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Presence Of Left Atrial Appendage Thrombus In Patients Presenting For Left Atrial Ablation Of Atrial Fibrillation Despite Pre-Operative Anticoagulation

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Abstract

Background: One of the recognised complications of left atrial ablation for atrial fibrillation (AF) is stroke. Left atrial (LA) thrombus, which may be dislodged by catheter manipulation, is an absolute contraindication to ablation. It is unclear whether imaging of the left atrial appendage (LAA) by transesophageal echo (TEE) is mandatory to exclude LA clot prior to ablation, particularly in "low-risk" patients with paroxysmal AF and normal left ventricular (LV) function.

Methods and Results: We carried out a retrospective analysis of pre-ablation TEE in patients presenting for ablation of AF. Images from 244 ablation procedures carried out in 148 patients were examined, including 106 patients with paroxysmal AF and normal LV function. Despite at least 4 weeks of pre-operative therapeutic anticoagulation with Warfarin (INR>2.0), LAA thrombus was identified in 4 patients (2.7% (0.1-5.3%)). These included 2 patients with paroxysmal AF and normal LV function, although both had a high arrhythmia burden. The thrombi regressed with intensification of anticoagulation.

Conclusions: Pre-operative imaging of the LAA remains advisable to exclude thrombus prior to ablation for AF even in patients with paroxysmal AF and normal LV function, especially if there is a high AF burden.

Key words: Left atrial thrombus, catheter ablation, atrial fibrillation, transesophageal echo

Introduction

Left atrial (LA) ablation is now a key therapeutic option for the treatment of symptomatic, drug-refractory paroxysmal and persistent atrial fibrillation (AF). Although a variety of techniques are used, all involve extensive manipulation of catheters within the LA and widespread ablation using either radiofrequency energy or cryoablation.[1] Periprocedural cerebrovascular accidents (CVAs) are a recognised complication. Clinically significant neurological events occur in around 0.5-1% of patients, but the incidence of silent embolic events is likely to be much higher.[2-4] The presence

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of LA thrombus is an absolute contraindication to manipulation of catheters within the LA.[1] AF is associated with the development of LA thrombus, particularly in the left atrial appendage (LAA), which can be visualized by transesophageal echocardiography (TEE).[5]

A number of strategies have been developed to reduce the incidence of peri-procedural stroke in patients undergoing ablation for AF.[1,6] These include routine anticoagulation of patients for at least one month prior to ablation and routine TEE immediately prior to the procedure to rule out the presence of LAA clot. It is not known whether TEE should be mandatory in all patients, particularly if they have been therapeutically anticoagulated prior to admission, or whether it can be restricted to high risk patients.[7] We carried out a retrospective study to identify the incidence and predictors of LAA thrombus in patients presenting for LA ablation of AF despite four weeks of therapeutic anticoagulation to determine whether pre-operative TEE should be recommended in all patients or only those deemed to be at high risk.

Methods

A retrospective review of the medical records and TEE findings in consecutive patients presenting for LA ablation of AF in our institution between December 2003 and November 2007. All received at least 6 weeks of anticoagulation with Warfarin prior to ablation aiming for a target international normalised ratio (INR) of 2.5. Following the loading period, INR was measured weekly for at least one month prior to admission. Any patient with an INR less than 2 during this period was excluded from the study. Warfarin was stopped 3 days prior to admission. All patients underwent a TEE on the morning of their ablation procedure. Procedures were regarded as separate when there was at least a three month gap between procedures.

Following a bolus of 10,000 u intravenous heparin, double transeptal punctures were performed with an Agilis (St Jude Medical) and SL0 sheaths (St Jude Medical) using standard techniques. Sheaths were perfused with heparinised saline at >100 mL/hr to maintain an ACT of 300-350 s. A 3D map was created of the LA geometry using either NavX (St Jude Medical) or Carto systems (Biosense Webster). A circular mapping catheter (Optima, St Jude Medical) was used to record electrograms in the pulmonary veins. Bilateral wide area circumferential ablation of the pulmonary vein antrum was performed in all cases with further ablation, including complex fractionated electrograms and lines, performed according to the patients clinical status at the discretion of the operator. Power was limited to 30 W in the left atrium, except where a mitral isthmus line was being performed (max 50W). Iv Protamine was administered at the end of the procedure and 4 hours following the procedure a 100 IU/kg Dalteparin was administered and patients were reloaded with oral warfarin. Twelve hours later 200 IU/kg Dalteparin was given. The same dose of Dalteparin was administered every 24 hours until the INR was greater than 2.0.

The TEE images were reviewed independently by two experienced blinded echocardiographers for the presence or absence of LAA thrombus. In cases of disagreement, the images were reviewed by a third independent echocardiographer; however in all cases where a definite thrombus was identified there was no disagreement between the original reviewers. A thrombus was considered to be present if a mass detected in the appendage appeared to be distinct from the underlying endocardium, was not caused by pectinate muscles, and was detected in more than one imaging plane.[8]

The patients' records were examined to identify risk factors for embolic events using the $CHADS_2$ scoring system[9] Atrial fibrillation was classified according to the ACC/AHA/ESC 2006 guidelines and HRS/EHRA/ECAS consensus statement.[1,10] Where appropriate measurements are given as the mean +/- standard deviation.

Results

One hundred forty eight consecutive patients were studied who had undergone a total of 244 LA ablation procedures for AF (median 1 per patient, range 1-5). The clinical details of the patients are shown in table 1. Thrombus was identified in the LAA prior to 4 procedures (1.6%). The first patient was a 61 year old male with a history of non-insulin dependent diabetes mellitus, impaired left ventricular (LV) function and a history of prior transient ischemic attacks ($CHADS_2$ score 4). 6

Table 1 Clinical characteristics of patients undergoing left atrial ablation for atrial fibrillation. TEE - Transesophageal echo, TIA – Transient ischaemic attack

Patients	148
Procedures	244
Number of procedures with thrombus identified by TEE	4
Type of atrial fibrillation	
Paroxysmal	107 (72%)
Persistent	36 (24%)
Long standing persistent	6 (3%)
Risk factors for thrombus	
Age	55 +/- 10 (range 27-74)
Hypertension	43 (29.1%)
Diabetes	6 (4.1%)
Congestive heart failure	5 (3.4%)
Previous stroke or TIA	10 (6.8%)
$CHADS_2$ score	
0	94 (63.5%)
1	42 (28.4%)
2	8 (5.4%)
3	3 (2.0%)
4	1 (0.7%)

months earlier he had undergone LA ablation for persistent AF. Following this he had suffered from recurrent episodes of paroxysmal AF and two episodes of persistent atypical flutter requiring cardioversion. At the time of his second procedure he was in sinus rhythm, but the ablation was abandoned following the detection of LAA thrombus by TEE. His Target INR was increased to 3. Three months later he was readmitted and TEE no longer showed LAA thrombus.

Patient 2 was a 61 year old male with severely impaired LV function and a very dilated LA on transthoracic echocardiogram (7.0 cm, $CHADS_2$ score 1). He had undergone two previous cardioversions for recurrent persistent AF. He was in sinus rhythm at the time of his ablation procedure, but TEE showed LAA thrombus and the procedure was abandoned. Intensification of his anticoagulation regime (target INR 3.0) led to a significant reduction in size of the thrombus, but even with further increases in anticoagulation (target INR 3.5), a filling defect persisted in the LAA and we were unable to exclude persistent LAA thrombus. He was referred for a surgical maze procedure.

Patient 3 was a 63 year old male with normal left ventricular function whose only risk factor for thromboembolism was hypertension ($CHADS_2$ score 1). He suffered from recurrent paroxysmal AF with frequent paroxysms lasting 2-3 days in duration despite treatment with amiodarone 200mg daily and previously sotolol. He was in AF at the time of his TEE which showed LAA thrombus. His left atrial dimension of 4.6 cm (compared to a mean LA dimension of 4.4 +/- 0.8cm for all patients with a $CHADS_2$ score of 1). The thrombus markedly reduced in size with more intensive anticoagulation (INR 3.0) but did not disappear completely despite increasing his target INR to 3.5 for 6 months. He was also referred for a surgical maze procedure. Patient 4 was a 42 year old female with no risk factors for thromboembolic events ($CHADS_2$ score 0) and normal left ventricular function. She had paroxysmal AF and spent a number of hours each day in AF. Prior to the procedure she was treated with flecainide 100mg twice a day, following previously unsuccessful treatment with sotolol. She was in AF at the time of her TEE which showed LAA thrombus. Her LA diameter was 4.1cm (compared to a mean of 4.0cm +/- 0.6cm in all patients with a $CHADS_2$ score of 0). The thrombus resolved completely with increased anticoagulation and she underwent a successful ablation 3 months later. Those patients where TEE did not show any LAA thrombus proceeded to LA ablation (240 procedures). Following ablation two patients suffered clinical cerebrovascular events. Both had low $CHADS_2$ scores (0 and 1), but underwent extensive left atrial ablation for persistent atrial fibrillation. Both patients recovered rapidly and were discharged with only minor neurological deficits within a few days of their ablations.

Discussion

In this study we have investigated the role of TEE to detect LAA thrombus prior to ablation for AF. Despite at least four weeks of therapeutic anticoagulation prior to ablation, thrombus was present in the LAA in 1.6% (95% confidence intervals 0.1%-5.3%) of procedures (2.7% (0.03-3.17%) of patients). Although two patients might be expected to be at high risk of thrombus with

impaired LV function and either a massively dilated LA or the presence of multiple risk factors for embolic events, thrombus was also identified in two patients with paroxysmal AF and a normal left ventricular ejection fraction. The presence of thrombus could not be excluded by the absence of conventional risk factors for embolic events. Previous studies have suggested that the risk of thrombus in such patients with structurally normal hearts and paroxysmal AF is so low as to make TEE redundant.[7] In our study 106 patients had paroxysmal AF and structurally-normal hearts yet there was still a 1.1% (0-3.1%) incidence of thrombus. Redfearn's survey of Canadian centres showed a similar overall 1.1% incidence of LAA thrombus in all patients presenting for ablation of atrial fibrillation in centres where TEE is routinely performed.[11] However this survey showed no apparent difference in the incidence of embolic events with a strategy of universal pre-procedure TEE compared to one of performing TEE on selected high-risk patients. Khan et al used CT to detect LAA thrombus in a large group of patients referred for pulmonary vein isolation with additional TEE in approximately half their patients, including all those where LAA thrombus was suspected from the CT scan. They identified an incidence of LAA thrombus of 0.4% in persistent AF and 0.14% in paroxysmal AF.[7] However, TEE was not performed in all their patients and only patients undergoing solely pulmonary vein isolation were included; patients where more extensive ablation was planned were excluded, which may explain the lower incidence of thrombi. Both the patients in our study who had paroxysmal AF and normal LV function had high AF burdens with many hours of AF each day which may have prevented any restoration of mechanical function in the LAA during periods of sinus rhythm, allowing thrombus to develop; however studies of thromboembolic risk in medically-treated patients have not shown differences between patients with persistent and paroxysmal AF.[12]

Pre-existing LAA thrombus is not the only cause of thromboembolic events resulting from LA ablation.[13,14] Ablation of the LA itself creates a thrombogenic environment, excessive temperatures can lead to coagulum formation, whilst soft thrombus may also form within the LA during ablation.[14] Despite universal screening for LAA thrombus two patients in this study had neurological events. Both these patients made a rapid and almost complete recovery. It is possible that the nature of the neurological events may differ considerably depending on etiology. In addition, although the presence of known LAA thrombus is a contraindication to LA ablation, the risk of embolic events as a result of LA ablation in the presence of an undetected LAA thrombus is unknown and is likely to be significantly less than 100%. Thus failure to identify all LAA thrombi prior to ablation is only likely to lead to a small increase in overall event rates. As the incidence of embolic events in patients undergoing left atrial ablation is already low, it is likely that any attempt to use randomised controlled trials to address the role of pre-ablation imaging of the LAA would be limited by the extremely large numbers of patients required to adequately power such a study.

Although all the thrombi identified in this study reduced significantly in size with intensification of anticoagulation, in two of our patients a small residual thrombus remained in the LAA and TEE was unable to show conclusively complete disappearance of clot. These observations are very similar to those observed by Benrhardt et al. who showed that in patients with long standing persistent AF, one year of anticoagulation reduced the size of all LAA thrombi but only led to complete resolution in 56% of patients.[15] In patients with pre-existing thrombus therefore, even 6 weeks of continuous anticoagulant therapy prior to ablation could not completely exclude persistent LAA thrombus.

Limitations

In the present study all patients received the same anticoagulation regime with Warfarin being continued until three days prior to the procedure. Some centres continue Warfarin or use bridging heparin until the day of the procedure itself to reduce the risk of thrombus formation and it is possible that our patients' thrombi may have developed in the short period prior to the procedure as the INR fell.[6] Continuing anticoagulation right up the day of ablation using either Warfarin or heparin may reduce the risk of thrombus obviating the need for TEE on the day of the procedure. The incidence of persistent thrombus using this approach has not been formally assessed.

Conclusion

Even with prolonged therapeutic anticoagulation prior to ablation, LAA thrombus can still be identified using TEE in patients presenting for ablation of AF who are apparently at low risk for this. The presence of paroxysmal AF, a normal ejection fraction and the absence of other risk factors for thromboembolism does not exclude the presence of LAA thrombus. Thus imaging of the LAA prior to ablation is recommended in all patients undergoing LA ablation for AF, particularly where anticoagulation is discontinued prior to the procedure even for a short period of time. TEE is currently the gold standard for imaging thrombus in the LAA, but increasingly other imaging modalities are being used for this purpose including CT and MRI. Further studies are required to identify the optimal strategy to maximise both operative success and efficiency whilst minimizing the risk of complications.[6]

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