Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Detection of Device-Related Thrombosis Following Left Atrial Appendage Occlusion

A Comparison Between Cardiac Computed Tomography and Transesophageal Echocardiography

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BACKGROUND: Device-related thrombosis (DRT) following left atrial appendage occlusion is a rare but feared complication. The diagnostic value of cardiac compute tomography (CT) for detection of DRT is unknown. This study sought to evaluate the clinical value of cardiac CT for detection of DRT using transesophageal echocardiography (TEE) as the reference standard and to provide insights into the causes, natural history, and risk of DRT.

METHODS: We reviewed 301 consecutive patients undergoing left atrial appendage occlusion at Aarhus University Hospital, Denmark, between 2010 and 2017. Of these, 248 patients had cardiac CT and TEE imaging available at 8-week follow-up; 139 had complete 12-month imaging. A blinded investigator analyzed all images. On TEE, an echo-dense mass attached to the device was defined as DRT. Cardiac CT was analyzed for presence of hypoattenuated thickening (HAT) on the device, which was subclassified as low grade or high grade. High-grade HAT was considered as definite DRT.

RESULTS: At 8 weeks, TEE detected 5 (2%) cases with DRT; and cardiac CT 6 (2.4%) cases with high-grade HAT. At 12 months, both TEE and cardiac CT detected 2 (1.4%) cases with DRT or high-grade HAT, respectively. Cardiac CT demonstrated low-grade HAT in 9 (3.6%) cases at 8 weeks; and 13 cases (9.4%) at 12-months. High-grade HAT/DRT was associated with thromboembolism in 2 cases, whereas low-grade HAT was not related to embolic events. Low-grade HAT resolved spontaneously over time.

CONCLUSIONS: Cardiac CT seems equally good as TEE for detection of DRT. In addition, cardiac CT demonstrates cases with low-grade HAT, not visualized by TEE. The clinical significance hereof requires further investigation.

VISUAL OVERVIEW: A visual overview is available for this article.

Key Words: atrial appendage ■ echocardiography, transesophageal ■ registries ■ risk ■ thrombosis

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WHAT IS KNOWN

- Cardiac computed tomography has gained increasing interest as follow-up imaging after left atrial appendage occlusion; however, the diagnostic value for detection of device-related thrombosis is unknown.

WHAT THE STUDY ADDS

- Cardiac computed tomography seems equally good as transesophageal echocardiography for detection of device-related thrombosis. It even demonstrates cases with low grades of hypoattenuated thickening on the surface of the left atrial appendage occlusion device, not visible by transesophageal echocardiography. This seems to be a temporary phenomenon.
- Cardiac computed tomography may be a valuable tool in clinical practice for follow-up after left atrial appendage occlusion and in future studies addressing the clinical impact and optimal treatment of device-related thrombosis.
- Further investigations are warranted to establish the clinical implications of hypoattenuated thickening of the left atrial appendage occlusion device.

Transcatheter left atrial appendage occlusion (LAAO) is an increasingly used alternative to oral anticoagulation in patients with atrial fibrillation and a high bleeding risk. The efficacy and safety of the procedure has been demonstrated in 2 randomized trials[1] and multiple large observational registries.[2–4] A feared complication following device implantation is thrombus formation on the atrial surface of the device.[5–8] The incidence of device-related thrombosis (DRT) ranges between 2% and 17% in observational case series.[3–6,8–10] The majority of patients with DRT were diagnosed during early routine follow-up imaging.[5] Still, the presence of DRT seems to be associated to post-LAAO thromboembolic events irrespective of timing of diagnosis,[5–8] and empirical treatment with low molecular weight heparin or oral anticoagulation seems to effectively resolve DRT.[6]

Transesophageal echocardiography (TEE) is regarded as the gold standard per device surveillance following LAAO, and for the diagnosis of DRT.[11] However, cardiac computed tomography (CT) is an appealing alternative because of its noninvasive nature. Despite TEE offers higher temporal resolution, cardiac CT has superior spatial resolution, is isotropic by nature with 3-dimensional (3D) and multiplanar capabilities, and is less operator dependent. Studies have suggested feasibility of cardiac CT for device-surveillance following LAAO; however, no comparative studies have evaluated the diagnostic performance to detect DRT.[12,13] This study aimed to compare cardiac CT and TEE for detection of DRT and to provide insights into the natural history of thrombus formation on the LAAO device using cardiac CT.

METHODS

Study Design and Population

This was a retrospective single-center, cohort study of consecutive patients undergoing LAAO with the Amplatzer Cardiac Plug or Amulet (Abbott, Lake Bluff, IL) device at Aarhus University Hospital, Denmark, between March 2010 and September 2017. All patients who underwent LAAO were scheduled for 8 weeks and 12 months follow-up with both cardiac CT and TEE per institutional routine device-surveillance. In patients with a glomerular filtration rate ≤30 mL/minute, the cardiac CT was omitted. Patients were included in the current analysis if both cardiac CT and TEE imaging were available at the 8-week follow-up visit. All imaging analyses were performed retrospectively by 1 investigator in a blinded fashion.

The study conformed to the declaration of Helsinki. The Danish Data Protection Agency (1-16-02-419-16) and Danish Patient Safety Authorities (3-3013-2736/1) approved the study, and according to Danish law, ethical approval was not required for the current study.

Transesophageal Echocardiography

A TEE was performed using the Philips x7-t2 probe or the GE 6VT-D probe. The LAAO device was visualized in multiple planes at 0°, 45°, 90°, and 135°. All patients had 2-dimensional TEE available, with 3D TEE images available in 174/248 (71%) at 8 weeks and 114/166 (69%) at 12-month follow-up. DRT by TEE was defined as a homogenous echo-dense mass visible in multiple planes with independent motion and adherence to the atrial surface of the LAAO device (Figure 1). The clinical decision to initiate anticoagulation was predominantly based on findings from TEE.

Cardiac CT Acquisition

Cardiac CT scans were performed using the Siemens Somatom Definition Flash or Force scanner (Siemens Healthcare, Forchheim, Germany). The imaging acquisition protocol has previously been described in detail.[14] In brief, a prospective ECG-gated scan was performed using a high-pitch single-heart-beat spiral acquisition protocol (Flash). A diastolic phase was targeted for heart rates below 70 beats per minutes, and a systolic phase for heart rates above 70 beats per minute. Tube voltage was set between 70 and 150 kV depending on body weight. Automated tube current modulation was used (CareDose 4D). Based on a test bolus, a single contrast injection (350 mg I/mL Iodine concentration) was administered through an antecubital vein at flow rates of 5 to 6 mL/s, followed by a 50 mL saline flush. Images were reconstructed with a 0.75-mm slice thickness using kernel Bv40.

The effective radiation exposure associated with the cardiac CT scan was calculated based on the dose-length product (mGy-centimeter) applying a 0.014 mSv/mGy/cm conversion factor.

Analysis of Cardiac CT Images

Images were analyzed using the syngo.via software package (Siemens Healthcare, Forchheim, Germany). The implanted LAAO device was identified in the multiplanar reconstructed view, and the axes were aligned with the disc and the center placed perpendicular through the screw hub.[14] The images were evaluated for signs of DRT defined as any

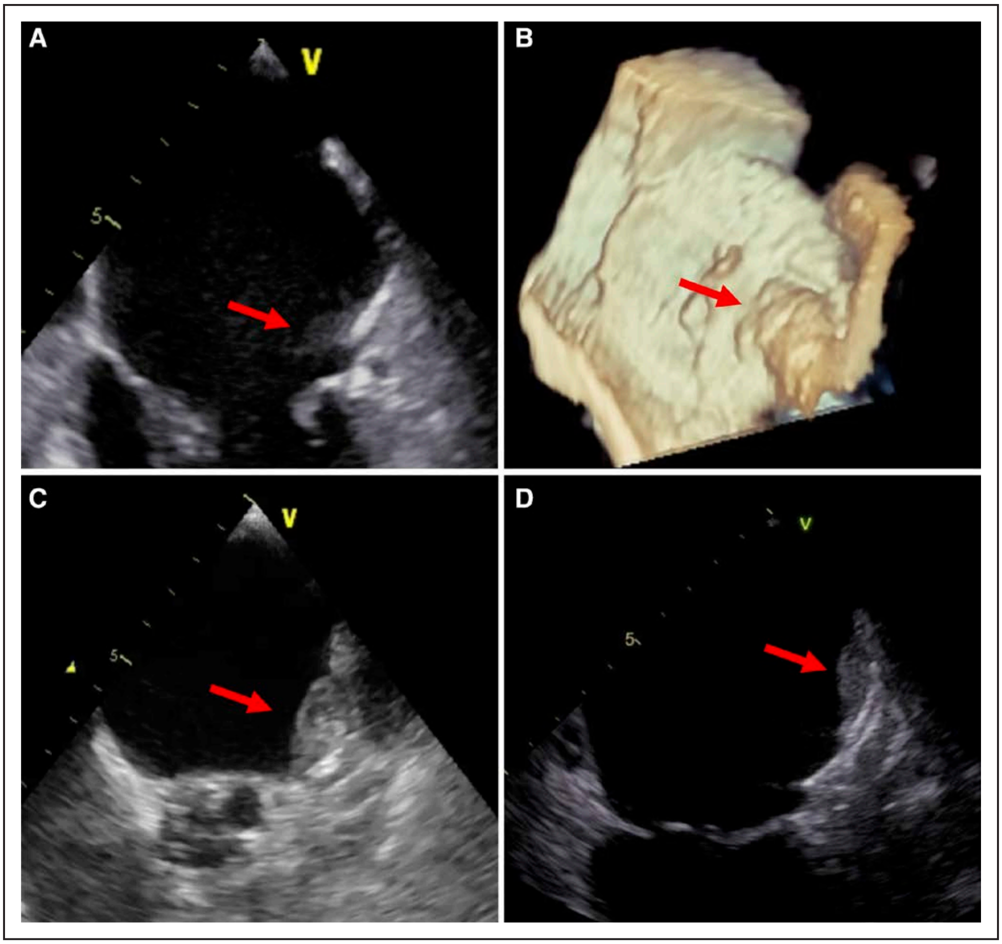

Figure 1. Illustration of device-related thrombosis on transesophageal echocardiography.
Small pedunculated device-related thrombus attached to the left atrial appendage occlusion device disc (**A**); large, laminar device-related thrombus on the disc (**B**); 2-dimensional and 3-dimensional illustration of a laminar device-related thrombus at the superior margin (**C** and **D**).

hypoattenuated thickening (HAT) on the atrial surface of the LAAO device (Figures 2 and 3). The cross-sectional area of a HAT was traced at the level of the device disc and related to the disc surface area. The Hounsfield attenuation values of HAT and at the center of the left atrium was measured, and a HAT/left atrium attenuation ratio was calculated. Three experienced investigators reviewed images with HAT, which was subsequently subclassified into low- or high-grade HAT (Figure 3). A high-grade HAT was a priori considered as definite DRT on cardiac CT.

Antithrombotic Therapy

Per institutional protocol, antithrombotic therapy following device implantation consisted of aspirin monotherapy 75 mg/day for 6 months in all patients, unless other indications necessitated life-long aspirin, dual antiplatelet therapy, or oral anticoagulation (ie, recent coronary stent implantation, carotid endarterectomy, or mechanical valve prosthesis).[10]

Clinical Events and Follow-Up

Adverse events were defined according to the Munich Consensus Document on definitions and end points for clinical studies on LAAO.[15] We registered ischemic stroke, systemic embolism, major bleeding, and all-cause death during follow-up. Clinical follow-up was conducted at patient visits 8 weeks and 12 months after the procedure, thereafter through systematic review of the patients' electronic medical files, and through a search in the Danish Civil Registration System.[16]

Statistical Analysis

The distribution of data was assessed using QQ-plot and histogram. Continuous variables were expressed as mean with SD, or median with interquartile ranges, and were compared using the Student *t* test or Mann-Whitney *U* test as appropriate. Categorical variables were reported as counts and percentages, and groups were compared using Fisher exact test. A 2-tailed $P<0.05$ was considered statistically significant. Statistical analysis was performed using STATA (STATA IC, version 14.2, StataCorp, College Station, TX).

RESULTS

A total of 301 patients underwent LAAO during the study period. Of these, 248 patients had an Amplatzer device implanted and complete imaging follow-up at 8 weeks with both cardiac CT and TEE available for analysis. These 248 patients formed the basis of the present

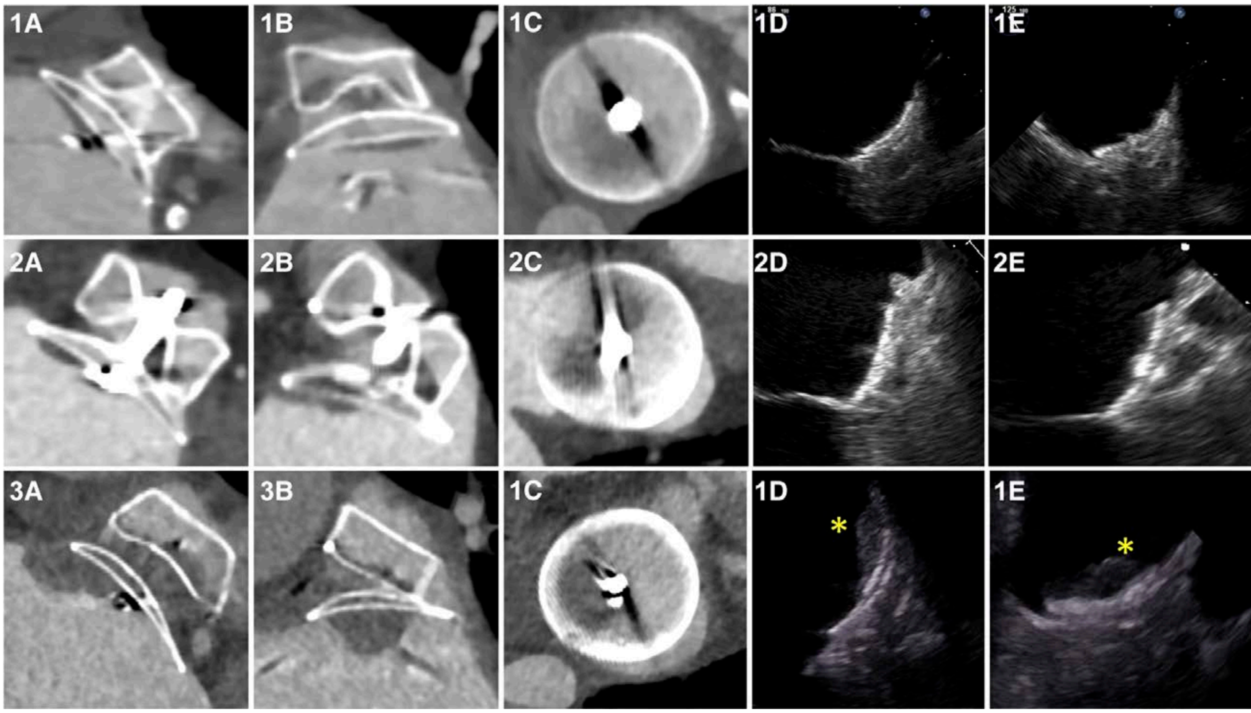

Figure 2. Appearance of device related hypoattenuated thickening on cardiac computed tomography and transesophageal echocardiography (TEE). Illustration of hypoattenuated thickening on the left atrial appendage occlusion device in 3 different patients, with corresponding TEE images. Images 1A through 1E and 2A through 2E illustrate low-grade hypoattenuated thickening, not visualized by TEE. Images 3A through 3E shows high-grade hypoattenuated thickening, visualized in the corresponding TEE.

study (Figure 4). Baseline characteristics are summarized in Table 1. Mean (SD) age of the study cohort was 73±8.4 years, 67% were male, mean (SD) body mass index was 26.8±4.3, and 44% had permanent atrial fibrillation at baseline. An Amplatzer Cardiac Plug was implanted in 62 (25%) cases, an Amplatzer Amulet device in 186 (75%).

8-Week Follow-Up Imaging

Mean (SD) time from LAAO to first cardiac CT was 60±21 days. In 236 of 248 (95%) patients, the cardiac CT and TEE were performed on the same day. The remaining 12 patients had a median (IQR) of 22 (5–42) days between cardiac CT and TEE. The follow-up cardiac CT was performed with 62% of patients in atrial fibrillation, and mean (SD, range) effective radiation exposure was 1.9±2.3 (0.45–24.6) mSv.

DRT was detected in 5 (2%) patients by TEE. Presence of HAT was detected in 15 (6%) patients by cardiac CT. HAT was classified as low- and high-grade in 9 (3.6%) and 6 (2.4%) patients, respectively. All patients with a DRT on TEE had high-grade HAT on cardiac CT. Image quality of the cardiac CT was inadequate for the diagnosis of HAT in 12 of 248 patients (4.8%) because of the presence of at least 1 compromising artifact (severe blooming, n=9; motion, n=4; low contrast opacification, n=2).

12-Month Follow-Up Imaging

Twelve-month follow-up imaging was available in 182 of 248 (73%) patients; 139 (56%) had both cardiac CT and TEE imaging performed (Figure 4). Impaired image quality was present in 11 of 169 (6.5%) cardiac CT scans (severe blooming, n=10; motion, n=2; low contrast opacification, n=1). Mean (SD) time from LAAO to 12-month cardiac CT was 366±85 days, and both cardiac CT and TEE was performed on the same day in 134 of 139 (96%) patients. Mean (SD, range) radiation exposure was 2±3.8 mSv (0.49–45), and 64% of patients were in atrial fibrillation during the scan.

Of the 139 patients with cardiac CT and TEE available for comparison, a DRT was detected in 2 (1.4%) patients on TEE, and the same 2 patients had high-grade HAT on cardiac CT. In addition, cardiac CT detected 13 (9.4%) cases of low-grade HAT on the device surface.

None of the patients examined by cardiac CT only demonstrated HAT, while 1 patient had DRT among those studied only by TEE.

Characteristics HAT

In total, 30 cases of HAT were detected in 27 patients (Table 2). HAT with a HAT/left atrium attenuation ratio

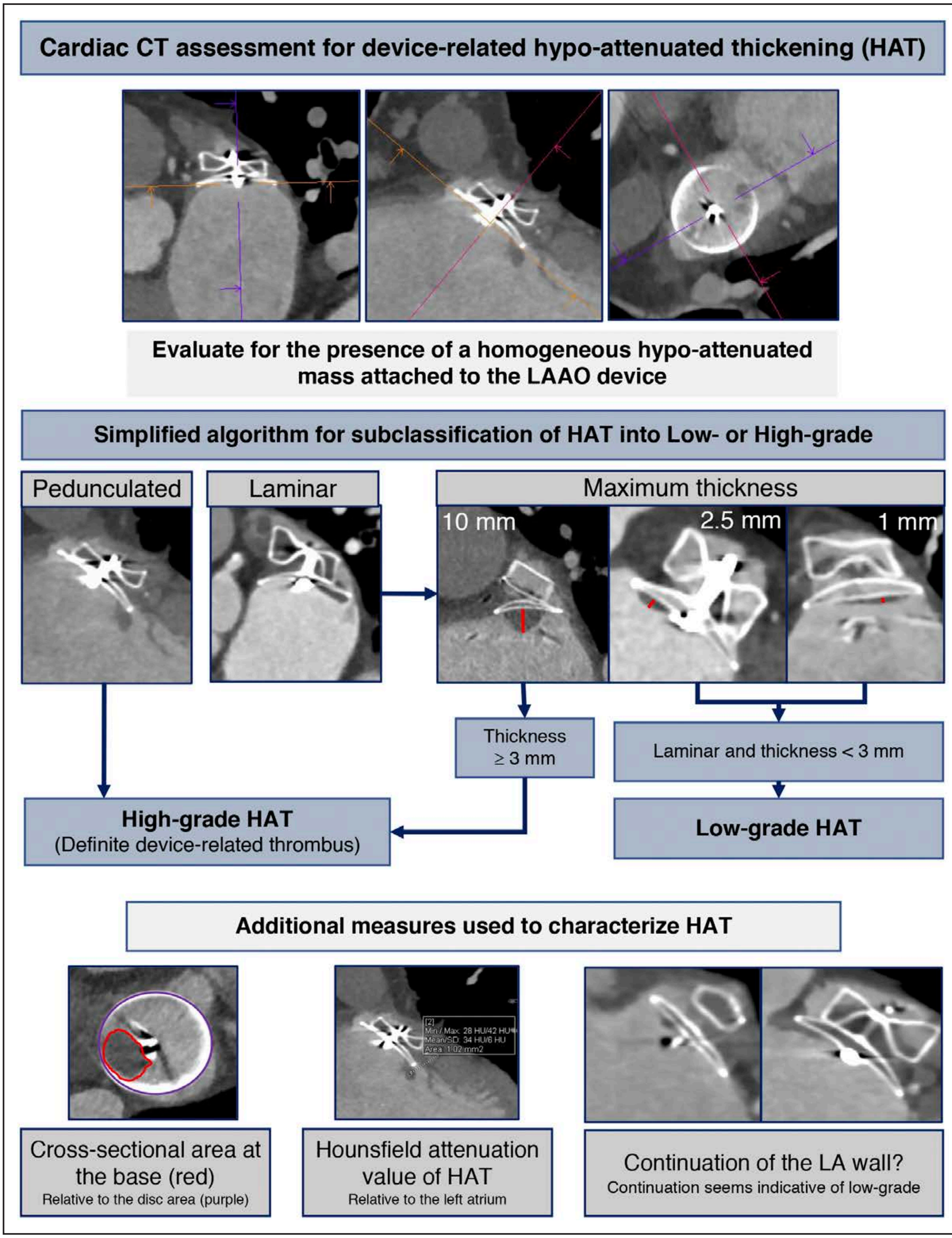

Figure 3. Illustration of the algorithm to detect and classify left atrial appendage occlusion (LAAO) device hypoattenuated thickening (HAT). CT indicates computed tomography; and LA, left atrium.

below 0.2 and no smooth continuation of HAT onto the left atrium wall was more likely to be categorized as high-grade (Table 2).

A second follow-up cardiac CT scan was available in 6 of 9 patients with low-grade HAT at 8 weeks. All showing complete resolution of low-grade HAT (Table 3; Figure 5). High-grade HAT resolved into low-grade HAT in 3 patients and completely resolved in 1 patient (Table 3). None of the patients with low-grade HAT at 12 months had additional cardiac CT available for analysis. The 2 patients with high-grade HAT at 12 months underwent repeated TEE with complete

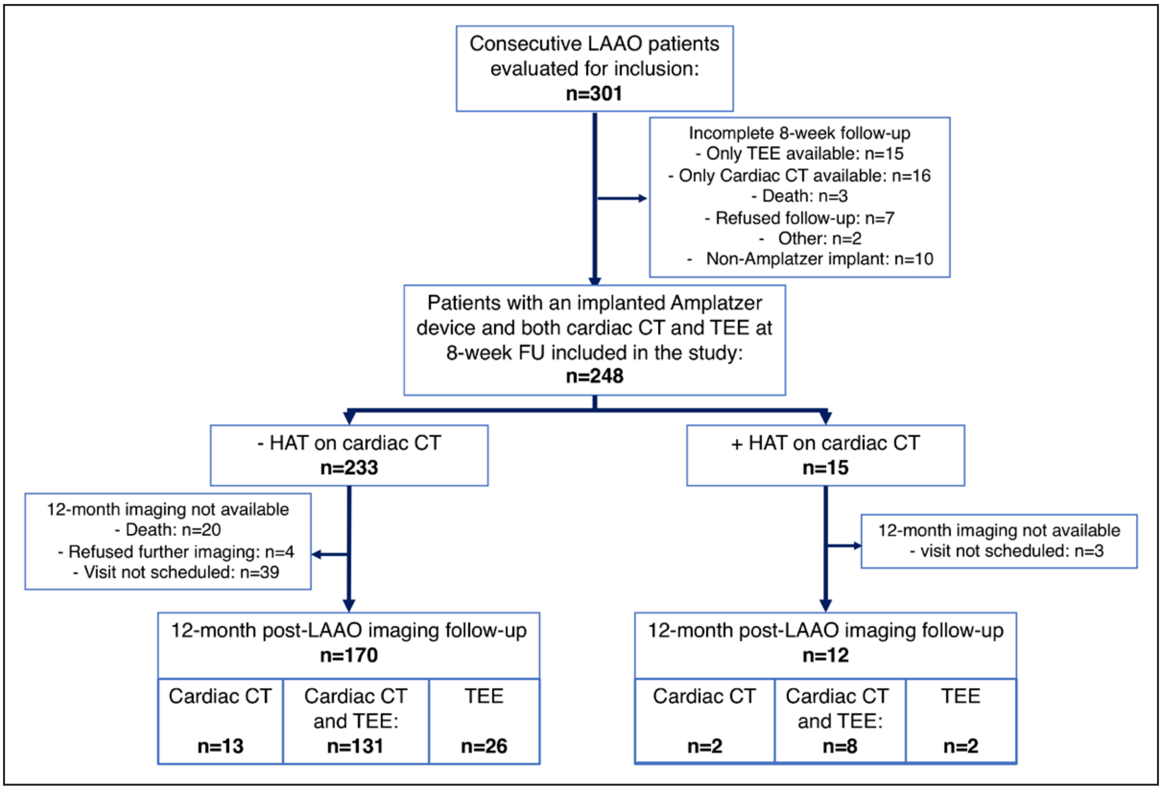

Figure 4. Flow chart of study patients.
CT indicates computed tomography; HAT, hypoattenuated thickening; LAAO, left atrial appendage occlusion; and TEE, transesophageal echocardiography.

resolution. The antithrombotic therapy in case of high-grade HAT consisted of low molecular weight heparin in 3 of 8 cases, oral anticoagulation in 3 of 8 cases, and continued aspirin therapy in 2 of 8.

A deep device implantation defined as the device disc being positioned at least 10 mm distal to the tip of the left upper pulmonary vein ridge[17] and thereby leaving a LAA remnant was more prevalent in patients with HAT. Otherwise, no statistically significant difference was seen in baseline characteristics, discharge antithrombotic therapy, or device characteristics between patients with HAT and those without (Table 4).

Clinical Outcomes

Mean (SD) follow-up time was 1.7±1.1 years. High-grade HAT appeared to be associated with a thromboembolic event in 2 patients (Table 5). One patient suffered ischemia in the lower extremities 20 days following LAAO. Both cardiac CT and TEE during the hospitalization showed high-grade HAT and DRT, respectively. The other suffered an ischemic stroke 119 days after LAAO, with an in-hospital TEE showing DRT. Cardiac CT and TEE follow-up was conducted 3 months later still showing high-grade HAT and DRT, respectively. Low-grade HAT was not associated with thromboembolic events.

DISCUSSION

In this large comparative cohort study of cardiac CT and TEE for detection of DRT, our principal finding was that cardiac CT is a highly valuable modality with an excellent ability to detect DRT on the atrial surface of the LAAO device. Cardiac CT even detects low grades of HAT on the disc surface. In addition, we propose a new clinical graduation of HAT for discrimination between definite thrombus and low-grade HAT which seems to be a benign and transient phenomenon.

Diagnostic Value of Cardiac CT

Smaller observational case series have reported feasibility of cardiac CT for device-surveillance, but the focus hitherto has been on peridevice leaks, without any systematic comparison of the ability to detect DRT.[12,18] A recent case series with cardiac CT performed in 117 patients following LAAO described an enhancement defect on the atrial surface of the device in 19 patients. A TEE examination of these 19 patients showed definite organized thrombus in 5 patients.[13] However, the latter report did not include systematic TEE examinations, and a second follow-up of patients suspected of DRT was not performed. Our results support the conclusion that cardiac CT is a more sensitive modality than TEE for detection of potential DRT, which likely is explained by the superior spatial resolution. The algorithm to discriminate

Table 1. Baseline Characteristics of Study Cohort and Excluded Patients

	Study Cohort n=248	Incomplete Imaging Follow-Up n=43	*P* Value
Age, y	73.0±8.4	73.9±10	0.53
Female sex	82 (33%)	23 (47%)	0.12
Body mass index	26.8±4.3	26.7±5	0.89
Permanent atrial fibrillation	110 (44%)	23 (54%)	0.32
Congestive heart failure	42 (17%)	9 (21%)	0.52
Baseline left ventricular EF (%)	60 (50–60)	60 (50–60)	0.28
Mechanical valve prosthesis	2 (1%)*	0 (0%)	>0.99
Hypertension	201 (81%)	38 (89%)	0.29
Diabetes mellitus	47 (19%)	11 (26%)	0.31
Ischemic stroke/TIA	117 (47%)	17 (40%)	0.41
Vascular disease	96 (39%)	15 (35%)	0.73
History of major bleeding	194 (78%)	35 (81%)	0.84
Chronic kidney disease stage 3–5	74 (30%)	22 (51%)	<0.01
Creatinine (µmol/L)	85 (71–104)	100 (75–174)	0.01
CHA_2DS_2-VASc Score	4.2±1.6	4.3±1.6	0.51
HAS-BLED score	3.8±1.1	4.2±1.1	0.02
Primary indication for LAAO			
Intracranial hemorrhage	96 (39%)	22 (51%)	0.13
Gastrointestinal bleeding	48 (19%)	5 (12%)	0.29
Urinary tract bleeding	15 (6%)	0 (0%)	0.14
Other spontaneous bleeding	27 (11%)	6 (14%)	0.60
Cerebral amyloid angiopathy	12 (5%)	1 (2%)	0.70
Stroke despite OAC	21 (9%)	1 (2%)	0.22
High bleeding risk/ intolerance to OAC	25 (10%)	8 (19%)	0.12
Other	4 (2%)	0 (0%)	>0.99
Implanted device			<0.01
ACP	62 (25%)	13 (30%)	
Amulet	186 (75%)	30 (70%)	
Mean device size, mm	24.2±4.3	23.7±4.8	0.51
Discharge antithrombotic therapy			
Aspirin monotherapy	207 (84%)	37 (86%)	0.82
Dual antiplatelet therapy	26 (11%)	5 (12%)	0.79
(N)OAC therapy	7 (3%)	0 (0%)	0.60
Clopidogrel monotherapy	8 (3%)	0 (0%)	0.61
No antithrombotic therapy	0 (0%)	1 (2%)	0.15

Data are reported as mean (SD), median (IQR) or numbers (%). ACP indicates amplatzer cardiac plug; EF, ejection fraction; LAAO, left atrial appendage occlusion; OAC, oral anticoagulation; and TIA, transient ischemic attack.

*Both had stroke on OAC as indication for LAAO and continued life-long OAC.

between low- and high-grade HAT seems to correlate well with DRT detected by TEE. However, future studies should aim to validate the proposed algorithm.

Table 2. Characteristics of HAT

	HAT n=27*	Low Grade n=20*	High Grade n=7*	*P* Value
Number of HAT cases	30	22	8	
Pedunculated, n/N	1/30 (3%)	0/22 (0%)	1/8 (13%)	0.26
Thickness, mm	2 (1–14)	1 (1–2.8)	5 (3–14)	<0.01
HAT/LA attenuation ratio	0.29 (0.10–0.82)	0.32 (0.10–0.82)	0.18 (0.12–0.38)	0.04
HAT/device disc cross-sectional area	0.17 (0.04–0.83)	0.15 (0.04–0.66)	0.36 (0.06–0.83)	0.14
Continuation of LA wall, n/N	20/30 (67%)	18/22 (82%)	2/8 (25%)	0.01

Data are presented as median (range). HAT indicates hypoattenuated thickening; and LA, left atrium.

*n indicates number of patients.

Though cardiac CT seems to be a valuable alternative to TEE, the limitations of cardiac CT imaging should be acknowledged. Contrast administration may be problematic in some patients, reducing the generalized feasibility of cardiac CT. In addition, radiation exposure might be a concern. Previous studies have reported mean radiation exposure between 3.5 and 6.6 mSv.[12,14,19] The mean effective radiation exposure was extremely low with the applied high-pitch prospective gated scan acquisition used in our study. The presence of metal in the CT scan field may cause artifacts, which can be worsened by motion. Hence, cardiac CT in an elderly, comorbid population with atrial fibrillation may be challenging. However, with the use of a high-pitch single-heart-beat protocol with very short acquisition time (allowing for a reduced contrast volume), we encountered significant artifacts in only ≈5% of the patients. This is despite ≈62% being in atrial fibrillation during the CT acquisition. Yet, artifacts could potentially be reduced with heart rate control, alternative postprocessing algorithms, or acquisition protocols (double-flash or multiphase retrospective-gated). However, the value of alternative postprocessing algorithms or an immediate re-scan to reduce the need for confirmative TEE examinations in patients with compromising artifacts needs further delineation.

Causes and Evolution of HAT

An autopsy study of 9 canine hearts and 4 human hearts explanted at different time points following LAAO revealed an initial fibrin-thrombus deposition on the device surface, followed by endocardial ingrowth of thin layers of smooth muscle cells and fibrous tissue.[20] Two devices from human hearts showed thin laminar fibrin thrombus masses on the atrial surface, which seemed neither fragile or substantive.[20]

Table 3. Antithrombotic Treatment and Temporal Evolution of Hypoattenuated Thickening Detected at 8-Week Cardiac CT

Patient			8-Week Cardiac CT			Additional Imaging Follow-Up				12-Month Follow-Up				
No	Device (Size)	Discharge Antithrombotics	Interval From LAAO, D	HAT	Post-8-Wk Antithrombotics	Interval From LAAO, D	Modality	HAT	DRT on TEE	Interval From LAAO, D	Cardiac CT Performed	TEE Performed	HAT	DRT on TEE
1	Amulet (25)	ASA	48	Low	ASA	…	…	…	…	…	No	No	…	…
2	Amulet (28)	ASA	48	Low	ASA	…	…	…	…	355	Yes	Yes	No	No
3	Amulet (28)	OAC*	66	Low	Clopidogrel	…	…	…	…	353	Yes	Yes	No	No
4	Amulet (18)	ASA	104	Low	No APT	…	…	…	…	…	No	No	…	…
5	Amulet (22)	ASA	54	Low	ASA	…	…	…	…	393	Yes	Yes	No	No
6	ACP (18)	ASA	104	Low	ASA	…	…	…	…	474	Yes	No	No	…
7	Amulet (22)	ASA	47	Low	Clopidogrel	…	…	…	…	…	No	No	…	…
8	ACP (22)	ASA	42	Low	ASA	…	…	…	…	503	Yes	Yes	No	No
9	Amulet (25)	ASA	74	Low	ASA	…	…	…	…	365	Yes	Yes	No	No
10	Amulet (22)	ASA	48	High	LMWH	142	Cardiac CT	Low	…	379	Yes	No	Low	…
11	Amulet (34)	ASA	74	High	LMWH	167	Cardiac CT	Low	…	544	Yes	Yes	High	Yes
12	Amulet (25)	DAPT	57	High	ASA	91	Cardiac CT	High	…	402	Yes	Yes	Low	No
13	Amulet (25)	ASA	57	High	ASA	…	…	…	…	349	No	Yes	…	No
14	ACP (28)	ASA	92	High	LMWH	124	TEE	…	No	377	Yes	Yes	No	No
15	ACP (20)	Clopigodrel	22	High	OAC+ASA	125	TEE	…	No	Death before 12-month visit				

ACP indicates amplatzer cardiac plug; APT, antiplatelet therapy; ASA, acetylsalicylic acid; DAPT, dual antiplatelet therapy; CT, computed tomography; DRT, device-related thrombosis; HAT, hypoattenuated thickening; LMWH, low molecular weight heparin; LAAO, left atrial appendage occlusion; OAC, oral anticoagulation; and TEE, transesophageal echocardiography.

*The patient underwent combined pulmonary vein isolation and left atrial appendage occlusion, hence oral anticoagulation was given for 3 mo post-procedural.

In our cohort, low-grade HAT was detected on cardiac CT in 9 patients at 8 weeks, and 13 patients at 12 months. Low-grade HAT detected at 8 weeks appeared to resolve spontaneously over time, and a few cases with high-grade HAT regressed into low-grade HAT on anticoagulation therapy. Although in our cases, the diagnosis of HAT was not confirmed by histology or autopsy, the spontaneous resolution may indicate that low-grade HAT represents temporary platelet aggregation and fibrin deposition as an early stage of thrombus formation. This seems to be supported by the autopsy and animal studies.[20,21] Likewise, studies on transcatheter aortic valve implantation have reported analogous results with hypoattenuation of the leaflets visualized by cardiac CT.[22] Hypoattenuation of the leaflets has been interpreted as early, subclinical stages of leaflet thrombosis, while, it similarly seems to spontaneously resolve.[23,24] The hypothesis of hypoattenuation of the leaflets representing thrombus material seems to be supported by a recently published histological study of explanted transcatheter heart valves.[25]

The mechanisms behind the development of high-grade HAT is unknown. However, it might be a continuum of low-grade HAT, exaggerated by slow flow phenomena, exemplified by the higher prevalence of deep device implantations, permanent atrial fibrillation, and congestive heart failure in patients with high-grade HAT (Table 2). However, the lack of histological or autopsy confirmation of HAT or DRT warrants further studies elaborating on the mechanisms and clinical implications of these findings.

Management of HAT

The treatment of DRT following LAAO is currently empirical. Observational studies have indicated an association between DRT detected by TEE and clinical thromboembolic events.[5,7] However, the clinical management of patients with low-grade HAT remains unclear, especially given the uncertainty of what these findings represent. The spontaneous resolution without clinical events seems to advocate a conservative approach, which has been the strategy in other centers.[13] Nonetheless, an intensified follow-up with repeat cardiac CT to monitor the progression of low-grade HAT is encouraged. In turn, studies are warranted to investigate the clinical significance, management, and optimal antithrombotic therapy in case of HAT.

Study Limitations

This study has the inherent limitations of an observational single-center design. However, the blinded analysis

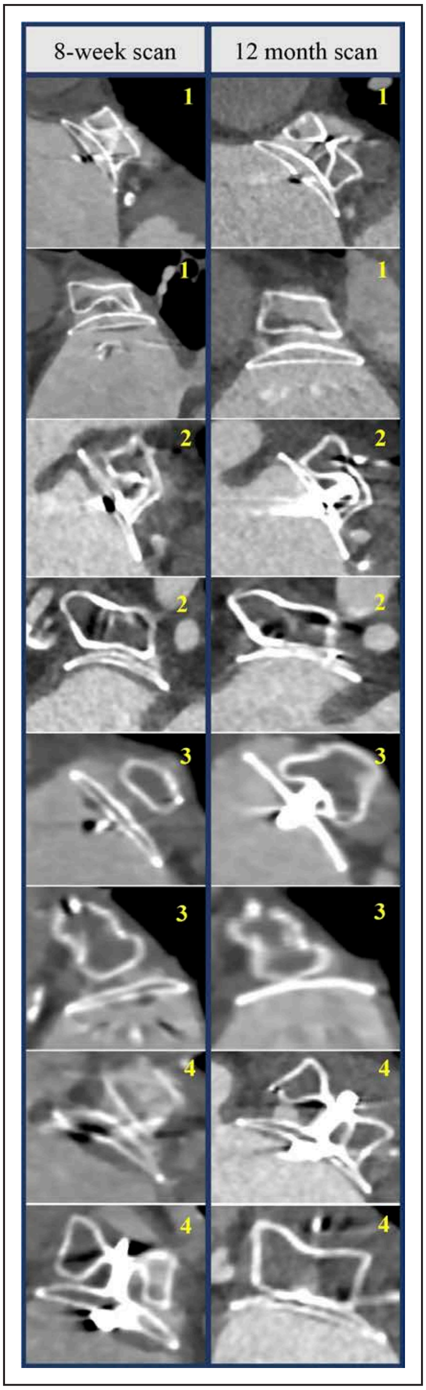

Figure 5. Temporal evolution of hypoattenuated thickening over time. Two orthogonal projections of the left atrial appendage occluder from 4 patients. On the left, the 8-week cardiac computed tomography (CT) images. On the right, the 12-month cardiac CT images. Images 1–3: low-grade hypoattenuated thickening (HAT) with complete resolution at 12 months on aspirin monotherapy. Images 4: high-grade HAT in a patient with simultaneous hypoattenuated leaflet thickening on a transcatheter aortic heart valve. Because of very high bleeding risk, aspirin was continued. Twelve-month scan showed regression to low-grade HAT.

of imaging data attempted to minimize bias of the results. The diagnosis of DRT was not confirmed by histology or autopsy; thus, the performance of cardiac CT was tested against the currently accepted gold standard for diagnosis of thrombus. The study did not

Table 4. Correlates of Hypoattenuated Thickening

	No HAT n=221	HAT n=27	*P* Value	Low-Grade n=20	High-Grade n=7
Patient characteristics					
Age, y	72.8±8.5	74.9±7.9	0.21	75.1±6.4	74.6±11
Female sex	72 (33%)	10 (37%)	0.67	7 (35%)	3 (43%)
Body mass index	26.8±4.3	26.8±3.9	0.99	26.1±3.7	28.8±4
Permanent atrial fibrillation	96 (43%)	14 (52%)	0.41	9 (45%)	5 (71%)
Congestive heart failure	36 (16%)	6 (22%)	0.42	3 (15%)	3 (43%)
Stroke/TIA	102 (46%)	15 (56%)	0.42	10 (50%)	5 (71%)
Vascular disease	86 (39%)	10 (37%)	0.99	7 (35%)	3 (43%)
Chronic kidney disease, stage 3–5	62 (28%)	13 (45%)	0.12	8 (40%)	4 (57%)
CHA_2DS_2-VASc score	4.1±1.6	4.6±1.6	0.12	4.2±1.4	5.7±1.8
HAS-BLED score	3.8±1.1	4.0±0.9	0.51	3.8±0.8	4.6±1
Preprocedural imaging					
Left ventricular EF on TTE (%),	60 (50–60)	60 (50–60)	0.10	60 (50–60)	50 (45–60)
LAA contrast filling defect on CT	57 (26%)	9 (35%)	0.35	6 (30%)	3 (43%)
Antithrombotic therapy					
Aspirin monotherapy at discharge	187 (85%)	20 (74%)	0.17	16 (80%)	4 (57%)
Device characteristics					
Size of device, mm	24.3±4.3	23.5±4.3	0.38	22.8±4	25.6±4.5
LAA remnant in front of the disc	30 (14%)	9 (33%)	0.02	5 (25%)	4 (57%)
Distance from LUPV to disc, mm	13.6±2.6	16.6±4.4	0.02	15.6±4.1	17.8±5
Completely thrombosed inside lobe of device	80 (36%)	12 (44%)	0.55	10 (50%)	2 (29%)

Data are presented as mean±SD, median (IQR), or numbers (%). CT indicates computed tomography; EF, ejection fraction; HAT, hypoattenuated thickening; LAA, left atrial appendage; LUPV, left upper pulmonary vein; TIA, transient ischemic attack; and TTE, transthoracic echocardiography.

allow assessment of the optimal timing of follow-up. The retrospective design did not permit investigation of postprocessing algorithms or alternative acquisition to reduce artifacts. In addition, the sample size and low event rate does not allow for statistical testing of an association between HAT and clinical events. Hence,

Table 5. Clinical Outcomes

	No HAT n=221	Low-Grade HAT n=20	High-Grade HAT n=7
Mean follow-up time, y	1.7±1.1	1.8±1.1	1.3±0.4
Ischemic stroke or thromboembolism	8 (4%)	0 (0%)	2 (29%)
Major bleeding	19 (9%)	3 (15%)	0 (0%)
Death	26 (12%)	1 (5%)	1 (14%)

Data are presented as numbers (%). HAT indicates hypoattenuated thickening.

the clinical importance of the reported imaging findings remains unclear as does the management of HAT; however, our observations may provide valuable insight into future focus of research on LAAO.

CONCLUSIONS

Cardiac CT is a sensitive modality for detection of potential DRT following LAAO. It seems equally good as TEE for the detection of device-related thrombosis. In addition, it demonstrates cases with low grades of HAT of the device disc. The clinical significance hereof requires further investigation.

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