Does Sex Affect Anticoagulant Use for Stroke Prevention in Nonvalvular Atrial Fibrillation?
The Prospective Global Anticoagulant Registry in the FIELD-Atrial Fibrillation

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Background—Among patients with atrial fibrillation (AF), women are at higher risk of stroke than men. Using prospective cohort data from a large global population of patients with nonvalvular AF, we sought to identify any differences in the use of anticoagulants for stroke prevention in women and men.

Methods and Results—This was a prospective multicenter observational registry with 858 randomly selected sites in 30 countries. A total of 17 184 patients with newly diagnosed (≤6 weeks) nonvalvular AF and ≥1 additional investigator-defined stroke risk factor(s) were recruited (March 2010 to June 2013). The main outcome measure was the use of anticoagulants (vitamin K antagonists, factor Xa inhibitors, and direct thrombin inhibitors) for stroke prevention at AF diagnosis. Of 17 184 patients enrolled, 43.8% were women. More women than men were at moderate-to-high risk of stroke (CHADS2 score ≥2: 65.1% versus 54.7%). Rates of anticoagulant use were not different overall (60.9% of men versus 60.8% of women) and in patients with a CHADS2 score ≥2 (adjusted odds ratio for women versus men, 1.00; 95% confidence interval, 0.92–1.09). In patients at low risk (CHA2DS2-VASc of 0 in men and 1 in women), 41.8% of men and 41.1% of women received an anticoagulant. In patients at high risk (CHA2DS2-VASc score ≥2), 35.4% of men and 38.4% of women did not receive an anticoagulant.

Conclusions—These contemporary global data show that anticoagulant use for stroke prevention is no different in men and women with nonvalvular AF. Thromboprophylaxis was, however, suboptimal in substantial proportions of men and women, with underuse in those at moderate-to-high risk of stroke and overuse in those at low risk.

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Key Words: atrial fibrillation ■ embolism ■ sex ■ stroke ■ women
WHAT IS KNOWN

- Women with atrial fibrillation are at higher risk of stroke than men with atrial fibrillation.
- The reasons for this elevated risk remain unclear, but they may include older age of women, use of hormone replacement therapy, undertreatment or suboptimal management with a vitamin K antagonist, and poor anticoagulation control.

WHAT THE STUDY ADDS

- The results from our worldwide study suggest that women are treated no differently to men in terms of anticoagulant therapy for stroke prevention.
- Thromboprophylaxis was, however, suboptimal in substantial proportions of men and women, with underuse in those at moderate-to-high risk of stroke and overuse in those at low risk.
- Improvements in anticoagulation prescription and management are needed for women and men.

Stroke or transient ischemic attack [Double],\textsuperscript{15} CHA\textsubscript{2}DS\textsubscript{2}-VASc,\textsuperscript{9} and HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio [INR], Elderly, Drugs/alcohol concomitantly).\textsuperscript{16} We hypothesized that anticoagulant use in women would be lower than that in men using data from the Global Anticoagulant Registry in the FIELD-Attrial Fibrillation (GARFIELD-AF).

Methods

Design

GARFIELD-AF is an ongoing, observational, worldwide study of adults with recently diagnosed nonvalvular AF.\textsuperscript{17} Independent ethics committee and hospital-based institutional review board approvals were obtained, as necessary, for the registry protocol. The registry is being conducted in accordance with the principles of the Declaration of Helsinki, local regulatory requirements, and the International Conference on Harmonisation-Good Pharmacopoeiological and Clinical Practice Guidelines. All patients provided written informed consent to participate. Confidentiality and anonymity of all patients enrolled into this registry are maintained at all times.

Study Population

Men and women aged ≥18 years with nonvalvular AF diagnosed according to standard local procedures within the past 6 weeks and with ≥1 additional factor(s) for stroke as judged by the investigator were eligible for enrollment.\textsuperscript{13} These risk factors were not prespecified in the protocol nor were they limited to the components of existing risk stratification schemes. Patients with a transient reversible cause of AF and those for whom follow-up to 2 years was unlikely were excluded. Data were collected using an electronic case report form.\textsuperscript{17} Patient enrollment was consecutive. Patients are being enrolled prospectively into 5 subsequent cohorts, each comprising n=10000 patients.\textsuperscript{13} Cohort 1 included a validation cohort of 5000 patients, enrolled at the same time as the first cohort, to describe the nature and characteristics of care for patients at participating sites before registry initiation; these patients were enrolled retrospectively and were excluded from the present analysis. This article reports only cross-sectional data at baseline.

Study Sites

A 3-step process was used for site selection to ensure proportional representation of the spectrum of care settings in each country. First, the national coordinating investigator identified the care settings, including office-based practice, hospital departments (neurology, cardiology, geriatrics, internal medicine, and emergency), anticoagulation clinics, and general or family practices, they believed most accurately represented the management of AF patients in their country. Second, the contract research organization provided a list (sampling frame) of sites from various database searches that reflected the care settings in the country. Third, the contract research organization contacted a random (ie, lack of selection of sites based on specific criteria rather than using random sampling) sample of sites for each care setting from the list, in accordance with the distribution specified by the national coordinating investigator. Sites that agreed to participate were recruited after a qualification telephone call, and the relevant investigator was required to complete a program providing guidance on patient screening, enrollment, and follow-up in the registry.

Data

Registry data were captured by trained data abstractors in electronic case report forms (designed by Dendrite Clinical Systems Ltd, Henley-on-Thames, United Kingdom, which is also responsible for ongoing database program management). Data collection and entry are managed by Quintiles (Durham, NC), which oversees all operational aspects of the program, apart from in the United Kingdom, where the tasks are undertaken by The University of Birmingham Department of Primary Care Clinical Sciences. Submitted data are examined by the coordinating center (Thrombosis Research Institute, London, United Kingdom) to ascertain their completeness and accuracy, and data queries are sent to participating sites. Data for this analysis, extracted on February 3, 2014, were analyzed by a statistician (Gabriele Accetta). The GARFIELD-AF registry uses a combination of techniques for quality control in monitoring of this study: frequent electronic database monitoring of all data entered into the registry database; remote site monitoring by clinical research associates on a monthly, quarterly, or 6-monthly basis depending on the site; on-site monitoring, which includes source document verification as per the monitoring plan; and ongoing monitoring of quality by the Audit Committee (Data Supplement).

Definitions

The term anticoagulation encompasses vitamin K antagonists, oral, injectable or undefined factor Xa inhibitors, and direct thrombin inhibitors. Vascular disease was defined as peripheral artery disease or coronary artery disease with a history of acute coronary syndrome (unstable angina or myocardial infarction). Hypertension was defined as a documented history of hypertension or blood pressure >140/90 mm Hg.

Statistical Analysis

Continuous variables are expressed as mean±SD or median (interquartile range) and categorical variables as frequency and percentage. Reported use at baseline of antithrombotic therapies was analyzed in relation to sex, according to CHADS\textsubscript{2} (\textsuperscript{17} CHA\textsubscript{2}DS\textsubscript{2}-VASc,\textsuperscript{9} and modified HAS-BLED (excluding fluctuations in the international normalized ratio) scores, calculated retrospectively from the data provided.\textsuperscript{16} For patients with a CHADS\textsubscript{2} score of ≥2, the strength of the association between independent factors and use of anticoagulation is expressed using odds ratios (ORs). Uncertainty related to OR estimates was assessed using 95% confidence intervals. Logistic regression models with only one independent factor as the explanatory variable in each were fitted to estimate crude ORs (univariate models). Adjusted ORs were estimated using a multivariable model. The models included variables judged to be of clinical relevance: sex, age, previous stroke, history of hypertension, congestive heart failure, diabetes mellitus, vascular disease, and geographic region. HAS-BLED
was not included in the models because of a high number of missing values. Patients with any missing values for confounders or unknown anticoagulant use did not contribute to the models. Age was categorized into 5 groups: ≤55, >55 to ≤65, >65 to ≤75, >75 to ≤85, and >85 years. Three different regions were included in the models: Europe (Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, the Netherlands, Norway, Poland, Russia, Spain, Sweden, Ukraine, and United Kingdom), Asia (China, India, Japan, Korea, Singapore, and Thailand), and non-Europe/non-Asia (Argentina, Australia, Brazil, Canada, Chile, Mexico, and South Africa). All other variables were treated as dichotomous, having only 2 possible values of yes and no. Adjusted ORs for risk factors were compared between women and men, fitting a model with first-degree interaction between sex and all other factors. Data analysis was performed with SAS statistical software, release 9.4 (SAS Institute Inc, Cary, NC).

Results

Study Population

Enrollment took place at 858 randomly selected sites in 30 countries in Europe (n=10851; 63.1%), Asia (n=3949; 23.0%), Central/South America (n=1443; 8.4%), Canada (n=348; 2.0%), Australia (n=427; 2.5%), and South Africa (n=166; 1.0%) between March 2, 2010, and June 7, 2013 (Table 1). Baseline characteristics for the 17184 patients are shown in Table 2. Of this population, 7530 (43.8%) were women. Women were older than men, with 47.5% aged ≥75 years versus 30.6% of men, and were less likely to be current or past smokers or heavy alcohol drinkers and to have coronary artery disease, peripheral artery disease, or a left ventricular ejection fraction of <40%. Women had higher prevalences of history of hypertension and moderate renal disease (ie, estimated glomerular filtration rate of 30–59 mL/min) and higher mean CHA2DS2-VASc scores because of their sex. A greater proportion of the women were at moderate-to-high risk of stroke (CHADS2 score of ≥2: 65.1% versus 54.7% of men). Almost all of the women (97.3%) had a CHA2DS2-VASc score of ≥2 versus 77.1% of the men. Of the 10882 patients in whom the HAS-BLED score could be calculated, 12.3% of men and 14.1% of women had a score of ≥3; the mean scores were similar in men and women.

Antithrombotic Therapy Use in Men and Women Overall and According to Risk Scores

Antithrombotic drugs given at diagnosis of AF are detailed in Table 3 and Figure 1. Aspirin was given to >30% of both men and women and adenosine diphosphate receptor inhibitors/P2Y12 inhibitors to 8.0% of men and 6.2% of women. Overall rates of anticoagulant use were no different in men and women (5788/9509 [60.9%] versus 4498/7404 [60.8%], respectively; Figure 1); 11.8% of men and 11.7% of women were receiving a factor Xa inhibitor or direct thrombin inhibitor (Table 3). Twenty-eight percent of men and 27.2% of women received an antiplatelet alone, and 12% of both men and women received no antithrombotic therapy. When analyzed by the level of stroke risk, approximately half of the men and women at low risk of stroke received some form of anticoagulant therapy, with similar patterns of antithrombotic use in men and women (Figure 2A). Among those with a CHADS2 score of 1, men had slightly higher levels of anticoagulant use compared with women. In patients with a CHADS2 score of ≥2, men were more likely than women to receive the combination of anticoagulant plus antiplatelet, but the overall rates of anticoagulant use were similar. After adjustment, use of an anticoagulant for stroke prevention in patients with a CHADS2 score of ≥2 was the same in women and men (OR, 1.00; 95% confidence interval, 0.92–1.09). In patients with a low risk of stroke, 41.8% (158/378) of men (CHA2DS2-VASc score of 0) and 41.1% (81/197) of women (CHA2DS2-VASc score of 1) received an anticoagulant (Figure 2B); the rate of antiplatelet use alone was slightly higher in women. In patients at high risk of stroke (CHA2DS2-VASc score of ≥2), 64.6% (4593/7108) of men and 61.6% (4329/7032) of women received an anticoagulant,
Table 2. Baseline Characteristics in Men and Women With Nonvalvular Atrial Fibrillation (n=17 184)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n=9654)</th>
<th>Women (n=7530)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (SD), y</td>
<td>68/9654 (12)</td>
</tr>
<tr>
<td>Age group, n (%)</td>
<td>&lt;65 y</td>
<td>3560/9654 (36.9)</td>
</tr>
<tr>
<td></td>
<td>65–74 y</td>
<td>3144/9654 (32.6)</td>
</tr>
<tr>
<td></td>
<td>≥75 y</td>
<td>2950/9654 (30.6)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>Mean (SD), kg/m²</td>
<td>27.7 (4.97)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Systolic blood pressure</td>
<td>130.0 (120.0–144.0)</td>
</tr>
<tr>
<td></td>
<td>Median (IQR), mm Hg</td>
<td>82.0 (70.0–100.0)</td>
</tr>
</tbody>
</table>

Continued...
The main reasons for not giving an anticoagulant to patients at moderate-to-high risk of stroke (CHADS\textsuperscript{2} score of ≥2) were similar between men and women and were largely because of physician choice (Table 4).

### Anticoagulant Use in Subgroups at Risk of Stroke

The univariate ORs for anticoagulant use in various subgroups of patients with a CHADS\textsuperscript{2} score of ≥2 are provided in Table 5, and the adjusted data for men and for women are presented in Figure 4. After adjustment, patients aged ≥85 years appeared to have a lower rate of use of anticoagulants than those aged ≤55 years, but the difference was not significant. Anticoagulant use was decreased in men and women aged ≥85 years. Men and women with a previous stroke were more likely than those without to receive anticoagulant treatment, whereas men and women with a history of hypertension were less likely to receive anticoagulants than those without a history.

### Discussion

In this large, contemporary, prospective, global cohort study of patients with newly diagnosed nonvalvular AF, overall use of anticoagulant therapy for stroke prevention was no different in men and women. Among patients with a CHADS\textsuperscript{2} score of 0, women were less likely than men to receive combination antithrombotic therapy. Use of anticoagulants in patients with a CHADS\textsuperscript{2} score of 0 could reflect suboptimal adherence.
to guidelines, or it may simply indicate that many clinicians think a CHADS2 score of 0 is not low risk and formally consider other risk factors when assessing risk. Among truly low-risk patients (CHA2DS2-VASc score of 0 in men and 1 in women), who are not considered candidates for anticoagulant therapy according to the guidelines, 60% of men and 40% of women received an anticoagulant. In contrast, among those with a CHA2DS2-VASc score of ≥2, in whom anticoagulation is a class I recommendation, one-third did not receive an anticoagulant. Of the women with a CHA2DS2-VASc score of 0, 41.1% were prescribed anticoagulants (some in combination with an antiplatelet) and 34.5% received an antiplatelet alone. Only 24.4% received no antithrombotic therapy, consistent with guideline recommendations. The high rate of use of antiplatelet therapy does not correlate with the rates of cardiovascular diseases among women, indicating that antiplatelets are still being given to low-risk women for stroke prevention, thus increasing bleeding risk. Similarly, 41.8% of men with a CHA2DS2-VASc score of ≥0 were prescribed anticoagulant therapy, and only 28.3% received no antithrombotic therapy. These findings of suboptimal thromboprophylaxis are of concern and indicate the need for improved stroke prevention in AF. These observations were evident from registries conducted a decade ago and show that anticoagulant use remains suboptimal in both sexes, reflecting the many limitations and difficulties with using vitamin K antagonists, and despite the recent introduction of direct anticoagulants.

Estimating bleeding risk in patients with AF can be difficult. The use of risk scores, such as HAS-BLED, may help clinicians make an informed decision about a patient’s potential risk for bleeding. In this study, the patterns of use of antithrombotic therapy were broadly similar when comparing men with women at low or at high risk of a bleed. The overall rates of anticoagulant therapy were higher in the low-risk group. However, combination antithrombotic therapy was more frequent in the high-risk group. Although the use of more intensive therapy in such patients may be somewhat unexpected, given that it is associated with an increased risk of bleeding complications, it probably reflects overlapping risk factors in stroke and bleeding risk scores. The presence of comorbid conditions such as coronary artery disease cannot, alone, account for the high rates of use of combination therapy in men and women at high risk of bleeding. Furthermore, a high HAS-BLED score per se should not be used to withdraw or preclude the use of anticoagulants; rather, it should be used to identify patients at higher risk of bleeding and to correct any potentially reversible risk factors for this event, and, in particular, to reconsider the use of combination antithrombotic therapy.

Reasons for the increased risk of stroke in women are uncertain. Stroke risk may be age dependent because, compared with that in men, it is increased only in women ≥65 years of age. Hormone replacement therapy may be a risk factor for ischemic stroke. Undertreatment or suboptimal management with an oral anticoagulant is also a possibility, with poor average time in the therapeutic range and frequent interruptions in anticoagulant therapy possibly contributing to the higher risk of stroke in women. The ORs for anticoagulant use in subgroups of men and women were similar, with the exception of men with a previous stroke or aged 65 to 75 years who were more likely to receive anticoagulants, whereas women with congestive heart failure and men with a history of hypertension were less likely to receive anticoagulants.

The prospective GARFIELD-AF registry is the largest worldwide initiative to study the risk of stroke among patients with newly diagnosed nonvalvular AF. The present analysis includes data spanning 30 countries across 6 continents. The population is representative of the spectrum of patients treated in everyday practice in each of the countries. This analysis is, however, limited by its observational design, although great efforts were made to standardize definitions of conditions, and missing data. No information has been included on race. The percentage of low-risk patients who were overtreated may have been overstated, as the primary indication for anticoagulant use was not recorded, no data were available for patients with a mechanical heart valve, and history of cardioversion or ablation was known for few patients (146 and 152, respectively). Of the low-risk patients (CHADS2 score of 0), only 10 men and 5 women had a history of venous thromboembolism. Recruitment preceded publication of the European Society of Cardiology 2010 guidelines on stroke prevention, which suggests the use of

Table 4. Main Reasons Why Vitamin K Antagonists Were Not Given to Men and Women With a CHADS2 Score of >2 (n=2643)

<table>
<thead>
<tr>
<th>Reason, n (%)</th>
<th>Men (n=1349)</th>
<th>Women (n=1294)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician’s choice</td>
<td>625 (46.3)</td>
<td>639 (49.4)</td>
</tr>
<tr>
<td>Bleeding risk</td>
<td>111 (17.8)</td>
<td>94 (14.7)</td>
</tr>
<tr>
<td>Concern over patient compliance</td>
<td>71 (11.4)</td>
<td>67 (10.5)</td>
</tr>
<tr>
<td>Guideline recommendation</td>
<td>15 (2.4)</td>
<td>19 (3.1)</td>
</tr>
<tr>
<td>Fall risk</td>
<td>49 (7.8)</td>
<td>123 (19.2)</td>
</tr>
<tr>
<td>Low risk of stroke</td>
<td>67 (10.7)</td>
<td>52 (8.1)</td>
</tr>
<tr>
<td>Not specified</td>
<td>312 (49.9)</td>
<td>283 (44.3)</td>
</tr>
<tr>
<td>Patient refusal</td>
<td>119 (8.8)</td>
<td>112 (8.7)</td>
</tr>
<tr>
<td>Already taking antiplatelet drugs for other medical conditions</td>
<td>91 (6.7)</td>
<td>68 (5.3)</td>
</tr>
<tr>
<td>Previous bleeding event</td>
<td>26 (1.9)</td>
<td>25 (1.9)</td>
</tr>
<tr>
<td>Alcohol misuse</td>
<td>13 (1.0)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Taking medication contraindicated or cautioned for use with vitamin K antagonist or anticoagulants</td>
<td>7 (0.5)</td>
<td>6 (0.5)</td>
</tr>
<tr>
<td>Other or unknown</td>
<td>468 (34.7)</td>
<td>442 (34.2)</td>
</tr>
</tbody>
</table>
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the CHA2DS2-VASc score to determine stroke risk. The results for the HAS-BLED score should be interpreted with caution because of the high number of missing values.

Conclusions
Overall rates of anticoagulant use in nonvalvular AF are no different in men and women. The results indicate suboptimal application of thromboprophylaxis in large proportions of men and women with AF, with underuse in moderate-to-high-risk patients and overuse in low-risk patients. Improvements in stroke prevention, as well as stroke and bleeding risk assessment, are clearly needed in men and women with AF.

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Disclosures
Dr. Lip is a consultant for Bayer, Astellas, Merck, Sanofi, Bristol-Myers Squibb/Pfizer, Daiichi-Sankyo, Biotronik, Medtronic, Portola, and Boehringer Ingelheim, and he is a Speakers’ Bureau member for Bayer, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, and Medtronic. Dr. Rushton-Smith is a consultant for Bristol-Myers Squibb, Boehringer-Ingehelm, MSD, Sanofi, and Servier. Dr. Goldhaber received research support from Bristol-Myers Squibb, Daiichi Sankyo, BTG, and National Heart, Lung, and Blood Institute, and he is a consultant/advisory board member for Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Janssen, and Portola. Dr. Fitzmaurice received honoraria from Bayer, Boehringer Ingelheim, and sanofi-aventis. Dr. Mantovani is a consultant for Bayer HealthCare Pharmaceuticals and received grants from Boehringer Ingelheim, Pfizer, BMS, and Daiichi Sankyo. Dr. Goto received research grants from sanofi-aventis (significant) and Pfizer (modest); he is a consultant for Bristol-Myers Squibb (modest), a Speakers’ Bureau member for Bristol-Myers Squibb/Pfizer (modest) and also received honoraria from Bayer, Daiichi Sankyo, and Bristol-Myers Squibb/Pfizer (modest), and sanofi-aventis (significant). Dr. Haas received honoraria

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Category</th>
<th>%</th>
<th>n</th>
<th>N*</th>
<th>Odds Ratio (95% CI)</th>
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<tbody>
<tr>
<td>Sex</td>
<td>Men (ref.)</td>
<td>66.0</td>
<td>3386</td>
<td>5133</td>
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<tr>
<td></td>
<td>Women</td>
<td>65.7</td>
<td>3147</td>
<td>4791</td>
<td>0.99 (0.91–1.07)</td>
</tr>
<tr>
<td>Age group, y</td>
<td>≤55 (ref.)</td>
<td>61.9</td>
<td>340</td>
<td>549</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>55–65</td>
<td>64.9</td>
<td>922</td>
<td>1420</td>
<td>1.14 (0.93–1.40)</td>
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<tr>
<td></td>
<td>65–75</td>
<td>67.6</td>
<td>1833</td>
<td>2713</td>
<td>1.28 (1.06–1.55)</td>
</tr>
<tr>
<td></td>
<td>75–85</td>
<td>67.2</td>
<td>2920</td>
<td>4343</td>
<td>1.26 (1.05–1.52)</td>
</tr>
<tr>
<td></td>
<td>&gt;85</td>
<td>57.6</td>
<td>518</td>
<td>899</td>
<td>0.84 (0.67–1.04)</td>
</tr>
<tr>
<td>Geographic region</td>
<td>Asia† (ref.)</td>
<td>55.2</td>
<td>1051</td>
<td>1904</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Europe‡</td>
<td>69.7</td>
<td>4589</td>
<td>6585</td>
<td>1.87 (1.68–2.07)</td>
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<tr>
<td></td>
<td>Non-Europe/non-Asia§</td>
<td>62.2</td>
<td>893</td>
<td>1435</td>
<td>1.34 (1.16–1.54)</td>
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<tr>
<td>Previous stroke</td>
<td></td>
<td>No (ref.)</td>
<td>65.3</td>
<td>5552</td>
<td>8497</td>
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<tr>
<td>History of hypertension</td>
<td></td>
<td>No (ref.)</td>
<td>69.3</td>
<td>735</td>
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<td>No (ref.)</td>
<td>65.8</td>
<td>4224</td>
<td>6421</td>
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<tr>
<td>Vascular disease#</td>
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<td>No (ref.)</td>
<td>65.9</td>
<td>5979</td>
<td>9076</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td></td>
<td>No (ref.)</td>
<td>66.6</td>
<td>4408</td>
<td>6621</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and ref., reference category.

*Fifty patients with missing data on anticoagulant use were removed.
†China, India, Japan, Korea, Singapore, and Thailand.
‡Austria, Czech Republic, Belgium, Denmark, Finland, France, Germany, Hungary, Italy, the Netherlands, Norway, Poland, Russia, Spain, Sweden, Ukraine, and United Kingdom.
§Argentina, Brazil, Chile, Mexico, Australia, Canada, and South Africa.
||Three patients with missing data on stroke were removed.
#Three patients with missing data on vascular disease were removed.
and is a Speakers’ Bureau member for Bayer, BMS, CSL-Behring, Boehringer Ingelheim, Daiichi Sankyo, Pfizer, and Sanofi. Dr Camm is a Speakers’ Bureau member for Bayer; he is a consultant/advisory board member for/received honoraria from Mitsubishi, Xanlem, ChanRx, Bayer, Biotronik, Boehringer Ingelheim, Takeda, Daiichi Sankyo, Menarini, St. Jude Medical, Pfizer, Bristol-Myers Squibb, Cardiovascular Therapeutics, Medtronic, Sanofi, Boston Scientific, Richmond Pharmacology, Novartis, and Servier. Dr Ambrosio received research support from Menarini International; he is a Speakers’ Bureau member for Boehringer Ingelheim, Menarini International, and Merck; he is a consultant/advisory board member for Menarini International, Merck, and ACRAF. Dr Janský is a consultant for/advisory board member for/received honoraria from Bayer, Sanofi, Daiichi Sankyo, Menarini, and Servier; he is an advisory board member for Bayer Healthcare, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, and Sanofi S.A.; he is a scientific advisory board member for Bayer Healthcare, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, and Sanofi S.A.; he is a scientific advisory board member for Bayer Healthcare, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, and Sanofi S.A.; he is a scientific advisory board member for Bayer Healthcare, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, Pfizer Inc, and Sanofi S.A. The other authors report no conflicts.

Figure 4. Use of anticoagulants at baseline in subgroups of men and women with a CHADS2 score of ≥2 (n=9974). *Reference group, no history. Fifty patients with missing data on anticoagulant use were removed. Four patients with missing data for independent variables were also removed. Likelihood ratio tests were performed to test the gain in the likelihood because of each interaction term. Interaction terms with sex were not statistically significant (P>0.05). Only the interaction term between sex and diabetes mellitus showed a P value of <0.1 (P=0.06). CI indicates confidence interval; OR, odds ratio; and ref., reference group.

Appendix

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References
Does Sex Affect Anticoagulant Use for Stroke Prevention in Nonvalvular Atrial Fibrillation?: The Prospective Global Anticoagulant Registry in the FIELD-Atrial Fibrillation


for the GARFIELD-AF Investigators

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