Effects of Exercise Training and Deconditioning on Platelet Aggregation Induced by Alternating Shear Stress in Men

Jong-Shyan Wang, Yu-San Li, Jin-Chung Chen, Yu-Wen Chen

Objective—Alternating shear stress, which resembles the flow condition in stenotic arteries, induces platelet aggregation. This study investigated how exercise training and deconditioning influence alternating shear-induced platelet aggregation (ASIPA) and clarify the mechanisms underlying ASIPA.

Methods and Results—Thirty healthy male sedentary subjects were randomly divided into control and trained groups. The trained men were trained on a bicycle ergometer at ~60% of maximal oxygen consumption for 30 minutes per day, 5 days per week for 8 weeks, and then were deconditioned for 8 weeks. The experimental results indicate the following: (1) short-term strenuous exercise increases the extent of ASIPA and is accompanied by increased the von Willebrand factor (vWF) binding and P-selectin expression on platelets in both the control and trained groups, whereas the enhancement of platelet function decreases after exercise training in trained subjects; (2) at rest and immediately after exercise, ASIPA and the vWF binding and P-selectin expression on platelets are reduced by training, but remain unchanged in the control group; and (3) deconditioning reverses the effects of training on resting and postexercise state.

Conclusions—Exercise training suppresses the extent of ASIPA, probably by reducing vWF binding to platelets and P-selectin expression on platelets. However, deconditioning reverses the training effects. (Arterioscler Thromb Vasc Biol. 2005;25:454-460.)

Key Words: training ▪ detraining ▪ shear stress ▪ platelets ▪ adhesion molecules

Lifestyle habits such as exercise may have significant influence on the risk of major vascular thrombotic events.1,2 Previous studies have suggested that the risk of primary cardiac arrest transiently increases during vigorous exercise,3,4 whereas regular exercise is associated with an overall decreased risk of cardiovascular diseases.5,6 Shear-induced platelet aggregation (SIPA) is important in arterial thrombosis, which is a major contributing factor for atherothrombotic occlusion of blood vessels.7 Therefore, it is important to distinguish the shear-mediated thrombotic events that occur between short-term bouts of exercise and physical conditioning. According to our earlier study of male patients with stable angina, strenuous acute exercise can increase the capacity of adhered platelets to withstand physiological flow shear stress.8 A previous investigation also demonstrated that SIPA increased after strenuous treadmill exercise in patients with effort angina.9 However, the effects of exercise training and detraining on shear-mediated platelet activation and its underlying mechanisms have not yet been studied.

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Pathological, high shear stress induces binding of von Willebrand factor (vWF) to the platelet glycoprotein (GP) Ib complex on platelets. This interaction transduces signals in platelets, subsequently activating GP IIb/IIIa complex. The activated GP IIb/IIIa complex then binds to fibrinogen, stabilizing the aggregated platelets.10,11 Our recent investigation showed that short-term intense exercise promoted SIPA, possibly by improving the ability of vWF to bind to platelets and the subsequent activation of GPIIb/IIIa complexes to sustained high shear stress.12 In fact, blood flow in stenotic vessel follows a complex pattern of hydrodynamics in that flow rate first increases dramatically in the throat of stenosis and then transits into a poststenosis turbulent flow, creating a region of slow recirculation.13,14 Such a complex flow pattern results in changes in blood shear stress that increases significantly at throat of stenosis, and then decreases very rapidly in the poststenosis recirculation region. Therefore, alternating shear stress, which comprises a high shear stress followed by a low shear stress, resembles those stresses in vivo in stenotic arteries rather than those stresses that occur in the sustained high-shear condition. Mimicking the pathological flow condition, a recent investigation indicated that P-selectin participates in alternating SIPA (ASIPA) in a manner distinct from the GP IIb/IIIa complex.15 This study was conducted to elucidate the effects of short-term exercise, exercise training, and deconditioning on ASIPA, and to explore the underlying mechanisms of ASIPA.
To specifically assess ASIPA, this work used a cone-plate viscometer that provided levels of shear stresses covering the physiological and pathological ranges in human circulation. The flow cytometric technique was applied to determine whether training and detraining can influence vWF binding to platelets, GP Ib/IIa activation, and P-selectin expression on platelets in response to varying shear stresses.

**Methods**

**Subjects**

The Ethics Committee of Chang Gung Memorial Hospital reviewed and approved the protocol for this investigation. The study procedures corresponded to institutional guidelines. We recruited 30 healthy nonsmokers, nonmedication/nonvitamin users, and infection-free or cardiovascular-risk-free subjects from Chang Gung University in Taiwan. None of the subjects had engaged in any regular physical activity for 1 year before the investigation. The subjects were studied after providing their informed consent, and the experimental procedures were explained to them. They were randomly divided into control (n = 15) and trained (n = 15) groups. The control and trained groups did not differ significantly in their anthropometric data: age, 24.7 ± 2.3 versus 23.5 ± 1.6 years; height, 171.6 ± 2.9 versus 171.9 ± 1.9 cm; and weight, 66.6 ± 4.3 versus 66.4 ± 4.3 kg, respectively. All subjects were abstained from all medication for at least 2 weeks before the study. The subjects in the trained group came to our laboratory to receive an exercise training program for 8 weeks, whereas the controls received no training during the experimental period. The subjects in the trained group were trained on a bicycle ergometer for 30 minutes per day. 5 days per week for 8 weeks, followed by 8 weeks of detraining. Training intensity was adjusted to ~60% of VO2max. Deconditioning defines the subjects as having not engaged in any regular physical activity, similar to conditions of the pretraining state; ie, exercise frequency ≤1 time per week, duration ≤20 minutes per time. The subjects must record their activities of daily life by a physical activity questionnaire, and we collected the questionnaire each week to check the subject’s activities of daily life until the end of this study.

**Exercise and Blood Collection Protocol**

On the day of the study, the subjects had a light mixed breakfast without any caffeine-containing drinks at 8:00 AM, and then fasted for 5 hours before participating in the study. At the beginning, a progressive exercise test was performed on each subject. During the experimental period, exercise tests were repeated at 8-week intervals in the trained group until the end of detraining. In contrast, the control group received 2 progressive exercise tests, at the beginning and 8 weeks later. All subjects arrived at the testing center at 1:00 PM to avoid possible diurnal influence. To avoid the short-term effects of exercise, the training group performed a progressive exercise test 48 test hours after exercise training. After the subjects arrived at the laboratory and rested for 30 minutes, blood samples were drawn from their forearm veins to provide baseline data on platelet function. Plasma was obtained by recentrifugation at 1600g at 120°C for 10 minutes, and the remainder of the blood sample was used to measure platelet function. Exercise began at 1:30 PM. The protocol comprised 2 minutes of unloaded pedaling, followed by increment of workload by 20 to 30 W every 3 minutes, until exhaustion (namely, strenuous exercise up to maximal oxygen consumption; VO2max). Immediately after the progressive exercise test, another blood sample was obtained for the measurement of postexercise platelet function.

**Platelet Aggregation Induced by Shear Stress**

Ten-mliliter blood samples were transferred into polypropylene tubes containing sodium citrate (3.8 g/DL: 1 vol to 9 vol of blood) (Sigma). Platelet-rich plasma (PRP) was prepared by centrifugation at 120g for 10 minutes at room temperature, whereas platelet-poor plasma was obtained by recentrifugation at 1600g for 10 minutes, also at room temperature. The number of platelets in platelet-poor plasma was adjusted to 2 × 10^10 cells/mL. For certain experiments, 10 μg/mL CD41 monoclonal antibody (Serotec), 10 μg/mL CD62P monoclonal antibody (Serotec), or 5 μmol/L yohimbine (an α1 adrenergic antagonist) (Sigma) were added to the platelet suspension, which was then warmed to 37°C for 10 minutes. Subsequently, 60 μL PRP was placed in a 1-ng/mL albumin-coated glass plate (32-mm diameter) and sheared at a controlled level of shear stress at 37°C for 5 minutes using a rotational viscometer (CAP2000; Brookfield). The PRP samples were exposed to either low shear stress alone (10 dyne/cm² for 5 minutes) or a combination of high and low shear stress (10 dyne/cm² for 20 seconds, and 100 dyne/cm² for 10 seconds, reduced to 10 dyne/cm² within 10 seconds, and then maintained at this level for the remainder of a total of 5 minutes) at 37°C. The PRP suspension was removed from the well immediately after exposure to shear stress, to count the single platelets, as described previously.

**GP Ib/IIa Activation and Expression, P-Selectin Expression, and vWF Binding on Platelets**

Platelet suspensions were exposed to various shear stresses, and aliquots then were incubated with a saturating concentration of fluorescein isothiocyanate (FITC)-conjugated CD41 (nonactivated and activated forms of GP Ib/IIa) (Serotec), FITC-conjugated PAC-1 (activated form of GP Ib/IIa) (Pharmingen), FITC-conjugated anti-CD62P (P-selectin) (Serotec), rabbit anti-human vWF IgG (Sigma) plus FITC-conjugated anti-rabbit IgG (Sigma), or FITC-conjugated anti-rabbit IgG control antibodies (Serotec) for 20 minutes in the dark. After fixation with 1% formaldehyde in phosphate-buffered saline, the fluorescence obtained from 10,000 events that represented the platelets was determined using a flow cytometer (Beckton Dickinson), as described previously. Parallel, nonsheared samples were used to correct for background fluorescence. In sheared samples, the increases in fluorescence resulting from anti-vWF, anti-CD62P, anti-CD41, and PAC-1 beyond this background were expressed as a percentage of the 10,000 counted events.

**Plasma vWF Antigen and Activity, Soluble P-Selectin, and Norepinephrine**

Plasma vWF antigen (Corgenix) and activity (American Biochemical and Pharmaceutical Co), as well as plasma soluble P-selectin (Ramco Systems) contents, were measured using commercial enzyme-linked immunosorbent assay, as described previously. Moreover, the blood sample was also analyzed for norepinephrine using high-performance liquid chromatography. Because short-term bouts of exercise caused hemococoncentration,8 postexercise vWF antigen and activity, soluble P-selectin, and norepinephrine levels in plasma were normalized with the changes in hematocrit after exercise. Additionally, analysis of these parameters showed a high reproducibility and a small intra-assay variation in replicates of all tested samples, ie, coefficient variation value in vWF antigen was 8.2%; vWF activity, 6.7%; soluble P-selectin, 9.5%; norepinephrine, 10.1%.

**Statistics**

Data were expressed as mean ± SEM. Additionally, the statistical software packages of StatView IV, running on a Macintosh computer, were used for data analysis. The comparison exercise performance, cardiorespiratory function, and platelet function in both the trained and control groups, both at the beginning of the study and after 8 weeks, were analyzed by ANOVA followed by Fisher multiple range test. To compare the differences of various parameters as mentioned in the trained group along with the experimental period, the results were analyzed by repeated measure ANOVA and Tukey multiple range test. The level of significance was set at P < 0.05.

**Results**

The trained subjects increased their exercise time, maximal workload (Wmax), maximal minute ventilation (VE,max), VO2max. The level of significance was set at P = 0.05.
and decreased systolic blood pressure and diastolic blood pressure after 8 weeks of exercise training (*P<0.05). However, the training effects on exercise performance reverted to the pretraining state after deconditioning. The subjects also displayed significantly higher exercise time, W_{max}, V_{Emax}, and VO_{2max}, and lower systolic blood pressure and diastolic blood pressure than the control subjects after 8 weeks of training (*P<0.05). In contrast, the control group displayed unchanged exercise performance after 8 weeks of the experiment (Table 1).

Plasma vWF antigen/activity and norepinephrine levels were increased by short-term strenuous exercise in both the control and trained groups. Plasma levels of resting and postexercise vWF antigen/activity and postexercise norepinephrine in trained subjects were reduced by exercise training. Furthermore, the trained group had markedly lower resting and postexercise plasma vWF antigen/activity and postexercise plasma norepinephrine levels than the control group after 8 weeks of training. Nonetheless, the training effects reversed to the pretraining state after 8 weeks of deconditioning. In contrast, plasma levels of soluble P-selectin had not significantly changed in both trained and control groups during this experimental period (Table 2).

In pilot experiments (n=6), we found that 80 to 120 dyne/cm² of shear stress for 10 seconds induced significant platelet aggregation (Figure 1; *P<0.05). Moreover, 100 dyne/cm² of shear stress for 10 seconds increased binding of vWF to platelet and expression of platelet P-selectin (CD62P), but had not changed PAC-1 binding and CD41 expression on platelets (online Figure I, please see http://atvb.ahajournals.org). However, an enhancement of PAC-1 bound to platelets occurred in the sustained high-shear condition (100 dyne/cm² of shear stress for 120 seconds) (Figure I). Accordingly to these results, we choose a combination of high (100 dyne/cm²) and low (10 dyne/cm²) shear stress as the pattern of alternating shear stress in this study. Moreover, the measured results revealed that alternating

### TABLE 1. Comparison of Basic Characteristics and Exercise Performance Between Trained and Control Groups During the Experimental Period

<table>
<thead>
<tr>
<th>Time, wk</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
<th>HRrest, bpm</th>
<th>HRmax, bpm</th>
<th>DBPrest, mm Hg</th>
<th>W_{max}, watt</th>
<th>VE_{Emax}, L/min</th>
<th>VO_{2max}, mL/min/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Trained</td>
<td>66.4±2.3</td>
<td>23.1±0.6</td>
<td>72±2</td>
<td>195±7</td>
<td>239±7</td>
<td>30.8±1.1</td>
<td>30.2±2.7</td>
</tr>
<tr>
<td>16</td>
<td>Control</td>
<td>66.6±4.3</td>
<td>22.7±1.7</td>
<td>74±5</td>
<td>194±11</td>
<td>196±7</td>
<td>37±6</td>
<td>32.8±1.0</td>
</tr>
<tr>
<td></td>
<td>Trained</td>
<td></td>
<td>66.7±1.6</td>
<td>22.6±0.6</td>
<td>74±2</td>
<td>239±7</td>
<td>39.0±0.8</td>
<td>32.8±1.0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td></td>
<td>69.1±3.1</td>
<td>23.4±0.9</td>
<td>76±1</td>
<td>196±7</td>
<td>39.0±0.8</td>
<td>32.8±1.0</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

*P<0.05 compared with pretraining data (0 weeks).

### TABLE 2. Comparison of Plasma Norepinephrine, vWF Antigen/Activity, and sP-Selectin Levels Between Trained and Control Groups During the Experimental Period

<table>
<thead>
<tr>
<th>Time, wk</th>
<th>Norepinephrine, pg/mL</th>
<th>vWF antigen, IU/dL</th>
<th>sP-selectin, ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Trained R 240.6±30.1 228.9±25.9</td>
<td>E 488.6±34.6 363.4±31.7††</td>
<td>Trained R 3.3 99.5</td>
</tr>
<tr>
<td>8</td>
<td>Control R 526.4±45.2 578.5±32.0*</td>
<td>E 154.9±9.7 112.5±10.0††</td>
<td>Control R 3.1 99.5</td>
</tr>
<tr>
<td>16</td>
<td>Trained R 238.5±35.4 252.5±18.0</td>
<td>E 56.4±45.2 578.5±32.0*</td>
<td>Control R 3.1 99.5</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

*P<0.05 rest (R) vs exercise (E).
†P<0.05 compared with pretraining data (0 weeks).
‡P<0.05 control vs trained.
shear stress induced higher platelet aggregation than low shear stress alone (Figure 2, \( P<0.05 \)). Short-term strenuous exercise increased the extent of ASIPA in both the control and trained groups at the beginning of the study, whereas this severe exercise-enhanced change in ASIPA was decreased after 8 weeks of exercise training in the trained group \((P<0.05; \text{ power}=1.000)\). Additionally, the resting and postexercise ASIPA of the trained group also reduced after 8 weeks of training \((P<0.05; \text{ power}=0.740)\). However, the training effects on ASIPA in the trained group reverted to the pretraining state after deconditioning (Figure 2).

During the experimental period, treating the platelet with CD62P monoclonal antibody effectively inhibited the extent of SIPA (from 71% to 92%; \( P<0.05 \)), whereas moderate suppression of ASIPA occurs when treating the platelet with yohimbine (from 24% to 51%, \( P<0.05 \)) in trained (Figure IIA and IIB) and control (Figure IIC and IID) groups. Although treating the platelet with CD41 monoclonal antibody did not alter the extent of ASIPA at rest (from -5% to 8%; \( P>0.05 \)), it slightly reduced the platelet response after short-term strenuous exercise (12% to 22%; \( P<0.05 \)). However, the short-term exercise effect on CD41-mediated ASIPA was attenuated after 8 weeks of training, and the training effects were reversed by deconditioning (Figure IIA and IIB).

Measured results demonstrated that alternating shear stress induced higher binding of vWF to platelet (Figure 3A) and expression of P-selectin (CD62P) on platelet (Figure 3B) than low shear stress, whereas no significant differences in expression (CD41) (Figure 3C) and activation (PAC-1) of GPIIb/IIIa (Figure 3D) on platelet were observed between the low and alternating shear flow conditions. Although the short-term effects of strenuous exercise increased vWF binding to platelet and P-selectin expression on the platelet at the beginning of this study \((P<0.05; \text{ power}=1.000)\), the platelet response was not changed by short-term exercise after 8 weeks of training (Figure 3A and 3B). Resting and postexercise vWF binding to platelets (Figure 3A) and postexercise P-selectin expression on platelets (Figure 3B) decreased after an 8-week training period in the trained group \((P<0.05; \text{ power}=1.000)\), but remained unchanged in the control group after 8 weeks of this experiment. However, deconditioning reverses the effects of training on resting and postexercise state (Figure 3A and 3B). In contrast, expression and activation of GPIIb/IIIa on the platelet did not change significantly in the trained and control groups during the experimental period (Figure 3C and 3D).

**Discussion**

To our knowledge, this investigation is the first to clearly show that moderate-intensity exercise training decreases resting and short-term severe exercise promoted ASIPA; moreover, this effect is accompanied by reduced capacity of vWF to bind to platelets and the expression of P-selectin on platelets undergoing alternating shear flow. However, the effects of training on ASIPA are reversed to the pretraining state after deconditioning.

Platelet activation induced by shear forces occurring in a stenosed coronary artery is one of the mechanisms of coronary thrombosis.7 Previous studies indicated that shear stress levels in stenotic arteries reach 60 to 3300 dynes/cm²,18 whereas physiological shear stress levels in the human arterial circuit range from 20 to 30 dynes/cm² and 0.8 to 8 dynes/cm² in the venous circuit.19 This investigation indicated that shear-induced platelet aggregation was more significant in alternating shear stress than in low shear stress. Furthermore, the ASIPA was associated with increased binding of vWF to platelets. According to this study, short-term strenuous exercise increased plasma levels of vWF antigen and activity, and was accompanied by enhanced capacity of vWF binding to platelets under alternating shear flow. Augmentation of ASIPA during severe exercise may be related to increased endogenous release of catecholamines; vigorous exercise can promote the release of catecholamines,20 and catecholamines can induce vWF release from vascular endothelial cells21 and also can increase shear-induced platelet aggregation by activating platelet \( \alpha \)-adrenergic receptors.22 Moreover, catecholamines can synergize with shear stress to induce platelet aggregation, and this synergistic response depends on vWF–GP Ib interactions.23 A previous study by the current authors demonstrated that strenuous exercise increased plasma levels of catecholamines and subsequently improved the performance of platelet \( \alpha \)-adrenergic receptors.24 Moreover, this present investigation also showed that treating the platelet with yohimbine, an \( \alpha \)-adrenergic antagonist, partially inhibited ASIPA. Consequently, short-term severe exercise increases the extent of ASIPA, possibly by enhancing the capacity of vWF to bind to platelet by increasing the intrinsic platelet-activating effect of catecholamines.

Clinical investigations observed elevated levels of P-selectin on platelets in conditions associated with arterial thrombosis.25 Even when treated with oral GPIIb/IIIa antagonists after initial thrombolysis, patients with acute coronary syndrome were found to have raised levels of P-selectin, indicating that P-selectin played a role in shear-induced platelet aggregation.26 P-selectin was found earlier to be of importance in cell adhesion under flow conditions; ie, neutrophil and platelet rolling on endothelial cells.27,28 The results from the present study show that treating the platelet with P-selectin antibody significantly blocks the ASIPA, implying a major role of P-selectin in platelet–platelet interactions under this shear condition. Parallel to increased P-selectin exposure, ASIPA also enhanced the capacity of vWF binding to platelets. The binding of vWF to platelet GPIIb complex under high shear stress has previously been demonstrated to cause platelet \([\text{Ca}^{2+}]\), elevation.29 When \([\text{Ca}^{2+}]\), increases in a platelet, P-selectin can be released from the \( \alpha \)-granules in the platelet, subsequently inducing the expression of P-selectin on the platelet membrane. PSGL-1 has been identified as the ligand for P-selectin on neutrophils and monocytes;30 however, the identity of P-selectin ligand on platelets is still unclear. Previous studies show that anti-PSGL-1 antibody had no effect on shear-induced platelet aggregation,15 it is unlikely that PSGL-1 is the ligand for P-selectin on platelets. Colling et al have suggested that sialyl Lewis X-containing gangliosides were potential ligands for P-selectin on platelets.31 The present data demonstrated that...
although the plasma-soluble P-selectin level remains unchanged in response to short-term severe exercise, this exercise enhanced alternating shear-induced expression of membrane-bound P-selectin on platelets. Additionally, a previous study by the present authors also found that short-term severe exercise increased $\alpha_2$-adrenergic receptor-mediated platelet $[\text{Ca}^{2+}]_i$ elevation, implying that vigorous exercise increased exocytosis of $\alpha$ granule and subsequent translocation of P-selectin in platelets. Therefore, the expression of platelet P-selectin induced by severe exercise may create the risk of stenotic-related thrombosis.

Enhanced ASIPA in short-term strenuous exercise noted in this investigation may accelerate the formation of hemostatic platelet plugging, in turn causing thrombosis, and thus increasing the risk of myocardial infarction in patients with coronary stenosis. Notably, the measured results presented in this study showed that moderate-intensity exercise training reduced the extent of ASIPA, as well as vWF binding and P-selectin expression on platelets, in turn reducing the risk of thrombotic events. This phenomenon may explain, at least partially, why regular exercise protects against cardiovascular diseases. Furthermore, the severe exercise-promoted ASIPA diminished after exercise training. This training effect may reduce the risk of thrombotic events in stenotic arteries during vigorous exercise. Therefore, it is plausible to consider moderate-intensity exercise training to be a “safe” exercise dosage for minimizing the risk of myocardial infarction by eliciting beneficial physiological changes.

Several possible mechanisms can explain why moderate-intensity exercise training reduced the extent of ASIPA. First, exercise training may decrease resting and short-term exercise-induced plasma catecholamine levels and down-regulate the performance of platelet $\alpha_2$-adrenergic receptors, thus reducing vWF–platelet interaction and platelet P-selectin expression. Second, previous studies showed that exercise training enhanced substantial release of nitric oxide from platelet and plasma, as well as expression of endothelial nitric oxide synthase, increasing platelet cGMP level and reducing the capacity of adhered platelets to withstand shear stress. Nitric oxide inhibits the formation of thrombus under high-shear flow and attenuates agonist-induced upregulation of P-selectin and the binding of vWF to platelet GPIb complex by negatively regulating the cGMP in platelets. By increasing nitric oxide release, exercise train-
ing may also somehow alter the performance of adhesion molecules on platelets, thereby reducing the platelet activation induced by shear stress. Additionally, chronic aerobic exercise reduces the susceptibility of the low-density lipoprotein of an exerciser to undergo oxidation, and suppresses the oxidized low-density lipoprotein-promoted capacity of adhered platelets to withstand shear stress via enhancing nitric oxide release. Accordingly, a third possibility is that exercise training changes the oxidative modification of lipid profiles in favor of antioxidant release or production, such as nitric oxide, which attenuates oxidative stress-promoted platelet activation under the pathological shear flow condition. However, the results presented here demonstrate that deconditioning reversed the training effect on ASIPA back to the pretraining state. This phenomenon can be explained by the reversed alteration of catecholamine, antioxidants, and lipoprotein patterns after deconditioning.

As in numerous other investigations, one limitation of the present work is that the subjects used tended to be young and healthy, and thus further clinical evidence was required to extrapolate the present results to patients with abnormal or diseased cardiovascular systems, for example, those with coronary stenosis or myocardial ischemia.

In conclusion, the extent of ASIPA can be desensitized by moderate-intensity exercise training. Furthermore, short-term severe exercise-enhanced ASIPA reduces after training. These changes are likely to be mediated by binding vWF to platelets and expression of P-selectin on platelets. However, these training effects are reversible after deconditioning. The findings presented here provide new insights into the possible protective effects of exercise training reducing the risk of thrombosis associated with stenotic arteries.

Acknowledgments

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References


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Figure I. Effects of high shear stress (100 dyne/cm²) for various time intervals on capacity of vWF binding to platelets, expression of P-selectin, and expression (CD41) and activation (PAC-1) of GPIIb/IIIa on platelets. * P<0.05, time= 0 vs. 10, 20, 30, 60, or 12 sec.
Figure II. Effects of CD62P monoclonal antibody (mAb), CD41 mAb, and yohimbine on platelet aggregation mediated by alternating and low shear stresses in both control and trained groups. **AS** indicates alternating shear stress; **LS**, low shear stress; (A), trained, at rest; (B), trained, after exercise; (C), control, at rest; (D), control, after exercise. * P<0.05 platelet + PBS (vehicle) vs. platelet + CD62P, CD41, or yohimbine.