Correlation of Platelet Survival Time with Occlusion of Saphenous Vein Aorto-Coronary Bypass Grafts

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SUMMARY Platelet survival time is frequently shortened in patients with coronary artery disease, and it is one of several factors that might contribute to graft occlusion after saphenous vein coronary artery bypass (CAB). In 35 patients with CAB, average platelet survival (autologous labeling with $^{51}$Chromium) was shortened in 20 with one or more saphenous vein grafts occluded and normal in 15 with all grafts open. Of 15 with all grafts open, individual levels of platelet survival were normal in 10 while in 20 with one or more grafts occluded platelet survival was normal in only one.

Platelet survival was not altered by coronary surgery and nine of ten with shortened platelet survival pre-operatively had graft occlusion. Platelet survival did not correlate with either parent artery occlusion or serum lipoproteins. These findings suggest a relationship between shortened platelet survival and saphenous vein graft occlusion and suggest that platelet suppressant therapy might be useful in preventing graft occlusion.

AORTO-CORONARY BYPASS GRAFTING utilizing autogenous saphenous veins is being performed with increasing frequency in patients with coronary artery disease. Clinical results have been encouraging but many vein grafts become occluded either early or many months after successful surgery. Several factors have been identified which may contribute to saphenous vein graft occlusion. These include technical considerations in performing the proximal and distal anastomoses, placing grafts to small diseased coronary arteries with limited distal vascular beds, elevated blood lipids, vein graft thrombosis, and fibrous intimal proliferation.

Pathological studies of patients with saphenous vein grafts have suggested that occlusion due to thrombosis generally occurs early following surgery, that is, within the first two months. Vein graft occlusion due to fibrous intimal proliferation seems to occur late, that is, beyond two months. Intimal fibrosis is a curious process in that it is almost invariably present after about one month but does not necessarily lead to complete occlusion. Some difference of opinion exists as to whether fibroblastic, smooth muscle cells, or both cell types participate in the proliferation occurring in the thickened vein intima. A similarity to early atherosclerosis is suggested by the finding of lipid inclusions in some smooth muscle cells, although this point is also disputed.

Fibrous intimal proliferation is uniform and its cause is not certain, although it may well reflect vein repair subsequent to being exposed to arterial pressure. In addition, diffuse damage of the vein endothelium is seen early after aorto-coronary grafting in pathological material from patients and from experimental animals. In the experimental animal platelets have been shown to adhere to the damaged luminal surface and microthrombi have been identified.

We have observed that platelet survival time is frequently shortened in patients with coronary artery disease. About 60% of patients with coronary disease have shortened platelet survival time and platelet suppressant drugs — sulfipyrazone and clofibrate — lengthen shortened platelet survival in these patients.

The present study was undertaken to examine the relationship between platelet survival time and saphenous vein graft occlusion in patients with coronary disease.

Patients

Thirty-five men (average age 48 years; range 34–56 years) were studied who had undergone aorto-coronary bypass for unstable or disabling angina. Sixty-nine saphenous vein grafts were constructed from the aorta to the distal coronary arteries in these 35 men. Cardiac catheterization with selective angiography of the native coronary circulation and of the saphenous vein grafts was undertaken from 3–44 months (average 21 months) following coronary surgery. Postoperative angiography was performed for evaluation of recurrent angina in most, although a few were studied to evaluate the results of surgery in patients without symptoms.

Platelet survival time was measured either just prior to postoperative angiography (in 32 men) or within four weeks following angiography (in three patients with all of their grafts occluded). The platelet survival time of the latter group was repeated 3–17 months later and no change found. Sixteen of these 35 patients underwent measurement of platelet survival before coronary surgery and again at the time of postoperative angiography (average 4 months, range 3–18 months).

Methods

Platelet survival time was measured by labeling the platelets from about 450 ml of the patients’ blood with $^{51}$Chromium, and following infusion, samples were drawn at 2–3 hours after infusion of labeled platelets and daily for seven days. By computer assisted least squares analysis a single exponent was fitted to the seven days of platelet count-rate data to obtain the survival half-time. In 18 normals, mean platelet survival half-time was 3.7 ± 0.19 days (mean ± SD) with a normal range of 3.3–4.2 days.
Serum cholesterol,\textsuperscript{16} triglyceride,\textsuperscript{16} and lipoprotein electrophoresis on paper\textsuperscript{17} were measured during the platelet survival study and patients classified as either normal or Type IV hyperlipoproteinemia.\textsuperscript{18} Blood for analysis was obtained after a fast of at least 14 hours.

Student's $t$-test was used to compare the means.

**Results**

Saphenous vein graft occlusion was associated with shortened postoperative platelet survival time. In 15 patients with patency of all of their saphenous vein grafts, average platelet survival time was normal ($3.5 \pm 0.11$ days; average $\pm$ SEM) and ten of the 15 (67\%) had normal platelet survival (fig. 1). Twenty men had one or more of their vein grafts occluded, and the average platelet survival was shortened ($2.6 \pm 0.08$ days) and significantly different from the average of those with all of their saphenous vein grafts patent ($P < 0.001$) (fig. 1). Nineteen of these 20 (95\%) had shortened platelet survival time.

Saphenous vein graft surgery did not alter platelet survival time. In the 16 patients studied before and again after bypass surgery average platelet survival was $3.2 \pm 0.15$ days and $3.2 \pm 0.16$ days, respectively, and none was altered by more than 0.2 days. Of these 16 patients six had normal platelet survival preoperatively and all six had all of their grafts open on postoperative angiographic study. Ten men had shortened platelet survival preoperatively and nine of these had one or more of their saphenous vein grafts occluded on postoperative study. Thus, it is reasonable to conclude that the postoperative platelet survival reflects the preoperative value.

Serum lipids and lipoproteins did not correlate with vein graft occlusion. Twenty patients had Type IV hyperlipoproteinemia. Nine of these had all their grafts open and 11 had one or more grafts closed. Of the patients with Type IV, 16 of the 41 vein grafts (39\%) were occluded. Fifteen patients had normal lipoproteins. Six had all grafts open and nine had one or more grafts occluded. Of the men with normal lipoproteins, 11 of 28 vein grafts (40\%) were occluded.

Serum lipids and lipoproteins did not correlate with platelet survival time in this small group of patients. Of the 20 men with Type IV hyperlipoproteinemia, six had normal platelet survival time (30\%). Five of the fifteen with normal lipoproteins (33\%) had normal platelet survival.

Occlusion of a previously open parent artery into which a saphenous vein graft was placed is a recognized complication of vein graft surgery.\textsuperscript{19-21} Platelet survival time did not correlate with parent coronary artery occlusion. Of patients with shortened platelet survival time, five of 15 previously patent parent coronary arteries were occluded (33\%) at postoperative study. In the 24 men with shortened platelet survival, 11 of 33 parent arteries were occluded postoperatively (33\%).

**Discussion**

Data suggest that saphenous vein aorto-coronary graft occlusion is associated with shortened platelet survival time. Shortened platelet survival time is common in patients with coronary artery disease.\textsuperscript{10, 11} The data in this report suggest that following saphenous vein aorto-coronary bypass the complication of vein graft occlusion is particularly likely to occur in those patients with shortened platelet survival time.

Although platelet survival time seems to be a quite sensitive measure for saphenous vein graft occlusion, it does not appear to be particularly specific. There seem to be many patients with patent vein grafts who have shortened platelet survival time. Since patients with shortened platelet survival time postoperatively appear to be those with shortened platelet survival time preoperatively, it is possible that those at high risk of vein graft occlusion may be identifiable prior to coronary surgery.

It is unlikely that the association between saphenous vein graft occlusion and shortened platelet survival time is due to late graft occlusion with subsequent shortening of platelet survival time. The interval between coronary bypass surgery and measurement of platelet survival time averaged 23 months in patients with all of their grafts patent and 20 months in those with one or more occluded grafts.

Although the cause and mechanism of fibrous intimal proliferation is uncertain, it is conceivable that platelets are involved and that patients with shortened platelet survival are at greater risk of intimal proliferation leading to occlusion. Diffuse endothelial damage is regularly seen early after vein grafting and is probably the result of arterial pressure.\textsuperscript{8, 9} The endothelial damage seen in vein grafts may be similar to the changes seen in the experimental animal subjected to balloon arterial injury. In this situation, platelets adhere to connective tissue constituents of the exposed subendothelium and then, intimal thickening, primarily due to smooth muscle cell proliferation occurs.\textsuperscript{22, 23} Cellular intimal thickening may progress and appear similar to the human atherosclerotic plaque. The intimal proliferation seen in saphenous vein grafts may reflect an injury-healing phenomenon in which the blood plays an important role.
The documentation that platelet survival time may be partially or completely corrected with available drugs, sulfipyrazone and clofibrate, affords the opportunity to evaluate the use of these drugs in patients who undergo coronary bypass surgery.

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References


Platelet Hyperaggregability in Idiopathic Recurrent Deep Vein Thrombosis

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SUMMARY Studies of platelet function were performed in 30 patients with idiopathic recurrent venous thrombosis. Evidence of platelet hyperactivity was found in 14 patients who exhibited spontaneous platelet aggregation and in 13 patients who had evidence of circulating platelet aggregates. No other differences in clinical characteristics or coagulation parameters could be elucidated between these two subgroups. In nine patients who had radioactivity-labeled platelet survival studies, there was a good correlation between the platelet hyperactivity and shortened platelet survival. Spontaneous platelet aggregation was inhibited both in vivo and in vitro by aspirin.

ALTHOUGH IT HAD BEEN THOUGHT earlier that platelets did not play a significant role in the pathogenesis of deep vein thrombosis (DVT), several recent studies have reported shortened platelet survival in patients with recurrent venous thrombosis. These observations have revived interest in the possible pathogenetic relationship between platelets and venous thromboembolic disorders. In order to help elucidate this problem, the present study was performed to assess the platelet aggregability in 30 patients with idiopathic recurrent deep vein thrombosis and to evaluate the effects of antiplatelet agents.

Patients and Methods

All patients were evaluated at the University of Iowa Medical Center. Only patients with recurrent idiopathic deep vein thrombosis were included. Criteria for the selection of patients in this prospective study included 1) ob-
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