A 100-point visual analog scale was used to measure the reported adherence of participants, whereas medication refill adherence was compared against self-reported adherence. Finally, degree of adherence was evaluated based on time in therapeutic range.

Results: This study included 192 participants. Half (n = 94, 49%) were women, and the mean age was 69.6 years. Mean scores were 92.2% for the visual analog scale and 87.3% for medication refill adherence. Medication adherence correlated significantly with age, as reflected in the visual analog scale scores (p < .05). The participants who were receiving polypharmacy with five types of medicines or less attained higher visual analog scale scores, whereas participants who were on warfarin for 2–12 months exhibited higher medication refill adherence. Time in therapeutic range correlated negatively with age, although stability improved with therapy duration.

Conclusions/Implications for Practice: Despite their high self-reported adherence levels, patients of advanced age require careful monitoring of their time in therapeutic range. The participants in this study who were on warfarin for a relatively longer time exhibited higher stability in the therapeutic range, despite their low medication refill adherence. The results of this study suggest that patient age, duration of warfarin therapy, and polypharmacy are factors associated with medication adherence. The findings may facilitate future assessments of warfarin adherence in patients as well as the implementation of more effective clinical nursing procedures and management practices.

Key Words: warfarin, adherence, polypharmacy.

Introduction

Nearly 610,000 new cases of cerebrovascular accidents and 180,000 cases of relapse are diagnosed annually in the United States (Lusardi, Jorge, & Nielsen, 2013), with one new cerebrovascular accident case diagnosed every 40 seconds and one stroke-related death occurring every 4 minutes on average (Benjamin et al., 2017). In Taiwan, cerebrovascular disease ranks as the second to fourth leading cause of death annually, taking away more than 10,000 precious lives every year (Ministry of Health and Welfare, Taiwan, ROC, 2019). Warfarin, an oral anticoagulant used mainly in the treatment and prevention of thromboembolism, is a vital medicine that cerebrovascular patients must take on a daily basis. However, in view of the difficulties in monitoring adherence to medication regimens and the extremely narrow therapeutic window of warfarin, medication adherence significantly influences the prognosis of these patients (Auyeung et al., 2016; Oterhals et al., 2014).

Medication adherence refers to the degree to which a patient takes medicine in accordance with the prescribed amounts and frequencies. Compliance and persistence constitute the two major concepts of medication adherence, with compliance referring to the intensity of medicine use during therapy and persistence referring to the overall duration of medicine use over the course of therapy (Zeber et al., 2013). Previous studies have employed various means to measure warfarin adherence, including objective methods such as medication event monitoring systems, the Millon Behavioral Medicine Diagnostic, and medication refill adherence (MRA) as well as subjective methods such as questionnaires, interviews, self-reports, and the visual analog scale (VAS). The findings of these prior studies indicate that, although patients tend

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to self-report high rates of adherence, objective assessment methods indicate otherwise, because of the presence of significant gaps in the time in therapeutic range (TTR; Cruess et al., 2010; Mayet, 2016; Wang, Kong, & Ko, 2013). Studies that have used electronic Medication Event Monitoring System medication bottle caps indicate that 36% of patients taking warfarin missed more than 20% of their doses, resulting in an international normalized ratio (INR) that did not reach the therapeutic condition (Kimmel et al., 2007). Thus, a deeper understanding of actual medication adherence is necessary.

Adherence may be measured using direct and/or indirect methods, each of which presents unique strengths and weaknesses. Direct methods obtain biological markers using direct observation, and although more accurate and objective than indirect methods, these methods are costly and may be affected by the “white-coat adherence” bias. By contrast, indirect methods, including self-reporting and pharmacy refill tracking, typically cost less to implement and provide quantitative medication-adherence data (McRae-Clark et al., 2015). Most related studies have used subjective self-reporting to monitor adherence as well as associated interviews and scales to examine the frequencies at which patients omit or increase their prescribed dosages (Cruess et al., 2010; Van Damme, Van Deyk, Budts, Verhamme, & Moons, 2011). In terms of objective measurements, previous studies have primarily used refill data, assessments of clinical responses, and biological markers as indicators of adherence (Wang et al., 2013; Yahaya, Hassali, Awaisu, & Shafie, 2009).

Albert (2008) showed that nonadherence is high among cardiovascular patients, particularly in terms of taking medications (31%–58%) and attending follow-up appointments (16%–84%). Subjective measurement methods tend to overestimate adherence, whereas objective measurement methods such as INR and TTR tend to show that patients fail to reach the therapeutic range (Marcatto et al., 2016; Van Damme et al., 2011). Yahaya et al. (2009) stated that, although reviews of medical records indicated that all patients adhered to clinical appointment schedules, the objectively observed MRA showed no correlation with the therapeutic range.

Numerous studies have verified that degrees of objectively and subjectively reported adherence, regardless of how high they are, do not adhere to the therapeutic range nor do reported adherence rates accurately correspond to TTR (Parker et al., 2007; Van Damme et al., 2011; Yahaya et al., 2009). Medication adherence and the prescribing behaviors of physicians affect the therapeutic range of warfarin (Kääriäinen, Paukama, & Kyngäs, 2013; Parker et al., 2007). However, identifying a method to accurately measure patient adherence has the potential to improve the safety and effectiveness of warfarin therapy.

The purpose of this study was twofold: (a) to verify warfarin adherence and use the mean therapeutic INR ratio range (i.e., TTR) as the ultimate indicator of medication adherence and (b) to assist clinicians to understand the factors associated with the effective attainment of the therapeutic range.

### Methods

#### Design, Sampling, and Setting

A cross-sectional design and purposive sampling method were adopted. From July 29, 2013, to July 28, 2014, patients who were taking warfarin and who met the inclusion criteria were recruited for inclusion as participants in this study. The researchers followed up with participants at the outpatient clinics, including cardiology, cardiovascular surgery, neurology, and general medicine, of a national-university-affiliated hospital in Yilan County, Taiwan. Inclusion criteria were as follows: (a) ≥ 20 years old, (b) receiving warfarin therapy with regular clinical follow-up, (c) mentally clear and free of mental disorders, and (d) able to communicate in either Mandarin or Taiwanese. Exclusion criteria included (a) death or loss to follow-up during the study, (b) refusal to participate, (c) receiving warfarin therapy for less than 1 month or having had only one INR reading, and (d) cessation of warfarin use after completion of therapy.

#### Instruments

This study reviewed medical records to collect the clinical characteristic and relevant laboratory data of the participants. The clinical characteristic data included indications, duration of warfarin therapy, weekly dosage of warfarin, comorbidities, and polypharmacy. The multifaceted method combines two or more measurement methods (Fatkullina, Morozkina, Suleimanova, & Khayrullina, 2016; Wu, Tsauo, Lin, Chang, & Lee, 2011). In this study, the 100-point VAS was used to assess self-reported medication adherence for warfarin. Demographic information, including age, gender, education, employment status, marital status, and smoking and drinking habits, was also collected. The time required to fill out the questionnaire was approximately 15 minutes.

#### Medication refill adherence

The participants were all required as patients to refill their prescriptions on a regular basis. Refill data were obtained from the outpatient information system and were compared with the physician-prescribed refill schedule (Gazmararian et al., 2006). The estimated annual average MRA was calculated using the following equation (Bieszk, Patel, Heaberlin, Wlasuk, & Zarowit, 2003):

\[
\text{MRA} \% = \frac{1 – \left( \frac{\text{days between refills} \times \text{days of medicine supply}}{\text{days between refills}} \right)}{100}
\]

The maximum value was 100%, with values below 80% indicating “low adherence.”

#### Medication adherence

The VAS was employed to measure the warfarin adherence of the participants. The range of the VAS was set to 0% (non-adherence) to 100% (absolute adherence), and test–retest reliability was .63 (p < .01), denoting nonadherence (0%) to absolute adherence (100%; Kalichman et al., 2005). The
scale was completed by participants based on their subjective perceptions, with scores less than 80% indicating low adherence (Gallagher, Muntner, Moise, Lin, & Kronish, 2015).

**Time in therapeutic range**
The INR was measured using an automated blood coagulation analyzer (Sysmex CA-1500, Japan). This reading is a calculation made to standardize prothrombin time (PT) and is presented as the ratio of a patient’s PT to the normal mean PT. INR was the measurement used during warfarin treatment to monitor the therapeutic range. TTR is defined as the duration of time during which the patient’s INR values were within the range of 2.0–3.0. TTR was calculated (Chan et al., 2016; Connolly et al., 2008) using the following equation:

\[
TTR \% = \frac{\text{Number of INR measurements within therapeutic range}}{\text{Total number of INR measurements}} \times 100
\]

A value of ≥ 58% indicates adherence, with values below 58% indicating nonadherence.

**Ethical Issues**
The researchers and advising professor for this study had completed instructional workshops that were hosted by the hospital’s institutional review board, and approval was obtained from the national-university-affiliated hospital (Serial Number RD2013-024). The autonomy of all the participants was maintained, and their privacy was protected throughout the data collection process. The participants and their families were informed of the study purpose and of their right to terminate or withdraw from the study at any time without jeopardizing their medical rights. Written, informed consent was obtained before participation. The personal information of each participant was anonymized using a numeric code to ensure anonymity, and all of the files remained confidential. Furthermore, all of the written materials were maintained in a locked and secure location.

**Data Analysis**
The collected information was coded and filed using SPSS software Version 22.0 (IBM, Inc., Armonk, NY, USA). Categorical variables were presented in the form of percentages and frequency, and continuous variables were presented in terms of mean, standard deviation, maximum, and minimum. The continuous variables were compared using the Student’s t test, and the categorical variables were compared using the chi-square test. Post hoc comparisons were used in addition to overall analysis of variance. Pearson and Spearman correlations were used to detect between-groups correlations. All of the tests were two-tailed, and the results were considered statistically significant when \( p < .05 \).

**Results**

**Sample Characteristics**
The sampling procedure is depicted in Figure 1. Four hundred sixty-eight participants were recruited and enrolled, and the data from 192 completed questionnaires were included in the analysis. The average age of the participants was 69.6 years (range = 34–91 years, SD = 12.6). The common indication for warfarin was atrial fibrillation (56.8%). Most participants reported a warfarin therapy duration of more than 1 year (75.6%), and the average therapy duration was 50 months (range = 1–492 months, SD = 60.5). Most had a prescribed warfarin dosage of less than 21 mg per week (65.1%), and the average dose was 21.7 mg (range = 5–87.5 mg, SD = 11.1). The participants had an average of 1.8 comorbidities (range = 0–5, SD = 1.0), with heart disease (54.2%) and hypertension (53.6%) being the two most common. Table 1 shows the demographic and clinical characteristics of the participants. An average of 6.2 medications (range = 1–15, SD = 3.0) were observed among the participants receiving polypharmacy, with up to 59.4% of these prescribed more than six medications, most of which (18.8%) were for treating other conditions and diseases (e.g., high cholesterol).

**Medication Adherence Measurement**
In terms of self-reported medication adherence, the mean VAS score was 92.2% (range = 30%–100%, SD = 12.5), and 91.1% of the participants were identified as “adherent” (> 80%). In terms of the objective methods, the mean MRA was 87.3% (range = 33%–100%, SD = 13.8%), and 79.2% of the participants were identified as adherent (above 80%). A comparison of the self-report and objective medication adherence measurements showed a positive correlation between the MRA and the VAS (\( r_s = .117, p < .05 \)).

In terms of the relationship between age and self-reported results, age was found to be positively correlated with medication adherence in the VAS (\( r = .183, p < .05 \)). The duration of warfarin therapy was significantly related to MRA,

![Figure 1](image-url)

**Figure 1.** Flowchart of sampling procedures. INR = international normalized ratio.
TABLE 1. 
**Demographic and Clinical Characteristics (N = 192)**

| Characteristic                          | n   | %    |
|-----------------------------------------|-----|------|
| Age (years; M and SD)                   |     |      |
| ≤ 65                                    | 69  | 12.6 |
| 66–75                                   | 69  | 35.9 |
| > 75                                    | 52  | 27.1 |
| Gender                                  |     |      |
| Male                                    | 98  | 51.0 |
| Female                                  | 94  | 49.0 |
| Educational level                       |     |      |
| Middle school or less                   | 122 | 63.6 |
| High school                             | 49  | 25.5 |
| College or more                         | 21  | 10.9 |
| Employment status                       |     |      |
| Unemployed                              | 83  | 43.2 |
| Employed                                | 32  | 16.7 |
| Retired                                 | 77  | 40.1 |
| Marital status                          |     |      |
| Married                                 | 153 | 79.7 |
| Othera                                  | 39  | 20.3 |
| Smoking status                          |     |      |
| Previous or current smoker              | 62  | 32.3 |
| Nonsmoker                               | 130 | 67.7 |
| Drinking status                         |     |      |
| Previous or current drinker             | 51  | 26.6 |
| Nondrinker                              | 141 | 73.4 |
| Number of indications                   |     |      |
| 1                                       | 164 | 85.4 |
| > 1                                     | 28  | 14.6 |
| Duration of warfarin therapy (months; M and SD) |     |      |
| 2–12                                    | 125 | 65.1 |
| 13–48                                   | 63  | 32.9 |
| > 48                                    | 75  | 39.1 |
| Dosage of warfarin per week (mg; M and SD) |     |      |
| ≤ 21.0                                  | 62  | 32.3 |
| 21.1–35.0                              | 125 | 65.1 |
| > 35.0                                  | 77  | 40.1 |
| Comorbidities (M and SD)                |     |      |
| Hypertension                            | 104 | 54.2 |
| Intracerebral disease                   | 51  | 26.6 |
| Heart disease                           | 104 | 54.2 |
| Renal failure                           | 42  | 21.9 |
| Liver disease                           | 19  | 9.9  |
| Thrombocytopenia                        | 3   | 1.6  |
| Cancer                                  | 8   | 4.2  |
| Thyroid disease                         | 11  | 5.7  |
| Polypharmacy (M and SD)                 |     |      |
| Antiplatelet                            | 18  | 9.4  |
| Antibiotics/antifungus                  | 2   | 1.0  |
| Antacid                                 | 19  | 9.9  |
| Antiarrhythmia                          | 21  | 10.9 |
| Othersb                                 | 36  | 18.8 |

aWidowed, single, or divorced. bAtrial fibrillation, valvular replacement, venous thromboembolism, and “other,” which include artery embolism, postmyocardial with stent placement, intracerebral embolism, and unknown cause. cMultiple choice. dNumber of treatments. eAntilipidemic agents.

Related to the VAS, F(189) = 3.41, p = .04, and polypharmacy was significantly related to the VAS, F(189) = 3.77, p = .03. The post hoc analysis revealed that the participants receiving ≤ 5 and 6–10 medications had higher VAS scores in their self-reports than those receiving ≥ 11 medications. Participants on warfarin for 2–12 months had a higher MRA than those on warfarin for ≥ 13 months. Participants with either atrial fibrillation or valvular replacements had higher MRA than others, F(190) = −0.231 and 0.672, p = .04 and .03, respectively. MRA decreased as therapy duration increased (r = −.240, p < .01). The related results are listed in Table 2.

**Relationship Between Medication Adherence and Time in Therapeutic Range**

This study found a mean TTR of 28.91% (range = 0%–100%, SD = 22.18%), with only 2.1% of the participants identified as adherent (above 58%). Moreover, TTR decreased with age (r = −.150, p < .05). In addition, the duration of therapy was found to significantly relate to TTR, F(189) = 3.10, p = .05. The post hoc analysis revealed that the participants on warfarin for 2–12 months had a lower TTR than those on warfarin for > 48 months. The demographic and clinical characteristics by TTR are shown in Table 3. Furthermore, the data showed that 41.1% of the participants obtained three INR readings in the range of 2–3.5 and the stability of TTR improved as the therapy duration increased (r = .146, p < .05). The age, therapy duration, and VAS of participants were found to be significantly associated with the stability of TTR. Regarding the indications for warfarin, this study found that the participants with a valvular replacement or other indications had a higher TTR than others, F(190) = −1.757 and 0.931, p = .01 and .02, respectively.

Although most participants exhibited high adherence in either their self-reports or the MRA (range = 55.7%–81.8%), fewer than 10% of the participants (range = 6.8%–9.4%) obtained favorable TTR values. The relationship between adherence and TTR is shown in Table 4.

**Discussion**

**Major Findings**

The major findings of this study are as follows: (a) A significant discrepancy exists between both self-reported adherence and prescription refills and actual medication taken in conjunction with warfarin therapy, and (b) medication adherence is influenced by age, duration of therapy, and polypharmacy. Because of the very narrow therapeutic window of warfarin, which easily induces serious complications when adherence is low, considerable research attention has been focused on the warfarin adherence of patients.

**Adherence Measures of Patients on Warfarin: Comparison With Previous Studies**

Several studies in the literature have compared the influence of subjective adherence measures on objective adherence...
measures in samples of patients with different characteristics. The VAS score of 92.2% in this study is similar to the 91.9% reported by Wang et al. (2013), with both VAS scores indicating high adherence. Furthermore, age was found in both studies to correlate positively and significantly with the adherence rates indicated by the VAS ($p < .05$). Although some participants in this study admitted that they occasionally forgot to take their medicine, they insisted that their adherence was high (90% or even 100%), signifying the possibility of overestimated subjective adherence. The MRA of 87.3% in this study is similar to the 93.6% reported by Wang et al., with both scores indicating high adherence.

The Clinical Characteristics Associated With Medication Refill in Time in Therapeutic Range

This study found a negative correlation between age and TTR, which contrasts with the findings of Pamboukian et al. (2008) and Platt et al. (2008). A possible reason is that the participants in this study were older than those in these two other studies, suggesting that most of the participants in this study required the assistance of family members to collect prescription refills. This situation is further complicated by the relative convenience for Taiwanese patients to seek medical attention from popular physicians. However, the overburdening of physicians has been shown to lower the refill rates of patients because of extremely long wait times at the clinic. The participants who had received warfarin for 2–12 months exhibited significantly higher MRA than those who had received warfarin for longer durations ($p < .05$). This indicates the necessity of strengthening instructions for patients who receive this therapy for more than 1 year to maintain their effective control of the disease and to prevent relapse, which may affect the perceived confidence of patients in their treatment and thus further discourage adherence. In addition, this study found that the participants on warfarin for 2–12 months had lower TTR than those on warfarin for > 48 months, indicating that the TTR of warfarin stabilizes over time, which confirms the findings of Kääriäinen et al. (2013).

| TABLE 2. Medication Adherence Measurement Results (N = 192) |
|---------------------------------------------------------------|
| Characteristic | Self-Reported Medication Adherence | Objective Medication Adherence |
|                | VAS | M (%) | SD | F/t | p | M (%) | SD | F/t | p |
| Age (years)    |     |       |    |     |   |       |    |     |   |
| ≤ 65           |     | 90.58 | 11.74 | 0.98 | .38 | 88.28 | 11.48 | 0.29 | .75 |
| 66–75          |     | 93.46 | 10.64 |     |   | 86.88 | 16.36 |     |   |
| > 75           |     | 92.96 | 14.82 |     |   | 86.59 | 14.04 |     |   |
| Smoking status |     |       |    |     |   |       |    |     |   |
| Previous or current smoker |     | 90.32 | 13.79 | −1.48 | .14 | 87.76 | 12.02 | −0.33 | .74 |
| Nonsmoker      |     | 93.15 | 11.75 |     |   | 87.05 | 14.65 |     |   |
| Drinking status|     |       |    |     |   |       |    |     |   |
| Previous or current drinker |     | 88.63 | 13.12 | −2.44 | .02* | 88.96 | 9.63 | 1.24 | .22 |
| Nondrinker     |     | 93.55 | 12.02 |     |   | 86.67 | 15.04 |     |   |
| Number of indications* |     |       |    |     |   |       |    |     |   |
| 1              |     | 92.01 | 13.02 | −0.61 | .54 | 87.00 | 14.25 | −0.67 | .51 |
| > 1            |     | 93.57 | 8.70  |     |   | 88.89 | 11.10 |     |   |
| Duration of warfarin therapy (months) |     |       |    |     |   |       |    |     |   |
| ① 2–12        |     | 92.55 | 11.51 | 0.58 | .56 | 91.77 | 10.89 | 3.41 | .04* |
| ② 13–48       |     | 93.20 | 12.86 |     |   | 86.13 | 12.87 |     |   |
| ③ > 48        |     | 91.00 | 12.76 |     |   | 85.49 | 15.94 |     |   |
| Post hoc       |     |       |    |     |   |       |    |     |   |
| Polypharmacy   |     |       |    |     |   |       |    |     |   |
| ① ≤ 5         |     | 92.44 | 11.19 | 3.77 | .03* | 87.04 | 13.23 | 0.67 | .52 |
| ② 6–10        |     | 93.33 | 11.95 |     |   | 86.87 | 14.08 |     |   |
| ③ ≥ 11        |     | 84.00 | 18.82 |     |   | 91.20 | 15.43 |     |   |
| Post hoc       |     |       |    |     |   |       |    |     |   |

Note. VAS = visual analog scale; MRA = medication refill adherence.

*Attrial fibrillation, valvular replacement, venous thromboembolism, and “other,” including artery embolism, postmyocardial with stent placement, intracerebral embolism, and unknown cause.

*p < .05.
Factors Associated With Time in Therapeutic Range

In this study, 41.1% of the participants had three INR readings between 2 and 3.5, which is similar to the 49% reported by Kääriäinen et al. (2013). However, the TTR of 28.91% in this study differed from the 64.5% reported by Wang et al. (2013), which may be attributable to the difference in the length of the research period between the two studies. Wang et al. examined the TTR values at 2 weeks and 3 months only, whereas this study examined the TTR values across the entire duration of therapy to explore the persistence of the participants. However, the RE-LY trial, which was conducted by Wallentin et al. (2010) and examined the TTR of participants from 44 countries, found that the TTR in Taiwan to be only 44%, which was lower than any of the other countries examined in that study. Further investigation is required to determine whether this is related to ethnic or cultural factors or to the prescribing behaviors of physicians. According to the TTR results in this study, regular prescription refills do not ensure that medication use remains within the therapeutic window. Further investigation of the relationship between the therapeutic window and the prescribing habits of physicians in different specialties indicated that, of the 192 participants recruited in this study, most (115) were prescribed warfarin by cardiologists. However, significant differences were found among the prescribing behaviors of physicians in different specialties that suggest that physicians tend to be highly conservative and cautious when prescribing warfarin, regardless of their field of specialty. Considering the therapeutic window of warfarin recommended under Japanese guidelines (Okumura et al., 2011), in which the value for patients aged ≥ 70 years was adjusted to be 1.6 – 2.6 because of the risk of intracerebral hemorrhage, the TTR for subjective adherence in this study was also unfavorable (28.91%). This further verifies the extreme caution of Taiwanese physicians regarding the clinical use of warfarin.

In summary, although the participants in this study exhibited high subjective adherence in their self-report and their prescription refill behavior, the TTR was lower than anticipated. In addition, the attitudes of physicians may be the main cause of the contradiction between the actual TTR and the high degree of adherence shown in the VAS and MRA.

Limitations of the Study

To ensure the continuity of the test data among participants, the data in this study were collected from the start of warfarin therapy until the end of the specified period, leading to

| TABLE 3. Demographic and Clinical Characteristics, by Time in Therapeutic Range (N = 192) |
| --- |
| Characteristic | Mean (%) | SD | F | p |
| Age (years) | | | | |
| ≤ 65 | 22.91 | 16.78 | | |
| 66–75 | 18.96 | 15.88 | | |
| > 75 | 16.89 | 14.38 | | |
| Smoking status | | | | |
| Previous or current smoker | 20.85 | 17.19 | | |
| Nonsmoker | 19.02 | 15.15 | | |
| Drinking status | | | | |
| Previous or current drinker | 17.49 | 16.12 | | |
| Nondrinker | 20.83 | 15.69 | | |
| Number of indicationsa | | | | |
| 1 | 0.19 | 0.16 | | |
| > 1 | 0.21 | 0.15 | | |
| Duration of warfarin therapy (months) | 14.94 | 18.44 | | |
| ≤ 5 | 19.67 | 16.57 | | |
| 6–10 | 19.65 | 15.71 | | |
| ≥ 11 | 19.13 | 13.27 | | |
| Polypharmacy | 0.99 | | | |
| ≤ 5 | | | | |
| 6–10 | | | | |
| ≥ 11 | | | | |

aAtrial fibrillation, valvular replacement, venous thromboembolism, and “other,” including artery embolism, postmyocardial with stent placement, intracerebral embolism, and unknown cause.

*p < .05.

| TABLE 4. Relationship Between Medication Adherence and Time in Therapeutic Range |
| --- |
| Medication Adherence | Time in Therapeutic Range |
| | Adherence | Nonadherence | OR | 95% CI | x² | p |
| Visual analog scale | | | | | | |
| Adherence | 18 | 9.4 | 157 | 81.8 | 0.958 | [0.683, 1.376] | 0.34 | 0.56 |
| Nonadherence | 1 | 0.5 | 16 | 8.3 | 1.757 | [0.247, 12.525] | 0.00 | 0.98 |
| Medication refill adherence | | | | | | |
| Adherence | 15 | 7.8 | 137 | 71.3 | 1.003 | [0.786, 1.281] | 0.395 | 2.475 |
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marked differences from the results reported in related studies. Moreover, the self-reported adherence assessment approach relies on memory and may be affected by the reaction of social expectations, which may limit or prevent the ability of researchers to accurately assess truly taken warfarin medication adherence. Adding qualitative interviews to the study may facilitate a better understanding of the gap between self-report and actual medication adherence. Furthermore, as anticoagulation with Vitamin K antagonists has some disadvantages, drug–drug and drug–food interactions require further monitoring, and pharmacogenetic differences may influence effective warfarin therapeutic concentrations in patients. These factors may reduce medication adherence and TTR in patients who take warfarin.

Conclusions
Medication adherence is an important issue for patients who take warfarin. Having simple tools to accurately identify patients’ medication adherence is thus of critical importance for treatment review and monitoring purposes. The VAS and MRA are tools that currently help healthcare professionals assess patient medication adherence quickly. In this study, the refill adherence of the participants was shown to be related to their subjective adherence, although a significant discrepancy was found between reported taken medicine and actual taken medicine. Participants with high objective medication adherence tended to exhibit high refill adherence. Age was found to potentially influence subjective adherence, and TTR was shown to decrease with patient age. In addition, reinforcing patient instructions and implementing long-term monitoring of the therapeutic window are strategies that may be used to achieve better medical adherence in patients with chronic diseases. Future research is needed to explore the major issue of discrepancy among self-reported medication adherence, prescription refills, and actual taken medication in the context of warfarin treatments.

Implications for Practice
The numerous regulations governing the use of medications that have been imposed on medical institutions render it difficult to accurately assess warfarin dosages, as warfarin dosages need to be adjusted frequently. The results of this study show a discrepancy between subjective adherence and TTR. We suggest that warfarin-related outpatient health education be provided and that nurses make related assessments and provide feedback in a manner that is appropriate to the educational level, medication compliance status, and INR data of each patient. Timely referral services (including to professionals such as pharmacists and dieticians) should be introduced to continuously improve patient instructions and communications based on individual patient characteristics. Dedicated nurses may analyze the medication adherence of patients, and the results may serve as a reference for clinicians to prescribe medicine. Furthermore, providing community and homecare services may give patients on warfarin treatments additional stability and support. Using information technology to provide effective medication reminders and monitoring is expected to be the next step in this field.

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Author Contributions
Conclusions
Study conception and design: All authors
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