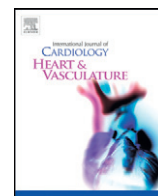


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Incidence of thromboembolism following detection by trans-oesophageal echocardiography of left atrial thrombus☆☆☆

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ABSTRACT

Background: Left atrial appendage (LAA) thrombus is an accepted risk factor for ischemic stroke. Following a literature review we were unable to identify a study that determined the incidence of ischemic stroke in patients with a confirmed LAA thrombus. The purpose of this study was to establish the incidence of ischemic stroke in patients with a LAA thrombus confirmed on trans-oesophageal echocardiography (TOE).

Method: A ten year retrospective single centre study was conducted for the period March 2005 to February 2014 in St. Vincent's University Hospital, Ireland. All TOE studies performed during this period were reviewed. A chart review was carried out on any patient who had a LAA thrombus, left atrial (LA) thrombus or pre-thrombus state identified. Charts were reviewed for documented neurological deficits consistent with ischemic stroke or transient ischemic attack within six months following TOE study.

Results: Overall 1903 TOE studies were reviewed. A total of 67 TOE studies detected a LAA thrombus, LA thrombus or pre-thrombus state. In the days prior to TOE, an ischemic stroke had occurred in two of the patients. Following detection of thrombus or pre-thrombus state on TOE and optimization of oral anti-coagulation (OAC), no patient had an ischemic stroke over the subsequent six months.

Conclusion: This is the only study to date that has looked at the incidence of ischemic stroke following a confirmed LAA thrombus, LA thrombus or pre-thrombus state. This single centre study found low stroke rates over a six month follow-up period in patients with a confirmed LAA thrombus, LA thrombus or pre-thrombus state and optimization of OAC. Larger studies would be required to confirm these findings.

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1. Introduction

At least 15% of ischemic strokes and more than a third of ischemic strokes in the elderly occur as a result of atrial fibrillation (AF) [1–5]. Patients with documented AF undergo a cardio-embolic risk stratification to determine their appropriateness for oral anti-coagulation (OAC). Patients with LAA thrombus are considered high risk for ischemic stroke. Low stroke rates are reported in patients in whom the LAA has been surgically removed [6,7]. However, data from retrospective or observational studies in different patient populations have shown inconsistent results of surgical LAA occlusion [8]. To our knowledge no study has looked at the incidence of ischemic stroke following the detection of LAA thrombus. The purpose of this retrospective study is to determine

the incidence of ischemic stroke over a six month period following a confirmed diagnosis of LAA thrombus, LA thrombus or pre-thrombus state.

2. Methods

A ten year retrospective single centre study was conducted for the period March 2005 to February 2014 in St. Vincent's University Hospital, Ireland. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. Ethical approval was obtained from the Hospital Ethics Committee. TOE studies were reviewed through the cardiac database TOMCAT. A pre-thrombus state was defined as spontaneous echo contrast together with pulsed Doppler recordings of inflow and outflow velocities of less than 25 cm per second in the LAA orifice. In studies in which a LAA thrombus, LA thrombus or pre-thrombus state was detected, a chart review was carried out. In addition neurological radiography was reviewed and was available to confirm clinical findings. OAC therapy at the time of diagnosis of thrombus or pre-thrombus state was noted.

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3. Results

Between March 2005 and February 2014 a total of 1903 TOE studies were performed. The indication for TOE was to find a cause for a cardio-embolic event in 414 studies, to exclude a thrombus prior to a planned cardio-version in 330 studies and assessment of structural heart disease in 1159 studies.

The average age of the patients was 62.9 ± 10.8 years. There was a higher number of male ($n = 38$) than female patients ($n = 29$), see [Table 1](#).

A LAA thrombus, LA thrombus or pre-thrombus state was identified in 3.5% ($n = 67$) of TOE studies. This sub divided into a LAA thrombus being identified in 2.7% ($n = 51$) of studies, a LA thrombus being identified in 0.1% ($n = 2$) of studies, a LAA and LA thrombi together being identified in 0.1% ($n = 3$) of studies and a pre-thrombus state being identified in 0.6% ($n = 11$) of studies.

In the 414 patients undergoing investigation for a cardio-embolic cause 0.48% ($n = 2$) had a thrombus or pre-thrombus state identified. In the 330 patients undergoing TOE prior to a planned cardio-version 16% ($n = 53$) had a thrombus or pre-thrombus state identified. In the 1159 undergoing assessment of structural heart disease 1% ($n = 12$) had a thrombus or pre-thrombus state identified.

A history of AF was identified in 65 of the 67 patients. One patient undergoing investigation for a cardio-embolic event and one patient with mitral valve disease had no documented history of AF.

Twenty five percent ($n = 17$) of these AF patients had an indication for OAC based on co-existing valvular heart disease. In AF patients without valvular heart disease 19% ($n = 13$) had a low ischemic stroke risk based on a CHADS₂-VASc score of 0, 7.5% ($n = 5$) had a low to moderate ischemic stroke risk based on a CHADS₂-VASc score of 1, 10.4% ($n = 7$) had a moderate ischemic stroke risk based on a CHADS₂-VASc score of 2, 20.9% ($n = 14$) had a moderate to high ischemic stroke risk based on a CHADS₂-VASc score of 3 and 13.4% ($n = 9$) had a high ischemic stroke risk based on a CHADS₂-VASc score of ≥ 3 , see [Table 2](#).

Only 27 patients were on OAC at the time of TOE. Patients with new onset AF were not considered to be on OAC if only commenced on treatment prior to TOE study. OAC was commenced in 38 patients following the TOE, see [Table 3](#). An increase in INR targets, reinforcement of compliance or a switch to novel OAC was made in 27 patients. One patient was deemed unsuitable for OAC given complicated liver disease with a previous bleed secondary to oesophageal varices. One patient declined OAC due to personal concerns.

Two patients had an ischemic stroke prior to the TOE study. Both patients were undergoing investigation for a cardio-embolic source of ischemic stroke. Neither patient was on OAC at the time. One patient was noted to go into AF at the time of TOE. The second patient had no documented arrhythmia or structural heart disease.

No patient had an ischemic stroke in the six-month period following the TOE study and optimal management of OAC.

Results are summarised in [Fig. 1](#).

Table 1

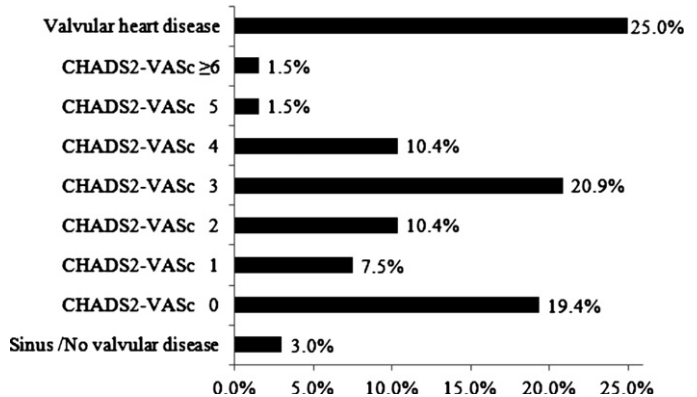
The gender and age distribution of patients with a LA thrombus, LAA thrombus or pre thrombus state.

	Male			Female		
	<64	65–74	>75	<64	65–74	>75
Age						
LAA thrombus	18	9	3	8	9	4
LA thrombus	1	1	0	0	0	0
LAA and LA thrombus	1	1	0	1	0	0
Pre-thrombus	4	0	1	5	1	0
Total	24	10	4	14	10	5

Abbreviations: LAA = left atrial appendage and LA = left atrial.

Table 2

Percentage of patient and their risk stratification for ischemic stroke.



4. Discussion

There is increasing interest in the field of cardio-embolic risk stratification in patients with AF and appropriate introduction of OAC. Although LAA thrombus is a well accepted risk factor for ischemic stroke, we were unable to find the incidence of ischemic stroke in patients with a confirmed LAA thrombus on literature review. We therefore carried out a retrospective study to determine the occurrence of ischemic stroke in patients following identification of a LAA thrombus and optimization of OAC in our own centre.

In 2 of our 67 patients AF had not been detected. It is possible that these 2 patients who developed LAA thrombus in the setting of “sinus rhythm” and normal cardiac anatomy had paroxysmal AF that had not been captured clinically. In non-valvular AF thrombus has a tendency to form in the LAA [7]. Thrombus may dislodge, embolize and lead to ischemic stroke [7 and 9]. LAA thrombus is infrequent in sinus rhythm. If it occurs in sinus rhythm it is typically associated with mitral valve disease or LA dysfunction [1]. Neither of these 2 patients had mitral valve disease. Sanna et al. recently reported paroxysmal AF detection rates (lasting >30 s) in 12.9% of patients with a diagnosis of cryptogenic stroke over a 12-month period following the index event, using implantable loop recorders [10].

A history of AF was documented in 65 of the 67 patients. The occurrence of thrombus or pre-thrombus was 0.48% in patients undergoing TOE following a cardio-embolic event, 16% in patients undergoing TOE prior to a planned cardio-version for AF and 1% in patients undergoing assessment of structural heart disease.

In the 65 AF patients 25% ($n = 17$) had valvular heart disease, 34.3% had moderate to high risk of ischemic stroke based on a CHADS₂-VASc score of ≥ 3 and 17.9% had low to moderate risk of ischemic stroke based on a CHADS₂-VASc score of 1 to 2. Interestingly 19.4% ($n = 13$) of AF patients had no valvular heart disease and a CHADS₂-VASc score of 0 and therefore would have been deemed by clinical criteria to be of low risk prior to TOE and identification of thrombus.

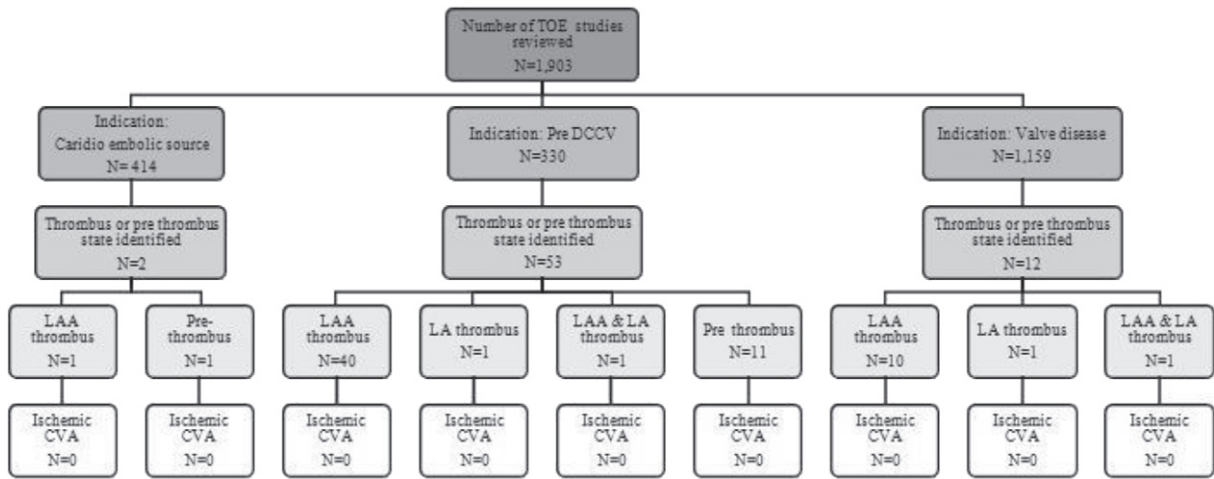
Only 28 of the 67 patients had an indication for OAC prior to identification of thrombus or pre-thrombus state on TOE or new onset AF.

Table 3

OAC status before and after diagnosis of LAA thrombus, LA thrombus or pre-thrombus state.

	OAC pre TOE	OAC post TOE
LAA thrombus	21	50
LA thrombus	1	2
LAA and LA thrombus	2	3
Pre-thrombus	3	10
Total	27	65

Footnote: LAA = left atrial appendage; LA = left atrial and OAC = oral anti-coagulation.



Footnote:: LAA= left atrial appendage; LA= left atrial and CVA= ischemic cerebrovascular events.

Fig. 1. Flow chart of indication for TOE reviewed and result of study. Footnote: LAA = left atrial appendage; LA = left atrial and CVA = ischemic cerebrovascular events.

Twenty of these patients were sub-optimally controlled and were undergoing TOE to exclude thrombus prior to the planned cardio-version.

Our study found a low rate (0 of 67) of ischemic strokes in patients following a confirmed LA thrombus, LAA thrombus or pre-thrombus state and introduction or adjustment of OAC. Only 2 patients had a prior ischemic stroke, and neither patient was on OAC at the time of their ischemic stroke.

Some series have reported a low stroke rate in patients in whom the LAA has been surgically removed. Notably, these patients were converted to sinus rhythm at the time of excision [12,13]. However, data from retrospective or observational studies in different patient populations have shown inconsistent results of surgical LAA occlusion [6–8]. More recently interventional techniques have been developed for percutaneous occlusion of the LAA to reduce ischemic stroke [11–13] however, these devices have not yet been approved in the US and the current ESC guidelines reflect ongoing concerns regarding LAA occlusion [14]. Our findings of a low rate of clinical thromboembolic events in patients in whom a thrombus or pre-thrombus state is identified and subsequently OAC optimally controlled are interesting. Larger studies would be required to verify these results. If confirmed a strategy of medical management could be justified without emergent surgical or percutaneous intervention in this acute setting.

4.1. Limitations

This single centre study was retrospective and the number of patients in whom thrombus or pre-thrombus was only 67. Given the small sample size further multicentre studies would be required to confirm our results. In addition the detection of neurological events was reliant not only on retrospective documentation, but also on patient's reporting of symptoms at follow-up visits. In the absence of symptoms, neurological imaging is not routinely obtained on patients following a documented LAA thrombus, and we therefore cannot rule out silent (sub-clinical) embolic events.

5. Conclusion

This is the only study to date that has looked at the occurrence of ischemic neurological events in patients following a confirmed LAA

thrombus, LA thrombus or pre-thrombus state and subsequent optimization of OAC. This study found a low rate (0 of 67 patients) of clinical thromboembolic events. Larger studies would be required to verify these results. If confirmed this might suggest that a strategy of medical management is appropriate without emergent surgical or percutaneous intervention in this acute setting.

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