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Sarah Gorgis

Mohammed F. Dabbagh

Kajali Mishra

Guneet Ahluwalia

Aeman Hana

See next page for additional authors

Authors

Sarah Gorgis, Mohammed F. Dabbagh, Kajali Mishra, Guneet Ahluwalia, Aeman Hana, Georgi Fram, Dilshan Dhillon, Alejandro Lemor, Arfaat Khan, Daniel Miller, Scott Kaatz, William W. O'Neill, and Dee Dee Wang

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Unprotected discharge: absence of stroke prevention strategies in patients with atrial fibrillation admitted for bleeding

Sarah Gorgis[1] · Mohammed F. Dabbagh[1] · Kajali Mishra[2] · Guneet Ahluwalia[2] · Aeman Hana[2] · Georgi Fram[2] · Dilshan Dhillon[2] · Alejandro Lemor[1] · Arfaat Khan[1] · Daniel Miller[3] · Scott Kaatz[2] · William W. O'Neill[1] · Dee Dee Wang[1]

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Abstract

Purpose Patients with atrial fibrillation or flutter (AF) on anticoagulation (AC) for stroke prevention are at an increased risk of bleeding. A common clinical dilemma is deciding when to safely restart AC following a bleed. Although studies have shown better outcomes with re-initiation of AC after hemostasis, there are clinical barriers to restarting AC. Left atrial appendage occlusion (LAAO) is a safe and efficacious alternative for patients who are unable to tolerate AC following major bleeding. We aimed to evaluate the rate of stroke prevention strategies instituted at time of discharge in patients with AF on AC who had been hospitalized for a bleeding event.

Methods We retrospectively identified patients with AF on AC admitted for bleeding between January 2016 and August 2019. The type of AC, form of bleeding, and CHA_2DS_2VASc were collected. Stroke prevention strategies upon discharge and at 3 months were noted.

Results One hundred seventy-four patients with AF on AC were hospitalized with a bleeding event, of which 10.9% died. Among patients who survived, AC was restarted in 45.2% of patients, 9.7% were referred for LAAO, and 45.1% were discharged without stroke prevention strategy. At 3 months, 32.6% of patients still had no documented stroke prophylaxis. Those referred for LAAO had, on average, higher CHA_2DS_2VASc (5 ± 1 vs 4 ± 1, $p = 0.007$).

Conclusions A significant number of patients with AF hospitalized for bleeding were discharged with no plan for stroke prophylaxis. Despite its safety and efficacy, LAAO appears to be an underutilized alternative in AF patients with high bleeding risk.

Keywords Atrial fibrillation · Stroke · Bleed · Left atrial appendage occlusion · Watchman

Abbreviations

AF	Atrial fibrillation or flutter
AC	Anticoagulation
GIB	Gastrointestinal bleed
ICH	Intracranial hemorrhage
LAAO	Left atrial appendage occlusion
HFrEF	Heart failure with reduced ejection fraction
CKD	Chronic kidney disease
ESRD	End-stage renal disease
DOAC	Direct oral anticoagulant
NSAIDs	Nonsteroidal anti-inflammatories
PPIs	Proton pump inhibitors

✉ Dee Dee Wang
Dwang2@hfhs.org

[1] Division of Cardiovascular Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202, USA

[2] Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA

[3] Department of Neurology, Henry Ford Hospital, Detroit, MI, USA

1 Introduction

Patients with atrial fibrillation or flutter (AF) on anticoagulation (AC) for stroke prevention have an increased bleeding risk. A common clinical dilemma is deciding when, or if, to restart AC after a clinically significant bleeding event. The 2017 ACC Consensus for Management of Bleeding on Anticoagulants recommends holding AC for bleeding requiring hospitalization [1]. Observational cohort studies suggest a potential mortality benefit with reinitiating AC following hemostasis, given the higher risk of thromboembolic events [2,

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3]. ACC and AHA recommend restarting AC 7 days following stabilization of gastrointestinal bleeds (GIBs) and 4 weeks following stabilization of intracranial hemorrhage (ICH) [1]. Despite these recommendations, AC is often not restarted due to the severity or frequency of bleeding, poor adherence, labile INRs, cost, or patient preference due to fear of rebleeding.

An alternative to long-term AC is left atrial appendage occlusion (LAAO). It is reported that 90% of atrial thrombi causing stroke originate from the left atrial appendage. LAAO became FDA approved following two prospective multicenter randomized controlled trials, PROTECT AF [4] and PREVAIL [5]. Subsequent registries have demonstrated that LAAO is a safe and efficacious alternative to AC [6–9].

Stroke can be a debilitating consequence of AF. However, the rate of instituting a stroke prevention strategy at the time of hospital discharge for patients with a history of AF who were admitted for bleeding is unclear. This study aims to assess the rate and type of stroke prevention strategies in patients with AF and $CHA_2DS_2VASc \geq 2$ hospitalized with a bleed.

2 Methods

2.1 Patient selection

We retrospectively analyzed patients with AF admitted to our tertiary care center with a bleed between January 2016 and August 2019. Patients were identified using ICD-10 codes: hemorrhage (R58), blood loss anemia (D50.0), anemia associated with acute blood loss (D62), acute blood loss with chronic anemia (D64.9), ICH (I62.9), subarachnoid hemorrhage (I60.9), blood in stool (K92.1), GIB (K92.2), gastritis with hemorrhage (K29.71), angiodysplasia of colon with hemorrhage (K55.21), hemoptysis (RO4.2), and hematuria (R31.9). Patients were excluded if $CHA_2DS_2VASc < 2$, they were not on AC pre-admission, AF was new onset, bleeding was peri-procedural, or if there were other indications for AC confounding decision-making (i.e., mechanical valves, left ventricular assist device, thromboembolism). Primary endpoint was defined as the presence or absence of documentation of a stroke prevention strategy at the time of hospital discharge. Stroke prevention strategy was defined as (1) resumption of AC or (2) referral for consideration of LAAO. Secondary endpoints were rates of stroke prevention strategy at 3 months post-discharge and rate of rebleeding, new stroke, or mortality at 30 days.

2.2 Data collection

The epidemiological, clinical, and laboratory data were manually extracted from electronic health records. Race was based on self-identification. Comorbid conditions were identified based on admission and discharge diagnoses. Prior bleeding was noted if identified using the "search" function in Epic or if mentioned in the provider notes. Anticoagulants on admission and discharge were identified based on admission and discharge medication reconciliation lists, respectively. Aspirin, clopidogrel, nonsteroidal anti-inflammatories (NSAIDs), steroids, and proton pump inhibitors (PPIs) on discharge were identified based on discharge medication reconciliation list. Thirty-day outcome data was manually extracted from electronic health records. CHA_2DS_2VASc score was calculated by using 1 point for congestive heart failure (defined as left ventricular ejection fraction < 40%), hypertension, age > 65, diabetes, vascular disease, and female sex, and 2 points for stroke or age ≥ 75. This study was approved by the Institutional Review Board (IRB# 11772), and informed consent was waived.

2.3 Statistical methods

Demographics, baseline characteristics, and clinical outcomes were evaluated. Numerical variables were described as mean and standard deviation, while discrete variables were described as proportions. Continuous variables were compared using Student's *t* test, while categorical variables were compared using the chi-squared test. The one-way analysis of variance (ANOVA) was used to determine any statistical significance between the means of three or more independent groups. Statistical analyses were considered significant if $p < 0.05$.

3 Results

3.1 Baseline characteristics

Of the 1300 patients analyzed, 174 patients met inclusion criteria of having known AF and $CHA_2DS_2VASc \geq 2$ on home AC with hospital admission for bleeding. The mean age was 76 ± 10 years; 51.7% were female, 71.8% were Caucasian, and 18.9% were African American. Warfarin was the most common anticoagulant pre-admission ($n = 87$, 50.0%), followed by apixaban ($n = 64$, 36.7%), rivaroxaban ($n = 20$, 11.5%), and dabigatran ($n = 3$, 1.7%). The average length of hospitalization was 7 ± 5.9 days and 44.3% of patients required intensive care unit (ICU) stay (Table 1).

3.2 Overall outcomes

Out of the 174 patients, 155 were alive at time of discharge, with in-hospital mortality of 10.9% (19/174). At time of discharge, 54.8% (85/155) of patients had some form of documented stroke prevention plan, and 45.2% (70/155) did not (Fig. 1). Table 1 compares the baseline characteristics of patients with and without stroke prevention plans. Patients with

Table 1 Baseline characteristics of patients discharged with and without stroke prophylaxis

			Stroke prophylaxis (AC or LAAO)		
	All ($N = 174$)	Discharged alive ($N = 155$)	Present ($N = 85$)	Absent ($N = 70$)	p value
Age (mean ± STD)	76 ± 10	77 ± 10	76 ± 9	78 ± 11	0.2
Female	90 (51.7%)	78 (50.3%)	41 (48.2%)	37 (52.8%)	0.6
Race					
Caucasian	125 (71.8%)	112 (72.2%)	63 (74.1%)	49 (70.0%)	0.6
African American	33 (18.9%)	28 (18.1%)	12 (14.1%)	16 (22.9%)	0.2
Other	16 (9.1%)	15 (9.7%)	10 (11.8%)	5 (7.1%)	0.4
Body weight (kg)	88.2 ± 26.5	87.6 ± 25.2	89.7 ± 27.3	85.1 ± 22.2	0.3
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.0
BMI (kg/m^2)	31.1 ± 8.2	31.0 ± 8.1	31.5 ± 8.6	30.3 ± 7.3	0.4
Comorbidities					
HFrEF (EF < 40%)	41 (23.6%)	33 (21.3%)	23 (27.1%)	10 (14.3%)	0.08
Hypertension	150 (86.2%)	135 (87.1%)	75 (88.2%)	60 (85.7%)	0.6
Diabetes mellitus	78 (44.8%)	68 (43.9%)	47 (55.3%)	21 (30.0%)	0.002
Peripheral vascular disease	76 (43.7%)	68 (43.9%)	44 (51.8%)	24 (34.3%)	0.02
Prior stroke/TIA	30 (17.2%)	26 (16.8%)	13 (15.3%)	13 (18.6%)	0.7
End-stage renal disease	6 (3.4%)	2 (1.3%)	1 (1.2%)	1 (1.4%)	1.0
Chronic kidney disease	59 (33.9%)	54 (34.8%)	29 (34.1%)	25 (35.7%)	0.9
Home O_2	13 (7.5%)	10 (6.5%)	7 (8.2%)	3 (4.3%)	0.5
Prior bleed	89 (51.1%)	81 (52.3%)	45 (52.9%)	36 (51.4%)	0.9
CHA_2DS_2VASc (mean ± STD)	4 ± 1	4 ± 1.4	4 ± 1.5	4 ± 1.0	1.0
Score of 2 (N)	20 (11.5%)	17 (11.0%)	6 (7.1%)	11 (15.7%)	0.1
Score of 3	33 (19.0%)	29 (18.7%)	18 (21.2%)	11 (15.7%)	0.4
Score of 4	43 (24.7%)	41 (26.5%)	18 (21.2%)	23 (32.9%)	0.1
Score of 5	45 (25.9%)	38 (24.5%)	24 (28.2%)	14 (20.0%)	0.3
Score of 6	20 (11.5%)	18 (11.6%)	10 (11.8%)	8 (11.4%)	1.0
Score of 7	10 (5.7%)	10 (6.5%)	8 (9.4%)	2 (2.9%)	0.1
Score of 8	3 (1.7%)	2 (1.3%)	1 (1.2%)	1 (1.4%)	1.0
Anticoagulant on admission					
Warfarin	87 (50.0%)	77 (49.7%)	45 (52.9%)	32 (45.7%)	0.4
Apixaban	64 (36.7%)	57 (36.8%)	27 (31.8%)	30 (42.9%)	0.2
Rivaroxaban	20 (11.5%)	18 (11.6%)	12 (14.1%)	6 (8.6%)	0.3
Dabigatran	3 (1.7%)	3 (1.9%)	1 (1.2%)	2 (2.9%)	0.6
Form of bleed on admission					
Gastrointestinal	150 (86.2%)	133 (85.8%)	74 (47.7%)	59 (84.3%)	0.7
EGD only	65 (43.3%)	58 (43.6%)	34 (25.6%)	24 (40.7%)	0.5
Colonoscopy only	12 (8.0%)	12 (9.0%)	6 (4.5%)	6 (10.1%)	0.8
Both EGD and colonoscopy	43 (28.7%)	40 (30.1%)	20 (15.0%)	20 (33.9%)	0.6
Hematuria	7 (4.0%)	7 (4.5%)	4 (2.6%)	3 (4.3%)	1.0
Hematoma	5 (2.9%)	5 (3.2%)	3 (1.9%)	2 (2.9%)	1.0
Intracranial hemorrhage	3 (1.7%)	1 (0.6%)	0 (0.0%)	1 (1.4%)	0.5
Other	9 (5.2%)	9 (5.8%)	4 (2.6%)	5 (7.1%)	0.7
Laboratory values					
Admission hemoglobin	8.6 ± 2.1	8.4 ± 2.1	8.5 ± 2.0	8.3 ± 2.1	0.6
Admission creatinine	1.7 ± 1.6	1.6 ± 1.3	1.4 ± 0.7	1.8 ± 1.7	0.5
Discharge hemoglobin	8.8 ± 1.3	8.9 ± 1.3	8.9 ± 1.4	8.8 ± 1.1	0.6
Discharge creatinine	1.6 ± 1.5	1.4 ± 1.1	1.3 ± 0.6	1.5 ± 1.5	0.3

Table 1 (continued)

	All ($N = 174$)	Discharged alive ($N = 155$)	Stroke prophylaxis (AC or LAAO)		
			Present ($N = 85$)	Absent ($N = 70$)	p value
Discharge medications					
Aspirin	–	67 (43.2%)	45 (52.9%)	22 (31.4%)	0.009
Clopidogrel	–	16 (10.3%)	14 (16.5%)	2 (2.9%)	0.007
NSAIDs	–	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.0
Steroids	–	10 (6.5%)	3 (3.5%)	7 (10.0%)	0.2
PPIs	–	90 (58.1%)	49 (57.6%)	41 (58.6%)	1.0
Inpatient outcomes					
Intensive care unit stay	77 (44.3%)	60 (38.7%)	30 (19.4%)	30 (42.9%)	0.4
Length of stay (mean ± STD)	7 ± 5.9	6 ± 5	7 ± 6	6 ± 4	0.2

AC anticoagulation, *LAAO* left atrial appendage occlusion, *BMI* body mass index, *EGD* esophagogastroduodenoscopy, *HFrEF* heart failure with reduced ejection fraction, *NSAIDs* nonsteroidal anti-inflammatories, *PPI* proton pump inhibitors, *TIA* transient ischemic attack

diabetes and peripheral vascular disease were more likely to have a documented stroke prevention plan ($p = 0.002$ and $p = 0.02$, respectively). Table 2 compares patients who were restarted on AC to those referred for LAAO. AC was restarted in 45.2% (70/155) of patients and 9.7% (15/155) were referred for LAAO. In patients restarted on AC, 48.6% (34/70) went home on warfarin, 37.1% (26/70) on apixaban, 12.9% (9/70) on rivaroxaban, and 1.4% (1/70) on dabigatran (Table 2). The majority of patients restarted on AC were continued on the same anticoagulant they were originally on (92.9%) (Fig. 2). The overall 30-day readmission rate was 22.6%, of which 48.6% were for rebleeding (Table 3).

3.3 Stroke prevention strategies based on bleeding type

GIB was the most common form of bleeding (86.2%, 150/174), followed by hematuria (4.0%, 7/174), hematomas (2.9%, 5/174), and ICH (1.7%, 3/174). Bleeding type did not influence the presence or absence of a stroke prevention strategy at time of discharge (Table 1). Patients with GIB largely had AC restarted (40.7%, 61/150) or held (39.3%, 59/150) after hemostasis, with only 8.7% (13/150) referred for LAAO. Procedural intervention was required in 80.0% (120/150) of GIBs: 43.3% esophagogastroduodenoscopy (EGD), 8% colonoscopy, and 28.7% undergoing both. There were only 3 patients with ICH: 2 died during hospitalization and 1 had AC held. Other forms of bleeding accounted for 12.1% (21/174) of patients, with similar patterns of stroke prevention strategies (Table 1).

3.4 Stroke prevention strategies based on medical history

The average CHA_2DS_2VASc was 4 ± 1, and comorbidities were as follows: 23.6% heart failure with reduced ejection fraction (HFrEF), 86.2% hypertension, 44.8% diabetes, 43.7% peripheral vascular disease, and 17.2%

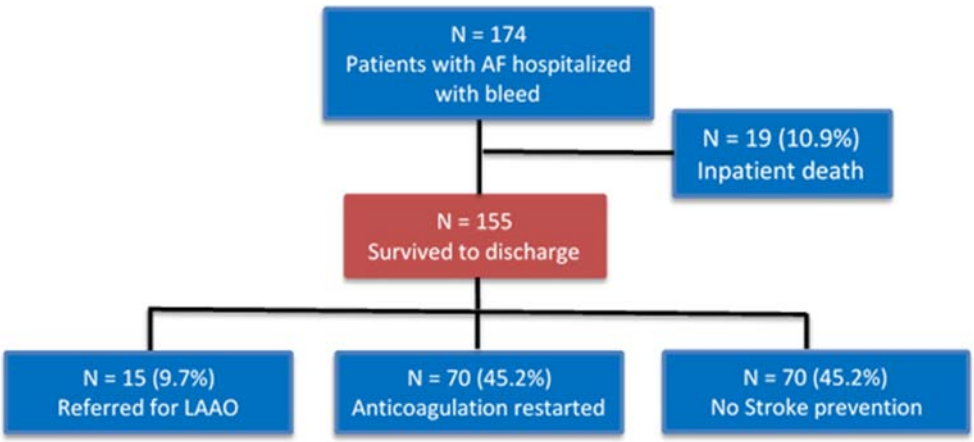

Fig. 1 Rates of stroke prevention strategies at discharge. One hundred seventy-four patients with known atrial fibrillation or flutter with $CHA_2DS_2VASc \geq 2$ on home AC hospitalized with a bleed were analyzed. 10.9% died inpatient, 45.2% were restarted on AC, 9.7% were referred for LAAO, and 45.2% had no form of stroke prevention

Table 2 Characteristics of patients discharged on anticoagulation versus referred for left atrial appendage occlusion

	All ($N = 85$)	Discharged on anticoagulation ($N = 70$)	Referred for LAAO ($N = 15$)	p value
Age (mean ± STD)	76 ± 9	75 ± 9	82 ± 8	0.007
Female	41 (48.2%)	34 (48.6%)	7 (46.7%)	1.0
Race				
Caucasian	63 (74.1%)	51 (72.8%)	12 (80.0%)	0.8
African American	12 (14.1%)	11 (15.7%)	1 (6.7%)	0.7
Other	10 (11.8%)	8 (11.4%)	2 (13.3%)	1.0
Body weight (kg)	89.7 ± 27.3	91.7 ± 28.1	80.8 ± 21.4	0.2
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.0
BMI (kg/m^2)	31.5 ± 8.6	32.2 ± 8.9	28.5 ± 6.1	0.1
Comorbidities				
HFrEF (EF < 40%)	23 (27.1%)	16 (22.9%)	7 (46.7%)	0.02
Hypertension	75 (88.2%)	62 (88.6%)	13 (86.7%)	1.0
Diabetes mellitus	47 (55.3%)	39 (55.7%)	8 (53.3%)	1.0
Peripheral vascular disease	44 (51.8%)	35 (50.0%)	9 (60.0%)	0.6
Prior stroke/TIA	13 (15.3%)	11 (15.7%)	2 (13.3%)	1.0
End-stage renal disease	1 (1.2%)	1 (1.4%)	0 (0.0%)	1.0
Chronic kidney disease	29 (34.1%)	24 (34.3%)	5 (33.3%)	1.0
Home O_2	7 (8.2%)	7 (10.0%)	0 (0.0%)	0.3
Prior bleed	45 (52.9%)	38 (54.3%)	7 (46.7%)	0.8
CHA_2DS_2VASc (mean ± STD)	4 ± 1.5	4 ± 1	5 ± 1	0.007
Score of 2 (N)	6 (7.1%)	6 (7.1%)	0 (0.0%)	0.6
Score of 3	18 (21.2%)	17 (20.0%)	1 (1.2%)	0.2
Score of 4	18 (21.2%)	14 (16.5%)	4 (4.7%)	0.7
Score of 5	24 (28.2%)	18 (21.2%)	6 (7.1%)	0.3
Score of 6	10 (11.8%)	7 (8.2%)	3 (3.5%)	0.4
Score of 7	8 (9.4%)	8 (9.4%)	0 (0.0%)	0.3
Score of 8	1 (1.2%)	0 (0.0%)	1 (1.2%)	0.2
Anticoagulant on admission				
Warfarin	45 (52.9%)	35 (50.0%)	10 (66.7%)	0.3
Apixaban	27 (31.8%)	26 (37.1%)	1 (6.7%)	0.03
Rivaroxaban	12 (14.1%)	8 (11.4%)	4 (26.7%)	0.2
Dabigatran	1 (1.2%)	1 (1.4%)	0 (0.0%)	1.0
Form of bleed on admission				
Gastrointestinal	74 (47.7%)	61 (87.1%)	13 (86.7%)	0.7
EGD only	34 (25.6%)	29 (47.5%)	5 (38.5%)	0.8
Colonoscopy only	6 (4.5%)	6 (9.8%)	0 (0.0%)	0.6
Both EGD and colonoscopy	20 (15.0%)	16 (26.2%)	4 (30.8%)	0.8
Hematuria	4 (2.6%)	2 (2.9%)	2 (13.3%)	0.1
Hematoma	3 (1.9%)	3 (4.3%)	0 (0.0%)	1.0
Intracranial hemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.0
Other	4 (2.6%)	4 (5.7%)	0 (0.0%)	1.0
Laboratory values				
Admission hemoglobin	8.5 ± 2.0	8.4 ± 2.1	8.6 ± 2.0	0.7
Admission creatinine	1.4 ± 0.7	1.4 ± 0.8	1.4 ± 0.4	1.0
Discharge hemoglobin	8.9 ± 1.4	9.0 ± 1.4	8.8 ± 1.1	0.6
Discharge creatinine	1.3 ± 0.6	1.3 ± 0.7	1.2 ± 0.3	0.6
Discharge anticoagulant				
Warfarin	34 (40.0%)	34 (48.6%)	0	–
Apixaban	26 (42.4%)	26 (37.1%)	0	–
Rivaroxaban	9 (10.6%)	9 (12.9%)	0	–
Dabigatran	1 (1.2%)	1 (1.4%)	0	–
Discharge medications				
Aspirin	45 (52.9%)	36 (51.4%)	9 (60.0%)	0.6
Clopidogrel	14 (16.5%)	6 (8.6%)	8 (53.3%)	0.0002
NSAIDs	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.0
Steroids	3 (3.5%)	1 (1.4%)	2 (13.3%)	0.08
PPIs	49 (57.6%)	39 (55.7%)	10 (66.7%)	0.6
Inpatient outcomes				
Intensive care unit stay	30 (19.4%)	26 (37.1%)	4 (26.7%)	0.6
Length of stay (mean ± STD)	7 ± 6	7 ± 6	6 ± 4	0.5

LAAO left atrial appendage occlusion, *BMI* body mass index, *EGD* esophagogastroduodenoscopy, *HFrEF* heart failure with reduced ejection fraction, *NSAIDs* nonsteroidal anti-inflammatories, *PPI* proton pump inhibitors, *TIA* transient ischemic attack

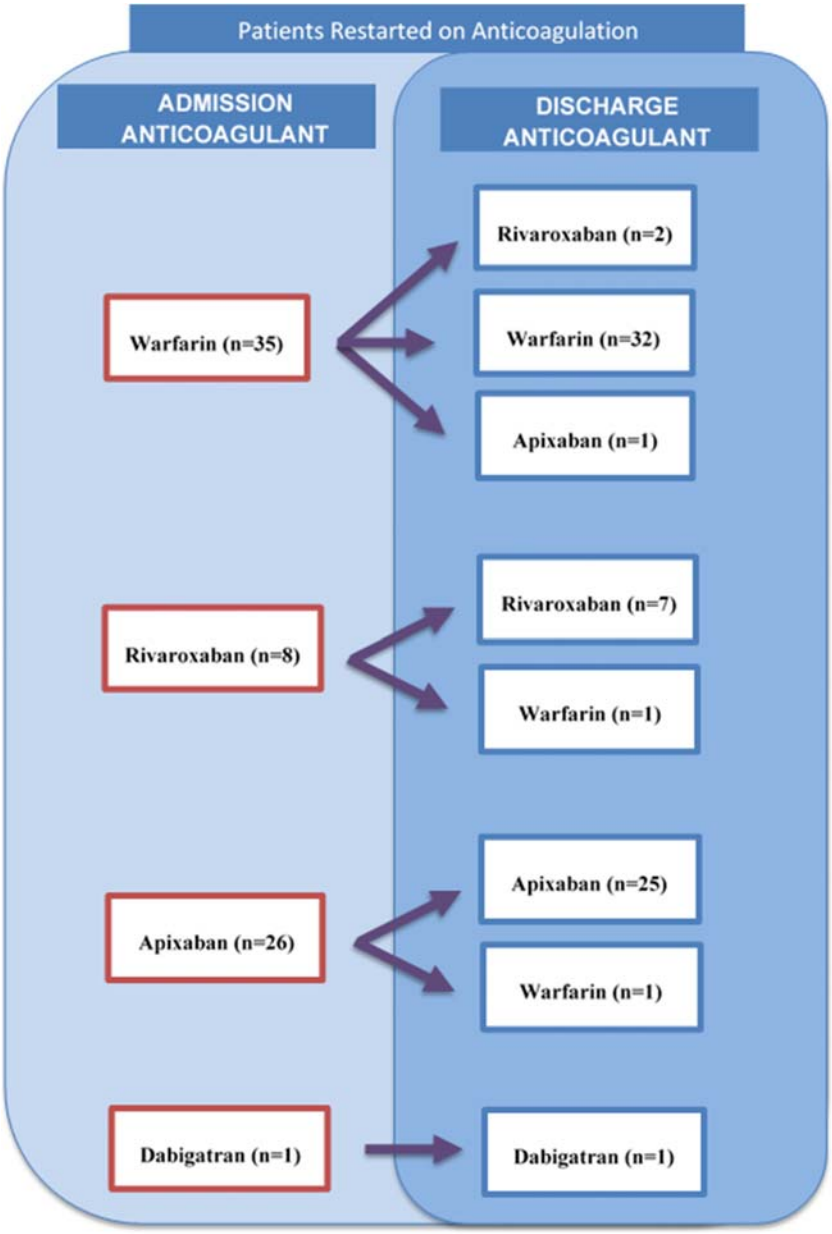

Fig. 2 In patients who were restarted on AC for stroke prophylaxis, 92.9% were discharged on the same anticoagulant they were originally on. Only three patients who were on warfarin were switched to DOACs. Two patients who were on DOACs were switched to warfarin; in these two patients, anticoagulant reversal agents had been used on presentation and the team favored warfarin for the ability to more readily reverse the anticoagulant if a major bleed were to recur

history of stroke. Patients with diabetes or peripheral vascular disease were more likely to have a documented stroke prevention plan at time of discharge ($p = 0.002$ and $p = 0.02$, respectively). Similarly, those who were on aspirin or clopidogrel on discharge were more likely to have a documented stroke prevention plan ($p = 0.009$ and $p = 0.007$, respectively) (Table 1). Age, HFrEF, and higher CHA_2DS_2VASc score were the only factors significantly associated with referral to LAAO, with older patients (82 vs 75 years old, $p = 0.007$), those with HFrEF (46.7% vs 22.9%, $p = 0.02$), and those with higher CHA_2DS_2VASc (5 ± 1 vs 4 ± 1, $p = 0.007$) being more likely to be referred (Table 2). As the CHA_2DS_2VASc score increased, the likelihood of referral to LAAO seemed to increase (Fig. 3). The majority of patients had a previous episode of bleeding (51.1%, 89/174) prior to the index hospitalization. In patients with prior bleeding, 47.2% (42/89) were on warfarin, 40.4% (36/89) on apixaban, 11.2% (10/89) on rivaroxaban, and 1.1% (1/89) on dabigatran. Of those with prior bleeding, 8.9% (8/89) died during hospitalization, 42.7% (38/89) were restarted on AC, 7.9% (7/89) were referred for LAAO, and 40.4% (36/89) were discharged without a documented stroke prophylaxis plan. In patients with prior stroke, 13.3% (4/30) died, 36.7% (11/30) were restarted on AC, 6.7% (2/30) were referred for LAAO, and 43.3% (13/30) were without stroke prophylaxis at discharge. Only 8.5% (5/59) of

Table 3 Clinical outcomes 30 days post-discharge

	All (*$N = 155$)	Discharged on anticoagulation ($N = 70$)	Referred for LAAO ($N = 15$)	None ($N = 70$)
30-day readmission	35 (22.6%)	14 (20.0%)	4 (26.7%)	17 (24.3%)
Bleeding	17 (48.6%)	8 (11.4%)	2 (13.3%)	7 (10.0%)
Stroke	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
Other	17 (48.6%)	6 (8.6%)	2 (13.3%)	9 (12.9%)

*From the original 174 patient cohort, there were 19 in-hospital deaths (10.9%)

patients with chronic kidney disease (CKD) and no patients with end-stage renal disease (ESRD) were referred for LAAO (Table 2).

3.5 In-hospital mortality

In the 19 patients with in-hospital mortality, 15.8% (3/19) died of ICH, 47.4% (9/19) died of massive GIB, and 10.5% (2/19) died of diffuse alveolar hemorrhage—making bleeding the cause of death in 73.7% of cases. The remaining patients died of hypoxic respiratory failure (15.8%, 3/19) and progression of underlying cardiomyopathy (10.5%, 2/19) in the setting of bleeding. 52.6% (10/19) of patients who died were on warfarin, 36.8% (7/19) were on apixaban, and 10.5% (2/19) were on rivaroxaban prior to admission. In those with in-hospital mortality, 63.2% (12/19) were female, 42.1% (8/19) had heart failure, 78.9% (15/19) had hypertension, 52.6% (10/19) had diabetes, 21.1% (4/19) had prior stroke, and 42.1% (8/19) had peripheral vascular disease.

3.6 Clinical outcomes 30 days post-discharge

The overall 30-day readmission rate was 22.6% (35/155); 48.6% (17/35) were for rebleeding, 2.9% (1/35) were for stroke, and 48.6% (17/35) were for other causes. There was no difference in 30-day readmission rates based on the stroke prevention strategy. The one patient who was readmitted for stroke had been discharged without a definitive stroke prevention strategy (Table 3). Out of the 8 patients who were discharged on AC and readmitted for bleeding, 4 were on apixaban and 4 were on warfarin.

3.7 Three-month follow-up

Stroke prevention strategy was collected at 3 months post-discharge. Out of 155 patients who survived to discharge, 4 died at 3 months and 10 patients had no follow-up. From the 141 patients with available 3-month follow-up data, 56.0% (79/141) were on AC, 11.3% (16/141) were referred for LAAO, and 32.6% (46/141) were still without documented stroke prophylaxis at 3 months (Fig. 4). In patients who were referred for LAAO, the average time from discharge to LAAO was 108 days.

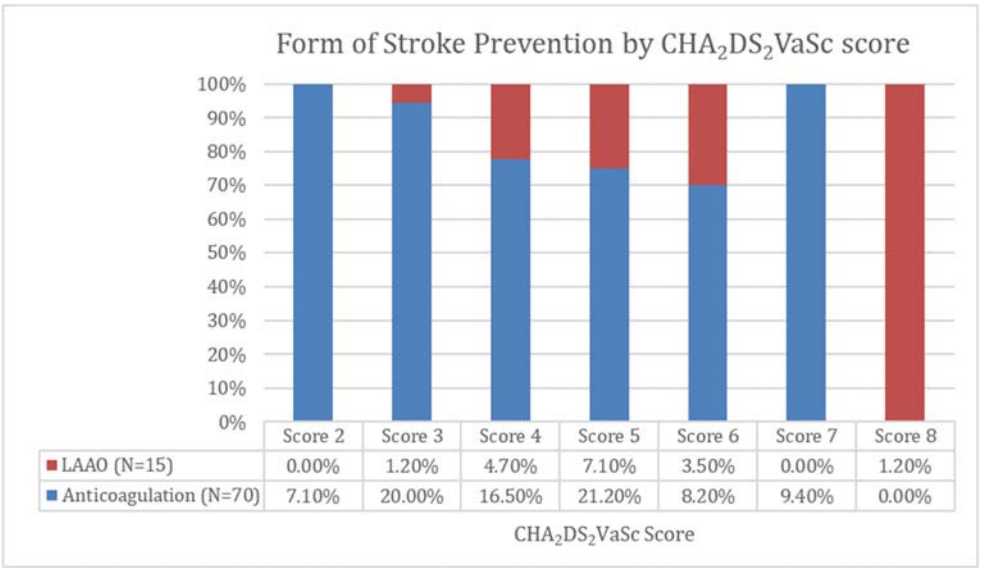

Fig. 3 Patients referred for LAAO had, on average, higher CHA_2DS_2VASc scores compared to those restarted on anticoagulation (5 ± 1 vs 4 ± 1, $p = 0.007$). The distribution of AC or referral to LAAO is depicted in the figure by each CHA_2DS_2VASc score

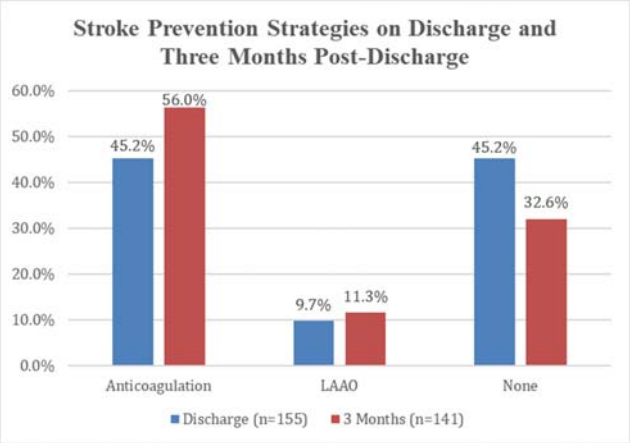

Fig. 4 Stroke prevention strategies at discharge were 45.2% restarted on AC, 9.7% referred for LAAO, and 45.2% none. In evaluating these strategies at 3 months post-discharge, 4 patients died at 3 months and 10 patients had no follow-up. From the 141 patients with available 3-month follow-up data, 56.0% (79/141) were on AC, 11.3% (16/141) were referred for LAAO, and 32.6% (46/141) were still without documented stroke prophylaxis at 3 months

4 Discussion

Balancing stroke risk with bleeding risk continues to be a clinical dilemma in patients with AF who require long-term AC for prevention of debilitating stroke. In our cohort, nearly 11% of patients on long-term AC for AF admitted with a bleed died during hospitalization, affirming that bleeding and its consequences can be life-threatening complications of AC. After hemostasis is achieved, it is vital to have a plan for stroke prevention.

Worldwide, stroke is the second most common cause of mortality and third most common cause of disability. In the USA, the annual incidence of new or recurrent stroke is approximately 795,000. The disabling nature of stroke imposes a significant economic burden on the healthcare system, with the total costs reported to be more than $65 billion for 2008 alone [10]. AF is one of the strongest risk factors for stroke [11], and its incidence is increasing with the aging population [12].

AC with warfarin or direct oral anticoagulants (DOACs) has been the main method of stroke prevention in patients with AF. Despite the advantages of DOACs over warfarin, there continues to be hesitancy in restarting AC in certain patients, depending on the bleeding type and severity. Our study revealed that, in patients with atrial fibrillation admitted with a major bleeding event secondary to long-term AC, 45.2% of patients were taken off of AC while inpatient, with no alternative stroke prevention plan at time of discharge. Furthermore, less than 10% of all patients were referred for consideration of LAAO at time of discharge. Although CHA_2DS_2VASc score was similar (range 4–5) in patients with and without stroke prevention plans, those who were referred for LAAO had higher CHA_2DS_2VASc on average.

LAAO is a safe alternative to AC in patients with AF [4–9]. Alternative short-course AC regimens following LAAO have demonstrated success in reducing risk of stroke and repeat bleeding in patients who cannot tolerate long-term AC [9]. The ASAP study prospectively looked at LAAO followed by short course of antiplatelet therapy in patients with contraindications to AC and revealed a successful device implantation rate of 94.7% and reduced stroke rate of 2.3% per year (compared to 7.3% with aspirin alone) [9]. This is being followed by the ASAP-TOO trial, a large randomized controlled trial which is currently underway to validate the safety and efficacy of LAAO followed by single or dual antiplatelet therapy in patients with AF who are at high risk for AC [13].

The majority of patients in our study had GIB requiring ICU level of care and procedural intervention, and yet 40.7% were discharged on AC with only 8.7% referred for LAAO. A recent large systematic review and meta-analysis of patients on AC admitted for GIB revealed that, while resumption of AC was associated with a decrease in thromboembolic events, it also resulted in a significant increase in recurrent GIB [2]. In patients with prior bleeding, Barakat et al. demonstrated stroke prevention strategies could be successfully instituted with LAAO followed by a short course of AC, with a low risk of recurrent spontaneous major bleeding [14]. Enomoto et al. have also shown that, in patients with high bleeding risk, AC can be abbreviated to aspirin plus clopidogrel for 6 months, followed by aspirin for lifetime [15]. In those who are at very high bleeding risk, DAPT following LAAO therapy can be shortened to 1 to 3 months [16]. Hence, stroke prevention strategies incorporating abbreviated AC regimens with LAAO should be strongly considered in patients at risk for recurrent bleeding.

In patients with chronic renal insufficiency, there is hesitancy in starting AC due to increased risk and lack of data [17]. A study looking at patients with AF and ESRD found that AC utilization was low, its use was not associated with reduced risk of stroke or death, and AC use was associated with increased risk of bleeding [17]. Although apixaban was recently FDA approved in AF and ESRD, data from a meta-analysis questioned its effectiveness [18]. Furthermore, the widely anticipated RENAL-AF study comparing the safety and efficacy of apixaban over warfarin in ESRD was stopped early due to lack of funding and produced inconclusive results. However, LAAO has been shown to be safe in CKD [19] and ESRD [20].

In patients with a prior history of atrial fibrillation and bleeding, patient comfort with medical regimen is extremely important for compliance with optimal medical care. A study comparing various blood thinners for AF showed less satisfaction with warfarin due to limitations on diet, lab draws, dose adjustments, and increased

feelings of burden [21]. RE-SONANCE, a large international prospective study, also revealed improved patient satisfaction with non-warfarin therapies [22]. Despite this, our study revealed that the majority of patients who were originally on warfarin were restarted on warfarin—with the choice largely driven by the patient's insurance coverage. Two patients who were on DOACs prior to admission were discharged on warfarin; in evaluating these patients, anticoagulant reversal agents had been used on presentation in both cases and the documented reason for choosing warfarin was the ability to more readily reverse the anticoagulant if a major bleed were to recur. LAAO provides the benefit of being an outpatient procedure which only requires short-term AC, reducing patient anxiety with long-term AC, testing, and overall pill burden.

The definitive stroke prevention strategy at discharge was ultimately determined by the patient's inpatient medicine team, which was internal medicine in 96 of the cases, cardiology in 35 cases, and other specialties in 24 cases. In patients who received LAAO, the decision was made by a cardiologist in 14/15 cases and the primary internist in 1/15 cases. This referral pattern can give some insight as to why so few patients were referred for LAAO, as not all patients who were hospitalized had a cardiology consult. Many patients who were discharged with no form of stroke prophylaxis had the decision deferred to an outpatient discussion. However, our 3-month data demonstrates that, if the decision to restart AC or refer to LAAO is not made at discharge, then rates of stroke prophylaxis are unlikely to improve at 3 months post-discharge. Generally, the suspected reasons for no stroke prophylaxis include the following: (1) fear of rebleeding due to multiple episodes of prior bleeding, hemorrhagic shock, or need of a reversal agent; (2) patient discomfort in restarting AC in the setting of recent bleed; (3) deferral of decision to an outpatient discussion with primary internist or cardiologist; and (4) lack of awareness of LAAO as an alternative to AC. Regarding LAAO referral, it appears that, when suggested by the cardiology service, patients were referred and ultimately received LAAO.

Ultimately, there are a large number of patients with AF and $CHA_2DS_2VASc \geq 2$ with major bleeding requiring hospitalization who end up with no stroke prevention plan at time of discharge. Increased awareness of LAAO as an alternative to AC can help assure more patients receive adequate stroke prevention.

4.1 Limitations

This is a single-center retrospective chart review study. This study may not have captured all patients with diagnosis of atrial fibrillation or flutter and concomitant admission for bleeding events given the variations in ICD-10 coding for hemorrhages. Although diligent chart review was performed, physicians may have made verbal plans with patients that were not documented.

5 Conclusion

A significant portion of patients with AF on AC hospitalized with a bleed are discharged with no definitive stroke prevention strategy. Despite its safety and efficacy, LAAO appears to be an underutilized alternative for stroke prevention in patients at high bleeding risk. Larger prospective studies are needed to identify the health and economic impact of unprotected stroke prevention discharges in this at-risk patient population.

Data availability Data and material are available for review.

Compliance with ethical standards

This study was approved by the Institutional Review Board (IRB# 11772), and informed consent was waived.

Conflict of interest Dr. Wang is a consultant for Edwards Lifesciences and Boston Scientific, and receives research grant support from Boston Scientific assigned to her employer, Henry Ford Health Systems.

Dr. O'Neill is a consultant to Abiomed, Medtronic, and Boston Scientific.

Dr. Miller received an honorarium from Boston Scientific as a speaker.

The other authors declare that they have no competing interests.

Code availability Not applicable.

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