Predictors of Warfarin Use Among Ohio Medicaid Patients With New-Onset Nonvalvular Atrial Fibrillation

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**Background:** Despite demonstrated efficacy in stroke prevention, warfarin is underused in patients with atrial fibrillation (AF). Reasons for warfarin nonuse are unclear.

**Methods:** We conducted a retrospective cohort analysis using Ohio Medicaid administrative billing data to ascertain determinants of warfarin use for patients with new-onset nonvalvular AF. The database included data from all institutions, providers, and pharmacies providing services to Ohio Medicaid enrollees. Subjects included all 11,699 continuously enrolled fee-for-service recipients of Ohio Medicaid with a new diagnosis of nonvalvular AF between January 1, 1998, and December 31, 2000. We determined incipient warfarin use and presence of risk factors for stroke and hemorrhage by searching claims records for corresponding International Classification of Diseases, Ninth Revision, Clinical Modification codes and National Drug Codes. Univariate and multivariable analyses were performed to examine the association of risk factors with warfarin use.

**Results:** Only 9.7% of all patients and 11.9% of those without apparent contraindications filled prescriptions for warfarin from 7 days preceding to 30 days after the development of AF. Hypertension and congestive heart failure independently predicted increased warfarin use. Older age (≥85 years), younger age (<55 years), prior intracranial hemorrhage, prior gastrointestinal hemorrhage, predisposition to falls, alcohol or other drug abuse, renal impairment, and conditions perceived as barriers to compliance predicted decreased warfarin use.

**Conclusions:** Few in this cohort of Ohio Medicaid patients with incident AF filled prescriptions for warfarin within 30 days of the diagnosis. Several factors, including alcohol or other drug abuse or dependence, psychiatric disease, homelessness or inadequate housing, and lack of a caregiver, were highly prevalent and seemed to bias against warfarin prescribing.

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in managed care populations in California and Massachusetts, 55% and 79%, respectively, of ambulatory patients with nonvalvular AF without contraindications received warfarin treatment.15,16

Several researchers have attempted to elucidate why warfarin is underused in patients with AF. Clearly, prescriber and patient characteristics play a role. Cohen and colleagues17 demonstrated that not all physicians were aware of the benefits of warfarin for stroke prevention and that certain patients (eg, elderly persons, those with language difficulties, and those with disabilities) were less likely to be treated. Beyth and colleagues18 showed that physicians were less likely to prescribe warfarin for older patients and for those with risk factors for bleeding. Two additional studies19,20 found that advanced age, female sex, and rural residency predicted underuse of antithrombotic therapy and that patients at risk for falls were less likely to receive anticoagulation, despite probable benefit. It seems likely that other factors associated with socioeconomic status, such as physician perception of probable poor adherence to treatment or inconsistent follow-up, might also impact decisions regarding anticoagulation and treatment outcomes. In light of these facts, we decided to study the use of warfarin in patients with AF enrolled in the Ohio Medicaid program.

METHODS

STUDY DESIGN AND DATA SOURCE

This study was a retrospective longitudinal analysis of Medicaid claims data obtained from the Ohio Department of Jobs and Family Services. The source data include all pharmacy, medical, and institutional claims for fee-for-service patients enrolled in the Ohio Medicaid program and Medicare crossover claims for coenrolled patients. Patients enrolled in capitated plans were excluded because capitated claims do not include claims for coenrolled patients. Patients enrolled in capitated plans were excluded because capitated claims do not include claims for coenrolled patients. Two additional studies19,20 found that advanced age, female sex, and rural residency predicted underuse of antithrombotic therapy and that patients at risk for falls were less likely to receive anticoagulation, despite probable benefit. It seems likely that other factors associated with socioeconomic status, such as physician perception of probable poor adherence to treatment or inconsistent follow-up, might also impact decisions regarding anticoagulation and treatment outcomes. In light of these facts, we decided to study the use of warfarin in patients with AF enrolled in the Ohio Medicaid program.

PATIENT SELECTION

We identified all adult patients whose first occurrence of a diagnosis of AF was between January 1, 1998, and December 31, 2000 (additional data available from the authors). To ensure that the cohort included only incident cases of AF, we excluded patients who did not have a full year of continuous Medicaid enrollment without a diagnosis of AF before their incident date. We next excluded patients with other clear indications for warfarin (eg, valvular heart disease and valve repair or replacement) and those with transient AF (ie, a single code for AF associated with a code for hyperthyroidism or with a code for operative procedures commonly associated with perioperative or postoperative AF). Finally, we excluded patients already receiving warfarin when first diagnosed as having AF. After all exclusion criteria were applied, the number of incident AF cases in adults occurring from January 1, 1998, through December 31, 2000, was 11,699.

DETERMINATION OF RISK FACTORS

For all patients selected, we extracted demographic information, including age, sex, and race. Patients were categorized into 1 of 3 age groups (<55, 55-84, and ≥85 years) and 3 racial groups (white, African American, and other). International Classification of Diseases, Ninth Revision, Clinical Modification codes and corresponding dates for all office visits and hospitalizations were used to establish the presence or absence of a set of predetermined diagnoses (additional data available from the authors). This information was used to create binary variables representing the presence or absence of the following risk factors for ischemic stroke and hemorrhage: prior TIA or stroke, hypertension, congestive heart failure, prior myocardial infarction, diabetes mellitus, prior intracranial hemorrhage, prior gastrointestinal hemorrhage, prior other hemorrhage, predisposition to falls, cirrhosis or hepatitis, and renal insufficiency. In addition, also using International Classification of Diseases, Ninth Revision, Clinical Modification codes, we examined several potential sociodemographic factors, such as alcohol or other drug abuse or dependence, psychiatric disease, homelessness or inadequate housing, and lack of a caregiver, that might negatively impact on patients’ ability to comply with warfarin therapy and its associated monitoring and, thus, influence physicians’ treatment decisions (additional data available from the authors).

WARFARIN USE

We used pharmacy and medical/institutional claims data to determine whether patients filled prescriptions for warfarin within a window of decision making subsequent to a diagnosis of AF. For each patient, we searched for National Drug Codes corresponding to warfarin and International Classification of Diseases, Ninth Revision, Clinical Modification codes indicating warfarin use (code V58.61). The presence of any such code from 7 days preceding until 30 days after the diagnosis of AF was considered evidence of the initiation of warfarin therapy in response to the new diagnosis of AF.

STATISTICAL ANALYSIS

We used the t test for continuous variables and the χ² test for categorical variables to determine the univariate association of demographic factors and risk factors for stroke and hemorrhage with warfarin use. We also examined the effect of varying stroke and hemorrhage risk profiles on warfarin use; for comparisons across subgroups of patients with additional risk factors for stroke and hemorrhage, we used the Mantel-Haenszel χ² test of trend.

We used a multivariable logistic regression analysis to determine independent predictors of warfarin use. Factors found to be significant univariate predictors at P <.10 and those previously shown to independently predict warfarin use (irrespective of P value) were considered for inclusion in multivariable models. A stepwise selection algorithm was used to identify the most significant predictors of warfarin use; P <.05 was used as the threshold criterion for inclusion in the final model. All statistical analyses were performed using SAS statistical software, version 8.2 (SAS Institute Inc, Cary, NC).
### Table 1. Characteristics of the Study Population*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (N = 11,699)</th>
<th>Warfarin Users (n = 1136)</th>
<th>Warfarin Nonusers (n = 10,563)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>73.7 (15.5)</td>
<td>71.0 (12.9)</td>
<td>74.0 (15.7)</td>
<td>&lt;.01</td>
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<tr>
<td>Female sex</td>
<td>71.5</td>
<td>69.6</td>
<td>71.7</td>
<td>.15</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>White</td>
<td>79.7</td>
<td>81.3</td>
<td>79.5</td>
<td>.15</td>
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<tr>
<td>African American</td>
<td>18.5</td>
<td>17.0</td>
<td>18.7</td>
<td>.17</td>
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<tr>
<td>Other</td>
<td>1.8</td>
<td>1.7</td>
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<td>.73</td>
</tr>
<tr>
<td>Probable risk factors for stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior transient ischemic attack or stroke</td>
<td>13.1</td>
<td>13.1</td>
<td>13.1</td>
<td>.99</td>
</tr>
<tr>
<td>Hypertension</td>
<td>43.4</td>
<td>52.4</td>
<td>42.4</td>
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<td>Congestive heart failure</td>
<td>31.2</td>
<td>37.5</td>
<td>30.5</td>
<td>&lt;.01</td>
</tr>
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<td>Prior myocardial infarction</td>
<td>13.9</td>
<td>14.7</td>
<td>13.8</td>
<td>.40</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31.0</td>
<td>34.7</td>
<td>30.6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Contraindications to warfarin</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior hemorrhage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial</td>
<td>2.8</td>
<td>1.4</td>
<td>3.0</td>
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<tr>
<td>Gastrointestinal</td>
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<td>7.6</td>
<td>10.9</td>
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<tr>
<td>Other‡</td>
<td>6.3</td>
<td>5.6</td>
<td>6.4</td>
<td>.31</td>
</tr>
<tr>
<td>Predisposition to falls§</td>
<td>24.2</td>
<td>15.4</td>
<td>25.1</td>
<td>&lt;.01</td>
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<tr>
<td>Alcohol or other drug abuse</td>
<td>2.5</td>
<td>1.4</td>
<td>2.6</td>
<td>.01</td>
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<tr>
<td>Perceived barriers to compliance§</td>
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<td>26.3</td>
<td>30.0</td>
<td>.01</td>
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<tr>
<td>Cirrhosis or hepatitis</td>
<td>1.6</td>
<td>1.0</td>
<td>1.7</td>
<td>.07</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>8.5</td>
<td>7.2</td>
<td>8.6</td>
<td>.12</td>
</tr>
</tbody>
</table>

*Data are given as percentage of each group unless otherwise indicated.
†Warfarin users compared with warfarin nonusers; the t-test was used for age and the χ² test was used for all other comparisons.
‡Includes retinal hemorrhage, hematuria, hemoptysis, and hemorrhage not otherwise specified.
§Includes dementia, epilepsy, cataplexy, orthostatic hypotension, syncope, convulsions, and past falls.
| Value† |

**RESULTS**

**PATIENT CHARACTERISTICS**

The mean (SD) age of this cohort of Ohio Medicaid patients was 73.7 (15.5) years (Table 1). Patients were predominantly women; 79.7% and 18.5% were white and African American, respectively. Many patients had a significant burden of chronic illness, with 1 or more probable risk factors for ischemic stroke, including past TIA or stroke, hypertension, congestive heart failure, prior myocardial infarction, and diabetes mellitus. Contraindications to warfarin therapy, such as prior gastrointestinal, intracranial, or other hemorrhage, were less common. Alcohol or other drug abuse was noted in 2.5% of the patients. Many patients also had conditions predisposing to falls or perceived as barriers to treatment compliance (Table 1).

**WARFARIN USE**

Only 9.7% of all patients filled prescriptions for warfarin from 7 days preceding to 30 days after the development of AF. In univariate analyses, there were several statistically significant differences between warfarin users and warfarin nonusers (Table 1). In general, warfarin users were more likely to be younger and to have conditions predisposing them to ischemic stroke (hypertension, congestive heart failure, and diabetes mellitus). Warfarin users were less likely to have had a prior gastrointestinal or intracranial hemorrhage, conditions predisposing them to falls, alcohol or other drug abuse or dependence, and perceived risk factors for poor compliance. No significant differences were noted in warfarin use by race or sex. Differences in the prevalence of past TIA or stroke, prior myocardial infarction, prior other hemorrhage, liver disease, and renal insufficiency were not significant. In general, patients with more risk factors for stroke were more likely to receive warfarin therapy (Mantel-Haenszel χ² test, P < .001), while those with more risk factors for hemorrhage were less likely to be treated (Mantel-Haenszel χ² test, P < .001) (Figure).

**MULTIVARIABLE PREDICTORS OF WARFARIN USE**

Ten variables were significant univariate predictors of warfarin use (Table 2) at P < .10 and were, thus, considered for inclusion in multivariable models. Age younger than 55 years, prior stroke, and renal disease were also considered, despite nonsignificant univariate associations in our data set, because they have been shown to be significantly associated with warfarin use in other studies. A stepwise algorithm selected 10 of these 13 candidate variables as significant independent predictors of warfarin use in the final multivariable model (Table 3). Hypertension and congestive heart failure increased the odds of receiving warfarin therapy, whereas age younger than 55 years and 85 years or older, prior intracranial and gastrointestinal hemorrhage, predisposition to falls, alcohol or other drug abuse or dependence, conditions perceived as barriers to compliance, and renal insufficiency decreased the odds. After inclusion of other model predictors, prior stroke, diabetes mellitus, and liver disease...
were no longer significant (P > .05 for all) predictors of warfarin use.

**COMMENT**

In this cohort of Ohio Medicaid patients diagnosed as having new-onset AF between January 1, 1998, and December 31, 2000, only 9.7% of all patients and 11.9% of those without an apparent contraindication to warfarin use had prescriptions for warfarin filled within 30 days of the diagnosis. While these numbers may underestimate the proportion of patients for whom physicians recommended or even prescribed treatment, the contrast between our findings and those reported in studies involving managed care populations is particularly striking. Using similar inclusion and exclusion criteria in a cohort of ambulatory patients with AF from the Kaiser Permanente Medical Care Program in northern California (the Anticoagulation and Risk Factors in Atrial Fibrillation [ATRIA] study cohort), Go and colleagues found that 55% of patients without contraindications received warfarin. In a smaller study, Gottlieb and Salem-Schatz found that nearly 79% of eligible patients in the Harvard Community Health Plan (a staff-model health maintenance organization in the greater Boston, Mass, area) were prescribed long-term warfarin therapy.

A comparison of patient characteristics in our study with those of patients studied in health maintenance organization environments provides several interesting insights (Table 4). Our population is slightly older and contains a much higher percentage of women, a reflection of the source population from which patients were drawn (women composed 69.6% of all eligible patients and 78.2% of all those aged ≥75 years). While the prevalence of stroke risk factors is similar, we noted significantly more contraindications to warfarin in our cohort compared with the ATRIA study cohort. Notably, conditions predisposing to falls were nearly 3 times as prevalent in our cohort as in the ATRIA study cohort, and were one of the strongest predictors of warfarin nonuse, although our definition was more inclusive than the one used in the ATRIA study. Equally impressive is the fact that we identified conditions perceived as barriers to compliance in 29.7% of the patients in our cohort; the presence of these conditions was also associated with a decreased chance of filling a prescription for warfarin. The
frequent occurrence of these adverse conditions may, in large measure, account for the discrepancy in the rates of warfarin use in our cohort and the managed care cohorts previously described. The high prevalence in the Medicaid population of conditions such as mental illness, substance abuse, homelessness, inadequate housing, absence of a caregiver, and noncompliance is not surprising, and these factors have been associated with adverse health outcomes in other clinical settings.22-27

Other findings of our study are consistent with those of other studies that have examined the use of warfarin in patients with AF. The most consistent and perhaps the most concerning finding is that older age predicts non-prescription of warfarin. The magnitude of the odds of warfarin use in patients older than 85 years in our population (odds ratio, 0.43) compared with younger patients is similar to that seen in several other studies (odds ratios, 0.25-0.60).13,17,19,28-30 Hypertension and congestive heart failure, which significantly predict warfarin use in our cohort, have less consistently predicted warfarin use in other studies. Multivariable odds ratios similar to those obtained for several of our significant negative predictors (past intracranial hemorrhage, past gastrointestinal hemorrhage, and predisposition to falls) have also been documented.15,28-30

To our knowledge, this is the first study to demonstrate the significant negative association of several adverse sociodemographic factors, such as alcohol or other drug abuse or dependence, psychiatric disease, homelessness or inadequate housing, and lack of a caregiver, with warfarin use. These findings are compelling and highlight areas for future study. Our findings are also unusual in that prior stroke or TIA is absent from the final list of significant multivariable predictors of warfarin use. In most other studies, prior stroke or TIA is one of the strongest predictors of warfarin use; the reasons for the lack of association in our study are unclear. Several additional observations may, in part, explain this finding. Of all patients with a prior stroke or TIA, 36.9% also had a predisposition to falls, 36.5% had perceived barriers to compliance, and 57.3% had one or the other of these risk factors. Only 31.7% had no risk factors for bleeding. While not significant, there was a trend toward greater warfarin use in these optimal candidates. Ultimately, it may be that physicians were obeying the ancient imperatives primum non nocere (first do no harm) in electing not to treat high-risk patients.

The strengths of this study relate to the nature of the Ohio Medicaid database. We used claims generated from a wide range of clinical encounters, including physician visits, hospitalizations, nursing home stays, and pharmacy visits. Information about the dependent variable (warfarin use) was derived primarily from claims resulting from prescriptions, described by Avorn31(186) as the “final common pathway in therapeutic decision making.” Medicaid pharmacy claims are perhaps the most reliable and valid data source for Medicaid patients; in one validation study,27 the correspondence between medical records and Medicaid pharmacy claims was 94%.

The use of administrative claims data also engenders serious limitations. Iezzoni23 has stressed that the ability to draw valid conclusions about quality of care using administrative data is limited because of gaps in the data and because of the billing context in which the data are generated. We acknowledge that while we are interested in studying physicians’ decisions to prescribe warfarin, we are in fact measuring prescriptions filled by patients, at best a proxy. Our implicit assumption, that patients once given a prescription for warfarin will have it filled reliably and in a timely fashion, is clearly not always valid.

Furthermore, while we tried to improve the reliability of our diagnostic data by requiring that codes be documented more than once for chronic conditions, we acknowledge that our disease attribution is less accurate than it might have been had we been able to perform a medical record review. The study could also have benefited from the use of other data sources, such as electrocardiograms to detect asymptomatic AF and echocardiograms to assess left ventricular function. Nevertheless, we are confident that the size of our sample and the magnitude of the associations seen in this exploratory study allow us to draw conclusions that are valid and highlight issues that should be investigated in greater depth using other data sources. However, our findings should not yet be generalized to non-Medicaid populations or even to Medicaid populations in other states, which may have different eligibility requirements and demographic characteristics.

In conclusion, few patients with a new diagnosis of nonvalvular AF in this cohort of Ohio Medicaid patients filled prescriptions for warfarin within 30 days of the diagnosis. We have identified several factors, such as predisposition to falls, substance abuse, and sociodemographic challenges, that are highly prevalent and seem

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### Table 4. Comparison of Medicaid and Kaiser Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Medicaid Patients (N = 11 699)</th>
<th>Kaiser Patients (N = 13 428)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>73.7</td>
<td>71.7</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Female sex</td>
<td>71.5</td>
<td>42.8</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>43.4</td>
<td>51.0</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31.0</td>
<td>17.3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>13.9</td>
<td>29.1 ‡</td>
<td>NA</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>31.2</td>
<td>30.8</td>
<td>.49</td>
</tr>
<tr>
<td>Prior transient ischemic attack or stroke</td>
<td>13.1</td>
<td>9.3</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: Kaiser, Kaiser Permanente Medical Care Program (in northern California); NA, statistical comparison not appropriate because different definitions were used.

†Ohio Medicaid patients compared with Kaiser patients; the test was used for age and the test was used for all other comparisons.

§Includes previous falls (3.9%), dementia (3.0%), and a seizure history (1.2%).

(1709)
to be strong deterrents to warfarin use in this population. Further studies are needed to better understand the impact of these conditions on physician decision making and to see whether these sociodemographic characteristics, which seemingly deter physicians from prescribing warfarin, are in fact associated with greater bleeding risks in patients undergoing anticoagulation. Additional investigations should assess the impact of warfarin underuse on clinical outcomes in this group of patients, and guide interventions aimed at improving their care.

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REFERENCES


