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Influence of The Prosthesis Type and Diameter in The Thrombocytopenia Associated with Aortic Valve Replacement Surgery

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ABSTRACT

Introduction: Aortic valve replacement with either mechanical or bioprosthetic valves is the gold standard treatment for severe aortic stenosis. Unfortunately, enhanced bleeding and hemodynamic decompensation thrombocytopenia is a frequent postoperative complication. The latter could be secondary to the shearing effect of mechanical prosthesis upon the blood flow that favors platelet aggregation or the presence of thrombogenic materials such as glutaraldehyde used to preserve bioprosthetic valves. Our aim was to discern which type of valve is associated with a more severe post-surgery thrombocytopenia so we compared postoperative platelet counts in patients treated with mechanical vs bioprosthetic valves.

Material and Method: Two hundred and fifty patients with severe aortic stenosis underwent valve replacement surgery were included in the analysis. 126 patients received a mechanical (group A) and 124 patients received a biological (group B) prosthesis. A conventional surgical procedure with Extracorporeal Life Supports (ECLS) was performed in all. Patients' age, gender, cardiovascular risk factors, type and time length of antiaggregant treatment, size of the implanted valve, and perioperative events were recorded. Pre-surgery platelet count and daily post-surgery registers of platelets count for a 10-day period was documented.

Results: Platelet count before surgery was within normal values in both groups. There was a significant decrease the first postsurgical day in both groups (127±48 vs 224±56 in group A, and 132±45 vs 229±54 in group B, p <0.001). Normal platelet count, was reached the fourth post-surgery day in group A patients compared to the eighth day of group B. The differences in platelet count between both groups, independently of the postsurgical day, were highly significant. Thrombocytopenia remained significantly lower and did not reach normal values (141) in the 10 days follow-up in patients that received the 19 mm prosthesis, whereas those receiving the 21 mm valves reached normal values (150) the eighth day.

Conclusion : Thrombocytopenia in patients undergoing aortic valve replacement is secondary to the synergic effect of ECLS, aldehydes present on the preservation solution of prosthesis, and the shear flow induced by the prosthesis diameter. The implant of small diameter prosthesis prolongs thrombocytopenia.

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Introduction

Aortic valve replacement with either mechanical or bioprosthetic valves is the gold standard treatment for severe aortic stenosis. The latter is the treatment of choice in patients >65 years old or in younger patients where oral prolonged anticoagulation therapy is not indicated (1, 2). Unfortunately, enhanced bleeding and hemodynamic decompensation due to extracorporeal circulation induced thrombocytopenia is a frequent postoperative complication.

Platelet derangements represent a short coming in cardiac surgery and extracorporeal life supports (ECLS). Thrombocytopenia is a clinically relevant entity and an intrinsic obstacle of cardiac surgery with a prevalence>30%, (3) associated with increased postoperative morbidity and mortality (4). The causes of the phenomenon are unidentified (5) but enhanced activation and adhesion of the platelets triggered by the plastic components of the extracorporeal circulation machine, (6) and the immune reactions or the oxidative stress induced by the extracorporeal circulation (7, 8) are plausible causes. Likewise, the shear and turbulence forces which mechanical prosthesis are subjected to by the blood flow specially in the short diameter ones (< 19 mm), or the biological effects exerted upon the vascular endothelium by the glutaraldehyde present in the preservation solution where bioprosthetic are maintained, are factors that reduce thrombo-resistance in fixed pericardium (9) and induce thrombocytopenia as Von Willebrand factor can be activated thus initiating the coagulation cascade and platelet aggregation (10-12).

Although we have detected differences in the postoperative thrombocytopenia levels between patients treated with mechanical or bioprosthetic valves, no clear correlation to mild or severe hemodynamic decompensation has been established. The aim of this project is to discern if our hypothesis is plausible.

Materials and Methods

Two hundred and fifty patients subjected to valve replacement surgery were included in the analysis. 126 received a mechanical prosthesis (Carbomedics) and 124 a biological prosthesis (Perimount). All the patients had severe aortic stenosis at arrival and were evaluated at the cardiovascular surgery division of CMN “20 de Noviembre”, ISSSTE. Patients with endocarditis, ischemic cardiopathy or concomitant mitral disease were not included. Intake of oral anticoagulants or platelet antiaggregant was suspended in all the patients seven days prior to the surgery .

The patients were treated with I.V. sodium heparin (3 mg/kg) before a conventional surgical procedure with ECLS and moderate hypothermia (34º C) was performed. Heart stoppage was obtained with cold Brechnaider solution before the ascendent aorta was ligated. Biological prosthesis were extensively washed (3 min) with physiological saline solution, in order to reduce aldehyde to alcohol, previous to the implantation. Regardless of the valve used, a transesophageal echocardiogram was carried out in all the patients to confirm the adequate positioning of the prosthesis and to exclude paravalvular leaks. All patients received 80 UI/kg/day of sodium heparin during the ten-days follow-up.

We kept a close record of the patients’ age, gender, cardiovascular risk factors, type and time length of antiaggregant treatment, size or the implanted valve, intraoperative events, pre-surgery platelet count and daily post-surgery registers of platelets count for a 10 days period. Platelet count was performed by an expert chemist, in the central clinical laboratory of CMN “20 de Noviembre” with 10 ml fresh blood obtained by venipuncture in an EDTA-containing tube using the CELL-DYN Sapphire (Abbott Lab., Chicago, USA) analyzer. The standard reference platelet count ranges from 150,000 to 450,000 platelets/µl of blood**.**

Statistical Analysis

Mean and SD in accord with Kolmogorov Smirnov normality test was used for descriptive analysis. The group comparison with Student’s t-test and Chi-square test were used for quantitative and qualitative variables, respectively. Significant statistic was considered with a p value < 0.05. The SPSS v28.0 statistical program for operating system Windows was used.

Results

The median age of patients implanted with a mechanical prosthesis (59±8 years) was significantly lower (74±6) than those implanted with a biological prosthesis (p= 0.001). Differences in co-morbidities, surgical procedure, or time length of ECLS between patients implanted with mechanical or biological prosthesis were not statistically significant (Table 1). None of the patients showed evidence of paravalvular leak as determined by the intraoperative echocardiography .

The platelet count before surgery was not different and was within normal values in both groups (224±56 µl vs 229±54 µl, p= 0.42). As expected, the platelet count showed a highly significant decrease at the first postsurgical day in both groups (127±48 vs 224±56 in patients treated with the mechanical valve, p < 0.001 and 132±45 vs 229±54 in patients treated with the biological valves, p < 0.001). The difference in platelet count between groups at the first and second postsurgical valve implantation days was not statistically significant (Table 2).

Table 1. Comparasion of relevant demographic variables.

	Type of valvular prosthesis		p *
	Mechanical	Biological	
Age (years)	59±8	74± 6	0.001
Gender			
Male (n)	94	99	0.20
Female (n)	32	25	
Cardiovascular risk factors			
Diabetes Mellitus (n)	29	38	0.35**
High blood pressure (n)	60	96	0.41**
Dyslipidemia (n)	46	54	0.24**
Transsurgical parameters			
Surgical procedure (min)	298±22	305±25	0.54
Aorta clapping (min)	95±5	97±4	0.45
ECLS (min)	111±12	108±18	0.37

Results are expressed as mean ± standard deviation of the mean,
*Student´s t test, ** Chi^2;
ECLS: Extracorporeal Life Support

Table 2. Differences in daily platelet count.

	Prosthesis		p *
	Mechanical	Biological	
Basal	224±56	229±54	0.42
Day 1	127±48	132±45	0.53
Day 2	126±29	124±28	0.39
Day 3	147±48	118±43	0.002
Day 4	152±46	115±45	0.001
Day 5	164±39	121±54	0.001
Day 6	176±43	132±43	0.001
Day 7	189±54	145±56	0.001
Day 8	197±62	150±42	0.001
Day 9	200±45	162±35	0.01
Day 10	245±56	170±47	0.01

Results are expressed as mean ± standard error of the mean.
Platelet value x103/µl of blood;
*Student´s t Test,

However, interestingly there was a clear tendency to return to normal platelet count, only patients who received the mechanical valve returned to pre-surgery values the tenth post-surgery day, whereas those receiving the biological prosthesis maintained counts similar to the count which was observed the first post-surgery day and initiated the recovery path from the 7th day onwards (Table 2) but clear thrombocytopenia persisted. The differences in platelet count between both groups, independently of the postsurgical day, were highly significant (Figure 1).

There was a clear difference in the postoperative platelet count when the 19 mm prosthesis was compared to the 21 mm. Although the tendency was identical to that shown in the previous figures and tables, thrombocytopenia remained significantly lower in patients who received the 19 mm prosthesis than those receiving the 21 mm valve (Table 3). The mean value of platelets was significantly different from day three onwards and platelet count reached normal values 8 days after surgery in the patients receiving the 21 mm prosthesis, as opposed to none of the patients with the 19 mm (Figure 2).

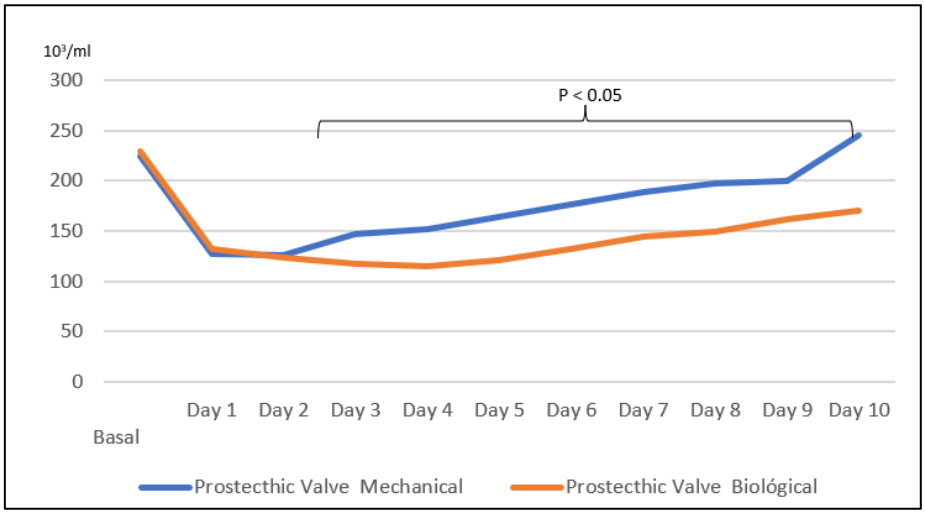

Figure 1. Postoperative platelet count evolution. Mechanical and biological prosthesis showed similar low platelet count, but with tendency to return to normal values after third postoperative day. Only patients who received the mechanical valve showed a significant. Recovery to pre-surgery values at tenth post-surgery day whereas those receiving the biological prosthesis the thrombocytopenia persisted.

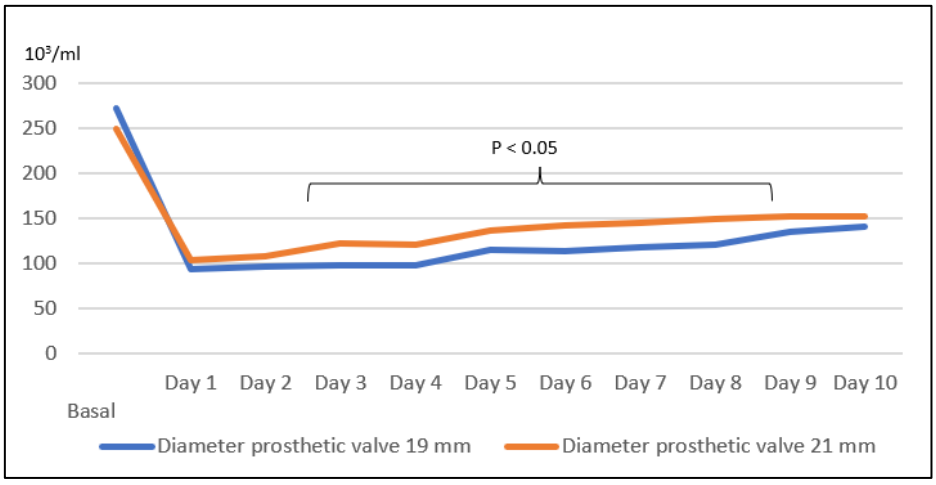

Figure 2. Platelet count domparation between 19 and 21 diameter prostethic vahve. There was a significant difference in the postoperative platelet count between 19mm and 21mm prosthetic valve, although the tendency was identical to recovery platelet count, the thrombocytopenia remained significantly lower in patient that received the 19mm.

Discussion

The majority of cardiac surgery patients have a nadir platelet count on postoperative days 2 to 3, with the platelet count returning to baseline by day 5 (13). This transitory decrease is probably secondary to immune mediators and Von Willebrand factor released from the vascular endothelium (14-16), which activates the coagulation cascade favoring platelet adhesion and consumption normally the first 12 post surgery hours. Thrombocytopenia is an intrinsic drawback of ECLS, however the mechanism underlying this phenomenon is unknown (17). Our results showed that in patients with extracorporeal life support in aortic valve replacement surgery, severe post-surgery thrombocytopenia was not only present but persisted for at least 10 days after surgery. This prolonged effect has been attributed to the severe shear forces that blood is subjected to when passing through the mechanical prosthesis (18-20) or the effect of the preservation solution of the bioprosthesis which contains glutaraldehyde (9).

The late platelet count recovery that we observed in the bioprosthesis group is probably secondary to the components of the preservation solution (21) as it may perpetuate endothelial aggression and inflammation (22). Our results confirm the observations reported in the literature.

A significant observation was the differences in platelet count detected in relation to the valve diameter. It is known that blood flow causes a shear stress on the vascular wall and that shear flow is determined by caliber, wall thickness and length (23); these forces affect endothelial cell behavior. It has been recognized that elevated shear stress promotes platelet dysfunction (24) and aggregation as von Willebrand factor is a shear-sensitive protein (25) through the glycoprotein1b-IX receptor complex (26). Valves, especially bioprosthetic valve, are made of nitinol, a super elastic rigid material with shape memory characteristics. It is well established that smaller diameter vessels have high shear rates, (27) thus enhancing the platelet dysfunction. It is clear that the decision as to which valve must be implanted in a patient depends in the size of the aortic annulus, however our results strongly favor the use of the 21 mm valves in order to facilitate a more rapid return of normal platelet counts thus avoiding the high morbidity-mortality of prolonged thrombocytopenia.

Limitations of the study

Being a retrospective study inflammation biomarkers nor biological endothelial status were determined.

Conclusion

Our results confirm that thrombocytopenia in patients undergoing aortic valve replacement is secondary to ECLS, effect of aldehydes present on the preservation solution of prosthesis especially the bioprosthetic valve, and the shear flow induced by the prosthesis, but it also demonstrates that the use of small diameter prosthesis prolongs thrombocytopenia.

Table 3. Platelet count in relation to prosthesis diameter.

	Diameter		P *
	19 mm	21 mm	
Basal	273±28	250±34	0.32
Day 1	94±48	104±46	0.09
Day 2	97±39	108±26	0.09
Day 3	98±48	122±32	0.03
Day 4	98±46	121±35	0.03
Day 5	115±34	136±44	0.02
Day 6	113±43	142±43	0.01
Day 7	118±34	145±46	0.01
Day 8	121±42	150±45	0.01
Day 9	135±35	192±35	0.001
Day 10	141±46	203±47	0.001

Results are expressed as mean ± standard deviation of the mean.
Platelet value x103/µl of blood,
* Student T test,

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