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ORIGINAL ARTICLE

Real-world survival data of device-related thrombus following left atrial appendage closure: 4-year experience from a single center

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Abstract

This study aimed to estimate the incidence and risk factors of device-related thrombus (DRT) following percutaneous left atrial appendage closure (LAAC) in real-world practices. Between February 2012 and December 2016, 319 consecutive patients with atrial fibrillation underwent percutaneous LAAC using WATCHMAN, WATCHMAN Flx, Amplatzer cardiac plug, and Amulet devices. All patients underwent transesophageal echocardiography (TEE) at a minimum of three time points; periprocedurally, at 45 days, and at 6 months. Other clinical parameters were also evaluated, and a comparison between patients with DRT and those not suffering from DRT was done. The percutaneous LAAC was successfully performed in 97.8% of the patients. DRT was detected in 14 (4.49%) patients; of the 14 patients, DRT was detected in 3 patients at acute phase, 8 patients at subacute phase, 2 patients at late phase and 1 patient at very late phase. Most of the DRT originated from the central screw of device. In 6 out of 14 patients, DRT was successfully resolved by oral anticoagulation. Higher HAS-BLED score (4.1 ± 1.2 vs. 3.5 ± 1.1, $p = 0.042$) was more frequent in patients with DRT. Multivariable analysis showed that residual peri-device leak may result in a predisposition to DRT ($p = 0.023$). The incidence of DRT after percutaneous LAAC was acceptable, as a part of the DRT was resolved with oral anticoagulation. Residual peri-device leak was associated with DRT. Optimal implantation without peri-device gap, individual antithrombotic regimens, and careful monitoring with TEE follow-up could be conducive to the prevention of DRT.

Keywords Percutaneous · Left atrial appendage closure · Thrombus · Anticoagulation

Introduction

Percutaneous left atrial appendage closure (LAAC) is a good alternative for oral anticoagulant in high stroke-risk patients with atrial fibrillation (AF), especially in patients with high bleeding risk [1–3]. The feasibility and safety of LAAC with Watchman, Watchman FLX (Boston Scientific, Natrick, MA, USA), Amplatzer Cardiac Plug (ACP), and Amulet (Abbott; Abbott Park, IL, USA) devices have been recently published [2–5]. LAAC is advocated as a potential therapeutic option in current ESC guidelines for the management of atrial fibrillation [6]. However, as with most invasive procedures, percutaneous LAAC has several patient-, device-, and procedure-related complications. These are mainly pericardial effusions with or without tamponade, air embolism with subsequent stroke, device migration or embolization, and device-related thrombus [7]. Recently, device-related thrombus (DRT) has been described after percutaneous LAAC with a number of different devices

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[8–15]. These cases indicate that early or late DRT is possible. Furthermore, DRT is still a major concern because it is a consequential finding which strongly associated with a higher risk of strokes and transient ischemic attack (TIA) during follow-up [12, 13]. Although the exact mechanism of DRT has not been fully investigated, this complication did not appear to be rare. Nowadays the prevalence and possible risk factors of DRT were discussed based on the main clinical trial [9–15]. As "real-world" data on device-related thrombus formation following LAAC are scarce, we aimed to determine the incidence and predisposing factors of DRT in patients undergoing LAAC with four types of devices from our real-world practices.

Methods

Study population

Between February 2012 and February 2017, 319 consecutive patients with AF and increased bleeding risk under oral anticoagulation underwent percutaneous LAAC at Helmut-G.-Walther-Klinikum after informed consent. All patients had a diagnosis of paroxysmal, persistent, or permanent AF, and had at least one indication (history of severe hemorrhage, unstable INR, patient refusal, history of fall, or recurrence of stroke/TIA despite taking warfarin). Exclusion criteria included symptomatic valvular disease, intracardiac thrombus, symptomatic carotid disease, the presence of a mechanical valve prosthesis, and pregnancy. All patients involved in this study gave their informed consent. Institutional review board approval of our hospital was obtained for this study.

Implantation procedure and definition of peri-device leak

The LAAC procedure has been described elsewhere [1–3]. The procedure was performed under general anesthesia and using intra-procedural transesophageal echocardiography (TEE) guidance. After transseptal puncture, heparin was administrated to maintain activated clotting time > 250 s. An important step is the irrigation of the device and delivery sheath with saline to avoid air embolism and stroke during the positioning. Then, the Watchman (WM), Watchman FLX (WMF) device, Amplatzer Cardiac Plug (ACP), or Amulet were positioned in the LAA, and it was released after all release criteria were met. All patients underwent TEE at 4 time points: baseline, periprocedurally, at 45 days, and at 6 months after procedure. The additional TEE evaluation after 6 months was at the physician's discretion. All the LAAC procedures were performed by the same operators. Color-flow Doppler was used to assess for residual leak around the device into the LAA. Peri-device leak was defined as the presence of a color jet around the device lobe that was detected at least 2 frames in the same location. According to the Munich LAAC consensus document for definition of peri-device leak, adequate LAA sealing was characterized by a jet < 5 mm. Further, the Munich LAAC consensus is to assess this parameter in studies on any type of LAA exclusion following a consistent methodology [16, 17].

Anticoagulation regimen after device implantation

The antithrombotic regimen at discharge differed between the patients treated with the 2 devices. After the WM or WMF device had been implanted, patients were treated with warfarin or non-vitamin K antagonist oral anticoagulants (NOACs) for 45 days. Patients discontinued warfarin therapy if the 45-day TEE showed either complete closure of the LAA or if there was residual peri-device flow (jet < 5 mm in width). After stopping warfarin treatment, once daily clopidogrel (75 mg) and aspirin (100 mg) were prescribed until completion of the 6-month follow-up visit, from which point aspirin alone was continued indefinitely. The recommendation by the ACP or Amulet device manufacturer was to prescribe aspirin 100 mg and clopidogrel 75 mg daily for 3 months and then only aspirin 100 mg for at least another 3 months.

Definition and resolution of DRT

TEE in follow-up was performed to evaluate device position, peri-device leak, pericardial effusion, and intracardiac thrombus formation. Multiple angles imaging (0°, 45°, 90°, 135°) and zoom imaging of the appendage of TEE were frequently used. The TEE findings were reviewed by two independent investigators (BAI and YU). In case of disagreement, a group review of TEE images was then conducted. According to the previous research from the PROTECT-AF trial [10], the consensus echocardiography diagnostic criteria for DRT included (1) an echo density on the left atrial aspect of the device; (2) unexplained by imaging artifact; (3) inconsistency with normal healing/device incorporation; (4) visibility in multiple TEE planes, (5) in contact with the device. Based on the time elapsed since device implantation, DRT can be classified as acute (≤ 45 days), subacute (46 days–6 months), late (6 months–1 year), and very late (≥ 1 year).

If a repeated TEE showed device-related thrombus, conservative drug treatment was used in this series. Resuming oral coagulation (warfarin/NOACs) or LMWH and returning in 3 months for a follow-up TEE to assess for DRT resolution was recommended in most of the patients. In a few patients with recurrent DRT, clopidogrel resistance was also a consideration. Changing to an alternative P2Y12 receptor

inhibitor (ticagrelor/prasugrel) or NOACs could be an option for these patients.

Data collection and statistics

From the patients' files, baseline clinical conditions, and comorbidities, the type of AF (paroxysmal atrial fibrillation or persistent atrial fibrillation) was documented, and $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED scores were retrospectively identified. Follow-up adverse events were defined according to the Valve Academic Research Consortium criteria [14]. All available follow-up TEEs were evaluated by at least two investigators independently. Disagreements on the DRT were discussed in a group. Clinical and demographic variables were subsequently compared for subjects with DRT versus all other device patients. Spontaneous echocardiographic contrast (SEC) of patients with DRT was graded with a score between 0 (none) and 4 (severe) [18].

All statistical analyses were performed using commercially available software (PASWStatisticsv 18.0.0; SPSS, Inc, Chicago, IL). Continuous variables were evaluated for a normal distribution with the Shapiro–Wilk test. Descriptive data for continuous variables were presented as a mean (SD). Categorical variables are presented as relative frequencies. Continuous variables were analyzed by unpaired *t* tests. To determine the predisposing factors of DRT, we compared the following variables between patients with and without DRT: age, gender, type of AF, $CHADS_2$ score, CHA_2DS_2-VASc score, HAS-BLED score, device size, prior heart failure, prior renal dysfunction, prior liver dysfunction, prior stroke/TIA, diabetes mellitus, residual peri-device leak, and so on. Stepwise logistic regression analysis was performed to estimate the odds ratio for multivariate risk factors. A p value < 0.05 was considered statistically significant. All probability values reported were two sided.

Results

Cohort characteristics and procedural results

From February 2012 to February 2017, 319 consecutive patients were enrolled and followed-up, including 5 patients receiving "Kissing Watchman" (two Watchman occluders in the LAA). The percutaneous LAAC was successfully performed in 97.8% of the patients. There were 7 patients in whom an implant was not attempted. Reasons for the aborted attempts were that a pre-implant TEE revealed a new LAA thrombus ($n = 1$), pericardial effusions induced by transseptal puncture ($n = 3$), and that LAA size and shape were not optimal for any device ($n = 3$). Device embolization occurred in three cases (1.05%) with WMF device that were all successfully retrieved percutaneously (WMF device has subsequently been pulled of the market). The study flow diagram is shown in Fig. 1. Data on baseline characteristics are displayed in Table 1. There were no perioperative strokes. One patient with 22 mm ACP device died of hemoptysis 3 months after LAAC, but no autopsy was done.

The characteristics of patient with DRT and follow-up

The study comprised a total of 406.05 patient-years of follow-up. 98% of patients received at least one TEE exam during follow-up. TEE follow-up after 6 weeks was complete for 303/312 (97.1%) patients. After 12 months, 281/312 (90.4%) patients had TEE follow-up. Device-related thrombus was detected in 14 patients (4.49%) after implantation. The baseline characteristics of patients with DRT are shown in Table 2. Among them, 13 patients were treated with the Watchman device and 1 patient received the WMF device. According to the classification of DRT, the thrombus was detected in 3 patients at acute phase (≤ 45 days), 8 patients at subacute phase (46 days–6 months), 2 patients at late phase (6 months–1 year), and 1 patient at very late phase (≥ 1 year). We found that most of the DRTs originated from the central screw ("threaded insert"). The DRT with a large

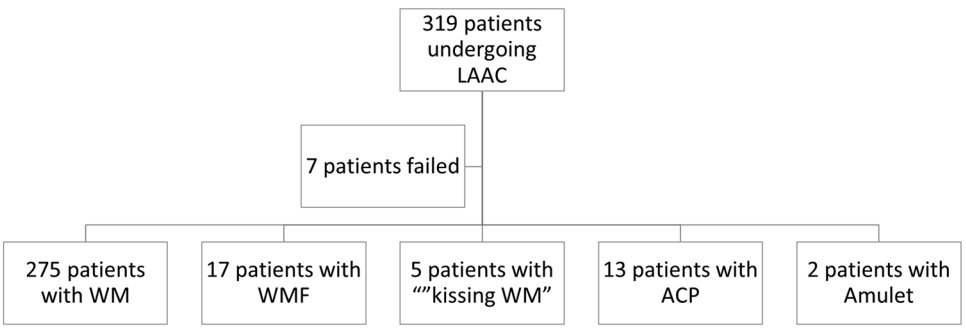

Fig. 1 The study flow diagram

Table 1 Baseline demographic characteristics and risk factors

Characteristics	No. (%)
Overall cases	324 (319 + 5)
Age mean ± SD, years	75.1 ± 7.6 (47 ~ 91)
Gender	
Male	217 (67.0%)
Female	107 (33.0%)
Type of atrial fibrillation	
Paroxysmal atrial fibrillation	103 (31.8%)
Permanent and persistent atrial fibrillation	221 (68.2%)
Risk	
CHADS2 score (continuous), mean ± SD	2.46 ± 1.19
CHA2DS2-VASc score (continuous), mean ± SD	3.83 ± 1.48
HAS-Bled score, mean ± SD	3.49 ± 1.09
Congestive heart failure	51 (15.7%)
Hypertension	260 (80.2%)
Age ≥ 75 years	186 (57.4%)
Diabetes	91 (28.1%)
Stroke/TIA	57 (17.6%)
Coronary artery disease	177 (54.6%)
Pre-closure antithrombotic regimens	
Warfarin	57 (17.6%)
Aspirin	116 (35.8)
NOAC	22 (6.8%)
Heparin	119 (36.7%)
Indications for LAAC	
Labile INR	90 (28.2%)
High bleeding risk	75 (23.5%)
Stroke on warfarin	70 (21.9%)
Coronary artery disease and stent	54 (16.9%)
Risk of falls	30 (9.4%)

CHADS2 congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, stroke or TIA, *CHA2DS2-VASc* congestive heart failure (or Left ventricular systolic dysfunction), hypertension, Age ≥ 75 years, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age 65–74 years, sex category (i.e., female sex), *HAS-Bled* hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (> 65 years), drugs/alcohol concomitantly, *TIA* transient ischemic attack, *NOAC* novel oral anticoagulation, *LAAC* left atrial appendage closure, *SD* standard deviation

laminar base centered on the atrial facing surface of the device were frequently less mobile (Fig. 2a, b), and part of the DRT spread toward the pulmonary vein (Fig. 2c). Until December 31 2016, in 6 out of 14 patients, thrombus was resolved successfully by LMWH or oral anticoagulation. No major bleeding was recorded during the treatment of DRT. There were no deaths in the patients with DRT. All of the patients remained completely asymptomatic, without any neurological event. Thrombus recurrence on the Watchman device occurred in three patients (numbers 2, 3, and 8) when they stopped anticoagulation. As a result, the three patients were to be treated with lifelong warfarin afterward. The remaining 5 patients with DRT were still under close monitoring (Table 3).

Comparison of patients without and with DRT

A comparison of potential risk factors for DRT is summarized in Table 4. HAS-BLED scores were higher in patients with DRT than without thrombus. There was a significant association between the presence of DRT and residual peri-device leak after percutaneous closure. There was no significant difference in other baseline and demographic characteristics between patients with and without DRT. Furthermore, we adopted a binary logistic regression model for the discovery of DRT risk factors. The residual peri-device leak was the only variable identified as a significant risk factor associated with DRT (OR 204.077, $p = 0.023$). Additionally, prior to device implantation, moderate to severe left atrial spontaneous echo contrast was noted on all patients with DRT (SEC 4° in 6 patients, SEC 3° in 7 patients and SEC 2° in one patient).

Discussion

This study of unselected, real-world AF patients demonstrated unexpected thrombus formation on the LAAC device and, therefore, raised safety concerns for this novel technique for patient with atrial fibrillation. Until recently, most descriptions of DRT after LAAC have been limited to isolated case reports or studies evaluating the general effects and complications of percutaneous therapy without detailed analysis of risk factors. We found the incidence of DRT in the single center data to be 4.49% and consistent with recent LAAC clinical studies (Fig. 3) [9–13, 18–21]. However, the incidence may be related to the follow-up duration. According to implanted patients reported in the literature, the incidence of DRT in PROTECT-AF was 5.7% of patients at the 1-year follow-up. Only three (0.7%) patients with DRT were detected at 4-month follow-up in a retrospective study of using NOACs as an alternative to warfarin to prevent DRT after LAAC with the Watchman device [20]. Moreover, in the prospective ASAP registry of investigating a dual antiplatelet regimen after LAAC, the rate of DRT (4%) at 341 days post-implant was comparable to other studies. Because of the possibility of late thrombosis, the number of DRTs may increase with a longer follow-up. In our study, the incidence of DRT is low within the 45-day follow-up (when patients are still receiving anticoagulation therapy) and peaks at the 6-month follow-up (when patients are receiving dual antiplatelet therapy). We also presented one case with very late DRT 24 months after WM device implantation

Table 2 Individual baseline characteristics of patients with DRT

Pts	Age	Sex	CHA2DS2-VASc	CHADS2	HAS-BLED	Type of AF	DM	LVEF %	SEC Grade	Pre-closure antithrombotic
1	71	M	5	4	5	Per	N	65	3	Aspirin
2	75	F	3	2	4	Per	Y	65	3	Wafarin
3	76	F	6	3	4	Per	N	60	3	LMWH
4	74	M	4	2	4	Per	N	55	4	Wafarin
5	61	M	2	1	3	Per	N	50	3	Aspirin
6	91	M	3	2	4	Per	Y	55	3	Wafarin
7	80	M	4	3	4	Per	N	65	3	Aspirin
8	86	M	4	4	5	Per	N	60	2	LMWH
9	77	M	5	4	3	Per	N	60	4	Wafarin
10	75	F	4	2	2	Paro	N	60	4	Wafarin
11	77	M	5	3	4	Per	Y	65	4	Aspirin + LMWH
12	74	F	6	4	7	Paro	Y	45	4	LMWH
13	77	F	3	2	2	Per	N	35	3	Wafarin
14	71	M	6	4	5	Per	Y	55	4	LMWH

DRT device-related thrombus, *M* male, *F* female, *AF* atrial fibrillation, *DM* diabetes mellitus, *Per* permanent/persistent, *Paro* paroxysmal, *LVEF* left ventricular ejection fraction, *SEC* spontaneous echocardiographic contrast, *LMWH* low-molecular-weight heparin

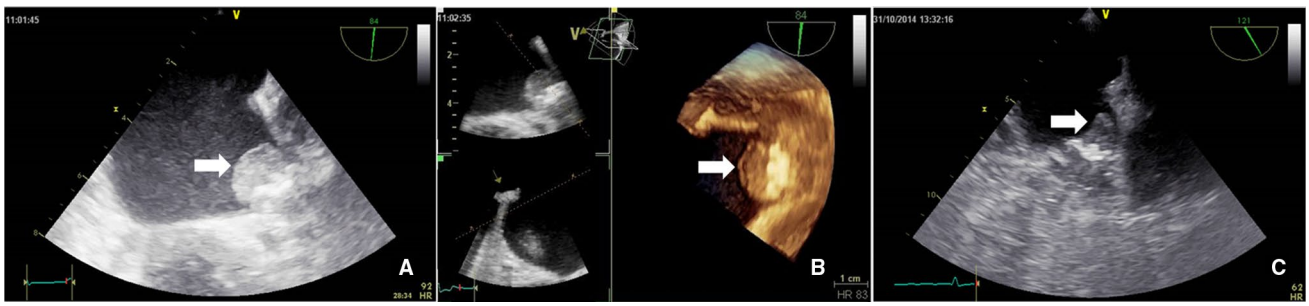

Fig. 2 Location of DRT. **a** DRT in the center; **b** DRT 3D image; **c** DRT spread toward pulmonary vein

(when this patient was receiving aspirin alone). In addition, all the patients with DRT received the WM or WMF device implantation and were asymptomatic. **Due to the limited 15 cases of ACPs and Amulet devices implanted in this study (less than 10%), it is difficult to compare which kind of device is more prone to thrombus formation.** And none of these 15 patients presented any problem during follow-up. Although all of the patients remained completely asymptomatic, without any neurological event in this study, the available evidence comes from current LAAC studies shown DRT is associated with a higher rate of stroke and systemic embolism. [11] However, DRT resolution is possible with anticoagulation, specifically NOACs.

In general, although the exact mechanism of DRT remains speculative, for all blood-contacting devices, it can be useful to classify risk factors as device-, procedure-, or patient-specific. One of the most commonly incriminated factors predisposing to DRT is the screw's threads on the atrial side of the device. Despite the fact that animal studies show the atrial surface of the Watchman device and the central screw threads were completely covered by neo-endocardial tissue as early as 28 days after implantation [22], most thrombi in this study originated from the connector pin of the device, suggesting there may be incomplete endothelialization. Massarenti L et al. also found incomplete endothelialization of left atrial appendage occlusion devices 10 months after implantation by postmortem examinations [23]. The Amulet device, an evolution of the ACP, has an inverted attaching end-screw on the disk to reduce the risk of DRT [5]. Furthermore, the ACP proximal disk composed of nitinol mesh and the permeable polyester fabric cover of Watchman may be other causes for thrombus formation. Therefore, the next generation of LAAC device should have a modified connector pin and disk.

Another finding from our study is that residual peri-device leak after LAAC was a significant risk factor

Table 3 Individual procedural characteristics and follow-up data of patients with DRT

Pts	Onset (month)	Antithrombotic strategy at discharge	Device	Device size(mm)	Thrombus size (mm)	Location of DRT	Peri-gap (mm)	Recapture	Therapy	Resolution (month)	Possible Reason	Repeated DRT
1	5	Warfarin	WM	27	8×10	Central	0	Y	LMWH + Clopidogrel	23	Poor drug compliance	No
2	6	Warfarin	WM	24	10×17	Central	0	Y	DAPT + LMWH	No/31	Clopidogrel resistance	Yes
3	1.5	Warfarin	WM	33	8×15	Central	3	N	DAPT + LMWH	No/30	Severe SEC	Yes
4	5	Warfarin	WM	27	12×15	Central	0	N	LMWH	7	Clopidogrel resistance	No
5	5	DAPT	WM	30	6×18	Central	3	N	LMWH	12	Clopidogrel resistance	No
6	24	Warfarin	WM	27	8×15	Spread to PV	2	Y	Warfarin	–	Unknown	No
7	6	Warfarin	WM	24	7×11	Spread to PV	3	N	LMWH + Dabigatran	3	Clopidogrel resistance	No
8	1.5	LMWH	WM	27	6×11	Central	3	N	DAPT + LMWH	No/31	Unknown	Yes
9	8	Warfarin	WM	27	8×14	Spread to PV	0	N	LMWH	5	Severe SEC	No
10	5	LMWH	WMF	35	5×13	Central	0	N	Dabigatran	2	Severe SEC	No
11	8	Warfarin	WM	21	13×19	Central	0	N	Warfarin	–	Severe SEC	No
12	6	Warfarin	WM	21	12×18	Spread to PV	0	N	Dabigatran	–	Severe SEC	No
13	4.5	DAPT	WM	24	9×11	Central	0	N	Warfarin	–	Unknown	No
14	1	Warfarin	WM	24	4×12	Central	0	N	Warfarin	–	Severe SEC	No

DRT device-related thrombus, *OP* operation, *WM* watchman, *WMF* watchman flx, *PV* pulmonary vein, *N* none, *Y* yes, *DAPT* dual antiplatelet therapy, *SEC* spontaneous echocardiographic contrast, *LMWH* low-molecular-weight heparin

Table 4 Comparison of patients without and with DRT

	Thrombus, $n=14$	No thrombus, $n=298$	p value
Age (years ± SD)	75.86 ± 6.97	75.03 ± 7.59	0.688
Female	5 (35.7%)	100 (33.6%)	0.902
Persistent/permanent AF	12 (85.7%)	201 (67.4%)	0.254
CHADS2	3.0 ± 1.0	2.4 ± 1.2	0.087
CHA2DS2-VASc	4.3 ± 1.3	3.8 ± 1.5	0.195
HAS-BLED	4.1 ± 1.2	3.5 ± 1.1	0.042*
Prior heart failure	2 (14.3%)	48 (12.1%)	0.848
Prior renal dysfunction	7 (50%)	133 (44.6%)	0.904
Diabetes mellitus	5 (35.7%)	75 (25.5)	0.589
Device size	25.9 ± 3.2	24.8 ± 3.1	0.180
Residual peri-device leak	5 (35.7%)	14 (4.7%)	0.000067*
Recapture	6 (42.9%)	83 (27.9%)	0.361
Previous stroke	3 (21.4%)	67 (22.5%)	0.813

*$p < 0.05$

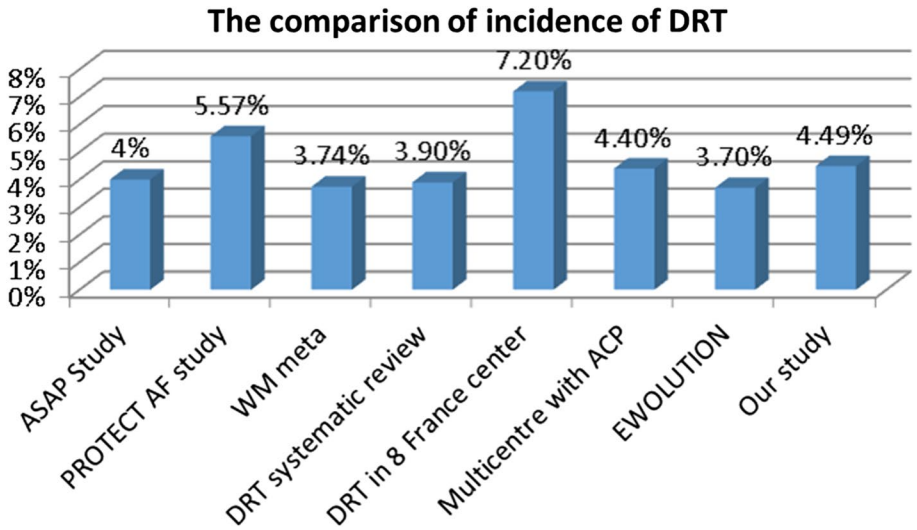

Fig. 3 The comparison on incidence of DRT with other studies

associated with DRT. This is one of the procedure-specific risk factors. Of the 14 patients with DRT, 5 patients had 2–3 mm residual peri-device leak during follow-up. Before we released the device, the LAA closure was deemed successful even in cases with a residual gap of up to 5 mm around the device according to the PROTECT-AF trial design. This degree of "acceptable" residual peri-device leak was chosen as a reasonable cut-off value and was not associated with an increased risk of thromboembolism in a post hoc analysis of the Watchman implantation cohort in the PROTECT-AF study. However, there was a statistical interaction between the presence of the residual peri-device leak and the subsequent risk of DRT in our study. Incomplete LAA closure with residual peri-device leak results in an open pouch with residual flow into the LAA, which may cause turbulence in blood flow in the residual LAA pouch [11]. It must be noted that the number of peri-device leak in our study is low. In the recently published PROTECT-AF follow-up study, the investigators report a prevalence of incomplete "closure" of only 32% at 12 months [24]. This difference compared with PROTECT-AF may lead to statistical bias. Potential differences in clinical outcome might be evident only after a longer follow-up period. In other small-scale study, it was suggested that a deep implantation of the device in the LAA, leaving an uncovered part of the LAA, may possibly be an important factor contributing to DRT [21, 24]. Another procedure-specific risk factor is the anticoagulation regimen postimplantation. 8 out of 14 patients in this study suffered from thrombus formation after their 45-day anticoagulation treatment (subacute phase). These findings indicate the current post-interventional anticoagulation/antiplatelet regime may require modification. Current post-procedural antithrombotic regimens are

empirical. The duration of anticoagulation therapy may be prolonged provided that there is a residual peri-device leak after device implantation. This observation also demonstrates that close monitoring of an LAA occluder device is required when anticoagulation or dual platelet therapy is withdrawn. In addition, HAS-BLED scores were higher in patients with DRT than without thrombus. Because the patient had a high HAS-BLED score, aspirin and clopidogrel without any anticoagulants were prescribed after the procedure because of a history of bleeding with oral anticoagulant therapy. So these patients with higher HAS-BLED score were under treated with antithrombotic therapy. The discontinuation of anticoagulation/dual antiplatelet treatment as a factor related to device thrombus was also discussed in another study [24]. However, the optimal duration of antithrombotic therapy remains to be clearly defined.

The third category of risk factors of DRT may be patient-related factors. Ketterer et al. investigated the presence of clopidogrel resistance in patients treated with LAAC. They reported that more than two-thirds of patients with DRT after percutaneous LAAC were clopidogrel-resistant [25]. This condition may be responsible for a series of unreported thromboembolic events occurring after LAAC. We also found 4 patients with DRT who had suspicious clopidogrel resistance. When the DRT was detected, we replaced the clopidogrel with NOACs or ticagrelor. Several months later, the DRT was dissolved completely. Notably, when we reviewed the TEE echo image of patient with DRT, the presence of spontaneous echo contrast ("dynamic smoke-like swirling echoes in the left atrium or the LAA") was observed in most cases. SEC $\geq 3°$ occurred in 13 patients (92.9%). Significant spontaneous echo contrast in LAA is a known marker of stasis and thromboembolic risk. Hematological studies have shown that SEC is a marker of an hypercoagulable state and a manifestation of red cell aggregation, arising from an interaction between red cells and plasma proteins such as fibrinogen, at low shear rates. Patients with SEC after LAAC should be considered for anticoagulant therapy. Therefore, future studies might aim to determine the association between spontaneous echo contrast and thrombus formation. Higher $CHADS_2$ score and reduced cardiac function were established risk factors for thrombus formation in previous studies and were not associated with thrombus formation in this study [10, 11]. Patients' compliance with antithrombotic therapy is also an important aspect; for example, patient #1 was an alcohol-addicted patient in this study. The patients' poor medication adherence, or non-adherence, limits effective antithrombotic management and control of DRT. NOACs have the advantages of ease of dosing, fewer drug interactions, and lack of need for ongoing monitoring. NOACs may lead to good adherence for the patients with DRT. Complete thrombus resolution under NOACs treatment was achieved in selected patients [19].

Limitations

Device-related thrombus was possibly underdiagnosed, considering the number of patients who did not undergo LAA imaging during follow-up. It is important to note that the compliance with follow-up TEE evaluation was significantly correlated with the incidence of DRT. The cases of delayed DRT up to 1 year after implantation may be underestimated due to inconsistent/incomplete routine postimplantation surveillance. This study is retrospective and not a randomized trial, and it was not possible to account for all confounding influences. For example, we did not have complete data on DRT characteristics such as protrusion of the shoulder of the device into the left atrium, platelet activity tests, and response to clopidogrel in patients. Such data would likely have improved both our understanding of the mechanism of DRT. In addition, due to the novelty of the technique, only a medium follow-up was documented. Considering the complexity of patients undergoing LAA closure, further studies with larger series and a longer follow-up are necessary not only to define evidence-based antithrombotic strategies to prevent DRT, but also to better determine predisposing factors of this feared complication.

Conclusions

This study illustrated that device-related thrombus after left atrial appendage closure might be an infrequent, but possible, complication, and its incidence was relatively low at 4.49%. This result is very consistent with other studies. Residual peri-device leak after LAAC may contribute to its occurrence. Higher HAS-BLED score was also associated with DRT. The role of TEE in detecting device-related thrombus was very important. The results also suggest that patients might need prolonged anticoagulation therapy once the presence of residual peri-device leak is detected. Antithrombotic regimen and duration after LAAC could be tailored according to the risk of device-related thrombus. Additional studies are needed to know if the current practice of antithrombotic regimens before endothelialization of the device is sufficient.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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