Analysis of Indium-111 Platelet Kinetics and Imaging in Patients with Aortic Grafts and Abdominal Aortic Aneurysms

Stephen R. Hanson, Harry F. Kotze, Henry Pieters, and Anthon du P. Heyns

To quantitatively characterize processes of platelet thrombus formation in vivo, the kinetics and incorporation into thrombus of autologous ln-111-labeled platelets were compared in six patients with aortic aneurysms and in seven patients with prosthetic aortic grafts. Although platelet survival was comparably shortened in both patient groups (mean, 5.8 days), the maximum radioactivity (percentage of whole body radioactivity) as determined by gamma camera imaging was higher in the aneurysms than in the grafts (3.3%±1.6% vs. 1.6%±1.1%, p=0.05). Maximum ln-111 uptake was also attained more quickly in the aneurysm patients (2.3±0.8 days vs. 3.5±1.3 days; p=0.07). The experimental platelet kinetic and imaging data were subsequently evaluated by compartmental analysis to estimate both normal and disease-related components of platelet destruction. This analysis indicated that deposited platelet radioactivity had a longer residence time on grafts (2.9±1.7 days vs. 1.4±0.9 days, p=0.07) but accumulated at a faster rate in aneurysms (5.0%±3.4% per day vs. 1.4%±0.9% per day, p=0.02). As determined by imaging, only a proportion of increased platelet destruction was specifically due to the aneurysms (55%±38%) or grafts (17%±11%, p=0.03). This result indicates additional components of platelet destruction unrelated to graft and aneurysm thrombus formation which, in some graft patients, may reflect a greater severity of vascular disease or other mechanisms causing a preferential shortening of platelet survival. Thus, the analytical approach described may be a useful one for discriminating components of in vivo platelet utilization including platelet removal due to normal hemostatic and senescent mechanisms, localized thrombus formation, and more generalized vascular disease.

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In patients with thromboembolic disorders and cardiovascular devices, measurements of reduced platelet lifespan and of localized platelet deposition have proven clinically useful for assessing the severity of disease and the effectiveness of antithrombotic therapy.1-9 Although these measurements are quantitative and objective, they are not readily interpreted in terms of rates of thrombus formation and dissolution. For example, platelet survival studies, which reflect all mechanisms of platelet utilization, cannot discriminate the interdependent processes of senescent platelet removal,1,6 normal platelet utilization for the maintenance of vascular integrity,10 and additional components of platelet destruction due to vascular disease. Similarly, measurements of localized platelet deposition by scintillation camera imaging or other methods may have little relation to overall platelet turnover.

In this study, we evaluated patients with aortic aneurysms and prosthetic aortic grafts since both are actively thrombogenic as demonstrated by shortened platelet survival times,1,2,6 imaging of ln-111 platelet deposition,3-8 and morphologic and clinical observations.11,12,13 In these patients, measurements of platelet lifespan have, in general, correlated poorly with measurements of ln-111 platelet deposition.6,14 Thus, in aortic graft recipients, platelet survival tends to normalize over the first postoperative year, while platelet accumulation onto such grafts may continue at a reduced rate for periods of up to 10 years and perhaps indefinitely.6,7 In addition, in both patient groups, it has been demonstrated by dynamic gamma camera imaging that the accumulation of platelet radioactivity may be nonlinear with time, suggesting an exchange or equilibration between circulating and deposited platelet pools.6,14 At present, the quantitative interpretation of these various observations remains uncertain.

In the aneurysm and prosthesis patients described in this report, the mechanisms of platelet removal (senescence, thrombosis, and hemostasis) were compared by a method of compartmental analysis of data from concurrent platelet kinetic and platelet imaging studies. It should be noted that it was not the objective of this study to
compare by scintillation camera imaging the uptake of In-111 platelets by aortic grafts and aneurysms, a process that has been described for both patient groups.\(^2\)\(^{-}\)\(^6\)\(^{14}\) Rather, we employed well-documented methods for platelet kinetics and imaging to more clearly define the different components of platelet utilization in these disorders and to estimate the steady-state rates of platelet destruction due to normal physiologic mechanisms and direct interactions with the grafts, aneurysms, and other sites of vascular disease.

**Methods**

**Patients**

Thirteen patients gave informed consent to take part in the study, which was approved by the Ethical Committee of the Provincial Administration and the University of the Orange Free State. Six patients (five men, one woman) having abdominal aortic aneurysms of similar size and location were diagnosed according to clinical criteria.\(^6\) The diagnosis was confirmed by ultrasonic examination. Seven other patients (five men, two women) had double velour Dacron aortobifemoral grafts (U.S. Catheter, Inc., Billerica, MA). The period from graft implantation ranged from 2 to 60 months (mean, 32±21 months). The mean age of the aneurysm patients was 60±12 years (45 to 75 years), and that of the prosthesis patients was 59±7 years (47 to 69 years). At the time of these studies, all grafts were patent as determined by Doppler scanning, and no patient was clinically symptomatic for peripheral ischemia or thromboembolism. Determination of platelet survival was also performed in six normal individuals ages 25 to 45 years. For a period of at least 2 weeks before each study, neither the patients nor the control subjects received any therapy that might have influenced platelet survival or function.

**Platelet Labeling and Survival Measurements**

Autologous platelets were isolated from whole blood under sterile conditions and were labeled with In-111-oxine as described.\(^15\)\(^{16}\) The labeled platelets were viable as documented by a normal aggregation response after exposure to adenosine 5'-diphosphate in vitro\(^15\) and by their normal recovery in the circulation after infusion (Tables 1 and 2).

The mean platelet lifespan was calculated by least-squares fitting the disappearance pattern of circulating In-111 platelet radioactivity to gamma functions.\(^17\)\(^{18}\) After the injection of labeled cells, the disappearance curve was generated by counting blood samples collected at 90 minutes and daily thereafter for 6 days. The recovery of labeled platelets in the circulation was calculated by estimating patient blood volumes and by back extrapolation of the disappearance curve to zero time.\(^17\)\(^{19}\)

**Platelet Imaging**

In-111 images were made with a Searle large-field-of-view scintillation camera and were analyzed with a Medical Data Systems A² image processing system. In patients with aortic aneurysms; the percentage of total injected radioactivity associated with the aneurysm was determined by using the geometrical mean method. This method corrects for the attenuation of gamma photons by intervening tissues.\(^15\)\(^{20}\)\(^{21}\) In brief, anterior and posterior images of the whole body were acquired daily; the count rates in the aneurysm and whole body were determined by region-of-interest analysis and were corrected for background radioactivity. Aneurysm radioactivity (counts/pixel) was corrected for sequestered bone marrow and circulating blood radioactivities by subtracting the count rate (corrected for background radioactivity) in an adjacent region positioned over an iliac artery. Whole body and aneurysm radioactivities were then corrected for In-111 decay (half-life, 2.8 days).

In patients with Dacron aortic prostheses, the deposition of In-111 platelets was measured as described elsewhere.\(^21\) The total amount of radioactivity injected was determined by counting the injectate with the scintillation camera. After administration of the labeled cells, 30-minute anterior images of the prostheses were acquired daily. The count rates in the prosthesis and in an adjacent area were determined by region-of-interest analysis. Prosthesis radioactivity was corrected for sequestered bone marrow and blood radioactivities by subtraction of the count rate in the adjacent area from that of the prosthesis. The attenuation of gamma photons by intervening tissue was measured by determining the depth of the prostheses and deriving an attenuation factor.\(^21\) Prosthesis depth ranged from 5 to 9 cm. The accuracy of this method of depth determination was confirmed in a human-like phantom with an In-111 source at depths ranging from 5 to 11 cm. The accuracy of determination of depth was 2.4%±5.1%. The prosthesis count rate was then corrected for tissue attenuation and radioisotope decay and was expressed as a percentage of the amount of radioactivity injected. Since little In-111-oxine radioactivity is lost from the whole body over time,\(^15\)\(^{16}\) the methods used to quantify the amount of radioactivity associated with both the aneurysms (fraction of whole body In-111) and arterial grafts (fraction of total In-111 dose) were essentially equivalent and in both cases reflected only deposited (noncirculating) radioactivity.

![Figure 1. Schematic representation of pathways of platelet destruction. Circulating platelets, in equilibrium with the splenic platelet pool, are removed by hemostatic, senescent, or disease-related mechanisms.](image-url)
Analysis of Platelet Kinetic and Imaging Data

The important pathways of platelet removal considered in this study are shown in Figure 1. In this scheme, circulating platelets are in dynamic equilibrium with the splenic platelet pool, which comprises about one-third of the total body platelets. Platelets are removed from the circulation by normal physiologic mechanisms (senescence and hemostasis). Therefore, this value was used in the subsequent analysis. Platelets are also lost from the circulation after direct interactions with thrombus associated with an arterial graft or aneurysm or at other sites of vascular disease.

In the present analysis, platelet utilization by both normal hemostatic and disease-related mechanisms were considered to be random processes, so that with increasing severity of disease, the extent of age-related platelet removal (senescence) would be reduced relative to the random component. The relative proportion of platelets destroyed by random vs. senescent mechanisms was calculated according to an application of the Mills-Dornhorst model:

\[
\frac{N(t)}{N(O)} = \frac{e^{-kt} - e^{-kT}}{1 - e^{-kT}} \tag{1}
\]

This model, which was originally developed to describe the survival of red cells, applies equally well to any element having a finite lifespan but which is also subject to risk of destruction by external hazards. In this formula, the number of labeled platelets circulating at time \(t\) after infusion, \(N(t)\), is determined by a maximum platelet lifespan \(T\), which will be reduced depending upon the rate of random platelet destruction \(k\) due to extrinsic mechanisms. Since the initial slope of the platelet survival curve, \(N(t)/N(O)\), intercepts the time axis at the mean platelet lifespan, it follows that:

\[
\tau = \frac{1 - e^{-kT}}{k} \tag{2}
\]

where \(\tau\) is the estimated mean platelet lifespan (days), and \(k\) is the rate of random platelet removal (fraction of circulating platelets per day). Equation 2 is the well-known expression of Mills-Dornhorst, which has been widely used for the interpretation of platelet survival data.

The application of Equations 1 and 2 to platelet survival curves obtained in normal subjects and in patients with decreased platelet production has suggested a finite platelet lifespan, \(T\), averaging approximately 10.5 days. Therefore, this value was used in the subsequent analysis. Similarly, a fixed hemostatic requirement of approximately 4700 platelets per microliter of whole blood per day has been determined.

With these approximations, both the normal and disease-related components of platelet utilization were calculated in the following manner. The fractional rate of random platelet destruction due to normal physiologic mechanisms (fraction per day) was determined by dividing the fixed platelet requirement (4700/µl/day) by the circulating platelet count (platelets per microliter) for each patient and normal subject. Given the mean platelet survival time \(\tau\) as determined in all individuals studied, the rate constant for random platelet removal \(k\) was calculated directly from Equation 2 with \(T=10.5\) days. It should be noted that when platelet lifespan is reduced significantly, as in the present studies, calculations of platelet destruction rates are relatively independent of assumed values of \(T\) within normal limits as well as possible variations in maximum lifespan of individual platelets in different subjects (i.e., when platelet survival is short, few cells reach their maximum possible lifespan).

The fractional rate of senescence platelet removal was calculated by subtracting the rate of random platelet destruction, \(kP\) (platelets per microliter per day), from the overall turnover rate of circulating platelets, \(P/\tau\), and dividing by the platelet count, \(P\). The fractional rate of senescence platelet removal was therefore calculated as:

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\]
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| Table 1. Platelet Utilization in Patients with Aortic Aneurysms |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | Platelet Count ($10^9$) | Recovery (%) | Lifespan (days) | % Whole body | Time (days) | Average residence (days) | Total destruction rates (% per day) | Aneurysm | Hemostasis | Other | Senescence | Random |
| 1 | 198 | 78 | 6.29 | 2.0 | 2.2 | 1.1 | 10.8 | 2.4 | 3.2 | 5.2 | 5.1 | 38 68 |
| 2 | 303 | 79 | 4.21 | 3.1 | 3.0 | 2.3 | 21.2 | 1.6 | 2.9 | 16.7 | 2.6 | 15 89 |
| 3 | 285 | 57 | 4.67 | 3.7 | 3.4 | 2.8 | 18.3 | 1.7 | 2.9 | 13.7 | 3.1 | 17 85 |
| 4 | 230 | 84 | 8.46 | 1.0 | 1.6 | 0.6 | 4.3 | 2.0 | 2.2 | 0.1 | 7.5 | 96 36 |
| 5 | 236 | 58 | 4.96 | 5.3 | 1.7 | 0.8 | 16.7 | 2.0 | 9.7 | 5.0 | 3.5 | 66 83 |
| 6 | 205 | 59 | 6.13 | 4.4 | 1.6 | 0.6 | 11.4 | 2.3 | 9.1 | 0.0 | 4.9 | 100 70 |
| Mean | 243 | 69 | 5.79 | 3.3 | 2.3 | 1.4 | 13.8 | 2.0 | 5.0 | 6.8 | 4.5 | 55 72 |
| 1 SD | 43 | 12 | 1.54 | 1.6 | 0.8 | 0.9 | 6.1 | 0.3 | 3.4 | 7.0 | 1.8 | 38 19 |
| Normals | 260 | 74 | 8.95 | 0 | 0 | 0 | 1.9 | 1.9 | 0 | 0 | 9.4 | 0 17 |
| 1 SD | 43 | 17 | 0.75 | 0.3 | 0 | 0 | 0.3 | 0.3 | 1.0 | 3 | |

Theoretically derived parameters included the average residence time for aneurysm-associated platelets ($\theta$) and rates of platelet destruction due to senescence and random mechanisms (hemostasis, aneurysm, other disease). % Aneurysm (column 13) is the percentage of pathological platelet destruction (aneurysm plus other) that can be attributed directly to the aneurysm. % Random (column 14) is the fraction of platelets destroyed by all random (vs. senescent) mechanisms throughout their lifespan. The calculations are described in the Methods section.

Equation or lysis, and $N(t)/N(O)$ is the fraction of injected platelets still circulating at time $t$ as given by Equation 1. Or, in brief, Equation 3 states that the rate of change of deposited radioactivity at time $t$, $dl(t)/dt$, is equal to the deposition rate, $K\cdot N(t)/N(O)$, minus the removal rate, $l(t)/0$, of platelet- associated Indium-111. The general solution to Equation 3 is obtained by direct integration as:

$$ l(t) = \theta K \left[ e^{-kT} \frac{(1-e^{-kT})}{1-kT} - e^{-\theta T} \right] $$

Equation 4 gives deposited Indium-111 activity, $l(t)$, as a function of time and four parameters ($k$, $K$, $T$, $\theta$) and was fitted to the dynamic imaging data obtained in the patients with grafts and aneurysms to determine values for the parameters, $K$ and $\theta$. In the curve fitting procedure, the value of $T$ was assumed to be equal to 10.5 days, $k$ was determined a priori from Equation 2, and the parameters, $K$ and $\theta$, were determined for each patient by least-squares regression analysis. The apparent maximum value of platelet uptake and the time required to reach this maximum were also calculated for each patient from the best-fit equation. By subtracting the components due to normal hemostasis and thrombosis associated with the grafts or aneurysms from the total rate of random platelet destruction, an additional component of platelet removal (presumably due to other disease processes) was calculated.

**Curve Fitting and Statistical Analyses**

Curve fitting of prosthesis and aneurysm time/activity data to Equation 4 was performed on a microcomputer (IBM PC-AT) according to the nonlinear least-squares iteration procedure of Snedecor and Cochran.26 Comparisons were made by using Student's t test (two-tailed) for unpaired sample groups. The data are expressed as the mean values±1 SD.

**Results**

**Platelet Survival Studies**

The mean values for platelet count and platelet recovery were similar (Tables 1 and 2) and not different from the control values obtained in six normal subjects ($p>0.1$). The mean platelet lifespans were also equivalent, averaging 5.79±1.54 days in the aneurysm patients (Table 1) and 5.75±1.46 days in the group with aortic prostheses (Table 2). The composite platelet disappearance patterns obtained in the patients and normal subjects are shown in Figure 2. In the aneurysm and graft patient groups, the averaged best-fit platelet survival curves derived from gamma function modeling were

**Figure 2. Platelet survival curves in patients and normal subjects.** In-111-platelet disappearance patterns were equivalent in patients with aortic aneurysms (○) and aortic Dacron grafts (■). Platelet clearance was increased as compared to normal control subjects (●). For both patient groups, mean platelet lifespans were reduced significantly ($p<0.01$) vs. control values (see Results).
Platelet Imaging Studies

Despite the similarities in platelet kinetics between the aneurysm and graft patients, dynamic imaging demonstrated markedly dissimilar patterns of In-111 platelet accumulation onto the abnormal endovascular surfaces (Figure 3). The maximum accumulation of platelet radioactivity and the time required to reach this peak value after injection of the labeled cells were calculated directly from Equation 4 following least-squares fitting to the time-radioactivity data for each patient. The aneurysms accumulated platelets more rapidly, with the peak uptake of radioactivity observed at 2.3±0.8 days compared to virtually coincident. In both cases, platelet survival was reduced significantly (p<0.01) compared to normal control values, which averaged 8.95±0.75 days.

Since platelet survival was comparably shortened in both patient groups, the calculated rates of total random platelet destruction (excluding senescent platelet removal) were also equivalent, and averaged 13.8%±6.1% per day in the aneurysm group and 13.8%±5.7% per day in the prostheses patents. These rates were significantly greater (p<0.0001) than the control values of 1.9%±0.3% per day, which in the normal individuals reflected only hemostatic platelet utilization (Tables 1 and 2). Similarly, senescent platelet removal averaged 4.4%±1.7% per day in the aneurysm patients and 4.4%±1.7% per day in the graft recipients (p=0.5). These rates were significantly reduced as compared to control values (9.4%±1.0% per day, p<0.001). Also, the fraction of platelets that were removed by random mechanisms throughout their lifespan (% random, Tables 1 and 2) was elevated in both the aneurysm patients (72%±19%) and graft patients (73%±19%) relative to the control group values (17%±3%, p<0.001). The platelet requirement to support hemostasis and/or other normal physiologic mechanisms averaged 1.8% to 2.0% per day in both the patient groups and normal subjects.

Table 2. Platelet Utilization in Patients with Aortic Prostheses

<table>
<thead>
<tr>
<th>Patient</th>
<th>Platelet Radioactivity</th>
<th>Average residence</th>
<th>Platelet destruction rates (% per day)</th>
<th>% Pros thesis</th>
<th>% Random</th>
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</thead>
<tbody>
<tr>
<td>Normal</td>
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<tr>
<td>1 SD</td>
<td>60</td>
<td>13</td>
<td>1.46 (1.1)</td>
<td>0.75</td>
<td>0.3</td>
</tr>
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<td>17</td>
<td>0.39 (0.3)</td>
<td>0.07</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Theoretically derived parameters included the average residence time for prosthesis-associated platelets (δ) and rates of platelet destruction due to senescence and random mechanisms (hemostasis, prosthesis, other disease). % Prosthesis (column 13) is the percentage of pathological platelet destruction (prosthesis plus other) that can be attributed directly to the prosthesis. % Random (column 14) is the fraction of platelets destroyed by all random (vs. senescent) mechanisms throughout their lifespan. The calculations are described in the Methods section.

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These differences between patient groups, which were demonstrated experimentally by dynamic imaging (Figure 3), were also reflected in the parameters derived from the analysis (Equation 4). Thus, the average residence time (δ) for aneurysm-associated radioactivity was 1.4±0.9 days, vs. an average residence time of 2.9±1.7 days for graft-associated In-111 radioactivity (p=0.07). The rate constant (K) for platelet deposition in aneurysms ("Aneurysm," Table 1) averaged 5.0%±3.4% of circulating platelets per day and was significantly greater (p=0.02) than the rate of platelet deposition onto the aortic prostheses, 1.4±0.8% per day ("Prosthesis,"...
These experimental observations are generally consistent with previous clinical studies in patients with aortic aneurysms and in patients with Dacron aortic prostheses, although the patterns of nonaneurysm components of platelet removal, platelet destruction by the aneurysms was clearly a major factor contributing to shortened platelet survival in most patients. However, in the seven prosthesis patients, the extent of abnormal platelet destruction that could be attributed directly to the vascular grafts (% Prosthesis, Table 2) averaged only 17%±11% (range, 6% to 40%). The difference between the aneurysm and graft patients in this regard was statistically significant (p=0.03).

**Discussion**

While both arterial grafts and aneurysms are thrombogenic, these vascular abnormalities differ in terms of their pathologic mechanisms of thrombus formation. Important variables may include the effects of altered blood flow patterns, the presence of synthetic (Dacron) vs. biologic (aneurysm) nonendothelialized surfaces and differences in the relative importance of platelet-mediated vs. coagulation-mediated pathways of platelet recruitment. Thus, aneurysms may contain large visible thrombi, while grafts generally accumulate thinner layers of platelets and compacted fibrin.

In the present study, the mean lifespan of circulating platelets was significantly and comparably shortened, both in patients with aortic aneurysms and in patients with Dacron aortic prostheses, although the patterns of In-111 platelet deposition, as determined from gamma camera imaging, were markedly different in the two patient groups. The aneurysms accumulated approximately twice as much injected In-111 platelet radioactivity as the vascular prostheses, and the maximum incorporation of isotope was observed at an earlier time in the aneurysm patients. Thus, measurements of platelet survival alone were clearly unable to predict the rate or extent of platelet incorporation by the grafts or aneurysms, suggesting additional and perhaps unrecognized components of platelet destruction in these disorders. These experimental observations are generally consistent with previous clinical studies in patients with aortic grafts and aneurysms. It should be noted that the control subjects for platelet survival studies were of a younger average age than the patients, and it is conceivable that the normal platelet lifespan may decrease modestly with advancing age. Nonetheless, platelet survivals in both patient groups were considerably reduced as compared to the generally accepted normal value of 9 to 10 days.

The analytical approach used to estimate the rates of platelet removal by different normal and pathological mechanisms allowed a broader interpretation of these findings. The results were well explained quantitatively on the basis that the aneurysms caused more destruction of circulating platelet than the grafts (5.4%±3.0% per day vs. 1.4%±0.8% per day), with platelets deposited in aneurysms having a shorter residence time than platelets associated with the Dacron prostheses (1.4±0.9 days vs. 2.9±1.7 days). Since rates of thrombus formation and dissolution are equivalent under steady-state conditions, the observations that aneurysms accumulated platelets more quickly and to a greater extent suggests that they are typically more thromboembolic/thrombolytic, as well as more thrombogenic, than vascular prostheses. This rapid turnover of aneurysm (vs. graft) thrombi could reflect a more active thrombin-mediated deposition process and locally enhanced fibrinolysis and/or the formation of thrombus, which is inherently less stable toward fluid shear forces or more susceptible to degradation by thrombolytic mechanisms. This concept is also consistent with clinical observations that aneurysms may produce a chronic consumption coagulopathy, while arterial grafts selectively remove platelets without increased turnover of fibrinogen and plasminogen or elevation of plasma levels of fibrinogen/fibrin degradation products. Our results are also consistent with the increased frequency of clinical embolic phenomena observed in aneurysm patients and support the view that aneurysm segment reconstruction by vascular grafting is therapeutically warranted.

Graft-related platelet deposition accounted for a relatively minor proportion of increased platelet turnover above normal physiologic levels (17%±11%) as compared to the aneurysm patients (55%±38%). This may explain, in part, the poor correlation found between platelet lifespan and maximum graft platelet deposition and may be consistent with observations of reduced platelet lifespan in preoperative atherosclerotic patients. The additional components of platelet removal could be related to unrecognized (by In-111 imaging) sites of vascular disease, particularly in the graft recipients. While there is no reason to speculate that graft patients have more unrecognized preoperative atherosclerosis than aneurysm patients, in the present study the graft patients were evaluated an average of 32 months postoperatively. Over this interval, significant progression of disease at sites removed from the grafts seems likely, at least in some patients. Alternatively, this result could reflect a reduced intrinsic lifespan of individual platelets, which continued to circulate, perhaps as a consequence of reversible or sublethal platelet interactions. We consider this explanation less likely since it has been shown in rabbits that platelets degranulated in vitro survive normally in vivo and that in primates with vascular prostheses, platelet survival and function are normal and independent of platelet aging in the circulation after platelet cross-transfusion into normal recipients or after removal of the thrombogenic stimulus. The analytical approach used here is consistent with either possibility since it demonstrates only that there is an additional
component of platelet removal (i.e., a shortening in platelet survival to a degree greater than expected) occurring through mechanisms that remain to be defined. Despite the heterogeneity of each patient population, the two groups differed most significantly with regard to the theoretically predicted rates of platelet deposition onto grafts vs. aneurysms (p=0.02) and were less well differentiated on the basis of experimental measurements such as the mean platelet survival time (p>0.5) or the maximum incorporation of radioisotope (p=0.05). This approach may, therefore, have a greater sensitivity for distinguishing thromboembolic disorders and for assessing the effects of therapy. In addition, information on platelet deposition rates and platelet thrombus turnover may be important in certain settings for the proper selection of radioisotopes or for the design of thrombus-directed probes (e.g., labeled monoclonal antibodies) to be used for thrombus detection. Moreover, this analytical method may also be useful for the interpretation of clinical assessments of peripheral thrombembolism or ischemia or for correlating laboratory measurements of ongoing thrombosis such as plasma levels of platelet specific proteins and other markers of active coagulation and fibrinolysis.

Finally, a plateau and subsequent decrease in graft or aneurysm radioactivity was observed in each patient studied, demonstrating both active platelet uptake and the reduction of platelet-containing thrombus, presumably by microembolization and/or lytic mechanisms. This phenomenon has generally not been demonstrated in previous reports, perhaps since imaging was not performed at later time points or, because the presentation of imaging data simply normalized with respect to reference areas or circulating blood radioactivity does not fully exploit the information contained in the dynamic curves. Thus, while measurements such as mean platelet lifespan and maximum incorporation of isotope have clearly proven useful for thrombus detection, we believe that the additional determination of both normal and pathological components of platelet destruction will provide a more thorough characterization of platelet mechanisms in thromboembolic disease.

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References


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