Mean Platelet Volume and Integrin Alleles Correlate With Levels of Integrins α1Ibβ3 and α2β1 in Acute Coronary Syndrome Patients and Normal Subjects

Thomas J. Kunicki, Shirley A. Williams, Diane J. Nugent, Mark Yeager

Objective—The interindividual variation in platelet α2β1 exceeds a 2-fold variance in platelet α1Ibβ3 level. Our objective was to parse the contribution of mean platelet volume (MPV) and integrin gene alleles to this variation in large cohorts of patients with acute coronary syndrome (ACS) and normal subjects.

Methods and Results—Platelet α1Ibβ3 and α2β1 levels were measured by flow cytometry in whole blood from 320 ACS patients and 128 normal subjects and compared with MPV, platelet count, ITGA2 rs28095, and ITGB3 rs5918 alleles. In all subjects, a strong direct correlation was found between MPV and α1Ibβ3 level (P<0.001). Neither MPV nor α1Ibβ3 level correlated with ITGB3 rs5918 alleles. In the case of α2β1 level, MPV contributed modestly, whereas ITGA2 rs28095 exerted a greater effect. An inverse correlation was found between MPV and the rs28095 minor allele.

Conclusion—MPV is the major effector of platelet α1Ibβ3 level, whereas the ITGA2 rs28095 alleles influence α2β1 level more than MPV does. The rs28095 minor allele, associated with lower MPV, likely exerts this effect via the influence of α2β1 on megakaryocyte maturation. Because of the hyperactivity of larger platelets, MPV is an accurate metric of risk for adverse outcome in ACS. (Arterioscler Thromb Vasc Biol. 2012;32:147-152.)

Key Words: arterial thrombosis ■ platelets ■ thrombosis ■ integrins ■ mean platelet volume

Differences in the level of integrins expressed on the surface membranes of platelets can have a significant effect on platelet reactivity and adverse outcomes in a variety of thrombotic and hematologic dyscrasias. Quantitative differences have been recorded in the plasma membrane levels of 2 relevant integrins, α2β1 (a receptor for collagen) and α1Ibβ3 (a receptor for fibrinogen and von Willebrand factor). Quantitative measurements of platelet surface membrane α1Ibβ3 among normal subjects, using direct binding of radiolabeled monoclonal antibodies or flow cytometry, have demonstrated a 2- to 3-fold difference, ranging from 25,000 to 75,000 molecules per platelet.1–5 An allelic variation involving either the α1Ib or β3 gene (ITGA2B and ITGB3, respectively) that can account for this difference has not yet been identified. In the case of α2β1, the range observed among normal subjects is greater, reported to be as high as 10-fold, and is strongly associated with allelic variants of the α2 gene ITGA2.6–8

The total number of integrin molecules and other receptors on platelets is influenced to a large extent by the total surface area of plasma membrane and consequently the mean platelet volume (MPV), which itself has a very strong genetic component.7,8 Giles et al10 noted a 7% increase in MPV in patients with acute myocardial infarction (n=14) and a 20% increase in platelet α1Ibβ3 relative to control subjects (n=14). In addition, Yakushkin et al11 recently provided the first association between MPV and α1Ibβ3 levels in acute coronary syndrome (ACS) patients (n=65).

The objective of this study was to parse the relative contribution of MPV and allelic variation to the basal levels of α2β1 and α1Ibβ3 in a larger cohort of patients with ACS (n=341), as well as a large cohort of normal subjects (n=128). Our results indicate that the relative contribution of MPV and allelic diversity differs for both α2β1 and α1Ibβ3, and our findings suggest that MPV is an accurate marker for risk in ACS.

Methods

Subjects

Blood from normal, healthy volunteers was obtained through the Normal Blood Drawing Service of the Scripps Research Institute and from the former Scripps General Clinical Research Center. Blood from patients with ACS was obtained through the Scripps General Clinical Research Center. This research study was approved by the Scripps Research Institute institutional review board, and all participants gave written informed consent.

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ACS patients included in this study were referred to the Division of Cardiovascular Diseases of Scripps Clinic for coronary angiography, with or without a preexisting history of ACS, as defined by American Heart Association/American College of Cardiology guidelines.12

Quantitation of $\alpha_{\text{IIb}}\beta_3$ and $\alpha_2\beta_1$ by Flow Cytometry

12F1 and 8C12, murine monoclonal antibodies specific for $\alpha_{\text{IIb}}\beta_3$, and AP2, a murine monoclonal antibody specific for $\alpha_{\text{IIb}}\beta_3$, were used to measure platelet plasma membrane levels of these integrins by flow cytometry of whole blood samples, as previously described.13,14

Using a 19-G butterfly needle and Vacutainer tubes, an initial volume of blood was discarded, and a subsequent blood sample was anticoagulated by mixing with one-sixth volume acid citrate dextrose-formula A. Not later than 4 hours after phlebotomy, 5 $\mu$L of blood was mixed with 40 $\mu$L of 2 mmol/L MgCl$_2$, 138 mmol/L NaCl, 12 mmol/L NaHCO$_3$, 2.6 mmol/L KCl, pH 7.4 (Tyrode buffer), containing 1% (wt/vol) bovine serum albumin. Five microliters of primary antibody (100 $\mu$g/mL AP2, 12F1, 8C12, or nonimmune mouse IgG1) was then added to the mixture, which was gently inverted and incubated for 30 minutes at room temperature.

Fluorescence intensity obtained from addition of control nonimmune mouse IgG1 was then added to the mixture, which was incubated for an additional 30 minutes at room temperature. Then, 950 $\mu$L of ice-cold 1% (v/v) parafomaldehyde in phosphate-buffered saline pH 7.4 was added, and the sample was stored at 4°C in the dark until it was assayed by flow cytometry, which was performed within the subsequent 3 days. Neither the time delay between phlebotomy and antibody assay (1–4 hours) nor the delay between antibody assay and flow cytometry (1–3 days) had an effect on the outcome of receptor antibody assay (1–4 hours) nor the delay between antibody assay and flow cytometry (1–3 days). Neither the time delay between phlebotomy and antibody assay (1–4 hours) nor the delay between antibody assay and flow cytometry (1–3 days) had an effect on the outcome of receptor antibody assay (1–4 hours) nor the delay between antibody assay and flow cytometry (1–3 days).

Levels of bound monoclonal antibody were expressed as geometric mean fluorescence intensity after subtraction of geometric mean fluorescence intensity obtained from addition of control nonimmune murine IgG1.

Measurement of Platelet Count and MPV

Whole blood platelet count and MPV were measured using a Coulter 9000 apparatus (Mallinckrodt Baker, Phillipsburg, NJ).

Genotyping

Genotypes were determined using primer sequences previously reported in a primer extension-based assay13 or a customized Nanogen-based single-nucleotide polymorphism analysis (Nanogen Inc., San Diego, CA, USA).14 When necessary, single-nucleotide polymorphisms were confirmed by direct Sanger sequencing. The single-nucleotide polymorphisms analyzed in this study were ITGB3 rs5918 (minor allele frequency = 0.17)17 and ITGA2 rs28095 (minor allele frequency = 0.38).6

Statistics

Statistical calculations were performed using SigmaStat, version 3.01 (SPSS Inc, Chicago, IL). For continuous variables (eg, platelet count, MPV, age, $\alpha_2\beta_1$ level, $\alpha_{\text{IIb}}\beta_3$ level), descriptive statistics were calculated and reported as mean and standard deviation. Linear and multilinear regression, using the adjusted $r^2$ statistic, was used to determine the contribution of independent variables that predict the dependent variable. Associations between discontinuous variables (eg, single-nucleotide polymorphisms) and continuous variables were described using the Pearson product moment correlation or Spearman rank order association, and probability values were corrected for multiple testing. Pairwise associations between variables were analyzed by 1-way ANOVA, Kruskal-Wallis 1-way ANOVA on ranks, or $t$ test. All tests are 2-sided and considered significant at $P<0.05$ after correction for multiple testing. The coefficient of variation is defined as the ratio of the standard deviation to the mean (SD/mean).

Results

Subject Parameters

The ACS patient cohort was deidentified, including sex and age. In the control subject cohort, the percentage of males was 51%, and the mean age was 39.3 ± 9.2 years. The MPV of ACS patients (7.46 ± 1.43 fl; n = 109) was not significantly different ($P = 0.079$) from that of control subjects (7.11 ± 1.64 fl; n = 128), and the same was true for the platelet count (214 ± 58 and 225 ± 56 × 10$^{-3}$/μL, respectively; $P = 0.219$) (Supplemental Table I, available online at http://atvb.ahajournals.org).

Quantitation of Integrin Levels

Intradonor variation in $\alpha_2\beta_1$ or $\alpha_{\text{IIb}}\beta_3$ levels was analyzed using 11 control and 6 ACS subjects by flow cytometric measurements performed on 2 separate occasions at least 30 days apart (Supplemental Figure 1). The coefficient of variation in geometric mean fluorescence intensity for each of the three monoclonal antibodies was as follows: AP2, 0.11; 12F1, 0.21; and 8C12, 0.10. On this basis, bound 8C12 is a more precise metric than bound 12F1 for the quantitation of $\alpha_2\beta_1$. The intersubject variation was similar in either ACS patients or control subjects with regard to platelet levels of $\alpha_{\text{IIb}}\beta_3$ (Figure 1) or $\alpha_2\beta_1$ (Figure 2), as summarized in Table 1. The metric of $\alpha_2\beta_1$ depicted in Figure 2 was bound 8C12, but

![Figure 1](http://atvb.ahajournals.org)

Interdonor variation in platelet-bound AP2 as a metric of the level of integrin $\alpha_{\text{IIb}}\beta_3$. Geometric mean fluorescence intensity (GMFI) is plotted on the ordinate. Measurements for each individual (320 acute coronary syndrome [ACS] patients; 128 controls) are plotted in chronological order (left to right) on the abscissa.

![Figure 2](http://atvb.ahajournals.org)

Interdonor variation in platelet-bound 8C12 as a metric of the level of integrin $\alpha_{\text{IIb}}\beta_3$. Geometric mean fluorescence intensity (GMFI) is plotted on the ordinate. Measurements for each individual (320 acute coronary syndrome [ACS] patients; 128 controls) are plotted in chronological order (left to right) on the abscissa.

Figure 1. Interdonor variation in platelet-bound AP2 as a metric of the level of integrin $\alpha_{\text{IIb}}\beta_3$. Geometric mean fluorescence intensity (GMFI) is plotted on the ordinate. Measurements for each individual (320 acute coronary syndrome [ACS] patients; 128 controls) are plotted in chronological order (left to right) on the abscissa.

Figure 2. Interdonor variation in platelet-bound 8C12 as a metric of the level of integrin $\alpha_{\text{IIb}}\beta_3$. Geometric mean fluorescence intensity (GMFI) is plotted on the ordinate. Measurements for each individual (320 acute coronary syndrome [ACS] patients; 128 controls) are plotted in chronological order (left to right) on the abscissa.
similar findings were made for bound 12F1 (Supplemental Figure II), and very high correlation was observed between bound 8C12 and 12F1 (adjusted $r^2 = 0.583; P < 0.001$) (Supplemental Figure III).

Multivariate analysis in ACS patients (Supplemental Table II) indicated a statistically significant direct association between MPV and the level of AP2 ($P < 0.001$), 12F1 ($P < 0.001$), or 8C12 ($P = 0.001$) bound per platelet (geometric mean fluorescence intensity). Not unexpectedly, there was also a very strong direct correlation between platelet-bound 12F1 and 8C12 (data not shown). Likewise, among control subjects (Figure 4), MPV accounted for 49% (bound AP2) of the variation in levels of $\alpha_{IIb}\beta_3$, whereas identical findings were observed for bound 12F1 as for bound 8C12 (data not shown). As shown in Table 2, the $ITGA2$ rs28095 alleles exert a significant effect on the levels of platelet $\alpha_{IIb}\beta_3$. In addition, there was a significant negative correlation between the rs28095 minor allele T and MPV itself. The presence of even 1 minor allele was associated with a decreased MPV. This likely accounts for the weak but significant correlation between the presence of the minor allele and decreased bound AP2 (that is, a decreased level of $\alpha_{IIb}\beta_3$).

Table 2. Control Subjects: Influence of $ITGA2$ rs28095

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<th>rs28095</th>
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<th>8C12</th>
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<tr>
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<td>49</td>
<td>7.7±1.7</td>
<td>8.2±2.0</td>
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<td>CT</td>
<td>58</td>
<td>6.8±1.6</td>
<td>5.2±1.2</td>
<td>10.1±2.5</td>
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<tr>
<td>TT</td>
<td>21</td>
<td>6.5±1.1</td>
<td>3.2±1.1</td>
<td>6.1±1.8</td>
<td>286.8±32.3</td>
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<table>
<thead>
<tr>
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<th>CC vs CT</th>
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<td>$&lt;0.01^*$</td>
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</table>

MPV indicates mean platelet volume.

*The power of the performed test with $\alpha = 0.05$ is $\geq 0.80$.

Table 1. Platelet Integrin Levels

<table>
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<th>Antibody</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>CV</th>
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<td>AP2</td>
<td>320</td>
<td>288.6*</td>
<td>61.7</td>
<td>113.3</td>
<td>547.8</td>
<td>0.21</td>
<td>0.898</td>
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<td>12F1</td>
<td>320</td>
<td>6.0</td>
<td>2.6</td>
<td>1.0</td>
<td>15.2</td>
<td>0.43</td>
<td>0.810</td>
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<tr>
<td>8C12</td>
<td>320</td>
<td>11.0</td>
<td>4.4</td>
<td>1.7</td>
<td>32.8</td>
<td>0.40</td>
<td>0.752</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; CV, coefficient of variation.

*Geometric mean fluorescence intensity.

**Discussion**

MPV is the most common metric of platelet size and correlates very well with platelet reactivity. Larger platelets have greater prothrombotic potential, and elevated MPV is associated with increased platelet aggregation, thromboxane synthesis, $\beta$-thromboglobulin release, and expression of adhesion molecules. A relationship between MPV and platelet count has not been established, and most studies do not find a significant correlation between these 2 variables. On the other hand, no correlation was observed between the level of bound 12F1 and 8C12 (data not shown). Likewise, among control subjects (Figure 4), MPV accounted for 49% (bound AP2) of the variation in levels of $\alpha_{IIb}\beta_3$, whereas identical findings were observed for bound 12F1 as for bound 8C12 (data not shown). As shown in Table 2, the $ITGA2$ rs28095 alleles exert a significant effect on the levels of platelet $\alpha_{IIb}\beta_3$. In addition, there was a significant negative correlation between the rs28095 minor allele T and MPV itself. The presence of even 1 minor allele was associated with a decreased MPV. This likely accounts for the weak but significant correlation between the presence of the minor allele and decreased bound AP2 (that is, a decreased level of $\alpha_{IIb}\beta_3$).
other hand, several studies have demonstrated a statistically
significant association between MPV and acute myocardial
infarction or other cardiovascular events, even after adjusting
for platelet count,21–23 whereas the majority of studies have
not found a statistically significant association between in-
creased platelet count and incidence of acute myocardial
infarction, restenosis, or long-term mortality in cardiovascu-
lar disease.21,22,24,26

Previous studies have found that the levels of \( \alpha_{\text{IIb}} \beta_3 \) and
glycoprotein (GP)Ib\( \alpha \) vary over a 2-fold range among normal
subjects or patients with ACS.5,11,27–29 As expected, these
increased levels of \( \alpha_{\text{IIb}} \beta_3 \) are associated with increased
platelet reactivity and decreased sensitivity to \( \alpha_{\text{IIb}} \beta_3 \) antago-
nists.11,28 Very recently, it has also been shown that the ability
of platelets to support thrombin generation may be defined by
a subpopulation of larger, perhaps reticulated, platelets bear-
ing nondissociable platelet-derived Factor Va and exhibiting
increased levels of the collagen receptor \( \alpha_{\text{IIb}} \beta_3 \) and
\( \alpha_{\text{Ia}} \beta_2 \).30 However, this procoagulant subpopulation
can represent as little a 8% to as much as 54%, depending on
the donor, and an association with MPV has not been
established. As in most studies of platelet physiology, another
confounding factor is platelet activation, because this has
been shown to increase the level of surface receptor expres-
sion, including \( \alpha_{\text{IIb}} \beta_3 \), by as much as 40% when the activa-
tion is conducted in vitro.31,32 However, the percentage of
platelet activation (percentage of maximum expression of
total \( \alpha_{\text{IIb}} \beta_3 \)) in whole blood from patients is not likely to be
as high as the maximum inducible in vitro. On the other hand,
there are no accurate data concerning the effect of platelet
activation on platelet volume, but any increase would cer-
tainly be affected by the nature of the agonist and the
conditions of the medium. As a relevant observation, it has
been reported that during storage of platelet concentrates,
the surface activation markers CD62P and PAC-1 increase up to
600% and 150%, respectively, but there is absolutely no
significant change in MPV.33 The best way to minimize this
confounding factor of platelet activation during platelet pro-
cessing is to fix platelets in whole blood before flow
cytometric analysis, as we have done in this study.

Our study examines larger cohorts of both ACS patients
and control subjects than hitherto reported and confirms that
levels of \( \alpha_{\text{Ia}} \beta_2 \) vary at least 2-fold. In addition, our results
establish that MPV accounts for 49% of the observed varia-
tion. Logically, the number of glycoprotein receptors per
platelet increases proportionately with MPV, and because
receptor density remains unchanged,11 the increase is likely
due to the increased surface area of platelet plasma mem-
brane. Although we found no influence of the common
\( ITGB3 \) alleles on expression level, a genetic component
cannot be ruled out, perhaps because of as yet unidentified
extragenic regulatory elements. At the same time, it is not
likely that \( ITGB3 \) rs5918 is in linkage disequilibrium with
genetic variants that contribute to MPV, because our results
and the results of a previous study34 found that neither MPV
nor platelet count correlates with the \( ITGB3 \) rs5918 minor
allele.

In the case of \( \alpha_2 \beta_1 \), the genetic component of variation is
more profound and exceeds the contribution of MPV. We
previously described a genetically determined variation in the
level of the collagen receptor \( \alpha_2 \beta_1 \) on platelets and argued
that this variation is largely independent of MPV. The fact
that genetically determined \( \alpha_2 \beta_1 \) levels are found on cells
other than platelets is consistent with this argument. None-
theless, differences in MPV must contribute to the overall
variability, and our objective in this study was to parse the
contributions of MPV and the genetic component. Our
findings indicate that allelic differences in \( ITGA2 \) rs28095,
previously documented to profoundly influence transcription
of this gene, are the most important factor that regulates \( \alpha_2 \beta_1 \)
levels (46% based on bound 8C12; 57% based on bound
12F1), with MPV exerting an independent but smaller con-
tribution (13% based on bound 8C12; 8% based on bound
12F1).

Perhaps the most intriguing finding of our study is the
inverse association of the \( ITGA2 \) rs28095 minor allele T with
MPV. This suggests that expression levels of integrin \( \alpha_2 \beta_1 \)
may be involved in the regulation of platelet size, which is
certainly consistent with previous observations that \( \alpha_2 \beta_1 \)
modulation of proplatelet formation is an important factor in
the production and size of platelets.35,36 In the bone marrow,
the interaction of hematopoietic stem cells with osteoblasts
inhibits megakaryocyte maturation and proplatelet formation
through a mechanism that is dependent on the engagement
of collagen I by megakaryocyte \( \alpha_2 \beta_1 \).37 Enhanced binding of
megakaryocyte \( \alpha_2 \beta_1 \) to collagen I attenuates or delays pro-
platelet formation. Conversely, in Wiscott-Aldrich syndrome
and X-linked thrombocytopenia, a deficiency of the protein
WASP is associated with loss of \( \alpha_2 \beta_1 \)-mediated inhibition of
proplatelet formation, resulting in ectopic shedding of
platelets into the bone marrow space and microthrombocyto-
penia.35 Likewise, familial thrombocytopenia 2 is characterized
by mutations of the gene ANKRD26, decreased MPV, and
decreased expression of integrin \( \alpha_2 \beta_1 \).37 Thus, it is reasonable
that megakaryocyte expression of the rs28095 minor allele T,
which is known to attenuate \( ITGA2 \) transcription, thereby
leading to diminished \( \alpha_2 \beta_1 \) expression and reduced platelet
adhesion to collagen I, may also result in a mild form of
accelerated platelet formation and consequently a decrease in
MPV.

The degree of \( \alpha_{\text{Ia}} \beta_2 \) variation that is observed likely
influences platelet reactivity and the risk of thrombosis but
can also complicate the detection of carriers of the hereditary

Figure 4. Control subjects: relationship between mean platelet
volume (MPV) and level of bound AP2 (left) or 8C12 (right). Cor-
responding regression lines are plotted. For AP2, adjusted
\( r^2=0.491, P<0.001 \); for 8C12, adjusted \( r^2=0.056, P<0.001 \). The
powers of the performed tests with \( \alpha=0.05 \) were 1.0 for MPV vs
AP2 and 0.82 for MPV vs 8C12.
deficiency of αIIbβ3, Glanzmann thrombasthenia (GT). In one of the earliest studies, McEver et al.1 used radiolabeled monoclonal antibody Tab to measure αIIbβ3 on platelets of 4 GT patients and their immediate family members. They found 30,000 to 50,000 molecules bound to platelets of normal subjects and normal members of the GT families, but 20,000 to 35,000 molecules bound per platelet by obligate GT heterozygotes (n=5). Four other possible GT heterozygotes expressed 15,000 to 30,000 molecules per platelet. This was the first indication that the range of platelet αIIbβ3 expression in GT heterozygotes might overlap the range of expression in normal subjects. Coller et al.3 produced similar results using radiolabeled monoclonal antibody 10E5, finding a range of αIIbβ3 levels in 37 obligate GT carriers of 18,000 to 47,000 per platelet, compared with a normal range of 27,000 to 50,000. It is possible that normalization of αIIbβ3 levels based on MPV may serve to increase the accuracy of detection of obligate GT carriers using monoclonal antibody-based methods.

Two other platelet-specific receptors have been found to vary to a degree similar to that seen with αIIbβ3 (2-fold). These are the von Willebrand factor receptor GPIbα11 and the collagen receptor GPVI.12,13,30 Logically, the observed variation in these receptors is most probably attributable to differences in MPV, although a direct correlation has yet to be reported. Indeed, several reports from one research group have noted that platelet GPVI levels are significantly elevated in ACS patients and strongly associated with myocardial ischemia.39–41 None of these reports, however, included a measurement of MPV.

In summary, our results provide compelling evidence that MPV is the greatest contributor to variation in levels of platelet αIIbβ3 among either normal individuals or patients with ACS and may be the major contributor to the variation seen in several other platelet receptors, such as GPIbα or GPVI. An exception is the collagen receptor αIIbβ3, whose level is influenced in part by MPV but to a larger extent by allelic variation in ITGA2. In addition, our results suggest that allelic variation in ITGA2 may itself contribute to the modulation of platelet size and MPV. Our findings also contribute to the argument that increased levels of platelet receptors, particularly integrins αIIbβ3 and αIβ1b, resulting from increased MPV, are responsible for the resultant increase in platelet reactivity. Larger platelets are hyperactive, owing in large part to the increased surface expression of all receptors, but most notably the integrins, which play a key role in initiation of platelet activation and perpetuation of the nascent thrombus. Additional studies of the clinical implications of our findings are warranted.

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**Disclosures**

None.

**References**


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Mean Platelet Volume and Integrin Alleles Correlate with Levels of Integrins $\alpha_{IIb}\beta_3$ and $\alpha_2\beta_1$ in Acute Coronary Syndrome Patients and Normals

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**Supplemental Figure I.** Intra-donor variation in A) bound AP2, as a measure of integrin $\alpha_{IIb}\beta_3$, and B) bound 8C12, as a measure of integrin $\alpha_2\beta_1$. GMFI was determined on two occasions (1st and 2nd) for each of 17 subjects (11 normal controls; 6 ACS patients). Comparable findings were obtained with measurements of bound 12F1 (not shown).

**Supplemental Figure II.** Inter-donor variation in platelet-bound 12F1, as a metric of the level of integrin $\alpha_2\beta_1$. GMFI is plotted on the ordinate. Measurements for each individual (320 ACS patients; 128 controls) are plotted in chronological order (left to right) on the abscissa.
Supplemental Figure III. Linear correlation between bound 12F1 (abscissa) and bound 8C12 (ordinate) for each donor (combined control subjects and ACS patients; n = 448). Adjusted $r^2 = 0.583$, $p < 0.001$.

Supplemental Table I. Subject Parameters

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*Correlation Coefficient; $p$-value; Highly significant correlations are in bold.

Supplemental Table II. ACS Patients: Pearson Product Moment Correlation

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*Correlation Coefficient; $^\dagger$ p-value; Highly significant correlations are in bold.
Supplemental Table III. Control Subjects: Pearson Product Moment Correlation

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*Correlation Coefficient; ¶p-value; Highly significant correlations are in **bold**.

For all comparisons, n = 128. At n = 128, the power of the performed test with $\alpha = 0.05$ will be $\geq 0.08$ given a correlation coefficient $\geq 0.246$. 
### LABORATORY RESULTS

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### Supplementary Table IV: Correlation between Laboratory Variables in ACS Patients determined by Pearson product moment correlation (SigmaStat 3.01).

For each variable entry, the following parameters are depicted:

- **Correlation Coefficient (top)**
- **p-value (center)**
- **number of pair-wise observations (bottom)**

**CHOL**

- p-values are corrected for multiple testing, as described by Bonferroni et al.

**HDL**

Entries highlighted in yellow are statistically significant (p < 0.05) after correction for multiple testing. In each case, the power of the performed test with α = 0.05 is > 0.8.

**TG**

A positive correlation coefficient indicates that there is a direct correlation between the two variables; a negative coefficient indicates that there is an inverse correlation.

**PT**

### ABBREVIATIONS

- AP2: Flow Cytometry GMFI anti-αIIBβ3
- 12F1: Flow Cytometry GMFI anti-α2β1
- 8C12: Flow Cytometry GMFI anti-α2β1
- MPV: Mean Platelet Volume (Coulter Counter)
- AGE
- PLT, platelet count (Coulter Counter)
- Hb, Hemoglobin
- Hct, Hematocrit
- WBC, white blood cell count
- CHOL, blood cholesterol level
- LDL, blood low density lipoprotein level
- HDL, blood high density lipoprotein level
- TG, blood triglyceride level
- PT, prothrombin time
- INR, international normalized ratio
- PTT, partial thromboplastin time
**Coronary Artery Disease**

**Cardiac Risk Factors**

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<th>Std. Error</th>
<th>t-value</th>
<th>p-value</th>
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**Medications**

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**Coronary Artery Disease Results**

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**Supplementary Table**

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**References**

- **Coronary Artery Disease**
- **Cardiac Risk Factors**
- **Medications**
- **Coronary Artery Disease Results**
- **Supplementary Table**
- **References**