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Clinical Research

Association Between Patient and Physician Sex and Physician-Estimated Stroke and Bleeding Risks in Atrial Fibrillation

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See editorial by Ding et al., pages 145–146 of this issue.

ABSTRACT

Background: Physicians treating nonvalvular atrial fibrillation (AF) assess stroke and bleeding risks when deciding on anticoagulation. The agreement between empirical and physician-estimated risks is unclear. Furthermore, the association between patient and physician sex and anticoagulation decision-making is uncertain.

Methods: We pooled data from 2 national primary care physician chart audit databases of patients with AF (**F**acilitating **R**eview and

RÉSUMÉ

Contexte : Les médecins qui traitent la fibrillation auriculaire non valvulaire évaluent les risques d'accident vasculaire cérébral (AVC) et d'hémorragie avant de décider d'instaurer un traitement anticoagulant. La concordance entre le risque empirique et celui estimé par le médecin n'a pas été étudiée. On ne sait pas non plus s'il existe une association entre le sexe du patient et du médecin et la décision prise en matière de traitement anticoagulant.

Atrial fibrillation (AF) is the most prevalent adult arrhythmia and is relevant from a public health perspective given the associated morbidity and mortality.[1] Guidelines recommend that patients be stratified with respect to stroke and bleeding risks, and that most should receive antithrombotic therapy.[2,3] The most widely used tools to estimate stroke and bleeding risk are the **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack ($CHADS_2$)[4] and **H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history, **L**abile international normalized ratio, **E**lderly,

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Education to Optimize Stroke Prevention in Atrial Fibrillation and Coordinated National Network to Engage Physicians in the Care and Treatment of Patients with Atrial Fibrillation Chart Audit) with a combined 1035 physicians (133 female, 902 male) and 10,927 patients (4567 female and 6360 male).

Results: **Male physicians underestimated stroke risk in female patients and overestimated risk in male patients. Female physicians estimated stroke risk well in female patients but underestimated the risk in male patients. Risk of bleeding was underestimated in all. Despite differences in risk assessment by physician and patient sex, > 90% of patients received anticoagulation across all subgroups. There was modest agreement between physician estimated and calculated (ie, $CHADS_2$ score) stroke risk: Kappa scores were 0.41 (0.35-0.47) for female physicians and 0.34 (0.32-0.36) for male physicians.**

Conclusions: **Our study is the first to examine the association between patient and physician sex influences and stroke and bleeding risk estimation in AF. Although there were differences in agreement between physician estimated stroke risk and calculated $CHADS_2$ scores, these differences were small and unlikely to affect clinical practice; further, despite any perceived differences in the accuracy of risk assessment by sex, most patients received anticoagulation.**

Méthodologie : **Nous avons regroupé les renseignements figurant dans deux bases de données nationales issues de programmes de revue des dossiers médicaux de médecins de soins primaires portant sur des patients atteints de fibrillation auriculaire (*Facilitating Review and Education to Optimize Stroke Prevention in Atrial Fibrillation* et *Coordinated National Network to Engage Physicians in the Care and Treatment of Patients with Atrial Fibrillation*) qui concernaient au total 1035 médecins (133 femmes, 902 hommes) et 10 927 patients (4567 femmes et 6360 hommes).**

Résultats : **Les médecins de sexe masculin avaient sous-estimé le risque d'AVC chez les femmes et surestimé ce risque chez les hommes. Les médecins de sexe féminin avaient estimé correctement le risque d'AVC chez les femmes, mais sous-estimé ce risque chez les hommes. Le risque d'hémorragie avait été sous-estimé chez tous les patients. Malgré les écarts dans l'évaluation du risque selon le sexe du médecin et celui du patient, plus de 90 % des patients avaient reçu un traitement anticoagulant dans tous les sous-groupes. Une concordance modeste a été observée entre le risque d'AVC calculé (c.-à-d. le score $CHADS_2$) et celui estimé par le médecin : les scores au test du Kappa étaient de 0,41 (0,35-0,47) pour les médecins de sexe féminin et de 0,34 (0,32-0,36) pour les médecins de sexe masculin.**

Conclusions : **Notre étude est la première à s'intéresser à l'association entre les influences exercées par le sexe du médecin et du patient et l'estimation du risque d'AVC et d'hémorragie dans la fibrillation auriculaire. Certaines différences entre le risque d'AVC calculé (c.-à-d. le score $CHADS_2$) et celui estimé par le médecin ont été notées, mais ces différences étaient mineures et non susceptibles d'influer sur la pratique clinique; de plus, malgré les différences apparentes de justesse de l'évaluation du risque selon le sexe, la plupart des patients ont reçu un traitement anticoagulant.**

Drugs/alcohol (HAS-BLED)[5] scores, respectively. Previous studies demonstrate disagreement between physician-estimated and calculated risks of stroke and major bleeding in patients with AF.[6,7] Sex-related disparities exist in the management of acute coronary syndromes,[8,9] heart failure,[10] and AF.[11,12] To date, there are few data describing the relationships between physician sex and patient risk assessment and evidence-based care in AF. Through 2 national chart audits of patients with AF in primary care practice, we sought to describe physician-assigned risk compared with empirically calculated stroke and bleed risks, further stratified by patient and physician sex.

Material and Methods

Facilitating **Re**view and **Ed**ucation to **O**pti**m**ize Stroke Prevention in **A**trial **F**ibrillation (FREEDOM AF)[13] was a knowledge translation initiative that provided guideline-recommended strategies to primary care physicians (PCPs) treating patients with nonvalvular AF at risk of stroke. The **Co**ordinated **N**ational **N**etwork to **E**ngage Physicians in the **C**are and **T**reatment of Patients with **A**trial **F**ibrillation (CONNECT AF)[7] Chart Audit was a similar initiative, focusing on risk stratification and stroke prevention therapy care gaps in Canadian patients with nonvalvular AF. Both programs were conceived and coordinated by the Canadian Heart Research Centre, a nonprofit physician-based organization. All management decisions were at the discretion of the treating physicians. Collected information included patient demographics, cardiovascular risk factors and diseases, AF history, rate- and rhythm-control medications, stroke risk assessment and method by which it was determined (including but not limited to the $CHADS_2$ score), major bleeding risk assessment and method by which it was determined (including but not limited to the HAS-BLED score), and current antithrombotic therapy.

We pooled data from these 2 national chart audit databases of patients $\geq$ 18 years of age without significant valvular disease: FREEDOM AF (February to September 2011), which included 4670 patients from 474 PCPs, and CONNECT AF (January to June 2013), which included 6346 patients from 647 PCPs (Fig. 1). Some PCPs participated in both databases, but they were included only once in the analyses (ie, a total of 1035 [133 female, 902 male] physicians). PCPs were recruited to participate by direct mail or fax campaigns, by continuing medical education events, and by virtue of participation in previous or ongoing clinical trials, observational studies, or knowledge translation programs with the coordinating centre. PCPs undertook a chart audit of 10 patients with AF seen in their practice.

We defined "intermediate-high" stroke risk as a calculated $CHADS_2$ score of $\geq$ 2; $CHADS_2$ score was the most widely used stroke risk estimator, because the **C**ongestive Heart Failure, **H**ypertension, **A**ge ($\geq$ 75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female) score was just emerging and not yet adopted into the guidelines at the time of data collection.[14] We defined physician-estimated stroke risk as "low" (< 3%/y in FREEDOM AF, < 2%/y in CONNECT AF) and "intermediate-high" (ie, threshold for oral

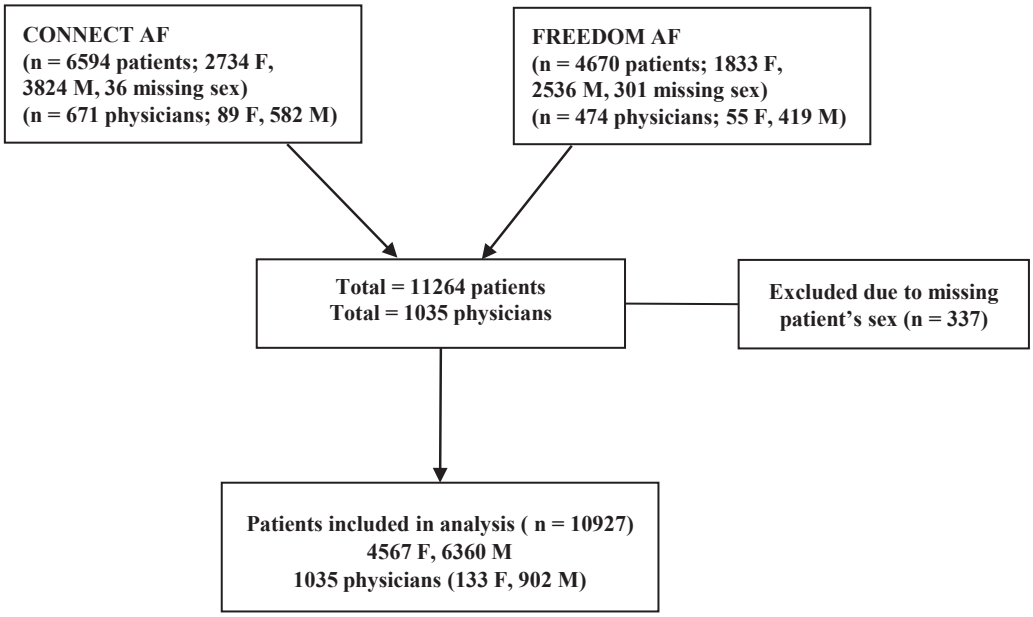


Figure 1. Study cohort. CONNECT-AF, Coordinated National Network to Engage Physicians in the Care and Treatment of Patients with Atrial Fibrillation Chart Audit; FREEDOM AF, Facilitating Review and Education to Optimize Stroke Prevention in Atrial Fibrillation.

anticoagulation); our definition of "intermediate-high" $CHADS_2$ score ≥ 2 would approximate an annual stroke risk of 4.0%.[3] Calculated risk estimates for stroke were derived from the data-collection forms for each patient using the $CHADS_2$ score[3] and defined a "high-risk" $CHADS_2$ score as ≥ 2, which estimates a stroke risk of $\geq 3\%$ to 5% per year.

We arbitrarily defined "intermediate-high" bleeding risk as a calculated HAS-BLED score of ≥ 2 (major bleeding risk of $\geq$ 2%-3% per year) because participating physicians were asked to estimate major bleeding risk as "low" if $< 2\%$ per year in CONNECT AF and $< 3\%$ per year in FREEDOM AF. Calculated risk estimates for major bleeding risk were derived from the data-collection forms for each patient using the HAS-BLED score.[4] Physicians' estimates of patient stroke and bleeding risks were grouped as "high risk," "non-high risk," "don't know," or "missing data." The Canadian AF guideline at the time of data collection recommended the use of the HAS-BLED score for estimating bleed risk.[14]

Statistical analysis

We stratified physicians and their patients by sex and compared potential differences in the baseline characteristics between physician sex and patient sex using a *P* value for interaction. We calculated the $CHADS_2$ (age, prior stroke/transient ischemic attack, hypertension, diabetes, and heart failure) and HAS-BLED (age, hypertension, prior stroke, kidney disease, liver disease, prior major bleed, heavy alcohol/drug use, nonsteroidal anti-inflammatory drug/antiplatelet, and time in therapeutic range [TTR] $< 60\%$) scores to estimate stroke and bleeding risks, respectively. We used $CHADS_2$ score ≥ 2 and HAS-BLED score ≥ 2 to define high stroke and bleeding risks, respectively. These values were then compared with the physician-reported risk estimates using the kappa statistic, which measures inter-rater agreement for categorical items after accounting for possible agreement occurring by chance.

Although FREEDOM AF and CONNECT AF had similar study designs and populations, some variables collection differed and 110 physicians participated in both studies; thus, 1145 clustering sites from both studies were used as a random effect in the multivariable logistic regression models to determine which patient characteristics might have influenced physicians' perception of their patients' risks of stroke and bleeding, and how this impact might differ according to patient sex and physician sex. In addition to patients' risk factors for stroke and bleeding (components of $CHADS_2$ and HAS-BLED risk scores), these models included physician sex, patient sex, interaction between physician and patient sex, interaction between risk factors and patient sex, and interaction between risk factors and physician sex. In the stroke risk multivariable model, the risk factors included those 5 variables listed, which are used to calculate the $CHADS_2$ risk score, whereas the bleeding risk model included the 9 variables mentioned, which are used to calculate the HAS-BLED scores. Data were also stratified to assess whether patient or physician sex influenced risk estimation.

Continuous variables were summarized as median (interquartile range) or mean and standard deviation, and categorical variables were summarized as percentages and frequencies. The data were analyzed with SAS software v. 9.4 (SAS Institute, Inc, Cary, NC).

Results

Baseline characteristics in women and men

Of the 1035 participating physicians, 133 were female and 902 were male. Of the 10,927 patients, 4567 were female and 6360 were male (Fig. 1). Baseline characteristics of the study population are presented in Table 1. Regardless

Table 1. Baseline patient characteristics

	Male physicians (n = 902)			Female physicians (n = 133)			*P* value for interaction (between physician sex and patient sex)
	Female patients (n = 3819)	Male patients (n = 5743)	*P* value	Female patients (n = 748)	Male patients (n = 617)	*P* value	
Age (y) mean ± SD	79 ± 9.35	74 ± 10.13	< 0.001	78 ± 10.14	75 ± 10.73	< 0.001	0.11
Age ≥ 75 y (%)	71.7	52.9	< 0.001	67.4	54.0	< 0.001	0.04
Age ≥ 65 y (%)	90.3	80.8	< 0.001	88.6	80.0	< 0.001	0.46
AF duration (y) median (Q1, Q3)	5 (3-10)	5 (3-10)	0.03	5 (2-10)	5 (3-10)	0.14	0.79
Weight (kg) Mean ± SD	72.1 ± 18.02	88.7 ± 19.22	< 0.001	72.1 ± 19.17	87.8 ± 19.94	< 0.001	0.50
Heart failure (%)	20.8	19.8	0.23	19.5	25.9	0.005	0.002
Hypertension (%)	71.6	65.2	< 0.001	75.0	74.2	0.74	0.05
Diabetes (%)	25.4	29.2	< 0.001	25.1	34.7	< 0.001	0.03
Prior stroke/TIA (%)	23.6	20.1	< 0.001	23.3	23.0	0.91	0.16
Current warfarin (%)	72.1	69.8	0.01	68.0	68.6	0.84	0.28
Other anticoagulation (%)	20.9	21.3	0.60	23.0	23.0	0.99	0.85
TTR > 60%	1680/2610	2553/3831	0.06	336/493	266/403	0.50	0.19
Coronary disease (%)	27.8	36.7	< 0.001	25.7	35.7	< 0.001	0.63
Peripheral artery disease (%)	7.2	8.8	0.004	4.4	10	< 0.001	< 0.01
Kidney disease (eGFR < 60 mL/min/1.73 m^2)	26.7	20.1	< 0.001	27.9	23.8	0.08	0.25
Liver disease (%)	0.6	1.1	0.01	1.3	2.8	0.06	0.80
Prior major bleeding (%)	7.6	7.1	0.30	8.8	10.9	0.21	0.12
Heavy alcohol/drug use (%)	2.7	7.7	< 0.001	2.4	7.8	< 0.001	0.64
Smoking, current or former (%)	25.7	49.9	< 0.001	25.1	52.9	< 0.001	0.43
NSAID/antiplatelet use (%)	22.2	28.7	< 0.001	19.0	28.4	< 0.001	0.20
$CHADS_2$ score median (mean ± SD)	2.36 ± 1.27	2.07 ± 1.3	< 0.001	2.33 ± 1.27	2.34 ± 1.32	0.90	< 0.001
HAS-BLED score median (mean ± SD)	2.2 ± 1.05	2.08 ± 1.13	< 0.001	2.13 ± 1.05	2.19 ± 1.14	0.34	0.005

AF, atrial fibrillation; $CHADS_2$, **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack; eGFR, estimated glomerular filtration rate; HAS-BLED, **H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history, **L**abile international normalized ratio, **E**lderly, **D**rugs/alcohol; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation; TIA, transient ischemic attack; TTR, time in therapeutic range.

of physician sex, female patients were more likely to be aged more than 75 years (71% vs 53%, $P < 0.001$) (or alternatively, can just use overall mean age 78 ± 9 vs 74 ± 10 years, $P < 0.001$). There was a statistically significant interaction ($P = 0.002$) between physician and patient sex, with the highest proportion of heart failure in male patients of female physicians. Male patients of male physicians had a statistically significant lower rate of hypertension and stroke (both $P < 0.001$).

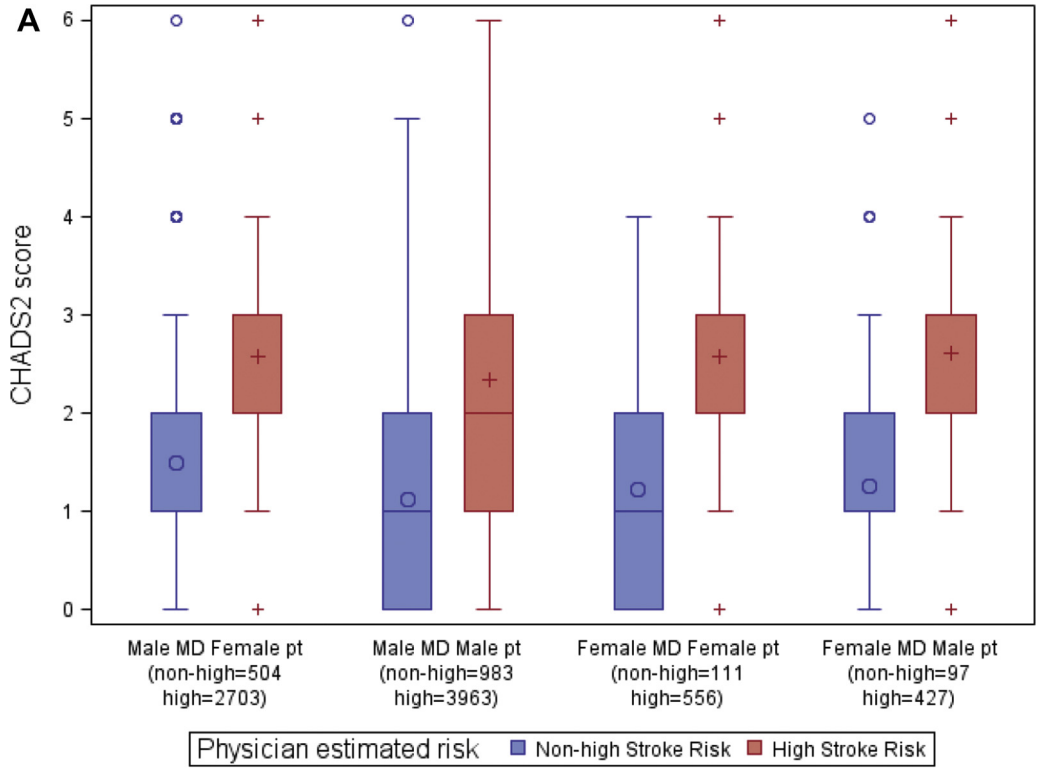
Within the female physician group, the mean $CHADS_2$ scores were 2.33 for female patients and 2.34 for male patients ($P = 0.86$). Within the male physician group, the mean $CHADS_2$ scores were 2.36 for female patients and 2.07 for male patients ($P < 0.001$). The $CHADS_2$ scores were similar between patient sexes within the female physician group, whereas the $CHADS_2$ score was significantly higher in female patients than male patients within the male physician group. That is, the relationships between $CHADS_2$ score and patient sex were actually different according to physician sex; this is indicated by the significant *P* for interaction (< 0.001). Similar patterns were observed for HAS-BLED scores.

Stroke risk stratification

PCPs estimated a > 2% per year stroke risk in 7649 patients (70.0%) of the overall 10,927 study population, with a sex-specific distribution of 3259 female patients (71.4%) and 4390 male patients (69.0%) (data not shown). By using a standard risk score estimation, 7558 patients (69.2%) had a $CHADS_2$ score ≥ 2, with this level of risk calculated in 3407 female patients (74.6%) and 4151 male patients (65.3%) (data not shown). The agreement between calculated $CHADS_2$ score and physician-estimated stroke risk is shown in Figure 2A.

Male physicians estimated "high risk" of stroke in 70.8% of their 3819 female patients and 69.0% of their 5743 male patients. Female physicians estimated "high stroke risk" in 74.3% of their 748 female patients and 69.2% of their 617 male patients. Among female physicians, the proportion of female patients estimated as "high risk" compared with male patients was higher than the proportion among male physicians ($p_{interaction} < 0.01$). In patients cared for by male physicians, when a formal risk calculation tool was used to determine the proportion of patients at higher risk of stroke ($CHADS_2$ score), 74.7% of their female patients and 64.4% of their male patients were deemed "high risk." In contrast, calculated $CHADS_2$ scores suggested 74.3% of female patients cared for by female physicians and 73.7% of their male patients were at high stroke risk. Among female physicians, the proportion of female patients calculated as "high risk" compared with male patients was higher than the proportion among male physicians ($p_{interaction} = 0.01$) (Table 2).

The overall kappa score between physician-estimated and calculated stroke risk was 0.35 (0.33-0.37) for all patients, 0.33 (0.30-0.37) for female patients, and 0.35 (0.33-0.38) for male patients (Table 3). Patients of female physicians had a kappa score of 0.41 (0.35-0.47) vs 0.34 (0.32-0.36) for patients of male physicians. Female physicians had moderate agreement in their female patients between estimated "high stroke risk" and calculated $CHADS_2$ score ≥ 2 (kappa 0.41, 95% confidence interval [CI], 0.33-0.49), as well as moderate agreement in their male patients (kappa 0.41, 95% CI, 0.32-0.50). Male physicians had fair agreement for their female patients (kappa 0.32, 95% CI, 0.28-0.35) and male patients (kappa 0.35, 95% CI, 0.32-0.37).



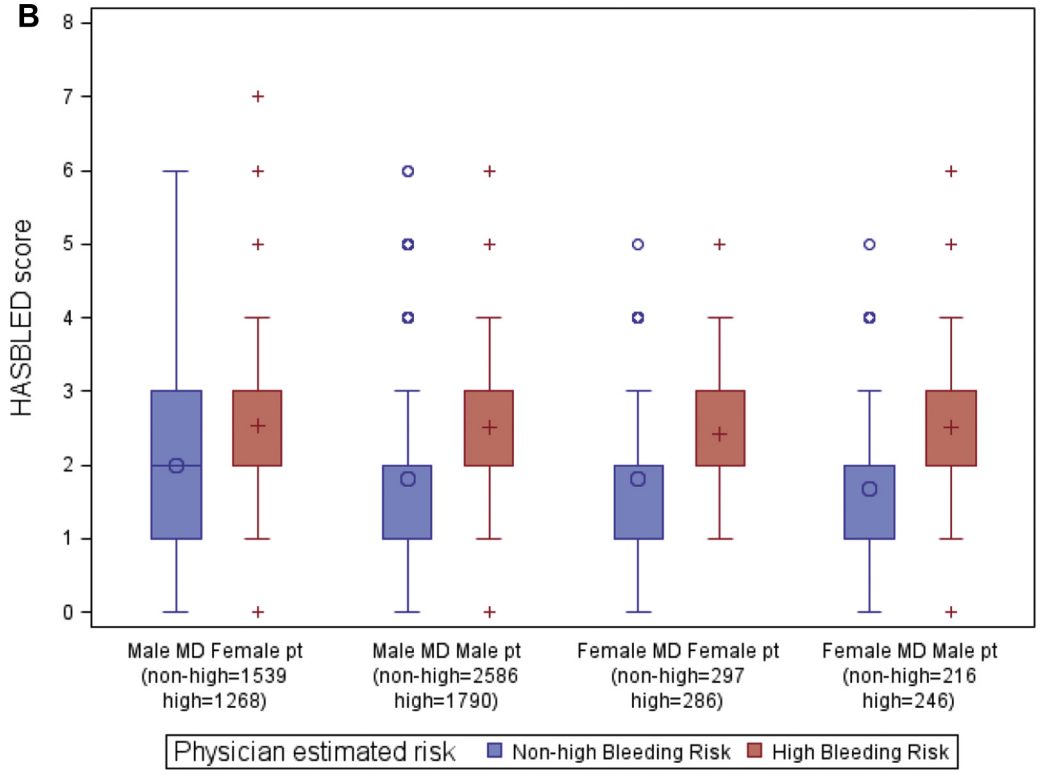


Figure 2. (**A**) Calculated **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack ($CHADS_2$) $\geq$ 2 score vs physician-estimated high stroke risk. (**B**) Calculated **H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history, **L**abile international normalized ratio, **E**lderly, **D**rugs/alcohol (HAS-BLED) score vs physician-estimated high bleeding risk.

Table 2. Estimated vs calculated high risk of stroke ($CHADS_2 \geq 2$) and major bleeding (HAS-BLED ≥ 2)

	Male physicians (n = 902)			Female physicians (n = 133)			*P* value for interaction (between physician sex and patient sex)
	Female patients (n = 3819)	Male patients (n = 5743)	*P* value	Female patients (n = 748)	Male patients (n = 617)	*P* value	
Physician-estimated* high-risk stroke (%)	70.8	69.0	< 0.001	74.3	69.2	0.05	< 0.01
Calculated high risk ($CHADS_2$) (%)	74.7	64.4	< 0.001	74.3	73.7	0.81	< 0.01
Physician-estimated* high-risk bleed (%)	33.2	31.2	< 0.001	38.2	39.9	0.17	< 0.001
Calculated high risk (HAS-BLED) (%)	73.9	67.3	< 0.001	69.4	72.0	0.30	< 0.001
Any anticoagulation (%)	92.9	90.9	< 0.001	90.9	90.8	0.93	0.21
Warfarin (%)	72.1	69.8	0.01	68.0	68.6	0.84	0.28
Other anticoagulation (%)	20.9	21.3	0.60	23.0	23.0	0.99	0.85
TTR > 60%†	1680/2610	2553/3831	0.06	336/493	266/403	0.50	0.19

Physician-estimated high risk for stroke and major bleeding was defined as ≥ 3%/y in FREEDOM AF but ≥ 2%/y for both risks in CONNECT AF. Calculated high-risk scores were defined as $CHADS_2 \geq 2$ and HAS-BLED ≥ 2.

$CHADS_2$, **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack; HAS-BLED, **H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history, **L**abile international normalized ratio, **E**lderly, **D**rugs/alcohol; TTR, time in therapeutic range.

*High risk (vs not high risk/don't know/missing information).

†Using up to 6 of the most recently available international normalized ratio values, estimates of the TTR were established with the therapeutic range defined as an international normalized ratio range from 2 to 3.

Multivariable analysis showed that female patients tended to be more likely categorized as high stroke risk compared with male patients (adjusted odds ratio, 3.01; 95% CI, 1.15-8.02; $P = 0.02$), regardless of physician sex. Independent predictors associated with physician-estimated high stroke risk included history of heart failure, hypertension, age, diabetes, and history of transient ischemic attack/stroke (all $P < 0.001$).

Major bleeding risk stratification

PCPs estimated a > 2% per year risk of major bleeding in 3590 patients (32.9%): 1554 female patients (34.0%) and 2036 male patients (32.0%) (data not shown). In comparison, 7650 patients (70.0%) had a HAS-BLED score ≥ 2 (ie, major bleed risk > 2% per year), including 3340 female patients (73.1%) and 4310 male patients (67.8%) (data not shown). Risk estimates by patient and physician sex are summarized in Table 2. The agreement between HAS-BLED score and physician-estimated bleeding risk is shown in Figure 2B.

The overall kappa score between physician-estimated and calculated bleeding risk was 0.19 (0.17-0.21) and 0.17 (0.14-0.20) in female patients and 0.21 (0.18-0.23) in male patients (Table 3). Overall kappa scores were 0.28 (0.22-0.33) for female physicians and 0.18 (0.16-0.20) for male physicians. Female physicians had fair agreement for their female patients, between estimated "high major bleeding risk" and HAS-BLED score ≥ 2 (kappa 0.27, 95% CI, 0.20-0.35), and

Table 3. Kappa analysis for physician-estimated high-risk vs calculated $CHADS_2 \geq 2$ and HAS-BLED ≥ 2 risks

	Physician-estimated stroke risk vs calculated $CHADS_2$ score Kappa coefficient (95% CI)	Agreement	Physician-estimated major bleeding risk vs calculated HAS-BLED score Kappa coefficient (95% CI)	Agreement
All patients	0.35 (0.33-0.37)	Fair	0.19 (0.17-0.21)	Slight
All female patients	0.33 (0.30-0.37)	Fair	0.17 (0.14-0.20)	Slight
All male patients	0.35 (0.33-0.38)	Fair	0.21 (0.18-0.23)	Fair
Patients of female physicians	0.41 (0.35-0.47)	Moderate	0.28 (0.22-0.33)	Fair
Patients of male physicians	0.34 (0.32-0.36)	Fair	0.18 (0.16-0.20)	Slight

Physician-estimated high-risk major stroke risk vs calculated CHADS2 ≥ 2 score			
Physician sex	Patient sex	Kappa coefficient (95% CI)	Agreement
Female	Female	0.41 (0.33-0.49)	Moderate
	Male	0.41 (0.32-0.50)	Moderate
Male	Female	0.32 (0.28-0.35)	Fair
	Male	0.35 (0.32-0.37)	Fair

Physician-estimated high-risk major bleeding risk vs calculated HAS-BLED ≥ 2 score			
Physician sex	Patient sex	Kappa coefficient (95% CI)	Agreement
Female	Female	0.27 (0.20-0.35)	Fair
	Male	0.28 (0.20-0.36)	Fair
Male	Female	0.15 (0.12-0.18)	Slight
	Male	0.20 (0.17-0.22)	Slight

$CHADS_2$, **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack; CI, confidence interval; HAS-BLED, **H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history, **L**abile international normalized ratio, **E**lderly, **D**rugs/alcohol.

fair agreement for their male patients (kappa 0.28, 95% CI, 0.20-0.36). Male physicians had slight agreement for their female patients (kappa 0.15, 95% CI, 0.12-0.18) and slight agreement for their male patients (kappa 0.20, 95% CI, 0.17-0.22).

Independent predictors associated with physician-estimated bleeding risk included age, hypertension, prior stroke, kidney disease, liver disease, history of major bleed, heavy alcohol/drug use, nonsteroidal anti-inflammatory drug/antiplatelet, and TTR < 60% (all $P < 0.001$), but not patient (with adjusted odds ratio, 1.87; 95% CI, 0.71-4.92 of being female patient) or physician sex.

Rates of anticoagulation

Overall, 74.6% of women and 65.3% of men met criteria for antithrombotic therapy based on $CHADS_2$ score ≥ 2 (data not shown). Of the 4567 women eligible for anticoagulation, 4229 (92.6%) were anticoagulated, compared with 5781 of 6360 men (90.9%).

Male physicians reported that of their 3819 female patients, 2851 (74.7%) had a $CHADS_2$ score ≥ 2, and overall 3549 (92.9%) were anticoagulated, whereas of their 5743 male patients, 3696 (64.4%) had a $CHADS_2$ score ≥ 2 and 5221 (90.9%) were anticoagulated (Table 2). Of the 748 female patients treated by female physicians, 556 (74.3%) had a $CHADS_2$ score ≥ 2 and 680 (90.9%) were anticoagulated, compared with 455 (73.7%) of 617 male patients with $CHADS_2$ score ≥ 2, and overall, 560 (90.8%) were anticoagulated.

Overall, the most commonly prescribed anticoagulant was warfarin. Male physicians had a TTR > 60% in 64.4% of their female patients and in 66.6% of their male patients. Female physicians had a TTR > 60% in 68.2% of female patients and 66.0% of male patients.

Discussion

The focus of this study was to describe physician decision-making in regard to anticoagulation for patients with AF at higher stroke risk. We sought to characterize whether physician decision-making was based on established risk criteria, specifically those outlined in formal stroke risk calculators (ie, $CHADS_2$ score), and whether patient and physician sex differences in risk estimation were observed. Although there were slight differences in the correlation between physician-estimated high stroke risk and calculated $CHADS_2$ score ≥ 2, with female physicians demonstrating slightly better rates of agreement, these differences were small and unlikely to be clinically relevant.

Risk of major bleeding was underestimated overall in all patients, regardless of patient or physician sex when compared with a HAS-BLED score ≥ 2. It is important to note that, according to Canadian AF guidelines in use at the time of the 2 national chart audits, the HAS-BLED score was not meant to dissuade the use of anticoagulation, but rather to identify opportunities to address potentially modifiable bleeding risk factors and to encourage closer monitoring and follow-up.[14] Prior literature has described a greater influence of stroke risk over bleeding risk on the decision to anticoagulate.[6] Given the high rates of anticoagulation in our study (> 90%), it is not surprising that this observation was also seen in our physicians' decision-making.

In our study, female patients were more likely to be estimated by physicians to be at "high stroke risk." Female sex itself has been considered an independent risk factor for thromboembolism.[12,15,16] However, more recent literature suggests the perceived differences in stroke risk are nonsignificant when female patients are appropriately anticoagulated for other stroke risk factors (ie, $CHADS_2$ components), and that the perceived disproportionality in stroke risk for women is perhaps due to sex disparity in anticoagulation.[12,17] Possible hypotheses for this discordance have included underestimation of female thromboembolic risk or overestimation of their bleeding risk.[18,19] Differences in stroke risk assessment may result in different rates of anticoagulation.[20]

In our population, there was directional discordance in the estimation of stroke risk according to physician sex. Specifically, male physicians tended to underestimate stroke risk in female patients and overestimate stroke risk in male patients, whereas female physicians tended to estimate stroke risk well in their female patients but tended to underestimate stroke risk in male patients. However, the magnitude of these differences was small; further, > 90% of patients received oral anticoagulation across all subgroups.

Although other studies have demonstrated discordance between physician-estimated and calculated risk in cardiovascular disease[21,22] and stroke risk in AF,[6,7] we believe this study is the first to examine this relationship with respect to both patient and physician sex. Steinberg et al.[6] found the association between empirical ($CHADS_2$ score) and physician-estimated stroke risk was low (kappa 0.1). Our study found female physicians had a kappa of 0.41 (0.35-0.47) compared with their male colleagues who had a kappa of 0.34 (0.32-0.36). Larger studies are needed to determine whether physician sex is associated with this apparent discordance.

Many hypotheses have been generated to explain the relationship between physician sex and quality of care. Some literature suggests that female physicians are more likely to adhere to clinical guidelines[10,23,24] and to use more patient-centered communication,[25,26] and perhaps have improved rates of hospital mortality and readmissions.[27] Data from the ambulatory care setting have suggested that differences exist between patients who seek care from male vs female physicians.[28] In our study, male patients of male physicians were the lowest risk of the 4 subgroups, with only 64% with a $CHADS_2$ score ≥ 2; all other groups (men and women followed by a female physician, and women under the care of a male physician) had > 74% of patients with $CHADS_2$ score ≥ 2. Of note, although male physicians tended to underestimate stroke risk in their female patients, this subgroup also had the highest rate of anticoagulation (92.9%).

Overall, the determination of stroke vs major bleeding risk remains challenging for physicians with potential room for improvement, especially as it relates to possible physician and patient sex influences.

Limitations

There are several limitations to be considered in this study. The patient populations between male and female physicians differed, albeit only slightly. There were a relatively smaller

number of female physicians represented in this study, and it is unknown whether they perhaps reflect a younger demographic more recently entered into clinical practice. In addition, participating physicians and patients are not a true population-based or random sample and, therefore, are not likely to be reflective of all practitioners or their patients with nonvalvular AF. Although consecutive eligible patient enrollment was encouraged, physicians provided the 10 patients with AF at their discretion. In addition, physicians were asked to include patients in both chart audits who they believed should be considered for anticoagulation, thus accounting for the high (> 90%) rate of anticoagulation. It is also unknown whether the treatment patterns we observed would change with the more widespread adoption of direct-acting oral anticoagulants; both chart audits were undertaken when direct-acting oral anticoagulants were just being introduced into clinical practice, and thus warfarin was the dominant oral anticoagulant. The focus of our analyses regarding stroke risk estimation is on the $CHADS_2$ score; although contemporary guidelines now recommend the use of the **C**ongestive Heart Failure, **H**ypertension, **A**ge ($\geq$ 75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female) score (including age $\geq$ 65 years), the $CHADS_2$ score was the most commonly used risk tool used during the time of the FREEDOM AF and CONNECT AF chart audits. Finally, because patients were not followed up in this simple chart audit, we cannot determine whether physician empirically estimated vs risk assessment scores were more accurate and how these treatment patterns would affect patient outcomes.

Conclusions

Our study is the first to examine the association between patient and physician sex influences and stroke and bleeding risk estimation in AF. Despite current clinical practices and consensus guidelines, there continues to be some disparity between sex- and evidence-based practice.

Although there were differences in agreement between physician-estimated stroke risk and calculated $CHADS_2$ scores, these differences were small and unlikely to affect clinical practice; further, despite differences in the accuracy of risk assessment by sex, most patients received anticoagulation. Further studies are needed to understand whether these sex differences are associated with differences in clinical outcomes.

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