Platelet Survival Time and Thromboembolism in Patients with Mitral Valve Prolapse

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SUMMARY Thromboembolism (TE) occurs in about 20% of patients with rheumatic mitral valve disease, and platelet survival time in these patients has correlated with TE. In patients with mitral valve prolapse, TE appears to occur very infrequently. Platelet survival (autologous labeling with chromium-51) was performed in 26 patients with mitral prolapse. Five patients had a history of stroke, as well as normal cerebrovascular arteriography and shortened platelet survival (average half-time ± SEM 2.3 ± 0.18 days; normal half-time 3.7 ± 0.03 days; n = 26; p < 0.01). Platelet survival was shortened in seven of 21 patients without TE (33%) (3.3 ± 0.06 days; p < 0.01 vs patients with TE). In 138 patients with rheumatic heart disease, platelet survival was shortened in 40 of 41 (98%) with a history of TE (2.3 ± 0.08 days) and in 76 of 97 (78%) without TE (2.9 ± 0.07 days; p < 0.001 vs patients with TE). In patients with mitral prolapse, sulfinpyrazone increased platelet survival (2.4 ± 0.16 to 2.7 ± 0.19 days; n = 7; p < 0.05). Our results suggest that platelet survival time is shortened in patients with mitral prolapse and rheumatic heart disease who have had TE. Of those without TE there is an increased frequency of shortened platelet survival in patients with rheumatic heart disease (78%) compared with those with mitral prolapse (33%), consistent with the infrequency of TE in mitral prolapse.

PATIENTS who have the mitral valve prolapse syndrome are frequently seen in clinical practice. Although this condition is usually considered to have a benign natural history — some authors even consider it to be a normal variant — a number of complications appear to occur infrequently. Patients with mitral valve prolapse may develop severe mitral regurgitation, may be prone to bacterial endocarditis and sudden death, and appear to have an increased frequency of ventricular arrhythmias. These patients may also have intracardiac thrombosis, which might result in systemic embolism. Kostuk and associates found 14 patients with stroke, normal cerebral arteriograms and mitral valve prolapse. In another patient with mitral prolapse, these authors observed a small thrombus at the junction of the prolapsing mitral leaflet and the left atrial endocardium.

Systemic embolism occurs in 10-20% of patients with rheumatic heart disease (mitral stenosis). In these patients, embolism tends to be recurrent and is unrelated to the severity of the mitral valve lesion. In this study, we measured platelet survival time in patients with the mitral valve prolapse syndrome and in patients with rheumatic mitral valve disease.

Patients

Platelet survival time was measured in 26 patients (10 men and 16 women, ages 27–45 years) with clinical and echocardiographic evidence of the mitral valve prolapse syndrome. All patients had either a mid-systolic apical click or a late systolic apical murmur and both, and all had echocardiographic systolic prolapse of either the anterior or posterior mitral leaflet. Five patients (two men and three women, ages 27–43 years) had a history of stroke. We evaluated platelet survival time in five patients tentatively diagnosed as having sustained a cerebral thromboembolism in association with mitral valve prolapse. After finding abnormal platelet survival in these five patients, and because of the relationship of platelet survival and systemic embolism in patients with rheumatic mitral valve disease, we measured platelet survival time in 21 other unselected patients with mitral prolapse who had not had thrombosis. The original five patients were selected for study because they had apparently had thromboembolism.

One woman without stroke had documented paroxysmal atrial tachycardia, and improved while taking digoxin. All patients who had undergone ambulatory electrocardiographic monitoring at least once, showing only occasional (less than 10 per hour) ventricular premature depolarizations. All five with stroke had cardiac catheterization and all had normal left ventricular performance, ventriculographic demonstration of mitral leaflet prolapse, mild mitral regurgitation and normal coronary arteriograms. Two of the patients without stroke had catheterization because of angina, and both had normal coronary arteries and mild or no mitral regurgitation. None of the other patients had clinical evidence of more than mild mitral regurgitation.

Strokes in the five original patients developed within an hour, and all had a satisfactory return of function within a week, although all have clinically apparent residual abnormalities. Two patients had right hemiparesis, one with aphasia; one patient had left-sided parietal lobe signs; one had cerebellar signs; and one had aphasia only. After the stroke (10–17 days), all patients underwent cerebral arteriography, which showed perfectly normal arteriograms. The other 21 patients have not had stroke or any other thromboemb-
bolic manifestation. No patient was receiving oral contraceptives or estrogen.

One hundred thirty-eight patients with rheumatic heart disease (66 men and 72 women, ages 18–53 years) were studied. Forty-one patients had a history of stroke or other embolism (19 men and 22 women, ages 26–45 years) and 97 did not. All patients with rheumatic heart disease had clinical evidence of mitral stenosis with or without mitral regurgitation or aortic valve involvement. In both patient groups, platelet survival was measured at least 3 months after thromboembolism. Patients with rheumatic heart disease were also selected to include those with and those without a history of thromboembolism.

Methods

Platelet survival time was measured by labeling the platelets obtained from the patient’s blood with 100–150 μCi of chromium-51.11 Using computer analysis, we fitted a single exponential to 7 days of platelet count-rate data to obtain the half-time. In 26 normal men, platelet survival time averaged 3.7 days (± 0.03 days ± SEM). The normal range of platelet survival time is 3.3–4.2 days. Serial measurement of platelet survival in patients receiving placebo, including patients with rheumatic heart disease, results in a variation of less than 0.2 days in half-time.

We compared the means of the various groups using the t test.

Results

Platelet survival time was shortened (< 3.3 days) in 12 of the 26 (46%) patients with mitral valve prolapse. Platelet survival was shortened in all five patients who had had stroke (average half-time (± SEM); 2.3 ± 0.18 days; normal half-time 3.7 ± 0.03 days; n = 26; p < 0.001) (fig. 1). Platelet survival was shortened in seven of the 21 (33%) who had not had stroke or other thromboembolism (3.3 ± 0.06 days; p < 0.001 vs patients with embolism). Platelet survival time did not correlate with patient age or sex.

In the patients with rheumatic mitral valve disease, platelet survival time was shortened in 116 of 138 (84%). Platelet survival time was shortened in 40 of 41 patients (98%) with a history of embolism (2.3 ± 0.08 days). Platelet survival was shortened in 76 of 97 (78%) patients who had not sustained an embolic event (2.9 ± 0.07 days; p < 0.001 vs patients with embolism). Platelet survival time did not correlate with patient age or sex or the severity of mitral valve disease. Most patients were in New York Heart Association functional classes I and II.

The platelet suppressant drug sulfinpyrazone (800 mg/day orally), was administered for 2–3 months to seven patients with mitral valve prolapse and shortened platelet survival. All five patients with stroke were studied with sulfinpyrazone. Sulfinpyrazone increased platelet survival time from 2.4 ± 0.16 to 2.7 ± 0.19 days (p < 0.05). Sulfinpyrazone increased platelet survival in patients with rheumatic heart disease from 2.1 ± 0.1 to 2.6 ± 0.11 days (p < 0.01; n = 27).

Discussion

In patients with the mitral valve prolapse syndrome and thromboembolic stroke, platelet survival time is shortened. All patients with mitral prolapse and a history of stroke had shortened platelet survival; this abnormality was infrequently observed in patients with mitral prolapse who had not had thromboembolism. The 20% frequency of embolism in this group of patients with mitral prolapse is not representative of the risk of thrombosis in these patients. The patients with mitral prolapse were selected to include those with and those without thromboembolism. In this preliminary study of a small number of patients, there were differences between average platelet survival in those with thromboembolism and those without embolism. The occurrence of stroke, presumably thromboembolic, in patients with mitral prolapse confirms the observations of Kostuk and associates.6

Patients with rheumatic heart disease have a much increased risk of thromboembolism compared with those with mitral prolapse. Platelet survival time was shortened in most patients with rheumatic mitral disease whether or not they had a history of embolism. In all but one patient with systemic embolism, platelet survival was abnormal, and there was a difference between average platelet survival in patients with and patients without a history of thromboembolism.

In both groups — mitral prolapse and rheumatic mitral valve disease — patients with a history of thromboembolism have shortened platelet survival. The frequency of shortened platelet survival in patients without a history of embolism differs between these groups — 33% in mitral prolapse vs 78% in

![Figure 1](https://i.imgur.com/3G5l5.png)
rheumatic heart disease. In these two groups of patients, shortened platelet survival time appears to be related to the frequency of thromboembolism.

Platelet survival appears to be a sensitive indicator of thrombosis in many clinical states. Platelet survival was shortened in 16 of 17 patients (average age 55 years; 11 men and six women) who had a stroke in the carotid arterial distribution and subsequently underwent carotid arteriography which showed definite atherosclerotic involvement (2.6 ± 0.08 days; average ± SEM). In 11 patients who had sustained a stroke in the carotid distribution and who were subsequently shown to have perfectly normal carotid arteriograms, platelet survival time was shortened in seven (64%) and normal in four (36%) (2.9 ± 0.11 days; average age 36 years; seven men and four women). None of these 11 patients had a clinically recognized risk factor for thrombosis. We have studied eight men with transmural myocardial infarction who were subsequently shown to have normal coronary arteriograms and all eight had shortened platelet survival time (24 ± 0.11 days; average age 34 years). Thus, arterial thrombosis in association with shortened platelet survival time occurs in patients who do not have either rheumatic heart disease or the mitral prolapse syndrome. The relationship in the present study between shortened platelet survival time, thromboembolism and mitral valve disease may reflect coincidence of two common problems—shortened platelet survival and stroke. Perhaps shortened platelet survival in patients with mitral valve disease who have not had thrombosis supports the idea that shortened platelet survival results, at least in part, from mitral valve disease.

Thromboembolism is common in patients with mitral stenosis, but uncommon in patients with aortic stenosis. In 18 patients with aortic stenosis, average platelet survival time was normal (3.4 ± 0.14 days) in 13 patients (72%). Thus, in patients with valvular heart disease there are differences in the frequency of shortened platelet survival time.

In patients with the mitral valve prolapse syndrome, platelet survival correlates with a history of thromboembolism, and sulfipyrazone increases platelet survival. This study was not designed to evaluate the effectiveness of platelet suppressant therapy in these patients. This would be a difficult undertaking in view of the infrequent occurrence of embolism in these patients. We do not advocate that patients with mitral valve prolapse receive platelet suppressant therapy. This therapy is not unreasonable, however, in patients with this syndrome who have sustained a stroke or other thromboembolic manifestation.

Acknowledgment
The authors acknowledge the expert technical assistance of Michael Adams, Jan Lacher, Carla Gilbert, Carol Vandello and Margie Anderson.

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P Steele, H Weily, J Rainwater and R Vogel

Circulation. 1979;60:43-45
doi: 10.1161/01.CIR.60.1.43
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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