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# Prevalence of Left Atrial Thrombus Detection by Transesophageal Echocardiography

## A Comparison of Continuous Non-Vitamin K Antagonist Oral Anticoagulant Versus Warfarin Therapy in Patients Undergoing Catheter Ablation for Atrial Fibrillation

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**CME Objective for This Article:** Upon completion of this activity, the learner should be able to discuss the incidence of left atrial thrombus among patients on continuous non-vitamin K antagonist oral anticoagulant or warfarin therapy prior to atrial fibrillation ablation and identify patients who are at highest risk of left atrial thrombus detection and would therefore benefit most from pre-ablation transesophageal echocardiography screening.

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From the Department of Medicine, Division of Cardiology, Weill Cornell Medical College, New York, New York. Dr. Markowitz serves on the Data Safety Monitoring Board for Boston Scientific; and has received a speaker honorarium from St. Jude Medical. Dr. Singh has received research funding from the Marfan Foundation. Dr. Lerman serves on the Scientific Advisory Board of Peroshpere. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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### ABSTRACT

**OBJECTIVES** The purpose of this study is to determine whether patients on  $\geq 4$  weeks of continuous non-vitamin K antagonist oral anticoagulant (NOAC) therapy require transesophageal echocardiography (TEE) before catheter ablation of atrial fibrillation (AF) or atrial flutter and to compare rates of left atrial (LA) thrombus and dense spontaneous echocardiographic contrast (SEC) in patients on NOAC versus warfarin therapy.

**BACKGROUND** The impact of NOAC therapy on the rates of LA thrombus detection by TEE in patients undergoing catheter ablation of AF is unknown.

**METHODS** Initial TEEs for 388 patients (median age, 65 years; 74% male) on  $\geq 4$  weeks of continuous NOAC ( $n = 183$ ) or warfarin therapy ( $n = 205$ ) undergoing catheter ablation of AF and flutter were reviewed.

**RESULTS** After  $\geq 4$  weeks of therapy, the prevalence of LA thrombus and LA thrombus/dense SEC among patients on NOACs was 4.4% and 6.0%, respectively, which was comparable with that of patients on warfarin. LA thrombus rates among patients on dabigatran, rivaroxaban, and apixaban were 5.4%, 4.8%, and 0%, respectively ( $p = 0.46$ ). Predictors of LA thrombus were congestive heart failure (odds ratio [OR]: 5.38; 95% confidence interval [CI]: 1.79 to 16.2;  $p = 0.003$ ); and persistent AF (OR: 3.27; 95% CI: 1.06 to 10.2;  $p = 0.040$ ).

**CONCLUSIONS** Despite  $\geq 4$  weeks of anticoagulation, the rate of LA thrombus in patients on NOACs before catheter ablation of AF or atrial flutter was 4.4%. This suggests that continuous NOAC therapy does not eliminate the need for TEE before catheter ablation of AF. (J Am Coll Cardiol EP 2016;2:295-303) © 2016 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is associated with the development of left atrial (LA) and LA appendageal thrombi, which are the main source of stroke and systemic embolism (1). Transesophageal echocardiograms (TEEs) are recognized as the gold standard for evaluating for the presence of LA thrombus and is routinely used before cardioversion and catheter ablation procedures to minimize the risk of periprocedural stroke (2). Risk factors such as structural heart disease, LA enlargement, and increased CHADS<sub>2</sub> scores have been identified as predictors of LA thrombus detection by TEE in patients undergoing pulmonary vein isolation (3-6). Despite  $\geq 3$  to 4 weeks of continuous warfarin

therapy, the rates of LA thrombus detection before cardioversion or catheter ablation have been shown to be substantial, with ranges reported between 1.6% and 7.7% (4,6,7).

Several non-vitamin K antagonist oral anticoagulants (NOACs) have been shown in randomized studies to result in significant reductions in stroke and systemic embolism when compared with warfarin (8). However, the impact of NOAC therapy on the rates of LA thrombus detection by TEE in patients undergoing catheter ablation of AF is unknown. With decreased variability in anticoagulant effect compared with warfarin, NOAC use may result in decreased rates of LA thrombus. This study sought

to determine whether patients with  $\geq 4$  weeks of continuous NOAC therapy still require TEE screening before catheter ablation of AF or atrial flutter and to compare the prevalence of LA thrombus and dense spontaneous echocardiographic contrast (SEC) in patients on NOAC versus warfarin therapy.

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**METHODS**

**STUDY POPULATION.** We retrospectively evaluated 627 consecutive patients undergoing their first TEE at New York Presbyterian Hospital-Weill Cornell Medical Center before catheter ablation of AF or atrial flutter. We excluded 93 patients who were not on any anticoagulation, 144 patients who did not have documented compliant continuous oral anticoagulation therapy for 4 weeks before TEE, and 2 patients who had previously documented LA thrombus determined by TEE at outside institutions. The final study population included 388 patients. The study was approved by the Weill Cornell Medical College Institutional Review Board.

**BASELINE ASSESSMENT AND ORAL ANTICOAGULATION THERAPY.** Baseline demographic and clinical information for each study patient at the time of TEE was collected. Data recorded for each patient included age, gender, cardiovascular risk factors, prior valve surgery, type of AF, and type and total duration of continuous oral anticoagulant therapy. Congestive heart failure (CHF) was defined as clinical history of heart failure or presence of left ventricular ejection fraction of  $\leq 40\%$  (9). A CHA<sub>2</sub>DS<sub>2</sub>-VASc score was calculated for each study patient as per Lip et al. (9) Paroxysmal AF was defined as AF lasting  $\leq 7$  days (10). Persistent AF was defined as continuous AF lasting  $>7$  days. Patients with a history of paroxysmal and persistent AF were adjudicated as having persistent AF. Long-standing persistent AF was defined as continuous AF lasting  $>1$  year. In all study patients, warfarin and NOAC were continued up through the day of TEE without interruption or enoxaparin bridging.

**TEE IMAGING.** TEEs were performed in all study patients within 3 days of planned catheter ablation. Imaging was performed using a General Electric Vivid 4 system (General Electric, Milwaukee, Wisconsin). Standard TEE acquisition was performed with focused imaging of the LA and LA appendage including a continuous 0° to 180° arc at the mid-esophageal plane in 10° to 30° intervals. LA thrombus was defined as a discrete echodense mass in the LA or LA appendage distinct from the LA endocardium or pectinate

muscles, respectively (Online Figure 1, Online Video 1) (11). SEC (indicative of blood stasis) was categorized as dense if slow swirling echodensities did not clear within 3 to 5 ventricular cycles (12) (Online Figure 1, Online Video 2) correlating with 3+ and 4+ SEC as graded by Fatkin et al. (13). SEC was categorized as clearing SEC if it cleared within 3 ventricular cycles, correlating with 1+ and 2+ SEC (13). LA size was graded semi-quantitatively as normal or mildly, moderately, or severely enlarged based on visualization in multiple imaging planes.

**FOLLOW-UP.** For all study patients who proceeded to catheter ablation after TEE, follow-up clinical data were collected to assess for stroke, transient ischemic attack, and systemic embolic events occurring within 30 days of the ablation procedure. For patients with LA thrombus on initial TEE, follow-up data from repeat TEE imaging studies were collected. Any changes in oral anticoagulation therapy regimen made among these patients at the discretion of the treating physician were recorded.

**STATISTICAL ANALYSIS.** Continuous variables are expressed as median values (interquartile range

**ABBREVIATIONS AND ACRONYMS**

- AF** = atrial fibrillation
- CHF** = congestive heart failure
- CI** = confidence interval
- NOAC** = non-vitamin K antagonist oral anticoagulants
- INR** = international normalized ratio
- IQR** = interquartile range
- OR** = odds ratio
- LA** = left atrium
- SEC** = spontaneous echocardiographic contrast
- TEE** = transesophageal echocardiography

**TABLE 1** Baseline Demographics (N = 388)

Age, yrs	65 (58, 71)
Male	287 (74)
Left ventricular ejection fraction, %	57.5 (52.5, 60.0)
Congestive heart failure	62 (16)
Hypertension	200 (52)
Diabetes	56 (14)
TIA/CVA	51 (13)
CAD/PAD	86 (22)
GFR $<50$ ml/min/1.73 m <sup>2</sup>	16 (4)
Prior MVR	21 (5)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	2 (1, 3)
Paroxysmal AF	204 (53)
Persistent AF	132 (34)
Long-standing persistent AF	11 (3)
Atrial flutter	133 (34)
Oral anticoagulant use	
Duration of continuous anticoagulation, weeks	13 (6, 36)
Warfarin	205 (53)
NOAC	183 (47)
Dabigatran	93 (24)
Rivaroxaban	62 (16)
Apixaban	28 (7)
Values are median (1st quartile, 3rd quartile) or n (%).	
AF = atrial fibrillation; CAD/PAD = coronary artery disease/peripheral arterial disease; GFR = glomerular filtration rate; NOAC = non-vitamin K antagonist oral anticoagulant; TIA/CVA = transient ischemic attack/cerebrovascular accident.	

[IQR]: 25th percentile, 75th percentile) and compared using the Mann Whitney U test. Categorical values were compared pairwise using the Fisher exact test or chi-square test as appropriate and across >2 groups using the chi-square test. Univariate logistic regression analysis was performed to estimate odds ratios of potential risk factors for LA thrombus or dense SEC detection by TEE. Any clinical variables identified in this analysis with  $p < 0.10$  were entered into a multivariate logistic regression model to identify independent factors associated with LA thrombus or dense SEC. For each variable, an odds ratio with 95% confidence intervals (CIs) was generated. For all comparisons,  $p < 0.05$  was considered significant. Statistical analysis performed with SPSS Version 19.0 (Chicago, Illinois).

## RESULTS

**STUDY POPULATION.** Baseline characteristics of the study population are shown in [Table 1](#). The median age was 65 years (IQR: 58 to 71 years) and 74% were male. The median duration of continuous anticoagulation before TEE was 13 weeks (IQR: 6 to 36 weeks) with 53%

patients on warfarin and 47% patients on a NOAC. The distribution of CHA<sub>2</sub>DS<sub>2</sub>-VASc scores among study patients were as follows: 52 (13%) with score of 0, 87 (22%) with score of 1, 103 (27%) with score of 2, and 146 (38%) with score of  $\geq 3$ . Comparison of baseline characteristics between patients on warfarin and NOAC therapy are summarized in [Online Table 1](#). Compared with patients on NOACs, patients on warfarin had significantly more CHF, hypertension, diabetes, coronary or vascular disease, and prior mitral valve surgery. CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were significantly higher among warfarin patients compared with NOAC patients ( $p < 0.001$ ). Warfarin patients were on continuous anticoagulation therapy for a longer duration than NOAC patients (median, 16 weeks [IQR: 7 to 77 weeks] vs. 11 weeks [IQR: 5 to 26 weeks];  $p < 0.001$ ).

**PREVALENCE OF LA THROMBUS AND SEC DETECTION BY TEE.** After  $\geq 4$  weeks of continuous anticoagulation therapy, the prevalence of LA thrombus, LA thrombus/dense SEC and LA thrombus/any SEC among study patients was 3.6%, 6.2%, and 14.2%, respectively. All 14 patients with LA thrombus and 2 of 10 patients with dense SEC alone had postponement of their catheter ablation procedure. A comparison of the clinical and echocardiographic characteristics of patients with and without LA thrombus is summarized in [Table 2](#). Patients with LA thrombus had a high prevalence of CHF, persistent AF, moderate to severe LA, and lower left ventricular ejection fractions. There was also a trend toward more renal dysfunction among patients with LA thrombus. A comparison of the characteristics of patients with and without LA thrombus or dense SEC is summarized in [Online Table 2](#). Patients with LA thrombus/dense SEC had significantly higher prevalence of CHF, persistent and long-standing persistent AF, enlarged LA as well as a trend toward more renal dysfunction and higher CHADS<sub>2</sub>VASc score.

**COMPARISON OF NOAC AND WARFARIN THERAPY.** There was no difference in the rates of LA thrombus detection (4.4% vs. 2.9%;  $p = 0.45$ ) or LA thrombus/dense SEC detection (6.0% vs. 6.3%;  $p = 0.89$ ) as assessed by TEE among patients on NOAC versus warfarin therapy ([Figure 1](#)). There was a higher prevalence of LA thrombus/any SEC detection among patients on warfarin when compared with patients on NOACs (18% vs. 9.8%;  $p = 0.021$ ). Among patients on NOAC therapy, the rates of LA thrombus detection among patients on dabigatran ( $n = 93$ ), rivaroxaban ( $n = 62$ ), and apixaban ( $n = 28$ ) were 5.4%, 4.8%, and 0%, respectively ( $p = 0.48$ ) ([Figure 2](#)). The rates of LA thrombus/dense SEC detection among patients on

**TABLE 2 Comparison Between Patients With and Without Left Atrial Thrombus**

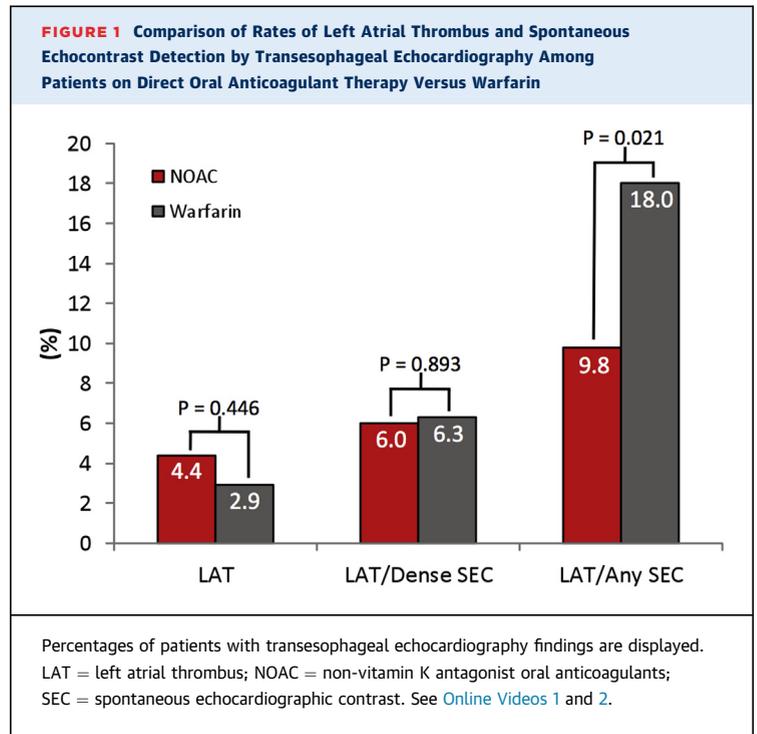
	(+) Left Atrial Thrombus (n = 14)	(-) Left Atrial Thrombus (n = 374)	p Value
Age, yrs	62 (53, 69)	65 (59, 71)	0.296
Male	13 (93)	274 (73)	0.101
Congestive heart failure	7 (50)	55 (15)	<0.001
Hypertension	7 (50)	193 (52)	0.906
Diabetes	1 (7)	55 (15)	0.703
TIA/CVA	2 (14)	49 (13)	0.705
CAD/PAD, n (%)	4 (29)	82 (22)	0.522
GFR < 50 ml/min/1.73 m <sup>2</sup>	2 (14)	14 (4)	0.051
Prior MVR	0 (0)	21 (6)	0.999
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	2.5 (1.0, 3.3)	2 (1, 3)	0.638
Paroxysmal AF	4 (29)	200 (54)	0.067
Persistent AF	9 (64)	123 (33)	0.015
Long-standing persistent AF	1 (7)	10 (3)	0.336
Atrial flutter	3 (21)	130 (35)	0.397
Oral anticoagulant use			
Duration of anticoagulation, weeks	22 (11, 37)	13 (6, 36)	0.347
Warfarin	6 (43)	199 (53)	0.446
NOAC	8 (57)	175 (47)	0.446
Dabigatran	5 (36)	88 (24)	
Rivaroxaban	3 (21)	59 (16)	
Apixaban	0 (0)	28 (7)	
Echocardiographic findings			
Left ventricular ejection fraction, %	50 (33, 58)	58 (53, 60)	0.005
Moderate to severe left atrial enlargement	9 (64)	135 (36)	0.033
Severe mitral regurgitation	0 (0)	13 (3)	0.999

Values are median (1st quartile, 3rd quartile) or n (%).  
Abbreviations as in [Table 1](#).

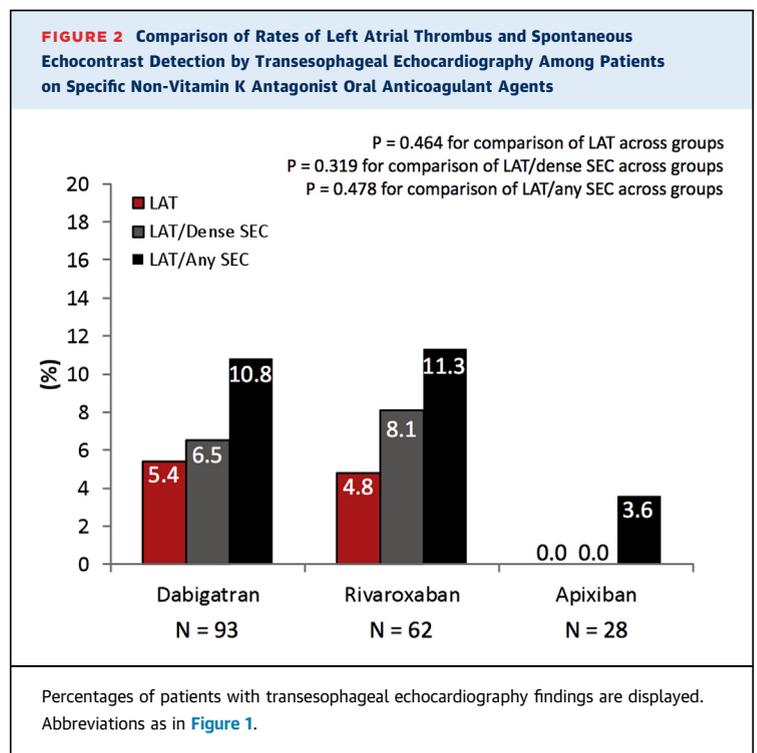
dabigatran, rivaroxaban and apixaban were 6.5%, 8.1%, and 0%, respectively ( $p = 0.34$ ). The rates of LA thrombus/any SEC detection among patients on dabigatran, rivaroxaban, and apixaban were 10.8%, 11.3%, and 3.6%, respectively. Apixaban was the only agent associated with the absence of any LA thrombus or dense SEC among treated patients. Comparisons of the individual NOAC agents with respect to the endpoints of LA thrombus, LA thrombus/dense SEC, and LA thrombus/any SEC showed no differences (Figure 2).

**INDEPENDENT PREDICTORS OF LA THROMBUS AND DENSE SEC.** Decreased left ventricular ejection fraction (<55%), CHF, persistent AF, and moderate-to-severe LA enlargement were identified as significant univariate predictors of LA thrombus detection on preablation screening TEE (Online Table 3). On multivariate logistic regression, CHF (OR: 5.38; 95% CI: 1.79 to 16.2;  $p = 0.003$ ) and persistent AF (OR: 3.28; 95% CI: 1.06 to 10.2;  $p = 0.040$ ) were significant independent predictors of LA thrombus. With respect to the combined endpoint of LA thrombus or dense SEC detection, CHF (OR: 2.62; 95% CI: 1.02 to 6.68;  $p = 0.044$ ), glomerular filtration rate of <50 ml/min/1.73 m<sup>2</sup> (OR: 4.48; 95% 1.04 to 19.3;  $p = 0.044$ ), moderate to severe LA enlargement (OR: 3.24; 95% CI: 1.29 to 8.15;  $p = 0.012$ ), and longstanding persistent AF (OR: 6.55; 95% CI: 1.51 to 28.5;  $p = 0.012$ ) were significant independent predictors of LA thrombus/dense SEC (Online Table 4). No patients with CHA2DS2VASc score of 0 and normal left ventricular ejection fraction ( $\geq 55\%$ ) had LA thrombus or dense SEC.

**FINDINGS FROM REPEAT TEES AFTER INITIAL DETECTION OF LA THROMBUS.** The clinical characteristics and outcomes of the 14 patients with LA thrombus are shown in Table 3. Patients with LA thrombus were on continuous oral anticoagulation for a median of 22 (IQR: 11 to 37) weeks. Among warfarin patients with LA thrombus, the median international normalized ratio (INR) at the time of TEE was 3.0 (IQR: 2.5 to 3.2). All patients with LA thrombus underwent a follow-up TEE after a median of 2.1 (IQR: 1.9 to 3.3) months. Five patients (36%) had resolution of their LA thrombus on the first repeat TEE with an additional 4 patients (29%) showing resolution of LA thrombus on a second repeat TEE performed a median of 3.2 months later. In summary, 9 patients (64%) had eventual resolution of LA thrombus after modification of the anticoagulation regimen. Of these, 3 patients (33%) had residual dense SEC on final TEE imaging. Among the 7 patients on warfarin who had LA thrombus on initial TEE, 3 remained on warfarin with a higher INR goal



(INR 3.0 to 3.5) and all subsequently had resolution of LA thrombus. The other 4 warfarin patients with LA thrombus were switched to a NOAC, and of these, 3 had resolution of LA thrombus. Among the 7 patients on NOAC who had LA thrombus on TEE, 4 were



**TABLE 3 Clinical Characteristics of Patients With Left Atrial Thrombus Detection by TEE**

Patient #	Age (yrs)	Sex	AF/AFL Type	Clinical Features	CHA <sub>2</sub> DS <sub>2</sub> VASc	LVEF (%)	OAC at TEE	Duration of OAC Before TEE (weeks)	OAC Change Before Final TEE	LAT on Final TEE	Time Between TEEs (weeks)
1	47	Male	Parox	CVA, DM	3	50	W	4	Yes (W → D)	No	18
2	56	Male	Pers	HCM, CVA	2	65	W	52	Yes (W → D)	Yes	25
3	73	Female	Parox	HTN	3	60	W	312	No (↑ INR goal)	No	6
4	60	Male	Pers	Mild LV dysfunction	0	45	W	24	Yes (W → D)	No	12*
5	67	Male	Pers	CM	1	41	R	12	Yes (R → A)	No	9
6	47	Male	Pers	HCM, CM	2	33	D	32	Yes (D → W)	Yes	9
7	78	Male	Pers	CAD, CABG	4	58	W	20	Yes (W → R)	No	24
8	54	Male	Parox	CM	1	23	D	4	Yes (D → W)	Yes	7
9	67	Male	LongPers	CAD, CM	4	33	D	4	D → W → D	No	26*
10	84	Male	Flutter	PPM	4	53	D	24	Yes (D → W)	Yes	18
11	53	Male	Parox	HCM	1	58	W	260	No (↑ INR goal)	No	13
12	65	Male	Pers	Renal transplant, CAD	3	53	W	32	No (↑ INR goal)	No	27*
13	64	Male	Pers	CM	2	34	R	12	R → A	Yes	13
14	52	Male	Pers	CM	2	31	R	9	R → D	No	15*

\*Patients with persistent left atrial thrombus at first repeat TEE who had a second repeat TEE. Times indicated pertain to time between first and final TEE.

A = apixaban; AFL = atrial flutter; CABG = coronary artery bypass graft; CM = cardiomyopathy; D = dabigatran; DM = diabetes mellitus; Flutter = atrial flutter; HCM = hypertrophic cardiomyopathy; HTN = hypertension; INR = International Normalized Ratio; LongPers = longstanding persistent; LV = left ventricular; OAC = oral anticoagulant; Parox = paroxysmal; Pers = persistent; PPM = hypertension; R = rivaroxaban; TEE = transesophageal echocardiography; W = warfarin; other abbreviations as in Table 1.

switched to warfarin and all of them still had LA thrombus on repeat TEE. Of these, 1 patient (patient #9) was switched back to dabigatran and eventually had resolution of LA thrombus.

**STROKE AND SYSTEMIC EMBOLIC EVENTS ON 30-DAY FOLLOW-UP.** Of the 388 study patients, 381 (98%) underwent catheter ablation of AF or flutter with 6 patients not undergoing ablation owing to persistent LA thrombus/dense SEC and 1 patient owing to physician discretion. Among the patients who underwent ablation, follow-up was available on 373 patients (98%). Overall, 2 patients (0.5%) had a stroke, transient ischemic attack, or systemic embolic event within 30 days of their ablation procedure. One patient with a history of prior cerebrovascular accident and paroxysmal AF had scattered small embolic cerebrovascular accidents detected by magnetic resonance imaging the day after ablation. She was on uninterrupted warfarin with an INR of 2.2 on the day of her procedure with a TEE that was negative for LA thrombus. One patient (Patient #7 in Table 3) with a history of persistent AF and coronary artery disease had LA thrombus initially detected by TEE that resolved on repeat TEE after switching from warfarin to rivaroxaban. The patient was found to have embolic right frontal cerebrovascular accident the day after ablation. His rivaroxaban had been held the night before ablation.

## DISCUSSION

Despite  $\geq 4$  weeks of continuous anticoagulation, the rates of LA thrombus and LA thrombus/dense

SEC among patients on NOAC therapy undergoing TEE before catheter ablation of AF or atrial flutter were 4.4% and 6.0%, respectively. To our knowledge, this is the first study to examine systematically the prevalence of LA thrombus and dense SEC before catheter ablation of AF and atrial flutter among fully anticoagulated patients on NOAC therapy. Despite a higher prevalence of significant comorbidities among patients on warfarin, there were no differences in the rates of LA thrombus and LA thrombus/dense SEC detection between patients on NOAC therapy and patients on warfarin therapy.

**PREVALENCE OF LA THROMBUS AND DENSE SEC DETECTION IN PATIENTS ON NOACs.** To date, there have only been limited data on the prevalence of LA thrombus detection among patients with AF on NOAC therapy. In a subgroup analysis of patients in the RELY (Randomized Evaluation of Long Term Anticoagulant Therapy) study, the rates of LA thrombus detection among patients undergoing TEE before cardioversion were 1.2% to 1.8% for patients on dabigatran (14). In the ARISTOLE (Apixaban for the Prevention of Stroke in Subjects With Atrial Fibrillation) study, TEE data were available in 86 patients on apixaban and none of these patients had LA thrombus (15). In an analysis of patients undergoing cardioversions or catheter ablation of AF in the ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) study, no TEE data were collected to

assess rates of LA thrombus detection among patients on rivaroxaban (16).

In our study, the rate of LA thrombus detection among patients on NOAC therapy in our study was 4.4%, specifically with rates of 5.4%, 4.8%, and 0% among patients on dabigatran, rivaroxaban, and apixaban, respectively. Although continuous NOAC therapy would theoretically circumvent the issues of subtherapeutic anticoagulation associated with warfarin use, the prevalence of LA thrombus or LA thrombus/dense SEC in patients before catheter ablation was not zero. We did not identify a difference in the rates of LA thrombus or dense SEC between patients on NOAC versus warfarin therapy despite a higher prevalence of comorbidities among patients on warfarin. The rate of LA thrombus detection among patients on warfarin in our study was 2.9%, which is comparable to rates ranging between 1.6% and 3.6% reported in other studies of patients fully anticoagulated with warfarin for  $\geq 4$  weeks duration before catheter ablation (4,6). On the other hand, 2 studies reported much lower rates of LA thrombus detection ( $<1\%$ ) among patients before pulmonary vein isolation. Khan et al. (3) reported a 0.25% prevalence of LA thrombus detection. However, this study evaluated only patients with paroxysmal AF and initial screening for LA thrombus was performed with cardiac computed tomography scans. Puwanant et al. (5) identified only a 0.6% rate of LA thrombus detection among patients before pulmonary vein isolation. Compared with our study, the patients in that study had a lower prevalence of comorbidities with a CHADS<sub>2</sub> score was  $\leq 1$  in 80% of the study population. Hence, the wide range in rates of LA thrombus detection among various studies may be attributed to differences in methods of LA thrombus detection and in clinical characteristics of the study population.

Our study was underpowered to detect a significant difference in the rates of LA thrombus and LA thrombus/dense SEC detection between the individual NOAC agents. Of note, we identified a 0% rate of LA thrombus and dense SEC detection among patients on apixaban, which is consistent with data from the ARISTOTLE study (15). Differences in the mechanism of action of direct thrombin inhibitors such as dabigatran versus factor Xa inhibitors such as apixaban may account for differences in the rates of LA thrombus. It has been postulated that inhibition of factor Xa, which is positioned earlier in the coagulation cascade and is therefore more thrombogenic on a molar basis compared with thrombin, may result in a greater antithrombotic effect compared with thrombin inhibition (17). Furthermore, differences in

pharmacokinetics and dosing frequency may explain differences in the rates of LA thrombus detection between rivaroxaban and apixaban. Studies with population sizes powered to detect differences in rates of LA thrombus detection between patients treated with specific NOAC agents are warranted.

**PREDICTORS OF LA THROMBUS AND DENSE SEC DETECTION.** The identification of CHF, LA enlargement, and persistent AF as significant independent predictors of LA thrombus and dense SEC in our study is consistent with findings from other studies (3,5,18-20). In our study, low-risk CHADS<sub>2</sub>VA<sub>2</sub>SC scores did not completely rule out the detection of LA thrombus. Of 14 patients, 4 (29%) with LA thrombus had a CHADS<sub>2</sub>VA<sub>2</sub>SC score of  $<2$ . No patients with CHA<sub>2</sub>DS<sub>2</sub>VASc score of 0 and normal left ventricular ejection fraction ( $\geq 55\%$ ) had LA thrombus in our study, thereby highlighting a patient subgroup where preablation TEE may not be necessary. However, it should be noted that this low-risk subgroup accounted for only 9.3% of our study population.

**RATES OF LA THROMBUS RESOLUTION.** Data on LA thrombus resolution among patients on NOAC therapy have been limited thus far to case studies (21-23), and rates of LA thrombus resolution among patients on warfarin have been previously reported to be 55% to 82% (7,24). We identified an overall 64% rate of LA thrombus resolution after initial TEE with modification of the oral anticoagulation regimen. Given the limited number of patients with LA thrombus and the heterogeneity in the follow-up regimen of these patients, we were unable to make conclusions about the optimal anticoagulation strategy for LA thrombus resolution. Moreover, the time course of LA thrombus resolution is an important factor to consider. In our study, only 5 of the 9 patients who had eventual LA thrombus resolution were thrombus-free at first repeat TEE performed at a median of 2.1 months after initial TEE. Three patients were found to have LA thrombus resolution only after repeated TEEs were performed  $>5$  months after initial study.

**STUDY LIMITATIONS.** Our study has several limitations, including its retrospective design. Second, among NOAC patients, the use of dabigatran, rivaroxaban, and apixaban was not evenly distributed. The low number of patients on apixaban reflects the later introduction of this drug into clinical use compared with the other NOAC agents during our study period. Therefore, our study was underpowered to assess for differences in LA thrombus and dense SEC detection between the individual NOAC agents. Future clinical studies are needed to explore

this comparison, especially given the absence of any LA thrombus or dense SEC detection among patients on apixaban in our study. Third, given the variable frequency of INR checks for patients on warfarin, we could not report the percentage of time in the therapeutic range before TEE. Moreover, among the patients on NOACs, we could not ensure that the patients were 100% compliant, although we did exclude patients with any documented history of missed NOAC doses in the 4 weeks before TEE in our study. Finally, although our study provided 30-day follow-up on thromboembolic events, we did not examine the clinical implications of LA thrombus and dense SEC detection with respect to thromboembolic events during long-term follow-up.

## CONCLUSIONS

Despite a minimum of 4 weeks of continuous anticoagulation, the rates of LA thrombus and LA thrombus/dense SEC among patients on NOAC therapy undergoing TEE before catheter ablation of AF or atrial flutter are not zero (4.4% and 6%, respectively). The rates of LA thrombus and dense SEC detection among patients on NOACs and warfarin were comparable. The presence of CHF, persistent AF, LA enlargement, and renal dysfunction are predictors of LA thrombus and dense SEC. The presence of such clinical factors should

guide the decision to perform TEEs before ablation of AF in high-risk patients.

**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Jim W. Cheung, Division of Cardiology, Weill Cornell Medical College, 520 East 70th Street, Starr 4, New York, New York 10021. E-mail: [jac9029@med.cornell.edu](mailto:jac9029@med.cornell.edu).

## PERSPECTIVES

### COMPETENCY IN MEDICAL KNOWLEDGE:

Despite continuous therapy, patients on non-vitamin K oral anticoagulants can still have LA thrombus detection by transesophageal echocardiography before catheter ablation of atrial fibrillation or flutter. Recognition of risk factors for LA thrombus such as congestive heart failure and LA enlargement would help to identify patients who would benefit most from preablation screening for LA thrombus.

**TRANSLATIONAL OUTLOOK:** Further studies are needed to compare the rates of LA thrombus detection among patients placed on specific NOACs. Any differences found between individual NOACs should be explored further with mechanistic studies to compare the antithrombotic properties of the agents.

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**KEY WORDS** anticoagulation, atrial fibrillation, catheter ablation, thrombus, transesophageal echocardiography

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 **APPENDIX** For supplemental tables, figures, and videos, please see the online version of this article.



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