

Bioprosthetic Mitral Valve Thrombosis. Importance of Transesophageal Echocardiography in the Diagnosis and Follow-up After Treatment

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Objective

To report the clinical and echocardiographic findings of bioprosthetic mitral valve thrombosis and the value of transesophageal echocardiography (TEE) in its diagnosis and monitoring of thrombolysis.

Methods

One hundred and eleven patients with mitral bioprostheses underwent TEE, and 4 out of 7 suspected of having a thrombus on these prostheses were included in the study (mean age = 60.2 ± 10.2 years; 2 men). The diagnosis was confirmed with serial TEE and clinical evolution. The morphologic features of the prosthetic leaflets, as well as the presence and characteristics of attached echogenic masses were investigated. The mean gradient through the prosthesis and the valvular area were obtained.

Results

The diagnosis of bioprosthetic mitral valve thrombosis was established 48.7 ± 55.2 months after surgery. Two patients had ischemic stroke in the early postoperative period. The mean overall gradient was high (11.4 ± 3 mmHg) and the valvular area reduced (1.24 ± 0.3 cm²). On TEE, echogenic masses on the left ventricular face of the mitral bioprosthesis suggestive of thrombus were evidenced in all patients. On serial TEE (136 ± 233 days), in 2 patients the thrombus had disappeared and in 2 others it was smaller after treatment, the mean gradient dropped to 6.2 ± 3 mmHg ($P = 0.004$; 95% CI), and the valvular area increased to 2.07 ± 0.4 ($P = NS$).

Conclusion

TEE proved to be useful for detecting bioprosthetic mitral valve thrombosis and was effective in monitoring the treatment in all patients.

Key words

thrombosis, bioprosthesis, transesophageal echocardiography

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One of the major advantages of bioprostheses is the fact that they have a low incidence of thrombosis¹ as compared with that of mechanical prostheses, and, therefore, do not require the use of anticoagulant drugs.

In an observational study by Grunkemeier and Rahimtoola², the analysis of the risk of thrombosis showed a significant difference between biological and mechanical prostheses. For the mechanical prostheses in the aortic position, the occurrence of thrombosis varied from 0.05% to 0.25% per year. For the bioprosthesis in the aortic position, the occurrence of thrombosis was 0.03% per year. The mitral prostheses followed a similar pattern, with a predominance of thrombosis occurring with the metallic type (0.28 to 0.62% per year) as compared with that with the biologic type (Hancock and Carpentier-Edwards – 0.02 to 0.07% per year)³.

The diagnosis of prosthetic valve dysfunction is usually confirmed on autopsy or through the surgical inspection of the removed prostheses, but the noninvasive diagnosis has been used with progressive safety in these cases.

Two-dimensional and M-mode echocardiography may be useful instruments for demonstrating obstruction of the bioprosthesis by a thrombus^{4,5}, the first cases being reported in 1976^{6,7}. However, transthoracic echocardiographic images usually do not allow a conclusive approach to thrombus definition due to its imprecision in defining the prosthetic leaflets.

Transesophageal echocardiography (TEE), on the other hand, provides a unique acoustic window for assessing the prosthetic leaflets, particularly in the mitral position, due to the greater proximity of the transducer with the cardiac structures and greater frequency of the crystals used, which results in greater resolution and absence of acoustic interference of the attenuating elements, such as the ribs and lungs, and even the components of the prosthesis⁸. This technique provides accurate images for the definition of the thickness of the leaflets and their mobility, allowing an adequate diagnosis of calcifications, stenoses, and ruptures⁹⁻¹².

Nonetheless, the descriptions of bioprosthetic mitral valve thrombosis on TEE are rare¹³⁻¹⁷.

In regard to the treatment of metallic prosthetic thrombosis, the thrombolytic agent has been efficient in a significant number of cases¹⁸⁻²¹, although the use of oral anticoagulants prior to the thrombolytic agent has also been effective on some occasions, when one is not dealing with an acute hemodynamic decompensation²².

In bioprosthetic thrombosis, therapy with oral anticoagulant agents has been rarely reported, although the results have been promising¹⁷.

The literature has shown that the effect of thrombolytic agents on this type of prosthesis has proved to be an effective alternative^{23,24}.

This study aims at reporting the echocardiographic findings (particularly those of TEE) in bioprosthetic mitral valve thrombosis and the role played by echocardiography in monitoring therapeutic efficacy.

Methods

One hundred and eleven patients with mitral bioprostheses who underwent transesophageal echocardiography due to different clinical indications between 1994 and 1998 were retrospectively analyzed. Thrombosis was evidenced in 7 patients. In 4 of these patients (mean age = 60.2±10.2 years; 2 males), the diagnosis of thrombosis could be confirmed through clinical evolution and serial assessment on TEE; therefore, the 4 were included in the study. In the remaining cases, although the transesophageal echocardiographic characteristics were suggestive of thrombus, the clinical evolution did not confirm it, and, therefore, the patients were not included in the study. All patients received intravenous heparin for the treatment of thrombosis; on one occasion, streptokinase was added.

The number of transesophageal echocardiographies performed and the time interval for their performance were decided by the cardiologist responsible for the case. In this analysis, the last transesophageal echocardiography of each patient was considered for comparison with the initial one. The serial echocardiographies were performed by the same examiner. The mean time between the 2 transesophageal echocardiographies was 136±233 days (11 days – 16.2 months). The mitral valve dysfunction was due to the rheumatic cause in all cases.

Two patients had undergone previous surgery for mitral prosthesis, and none had received a prosthesis in the aortic position.

Two patients were using oral anticoagulation prior to the echocardiographic diagnosis of thrombosis, and the medication was suspended on the occasion of the surgical procedures (mitral valve re-replacement in 1 case and renal surgery in another). Although the patient undergoing mitral valve re-replacement continued with intravenous heparin, both experienced ischemic stroke in the early postoperative period.

The following devices were used to perform transthoracic echocardiography: the Toshiba SSH-140 model; the SIM 7000 model of ESAOTE; and the Acuson XP-10 model. The Toshiba SSH-140

model with biplanar transducer was used for TEE. The measurements of the atrial and ventricular cavities were obtained through the left parasternal view, according to previously published recommendations²⁵.

The thickness and mobility of the leaflets of the mitral valve prostheses were analyzed using apical, parasternal, and subcostal mapping, and the presence of echogenic masses in the leaflets was assessed, as was the presence of left atrial thrombus.

The mean gradient through the mitral valve prosthesis was assessed with continuous Doppler using the apical 4-chamber view and the simplified Bernoulli equation²⁶. The prosthetic mitral valve area was calculated according to the atrioventricular pressure half-time method reported by Hatle et al²⁷.

The presence and degree of mitral insufficiency were analyzed with color Doppler²⁸.

Left ventricular systolic function was assessed through calculation of the ejection fraction according to the method reported by Teichholz et al²⁹.

The jet of tricuspid insufficiency was used to calculate the systolic pressure of the pulmonary artery adding 10 mmHg to the peak gradient through regurgitation³⁰.

Transesophageal echocardiography was performed with a 5MHz biplane transducer in the longitudinal and transversal planes, in the high and low esophageal, and gastric positions.

Thickness and mobility of the leaflets were assessed qualitatively and quantitatively; when the measure exceeded 3 mm, the prosthetic leaflet was considered thickened¹⁴.

The presence of echogenic masses in the leaflets was investigated, as was the presence of a thrombus in the left atrium or in its appendage.

The presence and severity of mitral regurgitation were also analyzed on TEE.

After treatment with an anticoagulant or thrombolytic agent, or both, the same parameters were reassessed on transthoracic and transesophageal echocardiography.

The paired Student *t* test was used for comparison between pre- and posttreatment parameters.

Results

The diagnosis of bioprosthetic mitral valve thrombosis was performed, on average, 48.7±55.2 months after surgery; in 1 patient, it occurred 11 days after surgery (tab. I). On the occasion of the echocardiographic diagnosis of thrombus, 1 patient was in NYHA functional class II congestive heart failure, another in functional class IV, and the 2 remaining in functional class I.

Table I - Clinical data

Case	Age (years)	Sex	BPM type	# BPM	Time of BPM (m)	AC	ASA	Rhythm	Symptoms	FC
1	59	F	BPH	NA	122	No	No	AF	CHF	II
2	73	M	Biocor	29	12.7	No	Yes	AT	Asymptomatic	I
3	61	F	NA	NA	60	No	No	AF	STR	I
4	48	M	Labcor	NA	0.36	Heparin	No	AF	CHF, STRIV	IV
Mean ± SD	60.2 ± 10.2				48.7 ± 55.2					

AT - atrial tachycardia; AF - atrial fibrillation; NA - not available; STR - stroke; CHF - congestive heart failure; FC - NYHA functional class; AC - anticoagulant; BPM - bioprosthetic mitral valve; m - months; # - number.



In 1 of these patients in functional class I, obstruction of the mitral bioprosthesis was found on transthoracic echocardiography in a routine assessment of the prosthesis 1 year after surgery, which showed an elevated transprosthetic gradient and leaflets with reduced mobility. The subsequent TEE showed a thrombus on the prosthesis causing the obstruction.

The other patient in functional class I underwent transthoracic echocardiography a few weeks after renal surgery due to the occurrence of stroke in the early postoperative period. The gradient through the prosthesis was increased, and the TEE performed on the same day revealed a thrombus on the mitral prosthesis causing the obstruction.

In the patient with functional class IV congestive heart failure and stroke in the early postoperative period, transthoracic echocardiography showed, in addition to the high prosthetic mitral valve gradient, thickened leaflets with reduced mobility, allowing only partial filling through the prosthetic ring on color flow mapping, raising the suspicion of a thrombus. Later, TEE confirmed these findings.

The transprosthetic gradient of the patient in functional class II on transthoracic echocardiography was not very elevated (8.8 mmHg), but as the patient's cardiac rhythm was that of atrial fibrillation, cardioversion was considered a possibility in an attempt to improve clinical condition. Prosthetic mitral valve thrombosis was only detected on routine TEE performed prior to cardioversion to investigate the emboligenic source.

Three patients had atrial fibrillation, and 1 had atrial tachycardia. No patient had fever or clinical suspicion of infective endocarditis.

All patients were treated with intravenous heparin after the diagnosis of thrombosis, streptokinase being added for 1 patient

due to lack of clinical/echocardiographic response to heparin. Oral anticoagulation was administered to all patients after hospital discharge.

On transthoracic echocardiography, the left atrium ranged from 51 to 60 mm (mean = 55.3±4.1 mm), and left ventricular overall systolic function was decreased only in 1 patient (EF = 35%), who also had a reduced right ventricular overall systolic function.

In 1 patient, transthoracic echocardiography suggested bioprosthetic mitral valve thrombosis, and in all patients the mean transprosthetic gradient was elevated, with an overall mean of 11.4±3 mmHg (tab. II). The valvular area was reduced (1.24±0.3 cm²), and only 1 patient had mild transprosthetic mitral insufficiency.

Three patients had tricuspid valvular incompetence, and the systolic pressure of the pulmonary artery could be measured in 2 of them, being elevated in both (tab. II).

On TEE, the leaflets were thickened and their mobility was reduced in all patients.

Echogenic masses suggestive of thrombi were seen in all patients carpeting the left ventricular face of the prosthetic leaflets, producing an increase in their thickness (5.7 ± 0.9 mm). In 1 patient, thrombi in the left atrial face with a pedunculated aspect were observed, adhered to the atrial margin of the prosthetic leaflet. In 3 patients, the thrombus affected 2 leaflets, and, in 1 patient, the thrombus affected 3 leaflets (tab. III).

A thrombus was observed in the left atrium in 2 patients, and formation of spontaneous contrast was seen in all patients (tab. III).

In 3 patients, the recent serial TEE (< 1 month) showed a reduction in size or disappearance of the thrombi (fig. 1); in 1 patient, however, the thrombus only disappeared on the second serial TEE (486 days after the initial study).

Table II - Transthoracic echocardiographic data

Case	LVDD (mm)	LVSD (mm)	LV EF (%)	LA (mm)	MG (mmHg)	MVA (cm ²)	LA TR	RV function	Bioprosthetic mitral valve				Tricuspid valve
									Thic	Mob	TR	MI	
1	42	20	84	51	8.8	1.34	No	NI	No	NI	No	No	N
2	49	27	76	60	15.0	NA	No	N	No	Dec	No	No	Mod/imp T1 PASP:65
3	46	24	79	52	13.0	1.5	No	NI	Yes	Dec	No	No	Mild/mod T1 PASP:48
4	63	51	35	54	9.0	0.9	No	Dec	Yes	Dec	Suspicion	Mild	Mild T1
Mean ± SD	50.0±9.1	30.5±13.9	68.5±22.5	54.2±4.0	11.4±3.05	1.24±0.3			Yes	Dec	Suspicion	Mild	

LVDD - left ventricular diastolic diameter; LVSD - left ventricular systolic diameter; LVEF - left ventricular ejection fraction; LA - left atrium; MG - mean mitral transprosthetic gradient; MVA - mitral valve area; TR - thrombus; Thic - thickening of prosthetic leaflets; Dec - decreased; NI - normal; Mob - mobility of the prosthetic leaflets; MI - mitral insufficiency; T1 - tricuspid insufficiency; PASP - pulmonary arterial systolic pressure (in mmHg); mod - moderate; imp - important.

Table III - Transesophageal echocardiographic findings

Case	LA		Bioprosthetic mitral valve							
	TR	SC	Thrombus				Leaflets		Insuf	
			Type	Site	Size (mm)	#	Thic (mm)	Mob		
1	No	Yes	Sessile	Ventricular face	15	2	Yes	6.0	Dec	no
2	Yes	Yes	Sessile	Ventricular face	17	2	Yes	6.7	Dec	no
3	No	Yes	Sessile and pedunculated	Ventricular and atrial face (free margin)	24	3	Yes	4.5	Dec	mild
4	Yes	Yes	Sessile	Ventricular face	16	2	Yes	5.7	Dec	mild
Mean ± SD					18 ± 4.0			5.7 ± 0.9		

SC - spontaneous contrast; Insuf - insufficiency; the other abbreviations are as in table II.

Intravenous heparin was administered followed by anticoagulation in all patients, and the mitral transprosthetic gradient subsided in 3 patients, 2 of whom also had disappearance of the thrombus, while the third had a decrease in its size. In the fourth patient, the isolated anticoagulant therapy did not have the effect desired, no modification in the transprosthetic gradient (from 9 to 10 mmHg) occurred, and no significant change in leaflet mobility on transthoracic echocardiography was observed. Due to clinical instability with persistence of dyspnea on minimal exertion, streptokinase was chosen to be administered at a dosage of 250,000 IU in bolus and 100,000 IU/h as maintenance until the transthoracic echocardiogram showed a reduction in the transprosthetic gradient, which occurred with 24 hours of infusion (5.6 mmHg). The transesophageal echocardiogram revealed disappearance of the thrombus in the left ventricular face and the presence of a minimum pedunculated mass measuring 3 mm in the margin of the leaflets (atrial face) (fig. 1).

On average, the mean mitral transprosthetic gradient after treatment (isolated anticoagulant in 3 patients and streptokinase + anticoagulant in 1 patient) decreased to 6.2 ± 3 mmHg ($P = 0.004$ versus basal; 95% CI of the difference 3.1 to 7.3), and the valvular area increased to 2.07 ± 0.4 cm² ($P = NS$).

Of the 2 patients, in whom pulmonary arterial systolic pressure could be calculated based on the tricuspid regurgitation jet, regression was observed in 1 (32 mmHg), who also had a reduction in the mean transmitral gradient (7.4 mmHg) in this short follow-

up period (tab. IV). The other patient initially showed a poor response to therapy, evidenced by maintenance of the same dimensions of the thrombus 1 week after the first serial TEE and no effective reduction in the mean transmitral gradient (11 mmHg) and in the pulmonary arterial systolic pressure (60 mmHg) on transthoracic echocardiography on the occasion. Only on the more recent second serial transesophageal echocardiogram (486 days of evolution – tab. IV), the thrombus completely disappeared and a reduction in the mean transmitral gradient (9.5 mmHg) was observed, although the pulmonary pressure levels were maintained (65 mmHg). The left atrial thrombus in the 2 present cases disappeared.

Discussion

Prosthetic mitral valve dysfunction usually occurs due to rupture or calcification of the leaflets, culminating in valvular insufficiency or stenosis^{31,32}. Bioprosthetic mitral valve thrombosis is rare^{2,3}. Thrombosis of the Hancock bioprosthesis was reported in 2/561 (0.3%) patients followed up for a mean period of 2.3 (0.1-7.3) years³³.

The low frequency of bioprosthetic thrombosis¹ is one of the major advantages of the bioprostheses as compared with the mechanical type, making the use of oral anticoagulants unnecessary in the long run in the first case³³.

However, the real prevalence of thrombosis in patients with mitral bioprosthesis is unknown. Thiene et al³⁴ reported that, analyzing the pathologic findings in 50 Hancock bioprostheses placed in the mitral position, thrombus in the leaflets was found in 5 cases (10%), similar to the findings in other reports³⁵. These data suggest that the prevalence of bioprosthetic mitral valve thrombosis could be more representative.

The frequency of occurrence of mitral bioprosthetic thrombosis on TEE has been controversial in the literature. Kandheria et al¹³ reported only 1 patient among 21 (4.7%) with mitral bioprosthetic thrombosis, and Daniel et al¹⁴ reported a thrombus in 1 out of 113 (0.8%) patients. On the other hand, Oliver et al¹⁷, studying 161 (9.3%) patients with mitral bioprosthesis of the porcine type with signs of prosthetic dysfunction assessed on TEE, reported 15 patients with thrombosis, a frequency similar to that of the pathological findings previously reported.

In our study, 7 (6.3%) patients out of 111 had images suggestive of bioprosthetic mitral valve thrombosis, 4 of whom were confirmed by clinical response and on serial TEE. In this study, all

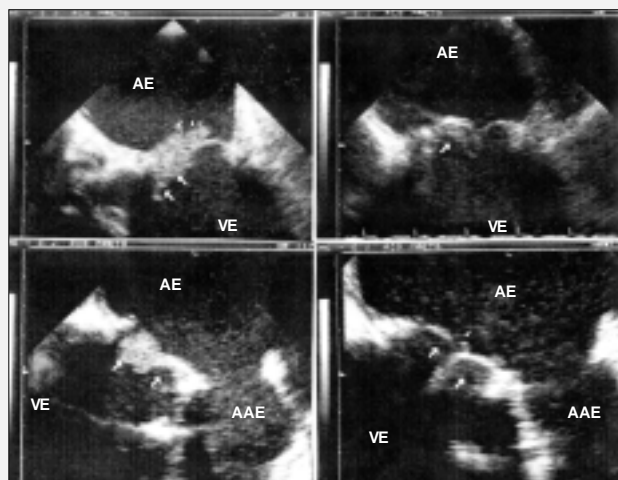


Fig. 1 - Transesophageal images of the patient 3 (superior) and 4 (inferior) before (left) and after treatment (right); the arrows point out the site of the thrombus on the leaflets of the mitral prosthesis, which decreased after treatment. VE - left ventricle; AE - left atrium; AAE - left atrial appendage; AO - aorta.

Table IV - Echocardiographic data on serial evolution after treatment

Case	Time (days)	LA TR	2nd TEE				2nd TTE		
			Bioprosthetic mitral valve thrombosis				MG (mmHg)	MVA (cm ²)	Tricuspid
			Type	Site	#	Size (mm)			
1	16	No	No	-	0	-	2.3	2.5	N
2	486	No	No	-	0	-	9.5	1.9	Mod/imp T1 PASP:65
3	22	No	Sessile and pedunculated	Ventricular face, free margin	2	11	7.4	1.6	Mild T1 PASP:32
4	25	No	pedunculated	Atrial face, free margin	1	3	5.6	2.3	N
Mean ± SD	136 ± 233					6.2 ± 3	2.07 ± 0.4		

Abbreviation as in the previous tables.



patients with a bioprosthesis in the mitral position undergoing TEE were analyzed, including those who were investigated for diseases other than the suspicion of prosthetic dysfunction, differently from the study by Oliver et al¹⁷.

Additional factors, such as age, sex, time of cardiac surgery, position of the valve, type of bioprosthesis, atrial cardiac rhythm, anticoagulant therapy, left atrial dimension, and left ventricular systolic/diastolic function, may influence in the formation of the thrombus¹⁷. In addition, situations of low transvalvular flow through the bioprosthesis, requiring circulatory assistance with centrifuge pumps¹⁵, may propitiate the formation of a thrombus in the early postoperative period.

In the present study, the left atrium was enlarged in all patients, the ventricular function was decreased in 1, all patients had atrial arrhythmia (3 had atrial fibrillation and 1 had atrial tachycardia), and only 1 patient was receiving anticoagulation (IV heparin) due to early postoperative period. The mean patients' ages were also advanced. The summation of these factors may have contributed to a greater prevalence of prosthetic mitral valve thrombosis in the present series.

It is important to note the significant role of atrial arrhythmias, mainly atrial fibrillation, in the pathophysiology of atrial thrombus formation, and this could be involved in triggering prosthetic thrombosis. Several studies³⁶⁻³⁸ have shown that the dysfunction of the atrial appendage present in certain arrhythmias, such as atrial fibrillation or flutter, is more related to the formation of spontaneous contrast or intracavitary thrombus, and with a greater occurrence of embolic events. Mugge et al³⁶ reported that the filling/emptying velocity of the left atrial appendage (reflecting the left atrial appendage function) was decreased (< 25 cm/s) in some patients with nonrheumatic atrial fibrillation, similarly to the group that had rheumatic atrial fibrillation. More embolic phenomena (5/10 patients) were observed in the group with low velocity as compared with the group with higher velocity (1/19 patients; $P < 0.05$). A greater occurrence of left atrial appendage thrombosis (30 vs 0%) and spontaneous contrast (80 vs 5%) were also observed.

In the present study, 2 patients had left atrial thrombosis, and all had spontaneous contrast. The left atrial appendage velocity was decreased in 1 patient (0.15 m/s), normal in another (0.46 m/s), and not available in 2 patients, making any conclusion about the significant role played by these data in the pathogenesis of prosthetic thrombosis risky.

The fact that thrombi are found on the ventricular and not on the atrial face of the prostheses is also relevant, and seems related to low flow, and areas of flow stagnation and turbulence through the prostheses. In an experimental study analyzing the characteristics of the flow through the different types of prostheses in an *in vitro* model, Schoepfoster et al³⁹ showed that, in bioprostheses, the region close to the periphery of the jet was relatively stagnant, and that the shear stress had greater stress in the margins of the jet with the greatest velocity. Yoganathan et al⁴⁰ correlated thrombus formation and tissue growth in valves with a single bascule disc with areas of stagnation and low shear rate in the region with the smallest valvular orifice. Some clinical studies also showed that the thrombus may occupy the sinus of the leaflet, either in the mitral^{15,16} or in the aortic¹⁶ position, and this fact could also be observed in pathological studies³⁴. The preservation of both mitral leaflets may cause relative prosthetic

stenosis, and mild abnormalities in blood rheology and local turbulence caused by the remaining leaflets might have a thrombotic effect⁴¹.

In this study, the thrombi were located in the ventricular face of the prostheses (sinuses of the leaflets) in all patients, corroborating the reports about the site of origin of the thrombi in previous studies.

The period of greater propensity for thrombus development seems not to be well established. Oliver et al¹⁷ reported that 70% of the patients studied had bioprosthetic mitral valve thrombosis after an 80-month follow-up of valvular replacement, early thrombosis (5 months) occurring in only 1 case. On the other hand, Hagley et al¹⁵ reported the occurrence of bioprosthetic mitral valve thrombosis early in the postoperative period related to conditions of low transvalvular flow. In the present study, 1 patient had a thrombus on a mitral prosthesis still in the early postoperative period associated with an episode of stroke. It is worth noting that this patient, although being on intravenous heparin therapy, had multiple factors contributing to thrombus formation, such as enlargement of the left atrium, a reduction in the left ventricular systolic function and atrial fibrillation. The patient evolved with NYHA functional class IV congestive heart failure, being discharged from the intensive care unit only after thrombolytic therapy, when thrombus resolution and a reduction in the transprosthetic gradient were obtained.

It is worth noting that in another patient the finding of the prosthetic mitral valve thrombus was occasional. The thrombus was suspected on transthoracic echocardiography, which showed a high gradient in an asymptomatic patient, the definitive diagnosis being established on TEE.

Treatment with thrombolytic agents for thrombosis on prostheses of the biological type has rarely been reported^{23,24}. The use of thrombolytic agents has been reported for prostheses in the aortic position with favorable results and complete resolution of the thrombus. The rationale for this is similar to that of their use for mechanical prostheses, and, in our study, this treatment was used for thrombosis of a prosthesis in the mitral position. Our decision was based on the clinical instability of the patient and on nonregression of the initial echocardiographic parameters. The patient's symptoms improved, and echocardiographic resolution of the mass on the bioprosthesis was observed on TEE with no complications resulting from the thrombolytic treatment.

However, it should be emphasized that the use of thrombolytic agents is not free of complications^{24,42}, especially when considering patients in the early postoperative period. One study²⁴ reported the occurrence of hemorrhage of the nose and of the venous accesses, which were clinically controlled.

Therefore, the use of thrombolytic agents should be carefully pondered, being basically restricted to those cases in which the clinical and surgical alternatives have been exhausted due the occurrence of other morbid factors that may impair the patient's evolution⁴². It is important to recall that the use of a thrombolytic agent does not prevent subsequent reinterventions, when indicated, and that the patient may be referred for surgery when in more stable clinical condition.

In regard to the effect of oral anticoagulants/heparin in thrombus resolution, Oliver et al¹⁷ and Waksmonski et al²² showed it to be a safe (no complications, such as embolism or bleeding, being

observed) and effective alternative with improvement of the functional class in all patients during follow-up. In their study, the treatment with oral anticoagulants was effective in 3 patients, and, 1 patient (receiving intravenous heparin and oral anticoagulation) required the additional thrombolytic treatment for thrombus resolution.

In regard to pulmonary pressure levels, one should recall that, in processes of mitral valvular obstruction, the degree of pulmonary arterial hypertension would be theoretically related to the severity of the stenosis⁴³. However, some patients with significant mitral stenosis may not develop pulmonary arterial hypertension. The left atrial pressure elevated by valvular obstruction initially increases pulmonary pressure passively with no significant elevation in pulmonary resistance. Chronically, a significant increase in left atrial pressure causes elevation in pulmonary arterial pressure due to an increase in pulmonary vascular resistance, secondary to arteriolar spasm or obstructive vascular changes. Some authors have shown a striking variability among patients in regard to the degree of pulmonary vascular reactivity in response to a chronic elevation in left atrial pressure⁴³, but the factors determining this variability remain undefined.

On the other hand, pulmonary arterial hypertension may regress following valvular clearing, which was shown in patients undergoing procedures for mitral valvular dilation. Prediction of this regression could be related to some clinical and echocardiographic factors, such as age⁴⁴, and to the immediate result of dilation⁴⁵. The initial reduction in pulmonary arterial pressure seems more related to a reduction in pulmonary capillary pressure in the period following percutaneous valvuloplasty, while the additional reduction throughout the first week seems more related to the decrease in pulmonary resistance⁴⁶.

Although the present study does not assess the specific case of interventional valvular clearance, but of thrombotic clearance, the evolution of pulmonary arterial systolic pressure could be followed up in 2 cases. By the time control TEE (22 days) was performed, only 1 patient showed regression of the pulmonary arterial systolic pressure after treatment (32 mmHg), accompanied by a reduction in the transprosthetic gradient (7.4 mmHg) and an increase in the valvular area (1.6 cm²). In the other patient, pulmonary arterial systolic pressure remained elevated (65 mmHg) on control TEE (486 days). In this case, the initial response to anticoagulant therapy did not produce the effect desired, because of the permanence of the thrombus on the prosthesis and the insignificant changes in the pulmonary arterial systolic pressure levels (60 mmHg) and in the transprosthetic gradient (11 mmHg) on the 28th day. This poor initial response to anticoagulant treatment could have contributed to a chronic change in pulmonary vascular resistance. In addition, the patient's more advanced age could have influenced the response of pulmonary arterial systolic pressure to therapy.

Finally, we emphasize the exceptional role played by TEE in assessing therapy efficacy, because of the demonstration of complete or partial resolution of the thrombus, a fact also reported by

Oliver et al¹⁷. In their study, in 6 cases, transesophageal echocardiography showed the complete disappearance of the thrombus after treatment with oral anticoagulants, and, in 2 cases, a significant reduction in the size of the masses was observed. In our study, disappearance of the masses was observed in 2 cases and a reduction in the thrombotic dimensions in the other 2.

The time of the examinations was oriented by the clinician responsible for the patient, and, therefore, the degree of resolution of the thrombi after treatment may have been influenced by it. This may be corroborated by the observation that in 1 patient, the transesophageal echocardiogram after 1 week showed no alteration in the size of the thrombus on the mitral bioprosthesis, which only disappeared on the last TEE, considered a control (486 days).

The "definitive" diagnosis of bioprosthetic thrombosis was established only by the response to the treatment instituted, and was not confirmed by any other methodology. Other abnormalities that could produce images of thickening and masses in the leaflets, such as lipid degeneration, vegetation, fibrocalcification, or hematomas, were excluded based on clinical and evolution findings.

Therefore, the favorable results after treatment, with size reduction or disappearance of the masses, allow inferring that those may have corresponded to thrombotic material, an opinion also shared by other authors¹⁷.

The use of other methodologies, such as tissue Doppler, may have contributed to a more definitive determination of the thrombus^{47,48}. In the study by Bartel et al⁴⁸, all patients with a thrombus in the left atrial appendage and 75% of the patients with an intraventricular thrombus had a coherent leaflet mobility, showing a small phase difference in relation to the adjacent tissue, due to an attenuated oscillation on tissue Doppler. In addition, tissue Doppler also allowed a more instantaneous identification of the structures investigated as compared with that provided by M mode or 2-dimensional echocardiography⁴⁸. This study suggests that thrombosis with a mitral valve prosthesis, mainly in patients not using anticoagulants, may be more prevalent than previously reported.

Some authors^{49,50} emphasize that due to the greater risk of thromboembolism in the first 3 months after biological replacement of mitral valve, oral anticoagulation is frequently recommended. Patients with thrombogenic risk factors, such as atrial fibrillation, enlargement of the left atrium, left ventricular dysfunction, previous thromboembolic episodes and hypercoagulability conditions, may have a greater risk of thrombotic obstruction of the prosthesis, and, in the absence of contraindications, these patients could be maintained under anticoagulant therapy.

The diagnosis of prosthetic thrombosis should be suspected in a setting of cerebral or peripheral ischemic findings, progressive symptoms of congestive heart failure or abnormal transprosthetic gradients, in prostheses with no significant signs of degeneration on transthoracic echocardiography.

Finally, this study showed the impact of TEE on the definition of the cause of prosthetic obstruction and on the assessment of therapeutic efficacy, and also the improvement of the symptoms and of valvular function in all patients.



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