

Platelet survival in patients with homograft and prosthetic heart valves

Correlation with incidence of thromboembolism

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Manohitharajah, S. M., Rahman, A. N., Donnelly, R. J., Deverall, P. B., and Watson, D. A. (1974). *Thorax*, 29, 639–642. **Platelet survival in patients with homograft and prosthetic heart valves.** Investigations in the past have demonstrated shortened platelet survival time in patients with prosthetic heart valves. This suggested that platelets contribute to thromboembolism in this group. Homograft valves and the newer models of the Starr-Edwards prosthesis have proved less thrombogenic than those previously employed, but platelet survival studies in patients with these valves are lacking. In this study platelet function, survival, and its relation to haemolysis were determined in 28 patients following mitral valve replacement and in two patients following mitral valvotomy: 14 patients had a frame-mounted homograft aortic valve; 13 patients had a Starr-Edwards prosthesis model 6310 or 6320, and one had a Starr-Edwards prosthesis model 6000. Normal platelet function and survival was found in both the homograft and the Starr valve groups. The patient with the earlier model of the Starr valve (model 6000) had a shortened platelet survival time. The two patients following mitral valvotomy had normal platelet survival. The fact that platelet abnormalities were not demonstrable in our patients with homograft valves and newer Starr-Edwards prostheses may explain the low incidence of thromboembolism in this group. Platelet survival studies are a useful parameter to determine the potential thrombogenic nature of prosthetic valves. Platelet survival time was not influenced by the presence or severity of haemolysis.

Valve replacement is an established form of treatment for acquired valvular heart disease. The value of this replacement may be compromised by two major complications—thromboembolism, which carries a significant morbidity and mortality (Duvoisin, Brandenburg, and McGoon, 1967; Starr, Herr, and Wood, 1967; Akbarian, Austen, Yurchak, and Scannell, 1968), and intravascular haemolysis (Grosse-Brockhoff and Gerhmann, 1967; Donnelly *et al.*, 1973). Thromboembolism is more common in patients with mitral valve prostheses, and anticoagulant therapy does not successfully eliminate the incidence of systemic emboli in this group (Duvoisin *et al.*, 1967; Akbarian *et al.*, 1968). Platelet studies have shown abnormally shortened platelet survival in these patients (Harker and Slichter, 1970; Weily and Genton, 1970), suggesting that platelets play a significant role in initiating thrombosis (Mustard, Jorgensen,

and Hovig, 1966) and contribute to thromboembolism.

On this assumption, homograft valves which are non-thrombogenic should show normal platelet survival and the newer prosthetic valves with a reduced incidence of thromboembolism should cause less alteration in platelet survival time. In this unit 52 patients with frame-mounted aortic homograft valves in the mitral position, followed for the past 0–42 months, showed no evidence of thromboembolism, and the incidence of thromboembolism with the newer Starr valves in the mitral position is 5%. The aim of this study was to correlate the thrombogenic potential of heart valves with platelet survival time and platelet function.

PATIENTS AND METHODS

Platelet function and survival and red cell survival were studied in 30 patients. Fourteen patients had a

frame-mounted aortic homograft in the mitral position. Thirteen had a composite seat Starr-Edwards prosthesis, model 6310 or 6320 (size 2M or 3M), one had a Starr-Edwards prosthesis model 6000, and two patients had had a mitral valvotomy. One of the patients in the Starr valve group had mitral and tricuspid prostheses. There was no clinical evidence of valve dysfunction or perivalvular leak in any patient. Investigations were carried out four and a half months to three and a half years after operation in the homograft series and seven months to five and a half years after operation in the prosthetic valve and valvotomy patients. The age distribution of the patients in each group was similar.

The platelet survival time and recovery was determined by using chromium-51 (⁵¹Cr) labelled autologous platelets, according to the method of Aster and Jandl (1964)—samples taken on the same day and thereafter daily for 10 days. The normal range for platelet survival in our laboratory is 8 to 11 days and recovery is 60–70%.

Platelet adhesiveness was measured by a modified method of Hellem (1960), using plastic syringes wetted with heparin to draw 2 ml of venous blood, which was passed through a standard glass-bead column in a constant time. Duplicate specimens were tested and results were within 10%. Normal adhesiveness by this method ranged from 28 to 45%. Platelet counts were performed on all patients by a semi-automated method using a thrombocounter (Coulter).

Red cell survival studies using radioactive ⁵¹Cr were carried out with autologous cells according to the method of Dacie and Lewis (1968). The normal value for red cell survival in our laboratory is $T_{\frac{1}{2}} 27 \pm 3$ days.

RESULTS

The red cell survivals were measured four to six months before the platelet survival study was

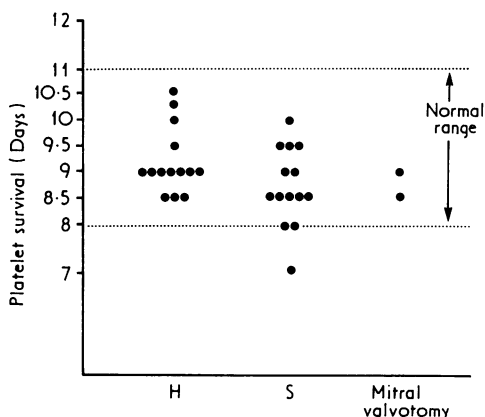


FIGURE Platelet survival time (days) in 14 patients with homografts, 14 patients with Starr valves, and two patients after mitral valvotomy. H=homograft; S=Starr-Edwards.

done. The platelet survival curves appeared to be composed of both a linear and an exponential component. The platelet survival in days (Figure) shows a range from 8.5 to 10.5 with a mean of 9.2 (\pm SD 0.64) in the homograft group and from 7 to 10 days with a mean of 8.8 (\pm SD 0.75) in the prosthetic valve group. There is no significant difference between the groups. The patient with a silastic ball Starr-Edwards prosthesis (model 6000) had a shortened platelet survival time of 7 days. Platelet recovery was estimated in 10 patients and values of between 60% and 70% were obtained. The Table indicates platelet counts, platelet adhesion, and red cell survival times in all

TABLE
PLATELET ADHESION AND SURVIVAL AND RED CELL SURVIVAL

No. of Cases	Heart Valve			Platelet Count Range (μ l)	Platelet Adhesion%		Platelet Survival (days)		Red Cell Survival $T_{\frac{1}{2}}$ ⁵¹ Cr (days)	
	Type	Position	Model Size		Range	Mean	Range	Mean	Range	Mean
14	H	M	—	154,000–307,000	27–45	37.6	8.5–10.5	9.2 (\pm SD 0.64)	25–28.5	27
12	SE CS	M	6310 2M or 6320 3M	118,000–260,000	25–46	34.3	7–10	8.8 (\pm SD 0.75)	14.8–24.4	18.2
1	SE (Silastic ball)	M	6000 No. 3	190,000	46	—	7	—	19	—
1	SE CS	M T	6320 3M 6310 2M	200,000	38	—	8.5	—	22	—
2	Mitral valvotomy	—	—	210,000–260,000	—	—	9–9.5	9.25	—	—

H = homograft; SE = Starr-Edwards; CS = composite seat; M = mitral; T = tricuspid.

patients studied. The platelet adhesion ranged from 27% to 45% with a mean of 37.6% in the homograft valve group and from 25% to 46% with a mean of 34.3% in the Starr valve group. The red cell survival figures ($T\frac{1}{2}$ ^{51}Cr) were in the normal range for the homograft valve group, but in the Starr valve group $T\frac{1}{2}$ ^{51}Cr ranged from 14.8 to 24.4 with a mean of 18.2 days. Red cell fragmentation was present in the majority of the Starr valve patients. Taken in conjunction with red cell $T\frac{1}{2}$ ^{51}Cr and haptoglobin estimations, 85% of these patients showed evidence of haemolysis.

DISCUSSION

It is accepted that deposition of platelets is the initiating event in the formation of a thrombus in the systemic arterial circulation and plays an important role in its propagation (Mustard *et al.*, 1966). The type of clot formed is 'white' and consists mainly of platelets and fibrin strands (Marcus, 1969). This may explain the fact that thromboembolism continues to be a cause of morbidity and mortality in patients with prosthetic heart valves despite adequate anticoagulation, and that the addition of platelet inhibitors has significantly reduced the incidence of thromboembolism in this group of patients (Sullivan, Harken, and Gorlin, 1968). Analysis of platelet function and survival should therefore represent a means of assessing the thrombogenic potential of artificial heart valves. Studies in patients with prosthetic heart valves, associated with a high incidence of thromboembolism, have shown shortened platelet survival time (Harker and Slichter, 1970; Weily and Genton, 1970). Recently, Weily, Steele, and Genton (1972) demonstrated normal platelet survival in patients with Beall valves in the mitral position, a valve with a low reported incidence of thromboembolism. As far as we are aware, there are no reported studies in patients with homograft valves in whom platelet survival was assessed.

It seemed logical to us to extend platelet studies to a wider group of patients with homograft mitral valve replacement which clinically have been non-thrombogenic, and composite-seat Starr-Edwards prostheses, a valve of low thrombogenic potential. Platelet survival times were normal in the homograft group which appeared to correlate with the non-thrombogenic nature of these valves. Normal platelet survivals were also found in patients with the prosthetic Starr valves (models 6310 and 6320), consistent again with the low thrombogenic potential of this type. This suggests that platelet survival is a useful means of assessing the thrombogenic potential of a particular prosthesis.

The only patient with the earlier model of Starr valve (model 6000) studied had a shortened platelet survival. This patient has had several embolic episodes in spite of adequate anticoagulation, and the addition of a platelet inhibitor, dipyridamole (Persantin), 400 mg daily, has eliminated further embolic episodes.

No significant difference in platelet adhesiveness or other platelet functions was demonstrated between the homograft and Starr valve groups. However, previous investigators, who found shortened platelet survival times with valves associated with a high incidence of thromboembolism, also found platelet adhesiveness to be of little value in assessing the valve thrombogenicity.

In our patients the presence and severity of haemolysis did not influence platelet survival time. If it is presumed that the trauma to the red cells caused by turbulence around the valve is the cause of the red cell fragmentation, the platelets seem to be far less vulnerable to this trauma than the red cells.

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