

Resolution of Left Atrial Appendage Thrombi with Anticoagulant Therapy in Candidates for Percutaneous Mitral Commissurotomy

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Fate of left atrial thrombi (LAT) among candidates of Percutaneous Mitral Commissurotomy (PTMC) after oral anticoagulant therapy, is not well documented. The aim of the study was to estimate the resolution rate of documented LAT and its predictors. In this prospective cohort study all consecutive patients with tight mitral valve stenosis and valve morphology suitable for PTMC on transthoracic ocardiography complicated by atrial fibrillation and LAT on Transoesophageal echocardiography (TEE), were followed between Jan 1998 and June 2002. Patients with multiple thrombi in LA cavity and very large and organized thrombi were excluded and referred for surgical intervention. All other patients received oral anticoagulation (INR 2-3). Serial TEE were performed at third and seventh months to observe the resolution of LAT. During study period a total of 42 patients were followed for 3- 7 months. LAT was totally dissolved in 32 patients with overall resolution rate of 76 %. Patients with resolved LAT underwent uneventful PTMC. The median period of resolution was 22 weeks. Significant predictors of LAT resolution were the size of LAT and severity of left atrial spontaneous echo contrast. Patients with pliable mitral stenosis complicated by atrial fibrillation and small LAT should be given a trial of OA therapy. Such patients can safely undergo PTMC on resolution of LAT.

Key words: Mitral stenosis, LAT, Transesophageal echocardiography

Percutaneous Transvenous Mitral Commissurotomy (PTMC) has been established as procedure of choice for treatment of severe mitral valve stenosis with pliable leaflets. It is a safe alternative to the surgical treatment if valve regurgitation and leaflet calcification are minimal¹. The presence of left atrial thrombi is generally considered a contraindication to the procedure because of the risk of systemic embolism associated with catheter and wire manipulation in LA^{1,2,3,4,5,6}. Resolution of left atrial appendage thrombi (LAAT) by oral anticoagulation treatment has been reported in small number of patients^{11,12,13} and it is suggested that PTMC can be attempted after resolution of atrial thrombi by oral anticoagulation of varying period. Purpose of this study was to establish the resolution rate of LAT among candidates for PTMC and to determine predictors of resolution.

Study population

Study design was prospective cohort conducted at Cardiology Department, Mayo hospital (from Jan 98 to 12-7-99) and at Punjab Institute of cardiology for rest of the period. Both units are professorial teaching units. All patients with tight mitral stenosis who fulfilled the criterion for PTMC on transthoracic echocardiography and atrial fibrillation underwent Transesophageal study (TEE). After exclusion (Table 1) 42 patients with LAT were found to be eligible for follow up. Study patients were given OA therapy to maintain INR between 2-3. If follow up TEE revealed resolution of LAT, PTMC was carried out 72-96 hours after discontinuing OA. Patients were closely followed for any deterioration in clinical status or non-compliance with OA.

Methods

Transthoracic Echocardiography (TTE) TTE were performed on the following Toshiba machines using color Doppler system and 2.5, 3.5 or 5.0 MHz transducers. 1) Powervision 7000. 2) Sonolayer SSH 140 A. 3) Corevision Pro.

Table 1. Exclusion criterion:

- Multiple thrombi in LAA and LA cavity.
- Large thrombus (more than 5mm in one axis)
- Organised clots especially adherent to LA walls and IAS.
- Freely mobile clots acting as ball valve thrombus and/or carrying high risk of embolism.
- Mitral valve judged as non pliable on TEE.
- Moderate to severe AR on TEE (under estimated on TTE).
- SEC in RA indicating organic TV disease.
- Severe symptoms or hemodynamic condition necessitating early surgical treatment.
- Patients with earlier closed or open mitral valvotomy
- Patients with history of systemic embolism but in sinus rhythm during TEE.

Routine measurements of chambers and valvular hemodynamics were made in different standard views. Mitral valve area (MVA) was calculated by planimetry and pressure half method of CW Doppler. Valves were classified as pliable, border line pliable (both suitable for PTMC) or non pliable (not suitable for PTMC). If LAT were suspected in patients with pliable mitral stenosis, their measurements were taken on TEE^{14,15,16}.

Transesophageal Echocardiography (TEE) TEE was performed with Toshiba Powervision 7000 system by biplane or multiplane (PIC) 2.5-3.75 MHz probe following usual protocol. Findings of TTE were confirmed and suitability for PTMC was rechecked. Left atrial

appendage (LAA) was viewed in multiple planes. Great care was taken to differentiate LAT from LAA hypertrophy. When confirmed LAT were measured in two perpendicular axes (width and length). LASEC was characterized by swirling echoes showing spiral movements in LA. Severity of LASEC was graded from 1-4 as described earlier^{17,18}.

Study Protocol

All patients with LAT were prescribed OA with objective INR between 2-3. LAT resolution was observed on serial TEE studies at 3 and 7 months. End point was complete dissolution of LAT. The patients in whom LAT were not resolved at seven months, open mitral valvotomy was opted for. Percutaneous Trans Septal Mitral Commissurotomy (PTMC): PTMC was performed with Inoue technique, using serial inflations of properly sized Inoue balloon catheter¹⁹. Interatrial septal puncture was performed by Brockenbrough technique²⁰. All patients with resolved LAT underwent PTMC without any complications. None regained sinus rhythm and OA was started 24 hours after PTMC.

Statistical Analysis

Patients were classified according to the sizes of LAT, density of LASEC and different measures of severity of mitral stenosis like MVA, peak pulmonary artery pressure (PPAP) and LA size. Rate of resolution of LAT of different groups were calculated from follow up TEE.

Results

Clinical features of study population are given in Table 2. Eleven patients had history of prior systemic embolism. Two had embolectomy for limb ischemia. Two of the patients with CNS embolism had residual defect, others had full recovery. Four patients were already on OA therapy of undetermined intensity but there initial INR was less than 1.7. Ninety five percent of patients were receiving digoxin and 83% were on low dose beta blockers for ventricular rate control. All patients had satisfactory rate control on follow up.

Table 2. Clinical variables

Age (Years)	19-33 (mean 21)
Men (No)	9(21.5%)
Women	33(78.5%)
Previous Embolism	11(28%)
NYHA II	18(43%)
NYHA III	24(57%)
Beta Blockers	35(83%)

LAT, LASEC and Resolution Rate of Clot: Patients were followed for 3-7 months. All patients showed decrease in clot size but complete resolution occurred in 32 (76%) patients. Degree of severity of mitral stenosis or pulmonary hypertension had no correlation with rate of resolution of LAT which was largely determined by size of LAT and density of LASEC (Tables 4,5). All clots with maximal dimension of less than 1.5cm were resolved at 7 month and large percentage (82%) of these were resolved

at 3 months. Only 33% of clots larger than 2.5 cm were dissolved.

Table 3. Echocardiographic variables

	Range	Mean
MVA (cm ²)	0.6-1.1	0.76
LA dimension (mm)	48-79	63
LVEF %	47-64	57
PPAP (mm Hg)	58-110	78
LAT Width (cm)	0.9-2.2	
LAT Length (cm)	0.7-4.2	
LAT Confined to LAA	32 (76%)	

Table 4. LAT characteristics and resolution rate

Size (larger dimension)	No	Resolution in Three Mon	Total Resolved
< 1.5 cm	12	10 (82%)	12 (100%)
1.5-2.5 cm	21	12 (57%)	17 (81%)
> 2.5 cm	09	01 (11%)	03 (33%)
Total	42	23 (55%)	32 (76%)

Table 5. LASEC score and lat resolution

LASEC Score	No	Resolution on 3 Mon	Total Resolved
2	14	10 (71%)	14 (100%)
3	26	13(50%)	15 (57%)
4	12	None	03(25%)

All patients with LAT had more than grade 1 LASEC. Patients with larger clots had more dense LASEC and these patients had lowest rate of resolution of LAT (25%). In all patients LASEC on TEE was most clearly detected at the inflow of the left inferior vein near the opening of LAA into LA. Patients with resolved LAT underwent uneventful PTMC. During follow up there were no embolic episodes in study population. Five patients had minor bleeding episodes largely due to local pathology.

Discussion

Reported Incidence of LAT in patients of rheumatic MS ranges between 8-12% in patients in sinus rhythm and 22-38% in patients with atrial fibrillation.^{17,21,22} This study was not designed to find out incidence of LAT in our population. Presence of LAT is a contraindication to PTMC because of the risk of systemic embolism during intervention. Few smaller reports^{21,23} have shown uneventful PTMC in the presence of non mobile LAA thrombus but unexpected placement of wires and catheters in LAA may dislodge the thrombus and cause systemic embolism. Due to very low risk of embolism in our study we cannot recommend PTMC in presence of such thrombi and an attempt to resolve these under strict follow up should be taken. Smaller studies^{11,12,13,23} have reported the complete resolution of LAT with OA, thus allowing such patients to undergo PTMC. This mode of management remained to be tested in our population. The present study also determines the predictors of clot dissolution.

Tsai et al¹¹ documented resolution of LAT by TEE in four patients who received OA for 4-12 months. Similarly

Pytlewski et al¹³ described resolution of LAT in two patients after short OA course. Kang et al¹² described successful resolution of LAT in 24 patients with rheumatic MS after two to 12 months of OA. Successful LAT resolution within four weeks of OA is described in a high proportion patients with non valvular atrial fibrillation²². A much longer duration of treatment with OA is required to resolve LAT in patients with MS complicated by atrial fibrillation²³. This increases the risk of systemic embolism which was not reported in study population. Risk of embolism can be further minimized by using intravenous heparin during discontinuation and reinitiation phases of OA. The risk of thromboembolic events with PTMC depends upon the location of LAT. Thrombi in LAA are associated with minor risk. This may explain absence of embolic events in study population.

The mechanism of clot resolution cannot be explained from this study. Probably endogenous fibrinolysis and prevention of formation of new clots play role. The study does demonstrate that complete resolution of LAT can be achieved in high percentage of patients awaiting PTMC. Most of the patients showed resolution within six months but extending OA for three months more did benefit patients with larger clot burden.

Study limitations:

The study protocol did not include methods to detect sub clinical embolism i.e., MRI and/or CT scan. Most of the TEE studies were performed and reported by single operator. We did not score the mitral valve with Wilkinsons²⁴ or any other parameters²⁵, an approach which was later established on observations that configuration of mitral ostium (central vs eccentric) and amount and location of calcification are the key determinants of the successful outcome of PTMC.

Conclusion

In brief the results of the study provide convincing evidence regarding efficacy and safety of OA therapy for nine months for resolution of LAT in patients otherwise suitable for PTMC. PTMC can be safely performed after resolution of LAT. Safety of longer duration of OA therapy for larger clots remains to be confirmed.

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