

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

Michael G. Fradley, MD,^a Kerry Ellenberg, BS,^b Mohammed Alomar, MD,^b Justin Swanson, MPH,^c Anant Kharod, MD,^b Anh Thy H. Nguyen, MSPH,^c Sara Khodor, MD,^b Shreya Mishra, MD,^b Linh M. Duong, MPH, MS,^c Nirav Shah, BS,^b Merna Armanious, MD,^b Isaac B. Rhea, MD,^b Matthew B. Schabath, PhD,^d Kevin E. Kip, PhD^c

ABSTRACT

BACKGROUND Atrial fibrillation (AF) is a common cardiovascular complication affecting patients with cancer, but management strategies are not well established.

OBJECTIVES The purpose of this retrospective cohort study was to evaluate cross-sectional patterns of anticoagulation (AC) use in patients with cancer with AF or atrial flutter (AFL) on the basis of their risk for stroke and bleeding.

METHODS Patients with cancer and electrocardiograms showing AF or AFL performed at Moffitt Cancer Center in either the inpatient or outpatient setting were included in this retrospective analysis. We described percentages of AC prescription by stroke and bleeding risk, as determined by individual CHA₂DS₂-VASc and HAS-BLED scores, respectively. Multivariable logistic regression evaluated clinical variables independently associated with anticoagulant prescription.

RESULTS The prevalence of electrocardiography-documented AF or AFL was 4.8% (n = 472). The mean CHA₂DS₂-VASc score was 2.8 ± 1.4. Among patients with CHA₂DS₂-VASc scores ≥2 and HAS-BLED scores <3, 44.3% did not receive AC, and of these, only 18.3% had platelet values <50,000/μL. In multivariable analysis, older age, hypertension, prior stroke, and history of venous thromboembolism were each directly associated with AC use, while current chemotherapy use, prior bleeding, renal disease, and thrombocytopenia were each inversely associated with AC use.

CONCLUSIONS Nearly one-half of patients with cancer, the majority with normal platelet counts, had an elevated risk for stroke but did not receive AC. In addition to known predictors, current chemotherapy use was independently associated with a lower odds of AC use. This study highlights the need to improve the application of AF treatment algorithms to cancer populations. (J Am Coll Cardiol CardioOnc 2020;2:747-54) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

TABLE 1 Baseline Characteristics According to Anticoagulation Status				
	Total (N = 472)	No AC (n = 259)	AC (n = 213)	p Value
Age (yrs)	73.0 ± 10.4	70.5 ± 11.4	76.0 ± 9.1	<0.001
Female	152 (32.2)	84 (32.4)	68 (31.9)	0.883
Hypertension	291 (61.7)	138 (53.3)	153 (71.8)	<0.001
Heart failure	37 (7.8)	14 (5.4)	23 (10.8)	0.031
Prior atrial fibrillation	216 (45.8)	79 (30.5)	137 (64.3)	<0.001
Diabetes	114 (24.2)	58 (22.4)	56 (26.3)	0.286
Prior stroke	37 (7.8)	12 (4.6)	25 (11.7)	0.004
Vascular disease	96 (20.3)	47 (18.1)	49 (23.0)	0.192
Renal disease	23 (4.9)	17 (6.6)	6 (2.8)	0.060
Liver disease	4 (0.8)	3 (1.2)	1 (0.5)	0.417
Prior major bleed	80 (16.9)	73 (28.2)	7 (3.3)	<0.001
Labile INR	5 (1.1)	2 (0.8)	3 (1.4)	0.413
VTE	33 (7.0)	13 (5.0)	20 (9.4)	0.095
Chemotherapy, current use	232 (49.2)	151 (58.3)	81 (38.0)	<0.001
Chemotherapy, not current but in prior 3 months	53 (11.2)	30 (11.6)	23 (10.8)	0.903
Perioperative atrial fibrillation	133 (28.2)	92 (35.5)	41 (19.2)	<0.001
NSAID	97 (20.6)	60 (23.2)	37 (17.4)	0.151
Ibrutinib	4 (0.8)	4 (1.5)	0 (0)	0.188
Platelet count <50,000/μl	63 (13.3)	61 (23.6)	2 (0.9)	<0.001
Karnofsky score	90 (70-90)	90 (70-90)	90 (80-90)	0.509
LVEF (%)*	63 (58-63)	63 (58-63)	63 (58-63)	0.301
Brain metastases	8 (1.7)	7 (2.7)	1 (0.5)	0.131
Cancer type				
Heme	116 (24.6)	92 (35.5)	24 (11.3)	<0.001
GI	73 (15.5)	39 (15.1)	34 (16.0)	0.887
Cutaneous	66 (14.0)	22 (8.5)	44 (20.7)	<0.001
GU	66 (14.0)	31 (12.0)	35 (16.4)	0.209
Lung	63 (13.3)	33 (12.7)	30 (14.1)	0.771
Breast	22 (4.7)	11 (4.2)	11 (5.2)	0.802
GYN	11 (2.3)	5 (1.9)	6 (2.8)	0.742
Sarcoma	11 (2.3)	3 (1.2)	8 (3.8)	0.120
Other	44 (9.3)	23 (8.9)	21 (9.9)	0.838
CHA ₂ DS ₂ -VASc score	2.8 ± 1.4	2.4 ± 1.4	3.2 ± 1.3	<0.001
CHA ₂ DS ₂ -VASc score ≥2	389 (82.4)	193 (74.5)	196 (92.0)	<0.001
HAS-BLED score	1.7 ± 0.9	1.7 ± 1.1	1.7 ± 0.8	0.788
HAS-BLED score ≥3	95 (20.1)	64 (24.7)	31 (14.6)	0.006
Values are mean ± SD, n (%), or median (interquartile range). *Echocardiographic data were available for 230 of the 472 patients. AC = anticoagulation; GI = gastrointestinal; GU = genitourinary; GYN = gynecologic; Heme = hematologic; INR = international normalized ratio; LVEF = left ventricular ejection fraction; NSAID = nonsteroidal anti-inflammatory drug; VTE = venous thromboembolism.				

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

TABLE 2 Clinical Variables According to Anticoagulation Status in Patients With CHA₂DS₂-VASc Scores ≥2 and HAS-BLED Scores <3: Full Cohort (N = 296)

	Total (N = 296)	No AC (n = 131)	AC (n = 165)	p Value
Age (yrs)	74.9 ± 8.3	73.8 ± 8.8	76.2 ± 7.6	0.003
Female	123 (41.6)	64 (48.9)	59 (35.8)	0.020
Hypertension	194 (65.5)	74 (56.5)	120 (72.7)	0.004
Heart failure	25 (8.4)	7 (5.3)	18 (10.9)	0.091
Prior atrial fibrillation	143 (48.3)	39 (29.8)	104 (63.0)	<0.001
Diabetes	81 (27.4)	34 (26.0)	47 (28.5)	0.634
Prior stroke	29 (9.8)	10 (7.6)	19 (11.5)	0.265
Vascular disease	61 (20.6)	25 (19.1)	36 (21.8)	0.564
Renal disease	8 (2.7)	5 (3.8)	3 (1.8)	0.293
Liver disease	3 (1.0)	2 (1.5)	1 (0.6)	0.433
Prior major bleed	27 (9.1)	26 (19.8)	1 (0.6)	<0.001
Labile INR	3 (1.0)	2 (1.5)	1 (0.6)	0.476
VTE	21 (7.1)	7 (5.3)	14 (8.5)	0.404
Chemotherapy, current use	142 (48.0)	77 (58.8)	65 (39.4)	<0.001
Chemotherapy, noncurrent, prior 3 months	36 (12.2)	18 (13.7)	18 (10.9)	0.592
Perioperative atrial fibrillation	81 (27.4)	47 (35.9)	34 (20.6)	0.006
NSAID	34 (11.5)	20 (15.3)	14 (8.5)	0.108
Ibrutinib	2 (0.7)	2 (1.5)	0 (0)	0.383
Platelet count <50,000/μl	26 (8.8)	24 (18.3)	2 (1.2)	<0.001
Karnofsky score	80 (70–90)	80 (70–90)	90 (70–90)	0.682
LVEF (%)	60 (58–63)	63 (58–63)	58 (58–63)	0.512
Brain metastases	5 (1.7)	4 (3.1)	1 (0.6)	0.246
Cancer type				
Heme	65 (22.0)	45 (34.4)	20 (12.1)	<0.001
GI	49 (16.6)	20 (15.3)	29 (17.6)	0.688
Cutaneous	41 (13.9)	8 (6.1)	33 (20.0)	<0.001
GU	41 (13.9)	15 (11.5)	26 (15.8)	0.357
Lung	40 (13.5)	19 (14.5)	21 (12.7)	0.805
Breast	16 (5.4)	8 (6.1)	8 (4.8)	0.841
GYN	10 (3.4)	4 (3.1)	6 (3.6)	0.783
Sarcoma	10 (3.4)	3 (2.3)	7 (4.2)	0.541
Other	25 (8.4)	10 (7.6)	15 (9.1)	0.797

Values are mean ± SD, n (%), or median (interquartile range).
Abbreviations as in Table 1.

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

TABLE 3 Clinical Variables Associated With Anticoagulation Prescription in Multivariable Logistic Regression Analysis: Full Cohort (N = 472)*

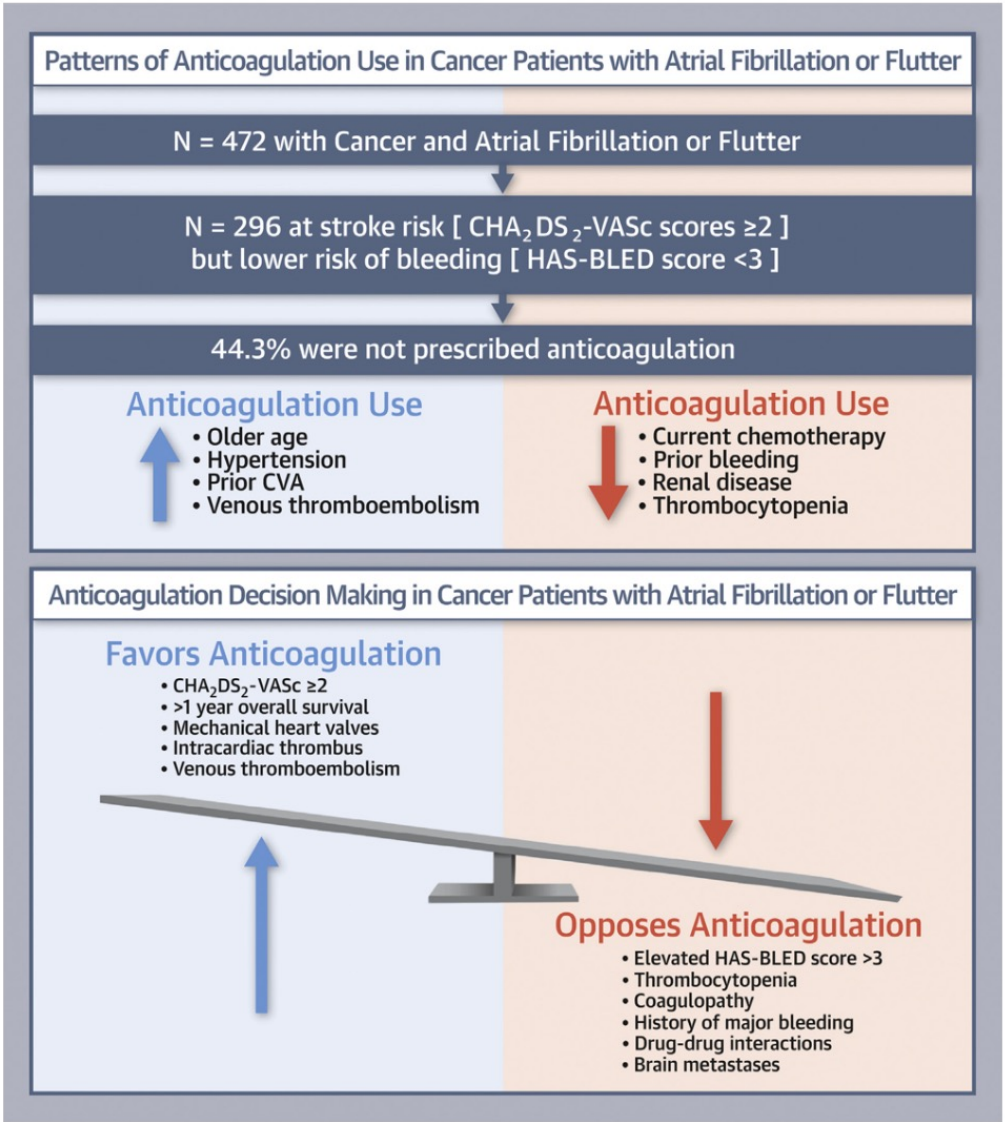
Covariate	Adjusted Odds Ratio (95% CI)
Age 65–74 yrs (vs. <65 yrs)	2.04 (1.01–4.25)
Age ≥75 yrs (vs. <65 yrs)	2.65 (1.30–5.52)
Gender (female vs. male)	0.74 (0.44–1.22)
Hypertension	2.50 (1.50–4.22)
Heart failure	2.38 (0.95–6.29)
Prior atrial fibrillation	3.02 (1.86–4.96)
Diabetes	0.84 (0.47–1.48)
Prior stroke	1.67 (1.03–2.82)
Vascular disease	0.82 (0.44–1.51)
Renal disease	0.24 (0.07–0.77)
Liver disease	0.89 (0.03–12.39)
Prior major bleeding	0.09 (0.03–0.23)
Labile INR	1.09 (0.13–12.22)
VTE	2.83 (1.04–8.24)
Chemotherapy, current use (vs. no use)	0.55 (0.32–0.93)
Chemotherapy, noncurrent, prior 3 months (vs. no use)	0.50 (0.24–1.05)
Perioperative atrial fibrillation	0.38 (0.22–0.65)
NSAID	0.31 (0.17–0.56)
Ibrutinib†	—
Platelet count <50,000/μl	0.10 (0.01–0.38)
Karnofsky score	1.00 (0.97–1.03)
LVEF	0.99 (0.94–1.04)
Brain metastases	0.12 (0.01–0.93)

*All variables listed in the table were included in the multivariable model; all variables were categorized as binary (yes or no), with the exception of age, categorized as <65 years, 65 to 74 years, or ≥75 years; Karnofsky score, categorized as 0 to 100; and LVEF, categorized as 0 to 100. All cancer subtypes indicated in **Tables 1** and **2** were also included in the model to control for confounding. †None of the patients treated with ibrutinib were prescribed anticoagulation.

CI = confidence interval; other abbreviations as in **Table 1**.

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

CENTRAL ILLUSTRATION Anticoagulation Decision Making in Cancer Patients With Atrial Fibrillation



Fradley, M.G. et al. J Am Coll Cardiol CardioOnc. 2020;2(5):747-54.

Anticoagulation for atrial fibrillation-related thromboembolism prophylaxis can be challenging in patients with concurrent cancer. In this population, decision making must be individualized weighing factors that promote the use of anticoagulation against those unique cancer-specific circumstances that are likely to increase bleeding risk and other complications. CVA = cerebrovascular accident.

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

Patterns of Anticoagulation Use in Patients With Cancer With Atrial Fibrillation and/or Atrial Flutter

PERSPECTIVES

COMPETENCY IN PATIENT CARE: AF is a commonly encountered cardiovascular complication in patients with cancer, and AF can increase the risk for stroke and systemic thromboembolism. This study demonstrates that patients with cancer may not be receiving adequate AC despite an increased risk for stroke and low bleeding risk. It is essential for cardiologists and electrophysiologists to work with oncologists to provide appropriate treatment to patients with cancer with AF.

TRANSLATIONAL OUTLOOK: Arrhythmias are a frequent and serious complication associated with cancer and cancer therapeutics. These clinical data motivate future clinical and translational studies to: 1) determine the true thromboembolic potential of cancer-associated AF; and 2) develop cancer-specific AF thromboembolism risk stratification and management algorithms.