Temporal Trends in the Use of Anticoagulants Among Older Adults With Atrial Fibrillation

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Background: Several recent randomized clinical trials have demonstrated that warfarin sodium treatment, and to a lesser extent aspirin, reduces risk of stroke and death compared with placebo in persons with atrial fibrillation. Insufficient documentation exists on the extent to which the use of these therapies following trial publications has continued to increase in the elderly with atrial fibrillation.

Methods: We used data from the Cardiovascular Health Study, a study of 5888 community-dwelling adults aged 65 years or older, to determine the prevalence of warfarin and aspirin use in persons with electrocardiogram-identified atrial fibrillation. Electrocardiogram examinations were conducted at baseline from 1989 through 1990, and at 6 subsequent annual examinations through 1995-1996. Medication data were collected by inventory methods at each examination. Temporal change in use of anticoagulants was analyzed by comparing percentage use in 1990 to use in each year through 1996.

Results: The use of warfarin increased 4-fold from 13% in 1990 to 50% in 1996 among participants with prevalent atrial fibrillation (P<.001). Daily use of aspirin did not increase over time. Participants younger than 80 years were 4 times more likely to use warfarin in 1996 (P<.001) than those 80 years and older. Use of aspirin did not vary significantly with age.

Conclusions: Warfarin use in community-dwelling elderly persons with electrocardiogram-documented atrial fibrillation increased steadily following the first publication of its treatment benefit, reaching 50% by 1996. In contrast, use of aspirin was unchanged during this same period. Continued efforts to promote appropriate anticoagulation therapy to physicians and their patients may still be needed.

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COMPARED WITH placebo, warfarin sodium treatment dramatically reduces the risk of stroke, systemic embolisms, and death in persons with atrial fibrillation.\(^1\)\(^3\) The benefits of aspirin treatment—with or without fixed-dose warfarin—are less pronounced than those of adjusted-dose warfarin,\(^6\)\(^7\) but are nonetheless significant.\(^1\)\(^3\)\(^8\)

The clinical use of warfarin to treat atrial fibrillation increased steadily through 1993.\(^9\)\(^10\) Yet treatment remained underutilized, especially among the very old.\(^9\)\(^11\) The extent to which the increase in the use of warfarin has continued over time and whether the oldest old have been party to any expanded treatment remains unknown. Furthermore, little is known about the prevalence of daily aspirin use among elderly persons with atrial fibrillation.\(^9\)\(^10\) In this article, we present temporal trend data from June 1989 through June 1996 on the use of warfarin and daily aspirin among participants aged 65 years and older who had electrocardiogram (ECG)-diagnosed atrial fibrillation.

RESULTS

The Table presents the number and the percentage of prevalent atrial fibrillation cases among CHS participants who had undergone ECG readings at baseline and at the 6 follow-up examinations, 1989-1996, and the number and the percentage of incident cases at each follow-up examination, 1990-1996. Among the 5888 subjects enrolled in the study, 1946 were missing ECG or medication data at the last examination due to death (47%), telephone contact only (30%), refusal to participate (11%), or other reasons (12%).

The use of warfarin increased 4-fold from 13% in 1990 to 50% in 1996 (Figure 1) among participants with prevalent paroxysmal or chronic atrial fibrillation (P<.001). The daily use of aspirin did not increase during the 6 years.
SUBJECTS AND METHODS

SETTING AND DESIGN

The Cardiovascular Health Study (CHS) is a population-based, prospective cohort study of risk factors for cardiovascular and cerebrovascular disease in the elderly. Participants were recruited from 4 US communities (Washington County, Maryland; Pittsburgh (Allegheny County), Pennsylvania; Forsyth County, North Carolina; and Sacramento County, California) based on a randomly-generated sampling frame from Health Care Financing Administration files. Annual examinations began in June 1989 and are ongoing. This study included data on the original cohort from the baseline examination and the first 6 years of follow-up, through June 1996.

SUBJECTS

The cohort consisted of 5201 community-dwelling adults aged 65 years and older who were recruited in 1989-1990 and an additional 687 African American adults who were recruited in 1992-1993. All study participants gave informed consent for their participation according to guidelines created by the appropriate institutional review boards. Participants who had atrial fibrillation and who did not have a mechanical pacing device were eligible for this study. Participants with atrial fibrillation who were too ill to participate further in the study or who were otherwise not available for follow-up were excluded from analysis since no medication data were available.

ATRIAL FIBRILLATION ASCERTAINMENT AND DEFINITION

Twelve-lead resting ECGs were performed at annual examinations. Tracings were read for atrial fibrillation or flutter at the CHS Electrocardiography Reading Center. Participants and their physicians were notified in writing when atrial fibrillation was detected. We relied exclusively on ECG-identified atrial fibrillation, which virtually restricted the study to persons with a chronic or paroxysmal dysrhythmia.

MEDICATION ASCERTAINMENT

Medication use was ascertained by inventory at annual clinic visits where participants brought all prescription medications used within the last 2 weeks. Interviewers transcribed drug information from the medication containers, including drug name, unit strength, and prescribed dosing instructions.

ANALYSIS

Trends in the use of anticoagulants were examined among participants who had atrial fibrillation at baseline or who developed atrial fibrillation during follow-up. A participant was classified as having prevalent atrial fibrillation at an examination if the abnormality was detected on ECG at that examination and there was at least 1 previous in-study ECG that identified atrial fibrillation. Baseline prevalence was exempted from the requirement for a previous ECG reading. A participant was classified as having incident atrial fibrillation at an examination if the abnormality was detected on ECG at that examination and there was at least 1 previous in-study ECG reading and all previous readings were free of atrial fibrillation. This precluded the possibility of incident atrial fibrillation at baseline.

Temporal change in the use of anticoagulants among participants with prevalent atrial fibrillation was analyzed by comparing the percentage use of anticoagulants among those with atrial fibrillation at baseline examination (1989-1990) with the percentage use of anticoagulants among those with atrial fibrillation at last follow-up examination (1993-1996). Since a subject could appear in both baseline and 6-year follow-up examinations, statistical tests of significance were conducted using a bootstrap technique, which accounts for the nonindependence of the study population. We also stratified the participants according to sex, age at examination (<80 years, ≥80 years), and elevated stroke risk (presence of ≥2 stroke risk factors defined as the presence of hypertension, diabetes, cardiovascular disease, or cerebrovascular disease at baseline for the 1990 comparisons or at last follow-up examination for 1996 comparisons) to determine if treatment trends were modified by these covariates. In addition, we identified participants who had potential contraindications to warfarin treatment, defined as those who “bleed easily,” consumed more than 28 drinks per week, scored in the lowest 5% of cognitive function measures, or had a history of falls. We compared the odds ratios (ORs) of anticoagulant use in 1990 with those of use in 1996 among participants in each age, sex, stroke risk, and potential contraindication stratum after adjusting for age, sex, stroke risk, race, and potential contraindication using multivariate logistic regression.

Temporal change in the use of anticoagulants over time to treat incident atrial fibrillation was based on reported use of an anticoagulant at the annual examination following the identification of the incident event. As such, we present incident atrial fibrillation data only through the fifth year of follow-up and medication data through the sixth year of follow-up. Change in use over time was assessed using a χ² test for trend.

of follow-up (28% in 1990 to 29% in 1996), and the use of warfarin or aspirin reached 74% by 1996.

Among prevalent cases, participants younger than 80 years were as likely to be using warfarin in 1990 (OR, 2.2; 95% confidence interval [CI], 0.47-10.8) and more than 4 times more likely to be using warfarin in 1996 (OR, 4.0; 95% CI, 1.9-8.4) when compared with participants who were 80 years or older at each examination after adjusting for sex, race, stroke risk, and potential contraindications to anticoagulation therapy (Figure 2). The use of aspirin did not vary significantly with age. Among those younger than 80 years, the use of warfarin or aspirin reached 83% in 1996 while their use in those 80 years and older was 63% in 1996.

Compared with participants who had a lower risk for stroke, higher-risk participants were more than 3 times more likely to be using warfarin in 1990 (24% vs 7%; OR, 3.2; 95% CI, 1.1-9.7) and as likely to be using warfarin by 1996 (55% vs 47%; OR, 1.3; 95% CI, 0.62-2.7) after adjusting for age, sex, race, and potential contraindica-
Overall, anticoagulation with warfarin in patients with paroxysmal or chronic atrial fibrillation reached 50% in 1996 and the use of either warfarin or aspirin reached 74% in that same year. By 1996, more than 80% of participants with atrial fibrillation younger than 80 years were receiving some form of anticoagulation, predominantly warfarin therapy. Interestingly, participants with elevated stroke risk were not using anticoagulation therapy more often than those at lower risk, nor were participants without potential contraindications to warfarin treatment using warfarin more often than those with potential contraindications. These factors appear to be benign in motivating the use of anticoagulation therapy. More detailed characteristics of users of anticoagulation therapy have been published elsewhere.20

Our findings differ from recently published data from the National Ambulatory Medical Care Surveys (NAMCS), which found that warfarin prescriptions increased to 33% for atrial fibrillation clinic visits in 1993 and remained flat through 1996.10 The NAMCS data represent clinic-based prevalence of treatment among visits by patients (all ages) to physician’s offices, whereas CHS data represent population-based prevalence among the elderly enrolled in the cohort. The NAMCS sampling design allows for an overrepresentation of patients who frequently visit physicians. These patients may have additional comorbidities that discourage the preventive use of warfarin. While our results demonstrating increased use through 1996 are encouraging, the results may in part reflect the cumulative benefit of repeated clinical monitoring with echocardiograms and annual feedback about atrial fibrillation to participants and their physicians.

**Figure 1.** Anticoagulant treatment of prevalent electrocardiogram-diagnosed atrial fibrillation according to warfarin sodium and daily aspirin use, 1990-1996.

**Figure 2.** Warfarin sodium treatment of prevalent electrocardiogram-diagnosed atrial fibrillation among those younger than 80 years and those 80 years and older, 1990-1996.

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**Prevalence and Incidence of Electrocardiogram-Identified Atrial Fibrillation Among Those Who Received an Electrocardiogram and Participated in the Medication Inventory, Cardiovascular Health Study, 1989-1996**

<table>
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<tbody>
<tr>
<td>(n = 5131)</td>
<td>144 (2.8)</td>
<td>111 (2.3)</td>
<td>114 (2.5)</td>
<td>119 (2.4)</td>
<td>116 (2.6)</td>
<td>130 (3.1)</td>
<td>135 (3.5)</td>
</tr>
<tr>
<td>Prevalent</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Incident</td>
<td>0</td>
<td>27 (0.6)</td>
<td>25 (0.6)</td>
<td>22 (0.4)</td>
<td>29 (0.7)</td>
<td>29 (0.7)</td>
<td>68 (1.8)</td>
</tr>
<tr>
<td>All Cases</td>
<td>144 (2.8)</td>
<td>138 (2.9)</td>
<td>139 (3.1)</td>
<td>141 (2.8)</td>
<td>145 (3.3)</td>
<td>159 (3.8)</td>
<td>203 (5.3)</td>
</tr>
</tbody>
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* New cohort added (new prevalent cases are added to cohort without their necessarily being incident that year). Percentage does not sum properly due to varying.

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both the CHS and NAMCS populations, it was shown that the oldest of the old were undertreated, a finding common to the use of other medical therapies among older adults.21-23

The robust change over time in the use of warfarin in people with atrial fibrillation certainly upsets change in the practice patterns related to other clinical conditions. Specifically, the increase in the use of angiotensin-converting enzyme inhibitors in persons with congestive heart failure and of β-blockers after myocardial infarction.24,25 The extent to which warfarin treatment trends will continue to rise will ultimately be limited by the inappropriateness—real or perceived—of treatment.

Clinical-trial exclusion-criteria data suggest that 50% to 60%3,4 of persons with atrial fibrillation have no contraindications to warfarin treatment and are appropriate candidates for warfarin therapy. Although self-reported and hospital-identified cases of atrial fibrillation were recorded within the CHS,26,27 we chose not to report, and (2) a validation study on a portion of the hospital-identified cases revealed that 93% of the atrial fibrillation had resolved at discharge from the hospital,27 suggesting that many of these persons may not have had indications for warfarin treatment. Other studies that have estimated the prevalence of atrial fibrillation in communities have both included28 and excluded29 self-reported data; those that have excluded self-reports have estimated atrial fibrillation prevalence to be 3.5% in those 65 years or older, similar to what we report.

We were not able to exclude incident ECG-identified atrial fibrillation from prevalent cases at baseline owing to the absence of a previous, in-study ECG. Including these subjects presumably lowered the prevalence of warfarin use at baseline since the medication inventory was conducted on the same day as the ECG and newly diagnosed atrial fibrillation would not have had the opportunity to be treated. The sharp rise in the number of incident cases in 1995-1996 was unexpected and cannot be explained by any known deviations from ECG protocols. We also did not exclude participants who might have been using warfarin for other conditions (the baseline prevalence of self-reported “deep vein thrombosis or blood clots in your legs” was 5%) since their number was small, nor did we exclude those who presented with potential contraindications to warfarin treatment since we found that the presence of relative contraindications was not associated with warfarin use.

Because of the limited number of subjects with atrial fibrillation, we were not able to examine trends in treatment by race, even with the addition of the new cohort in 1992-1993. We were also not able to give tight approximations of estimated risks associated with age, sex, stroke risk, and potential contraindications to anticoagulation therapy. As such, subanalyses can only be used to suggest changes in trends in treatment over time.

Treating persons who have atrial fibrillation with warfarin is not without costs, increased risk of hemorrhage, and increased expense and inconvenience of monitoring and therapy. A recent cost-effectiveness analysis of warfarin and aspirin for prophylaxis of stroke in patients with atrial fibrillation demonstrated that warfarin treatment was actually cost saving when administered to those with 2 or more stroke risk factors.19 In persons with 1 other stroke risk factor and aged 75 years or older, the cost per quality-adjusted life-year was $500. With nearly 75% of CHS participants with atrial fibrillation having 1 or 2 additional risk factors for stroke apart from age at their 1996 examination (45% with 1 risk factor and 28% with ≥2), the public health impact from warfarin undertreatment can be measured in both health and monetary costs.

In summary, the prevalence of warfarin anticoagulation in community-dwelling persons with atrial fibrillation increased steadily from the early 1990s and reached 50% overall by 1996. The use of aspirin, on the other hand, was unchanged during this same period. Noteworthy is the finding that 84% of the cohort younger than 80 years at study entry were using some type of anticoagulation treatment by 1996 and more than 68% of them were receiving warfarin. The results are much less encouraging for those 80 years and older. We conclude that continued efforts to actively promote the substantial health benefits of warfarin to physicians and their patients may still be needed, especially among persons 80 years and older and those with multiple stroke risk factors.

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The authors dedicate this article to the late William Feinberg, MD, whose initial contributions were instrumental in shaping this work.

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REFERENCES


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