FIBRINOLYTIC TREATMENT OF PROSTHETIC VALVE THROMBOSIS: A SINGLE-CENTER STUDY OF 72 CASES

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ABSTRACT

Objectives: *To analyze the results of fibrinolysis in a large single-center group of patients with prosthetic heart valve thrombosis.*

Methodology: *This descriptive study was conducted at Rehman Medical Institute Peshawar, Pakistan. A total of 72 consecutive patients presenting with Prosthetic heart valve thrombosis received Fibrinolysis treatment between 2003 and 2008. The diagnosis of Prosthetic heart valve thrombosis was established mainly by echocardiography. The fibrinolytic agent used was streptokinase. The outcome of Fibrinolysis treatment was assessed through hemodynamic parameters via echocardiography and also on clinical grounds.*

Results: *Complete success of hemodynamic abnormalities was noted in 61 of 72 patients, partial resolution in 6/72 patients, and failure in 5/72 patients after one or more consecutive fibrinolytic regimens. Only streptokinase was used as a fibrinolytic as previous studies have clearly established its supremacy. One death was reported. Major bleed, requiring transfusion occurred in just one patient. Three documented Cerebrovascular accidents with two embolic events and one cerebral haemorrhage occurred during Fibrinolysis treatment.*

Conclusions: *These results demonstrate that Fibrinolysis treatment is effective in Prosthetic heart valve thrombosis, regardless of prosthetic site involved. It also failed to show any significant difference between outcomes of success in different New York Heart Association classes and thus supports FT in New York Heart Association classes I and II as well.*

Key Words: *Fibrinolysis treatment(FT), New York Heart Association(NYHA), Cerebrovascular accident(CVA), Prosthetic heart valve thrombosis(PHVT), Streptokinase(SK), Transoesophageal echocardiography(TOE), Transthoracic echocardiography(TTE).*

INTRODUCTION

Prosthetic heart valve thrombosis (PHVT) is a rare but a major complication associated with high mortality, requiring urgent management. The incidence of such complications has been reported in the range of 0.03% to 4.3% patient-years, which in turn is said to be dependant on the thrombocity of the prosthetic valve, the location, and the level of anticoagulation[1-3]. Choice of treatment for such patients remains controversial, although surgery is usually preferred[4].

The proethetic valve thrombosis may be suspected in a patient who approaches, with shortness of breath especially with back ground of poor compliance with warfarin. Investigations such as Echocardiography (transthoracic or transoesophageal), will confirm the diagnosis, based on increased gradient across the prosthetic valve, or valve area calculation, or by visualization of thrombus burden.

Fibrinolytics as treatment option has been discussed since 1971[5-9]. One reason for that is the risk of surgery in such cases. FT has been suggested by many as the first line of therapy for PHVT. The results have been encouraging. However, there remains a real risk of thromboembolism[8,9].

Our studied population mostly comprised of non affording patients with prosthetic heart valve thrombosis, who due to lack of financial resources have no option but to undergo fibrinolytic therapy. This study was thus designed to analyze the result of fibrinolysis in a large single center group of patients with prosthetic heart valve thrombosis.

By doing this single centre study, we aimed to look further deep into the risks involved in the FT of PHVT and also to define further if there is any real difference in the outcome of different NYHA classes.

METHODOLOGY

A total of 72 patients were included in the study that had prosthetic heart valve thrombosis, from 2003 to 2008. The data was collected from the hospital records. All the patients of prosthethetic valve thrombosis which had Fibrinlytic therapy were included in the study. Any patient of prosthethic valve thrombosis, who had any other form of management apart from fibrinolytic therapy (re do surgery, conservative management with heparin and warfarin) were excluded from the study.

Doppler transthoracic echocardiography (TTE) was performed in all cases (n=72), augmented by Transoesphageal echocardiography (TEE) in some cases (n=16) who were stable enough to tolerate the procedure.

Streptokinase was used as a fibrinolytic agent in all the patients, with a loading dose of 500,000 IU in 30 min followed by 100,000 IU per hour for 10 h.

Success of the treatment was judged by taking into account the clinical data and imaging through echocardiography and defined it as,

1. Complete success: Normalization of transprosthetic gradient and valve area, with normal mobility of leaflet using echocardiographic data.
2. Partial success: Significant clinical improvement without complete normalization of transprosthetic gradient.
3. Unsuccessful: No clinical improvement, or may be associated with death or complications.

There were 4 cases with partial or complete resolution of the thrombosis of prosthetic valves but were labeled as unsuccessful because of the complications encountered.

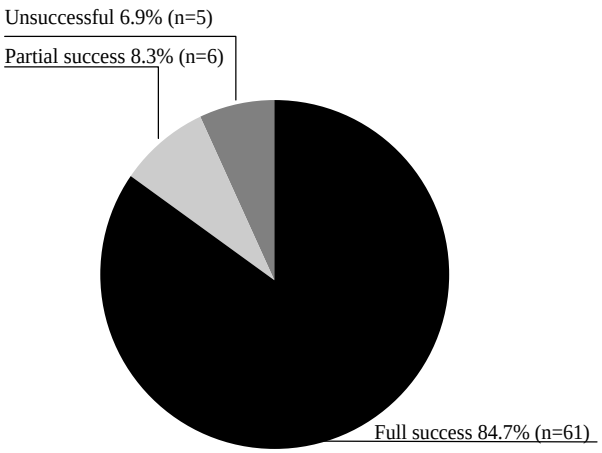
The success of FT for resolution at different prosthetic sites was compared using the Pearson chi-squared test.

RESULTS

There were 26 men (36.1%) and 46 women (63.9%) in the group. The mean age was 53 ± 11 years (range 32 to 76 years). The mean time since prosthetic valve was implanted was 5.9 ± 4.4 years (range 6 months to 17 years).

Complete success with one or more consecutive fibrinolytic regimens was achieved in 61 out of 72 cases (84.7%). Valve site wise it was 20/27(74.07%) in aortic valve, 41/45 (91.1%) in mitral valve prosthesis. The difference in the success of the two valves was not found to be statistically significant (p=0.051). Complete success was obtained in 45 patients (73.7%) with a single fibrinolytic agent, and in 16 other patients using a second fibrinolytic agent consecutively. Partial success was obtained in 6 patients (8.3%). Failure was noted in 5 patients (6.9%) (Figure 1).

Figure 1: Success rate



There was no significant difference in efficacy of FT between the Aortic and Mitral valve patients. (20/27 [74%] vs. 41/45 [91.1%], p=0.051) (Table 1). Note that all patients had tilting disc prosthetic valves.

Fibrinolytic therapy improved the clinical status in all functional classes, and failed to show any statistical difference. NYHA functional classes I and II (13/14. 92%) as compared to patients in NYHA functional classes III (17/22, 77%) and IV (31/36, 86.1%), (p=0.65).

Complications were observed in 4 patients (5.5%). Major bleeding occurred in one patient (1.3%), three cerebrovascular events with one brain hemorrhage [(1.3%) one death] and two embolic infarctions (2.8%).

Death occurred in 1 patient (1.3%), secondary to brain haemorrhage, which resulted in

failure to continue the FT, with partial success as far as the haemodynamic across the valve was concerned.

No relation was found between the number of FT regimens and the incidence of complications (thromboembolism, hemorrhage, death).

The incidence of complications was higher in patients in NYHA functional classes III and IV (2/22, 9% and 1/36, 2.7%) than in patients in NYHA functional classes I and II (0/14), but statistically there was no difference (p 0.34). (Figure 2, 3)

Table 1: Efficacy According to the prosthetic Valve Site

Site	complete success	Partial success	Un-successful	Total	p Value
Mitral Valve	41	1	3	45	.051
Aortic Valve	20	5	2	27	
Total	61	6	5	72	

Figure 2: Relationship of major bleed incidence with NYHA class

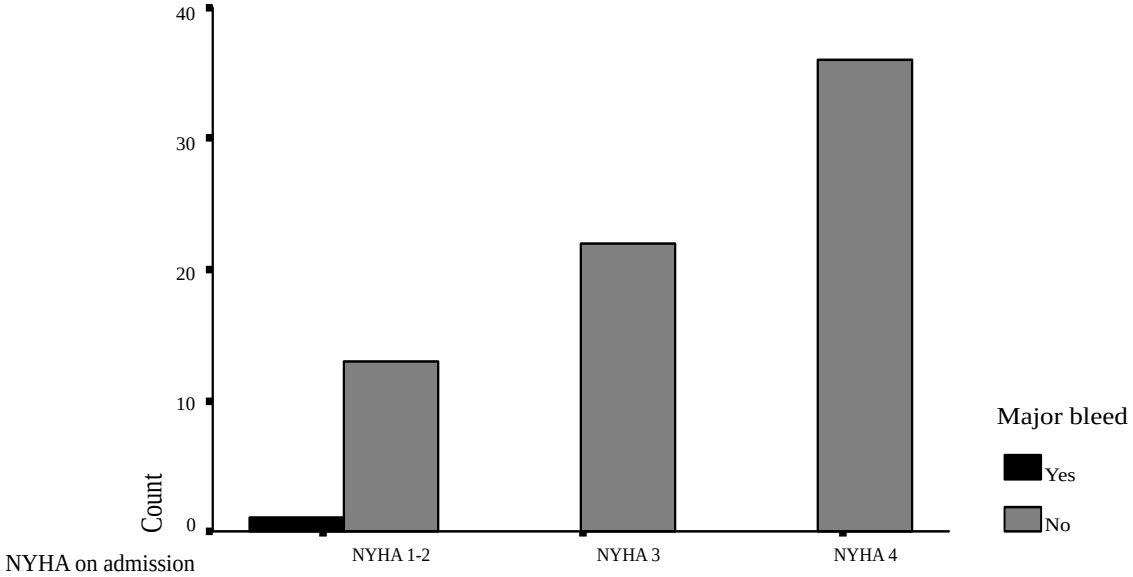
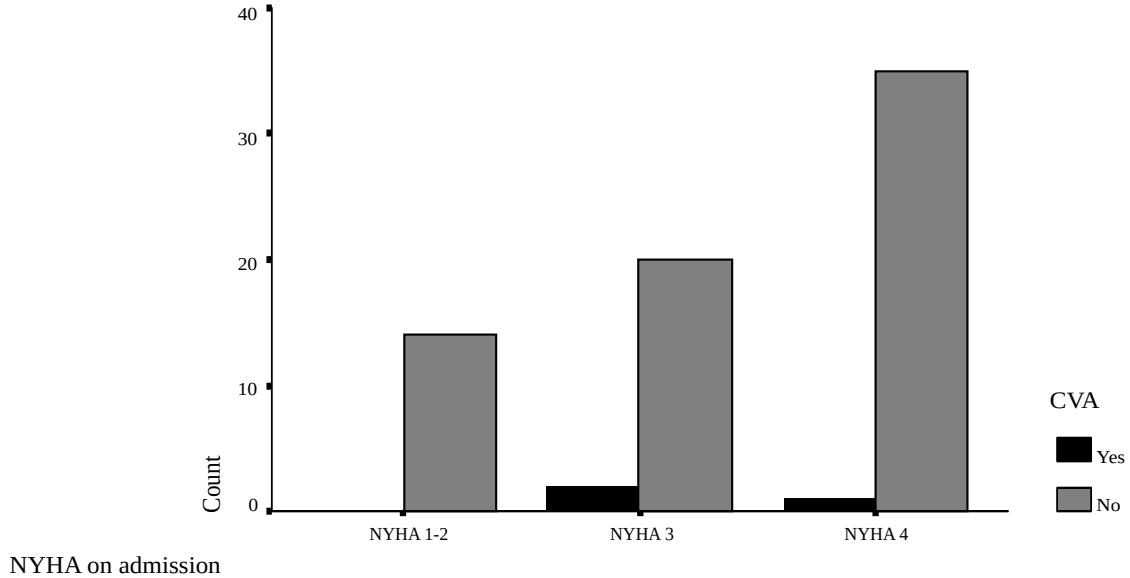


Figure 3: Relationship of CVA with NYHA class.



DISCUSSION

Prosthetic Heart Valve Thrombosis is a serious complication associated with a high mortality. Early diagnosis of obstructive thrombosis is very important and can be life saving.

We report a single-center study of 72 cases of PHVT, over a period of five years, who were treated with fibrinolysis. The efficacy of FT was assessed by using already known hemodynamic parameters derived from echocardiography as well as by clinical evaluation. We observed complete resolution of hemodynamic abnormalities in 84.7% of the cases, partial success in 8.3%, and no improvement in 6.9%. Major bleed was observed in 1.3% of the cases, with 3 cases of CVA (4.2%), of which one was cerebral haemorrhage and two were embolic events. Just One patient died (1.3%), because of the cerebral haemorrhage.

In 1997, a review of Lengyel et al[10] of 200 published reports of prosthetic heart valve thrombolysis has shown 82% initial success rate, with thromboembolism rate of 12%, and a mortality of 10%. This lead to the inference that FT of PHVT should be the way forward for the high risk patients, in whom surgical option is too risky. On the other hand NYHA class I and II have reasonably less surgical risk and thus outweighed by the thromboembolism risk of 12% to 17%.

However, the series of Roudaut et al[11] demonstrated that embolic events following medical therapy are mostly of a benign nature. Thus, reconsideration is advised on the recommendations of Lengyel et al[10].

We, in our setup are forced to employ conservative non invasive strategy, mainly because of the financial restraints. Under the circumstances, where there is a lot of illiteracy, and lack of patient education, many cases of prosthetic valve replacements, have been reported, who come back with thrombosis. In almost hundred percent cases, we have no option but to thrombolyse, whatever the NYHA class or thrombus burden be.

Our study is encouraging, where it has shown very low complication rate and mortality, unlike the previous review by Lengyel and Vandor[12] from a compilation of 10 studies each from 16 to 110 patients (515 cases). The success rate was 84%, mortality 5%, major bleeding 3%, systemic embolism 9%. Similarly another study of Gupta et al[13], of 110 consecutive patients showed a complete success in 81.8%, a partial response in 10%, and failure rate of 8.2%. There were 21 (19.1%) embolic episodes during therapy, including 6 strokes.

Various fibrinolytic protocols have been used[7,9,10,14-19]. In our study Streptokinase was the only agent used, following a simple and easy to follow regimen with a loading dose 500,000 IU in 30 min followed by 100,000 IU per hour for 10 h. Use of SK as the only agent was based on the previous study[11].

There are not many studies which have compared Thrombolysis and surgical treatment. In one such study[20], rtPA treatment was found successful without complications in eight cases of partial or non obstructive thrombosis with (NYHA functional class II to III, and on the other hand one death among 20 surgical patients in NYHA functional class III to IV was reported. The opinion of the authors was that thrombolysis was an appropriate treatment in selected cases.

CONCLUSION

This study demonstrates that, thrombolysis is effective in PHVT. It also failed to show any statistically significant difference between outcomes in different NYHA classes.

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