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Contrast-enhanced transesophageal echocardiography predicts neo-intimal coverage of device post-left atrial appendage closure

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Abstract

Background: *Left atrial appendage (LAA) closure (LAAC) is a viable alternative to anticoagulation for stroke prevention in non-valvular atrial fibrillation. However, device-associated thrombosis (DAT) is known as a complication of LAAC as observed within the first few weeks after implantation. A noninvasive method is needed to predict the progress for endothelialization surveillance. The aim of the study was to develop a noninvasive visual contrast-enhanced transesophageal echocardiography (cTEE) method for monitoring the communication between left atrium (LA) and LAA post-LAAC by cTEE-score evaluating the contrast enhancement in LAA.*

Methods: *A total of 29 healthy dogs were studied by LAAC at < 24 h and 1, 2, 3 and 6-months. The LAAC procedure was assessed by TEE with color Doppler flow imaging (CDFI) and contrast imaging. The cTEE score was calculated based on the differential contrast opacification of LA and LAA cavities, the CDFI on the width of peri-device color flow, and that of histology on the level of occluder surface endothelialization in postmortem histological examination. Spearman's correlation analysis was used to correlate these scores.*

Results: *The correlation between cTEE and histology scores was superior to that between CDFI and histology scores. The trend of average cTEE score was tracked with that of histology, while that of CDFI was far from that of histology. The correlation coefficient of CDFI and histology scores was not significant ($p > 0.05$).*

Conclusions: *The noninvasive visual cTEE is feasible and reliable to monitor communication between the LA and LAA post-LAAC. cTEE is superior to CDFI as a tool in predicting the progress for endothelialization surveillance.* (Cardiol J)

Key words: left atrial appendage closure, endothelialization, contrast echocardiography, histology, noninvasive surveillance

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Introduction

Left atrial appendage closure (LAAC) is an important alternative to life-long oral anticoagulation (OAC) in patients with high stroke risk and contraindication for OAC [1]. The Watchman device (Boston Scientific Inc., USA) and Amplatzer Cardiac Plug (ACP) device (St. Jude Medical Inc., USA) are the most commonly used devices [1–3]. Clinical trials with the Watchman device suggested that LAAC was similar to warfarin therapy for stroke prevention in non-valvular atrial fibrillation patients [4, 5]. The 5-year outcomes of the PREVAIL and the PROTECTAF trials demonstrated that LAAC by the Watchman device prevented stroke in non-valvular atrial fibrillation as compared to warfarin with fewer hemorrhagic strokes and mortalities [6, 7].

Interestingly, if the foreign material of LAAC devices is not fully covered by endothelial cells, thrombus develops on the left atrial surface of the device, followed by thromboembolization [8]. Reportedly, device-associated thrombosis (DAT) is a complication that occurs after LAAC with an incidence of 0–17.6% [1, 8–13]. Typically, the incidence of thrombus formation is frequent in the first few weeks after LAAC, followed by a decline with complete endothelialization of the device surface [10]. DAT and the peri-device leak showed a correlation with late thromboembolic events after technically successful LAAC [12]. Therefore, the optimal regimen of post-procedural anticoagulation or platelet inhibition after LAAC is recommended for both the Watchman and ACP devices [11].

However, the correlation between endothelialization of the left atrial appendage (LAA) occluder surface during healing and the blood flow between the left atrium (LA) and LAA is yet to be elucidated. The communication flow between LA and LAA, including central-device flow and peri-device flow (residual flow), may be associated with incomplete endothelialization of occluder surface and the risk of DAT formation. Both color Doppler flow imaging (CDFI) and contrast-enhanced transesophageal echocardiography (cTEE) is used to monitor the blood flow [14]. CDFI has been used to identify the residue flow by measuring the width of peri-device flow in PROTECTAF, PREVAIL, and EVOLUTION trials [4, 5]. However, the use of cTEE for post-LAAC follow-up examination has not yet been explored despite it being a valuable tool for differentiating between spontaneous contrast and thrombus in LAA [14].

Herein, we sought to monitor the communication between LA and LAA by applying cTEE after LAAC and found complete closure of LAA and endothelialization of the surface of the device in the absence of contrast agent within the LAA. However, the LAA opacification indicated the presence of communication between LA and LAA, although it could not be quantified. Furthermore, the correlation between CDFI, cTEE, and endothelialization is unclear.

Because complete cessation of flow by CDFI is the current "gold standard" for discontinuation of anticoagulation post-LAAC clinically, we focused on the correlation between cTEE, CDFI, and the histological evidence of complete endothelialization. In this study, we proposed that cTEE is a noninvasive method to evaluate not only the LAAC effectiveness but also the degree of endothelialization (related to histological analysis) and that it is a superior tool to CDFI for endothelialization surveillance.

Methods

Animal preparation

A total of 29 healthy dogs (7 females, 28.0 ± ± 3.7 kg) were divided into five groups randomly and euthanized at < 24 h, 1-, 2-, 3-, and 6-months after LAA device implantation. The study protocol was approved by the Committee on Animal Research of Beijing Pinggu District Hospital's Animal Experimental Center (Beijing, China). For the LAAC procedure and follow-up transesophageal echocardiography (TEE) examinations, the animals were under general anesthesia with xylazine hydrochloride (0.1 mg/kg) and propofol intramuscularly after 12 h of fasting.

TEE and cTEE examinations

A GE Vivid E9 with XD clear ultrasound system (GE Vingmed Ultrasound AS, Norway) containing a 6VT-D TEE transducer (3–8 MHz) was used. The TEE probe was inserted at a depth of 50–60 cm from the incisors. At 0, 45–60, 80–90, and 120–135°, the following were recorded: the LAA lobes, orifice diameter and depth, and the distance between left superior pulmonary vein and mitral annulus. The peri-device flow post-LAAC was assessed by CDFI with > 10 frames/s.

By adjusting in the left ventricular contrast mode, the mechanical index was set between 0.3 and 0.4, while the soft tissue thermal index was 0.2. After focusing the LAA and placing the

sample volume on the LAA orifice, 1.0–1.5 mL contrast agent (SonoVue™, Bracco Diagnostics, Princeton, NJ, USA) was injected intravenously in the femoral vein by bolus application, followed by a flush of saline. The images were acquired in 3–5 cardiac cycles after microbubbles was gradually flushed into the LAA. The time intensity curves of micobubble concentrations were acquired from the sample points (2.0-mm high and 2.0-mm wide). The curves were fitted using Time Intensity Curve Manual (Ultrasound Lab, 2005) and: *Fitting Curve* $= A\,[1 - exp(-kt)] + B$, where A is the difference between B and the maximum intensity at t is infinity, B is the intercept intensity at $t = 0$, k is a constant, $1 - exp(-kt)$ is the increasing function for wash-in.

The definition of cTEE score is three scores: 2, 1, and 0. The cTEE score of 2 is defined as microbubbles in both LA and LAA simultaneously with in 3 heart beats that fully fill the LAA, and 1 as microbubbles that slowly appear in LAA, following 3–5 heartbeats after LA is fully or partially filled. The final filling of LAA may be partial or complete. The cTEE score of 0 is defined as non-visible microbubbles in LAA, in which, there is no communication between LA and LAA. The cTEE scores 2 and 1 represent at least partial blood flow between LA and LAA.

The CDFI scores are based on the width of the residual flow into LAA. The CDFI score of 2 is defined as the width of peri-device flow > 5 mm, 1 as the width of peri-device flow ≤ 5 mm, and 0 as non-detectable peri-device flow.

LAA occlusion

The procedure was performed through a femoral vein under fluoroscopic and angiographic guidance. Based on the measurements by angiography and TEE, a self-expanding device (LAMax™ LAAC occluder, ShenZhen KYD Biomedical Technology Co., Ltd, China) was chosen, which comprises a proximal cover-disc to seal the ostium of the LAA and a distal embedded-hook anchor to be positioned within the LAA; a short central waist was connected with the two parts. Both the disc and the anchor were constructed from nitinol mesh and incorporate with fabric. Prior to the device release, five signs (acronym COVER) should be observed: 1) Concavity of the cover-disc to ensure adequate sealing; 2) Oversizing, i.e., the diameter of the anchor is 20–50% larger than the measured zone; 3) Verifying the position and impingement on the surrounding structures; 4) Ensuring stability for tug test; and 5) Residual flow assessed to be < 5 mm.

Follow-up gross and microscopic examinations

After postoperative TEEs, the dogs were euthanized with an overdose of intravenous injection of pentobarbital (86 mg/kg). The chest and pericardial cavities were inspected. The heart was opened from the right atrial. The device migration, DAT, the surface of the cover-disc, and the correlation with left superior pulmonary vein and mitral annulus were analyzed. The anchor of the device was inspected by cutting through the LAA. A histology score of 2 is defined as no neo-intimal coverage on the atrial surface of the cover-disc, 1 as partial neo-intimal coverage on the atrial surface or full neo-intimal coverage but gaps are present between the periphery of the cover-disc and the LA tissue, indicating incomplete LAAC, and 0 as full neo-intimal coverage on the surface of the cover-disc without any gap between the periphery of the cover-disc and the LA tissue, indicating complete LAA occlusion.

Subsequently, the device and the surrounding tissue underwent dehydration, followed by infiltration and were embedded in methyl methacrylate. The device was cut along the long axis of the appendage with an EXAKT 300CP diamond band saw, polished with an EXAKT 400CS grinding system (EXAKT, Norderstedt, Germany), stained with toluidine blue, and analyzed under light microscopy.

Statistical methods

Data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Values were displayed as mean ± standard deviation (SD). Spearman's correlation coefficients were computed among the cTEE, CDFI, and histology scores. $P < 0.05$ was considered statistically significant. The total scores were computed as the sum of the scores of all accountable dogs at that time point. The average score was computed by using total score divided by the animal count in a group. Plots were created with Microsoft Excel.

Results

Transesophageal echocardiography was performed in 29 dogs before LAAC. At 3–5 s after the intravenous injection of contrast agent, microbubbles could be seen filling the LAA (Fig. 1). No contrast filling defect was detected in any of them. The success of device implantation was 100%. There was no evidence of infarction in the major organs, as assessed by gross examinations.

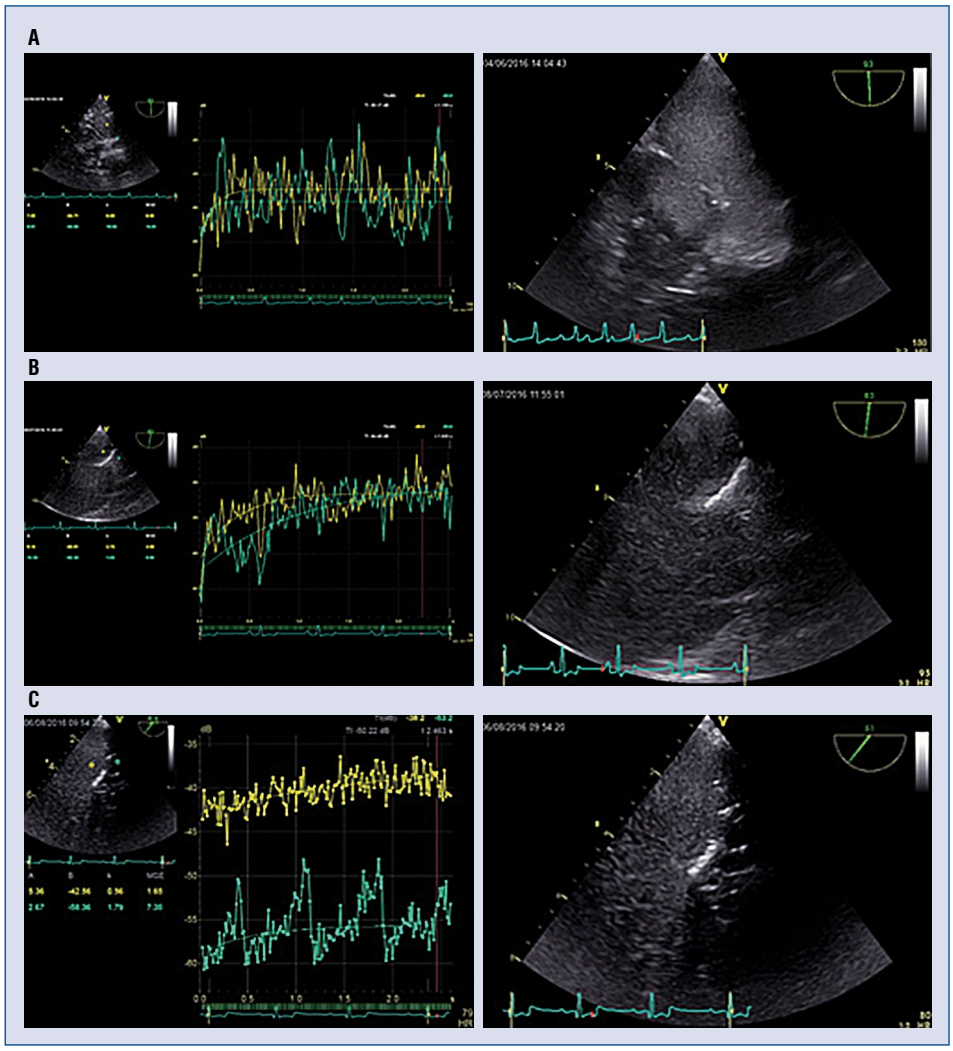

Figure 1. Representative contrast-enhanced transesophageal echocardiography (cTEE) graphs of different score gradings; **A.** cTEE-score 2: Microbubbles appeared in both left atrium (LA) and left atrial appendage (LAA) simultaneously within 3 heart beats, and fully filled in LAA; both time intensity curves (TIC) for the concentrations in LA (yellow TIC) and LAA (green TIC) were mingled and reached their plateaus at the same time; **B.** cTEE-score 1: Microbubbles appear slowly in LAA by 3 heart beats after the LA was fully filled with microbubbles; the rising speed of TIC in LAA (green) was slower than the one in LA (yellow), and finally both TICs mixed together although the yellow TIC reached its plateau earlier; **C.** cTEE-score 0: None visible microbubble in LAA, both TICs were separated with the TIC in LAA lower than that in LA.

At the follow-up visit, all animals had TEEs. The post-mortem pathology showed the LAA orifices were occluded by the cover-disc, and no thrombi were detected at any of these stages. Beginning from 1-month post LAAC, the atrial surface of the cover-discs started to be covered by a glistening white neo-endocardial layer. Bytheendof 6-month, the neo-endocardialization was 100% (Table 1). The neo-intima covered the device-left atrial interfaces, thereby sealing the LAA orifices completely. The claws of the anchor were well opposed to the LAA walls, without any evidence of tissue necrosis.

Figures 2 and 3 present examples of cTEE scores 0, and 2, respectively. As shown in Figure 4, the local atrial tissue tolerated the device well, as shown histologically.

Table 1 summarizes the results of cTEE-score, peri-device flow detected by CDFI, and histology score. In Table 2, at the < 24 h time point, only 17 dogs exhibited cTEE scores; the average cTEE score was 1.41. The average CDFI-score of 29 dogs

Table 1. Results of contrast-enhanced transesophageal echocardiography (cTEE)-score, peri-device flow detected by color Doppler flow imaging (CDFI)-score, and histology score.

Group	Case No.	cTEE-score					Peri-device flow detected by CDFI score					Histology score
		< 24 h	1 m	2 m	3 m	6 m	< 24 h	1 m	2 m	3 m	6 m	
< 24 h	1	2	–	–	–	–	0	–	–	–	–	2
	2	1	–	–	–	–	0	–	–	–	–	2
	3	1	–	–	–	–	0	–	–	–	–	2
	4	1	–	–	–	–	0	–	–	–	–	2
	5	2	–	–	–	–	0	–	–	–	–	2
	6	2	–	–	–	–	0	–	–	–	–	2
1–month	7		0	–	–	–	0	0	–	–	–	0
	8		1	–	–	–	0	0	–	–	–	1
	9		1	–	–	–	0	0	–	–	–	1
	10		0	–	–	–	0	0	–	–	–	0
	11		1	–	–	–	2	0	–	–	–	1
	12		0	–	–	–	0	0	–	–	–	0
2–months	13	1	0	0	–	–	0	0	0	–	–	0
	14	2	1	1	–	–	1	0	0	–	–	1
	15	2	1	0	–	–	0	0	0	–	–	0
	16	1	1	0	–	–	0	0	0	–	–	0
	17	1	1	0	–	–	0	0	0	–	–	0
3–months	18		1	0	0	–	0	0	0	0	–	0
	19		1	1	1	–	0	0	0	0	–	1
	20		1	0	0	–	0	0	0	0	–	0
	21	2	2	2	2	–	1	1	1	1	–	1
	22	1	0	0	0	–	0	0	0	0	–	0
	23	1	1	1	1	–	1	1	0	0	–	1
	24	2	2	2	1	–	1	1	1	1	–	1
6–months	25		x	0	0	0	0	0	0	0	0	0
	26		0	0	0	0	0	0	0	0	0	0
	27		0	0	0	0	0	0	0	0	0	0
	28	1	0	0	0	0	0	0	0	0	0	0
	29	1	x	0	0	0	0	0	0	0	0	0

–: the animal was euthanized; x: no CDFI or cTEE measurement; h — hour; m — month

was 0.17. Six dogs were sacrificed for autopsy. The average cTEE, CDFI and histology scores of these 6 dogs were 1.5, 0, and 2, respectively.

At the 1-month time point, the 6 dogs were sacrificed. The average cTEE, CDFI and histology scores of these dogs were 0.5, 0 and 0.5, respectively. One device malposition was found with a histology score of 1 (Case No. 11, Table 3). At the 2-month time point, no device migration was found.

At the 3-month time point, 7 dogs were sacrificed. Their average cTEE, CDFI and histology scores were 0.71, 0.29 and 0.57, respectively. There was peri-device flow in 2 cases (Case No. 21 and 24) with a width of 2-mm detected by a CDFI and cTEE score of 2 or 1 at post-LAAC. CDFI demonstrated that 3/7 animals had peri-device flow at both < 24 h and 1-month post-LAAC time points. Among these 3 animals, a peri-device flow was no longer apparent at 2 months, as assessed by CDFI but was detected by cTEE (Table 1). At the 6-month time point, the cTEE, CDFI, and histology scores of the remaining dogs were 0. The LSPV was partially obstructed and the MA was compressed by the cover-disc of the same device.

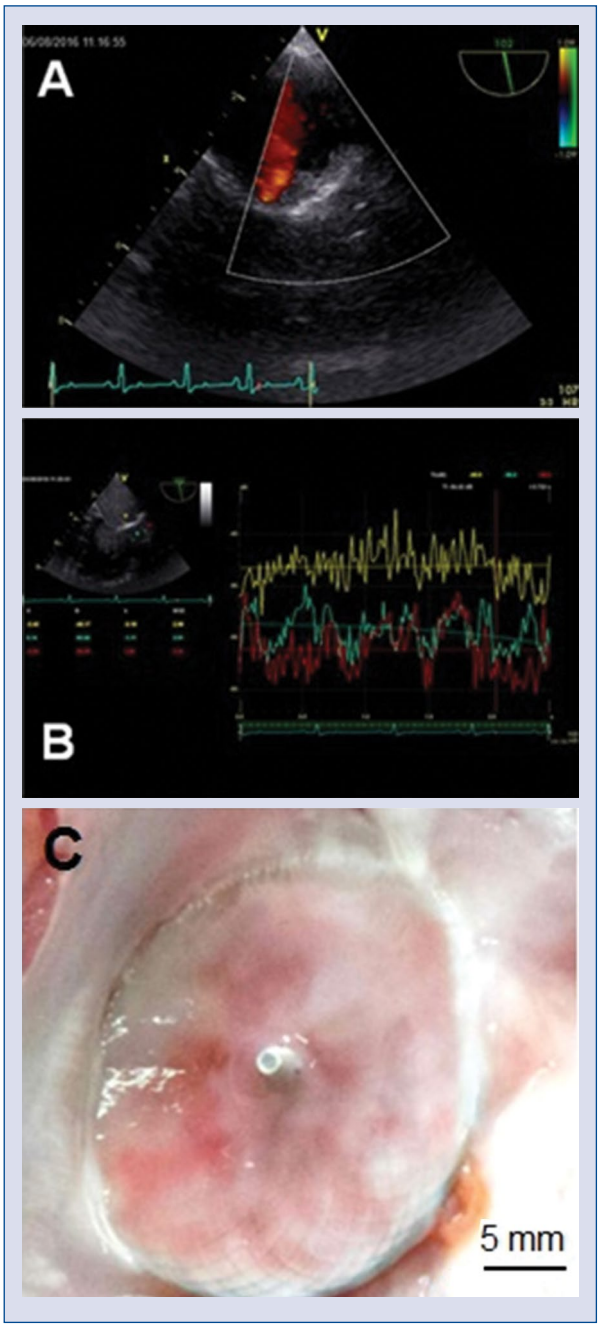

Figure 2. Example of contrast-enhanced transesophageal echocardiography (cTEE)-score 0 (2-months post--left atrial appendage closure); **A.** Color Doppler flow imaging (CDFI): none peri-device flow into left atrial appendage (LAA); **B.** cTEE and time intensity curves (TIC): none visible microbubble in LAA, two mixed TICs (red, green) in two different locations of LAA were much lower than that in left atrium (yellow); **C.** Gross examination: fully endothelialization of LAA occluder's atrial-surface, and the occluder was well coupled with the surrounding tissue.

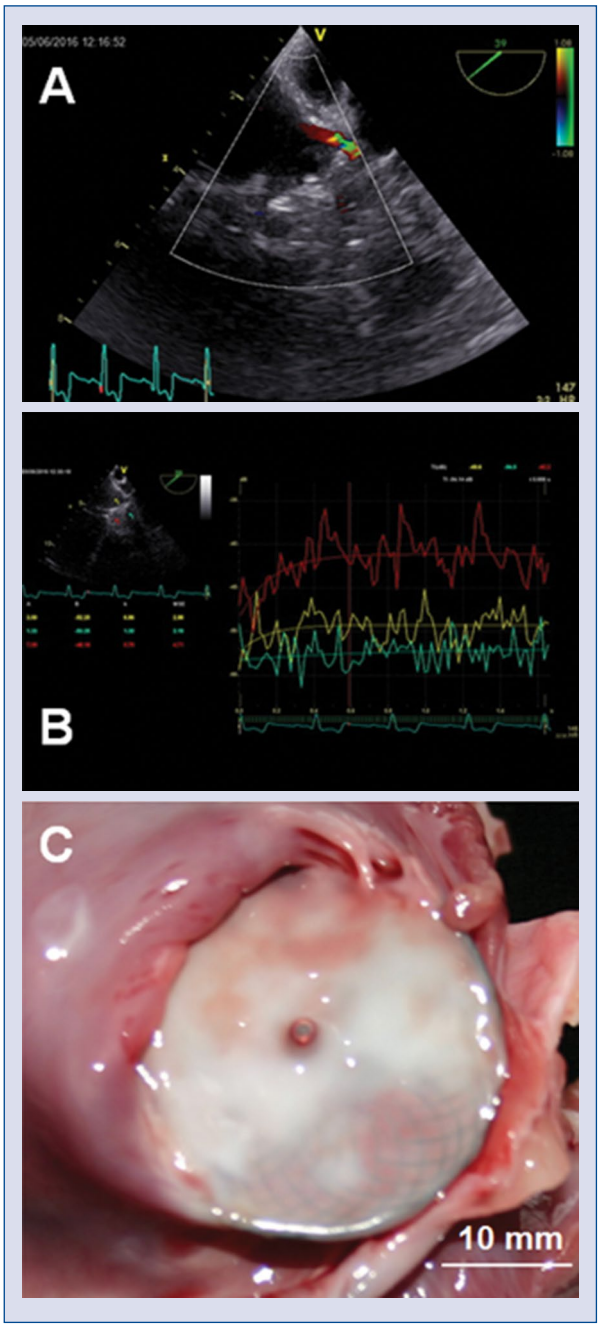

Figure 3. Example of contrast-enhanced transesophageal echocardiography (cTEE)-score 2 (3-months post--left atrial appendage closure [LAAC]); **A.** Color Doppler flow imaging (CDFI): a width of 2 mm peri-device flow into left atrial appendage (LAA); **B.** cTEE and time intensity curves (TIC): microbubbles got into LAA through a communication channel quickly from left atrium (LA) to LAA after LAAC, the TIC in LAA (red) was higher than the one in LA (yellow) due to the effect of an echo by the cover-plate; **C.** Gross examination: fully neo-intimal coverage of occluder's atrial-surface, the left edge of cover-plate was inside LAA, and an irregular fissure along the cover-plate's edge was found and passed with a 18-gauge hypodermic needle from LA to LAA.

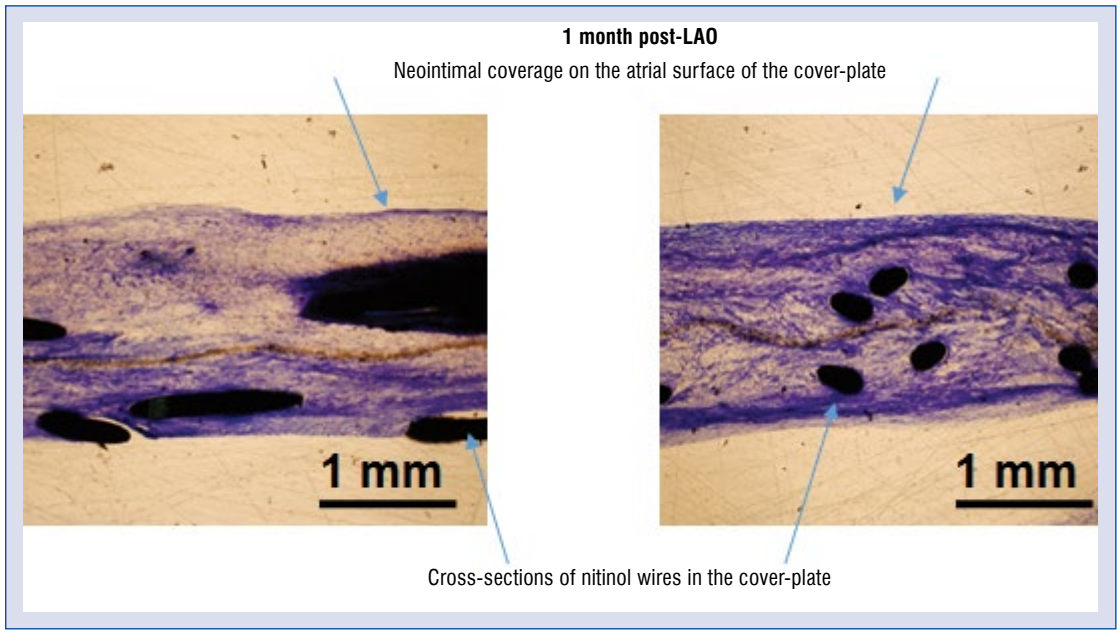

Figure 4. Histological section of the left atrial appendage closure (LAAC) device's cover-plate. Sagittal section through the center of the left atrial appendage and device in a dog (1-month post-LAAC). Microscopic views showed neointimal coverage over the atrial surface of the cover-plate.

Table 2. Summary of total score, average score for the contrast-enhanced transesophageal echocardiography (cTEE)-score, color Doppler flow imaging (CDFI)-score, histology-score at < 24 h, 1-month, 2-months, 3-months, and 6-months post-left atrial appendage closure (LAAC).

	< 24 hours	1-month	2-months	3-month	6-months
cTEE-score:					
Total	24 (17*)	15 (21)	7 (17)	5 (12)	0 (5)
Average	1.41**	0.71	0.41	0.42	0
CDFI-score:					
Total	5 (29)	3 (23)	2 (17)	2 (12)	0 (5)
Average	0.17	0.13	0.12	0.17	0
Histology-score:					
Total	12 (6)	3 (6)	1 (5)	4 (7)	0 (5)
Average	2	0.5	0.2	0.57	0

*Animal count; **1.41 = 24/7

Table 3. Three special cases.

Case	Description
No. 11	In case no. 11 (1-month post-LAAC), although the LAAC orifice was blocked by the anchor of the device while the cover-disc was in the left atrium (LA) but not attached to the orifice at all; the atrial surface of the device, including the central screw, was well covered by the neo-intimal tissue, while the incomplete neo-intimal coverage was found on the LAA surface of the cover--plate and the short central waist; no communication between LA and LAA was detected.
No. 21 and 24	In case no. 21 (3-months post-LAAC) and case no. 24 (3-months post-LAAC), the gross examination showed that in both animals, the left edge of the cover-plate was inside the LAA and there was a fissure along the cover-plate's edge; an 18-gauge hypodermic needle was used to examine the hole and could be passed from LA to LAA.

LA — left atrium; LAA — left atrial appendage; LAAC — left atrial appendage closure

Table 4. The correlation coefficients among contrast-enhanced transesophageal echocardiography (cTEE)-score, color Doppler flow imaging (CDFI)-score, and histology score.

	cTEE score (n)	CDFI score (n)	Histology score (n)
cTEE score	1.00 (72)	0.55* (72)	0.95** (29)
CDFI score	0.55* (72)	1.00 (72)	0.16 (29)
Histology score	0.95* (29)	0.16 (29)	1.00 (29)

*Correlation is significant at the 0.01 level (2-tailed).

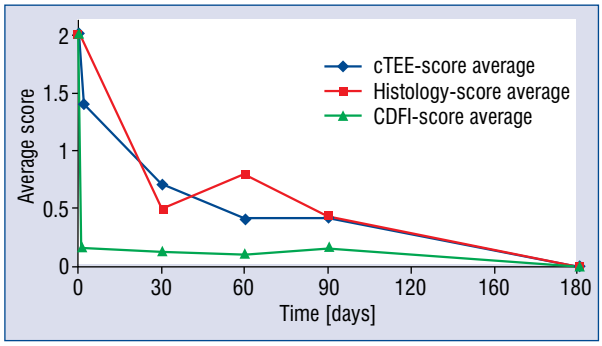

Figure 5. The trends of the average score number of contrast-enhanced transesophageal echocardiography (cTEE)-score, histology-score, color Doppler flow imaging (CDFI)-score, respectively, from the time before left atrial appendage closure (LAAC) (i.e., the time was 0) to 1-, 30-, 60-, 90-, 180-days post-LAAC.

Table 4 shows the Spearman's correlations of the cTEE, CDFI, and histology scores at time points < 24 h, and 30, 60, 90, and 180 days post-LAAC, respectively. The correlation between cTEE and histology scores was superior to that between CDFI and histology scores. In Figure 5, shows the trend of the average cTEE score tracks with that of the histology score at different time points, but the curve of the average CDFI score declines sharply after device implantation immediately, which is distal from that of the histology score.

Discussion

This study introduced a noninvasive visual cTEE score method to monitor the communication between LA and LAA and predict the progression of the LAAC endothelialization process. By comparing with the conventional CDFI method, as well as correlating with the post-mortem anatomical and histological examinations, we found that cTEE is superior to CDFI as a tool for endothelialization surveillance.

The post-LAAC healing reactions are similar between canine and human, and the canine model is suitable for pre-clinical evaluation of LAA occlusion devices [2]. Usually, the LAAC devices consist of nitinol frame and polyester fabric membrane. If not fully endothelialized, the left atrial surface of the devices have the potential to promote subsequent thrombosis [8]. In a systematic review of DAT after LAAC, the overall incidence of DAT was 3.9%. The median time from procedure to diagnosis of DAT was 1.5 months. These early cases of DAT are related to delayed device surface endothelialization, and the late cases could be secondary to mechanical factors or systemic patient factors [5, 10, 15]. Thus, the endothelialization of the LAA occluder's atrial surface is clinically critical in DAT prevention postoperatively in patients. Therefore, in the clinical trials, human subjects were given warfarin by Watchman devices for 45 days after LAAC. If the 45-day TEE documented either complete closure of the LAA or if peri-device flow was < 5 mm in width and there was no visible large thrombus on the device, warfarin was discontinued [4, 5]. Interestingly, the conformation of LAA surrounding structures exhibited variable healing responses among different LAAC devices, which might affect the progress of endothelialization [2]. In this study, LAMax™ LAAC occluder was applied, and the shape of the cover-disc was similar to the disc of ACP.

The following questions remain unanswered: Can the device endothelialization process be effectively monitored *in vivo*? Is the device endothelialization process associated with the communicated flow between LA and LAA? Intriguingly, TEE has been applied widely to guide LAAC implantation and follow-up anticoagulation. Routine device surveillance by TEE at intermediate follow-up provides the opportunity to assess DAT, peri-device leak, device positioning, surrounding structures. However, CDFI and cTEE monitor the blood flow by different mechanisms [14]. Echo contrast agents are lipid-encapsulated microbubbles, which are 1–7 μm in diameter and similar in size to red blood cells. The microbubbles are injected intravenously and remain within the blood pool to circulate in a manner similar to the red blood cells for a short interval. The use of cTEE has been described for delineation of an LAA thrombus and distinction between spontaneous contrast and thrombus [16].

In this study, cTEE was found to be superior to CDFI with respect to communication between LA

and LAA post-LAAC as well as the progression of device endothelialization *in vivo*. The CDFI score decreased precipitously immediately post-implantation in > 83% of the cases. This phenomenon indicated that in most cases, the communication between the LA and LAA reduces to the level below the detection of CDFI after successful device deportment. However, the CDFI score of 0 does not mean total cessation of the flow as seen in this cohort. There were 28/57 cases with a CDFI score of 0 zero, but their cTEE scores were 1 or 2, indicating at least partial flow between the LA and the LAA. Moreover, the positive predictive value was 100% with 12 CDFI score-positive (1 or 2) studies, which also had positive cTEE scores (1 or 2). Furthermore, in the set of < 24 h post-LAAC group with no neo-intimal coverage on the surface of cover-plate, all 6 dogs had a CDFI score of 0 and the cTEE score was 1 or 2. This indicated that cTEE can detect the communicated flow between LA and LAA post-LAAC beyond the resolution of CDFI.

Left atrial appendage closure device surface endothelialization is a slow process. It was shown that at the end of 1 month, 50% (3/6) of the dogs had complete device endothelialization, and by the end of 6 months, 100% of the devices' cover-discs were completely covered, and the neoendocardial covering was continuous from the left atrial wall to the device. At different time points, the histology scores of 15 dogs were 0; also, their cTEE and CDFI scores were uniformly 0, with a positive predictive value of 100%. However, when the endothelial process occurred partially with a histology score of 1, the cTEE score was superior to the CDFI score. In the 8 dogs with the histology score of 1, 7/8 had cTEE score of 1, and one had a score of 2, while 2/8 dogs had a CDFI score of 1, and the remaining had a score of 0. Overall, the cTEE-score was correlated to the histology score with a coefficient of 0.95. It is shown that a trend of the average cTEE score tracked with that of the histology score, but the trend of the average CDFI score was far from that of the histology score. This finding indicates that cTEE has a better temporal resolution than CDFI in monitoring the device endothelialization process *in vivo*.

The present study also showed that the effective healing response after implantation of LAAC devices was related to the achievement of concavity of the cover-plate and less peri-device flow. Especially, in 3-months post-LAAC group, both the average cTEE and histology scores were higher than that of the 2-month post-LAAC group. This is due to a higher number of cases with immediate post-LAAC peri-device flow present in this group. Therefore, it is important to avoid the incidence of residual flow during the LAAC procedure; if the residual flow is unavoidable, it may be necessary to monitor the healing progress by cTEE before terminating the use of anticoagulants.

Despite a satisfactory correlation with the histology score, the clinical significance of cTEE score is yet uncertain. Thus, a large-scale clinical study with DAT as the endpoint is imperative. For clinical application, it is better to have cTEE assessment before 1 month after LAAC. If cTEE score remains not 0, cTEE should be done again before terminating the OAC. If the residual flow is found by CDFI, cTEE could be avoided. Nevertheless, we speculated that cTEE could be used as a noninvasive tool for endothelialization surveillance after LAAC for the future.

Limitations of the study

The number of animals studied is relatively small. Since LAA occlusion devices are usually tested in canines before clinical application, the present study has extended these methods to healthy adult dogs as the animal model. However, clinical trials are required for further evaluation.

Conclusions

The noninvasive visual cTEE is feasible and reliable to monitor the communication between LA and LAA post-LAAC. The cTEE is superior to the currently used CDFI to predict the progress of neo-intimal coverage on the atrial surface of the LAAC device in dogs.

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