Why Do Patients With Atrial Fibrillation Not Receive Warfarin?

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Atrial fibrillation (AF) is a growing public health problem associated with significant morbidity and mortality. Numerous randomized controlled trials of warfarin have conclusively demonstrated that long-term anticoagulation therapy can reduce the risk for stroke by approximately 68% per year in patients with nonvalvular AF, and even more in patients with valvular AF. However, available data show that of those patients with AF and no contraindication to warfarin therapy, only 15% to 44% are prescribed warfarin. Our literature review has identified patient-, physician-, and health care system–related barriers to warfarin prescription. However, the relative importance of these specific barriers remains unknown. Further work is needed to understand the discrepancy between the randomized controlled trial evidence and clinical practice patterns.

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Atrial fibrillation (AF) is a growing public health problem associated with significant morbidity and mortality.1 Patients with AF have an increased risk for ischemic stroke; those with nonvalvular AF have at least a 5-fold increased risk,2-4 whereas those with valvular AF have an estimated 17-fold increased risk.4 The initial stroke occurring with AF is often severe; in 1 series, 71% of patients died or had severe permanent neurologic deficits.2 Approximately 15% of all strokes are associated with this dysrhythmia, and the association increases steadily with age, from 6.7% of all strokes for patients aged 50 through 59 years to 36.2% of all strokes for patients aged 80 through 89 years.3

Numerous randomized controlled trials of warfarin therapy have conclusively demonstrated that long-term anticoagulation therapy can reduce the risk for ischemic stroke by approximately 68% in patients with nonvalvular AF,6-11 and even more in patients with valvular AF. Despite this conclusive evidence of efficacy, several studies have shown that “real-world” use of warfarin in patients with AF is suboptimal.12-27 The reasons for this low use are unclear, despite the availability of multiple physician surveys investigating the barriers to the prescription of warfarin.15,17,28-34 Our purpose is to review the evidence of the widespread underuse of warfarin therapy in AF as well as the proposed reasons (barriers) for underuse.

MATERIALS AND METHODS

Articles published in English from January 1, 1966, through December 31, 1998, were identified through MEDLINE by using the following keywords and Medical Subject Headings: atrial fibrillation, prophylaxis, anticoagulation, warfarin, barrier, survey, questionnaire, and underutilization. The reference lists of the articles were reviewed for additional relevant articles, and experts within the field were contacted to identify other articles. All articles assessing practice patterns and barriers to using warfarin in AF were reviewed and are included herein.

EVIDENCE OF THE UNDERUSE OF WARFARIN IN AF

Despite conclusive evidence demonstrating benefit from the use of thromboembolic prophylaxis,6-11 practice pattern
evaluations consistently identify suboptimal use (Table). In a study of 12 Canadian hospitals and 3375 patients, the Clinical Quality Improvement Network reviewed the medical records of consecutive patients admitted to the participating hospitals during 1993 and 1994 with the primary, most responsible, or complicating diagnosis of AF. Only 23.8% of the patients were prescribed warfarin during their hospital stay or at discharge, 29.8% received aspirin, 8.0% received both, and 33.2% received no thromboembolic prophylaxis. Although these rates improved during hospitalization (16.4% received warfarin on admission, compared with 32.0% at discharge), these findings indicate suboptimal care in light of the aforementioned randomized controlled trial evidence. A repeated pattern of practice analysis comparing 1993-1994 with 1995-1996 admissions at an institution within the Clinical Quality Improvement Network showed little change in warfarin use.

There are several other studies confirming the underuse of anticoagulant therapy. In those patients with no contraindications to warfarin therapy, studies report that anywhere from 15% to 79% of patients actually receive this therapy. Excluding a study that looked at warfarin use in a center that had participated in one of the large randomized controlled trials of anticoagulation for AF, warfarin was prescribed for only 15% to 44% of patients. A national survey of randomly selected office-based physicians found a significant increase (from 7% in 1980-1981 to 32% in 1992-1993) in warfarin use, although use still remained low. In fact, the low rate likely overestimates actual use, as individuals were captured on a per-visit basis (not a per-patient basis), and patients receiving warfarin were more likely to see physicians. In another study, physicians reported prescribing warfarin to 51% of their patients on a survey, but an audit of their practices revealed only 24% had received a prescription. Despite evidence that informed patients want to receive warfarin therapy and that warfarin therapy is highly cost-effective in the prevention of stroke, warfarin still is not prescribed to most patients with AF.

### Table: Reported Rates of Warfarin Use in Patients Without Contraindications

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of Patients†</th>
<th>Patient Population</th>
<th>Setting</th>
<th>Warfarin Prescribed, No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albers et al, 1997</td>
<td>171 (60)</td>
<td>AF and stroke, mean age of 75 y</td>
<td>6 University hospitals in United States</td>
<td>22 (19.8)</td>
</tr>
<tr>
<td>Antani et al, 1996</td>
<td>98</td>
<td>AF, mean age of 76 y</td>
<td>2 Hospitals and 5 general practices in United States</td>
<td>36 (36.7)†</td>
</tr>
<tr>
<td>Bath et al, 1993</td>
<td>95 (20)</td>
<td>AF, aged 32-100 y</td>
<td>Hospital in England</td>
<td>22 (29.3)</td>
</tr>
<tr>
<td>Beyth et al, 1996</td>
<td>189</td>
<td>NVAF</td>
<td>United States hospital (n = 104) and office-based visits (n = 85)</td>
<td>(24)§</td>
</tr>
<tr>
<td>Brass et al, 1997</td>
<td>488 (184)</td>
<td>AF, aged ≥ 65 y; 54% were aged 65-74 y</td>
<td>Medicare patients in United States</td>
<td>117 (38.4)</td>
</tr>
<tr>
<td>Gottlieb and Salem-Schatz, 1994</td>
<td>238 (40)</td>
<td>AF, mean age of 69 y</td>
<td>HMO patients in hospitals in United States</td>
<td>156 (78.8)</td>
</tr>
<tr>
<td>Gurwitz et al, 1997</td>
<td>413</td>
<td>AF, 66% aged ≥ 85 y</td>
<td>Long-term care facility in United States</td>
<td>130 (31.5)</td>
</tr>
<tr>
<td>Hendry et al, 1994</td>
<td>131 (52)</td>
<td>NVAF, aged 53-95 y</td>
<td>Geriatric and medical units in Scotland</td>
<td>12 (15.2)</td>
</tr>
<tr>
<td>Lip et al, 1997</td>
<td>111</td>
<td>AF, aged 50-105 y</td>
<td>2 General practices in England</td>
<td>27 (22.3)</td>
</tr>
<tr>
<td>Lip et al, 1994</td>
<td>170 (49)</td>
<td>AF, aged 38-95 y</td>
<td>General hospital in Scotland</td>
<td>40 (36.0)</td>
</tr>
<tr>
<td>Munschauer et al, 1997</td>
<td>651 (42)</td>
<td>Chronic AF</td>
<td>2 Community and 2 tertiary referral hospitals in United States</td>
<td>232 (38.1)</td>
</tr>
<tr>
<td>O’Connell and Gray, 1996</td>
<td>91 (22)</td>
<td>AF, mean age of 77 y</td>
<td>General practice in England</td>
<td>14 (24.1)</td>
</tr>
<tr>
<td>Stafford and Singer, 1994</td>
<td>3.1 × 10^6 Visits</td>
<td>AF, mean age of 70 y</td>
<td>Office-based physician visits in United States</td>
<td>(32.0)§</td>
</tr>
<tr>
<td>Sudlow et al, 1998</td>
<td>207</td>
<td>AF, aged ≥ 65 y</td>
<td>26 General practices in England</td>
<td>44 (23)§</td>
</tr>
<tr>
<td>CQIN Investigators, 1998</td>
<td>3575</td>
<td>AF, aged 19-104 y</td>
<td>12 Canadian hospitals</td>
<td>852 (23.8)</td>
</tr>
<tr>
<td>Whittle et al, 1997</td>
<td>172</td>
<td>AF, mean age of 80 y</td>
<td>Medicare beneficiaries at 5 hospitals in United States</td>
<td>76 (44.1)</td>
</tr>
</tbody>
</table>

* CQIN indicates Clinical Quality Improvement Network; AF, atrial fibrillation; NVAF, nonvalvular AF; and HMO, health maintenance organization.
† Number in parentheses indicates number of patients with contraindications to warfarin.
‡ Indicates those in whom therapy with warfarin was deemed appropriate by a physician panel.
§ Exact number of patients not available.
|| Data are given as presented in Sudlow et al.

### BARRIERS TO THE USE OF WARFARIN

Several physician surveys have been performed to examine the barriers to prescribing anticoagulant therapy. With a single exception, these surveys have used vignettes (case scenarios) to depict various clinical situations. Central to these depictions are factors believed to influence the clinician’s decision to prescribe anticoagulants. The decision to implement therapy with warfarin necessitates close follow-up because of the narrow therapeutic index that is influenced by multiple factors (eg, drugs, diet, patient health status). Our review of the studies evaluating barriers to the prescription of warfarin demonstrates 3 general categories of barriers (Figure), ie, patient-, physician-, and health care system-related factors.

### Barriers Pertaining to the Patient

Patient-related factors such as age, perceived embolic risk, and perceived risk for hemorrhage are consistently identified as influencing the decision of...
prescribing anticoagulation in vignettes. For example, increasing age has been identified consistently as a barrier to anticoagulation therapy, and even those physicians who are willing to prescribe anticoagulation for elderly patients aim for a lower intensity than that supported by the randomized controlled trial evidence. In contrast, physicians are more enthusiastic about and more aggressive with anticoagulation therapy in patients with a history of stroke. A strong relationship has been documented between physician estimates of the patient’s relative risk for embolism compared with that for hemorrhage and the decision to implement anticoagulation therapy. Surveyed physicians have reported withholding warfarin based on the belief that patients would refuse therapy or be noncompliant. More detailed explanations are not available.

When given the choice of warfarin prophylaxis, patients in one study decided to take warfarin 93% of the time. These data originate from a site that was actively involved in recruiting patients for the Boston Area Anticoagulation Trial for Atrial Fibrillation, and thus adopted the practice of recommending anticoagulation therapy in almost all patients. Although these data may not be representative of other settings, they demonstrate patient willingness to undergo anticoagulation therapy with warfarin. Patients presented with visual aids depicting the risks and benefits of warfarin therapy elected to take warfarin at a lower level of stroke risk than their physicians preferred to prescribe it. Very few physicians (approximately 10%) believed that the patient’s quality of life would be significantly impaired if warfarin was administered.

Overall, the vignettes are targeted at assessing patient clinical characteristics that may influence the prescribing of warfarin. Although consistently identifying age, embolic risk, and risk for hemorrhage as major determinants of the decision to prescribe anticoagulation therapy, the surveys undertaken are highly variable in assessing any other factors influencing warfarin use. In evaluating studies analyzing patient-related barriers, it is not possible to determine how these barriers relate to the numerous potential obstacles in daily practice (ie, whether identified barriers actually prevent the prescription of warfarin).

**Barriers Pertaining to the Physician**

Although most surveys have made inferences about the barriers to the prescription of anticoagulants based on physicians’ treatment decisions in vignettes, few have directly questioned physicians regarding their perceived barriers to anticoagulation. Surveys suggest that the primary determinant of the use of anticoagulants is a weighting of the benefit vs risk in each individual patient. In an evaluation by Chang and colleagues, cardiologists believed the risk for embolism relative to hemorrhage to be lower than did general practitioners, and therefore cardiologists were less likely to prescribe warfarin. In fact, the physician’s perception of the benefit vs risk of therapy appears to be the only consistent finding influencing the implementation of warfarin therapy. This perception, in part, likely is derived from the physician’s previous experience with the use of warfarin. Physicians with good or excellent experiences with warfarin were more likely to prescribe it, but nonetheless still did not prescribe warfarin for half of their patients.

Clinical uncertainty, although commonly reported, is not defined clearly within surveys, and it ranges in relative importance. In these evaluations, clinical uncertainty has been interpreted to mean that physicians were not aware of the current literature, were aware of the literature but did not accept the results, or believed the clinical vignette had features not addressed by previous studies. The relative importance of clinical uncertainty as a barrier ranges from being uncommon to being common enough to justify most surveyed physicians to request practice guidelines pertaining to candidacy for anticoagulation therapy. However, guidelines may vary markedly in their recommendations. For example, a study evaluating AF guidelines available in Great Britain found that the variation among the guidelines would result in vastly different prescribing practices, with 13% to 100% of patients being prescribed warfarin.

This widespread lack of consensus may contribute to the varying practice patterns observed, although the precise reasons for this are unknown. Perhaps physicians are unaware of how infrequently they prescribe warfarin, as the rates they report are often greater than those used in clinical practice. Rarely reported, and infrequently investigated, is the fear of litigation by physicians. One survey reported that 79% of physicians cited a lack of patient reliability as a contraindication to therapy, and greater than 90% of the same group did not prescribe warfarin to patients with a history of chronic alcoholism. In a clinical scenario depicting a patient with a history of falls, 71% of physicians believed anticoagulation therapy was contraindicated. Another survey specifically questioned physicians regarding the cost-effectiveness of warfarin, and most recognized that it was cost-effective. Some physicians reported difficulty in maintaining therapy within the therapeutic range, stating that further training, the availability of consultant advice, or guidelines on managing anticoagulation therapy would increase willingness to use it, whereas a few physicians (17%) believed patient noncompliance was responsible for the difficulty in monitoring the prothrombin ratio.

Of those physicians aware of clinical practice guidelines, several believed the guidelines were not applicable to their patients. In an evaluation of anticoagulation...
therapy within a health maintenance organization, Gottlieb and Salem-Schatz found patients to have a significantly greater prevalence of angina, previous myocardial infarction, congestive heart failure, and diabetes than patients in clinical trials. In this analysis, patients were not monitored as closely as those in clinical trials, and control of anticoagulation was found to be inferior, with prothrombin time ratios being in the target range on only 50% of the days compared with 68% of days in clinical trials. In another evaluation of warfarin therapy, patients were reported to be within the therapeutic range only 40% of the time. In assessing patients being admitted to the hospital with the diagnosis of acute stroke and AF, Albers et al found that half of the patients with no contraindication to anticoagulation therapy were not receiving any antithrombotic agent on admission. Of those having an international normalized ratio performed on admission, 72% were below the therapeutic range of 2.0 to 3.0.

Barriers Pertaining to the Health Care System

To expect the same reduction in stroke and rates of hemorrhage as that seen in clinical trials, it is logical to require an equivalent level of anticoagulation to that achieved in clinical trials. Of those patients admitted to hospital with a stroke while receiving warfarin therapy, most have subtherapeutic international normalized ratios. Clinical trials contain the expertise and resources dedicated to delivering therapeutic interventions in an efficient, controlled setting. In clinical practice, however, there are numerous potential barriers related to the health care system. The surveys performed largely focus on clinical characteristics of patients, with many reports only indirectly assessing barriers outside of a patient’s candidacy for warfarin prophylaxis.

Surveys of these barriers to warfarin therapy have produced highly variable results. This reported variance may be due to regional differences or could be a result of the method in which surveys elicited responses from physicians (which range from a ranking system to creation of a list). Many physicians surveyed believed that monitoring therapy was inconvenient because of a lack of time, delay in laboratory result reporting, or space constraints. Some physicians believed there was a need for further remuneration, whereas some believed the availability of consultant advice would increase physician willingness to use anticoagulant prophylaxis. Most physicians surveyed in Great Britain (94%) reported a desire for someone else to manage anticoagulation clinic. Given these logistical concerns, there may be a lack of resources and experienced personnel in the community to adopt practice recommendations and to provide anticoagulation therapy at rates similar to those of controlled clinical trials.

Despite the potential scarcity of resources, physicians surveyed in Great Britain appear to believe that the management of anticoagulation should be undertaken in the community or primary care setting. When comparing primary with secondary care, British physicians agree that primary care offers improved access for patients and continuity of care. Given the expectation of managing anticoagulation at the level reported in clinical trials, it seems prudent to ensure that services are carefully planned, that appropriate resources are available to meet patient demand, and that measures are in place to ensure quality control in the primary care setting.

Surveys performed to date offer little information about barriers pertaining to the health care system, particularly in the North American setting. In assessing the barriers to warfarin use, such information is crucial because of the complexities of warfarin therapy and the necessity to arrange frequent laboratory tests to ensure an appropriate level of anticoagulation.

LIMITATIONS OF PREVIOUS RESEARCH ON PRESCRIBING BARRIERS

Available data evaluating the barriers to the prescription of warfarin in patients with AF have several important limitations. With the exception of 1 survey, all evaluations have used case vignettes, which have several methodological limitations. First, vignettes attempt, but often are not successful in, mimicking a clinical scenario for the physician. Their use rests on the assumption that responses in hypothetical situations reflect actual clinical practice patterns. Comparative data indicate that physician responses to vignettes may not be representative of their clinical practice patterns, and thus this type of analysis may not identify the true barriers present in clinical practice. In fact, only a few studies (11 of 74) using written case simulations assess validity. Attempts at validating vignettes have not been successful, and reliability testing has produced disappointing results. Second, the identification of prescribing barriers is inferred or measured indirectly from vignettes. On interpreting the decision to prescribe anticoagulation therapy, assumptions must be made regarding factors triggering the physician’s decision. These assumptions may be factors in the vignette, eg, patient age or type of AF. However, there may be circumstances outside of the case that may influence this decision (eg, health care system factors). This information cannot be captured in this format. Third, use of the vignette format does not allow for the assessment of the relative importance of each of the barriers in prescribing warfarin. For example, several factors required when using warfarin (eg, arrangement of laboratory testing, dosage modification) may be identified as barriers to prescribing warfarin, but may not be inconvenient enough to prevent prescription. To identify this information, a rating scale of barrier importance directly eliciting physician responses would be required. Finally, no single study has evaluated the complete spectrum of prescribing barriers for anticoagulation therapy. In general, instruments typically assess patient-related barriers while not assessing physician- and health care system–related barriers. In the only study not using case vignettes, only a partial list of possible barriers is assessed.
given survey, certain barriers may be recognized only because they were highlighted, whereas the same barrier may have gone unrecognized in another survey.

FUTURE DIRECTIONS

To understand more completely the problem of warfarin underuse in AF, all aspects pertaining to the provision of health care must be evaluated. A direct and systematic analysis of the importance of patient-, physician-, and health care system-related barriers is warranted. This might be accomplished by listing potential barriers with a rating scale to indicate the importance of these barriers in relation to one another. By clarifying the relative importance of barriers representing different aspects of patient care, an in-depth understanding of the mechanisms of this problem would be facilitated. Once important barriers are identified, future interventions can be developed to address the current limitations in practice. Through targeting interventions toward the identified barriers, positive changes in behavior are more likely to occur. 34

CONCLUSIONS

With an aging population, AF is a growing public health problem with significant clinical consequences. Despite conclusive evidence from randomized controlled clinical trials, the use of warfarin for the prevention of ischemic stroke in AF is suboptimal. Physician surveys assessing the barriers to warfarin use have numerous limitations. As a result, more research is needed to identify and to clarify the relative importance of patient-, physician-, and health care system-related barriers. Thus, future interventions can be targeted to make an impact on prescribing patterns, with the ultimate goal of improved outcomes for patients with AF. 34

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