Factors associated with new oral anticoagulant versus vitamin K antagonist use in 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 in those at elevated risk.
- Novel oral anticoagulants (NOAC) have revolutionized OAC use in the current era. Presently, 3 NOAC agents are available in Canada for AF stroke prevention (Dabigatran, Rivaroxaban, Apixaban).
- Currently, little is known with regards to how clinical, patient-, and physician- factors influence the use of vitamin K antagonist (VKA) vs. NOAC for AF stroke prevention in contemporary Canadian clinical practice.

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

PRIMARY

- To determine how Canadian physicians assess stroke risk in adults with AF and make therapeutic decisions with respect to 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.

Statistical Analysis Plan:

- To assess for factors associated with VKA vs. NOAC use, we performed a multivariable logistic regression model.
- The primary outcome (binary) was use of VKA or NOAC at the end of the most recent clinic visit.
- A backward elimination algorithm was performed to identify factors associated VKA vs. NOAC use in the final model, with the significance level for staying in the model set at $p<0.05$.
- Statistical measures of significance were reported as odds ratios (OR) with 95% confidence intervals (CI).
- The reported OR denotes the ratio of the odds of warfarin use vs. NOAC use (VKA / NOAC).

RESULTS

- Of the 850 subjects enrolled in phase 1 of SPRINT-AF, 705 (87.3%) subjects were treated with OAC.
- Amongst those treated with OAC, 369 (52.3%) subjects were treated with VKA and 336 (47.7%) were treated with NOAC agents.

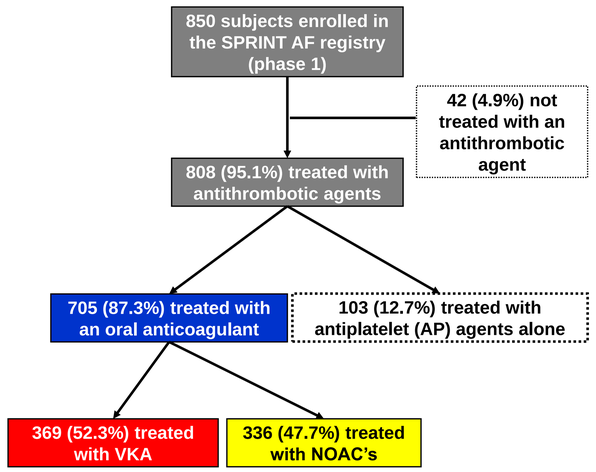

Figure 1. Study flowchart.

RESULTS

	VKA (n=369)	NOAC (n=336)	P-value
Male (n,%)	222 (60.2%)	202 (60.1%)	1.0
Age (median, IQR)	78 (71, 83)	76 (67, 83)	0.006
Age ≥75 (n,%)	224 (60.7%)	177 (52.7%)	0.033
Hypertension (n,%)	281 (76.2%)	261 (77.7%)	0.655
Dyslipidemia (n,%)	237 (64.2%)	216 (64.3%)	1.0
Diabetes (n,%)	125 (33.9%)	92 (27.4%)	0.072
History of smoking (n,%)	179 (48.5%)	143 (42.6%)	0.130
History of CAD (n,%)	114 (30.9%)	75 (22.3%)	0.011
Previous ACS (n,%)	87 (23.6%)	40 (11.9%)	<0.001
Previous PCI (n,%)	41 (11.1%)	29 (8.6%)	0.314
Previous CABG (n,%)	39 (10.6%)	23 (6.8%)	0.085
Stroke or TIA (n,%)	68 (18.4%)	50 (14.9%)	0.226
PAD (n,%)	22 (6%)	21 (6.2%)	0.876
Congestive heart failure (n,%)	87 (23.6%)	67 (19.9%)	0.273
Kidney disease (n,%)	29 (7.9%)	18 (5.4%)	0.227
Non-paroxysmal AF (n,%)	279 (79.3%)	213 (66.4%)	<0.001
Rhythm control (n,%)	105 (32.3%)	128 (43.1%)	0.006
$CHADS_2$≥ 2 (n,%)	282 (76.6%)	221 (65.8%)	0.005
CHA_2DS_2-VASC ≥2 (n,%)	349 (94.8%)	300 (89.3%)	0.019
HAS-BLED (n,%)			<0.001
0	10 (2.7%)	43 (13%)	
1-2	286 (77.5%)	266 (80.1%)	
≥3	73 (19.8%)	23 (6.9%)	
History of significant bleed (n,%)	24 (6.5%)	25 (7.4%)	0.668
Recruitment from Family Medicine practice (n,%)	282 (76.4%)	255 (75.9%)	0.930
Statin use (n,%)	230 (62.3%)	210 (62.5%)	1.0
NSAID use (n,%)	9 (2.4%)	18 (5.4%)	0.050
PPI use (n,%)	97 (26.3%)	100 (29.9%)	0.313

Table 1. Baseline demographics of patients treated with VKA vs. NOAC. *ACS indicates acute coronary syndrome; AF, atrial fibrillation; AP, antiplatelet; CABG, coronary artery bypass surgery; CAD, coronary artery disease; CNS, central nervous system; IQR, interquartile range; NOAC, new oral anticoagulant; NSAID, non-steroidal anti-inflammatory drug; OAC, oral anticoagulant; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PPI, proton pump inhibitor; TIA, transient ischemic attack.*

	VKA (n=369)	NOAC (n=336)	P-value
Decision to prescribe warfarin vs. NOAC:			
Better side effect profile (n,%)	30 (8.1%)	131 (39%)	<0.001
Improved efficacy (n,%)	174 (47.2%)	206 (61.3%)	<0.001
Lower costs (n,%)	222 (60.2%)	89 (26.5%)	<0.001

Table 2. Decision influencing choice of VKA vs. NOAC.

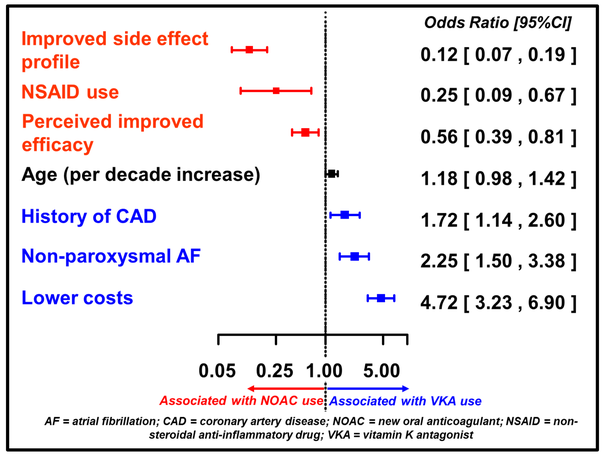

Figure 2. Factors associated with VKA vs. NOAC use.

The odds ratio was expressed as (odds of VKA/odds of NOAC use). An OR <1 indicated that the covariate was associated with NOAC use where as an OR > 1 indicated that the covariate was associated with VKA use.

RESULTS

	Unadjusted analysis			Multivariable logistic regression analysis		
Covariate	OR	95% CI	P-value	OR	95% CI	P-value
Age (per decade increase)	1.24	1.06 to 1.44	0.006	-	-	-
History of CAD	1.56	1.11 to 2.18	0.012	1.72	1.14 to 2.60	0.009
Antiplatelet use	1.71	1.16 to 2.52	0.006	-	-	-
Non-paroxysmal AF	1.94	1.37 to 2.74	<0.001	2.25	1.50 to 3.38	<0.001
Anti-arrhythmic drug use	0.63	0.45 to 0.87	0.006	-	-	-
$CHADS_2$ ≥2 (vs. 0)	2.15	1.13 to 4.10	0.019	-	-	-
Improved side effect *(as perceived by the patient)*	0.14	0.09 to 0.21	<0.001	0.12	0.07 to 0.19	<0.001
Improved efficacy *(as perceived by the clinician)*	0.56	0.42 to 0.76	<0.001	0.56	0.39 to 0.81	0.002
Lower costs	4.19	3.05 to 5.77	<0.001	4.72	3.23 to 6.90	<0.001
NSAID use	0.44	0.19 to 0.99	0.048	0.25	0.09 to 0.67	0.006

Table 3. Unadjusted and adjusted odds ratio for factors associated with VKA vs. NOAC use.

The odds ratio was expressed as (odds of VKA/odds of NOAC use). An OR <1 indicated that the covariate was associated with NOAC use where as an OR > 1 indicated that the covariate was associated with VKA use.

SUMMARY AND CLINICAL IMPLICATIONS

- In this contemporary national registry, NOAC agents are prescribed in about 50% of the enrolled subjects.
- Improved side effect profile, as perceived by the patient, was strongly associated with NOAC use (vs. VKA) (OR 0.12, 95% CI: 0.07 to 0.19, $p<0.01$). Lower cost was strongly associated with VKA use (vs. NOAC) (OR 4.72, 95% CI: 3.23 to 6.90, $p<0.01$). These findings suggested that patient-based preferences were important factors in the choice of OAC that was prescribed.
- Improved efficacy, as perceived by the clinician, was associated with NOAC use (vs. VKA use) (OR 0.56, 95% CI: 0.39 to 0.81, $p<0.01$). This suggested that the results of randomized clinical trials comparing NOAC vs. VKA for AF stroke prevention had been effectively translated into clinical practice.
- After adjustment of baseline antiplatelet (AP) use, a history of coronary artery disease was associated with VKA use (vs. NOAC) (OR 1.72, 95% CI: 1.14 to 2.60, $p<0.01$).
- The prescription patterns of OAC + AP in contemporary clinical practice deserve further analysis.

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DISCLOSURES

Dr. Gupta has received consulting fees and research funding from Bayer, Bristol-Myers-Squibb, and Pfizer. Dr. Ha has served on an advisory board for 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. 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. The other authors have no disclosures to report.

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