Eastern Journal of Medicine: 10 (2005): 10-14

Original Article

Management of prosthetic mitral valve thrombosis

Hasan Ekim[a], Hakan Akbayrak[b], Halil Başel[a], Abdüssemet Hazar[b], Melike Karadağ[b], Veysel Kutay[a], İsmail Demir[b], Cevat Yakut[a]

[a]*Yüzüncü Yıl University Department of of Cardiovascular Surgery*

[b]*Yüksek Ihtisas Hospital Department of Cardiovascular Surgery, Van, Turkey*

Abstract. Prosthetic mitral valve thrombosis is a lifethreatening complication. Data on complications and outcome are limited. The purpose of this study was to review the clinical experience with the thrombolytic therapy and surgical management of prosthetic mitral valve obstruction in our hospital. Between the January 2001 and April 2005, twelve patients with obstructed prosthetic mitral valve were admitted to our hospital. There were 8 female and 4 male patients ranging in age from14 to 60 years, with a mean age of 34±12 years. In all patients, the diagnosis of prosthetic valve thrombosis was confirmed by echocardiography including transesophageal echocardiography. All patients showed absence or muffering of prosthetic valve sounds. Two of 12 patients received thrombolytic therapy by using streptokinase. In the remaining 10 patients, operations were performed on an emergency basis with median sternotomy and cardiopulmonary bypass techniques using antegrade-retrograde combinated isothermic blood cardioplegia and moderate hypothermia. The principal risk factors of prosthetic valve thrombosis are inadequate anticoagulation or fluctuation in anticoagulation levels. Its treatment is either surgical or with thrombolytics. Although both treatment methods are effective, the latter is gaining favor. However, surgery is often required due to large thrombi and a presence of pannus formation.

Keywords: Prosthetic mitral valve thrombosis, pannus, thrombolysis

1. Introduction

Mechanical heart valves have the advantage of longevity but carry a risk of thrombosis which is dependant on valve design, materials and host-related interface (1). While endocarditis dehiscence and pannus are common to both biologic and mechanical valves, acute prosthetic thrombosis is mostly a complication of mechanical valves (2).

Prosthetic valve thrombosis is defined by any thrombus, in the absence of infection, attached to or near an operated valve, occluding part of the blood flow or interfering with valvular function (3). It is a dreaded complication of patients with mechanical heart valves, particularly those in the mitral position (4).

*Correspondence:Dr. Hasan EKİM

Y.Y.Ü. Tıp Fakültesi Kalp ve Damar Cerrahisi AD

E-mail: drhasanekim@yahoo.com Tel: 535 417 65 39

An acute obstruction is a life-threatening complication of mechanical valve prosthesis, and is caused by the formation of fresh clot or fibrous tissue overgrowth, or both (5).

In this study we focused on obstructive complication, pannus and thrombosis, which are the most common complications of mechanical heart valves.

2. Materials and methods

Between January 2001 and April 2005, twelve patients with obstructed prosthetic mitral valve were admitted to our hospital. There were 8 female and 4 male patients ranging in age from14 to 60 years, with a mean age of 34±12 years.

In all patients, the diagnosis of prosthetic valve obstruction was confirmed by echocardiography including transesophageal echocardiography (TEE). Each patient was carefully interrogated for the presence of any clot or pannus. Two-dimensional echocardiography was performed with special emphasis on looking for opening

Table 1

Baseline clinical characteristics.

Characteristics	Results
Number of patients	12
Age (years)	14-60 (38,9±14,1)
Gender (female/male)	8/4
Atrial fibrillation	9 patients
Time from valve replacement to redo operation (months)	5-48 (22,5±15,1)
Initial functional class (lll-lV)	10 patients
Average systolic pulmonary arterial pressure	71,2±12,6 mmHg (range 50-120)
Thrombosed prosthetic valves (Bileaflet/monoleaflet)	4/8

excursion and completeness of closure of the mechanical prosthesis. Doppler echocardiography was performed to measure the pressure gradients across the mechanical valve. None of the patients underwent cardiac catheterization. Inadequate anticoagulation was defined as interruption of anticoagulant therapy or an international normalized ratio (INR) level of less than 2,5 at the time of diagnosis of valve obstruction.

Thrombolytic therapy: Streptokinase was given in a loading dose of 500 000 units over 30-45 minutes, following by an infusion of 100000 units/hour. Methyl prednisolone was administered (80 mg intravenously) before the initiation of thrombolytic therapy. The patients were monitored hourly. Serial echocardiographic examination was done at 6 hours intervals after the start of thrombolytic therapy. The endpoint of therapy was taken as near-normalization of Doppler echocardiographic transvalvular gradients.

Surgery: In patients with mobile or large thrombi or combined with pannus formation, operation was preferred rather than thrombolytic therapy. Operations were performed with median sternotomy and cardiopulmonary bypass techniques using antegrade-retrograde combinated isotermic blood cardioplegia and moderate hypothermia.

In ten patients, the diagnosis was confirmed by the gross pathological appearance of the prosthetic valves during surgery and by subsequent histophatological examination. In the remaining two patients who underwent thrombolysis, diagnosis was confirmed by the echocardiography revealing resolution of the thrombus following thrombolysis.

Follow-up: The patients were discharged with an INR in the target range of 2,5-3,5 and were followed at our policlinic. Oral anticoagulation regimen after surgical treatment or thrombolytic therapy consisted of a combination of warfarin and low dose aspirin (150 mg daily).

3. Results

All patients of prosthetic valve thrombosis showed absence or muffering of prosthetic valve sounds. The period between initial mitral valve replacement (MVR) and redo operation or thrombolysis ranged from 5 months to 48 months with a mean of 22,5±15,1 months. Majority of patients (n:8) were admitted in the winter months. The median time between the diagnosis of prosthetic valve obstruction and thrombolytic therapy or surgical procedure was 3 days (range 0-6 days). Eight thrombosed prostheses were bileaflet and the remaining four were monoleaflet. The baseline clinical characteristics of the patients are summarized in table 1.

The main clinical signs at the time of obstruction were dyspnea, orthopnea and congestive heart failure. Two patients were class ll according to the New York Heart Association (NYHA) functional classification, seven were class lll, and three were class lV. The diagnosis of prosthetic valve thrombosis was made with transthoracic echocardiography (TTE) in nine patients and TEE in three patients. Nine patients were in atrial fibrillation and 3 were in sinus rhythm before the treatment procedures. Management of anticoagulant therapy was inadequate according to international recommendations, at the time of diagnosis of valve obstruction, in ten patients (the INR recorded at the time of diagnosis was less than 2,5). This inadequate anticoagulant therapy was favored in two patients due to dental procedures.

Doppler examination revealed significant pressure gradients across the valve in all patients. The average systolic pulmonary arterial pressure was 71,2±12,6 mmHg (range 50-120 mmHg). Mean valvular area was 0,79±0,2 cm^2. Eleven

valves had severe obstruction alone, and one had combined severe obstruction and regurgitation.

All patients were started on intravenous heparin as soon as the diagnosis was suspected. Two of 12 patients received thrombolytic therapy. In these patients, after successful thrombolysis, there was near normalization of transvalvular gradients and pulmonary arterial pressures with disappearance of regurgitation across the prosthetic valves. In the remaining 10 patients, operations were performed on an emergency basis. A redo median sternotomi was used. Prosthetic valve replacement was performed in nine patients, of whom one required additional right atrial thrombectomy. The remaining one patient with fresh thrombi underwent thrombectomy and radiofrequency ablation due to chronic atrial fibrillation.

The cross clamping time averaged 64,4±13,1 minutes (range 35-135 minutes), and the cardiopulmonary bypass (CPB) time was 107,4±30,1 minutes (range, 71-150 minutes).

The obstruction was caused by thrombus alone in 10 patients; but in two patients obstruction was mainly due to a combination of pannus and thrombus (figure 1). Of the 10 patients operated on, one died. The cause of death was low cardiac output syndrome.

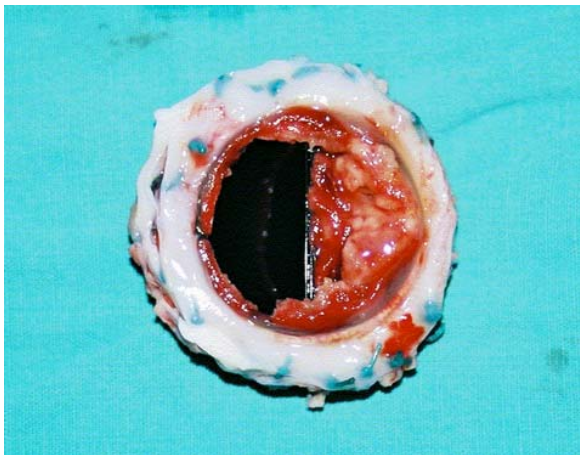

Figure 1. A combination of valve thrombosis and pannus formation of prosthetic mitral valve.

4. Discussion

There are many complications associated with mechanical valve replacement. These include thromboembolism, acute thrombotic occlusion, complications of long-term anticoagulation, prosthetic valve endocarditis, periprosthetic leakage, chronic hemolysis and reoperation. Acute thrombotic occlusion occurs primarily in patients with suboptimal anticoagulant therapy, which usually results when therapy is stopped or interrupted for a surgical procedure. The only other risk factor that has been identified is female sex (6).

Prosthetic valve thrombosis has been defined as any obstruction of a prosthesis by non-infective thrombotic material (7). Despite innovations in valve design and use of pyrolytic carbon or other material to coat valve surfaces, the reported incidence of thrombosis of prosthetic heart valves still ranges from 0,03 to 4,3% per year (8).

The presentation of patients with valve obstruction ranges from asymptomatic thrombotic occlusion detected by means of routine echocardiography to cardiogenic shock. The most common symptoms include those of pulmonary venous hypertension: dyspnea, orthopne a and paroxysmal nocturnal dyspnea. Other signs and symptoms include a decrease in the intensity of the prosthetic heart valve sounds, systemic thromboembolism, or the signs and symptoms of congestive heart failure. Cardiac examination reveals a prominent apical middiastolic murmur of mitral stenosis (9).

Thrombus formation generally occurs either from the sewing ring to the annulus or on the leading edge if tissue ingrowth, and extends along the struts and hinge points in disc and bileaflet-type valves (10). Pannus may be the only cause in 11-31% of the cases, and may be associated with thrombus formation in 46-78 % of the cases (11).

The most common precipitating factors for valve thrombosis are inadequate anticoagulation and poor patient compliance, underscoring the need for both patient-and physician-oriented education (12). Apart from anticoagulation failure, recurrent embolism, size and design of the prosthesis, atrial rhythm, cardiac failure and individual propensity are concomitant risk factors (13).

When thrombectomy is performed; the ventricular surface of the valve is inspected with a videothoracoscope. A laryngeal mirror can also be useful in this situation. Prosthetic valve thrombectomy is a safe, rapid, and simple procedure in a limited number of patients. Before discharge, aspirin is added to warfarin treatment. By optimizing the level of anticoagulation and by helping endothelialization of the prosthetic valve, aspirin might improve survival (12). Our one patient with fresh thrombi underwent thrombectomy and radiofrequency ablation treatment due to chronic atrial fibrillation. We suggest that radiofrequency ablation will minimize rethrombosis of the prosthetic valve.

Distinguishing thrombus from pannus on obstructed prosthetic valves is essential, since pannus formation is an indication for immediate surgery without prior thrombolytic therapy. Pannus formation is the result of an inflammatory reaction to a foreign body, as is confirmed by the histological features of pannus, involving giant cells, fibroblastic proliferation, and neoformed vessels (14).

The best discrimators between thrombus and pannus are duration of symptoms, anticoagulation status and ultrasound intensity of the mass. Extension of the thrombus into the left atrium has been considered specific for thrombus formation (15), as seen in our one patient

Heparin for nonobstructive prosthetic valve thrombosis is successful only in some (50%) of patients with small thrombi in functional class l or ll (16). Thrombolysis is usually superior to heparin. Success rates of thrombolytic therapy for prosthetic valve thrombosis have been estimated at 62-82 % (17). Complications of thrombolytic therapy include embolization, bleeding and allergic reactions. A neurological or circulatory deficit is rare (10).

Although there is no statistically difference in outcome between urakinase and streptokinase, some usually use urokinase because rheumatic heart disease has the risk of an allergic reaction to streptokinase (10). Rt-PA may be an recombinant tissue-type plasminogen activator alternative. However, (rt-PA) is costly and may actually increase the risk of embolism and bleeding (18).

Absolute contraindications to thrombolysis include active internal bleeding, history of hemorrhagic shock, recent cranial trauma or neoplasm, blood pressure more than 200/120 mmHg and diabetic hemorrhagic retinopathy (18).

Thrombolytic therapy should be reserved for patients with prosthetic valve thrombosis and NYHA class lV, a low-out-put state or any patients in whom operation carries an unacceptable risk, or for small thrombi of less than 5 mm size (19). However, some do not agree with the policy of carrying out thrombolysis in patients hemodynamically too unstable to undergo operation (9, 18, 20). They suggest that thrombolysis should only be used in patients without signs of cardiogenic shock. Patients with contraindications to thrombolytic therapy or those in low-output states should undergo emergency operations (9). Thrombolytic therapy is also emerging as a suitable alternative to reoperation in children with prosthetic valve occlusion.

The most common etiology of obstructive prosthetic valve thrombosis is inadequate anticoagulation, as seen in our series. Surgery is often required, in particular due to large thrombi and the frequent coexistence of pannus.

Thrombolysis in tilting disc valves is reserved only for nonobstructive thrombosis, because obstructive thrombosis in this valve model is generally sustained by pannus (21). On the other hand, bileaflet valves are more prone to primary thrombosis than fibrous tissue overgrowth and sometimes the obstruction affects only one leaflet. Therefore thrombolysis can be considered also when a reduced leaflet excursion is noted (21).

Fibrinolytic activity should be monitored every 6 hours by determining the fibrinogen concentration and fibrinogen breakdown products (7). After successful thrombolysis, heparin infusion is started and activated partial thromboplastin time is maintained at twofold baseline values (22).

A major disadvantage of thrombolytic therapy is the relatively high incidence of recurrent thrombosis during follow-up. Recurrent thrombosis was observed in 20% after thrombolysis as compared with 3% after valve rereplacement and 8% after valve thrombectomy (22).

Thrombosis of a prosthetic heart valve generally leads to progressive heart failure and ultimately, if untreated, to death (23). Traditionall therapy for this condition is emergency thrombectomy, with valve re-replacement as needed. When patients are taken to the operating room, valve thrombectomy is attempted first. However, there are times when thrombectomy is not feasible and valve rereplacement is required. Most commonly, this results from organization and fibrosis of the thrombotic material or when the thrombus is located on the ventricular side of the valve and cannot be extracted without removing the prosthesis (9). We preferred valve re-replacement rather than valve thrombectomy, in all patients except one patient with fresh thrombi.

A seasonable variation has been noted to prosthetic heart valve thrombosis with an increased frequency in the winter months, coinciding with an increased plasma fibrinogen and viscosity (24), as seen in our series.

In conclusion, the principal risk factors for prosthetic valve thrombosis are inadequate anticoagulation or fluctuation in anticoagulation levels. Prompt diagnosis and treatment of prosthetic valve obstruction is important. Its treatment is either surgical or with thrombolytics.

Thrombolytic therapy is an alternative to reoperation.

Although both treatment methods are effective, the thrombolytic therapy is gaining favor (23). However, thrombolytic therapy harbors not only the risk of embolism but also the probability of incomplete success such as pannus formation and vegetations (10). Surgery is often required due to large thrombi and a presence of pannus formation, as seen in our series.

References

1. Edmunds LH. Thrombotic and bleeding complications of prosthetic heart valves. Ann Thorac Surg. 1987;44:430-445.
2. Deviri E, Sareli P, Wisenbaugh T, et al. Obstruction of mechanical valve prostheses: clinical aspects and surgical management. J. Am Coll Cardiol 1991;17:646-650.
3. Edmunds LH, Clark RE, Cohn LH, et al. Guidelines for reporting morbidity and mortality after cardiac valvular operations. J Thorac Cardiovasc Surg. 1996;112:708-711.
4. Vongpatanasin W, Hillis LD, Lange RA, et al. Prosthetic heart valves. N Engl J Med 1996;33:407-416.
5. Vitale N, Renzulli A, Cerasuolo F, et al. Prosthetic valve obstruction: Thrombolysis versus operation. Ann Thorac Surg 1994;57:365-370.
6. Kirklin J, Barrat Boyes B. Cardiac Surgery. New York: Churchill Livingstone; 1993.
7. Horstkotte D, Burckhardt D. Prosthetic valve thrombosis. J Heart Valve Dis 1995;4:141-153.
8. Silber H, Khan SS, Matloff JM, et al. The St. Jude valve. Thrombolysis as the first line of therapy for cardiac valve thrombosis. Circulation 1993;87:30-37.
9. Kogon B, Kirshbom PH, Forbess JM, et al. Thrombolytic therapy for prosthetic valve thrombosis in children: Two case reports and review of the litareture. J Thorac Cardiovasc Surg. 2004;127:1519-1522.
10. Bollag L, Jost CHA, Vogt PR, et al. Symptomatic mechanical heart valve thrombosis: high morbidity and mortality despite successful treatment options. Swiss Med WKLY. 2001;131:109-116.
11. Roudaut R, Roques X, Lafitte S, et al. Surgery for prosthetic valve obstruction. A single center study of 136 patients. Eur J Cardio-Thorac Surg. 2003;24:868-872.
12. Dürrleman N, Pelerin M, Bouchard D, et al. Prosthetic valve thrombosis: Twenty-year experience at the Montreal Heart Institute. J Thorac Cardiovasc Surg 2004;127:1388-1392.
13. Rizzoli G, Guglielmi C, Toscano G, et al. Reoperations for acute prosthetic thrombosis and pannus: an assessment of rates, relationship and risk. Eur J Cardio-Thorac Surg 1999;16:74-80.
14. Czer LS, Weis M, Bateman TM, et al. Fibrinolytic therapy of St. Jude valve thrombosis under guidance of digital cinefluoroscopy. J Am Coll Cardiol 1985;5:1244-1249.
15. Gueret P, Vignon P, Fournier P, et al. Transesophageal echocardiography for the diagnosis and management of nonobstructive thrombosis of mechanical mitral valve prosthesis. Circulation. 1995;91:103-110.
16. Graver LM, Gelber PM, Tyras DH, et al. The risks and benefits of thrombolytic therapy in acute aortic and mitral prosthesis valve dysfunction: report of a case and review of the literature. Ann Thorac Surg 1988;46:85-88.
17. Kurzrok S, singh AK, Most AS, et al. Thrombolytic therapy for prosthetic cardiac valve thrombosis. J Am Coll Cardiol 1987;9:592-598.
18. Lengyel M, Fuster V, Keltai M, et al. Guidelines for management of left-sided prosthetic valve thombosis: a role for thrombolytic therapy. Consensus Conference on Prosthetic Valve Thrombosis. J Am Coll Cardiol. 1997;30:1521-1526.
19. Shapira Y, Herz I, Vaturini M, et al. Thrombolysis is an effective and safe therapy in stuck bileaflet mitral valves in the absence of high-risk thrombi. J Am Coll Cardiol 200;35:1874-1880.
20. Vitale N, Renzulli A, Schinosa L, et al. Prosthetic valve obstruction :Thrombolysis versus operation (updated in 2000). Ann Thorac Surg 2000 ;70 :2182-2183.
21. Vitale N, Renzulli A, Agozzino A, et al. Obstruction of mechanical mitral prostheses: analysis of pathologic findings. Ann Thorac Surg 1997;63:1101-1106.
22. Hering D, Piper C and Horstkotte D. Management of prosthetic valve thrombosis. Eur Heart J 2001;3 (supplement Q);Q22-Q26.
23. Dieter RS, Dieter RA, Dieter RA, et al. Prosthetic heart valve thrombosis: An overview. Wisconsin Med J 2002;101:67-69.
24. Horstkotte D, Piper C, Schulte HD. Thrombosis of prosthetic heart valves: diagnosis and management. Zeitschrift fur Kardiologie. 1998;87 suppl 4:20-32.