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Original Research Article

The Dilemma of Management of Prosthetic Mitral Valve Thrombosis: All Need Surgery?

Haiyong Wang[1], Tianci Qian[1], Zhenzong Du[2], Jianfei Song[2], Fugui Ruan[1], Xiaolin Sun[1], Jiangbin Sun[1]
[1]Department of Cardiovascular Surgery, Affiliated Hospital of Guilin Medical University, Guilin 541001, China
[2]Department of Cardiothoracic Surgery, the Second Affiliated Hospital of Guilin Medical University, Guilin 541199, China

***Corresponding author**
Haiyong Wang
Email: docwanghy@gmail.com

Abstract: The objective of this study is to investigate the diagnosis and treatment of prosthetic mitral valve thrombosis complicated with dysfunction, so as to deepen our knowledge on management of mechanical prosthetic valve thrombosis. The clinical data of 7 patients with prosthetic mitral valve thrombosis complicated with dysfunction were retrospectively analyzed, and the relevant literatures were reviewed. Re-operation (mechanical prosthetic valve replacement) was performed in 2 patients. Four patients were gave warfarin which increase INR to 2.5-3.0. One patient died of multi- organ failure and sepsis after intubation due to low cardiac output syndrome. Six patients recovered well; the cardiac function was obviously improved; and there were no early complications. Prosthetic mitral valve thrombosis should be strongly suspected when they have symptoms indicating valvular obstruction. A complication of prosthetic mitral valve thrombosis is not difficult to diagnose, and favourable management is important to save the life of urgent patients.

Keywords: Mechanical prosthetic valve, Surgery, Thrombosis, Treatment

INTRODUCTION

Mechanical prosthetic valve replacement was first introduced in 1960 and many improvements in design and structural properties have increased the hemodynamic performance and durability since then [1]. However, during the last fifty years, prosthetic mitral valve thrombosis has continued to be a potential complication with a high mortality risk because of the thrombogenic potential and need for urgent surgery or anticoagulation therapy. Obstructive prosthetic mitral valve is frequently related to thrombus formation due to inadequate anticoagulation. Prosthetic mitral valve thrombosis has other causes, such as failure of hemodynamic performance [2]. The prosthetic mitral valve thrombosis is also related other factors, including the surface characteristics of the prosthetic valve related with the design and the material, blood turbulence and the properties of the patient's blood due to hypercoagulability and blood flow depending on cardiac output[3]. A lack of cooperation between the cardiac surgeon and patients based on information is the main factor in prosthetic mitral valve thrombosis all over the world.

THE PATIENTS AND METHODS

Between January 2012 and January 2016, 482 patients were operated on in our department for mechanical prosthetic valve replacement. This number includes valve replacements with or without coronary artery bypass, Maze or other procedures. Seven (1.5%) of these patients were readmitted on with the diagnosis of obstructive prosthetic valve due to thrombus. Patients reoperated on for valve insufficiency following prosthetic valve endocarditis with thrombus were excluded. Information about the patients was investigated retrospectively.

RESULTS

Their ages ranged from 32 to 58 years, and there were 5 females and 2 males. Among them, 6 patients were operated on for mitral, 1 for both aortic and mitral valve replacement. The diagnosis was confirmed by transthoracic echocardiography (TTE) in all patients. The time interval between the first operations and the read mission ranged 1 to 40 months (Table 1). Two patients had cerebrovascular event before they were admitted to our hospital.

Two patients were operated on under emergency conditions, 4 patients and their relatives refused the operation and couldn't accept the adverse effects of thrombolytic drugs (urokinase and streptokinase). So warfarin was used in these four patients. INR was monitored every day. The ideal INR was 2.5-3.0. In two operative cases, median sternotomy was performed using an oscillating saw. The ascending

aorta was cannulated. Venous cannulation was performed bicavally. A vent cannula was inserted into the right upper pulmonary vein for left ventricular venting. Antegrade blood cardioplegia was used for myocardial protection; 30.0 ^{o}C systemic hypothermy was maintained. The mitral valve was exposed following the right atriotomy and the transseptal approach was preferred due to severe adhesions. Thrombosis was cleared. The artificial heart valve was replaced by a new one.

Table 1: The patients' data

	Age	Sex	Surgery	Interval time (month)	INR	Mitral valve opening area(cm^2)	Cardiac Function (NYHA, New York Heart Association)
Case 1	32	Female	MVR	13	1.3	0.8	III
Case 2	36	Male	DVR	18	1.6	1.1	II
Case 3	58	Female	MVR+TVP	40	1.7	1.2	II
Case 4	42	Female	MVR+TVP	1	1.2	0.9	III
Case 5	46	Female	MVR	26	1.7	1.3	IV
Case 6	51	Male	MVR+TVP	21	1.3	1.1	II
Case 7	56	Female	MVR+Maze	30	1.8	1.0	II

MVR: mitral valve replacement; DVR: double valve replacement; TVP: tricuspid valve plasty

Table 2: The patients' treatment and outcome

	treatment	Mitral valve opening area(cm^2) at discharge	Cardiac Function (NYHA, New York Heart Association)	outcome
Case 1	Surgery	2.1	I	Good recovery
Case 2	Anticoagulant therapy	2.0	I	Hemiplegia sequelae
Case 3	Anticoagulant therapy	1.8	I	Good recovery
Case 4	Surgery	2.3	I	Good recovery
Case 5	Rescue			Died
Case 6	Anticoagulant therapy	1.9	I	Hemiplegia sequelae
Case 7	Anticoagulant therapy	2.3	I	Good recovery

Among them, one patient was died at the first day of hospitalization. The cause of death was multi-organ failure and sepsis after intubation due to low cardiac output syndrome. All thrombus was located on the atrial side of the prosthesis. Four patients recovered fully. The follow-up echocardiograms showed preservation of left ventricular function(Table 2). The regular INR were monitor after the discharge. They are currently on anticoagulation and in good general condition.

DISCUSSION

Patients with bioprosthetic mitral valve replacement have excellent long-term hemodynamics. But prosthetic valve thrombosis is one of the serious complications postoperatively, with rates between 1–2% per patient-year depending on the type of anticoagulation used and compliance to the therapy[4]. The most common cause of the occurrence of a thrombosis is an inadequate anticoagulation therapy. Some precipitating factors of the thrombotic process include acting as surgery technique, left ventricular dysfunction, low cardiac output, atrial fibrillation, large LA size, valve type, and localization of the prosthetic valve [5].

Currently available tools for the diagnosis of prosthetic mitral valve thrombosis include TTE, transesophageal echocardiography (TEE) and fluoroscopy. In patients with a high clinical suspicion of prosthetic mitral valve thrombosis, TEE should be considered. TEE should play a central role in every step of the management of patients with PVT, including the initial diagnosis and evaluating the therapy and outcome. TTE is the first line choice that would provide clues for the assessment of mitral valve hemodynamics (immobility of leaflet, high valve gradients), but its utility is limited by its dependence on optimal windows and artifact from metallic valves. However, in the current condition, we used only transthoracic echocardiography for the clinical decision making of the patient. But, during the operation, we performed the TEE as a routine method, which was recommended as many cardiac surgeons [6-8].

Diagnosis is based on echocardiography findings, including reduced or absent leaflet mobility, elevated transprosthetic gradients, decreased effective orifice area and thrombus visualization. In some cases, computed tomography (CT) may be helpful in differentiating thrombosis from pannus. In the future, 3-dimensional echocardiography, CT, and magnetic resonance imaging may have a role in diagnosis of

prosthetic valve thrombosis as well as differentiating this from pannus.

There are no enough data from randomized controlled trials on approach to management of prosthetic heart valve thrombosis. In the current guidelines, there is no consensus on the treatment of patients with prosthetic mitral valve thrombosis. There are two methods for prosthetic mitral valve thrombosis —medical therapy and surgical intervention. Because the guidelines are based on limited data from observational studies, most of these small studies do not provide reasons for the choice of thrombolysis or of surgery as initial therapy.

Thrombus is a condition stimulated by thrombocyte activation and factors such as the adequacy of anticoagulation, cardiac rhythms and blood flow characteristics [9]. Thrombus on the mechanical valve may often lead to congestive heart failure. Obstructive prosthetic valve due to thrombus is related mainly to the surface characteristics of the prosthetic valve and irregular blood flow patterns arising around the prosthetic mitral valves.

Although limited by quality of primary studies, current provided evidence that suggests an important role for thrombolysis in patients with prosthetic mitral valve thrombosis [10]. Several therapeutic modalities can be considered: heparin treatment, fibrinolysis or optimisation of anticoagulant and antiplatelet therapy. Fibrinolysis can be attempted as the first-line therapy in some valve thrombosis. The fibrinolytic agents used for treatment of prosthetic valve thrombosis are urokinase, streptokinase, and recombinant tissue plasminogen activator (alteplase) [11]. In patients with left-sided valve thrombosis and recent onset of symptoms (less than 2 weeks), NYHA class I/II and smaller thrombus ($\leq$0.8 cm^2), fibrinolysis can be attempted if initial intravenous heparin therapy fails to resolve thrombosis (class IIa). Surgery can be reserved for those in whom thrombolysis is ineffective.

A smaller amount of thrombus at the hinges of a mechanical valve can result in thrombosis of the mechanical valve with obvious symptoms. This forms the basis for use of thrombolytic agents in patients with prosthetic mitral valve with a lower thrombus burden. However, thrombolysis in patients who are very symptomatic (NYHA class III/IV) may delay the timing of surgical intervention and lead to a higher mortality. The waiting time for operation after thrombolysis is 24 hours after discontinuation of the fibrinolytic infusion[12]. In fact, it was also a common practice to leave thrombolysis as an alternative to patients too ill to be operated. Therefore, they could have died because of their previously serious state and not because of the treatment choice. Recent data have shown that thrombolysis is superior to surgery, even in the most critical patients with prosthetic mitral valve thrombosis [13].

Although guidelines have recommended surgery for prosthetic mitral valve thrombosis[14], Özkan reported that low dose (25 mg) and slow infusion (6 h) of recombinant tissue plasminogen activator (t-PA) are very safe and are associated with a very high success in this regard [15]. In their study, repeated low-doses and slow infusions of alteplase regimen under the guidance of serial TEE was superior to faster infusion thrombolytic therapy protocols. Rapid thrombolysis should only be reserved for certain circumstances, including critically ill patients with prosthetic valve thrombosis or those with stroke [13] or acute myocardial infarction. The rapid infusion of t-PA with bolus dose and concomitant UFH jeopardizes prosthetic valve thrombosis patients who may suffer risks of hazardous consequences (death, embolism, hemorrhage).The clinicians should avoid the routine use of such a regimen.

When the diagnosis of stuck leaflet occurs, thrombolysis should be suspicions as an attempt to assure the reason of abnormal leaflet mobility [16], in spite of the fact that only in one of our patient's thrombus was the probable mechanism and in another one thrombolysis was ineffective. If this treatment does not succeed, we do not recommend rushing into surgery if the patient is in NYHA class I/II. By taking into consideration the risk of reoperations and the low probability of critic valve occlusion or systemic embolism in the absence of thrombus or strands on echocardiography. The possibility of spontaneous recovery of leaflet mobility, as happened in the other 4 patients, strengthens our point of view. The question to be answered is how long should we wait? In our two operative patients, we performed routine intraoperative TEE. Now we agree the opinion of most of the experts that recommend routine intraoperative TEE in all patients submitted to mitral valve surgery [17].

Previously available evidence favored surgical treatment for patients with left-sided valve thrombosis, especially if patient is highly symptomatic (NYHA class III/IV) or patients who is highly symptomatic unless patient is unstable for the operation or if surgery is unavailable or patient cannot be transferred to a heart center [11]. American College of Cardiology guidelines recommend emergent surgery in all patients with thrombosis left sided prosthetic heart valve with NYHA class III/IV symptoms (class I recommendation). Also, urgent surgery is a reasonable alternative in patients with left-sided prosthetic mitral valve thrombosis with a higher thrombus burden (›0.8 cm^2) [4]. In a systematic review of 662 patients with prosthetic mitral valve thrombosis from 13 studies who were treated surgically, 91% had surgery as the initial therapy, whereas 9% had surgery after failed thrombolysis. Of these patients, 81% were in NYHA class III/IV and 9% in NYHA

class I/II. Complete success was achieved in all. The incidence of embolic complications was 6% and recurrent thrombosis occurred in 6% of patients. The mortality with surgery was 15%, which may be partly due to the sicker population of patients who underwent surgery. Our patient underwent successful bioprosthetic mitral valve replacement in view that was demonstrated on TEE.

In a meta-analysis of 2,239 patients, compared surgery with thrombolytic therapy for the treatment of prosthetic mitral valve thrombosis, there were 27 studies in the surgery cohort (1,132 patients) and 26 studies or study arms evaluating cohorts of patients that received thrombolytic therapy (1,107 patients). There was a highly significant difference in mortality between the two groups: surgery and thrombolysis group was 18.1%, 6.6%, respectively. Surgical mortality appeared to increase with NYHA class [18]. Even considering the possibility of a multicenter study, it would be very difficult to achieve such a sample size. We still need a large prospective observational multicenter registry.

We believe the best way to prevent prosthetic valve thrombosis is to keep the INR within the ideal range and avoid periods of inadequate anticoagulation. Careful follow up for patients of valve replacement by a team including a cardiologist, a cardiac surgeon and a community physician also plays an important role.

CONCLUSION

Thrombosis of mechanical prosthetic mitral valves is associated with high morbidity and mortality and treatment options available can also be associated with serious complications. Careful anticoagulant medication should be maintained and echocardiographic surveillance should be considered for these patients. Thus, suspicion of prosthetic mitral valve thrombosis is an urgent clinical condition, which warrants prompt diagnostic assessment. Therapeutic strategy will be influenced by the presence or absence of valvular obstruction and by the patients' clinical status.

AUTHOR'S CONTRIBUTION

Haiyong Wang and Jiangbin Sun wrote the paper. Zhenzong Du, Jianfei Song, FuguiRuan, Tianci Qian, Donghua Pan and Xiaolin Sun supervised the composition of the paper. All authors read and approved the final paper.

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REFERENCES

1. Pibarot P, Dumesnil JG; Prosthetic heart valves: selection of the optimal prosthesis and long-term management. Circulation., 2009; 119(7):1034-48.
2. Deviri E, Sareli P, Wisenbaugh T, Cronje SL; Obstruction of mechanical heart valve prostheses: clinical aspects and surgical management. J Am CollCardiol., 1991; 17(3): 646-50
3. Roudaut R, Serri K, Lafitte S; Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart. 2007; 93(1): 137–142.
4. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP; 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; American College of Cardiology/American Heart Association Task Force on Practice Guidelines.. 2014 AHA/ACC Guideline for the Management of Patients WithValvular Heart Disease: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol., 2014; 63:e57–e185.
5. Moreno-Cabral RJ, McNamara JJ, Mamiya RT, Brainard SC, Chung GK; Acute thrombotic obstruction with Björk-Shiley valves: diagnostic and surgical considerations. J Thorac Cardiovasc Surg., 1978; 75(3):321-30.
6. Masiello P, Mastrogiovanni G, Leone R, Del Negro G, Iesu S, Triumbari F, Di Bennedeto G; One leaflet immobilization after mitral valve replacement with a bileaflet prosthesis. J Heart Valve Dis., 1996; 5(1):114-6.
7. Kumano H, Suehiro S, Shibata T, Hattori K, Kinoshita H; Stuck valve leaflet detected by intraoperativetransesophageal echocardiography. Ann Thorac Surg., 1999; 67(5):1484-5.
8. Fujii H, Suehiro S, Shibata T, Hattori K, Watanabe H, Yoshikawa J; Value of intraoperative transesophageal echocardiography in preventing serious complications during valvular surgery. A report of four cases. J Heart Valve Dis., 2002; 11(1):135-8.
9. Martinell J, Jimenez A, Rabago G, Artiz V, Fraile J, Farre J; Mechanical cardiac valve thrombosis. Is thrombectomy justified? Circulation, 1991; 84(5 Suppl):III70-5.
10. Jeffrey RR; Clots and cardiac valve prostheses. J ThrombHaemost., 2014; 12(8):1216-7.
11. Lengyel M, Horstkotte D, Völler H, Mistiaen WP; Working Group Infection, Thrombosis, Embolism and Bleeding of the Society for Heart Valve Disease. Recommendations for the management of prosthetic valve thrombosis. J Heart Valve Dis., 2005; 14(5): 567-75.
12. Bonou M, Lampropoulos K, Barbetseas J; Prosthetic heart valve obstruction: thrombolysis or surgical treatment? Eur Heart J Acute Cardiovasc Care, 2012 1(2): 122–127.
13. Özkan M, Gündüz S, Biteker M, Astarcioglu MA, Çevik C, Kaynak E, Yıldız M, Oğuz E, Aykan AÇ, Ertürk E, Karavelioğlu Y, Gökdeniz T, Kaya H, Gürsoy OM, Çakal B, Karakoyun S, Duran N, Özdemir N; Comparison of different TEE-guided thrombolytic regimens for prosthetic valve

thrombosis: The TROIA trial. JACC Cardiovasc Imaging, 2013; 6(2):206–216

14. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP; 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; ACC/AHA Task Force Members. AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation, 2014; 129(23):e521-643.
15. Özkan M, Gürsoy OM, Atasoy B, Uslu Z; Management of acute ischemic stroke occurred during thrombolytic treatment of a patient with prosthetic mitral valve thrombosis: continuing thrombolysis on top of thrombolysis. Anatol J Cardiol., 2012; 12: 689-90.
16. Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davis JL, Douglas PS, Faxon DP, Gillam LD, Kimball TR, Kussmaul WG, Pearlman AS, Philbrick JT, Rakowski H, Thys DM; ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography--summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography. J Am CollCardiol., 2003; 42(5):954-70.
17. Shapira Y, Herz I, Vaturi M, Porter A, Adler Y, Birnbaum Y, Strasberg B, Sclarovsky S, Sagie A; Thrombolysis is an effective and safe therapy in stuck bileaflet mitral valves in the absence of high-risk thrombi. J Am Coll Cardiol., 2000; 35(7):1874-80.
18. Castilho FM, De Sousa MR, Mendonça AL, Ribeiro AL, Cáceres-Lóriga FM; Thrombolytic therapy or surgery for valve prosthesis thrombosis: systematic review and meta-analysis. J Thromb Haemost., 2014; 12(8):1218-28.