Disagreement between physician-reported and scoring system-based stroke and bleeding risks in patients with atrial fibrillation: Insights from the Stroke Prevention and Rhythm Interventions in Atrial Fibrillation (SPRINT-AF) registry

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BACKGROUND

- Stroke prevention with oral anticoagulation (OAC) is an important treatment goal for patients with atrial fibrillation (AF), particularly those at elevated risk. However, use of OAC is associated with bleeding as well.
- Clinical practice guidelines recommend the use of validated algorithms to assess risk of stroke and risk of bleeding in patients with AF.
- Whether physician-reported stroke and bleeding risks are congruent with those derived from validated scoring schemes is unknown.
- To answer this question, we used data from the **S**troke **P**revention and **R**hythm **Int**erventions in **A**trial **F**ibrillation (SPRINT-AF) registry.

Overview of study objectives: SPRINT-AF (phase 1)

PRIMARY

- To determine how Canadian physicians assess stroke risk in adults with atrial fibrillation and make therapeutic decisions around oral anticoagulation.

SECONDARY:

- To assess the adequacy of anticoagulation in treated patients.
- To understand how new oral anticoagulants are incorporated into clinical practice.
- To evaluate regional differences in care.
- To compare management strategies between primary care physicians and cardiovascular specialists.

Inclusion criteria

- Documentation of AF (based on a 12-lead electrocardiogram (ECG), rhythm strip, or from device interrogation) within the past 36 months.
- The patient must have been assessed by the participating physician within 12 months from the date of enrollment.
- Age ≥ 18 years.

Exclusion criteria

- Presence of prosthetic heart valve or significant valvular heart disease (defined as: mitral stenosis, moderate or severe aortic stenosis, or severe mitral regurgitation).
- Active malignancy.
- Life expectancy < 12 months.
- An existing clinical indication for OAC treatment other than AF (e.g. venous thromboembolism, hypercoagulable disorders)
- Prior participation in an OAC randomized trial.

METHODS

Study Design:

- Phase 1 of SRPINT-AF was a multicenter, cross-sectional, retrospective study involving 101 clinical practices in 10 Canadian provinces.
- Subjects were recruited from December 1 2012 to July 31 2013.
- During the entire study period, Dabigatran and Rivaroxaban were included in the provincial formulary coverage plans in all Canadian provinces. There was limited provincial formulary coverage for Apixaban during the study period.
- Eligibility criteria to qualify for formulary coverage of NOAC agents varied amongst provinces.

METHODS

Statistical Analysis Plan:

- Agreement between physician-reported and score-derived risks was reported by the weighted kappa with 95% confidence intervals (CI).
- Weighted kappa values of 0.01-0.20, 0.21-0.40, 0.41-0.60, 0.61-0.80, and 0.81-0.99 represent slight, fair, moderate, good, and excellent agreement, respectively.
- The weighted kappa was used since the categorization of bleeding and stroke risk consisted of 3 levels (low, moderate, high).

Primary analysis:

- We assessed the degree of agreement between physician-reported stroke and bleeding risks vs. those derived from $CHADS_2$ and HAS-BLED, respectively.

Subgroup analysis:

- A subset of clinicians reported using the $CHADS_2$ and HAS-BLED scores to assess risk, rather than using other methods.
- We performed a pre-specified analysis in this subset to assess the degree of agreement between physician-reported and score-derived risks.

Assessment of stroke and bleeding risk

Physician-reported risks:

- In SPRINT-AF, physicians were asked to categorize patients as low, moderate, or high risk for bleeding and for stroke based on one of the following methods: i) overall clinical judgment, ii) individual patient factors, or iii) existing scoring schemes.

Centrally-calculated risks:

- Based on the baseline demographics collected, we centrally calculated the stroke and bleeding risks of each patient.
- Stroke risk was evaluated by the $CHADS_2$ scoring system. In accordance with published guidelines, risks were categorized as low (0 point), moderate (1 point), or high (≥ 2 points).
- Bleeding risk was evaluated by the HAS-BLED scoring system. In accordance with published guidelines, risks were categorized as low (0 point), moderate (1-2 points), or high (≥ 3 points).

Assessment of stroke risk in AF: $CHADS_2$

	Clinical feature	Score
C	Congestive heart failure	1
H	Hypertension	1
A	Age ≥ 75 years	1
D	Diabetes	1
S	Stroke / TIA / Thromboembolism	2
	Maximum Score	6

TIA=transient ischemic attack.

ACC/AHA/ESC guidelines: Fuster V *et al. Circulation 2006;114:e257–e354*

Assessment of bleeding risk in AF: HAS-BLED

	Clinical Characteristic	Score
H	Hypertension	1
A	Abnormal renal or liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly age	1
D	Drugs or alcohol (1 point each)	1 or 2
	Maximum Score	9

Hypertension: SBP > 160 mmHg; Abnormal renal function: Chronic dialysis, renal transplant, serum creatinine ≥ 200μmol/L; Abnormal liver function: Chronic hepatitis, bilirubin > 2x upper limit of normal (ULN) in association with AST/ALT/ALP > 3 x ULN; Bleeding: Previous history, predisposition; Labile INRs: unstable/high INRs, in therapeutic range < 60%; Age > 65 years; Drugs/alcohol: Concomitant use of antiplatelet agents, non-steroidal anti-inflammatory drugs, etc.

Pisters R, et al. *Chest* 2010;138:1093-100

Rates of stroke and bleeding according to the $CHADS_2$ and HAS-BLED scores

$CHADS_2$	Annual stroke risk (%)	HAS-BLED	Annual bleeding risk (%)
0	1.9%	0	1.1%
1	2.8%	1	1.0%
2	4.0%	2	1.9%
3	5.9%	3	3.7%
4	8.5%	4	8.7%
5	12.5%	5	12.5%
6	18.2%		

ACC/AHA/ESC guidelines: Fuster V et al. *Circulation* 2006;114:e257-e354.
Pisters R. et al. *Chest* 2010;138:1093-1100.

RESULTS

	Overall SPRINT-AF cohort (n=850)
Male (n,%)	523 (61.5%)
Caucasian (n,%)	740 (87.5%)
Age (median, IQR)	76 (67, 83)
Age ≥ 75 (n,%)	444 (52.2%)
Hypertension (n,%)	626 (73.6%)
Dyslipidemia (n,%)	519 (61.1%)
Diabetes (n,%)	246 (28.9%)
History of smoking (n,%)	390 (45.9%)
History of CAD (n,%)	213 (25.1%)
Stroke or TIA (n,%)	133 (15.6%)
PAD (n,%)	48 (5.6%)
Congestive heart failure (n,%)	164 (19.3%)
Kidney disease (n,%)	53 (6.2%)
New AF diagnosis (n,%)	30 (3.5%)
Non-paroxysmal AF (n,%)	562 (69.6%)
Anti-arrhythmic drug use (n,%)	296 (39.4%)
Recruitment from Family Medicine (n,%)	626 (73.6%)
$CHADS_2$ ≥2 (n,%)	552 (65.0%)
CHA_2DS_2-VASC ≥2 (n,%)	736 (86.7%)
HAS-BLED (n,%)	
0	75 (8.9%)
1 or 2	653 (77.3%)
≥3	117 (13.8%)
Statin use (n,%)	502 (59.1%)
PPI use (n,%)	221 (26.1%)

Table 1. Baseline demographics of patients in SPRINT-AF

AF indicates atrial fibrillation; AP, antiplatelet; CAD, coronary artery disease; IQR, interquartile range; OAC, oral anticoagulant; PAD, peripheral arterial disease; PPI, proton pump inhibitor; TIA, transient ischemic attack.

Table 2. Agreement between physician-reported stroke and bleeding risks and CHADS and HAS-BLED scores (overall cohort)

Physician-reported stroke risk — $CHADS_2$ Score

	Low (0)	Moderate (1)	High (≥2)	*Sum*
Low	57	66	21	144
Mod	20	115	199	334
High	4	33	328	365
Sum	81	214	548	843

Weighted Kappa: 0.42 (95% CI: 0.35, 0.50)

The greatest area of disagreement occurred in $CHADS_2$ ≥ 2, as 220 (40%) patients in this risk category were deemed to be at low/moderate risk for stroke by physicians.

Physician-reported bleeding risk — HAS-BLED Score

	Low (0)	Moderate (1-2)	High (≥3)	*Sum*
Low	64	293	24	381
Mod	7	274	67	348
High	3	79	26	108
Sum	74	646	117	837

Weighted Kappa: 0.14 (95% CI: 0.07, 0.21)

The greatest area of disagreement occurred at HAS-BLED 1-2 (moderate bleeding risk), as 293 (45%) of patients in this category were considered low risk for bleeding by physicians.

Table 3. Agreement between physician-reported stroke and bleeding risks and $CHADS_2$ and HAS-BLED scores *(subgroup analysis of physicians who used $CHADS_2$ and HAS-BLED to estimate stroke and bleeding risk)*

Physician-reported stroke risk — $CHADS_2$ Score

	Low (0)	Moderate (1)	High (≥2)	*Sum*
Low	52	50	15	117
Mod	12	91	149	252
High	2	30	261	293
Sum	66	171	425	662

Weighted Kappa: 0.45 (95% CI: 0.36, 0.54)

Physician-reported bleeding risk — HAS-BLED Score

	Low (0)	Moderate (1-2)	High (≥3)	*Sum*
Low	25	150	8	183
Mod	3	108	29	140
High	2	40	12	54
Sum	30	298	49	377

Weighted Kappa: 0.11 (95% CI: 0.01, 0.27)

CONCLUSIONS

- In SPRINT-AF, we observed that physicians tended to under-estimate the stroke and bleeding risks of AF patients, when calibrated against existing scoring schemes ($CHADS_2$ and HAS-BLED, respectively).
- We observed modest agreement between physician-reported stroke risk and $CHADS_2$ (weighted kappa 0.42, 95% CI: 0.35 to 0.50).
- The greatest disagreement occurred in $CHADS_2$ ≥ 2 (high stroke risk), with 40% of patients in this category deemed to be at low/moderate risk for stroke by physicians.
- We observed weak agreement between physician-reported bleeding risk and HAS-BLED (weighted kappa 0.14, 95% CI: 0.07 to 0.21).
- The greatest disagreement occurred at HAS-BLED 1-2 (moderate bleeding risk), as 45% of patients in this category were considered to be at low bleeding risk by physicians.
- Among physicians who used $CHADS_2$ and HAS-BLED to estimate patients' stroke and bleeding risk, the level of agreement with centrally-calculated scores was no better than the results of the overall cohort.

SUMMARY

- Our results suggest the possible existence of a knowledge translation and/or care gap in the estimation of stroke and bleeding risk in contemporary Canadian AF clinical practice.
- Further efforts are needed to delineate the reasons to account for the discrepancy between physician-reported and score-derived stroke/ bleeding risks.

FUNDING SOURCE

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DISCLOSURES

Dr. Ha has served on an advisory board for Bayer. Dr. Verma has received speaker's honoraria from Astrazeneca, Bayer, Boeringher Ingelheim, Merck, Pfizer, Sanofi, and Takeda, has served on advisory boards for Astrazeneca, Bayer, Boeringher Ingelheim, Sanofi, Merck, Pfizer, and Takeda, and has received research funding from Bayer. Dr. Cox has received consulting fees and speaker's honoraria from Bayer, Boehringer Ingelheim, Bristol-Myers-Squibb, Pfizer and has received research funding from Bayer. Dr. Dorian has received consulting fees and research funding from Bayer, Boehringer-Ingelheim, Bristol-Myers-Squibb, Pfizer, and Sanofi. Dr. Fournier has served on advisory boards for Amgen, Astrazeneca, Boeringher Ingelheim, Bristol-Myers-Squibb, Forest Laboratories, Janssen, Merck, Novo Nordisk Canada, Sanofi, Takeda, Valeant Canada and has received speaker's honoraria from Amgen, Astrazeneca, Boeringher Ingelheim, Bristol-Myers-Squibb, Eli-Lilly, Forest Laboratories, GlaxoKlineSmith, Merck, Sanofi and Valeant Canada. Dr. Lockwood has received consulting fees and speaker's honoraria from Bayer, Boehringer Ingelheim, Bristol-Myers-Squibb, and Pfizer, research support from Medtronic and St. Jude Medical, and fellowship support from St. Jude Medical. Dr. Singh has received speaker's honoraria from Boeringher Ingelheim and Bristol-Myers-Squibb and has received research funding from Boeringher Ingelheim and Janssen. Dr. Gupta has received consulting fees and research funding from Bayer, Bristol-Myers-Squibb, and Pfizer. The other authors have no disclosures to report.

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