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Thrombocytopenia Following Perceval Suture-Less Aortic Valve Implantation

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Abstract

Objectives: Thrombocytopenia has been reported following implantation of Perceval suture-less aortic valve. However, the time course of thrombocytopenia and platelet recovery is unknown. In addition, the effect of thrombocytopenia on post-operative outcome is unknown. We sought to study this observation and correlate that with short-term outcome. **Methods:** This is a retrospective review of a prospectively collected database over a 3-year period of all isolated aortic valve replacements (70 patients) using bioprosthetic valves (sutured Magna and suture-less Perceval). All preoperative, intraoperative and postoperative variables were collected and analyzed. Platelets count and mean platelet volumes were collected and analyzed in respect to the type of valve used and their time course. **Results:** The cohort consisted of 70 consecutive patients of which 42 underwent Perceval suture-less valve (group Perceval) and 28 underwent bioprosthetic sutured valve (group Magna). There was no difference in platelets count and mean platelet volume at baseline. However, Perceval group had significant drop in platelet count from day 1 to day 3 post-operatively, followed by a gradual increase in platelet count until discharge. Mean platelet volume, however, was not different between the two types of valves. Postoperative outcomes were similar in the two groups with exception of intensive care and a hospital stay which were significantly shorter in Perceval group. **Conclusion:** Thrombocytopenia following Perceval suture-less valve is observed from day 1 postoperatively and it is a transient phenomenon. It does not correlate with worse clinical outcomes postoperatively. Larger studies are needed to elucidate the mechanism and its impact.

Keywords

Thrombocytopenia, Perceval, Aortic Valve Replacement, Suture-Less

1. Introduction

Few studies have observed the high incidence of thrombocytopenia after suture-less Perceval valve implantation [1]-[6]. However, the time course of decline and recovery has not been fully reported previously. In addition, the impact of this thrombocytopenia on clinical outcomes is not clear. As such, we have examined our experience with both suture-less Perceval valve and sutured bioprosthetic valve (Magna) on the platelets count and correlated that with clinical outcomes.

2. Materials and Methods

2.1. Patients

This is a retrospective review of a prospectively collected departmental database (Cardio science Lifeline EMR, Manorama infosultions Pvt. Ltd. India). All patients who underwent isolated bioprosthetic aortic valve replacement (AVR) in the department of cardiac surgery at Chest Diseases hospital in Kuwait from January 2018 to January 2021 were reviewed. A total of 70 consecutive patients were enrolled in this study. Patients were divided into two groups based on the type of biological valve used (Perceval suture-less valve and Magna bioprosthetic valve). Patients who underwent any combined surgery or isolated AVR using mechanical valve or those requiring redo operations were excluded from the study. All data were collected prospectively in a departmental database through the input of a dedicated database manager. The database was strictly controlled with yearly departmental reports generated of departmental performance for audit purposes. Any missing information and all laboratory blood results were collected by reviewing patients' charts and accessing hospital laboratory system. Outcome measured studied included postoperative complications, in hospital mortality, length of hospital and intensive care unit stay. This study and the database were both approved by the ministry of health and our institutional review board. Individual patient consent was obtained for entry into the database. However, our review board waived the need for individual patient consent for this study.

2.2. Cardiopulmonary Bypass (CPB) and Definitions

All isolated AVR were performed through sternotomy (either mini sternotomy or full standard sternotomy) with full CPB. Following full anticoagulation with heparin given at a dose of 300 IU/Kg to maintain activated clotting time of 450 - 600 seconds, CPB was instituted using ascending aorta cannulation and two-stage right atrial venous cannulation. A roller pump (Sorin S5) and hollow fiber membrane oxygenator (Sorin Inspire 8F) were used. The extracorporeal circuit was primed with 1200 ml of Plasma-Lyte and 5000 IU of heparin. CPB was maintained with non-pulsatile flow with a minimum flow rate of 2.4 L/min/m^2 at normothermia with temperature allowed to drift to 34 degrees Celsius. Shed blood was recycled using cardiotomy suction. Acid/base managed

with alpha stat control. Myocardial protection was achieved with intermittent antegrade cold blood cardioplegia with/without retrograde cardioplegia in case of significant aortic regurgitation. Left ventricular vent was used in all cases. Following the closure of aortotomy, hot shot warm cardioplegia is given antegrade and aortic cross clamp removed. Heparin was reversed with protamine at 1:1 ratio after weaning from CPB.

Thrombocytopenia is defined as low platelet count of $<140 \times 10^9$/L (normal reference range (140 - 400) $\times 10^9$/L). Renal complications refer to postoperative renal failure that required dialysis or managed conservatively in patients with no prior history of same or patients with pre-existing renal impairment that worsened after surgery requiring new onset dialysis. Neurological complications refer to the incidence of transient ischemic attacks or permanent stroke or reversible ischemic neurological deficits. Pulmonary complications refer to postoperative chest infection, re-intubation, tracheostomy insertion, acute respiratory distress syndrome, respiratory arrest and pleural effusion requiring drainage. In hospital mortality refer to all deaths that occurred within 30 days of surgery.

2.3. Valve Implantation Technique

After transverse aortotomy is made, native aortic valve is de-calcified and debrided followed by irrigation and sizing of the annulus. For Perceval valve, aortotomy is made 1 - 2 cm higher than the level used for Magna valve. Perceval valve is constructed from bovine pericardium fixed in a metal cage made of Nitinol. Currently, 4 sizes are available: small (19 - 21 mm), medium (22 - 23 mm), large (24 - 25 mm) and extra-large (>25 mm) [7]. To place the valve in position, 3 guiding sutures (4/0 prolene) are placed in the nadir of each cusp of aortic valve. These are then passed through the corresponding loops of the Perceval valve and the prosthesis is then lowered to position. Once the delivery system is in position, the stent is deployed leaving the new valve in place. Then, the delivery system and guiding sutures are removed. The field is rinsed with warm saline and post dilatation balloon is inserted in the valve and dilated for 30 seconds at 4 atmospheric pressure to optimize the area of contact between prosthesis and aortic annulus [8]. Standard two-layer closure of aortotomy is then made with running 4/0 prolene suture. Trans-esophageal echo is used after weaning from cardiopulmonary bypass to assess the new valve and the presence of any para valvular leak.

2.4. Data Analysis

Statistical analysis was performed using SPSS software version 17 (IBM, Armonk, NY, USA). Univariate analysis was used to compare the variables between the two groups. Student t-test was used to compare numerical variables and continuous variables. Fischers Exact test was sued to compare discrete categorical variables. P-value < 0.05 was used as a point of statistical significance in the analysis.

3. Results

Our cohort consisted of 70 patients (42 patients with Perceval suture-less valve and 28 patients with Magna bioprosthetic valve). Age ranged from 17 to 82 years old with mean (± SD) of 56.1 ± 15.6. There were 35 females and 35 males (50% each). There was one in hospital death in the whole cohort in the Perceval group (1.4% mortality due to pneumonia and sepsis). Preoperative factors and patients' characteristics are summarized in Table 1. As shown in this table, the two groups were similar in most baseline characteristics with the exception of age, hyperlipidemia and ejection fraction. Patients receiving Magna valve were on average 10 years younger compared to those receiving Perceval valve with lower incidence of dyslipidemia and lower ejection fraction. As expected, aortic cross clamp time and cardiopulmonary bypass time were both significantly shorter in the suture-less Perceval group compared to the sutured Magna valve group reflecting the difference in the implantation technique [9].

Table 2 shows the platelet count and mean platelet volume between the two groups. As shown, the mean platelets count at baseline was similar in the two valve groups. However, by day 1 onwards until day 7, the mean platelet counts were significantly lower in the suture-less Perceval valve group than in the Magna

Table 1. Preoperative and intra-operative variables among the two groups.

Variable	Perceval valve (n = 42)	Magna valve (n = 28)	P-value
Age (years)			
Mean ± SD	60.0 ± 13.3	50.3 ± 17.1	0.01*
Gender			
Male	20 (48%)	15 (54%)	N/S
female	22 (52%)	13 (46%)	
Ejection fraction (%)			
Mean ± SD	60.1 ± 7.1	51.7 ± 13.1	0.001*
CPB time			
Mean ± SD (minutes)	109.5 ± 27.3	138.1 ± 33.8	0.001*
Cross clamp time			
Mean ± SD (minutes)	76.1 ± 24.7	96.8 ± 25.5	0.001*
Hypertension	29 (69%)	16 (57%)	N/S
Diabetes mellitus	17 (40%)	6 (21%)	N/S
Dyslipidemia	15 (36%)	3 (11%)	0.025 *
Cerebrovascular accident	1 (2%)	0	N/S
Atrial fibrillation	2 (5%)	1 (4%)	N/S
Renal failure	4 (10%)	4 (14%)	N/S
Ischemic heart disease	11 (26%)	3 (11%)	N/S
COPD/asthma	4 (10%)	2 (7%)	N/S

SD: standard deviation. N/S: not significant. COPD: chronic obstructive pulmonary disease. CPB: cardiopulmonary bypass.

Table 2. Platelets count and mean platelet volume in the two groups. Data presented as mean ± standard deviation.

Variable	Perceval valve	Magna Valve	P-value
Baseline platelet count	245.9 ± 59.1	255.8 ± 77.6	N/S
Platelet count day 1	105.8 ± 45.3	131.5 ± 42.8	0.019*
Platelet count day 2	81.9 ± 38.2	122.5 ± 44.4	0.001*
Platelet count day 3	69.6 ± 38.4	126.2 ± 56.4	0.001*
Platelet count day 4	76.6 ± 44.5	159.9 ± 62.2	0.001*
Platelet count day 5	100.5 ± 73.9	159.6 ± 64.0	0.008*
Platelet count day 6	94.4 ± 44.8	189.8 ± 80.8	0.001*
Platelet count day 7	125 ± 62.4	219 ± 108.4	0.004*
Baseline mean platelet volume	10.4 ± 1.4	9.75 ± 1.43	N/S
Mean platelet volume day 1	9.6 ± 1.8	9.42 ± 1.26	N/S
Mean platelet volume day 2	10.3 ± 1.1	9.60 ± 1.18	0.022*
Mean platelet volume day 3	10.5 ± 1.0	9.80 ± 1.61	0.03 *
Mean platelet volume day 4	10.7 ± 1.3	9.57 ± 1.42	N/S
Mean platelet volume day 5	10.1 ± 1.4	9.49 ± 1.37	N/S
Mean platelet volume day 6	9.9 ± 1.1	9.77 ± 1.48	N/S
Mean platelet volume day 7	9.5 ± 1.3	9.49 ± 1.36	N/S

N/S: not significant.

sutured valve group. This effect is also shown in **Figure 1(A)**, where the platelet count dropped significantly until day 3 postoperative and then slowly increased until day 7 and returned to normal levels in follow up period (2 weeks post-operative). In the Magna group, platelet count dropped slightly by day 1 and then remain at plateau until day 4 where they started to increase towards baseline by day 7 and became higher than baseline at follow-up (**Figure 1(B)**). Mean platelet volume (MPV) was not different between the two groups in most of the time points collected and remained around the level of baseline values. By examining the time curves of MPV in both groups, they remained around the baseline value (**Figure 2(A)** and **Figure 2(B)**).

In hospital mortality was similar between the two groups (**Table 3**). In addition, the rate of blood product transfusion (especially platelets) and rate of re-exploration for bleeding were similar between the two types of valves. The postoperative complications were also similar between the two groups. As shown in the table, suture-less Perceval group had significantly shorter intensive care unit and hospital stay compared to the Magna valve. The observed thrombocytopenia in the Perceval valve group had no effect on the rate of postoperative complications when compared to the Magna bioprosthetic valve.

4. Discussion

One of the proposed advantages of the suture-less valves is lack of sewing ring

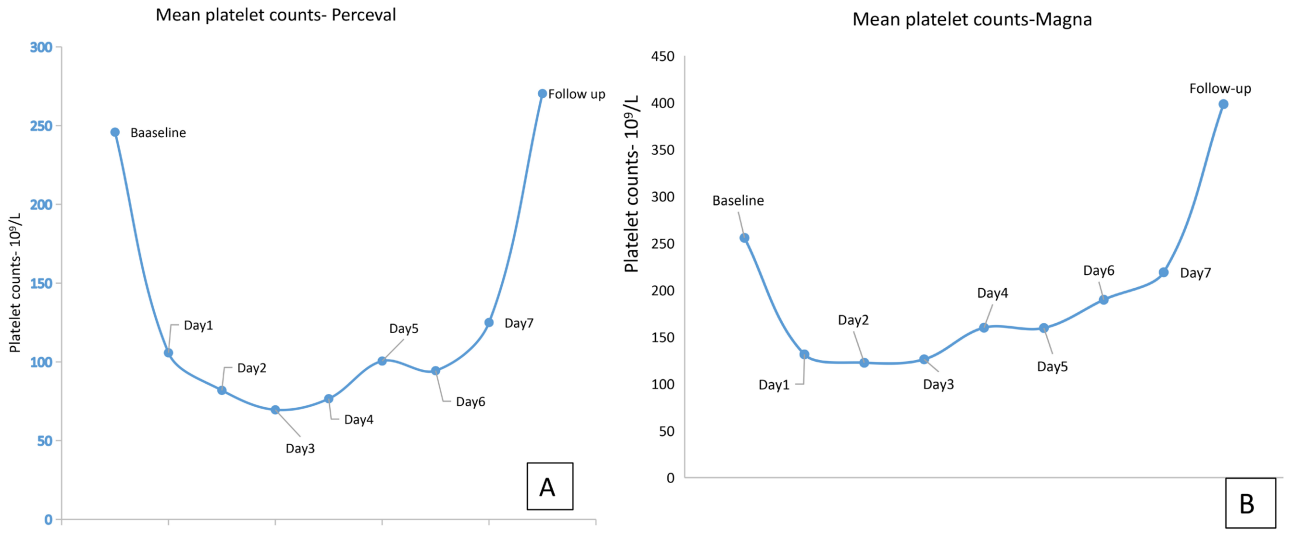

Figure 1. Mean platelet count in Perceval valve (A) and Magna valve (B).

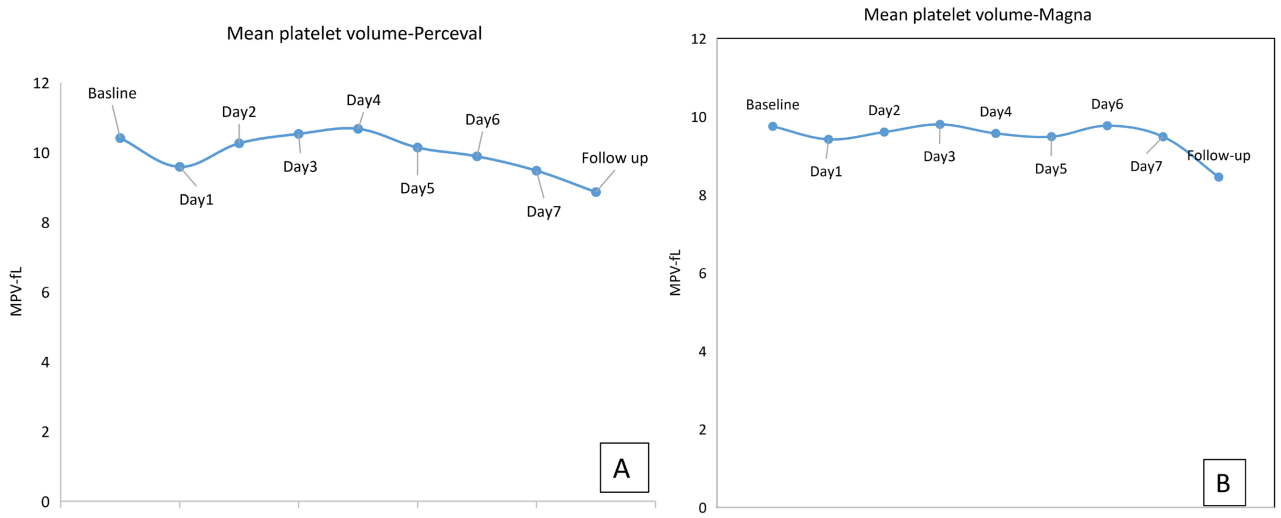

Figure 2. Mean platelet volume in Perceval valve (A) and Magna valve (B).

Table 3. Postoperative outcome in the two groups.

Outcome variable	Perceval (n = 42)	Magna (n = 28)	p-Value
Platelet transfusion	10 (24%)	10 (36%)	N/S
Fresh frozen plasma transfusion	12 (29%)	12 (43%)	N/S
Cryoprecipitate transfusion	3 (7%)	1 (4%)	N/S
In-hospital mortality	1 (2%)	0	N/S
Re-explored for bleeding/tamponade	3 (7%)	1 (4%)	N/S
Length of ICU stay (days) Mean ± SD	4.1 ± 1.9	6.9 ± 13.8	0.001*
Length of hospital stay (days) Mean ± SD	13.7 ± 7.0	17.7 ± 14.5	0.001*
Neurological complication	0	1 (4%)	N/S

Continued

Atrial fibrillation	4 (10%)	2 (7%)	N/S
Renal complication	2 (5%)	1 (4%)	N/S
Permanent pacemaker	2 (5%)	3 (11%)	N/S
Low cardiac output state	0	2 (7%)	N/S
Respiratory complications	4 (10%)	2 (7%)	N/S
Sternal Wound infection	1 (2%)	0	N/S

SD: standard deviation. N/S: not significant. ICU: intensive care unit.

resulting in the implantation of larger size valve and potentially improving valve hemodynamics [7] [8] [10]. In addition, both aortic cross clamp time and cardiopulmonary bypass time are significantly shorter in the suture-less valves compared to the conventional sutured valve resulting in a potential advantage in terms of postoperative complications as we had previously reported [11]. However, there is an increased risk of permanent pacemaker insertion associated with the use of suture-less valves compared to the conventional valves as reported in a recent meta-analysis [12]. The observation of postoperative thrombocytopenia in the Perceval valve remains a concern and its effect and time course are not well understood.

Our data are consistent with a study reported previously [4]. In that study, the authors had observed a decline of platelet count in suture-less Perceval valve until day 3 with a slight increase by day 5 postoperative and mild improvement at discharge but never reached preoperative levels. Mean platelet volume (MPV) showed significantly increased values in the Perceval vs Intuity suture-less valves post-operatively. However, careful examination of their data also showed that the MPV values of the Perceval subgroup were similar to the baseline preoperative values (as we showed in our study). In addition, they showed by using multivariate analysis that Perceval valve was as independently associated with postoperative thrombocytopenia (compared to Intuity sutures less valve). They also reported that at 1 year the platelet count was not significantly different from preoperative values in the Perceval suture-less valve. Our data were also consistent with another report [5]. In their work, thrombocytopenia was also observed post operatively in Perceval valve recipients more than Magna valve recipients. The maximal decline was at day 3 postoperatively with gradual increase from day 4 onwards but still not reaching the baseline on day 7 postoperatively. They also showed no difference in major complications postoperatively among type of valve used although their platelet transfusion was significantly higher in Perceval group when compared to Magna bioprosthetic group.

The observed thrombocytopenia in the postoperative period following Perceval suture-less valve implantation could be a transient direct toxic effects of these valves on platelets caused by the storage solutions used or the micro hemodynamic effects of the prosthetic structure. It has been reported that the anti-calcification treatment with Homocysteic acid (HCA) was the underlying

mechanism for thrombocytopenia associated with Sorin valve (including Sorin S Perceval valve) [2]. Our data does correlate with the thrombocytopenia that is observed with Perceval valve and shows that it is a temporary phenomenon with return to normal counts 2 weeks' post-operative. In addition, lack of correlation between the post-operative outcome and the type of valve used show that the thrombocytopenia is a benign phenomenon.

5. Limitations

Although our data were prospectively enrolled in the departmental database, the analysis was a retrospective design which only can raise association rather than casualty. In addition, our sample size of isolated aortic valve surgery enrolled was small (70 patients total). Another limitation is that the platelet counts, and mean platelet volume were measured based on the clinical situation and not consistently in the same exact time points in all patients. However, within these limitations, we believe that our work will shed more light on the observation of thrombocytopenia following Perceval valve implantation and can stimulate more research into the subject.

6. Conclusion

Thrombocytopenia occurs following Perceval valve implantation and it is a transient phenomenon with improvement after 3 days post-surgery and full recovery within 2 weeks of surgery. This observation does not seem to have an effect on the postoperative outcomes of patients receiving Perceval valve. This phenomenon is not seen to that extent in the sutured bioprosthetic valve and may be due to the design or the preservation method used in the Perceval valve.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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