

Absolute Eosinophil Count with Prosthetic Heart Valve Thrombosis

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Abstract

Background: Prosthetic heart valve thrombosis (PHVT) is a very rare complication after the replacement of a damaged valve by a mechanical valve. It contributes significantly to the late morbidity and mortality after heart valve surgery. The incidence varies across the world depending on the type of mechanical heart valve and its position. A little study was done on the absolute eosinophil count in prosthetic heart valve thrombosis. So in the present study, we are evaluating the risk factors, clinical profile and levels of absolute eosinophil count in prosthetic heart valve thrombosis cases.

Methodology: A prospective observational study was carried out at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru from November 2015-December 2017. A total of 73 patients with PHVT were studied during this period. Data was collected by detailed clinical and treatment profiles and analyzed using SPSS V 23 software and results were represented in tables, figures, percentages, and graphs under descriptive statistics.

Results: Mean age of study participants was 39.7±11.8 years. The percentage of females was higher than males. The main predisposing factor for valve replacement was found to be Rheumatic heart disease (94.5%) and degenerative aortic valve disease was found only in 5.5% of the cases. Mitral valve position (60.3%) was most commonly involved in PVT. After replacement of the valve, 32.9% of patients presented the PHVT after 5 years and 9.6% within 6 months of surgery. Out of 73 patients, 50.7% of cases presented with NYHA class II symptoms, and 69.9% had INR in the non-therapeutic range. Atrial fibrillation was observed in 23.3% of cases atrial tachycardia in 5.5% of cases. Recurrent PVT was observed in 20.5% of cases. The absolute eosinophil count (AEC) was measured in our study 39.7% of cases had elevated levels of AEC.

Conclusion: Prosthetic valve thrombosis is a major cause of morbidity and mortality in cases with heart valve replacement. There is a strong correlation between incidence of PHVT and elevated AEC. Eosinophilia increases the incidence of recurrent PHVT and interferes with events of thrombolysis. Hence it is necessary to check AEC for all cases of PVT for better assessment and management.

Keywords: Prosthetic heart valve thrombosis (PHVT), Absolute eosinophil count (AEC)

Introduction

The heart valve keeps the blood flowing in the correct direction through the heart. Rheumatic

heart disease and degenerative aortic valve disease are major causes of valve damage. Damaged heart valves will be replaced by biological (pig, cow, or human heart tissue) or mechanical (man-made) valves. After 10 -15 years, the biological valve is to be replaced by a new one whereas mechanical valves don't have to be replaced, however anticoagulants should be taken throughout the life to prevent thrombosis in case of mechanical valve procedure. Inadequate anticoagulation or cessation of anticoagulation leads to prosthetic heart valve thrombosis (PHVT)^[1]. Prosthetic heart valve thrombosis (PHVT/PVT) is defined as 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^[2]. Even though it is very rare, it is a serious complication after a heart valve replacement procedure. The incidence of Prosthetic heart valve thrombosis will vary across countries. Saksena *et al.* reported that the annual rate of valve replacement was found to be 27,500-3, 70,000 of which 45% are bio prosthetic heart valves and 55% are mechanical heart valves (MHVs) worldwide. Globally, prosthetic valve implantations are increasing at a rate of 5-7% per year^[3]. Hermans *et al.* reported that the incidence of prosthetic heart valve thrombosis was 0.6% to 6% in the left-sided valves and up to 20% in tricuspid valves^[4]. According to Karthikeyan *et al.*, the incidence of PHVT escalates even up to 10% per patient-year in developing countries, which will contribute significantly to the late morbidity and mortality after heart valve surgery^[5]. Thus for prosthetic heart valve thrombosis, thrombolysis and re-operation (de-clotting/valvular replacement) treatment procedures are widely accepted.

Generally, the absolute eosinophil count will be elevated due to infection, inflammation and clinical conditions in the body. Only limited studies have stated the levels of absolute eosinophil count in PVT. So in the present study, we are evaluating the clinical complications, treatment, outcome and levels of absolute eosinophil count in PVT cases.

Materials and Methods

Study design

It is a prospective observational study conducted at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru for 2 years 10 months from November 2015-December 2017 after obtaining the ethical clearance from the Institutional Ethical Committee. A total of 73 cases with PHVT were recruited for our study. Cases with a history of prosthetic heart valve replacement and symptoms related to prosthetic valve thrombosis admitted to ICU were recruited and the cases with high gradient due to pannus, Infective Endocarditis, Vegetation and Degenerated/ruptured bioprosthetic valve were excluded from the study. Using a pre-tested, semi-structured questionnaire data such as pre-operative clinical data, initial valve procedure, diagnostic features of valve thrombosis and management (before, during and after the treatment) with absolute eosinophil count (AEC) and outcome were recorded after obtaining the Informed consent from the patients and their attendees.

Statistical analysis

Time-bound sampling was done for this study. The data was entered and compiled in a Microsoft Excel sheet. Analysis was done using statistical software SPSS version 23. Descriptive statistics such as frequencies and percentages; mean and standard deviation were calculated.

Result

In the present study, a total of 73 cases with prosthetic valve thrombosis were identified and analyzed. The female (60.3%) cases were more predominant than the male (39.7%) cases.

The mean age of the study population was found to be 38.8 ± 11.8 years and the majority of the cases were in the age group 31-40 years and the least cases were in the < 20 yrs age group (Table 1).

Out of 73 cases, major prosthetic valves affected in the study subject were found to be mitral prosthesis (60.3%) followed by Aortic (19.2%) and 20.5% of cases had double valve replacement (Table 1). In study subjects, the most common type of prosthesis used was - St.JUDE mechanical valve (42.5%) followed by Medtronic ATS (27.4%), TTK Chitra (16.4%), bioprosthetic (1.4%) and others (12.3%)(Table 1).The main predisposing factor for valve replacement was found to be Rheumatic heart disease (94.5%) and degenerative aortic valve disease was found only in 5.5% of the cases. (Table 1).

Nearly 19.2% of patients were poorly compliant with drugs and monitoring of prothrombin time. More patients in economically underprivileged groups had discontinued medications when compared to those who were in a better socioeconomic group. Prothrombin time was altered in 19.2% of the cases whereas drug compliance was found to be good in 80.8% of the cases.

Almost all patients presented with symptoms, however in 2 patients the diagnosis was made on a routine follow-up Echocardiogram. According to the New York Heart Association (NYHA) classification of heart failure, in our study, most of the patients show the NYHA class II (50.7%) and III (37%) symptoms.

After primary valve implantation, majority of cases presented after five years of surgery (32.9%) and 9.6% of patients presented within six months of surgery. After primary surgery, the first time thrombosis was noticed in 79.5% followed by 17.8% with prior history of thrombosis and 2.7% of the cases with two prior episodes of thrombosis in our study (Table 1).

At the presentation of cases, the international normalized ratio (INR) of less than 2 was observed in 69.9% of the cases, followed by INR 2-3 range (19.2%) and INR greater than 3 in 11% of the cases (Table 2). Then mean and standard deviation of the peak and mean gradient levels at presentation were found to be 43.5 ± 28.6 and 27.4 ± 17.6 . Based on ECG findings, atrial fibrillation was noted in 23.3% of cases atrial tachycardia in 5.5% of cases (Table 2). In this study absolute eosinophil count (AEC) was elevated in 39.7% of cases (Table 2).

Table 1: Baseline characteristics

Baseline characteristics	Number (N)	Percentage (%)
Age group (Yrs)		
< 20 years	2	2.7
21-30 years	16	21.9
31-40 years	28	38.4
41-50 years	16	21.9
>50	11	15.1
Gender		
Male	29	39.7
Female	44	60.3
PV Position		
Mitral	44	60.3
Aortic	14	19.2
Double Valve Replacement	15	20.5
Prosthetic Valve type		
St.Jude	31	42.5
Medtronic ATS	20	27.4
TTK Chitra	12	16.4
Bioprosthetic	1	1.4

Others	9	12.3
Predisposing factor		
Rheumatic heart disease	69	94.5
Degenerative aortic valve	4	5.5
Drug Compliance		
Good	59	80.8
Poor	14	19.2
Symptomatic		
Yes	71	97.3
No	2	2.7
New York Heart Association (NYHA) Class		
Asymptomatic	2	2.7
Class I	1	1.4
Class II	37	50.7
Class III	27	37
Class IV	6	8.2
PVT after Surgery		
<6 Months	7	9.6
6M-1 yr	10	13.7
1-2 yrs	11	15.1
2-3 yrs	10	13.7
3-4 yrs	5	6.8
4-5 yrs	6	8.2
> 5 yrs	24	32.9
Recurrent Valve Thrombosis		
Never	58	79.5
Once	13	17.8
Twice	2	2.7

Table 2: Clinical findings

Clinical findings	Number(N)	Percentage (%)
International normalized ratio (INR)		
<2	51	69.9
2 – 3	14	19.2
>3	8	11
Atrial fibrillation		
Atrial fibrillation	17	23.3
Sinus rhythm	52	71.2
Atrialtachycardia	4	5.5
Absolute Eosinophil Count (AEC)		
Normal	44	60.3
High	29	39.7

Discussion

In our study, female cases were more than males and the mean age of the study population was found to be 38.8 ± 11.8 years and the majority of the cases were in the age group 31-40 years which is similar to the studies of Hirachan *et al.*^[6] and Özkan *et al.*^[7]. According to the Hirachan *et al.*^[7] study, in a majority of the cases, the mitral prosthetic valve was affected due to the increased vascular stasis around the mitral valve, which is similar to our study.

We had known that due to rheumatic heart disease the PVT is still on the rise. In our study population, 94.5% of the cases had a predisposing factor for valve replacement as Rheumatic heart disease. The majority of cases presented after five years of surgery (32.9%) and 9.6% of patients presented within six months of surgery. The total recurrence rate of PVT in our study was found to be 20.5%, which is similar to the Khajali *et al.*^[8] this may be due to poor response to treatment as noticed by us, 19.2% of the cases were poorly compliant with the drugs. More patients in economically underprivileged groups had discontinued medications when compared to those who were in a better socioeconomic group^[9]. Therefore proper follow-up is needed to reduce the recurrence rate.

In our study, only 2 patients were admitted without symptoms and most of the cases had symptoms of PVT with NYHA class II-III whereas Karthikeyan *et al.*^[5] study the high percentage of cases were in NYHA functional class I/II (69%). As in Hassouna *et al.*^[10] study, at the time of presentation of cases, the international normalized ratio (INR) of less than 2 was observed in 69.9% and the peak and mean gradient levels were found to be high compared to the normal valve.

At presentation, the elevated levels of absolute eosinophil count (AEC) was found in 39.7% of cases as in Rai *et al.*^[11] and Zhang *et al.* study. Elevated levels of eosinophils may induce cardiovascular damage by intracardiac thrombosis. Products of hypereosinophilia are thrombogenic and lead to prosthetic valve thrombosis. During granulation of eosinophils, the basic protein of eosinophils will release and inhibit the process of activation from thrombomodulin to active protein C and enhance the thrombotic activity. Further, eosinophils are involved in the high maintenance of high tissue factors in the blood and lead to thrombogenesis. Elevated levels of AEC in these cases decrease the thrombolytic activity and the recurrent rate of PVT increases^[12-15]. Thus we should also monitor the AEC before and after treatment which may help in better treatment and management.

Conclusion

Prosthetic valve thrombosis is a major cause of morbidity and mortality in cases with heart valve replacement. There is a strong correlation between incidence of PHVT and elevated AEC. Eosinophilia increases the incidence of recurrent PHVT and interferes with events of thrombolysis. Hence it is necessary to check AEC for all cases of PVT for better assessment and management. Studies with PVT and AEC are limited in the literature. Further larger studies should be carried out to find the association between PVT and AEC.

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