Effect of Strenuous, Acute Exercise on $\alpha_2$-Adrenergic Agonist–Potentiated Platelet Activation

Jong-Shyan Wang, Lee-Ju Cheng

Abstract—Vigorous exercise transiently increases the risk of primary cardiac arrest. Strenuous, acute exercise can also increase the release of plasma epinephrine. Previous investigations have indicated that epinephrine can potentiate platelet activation by activating platelet $\alpha_2$-adrenoceptors. This study investigated how strenuous, acute exercise affects $\alpha_2$-adrenergic agonist–potentiated platelet activation by closely examining 15 sedentary men who exercised strenuously on a bicycle ergometer. Before and immediately after exercise, platelet adhesiveness on fibrinogen-coated surfaces, $[\text{Ca}^{2+}]$, in platelets, the number and affinity of $\alpha_2$-adrenergic sites on the platelet surface, and plasma catecholamine levels were determined. The results of this study can be summarized as follows: (1) The affinity of $\alpha_2$-adrenergic receptors on platelets decreases while the maximal binding number significantly increases after strenuous exercise, thereby correlating with the rise in plasma catecholamine levels. (2) Basal, clonidine-treated, ADP-treated, and clonidine plus ADP–treated adhesiveness and $[\text{Ca}^{2+}]$, in platelets increased after strenuous exercise. (3) Strenuous exercise is associated with higher percentages of ADP- and clonidine plus ADP–enhanced platelet adhesiveness and $[\text{Ca}^{2+}]$, than at rest. (4) The synergistic effects of clonidine on ADP-enhanced platelet adhesiveness and $[\text{Ca}^{2+}]$, after strenuous exercise are much greater than those at rest. Therefore, we conclude that strenuous, acute exercise enhances platelet activation, possibly by altering the performance of platelet $\alpha_2$-adrenergic receptors, facilitating the ability of ADP-activated fibrinogen receptors, and enhancing fibrinogen binding to platelet fibrinogen receptors. (Arterioscler Thromb Vasc Biol. 1999;19:1559-1565.)

Key Words: exercise ▪ platelets ▪ adhesiveness ▪ $[\text{Ca}^{2+}]$ ▪ catecholamines

Platelets play a critical role in the pathogenesis and progression of cardiovascular diseases.1-3 Other investigators have postulated that vigorous, short-term exercise may enhance the risk of major vascular thrombotic events and transiently increase the incidence of primary cardiac arrest.4-6 According to our previous studies of healthy men and of male patients with stable angina, strenuous, acute exercise can enhance platelet function (ie, platelet adhesiveness on a fibrinogen-coated surface and ADP-induced aggregation).7,8 However, the underlying mechanisms of strenuous, acute exercise–induced changes on platelet function remain unclear.

Although strenuous, acute exercise can enhance epinephrine release,9,10 the ability of epinephrine to induce human platelets has been the subject of extensive debate.11-22a Related investigations have confirmed that epinephrine potentiates human platelet activation; however, epinephrine is not, by itself, an activating agent.15,17-20,22a Moreover, apyrase blocks epinephrine-induced platelet activation.19,20,22a The aforementioned studies indicated that the platelet-stimulating effect of epinephrine occurs only in the presence of extracellular ADP or another agonist. By acting through $\alpha_2$-adrenergic receptors, epinephrine can enhance the opening of glycoprotein IIb/IIIa binding sites for fibrinogen in the presence of ADP; fibrinogen binding to the active form of the fibrinogen receptor produces platelet aggregation as well.15,17,18,21 Therefore, we hypothesized that strenuous, acute exercise might alter the performance of platelet $\alpha_2$-adrenergic receptors by increasing the endogenous release of epinephrine, thereby modifying the ability of ADP-activated fibrinogen receptors and fibrinogen to bind to platelet fibrinogen receptors.

In light of the above discussion, this study elucidates how strenuous, acute exercise affects $\alpha_2$-adrenergic agonist–potenti- ated platelet activation. To specifically assess platelet adhesiveness under various experimental conditions, this study used a tapered, parallel-plate chamber (ie, linear shear stress flow chamber) that provided levels of shear stress covering the entire physiological range in the human circulation.7 In addition, platelet $[\text{Ca}^{2+}]$, was measured by a dual-wavelength fluorescence spectrophotometer. Moreover, the number and affinity of $\alpha_2$-adrenergic sites on platelet surfaces were assayed by a receptor binding assay, and plasma catecholamine levels were measured by high-performance liquid chromatography.

Methods

Subjects

The protocol had been previously reviewed and approved by an institutional committee for the protection of human subjects. Fifteen...
sedentary men who were young and healthy were studied after they had given their informed consent and understood the experimental procedures. The physical characteristics of these subjects, expressed as mean±SEM, were age, 24.3±1.1 years; height, 169.6±1.7 cm; and body weight, 69.5±3.4 kg. These subjects had not engaged in any regular physical activity for 1 year before the study. To prevent the confounding effect of smoking, all subjects were nonsmokers. They abstained from all medications for at least 2 weeks before the study. Before the activity study, subjects were familiarized with the exercise protocol on a bicycle ergometer (Corival 400) to eliminate the effect of a new experience. They completed a medical history form and a physical activity questionnaire. The subjects then came to the laboratory to receive the exercise protocol. All subjects arrived at 1:30 PM to participate in this study to avoid a possible diurnal influence, as mentioned in a previous study.28

Exercise and Blood Collection Protocols

After the subject had arrived at the laboratory and rested for 30 minutes, blood samples were drawn from a forearm vein. The first 2 mL was discarded, and the remainder of the blood sample was used for the baseline determination of hematological parameters and platelet function. The exercise protocol began at 3 PM and consisted of 2 minutes of unloaded pedaling, followed by pedaling with a continuous increment in workload, 20 to 40 W every 3 minutes, until exhaustion (ie, strenuous exercise up to maximal oxygen consumption; VO2 max). Immediately after exercise, another blood sample was collected for the measurement of the same hematological parameters and platelet function.

During exercise, the ECG was continuously monitored by a Gould ECG/Biotach, recorded on a 4-channel polygraph (Gould 2400 S portable ink recorder), and converted to a digital display of the heart rate. The airflow was monitored by a pneumotachometer (Hans Rudolph), and the inspiratory and expiratory airflow were determined by vacuum filtration (cell harvester, FH225V, Hoefer Scientific Instruments) over 0.2% polyethylene imine–pretreated Whatman GF/B glass fiber filters. The filter discs were washed 3 times with an ice-cold, mineral oil–treated centrifuge tube, and the amount of radioactivity retained on the filter. The platelet count was adjusted to 1.5 to 2.0 million/mL. Platelet-rich plasma was then mixed with 4 mL of Tyrode’s-HEPES buffer, and the mixture was then placed in a cold centrifuge tube containing EDTA (1.8 mg/mL of blood, Sigma) and glutathione (1.2 mg/mL of blood, Sigma), followed by centrifugation at 120 g for 10 minutes at 4°C. The plasma was stored at −80°C until assay. It was analyzed for norepinephrine and epinephrine by high-performance liquid chromatography.29

Radioligand Binding Studies

The method used for adrenergic receptor binding assays was adopted from Gleason and Hieble.27 For saturation studies, aliquots of washed platelets (≈140 mg of protein) were incubated in an assay buffer with various concentrations of [3H]clonidine (ranging from 0.01 to 10 nM/L; specific activity, 61.9 Ci/mmol; DuPont-NEN) in a final volume of 500 mL. After incubation for 30 minutes at room temperature, the bound and free forms of [3H]clonidine were separated by vacuum filtration (cell harvester, FH225V, Hoefer Scientific Instruments) over 0.2% polyethylene imine–pretreated Whatman GF/B glass fiber filters. The filter discs were washed 3 times with an ice-cold, binding-assay buffer (3 mL for each time). Nonspecific binding was determined in a similar manner in the presence of a 100-fold excess of cold clonidine. Specific binding was the difference between the total and nonspecific binding. The amount of radioactivity retained on the filter was determined by liquid scintillation counting (Beckman). Affinity (Kd) and receptor number (Bmax) were calculated from a Scatchard plot.

Plasma Levels of Catecholamines

From all subjects, an additional 5-mL blood sample was obtained, placed in a cold centrifuge tube containing EDTA (1.8 mg/mL of blood, Sigma) and glutathione (1.2 mg/mL of blood, Sigma), and immediately centrifuged at 3000 g for 10 minutes at 4°C. The plasma was stored at −80°C until assay. It was analyzed for norepinephrine and epinephrine by high-performance liquid chromatography.29

Statistical Analysis

All data were expressed as mean±SEM. To compare the differences in platelet adhesiveness on fibrinogen-coated surfaces and [Ca2+]i, statistical analysis was performed using the randomized block ANOVA and Tukey’s multiple range test. The Kd and Bmax of α2-adrenergic receptors on platelets and the plasma levels of catecholamines at rest and immediately after exercise were analyzed by paired t test. Differences were considered significant at P<0.05.

Results

Cardiorespiratory variables at rest and maximal exercise performance are shown in Table 1. The plasma levels of both norepinephrine and epinephrine were increased immediately after strenuous, acute exercise (Table 2, P<0.05).
shows an example of a Scatchard plot of [3H]clonidine binding to platelets obtained at rest and during strenuous exercise. Results demonstrated that strenuous, acute exercise decreased the binding affinity, indicated by a higher dissociation constant (Kd), but increased the number of binding sites (Bmax) for platelet α2-adrenergic receptors (Figure 2 and Table 2). Furthermore, the plasma levels of both epinephrine and norepinephrine were positively correlated with α2-adrenergic density on platelets, but only epinephrine was negatively correlated with affinity (Table 3).

The average percentages of attached platelets at the 6 locations under various shear stresses at rest and after severe exercise are shown in Figure 3a and 3b, respectively. Although ADP and clonidine plus ADP could enhance platelet adhesiveness, indicated as the shear versus adhesion area slope, it was not changed significantly by clonidine (Figure 4a). Moreover, ADP plus clonidine—enhanced platelet adhesiveness was much greater than ADP-treated platelet adhesiveness only (Figure 5a). Therefore, although clonidine may potentiate platelet adhesiveness on fibrinogen-coated surfaces, it is not, by itself, an activating agent. Basal, clonidine-treated, ADP-treated, and clonidine plus ADP–treated platelet adhesiveness levels were all increased after strenuous exercise (Figure 4a). However, the synergistic effect of clonidine on ADP-evoked platelet [Ca2+]i elevation was more pronounced after strenuous exercise than at rest (Figure 5b, P < 0.05).

Clonidine apparently did not induce platelet [Ca2+]i changes at rest and after strenuous, acute exercise (Figures 4b and 5b). In contrast, platelet [Ca2+]i, was increased by ADP and by clonidine plus ADP (Figure 4b). Moreover, clonidine could potentiate ADP-evoked platelet [Ca2+]i elevations (Figure 5b). Basal, clonidine-treated, ADP-treated, and clonidine plus ADP–treated platelet [Ca2+]i, levels were increased significantly after strenuous, acute exercise (Figure 4b). An example is demonstrated in Figure 6. However, the synergistic effect of clonidine on ADP-evoked platelet [Ca2+]i elevation was more pronounced after strenuous exercise than at rest (Figure 5b, P < 0.05).

**Discussion**

The results of this study can be summarized as follows: (1) Strenuous, acute exercise increases platelet α2-adrenergic

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**TABLE 1. Cardiorespiratory Variables at Rest and After Maximal Exercise Performance**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Resting</th>
<th>Maximal Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE, minutes</td>
<td>...</td>
<td>14.55±1.25</td>
</tr>
<tr>
<td>Workload, W</td>
<td>...</td>
<td>130±8.9</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>71±2</td>
<td>190±2</td>
</tr>
<tr>
<td>VO2, mL·min⁻¹·kg⁻¹</td>
<td>10.32±0.98</td>
<td>83.31±3.48</td>
</tr>
<tr>
<td>VCO2, mL·min⁻¹·kg⁻¹</td>
<td>2.98±0.26</td>
<td>31.93±1.99</td>
</tr>
<tr>
<td>R</td>
<td>2.11±0.16</td>
<td>38.71±3.28</td>
</tr>
</tbody>
</table>

Values are mean±SEM. TE indicates time to exhaustion; R, respiratory exchange ratio.

**TABLE 2. Comparison of Plasma Catecholamine Levels and Receptor Number (Bmax) and Affinity (Kd) for [3H]Clonidine Binding Platelets During Rest and After Strenuous, Acute Exercise**

<table>
<thead>
<tr>
<th>Catecholamines</th>
<th>At Rest</th>
<th>After Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine, pmol/mL</td>
<td>2.41±0.09</td>
<td>26.76±0.67*</td>
</tr>
<tr>
<td>Epinephrine, pmol/mL</td>
<td>0.32±0.01</td>
<td>3.37±0.09*</td>
</tr>
<tr>
<td>[3H]Clonidine binding to platelets</td>
<td>2.85±0.59</td>
<td>8.05±0.83*</td>
</tr>
<tr>
<td>Bmax, fmol/mg protein</td>
<td>0.46±0.11</td>
<td>0.97±0.24*</td>
</tr>
</tbody>
</table>

Values are mean±SEM. *P<0.05 vs exercise, analyzed by paired t test.

Figure 1. Scatchard plot of [3H]clonidine binding to platelets obtained at rest and after strenuous exercise. Strenuous, acute exercise decreased the binding affinity, indicated by a higher dissociation constant (Kd), but increased the number of binding sites (Bmax) for platelet α2-adrenergic receptors. Open circles denote values at rest; solid circles represent those immediately after strenuous, acute exercise.

Figure 2. Graphs displaying the relationship between plasma catecholamine levels and receptor number (Bmax) and affinity (Kd) for [3H]clonidine binding to platelets at rest versus after strenuous, acute exercise. Open circles indicate values at rest; solid circles represent those immediately after strenuous, acute exercise (n=10).
receptor density and is accompanied by a decrease in affinity, thereby correlating with the rise in plasma catecholamine levels. (2) Strenuous exercise increases basal, clonidine-treated, ADP-treated, and clonidine plus ADP–treated platelet adhesiveness and \([\text{Ca}^{2+}]_i\). (3) The percentages of ADP- and clonidine plus ADP–enhanced platelet adhesiveness and \([\text{Ca}^{2+}]_i\), after strenuous, acute exercise are greater than those at rest. (4) Strenuous, acute exercise can enhance clonidine-potentiated platelet adhesiveness on fibrinogen-coated surfaces and \([\text{Ca}^{2+}]_i\), elevations.

As is well known, the risk of primary cardiac arrest transiently increases during vigorous exercise.\(^{4-6}\) In addition, strenuous, acute exercise can significantly increase the release of plasma epinephrine.\(^{9,10}\) In vivo and in vitro observations confirm the relevance of epinephrine-mediated platelet activation in thrombosis. In experimental studies, thrombosis has been induced by injecting epinephrine into animals with coronary artery stenosis.\(^{29}\) In vitro studies have demonstrated that epinephrine induces the aggregation of human platelets and potentiates the aggregation induced by low concentrations of various platelet agonists such as ADP,\(^{15}\) platelet-activating factor,\(^{20}\) and thrombin.\(^{22}\) Previous studies have suggested that the intrinsic platelet-activating effect of epinephrine may play a role in activating \(\alpha_2\)-adrenoceptors in human platelets to (1) inhibit the adenylate cyclase system through coupling to a \(G_i\) protein\(^{16}\) and (2) enhance the opening of glycoprotein IIb/IIIa binding sites for fibrinogen in the presence of ADP or other agonists.\(^{18}\) Our previous study with healthy women as subjects indicated that although the platelet cAMP content remains unchanged after strenuous, acute exercise, severe exercise can enhance prostacyclin production.\(^{30}\) Although epinephrine levels enhanced by severe exercise could inhibit adenylate cyclase activity through activating platelet \(\alpha_2\)-adrenergic receptors, the effect may be attenuated by exercise-induced prostacyclin production. This study reports, for the first time, that strenuous, acute exercise may alter the performance of platelet \(\alpha_2\)-adrenergic receptors by increasing the endogenous release of catecholamines, thereby facilitating the ability of ADP-activated fibrinogen receptors and enhancing fibrinogen binding to platelet fibrinogen receptors. The enhanced platelet activity in severe exercise may accelerate the formation of hemostatic platelet

### Table 3. Correlation Between Plasma Catecholamine Levels and \(B_{\text{max}}\) and \(K_d\) of Platelet \(\alpha_2\)-Adrenoceptors

<table>
<thead>
<tr>
<th></th>
<th>(B_{\text{max}})</th>
<th>(K_d)</th>
<th>(r)</th>
<th>(P)</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>0.798</td>
<td>0.442</td>
<td>0.820</td>
<td>0.467</td>
<td>0.0001</td>
<td>0.0577</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>0.0001</td>
<td>0.0340</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Figure 3

Graphs displaying average percentages of attached platelets at the 6 locations under various shear stresses at rest (a) and immediately after strenuous, acute exercise (b). Solid squares indicate saline-treated; solid diamonds, clonidine-treated; solid circles, ADP-treated; and solid triangles, ADP plus clonidine-treated values.

### Figure 4

A comparison of saline (basal), 1 \(\mu\)mol/L clonidine-treated, 1 \(\mu\)mol/L ADP-treated, and 1 \(\mu\)mol/L clonidine plus 1 \(\mu\)mol/L ADP–treated (a) platelet adhesiveness on fibrinogen-coated-surfaces (indicated as the slope on the y axis) and (b) \([\text{Ca}^{2+}]_i\) at rest and after exercise. Basal, clonidine-treated, ADP-treated, and ADP plus clonidine–treated platelet adhesiveness and \([\text{Ca}^{2+}]_i\) levels were increased by strenuous exercise. Clo indicates clonidine. \(+P<0.05\) compared with saline. \(\ast P<0.05\) rest vs exercise; analyzed by randomized block ANOVA followed by Tukey’s multiple range test.
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platelets decreases while the B max significantly increases after exercise, 31 or remains unchanged, 32,33 in response to exercise, this study; ie, the affinity of α2-adrenergic receptors.

A decrease in affinity, thereby correlating with the rise in plasma catecholamines levels. However, according to a previous investigation, platelet α2-adrenergic receptor density increases, 31 or remains unchanged, 12,23 in response to exercise, whereas platelet α2-adrenergic receptor affinity decreases 31,32 or remains unchanged. 33 Kempen et al 33 found that moderate exercise (45% peak mechanical power) does not modify the density or affinity of platelet α2-adrenergic receptors. In contrast, the findings of Berlin et al 31 correspond to those of this study; ie, the affinity of α2-adrenergic receptors on platelets decreases while the B max significantly increases after strenuous, acute exercise. Other investigators observed similar results when strenuous, acute exercise increased lymphocyte β-adrenergic receptor density.34,35 However, submaximal exercise protocols have failed to demonstrate a change in the density of lymphocyte β-adrenergic receptors with exercise.36 Therefore, acute exercise in an intensity-dependent manner, such as with lymphocyte β-adrenergic receptors in previous studies 34,35, may affect the characteristic platelet α2-adrenergic receptors.

Several possible mechanisms could account for why exercise increases platelet α2-adrenergic receptor density. New receptors could be synthesized, or preexisting receptors could be externalized. Alternatively, the apparent increase in receptor density could simply be attributed to an exercise-induced alteration in the pool of circulating platelets. Exercise is known to increase the release of platelets from the spleen by α2-adrenergic stimulation.37 Therefore, acute changes in receptor density could be ascribed to an increase in the population of splenic platelets with a high density of receptors. However, the splenic platelet population (though having a larger mean platelet volume) appears to have an age and a density distribution similar to those of the population of platelets in the basal circulation.38 Further studies involving α2-adrenergic receptors on exercise-released splenic platelets are necessary to clarify this issue.

In the current study, changes in the density of receptors occurred rapidly, ie, over ~15 minutes. It is unlikely that new receptors could be synthesized during such a short period of time. However, externalization of receptors could have occurred over this period. Previous investigators have observed the rapid externalization of myocardial α1- and β-adrenergic receptors, accompanied by a local release of endogenous

Figure 5. Changes in (a) platelet adhesiveness on fibrinogen coated-surfaces and (b) [Ca2+] levels by 1 μmol/L clonidine, 1 μmol/L ADP, and 1 μmol/L clonidine plus 1 μmol/L ADP at rest and after exercise. Results are expressed as a percentage of agonist-treated platelet adhesiveness to basal platelet adhesiveness on fibrinogen coated-surfaces and [Ca2+], by using the following formula: (agonist-treated minus saline-treated platelet adhesiveness on fibrinogen coated-surfaces and [Ca2+]) divided by (saline-treated platelet adhesiveness on fibrinogen coated-surfaces and [Ca2+] multiplied by 100. In addition, (Clo+ADP) minus the summation of (ADP) and (Clo) was viewed as a synergistic effect of clonidine (Clo). Strenuous exercise was associated with higher percentages of ADP- and clonidine plus ADP-enhanced platelet adhesiveness and [Ca2+] than at rest. Moreover, the synergistic effects of clonidine on ADP-enhanced platelet adhesiveness and [Ca2+] after strenuous exercise were much greater than those at rest. P<0.05 compared with Clo. *P<0.05 rest vs exercise. #P<0.05 ADP vs Clo+ADP; analyzed by randomized block ANOVA followed by Tukey’s multiple range test.

Figure 6. Examples of clonidine-potentiated platelet [Ca2+] elevation at rest (a) and after strenuous, acute exercise (b). Clonidine did not induce changes in platelet [Ca2+] either at rest or after exercise. In contrast, platelet [Ca2+] was increased by ADP and ADP plus clonidine. Moreover, clonidine potentiated the ADP-evoked platelet [Ca2+] elevation. However, the synergistic effect of clonidine on ADP-evoked platelet [Ca2+] was more pronounced after strenuous exercise than at rest.
catecholamines, after the onset of myocardial ischemia (15 minutes).38,39 A previous study also revealed that agonist-promoted internalization and functional uncoupling of the receptors are abolished after acute myocardial ischemia.38 In addition, strenuous, acute exercise can increase the release of endogenous catecholamines.9,10 Moreover, with the increased extraction of oxygen from the arterial blood during strenuous exercise, the venous blood leaving the muscles has an extremely low oxygen content.40 Therefore, venous hypoxia accompanied by the increased epinephrine release due to strenuous, acute exercise may upregulate platelet \( \alpha_2 \)-adrenergic receptors and attenuate the extent of agonist-promoted downregulation, as with myocardial adrenergic receptors after acute ischemia, thus further enhancing \( \alpha_2 \)-adrenergic agonist–potentiated platelet activity.

Previous investigations have demonstrated not only that platelets stimulated by ADP expose fibrinogen receptors (ie, glycoprotein Ib/IIa) on their surfaces but also that fibrinogen binding to the active form of the fibrinogen receptor produces platelet aggregation.41,42 Figures et al17 have suggested that the promotion of platelet aggregation and the exposure of fibrinogen receptors by epinephrine depend on ADP. In addition, epinephrine-mediated platelet activation may be attributed to an alteration in the avidity of ADP binding. Moreover, epinephrine that promotes exposure of glycoprotein Ib/IIa sites for fibrinogen binding is also a possible requirement for Ca\(^{2+}\) influx.18 Clonidine is an agonist with a high affinity for \( \alpha_2 \)-adrenoceptors.43 Results of this study demonstrate that platelet adhesiveness on fibrinogen-coated surfaces and \([Ca^{2+}]\), levels, though enhanced by both ADP and clonidine plus ADP, were not significantly changed by clonidine alone. Moreover, ADP plus clonidine enhanced these platelet functional parameters to a much greater extent than did ADP alone. These results indicate that clonidine may potentiate human platelet activation but is not, by itself, an activating agent.

Regarding the effect of exercise, strenuous exercise increased basal, clonidine-treated, ADP-treated, and clonidine plus ADP–treated platelet adhesiveness on fibrinogen-coated surfaces as well as \([Ca^{2+}]\). In 1993, Kestin et al44 found that strenuous exercise could activate fibrinogen receptors. Their findings correspond to some of our results. Our results further demonstrate that the synergistic effects of an \( \alpha_2 \)-adrenergic agonist on ADP-enhanced platelet adhesiveness and \([Ca^{2+}]\), elevation are more pronounced after strenuous exercise than at rest. Therefore, strenuous exercise can enhance \( \alpha_2 \)-adrenergic agonist–potentiated platelet activation.

In conclusion, strenuous, acute exercise can enhance \( \alpha_2 \)-adrenergic agonist–potentiated platelet adhesiveness on fibrinogen-coated surfaces and \([Ca^{2+}]\), elevation, possibly attributed to the acute increase in catecholamines in response to exercise, and ultimately enhancing \( \alpha_2 \)-adrenoreceptor performance. The enhanced performance facilitates the activity of fibrinogen receptors and the fibrinogen binding to platelet fibrinogen receptors. Therefore, our findings provide further insight into the notion that strenuous, acute exercise augments the risk of major vascular thrombotic events partially because severe exercise may increase endogenous catecholamines (ie, epinephrine and norepinephrine), which in turn may augment platelet activation.

Acknowledgments

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