Abstract

- **Objective:** To present an overview of factors that impact warfarin adherence.
- **Methods:** Review of the literature.
- **Results:** Warfarin is an anticoagulant medication commonly prescribed to prevent blood clots and thus reduce risk of stroke and venous thromboembolism. Although warfarin is highly effective in clinical trials, outcomes are optimized if patients are adherent and remain within a very narrow therapeutic range. This clinical review highlights some of the main factors that impact adherence to warfarin. Specifically, we identify a number of psychosocial factors that may act as potential barriers to warfarin adherence and discuss ways to modify these factors.
- **Conclusion:** There are a number of factors that impact whether or not patients are adherent to warfarin therapy. Identifying these factors can lead to the development of interventions to enhance adherence and perhaps promote improved health outcomes.

Warfarin is an oral anticoagulant commonly prescribed to prevent clotting among patients at risk for stroke or venous thromboembolic events (VTE). Warfarin has a narrow therapeutic range, with a target international normalized ratio (INR) of 2.0 to 3.0 for nonvalvular atrial fibrillation [1,2]. Underanticoagulation on warfarin can lead to increased risk of stroke or recurrent VTE, whereas overanticoagulation on warfarin can lead to adverse events such as excessive bleeding and potentially fatal hemorrhage [3–7]. It is paramount to understand the wide range of factors underlying effective warfarin therapy to help prevent adverse health outcomes.

Among patients with atrial fibrillation who are on warfarin therapy, nonadherence rates are estimated between 10% and 26% [8]. Warfarin nonadherence is a significant cause of out-of-range INRs. For example, in a recent study on the effects of warfarin nonadherence, poorer adherence was significantly associated with underanticoagulation [9]. This study found that for each 10% increase in nonadherence (as measured by missed pill bottle openings), there was a 14% increase in the odds of underanticoagulation and a 10% increase in the odds of out-of-range INR. This association existed independent of many key demographic factors, such as age, race, employment status, gender, marital status, and insurance. In addition, this association was independent of important clinical characteristics, such as body mass index, weekly alcohol intake, smoking status, and medical history (eg, abnormal clotting, cancer, peptic ulcer disease, pulmonary embolism). Thus, it is important for physicians to monitor the many factors that might impact adherence among patients on warfarin therapy.

Factors Associated with Warfarin Nonadherence

Investigations into medication management have tended to focus heavily on clinical factors and medical history. However, demographic (eg, age, race, education), psychosocial (eg, mental health and cognitive functioning), and health care utilization factors (eg, insurance, patient-provider relationship) are increasingly viewed as important and have begun to be more widely investigated.

Poor adherence has been linked to psychosocial factors among diverse medical patient populations. For example, higher depressive symptoms [10,11], greater pessimism versus optimism [12–14], and perceived lack of social support [15] have been found to be associated with medication nonadherence and, therefore, may play an important role in warfarin adherence. Many psychosocial associations are thought to arise from the difficulty patients with psychological distress have in processing and remembering medication recommendations; these patients also tend to have low self-efficacy and are at increased risk for motivational impingements [16,17]. The relationship between perceived social support and adherence may also be a key factor to examine because social support can buffer, or exacerbate, negative psychological factors [18].

Only a limited number of studies have looked directly at
risk factors related to warfarin nonadherence. A recent study by our research team investigated a number of key factors and found that poorer adherence to warfarin was related to higher education level (education beyond high school), lower levels of mental health functioning (as measured by the Medical Outcome Study Short Form-36), and poor cognitive functioning (as measured by the Cognitive Capacity Screening Examination) [19]. In addition, unemployed and retired individuals had greater adherence to their medication regimens than currently employed individuals.

Another study provided additional insight into the factors predictive of nonadherence in a low-income outpatient population on warfarin therapy [20]. In this study, perceived barriers, marital status, living arrangements, and drug regimen played significant roles in nonadherence. More specifically, the researchers found that nonadherence decreased as perceived benefits of warfarin therapy increased (eg, warfarin improves my quality of life; warfarin makes one feel healthier) and perceived barriers of warfarin therapy decreased (eg, I have too many pills to take; it is too hard to remember to take pills). In addition, lower refill adherence was associated with being divorced or never married. Unstable living conditions (eg, living in a shelter; living with friends) and taking warfarin on an alternating schedule was also associated with nonadherence.

In addition to negatively impacting warfarin adherence, certain psychosocial factors have been identified as risk factors for negative clinical outcomes. For example, a study of patients with nonvalvular atrial fibrillation on warfarin therapy found that those patients with specific psychosocial characteristics were at heightened risk for adverse events [21]. In this study, patients with psychiatric illness (eg, schizophrenia, major depressive disorder, bipolar disorder) had a 36% increased risk for stroke, a 46% increased risk for intracranial hemorrhage, and a 19% increased risk for gastrointestinal bleeding compared with patients without these illnesses. Patients with substance abuse had a 135% increased risk for intracranial hemorrhage and a 41% increased risk for gastrointestinal bleeding compared with patients who were not substance abusers. Lastly, patients with social risk factors (eg, lack of housing, inadequate housing and material resources, living alone, and/or non-compliance with medical treatment) had a 28% increased risk for gastrointestinal bleeding.

It is important to note that many patients with chronic illness may have problems with medication adherence. This is particularly relevant for warfarin patients who suffer from chronic conditions such as atrial fibrillation. Research shows that among patients with chronic illness, adherence rates drop after the first 6 months of regimen initiation [22]. This may be due to beliefs about disease state and medication regimens, which have both been shown to impact adherence in general. For example, a study among 151 patients with diabetes found that disease and medication beliefs inconsistent with a chronic disease model of diabetes were significant predictors of poor medication adherence [23]. These patients were asked a number of questions regarding their beliefs about the chronicity, causes, consequences, and controllability of their illness, as well as medication beliefs about necessity, concerns, and regimen complexity. The authors point out that because patients on warfarin suffer from chronic conditions, illness and medication beliefs may be an important area to assess in these individuals.

Patient-provider communication issues (including language barriers) and health literacy are additional factors associated with warfarin nonadherence and may increase individual risk for negative clinical outcomes. One recent study examined rates of doctor-patient concordance in warfarin regimens by utilizing verbal communication and visual aids [24]. Patients were asked to verbalize their weekly warfarin regimen and to also visually identify their regimen from a color menu of warfarin pills. Patient language and health literacy were assessed to establish their role in concordance. These researchers found that doctor-patient discordance in weekly warfarin regimens was common. Specifically, verbal concordance was lower for nonnative English speakers and those with inadequate health literacy scores. In addition, visual concordance rates were greater than verbal concordance rates and were not associated with communication barriers or health literacy. The authors note that these findings have important implications for the use of visual aids in assessment of warfarin adherence, especially for patients with limited English proficiency and health literacy.

**Identifying Patients at Risk for Warfarin Nonadherence**

Identifying those at greater risk for warfarin nonadherence may perhaps help avoid adverse health outcomes (eg, stroke, hemorrhage) [20], and there are a variety of psychosocial assessments that could be used to identify patients at risk for nonadherence. Our group evaluated a screening tool based on 9 demographic, clinical, and psychosocial factors to identify patients at 2 anticoagulation clinics at risk for warfarin nonadherence [25]. The mean age of patients in this study was 55 years, two-thirds were men, and 54% identified as African American. Based on our predictive model, we found that patients with lower point scores were at lower risk for nonadherence compared with patients with higher point scores. Therefore, patients with higher scores may benefit from increased monitoring, education, and counseling. Although this novel clinical prediction tool has yet to be validated in other patient populations and settings, it offers promising potential to help identify patients at high and low risk for nonadherence. Ultimately, proper identification
of at-risk patients can assist providers in medical decision making.

Our group has also utilized a comprehensive psychosocial assessment instrument called the Millon Behavioral Medicine Diagnostic (MBMD) among patients on warfarin therapy at 2 anticoagulation clinics [26,27]. This instrument was developed specifically for medical patient populations and provides a broad assessment of patient adjustment to medical illness. It includes indicators of psychiatric problems, coping styles, and treatment prognostics scales to identify those at risk for adjustment difficulties. The MBMD Treatment Prognostics scales (Interventional Fragility, Medication Abuse, Information Discomfort, Utilization Excess, and Problematic Compliance) identify issues that might impact future health status. Our recent study utilizing the MBMD among patients on warfarin therapy found that those reporting a greater sensitivity to receptivity of details regarding illness-related information (MBMD Information Discomfort scale) were at a heightened risk for warfarin nonadherence even after controlling for a number of pertinent demographic and medical variables [27]. Future pessimism was also related to poorer warfarin adherence. The MBMD takes only 20 to 30 minutes to complete in the medical setting, provides a wealth of psychosocial data across a number of important domains, and can easily serve as a useful assessment tool in clinical practice. Information gathered from the MBMD might aid in the identification of patients at risk for nonadherence. By identifying and targeting patient-specific psychosocial factors through interventions, warfarin adherence may be enhanced and adverse medical events may be reduced.

Interventions to Enhance Warfarin Adherence

To date, the research on interventions designed to enhance warfarin therapy is limited. However, intervention research from other domains may be helpful in informing warfarin adherence strategies. For example, among patients with HIV, both cognitive-behavioral and educational interventions and dose training in combination with behavioral reinforcement have been shown to improve adherence [28,29]. In addition, among patients with psychiatric illness, both cognitive-behavioral and educational/supportive interventions involving patients and family members have been shown to improve adherence [30,31]. Cognitive-behavioral interventions are likely effective because they work to educate patients about their illness and the importance of adhering to their medication regimens. They also work to target, train, and reinforce adherence behaviors that have been thoughtfully tailored to each patient’s lifestyle [28]. In addition, these interventions help increase self-efficacy and motivation, and involving family members improves perceived social and emotional support.

Interventions to improve adherence are most effective if implemented by physicians, pharmacists, nursing staffs, and behavioral specialists throughout the entirety of treatment [22]. It is important to note that when compared with routine medical care, anticoagulation clinic management has been found to result in better clinical outcomes for patients [32]. For example, reduced thrombosis and bleeding complications have been directly attributed to services received at anticoagulation clinics [33]. These positive outcomes may exist because at specialized clinics, management details (eg, scheduling, changes in dosage, patient education) are often covered by health care workers throughout treatment [1].

In regards to warfarin therapy, increasing patient education, improving dosing schedules, and developing greater communication are potential ways to maximize patient adherence [24,34–37]. Interventions aimed at improving patient education and use of INR devices at home can improve clinical outcomes. For example, educating patients about the effects of lifestyle factors (eg, diet, smoking, drinking) on warfarin therapy is considered important since these factors heavily affect INR [8]. Educating patients about how to self-administer home INR monitoring is also possible and has been shown to improve the quality of anticoagulation management [38]. Based on recent studies by our group, effective interventions should also focus on memory prompts and other patient attitudinal factors, such as trait sensitivity to medical information [19,27]. Overall, depending on the individual patient, factors such as psychosocial distress, trust issues, patient-provider communication problems, and suboptimal beliefs are potentially modifiable and are logical targets for interventions to enhance adherence.

Conclusion

Warfarin therapy is recommended and commonly utilized to reduce the risk of stroke and VTE. Although warfarin is highly effective, optimal results occur when patients are adherent and have stable INR levels within a very narrow range. We have identified a number of important factors that impact adherence to warfarin therapy; it is advised that physicians and other health care professionals take the time to thoroughly assess for these factors that may impact patient health. In addition, we have also highlighted a number of barriers to warfarin adherence including key psychosocial factors. A comprehensive assessment of these types of factors may help to identify those patients most at risk for warfarin nonadherence and to assist in making appropriate referrals for intervention. Finally, future research should focus on developing interventions targeting the factors most relevant to warfarin adherence and study ways to incorporate them directly into patient care in order to help enhance health outcomes without burdening patients or negatively impacting medical care.
WARFARIN ADHERENCE

Corresponding author: Dean G. Cruess, PhD, Dept. of Psychology, Univ. of Connecticut, 406 Babidge Rd., Unit 1020, Storrs, CT 06269.

Funding/support: Dr. Kimmel discloses that NIH and Aetna provided funding for some of the research cited in the paper.

Financial disclosures: None

References


fibrillation and at high risk of stroke in the U.S. Pharmacoeconomics 2006;24:1021–33.


