Effects of a single bout of walking exercise on blood coagulation parameters in obese women

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The majority of the studies suggesting an anticoagulant effect of vigorous exercise were performed in young and healthy men, so are not applicable to obese women. The aim of this study was to quantify coagulation changes in response to a single controlled exercise bout with vigorous intensity at 70% of individual peak oxygen uptake (V̇O2) in obese premenopausal Austrian women at risk for thromboembolic complications (34).

Most studies dealing with the effects of exercise on hemostasis were performed in platelet-poor plasma (PPP) samples. However, while PPP contains many of the coagulation factors implicated in the coagulation process, whole blood (WB) includes phospholipid-bearing cells and platelets, which support coagulation. Therefore, in the present study, hemostatic profiling was performed in both WB samples (blood cell counts, course of clot development, platelet function) as well as in PPP samples [coagulation times, i.e., activated partial thromboplastin time (APTT) and prothrombin time (PT)]; thrombin generation curves; markers of thrombin formation; fibrinolytic parameters; levels of the pro- and anticoagulatory factors; and microparticle procoagulant activity.

MATERIALS AND METHODS

Subjects. Forty-two overweight and obese women participated in this trial. Inclusion criteria were as follows: female, age 35–50 yr, pre- or perimenopausal, eligible to participate in exercise, nonsmokers, sedentary work and lifestyle, body mass index between 28 and 40 kg/m², no dietary or nutritional supplement use within 4 wk prior to and immediately after exercise. Standard coagulation times, thrombin generation curves, markers of thrombin generation, fibrinolytic parameters, plasma levels of pro- and anticoagulatory factors, and microparticle procoagulant activity were determined in platelet-poor plasma samples. Thrombelastometry revealed a significant prolongation of clot formation time (P = 0.037) and a significant deceleration of fibrin build up (alpha angle, P = 0.034) after exercise. Calibrated automated thrombography revealed a significant exercise-induced decrease in endogenous thrombin potential (P = 0.039). Moreover, thrombin formation stopped earlier postexercise, reflected in shortened StartTail (P = 0.046). Significantly elevated tissue-plasminogen activator levels (P = 0.001) indicate an exercise-induced activation of the fibrinolytic system. Whole blood cell count increased significantly from pre- to postexercise (P = 0.045), indicating a mild exercise-induced leukocytosis. The results of this study demonstrate that vigorous aerobic exercise might be a suitable tool to protect obese women from thrombotic events. We show that a single bout of vigorous aerobic exercise is clearly associated with an activation of the fibrinolytic system and a decreased readiness of the postexercise samples to form a clot and to generate thrombin, the pivotal enzyme of hemostasis.

coagulation; exercise; obese women; thrombelastometry; thrombin generation}

CARDIOVASCULAR DISEASE (CVD) is a major cause of mortality and morbidity in the Western world. Obesity and sedentary lifestyle have been shown to be associated with increased prevalence of CVD and disturbed hemostasis (24, 39). As a consequence, official recommendations suggest that each individual should conduct 20–60 min of cardiorespiratory exercise 3–5 days/wk (8, 15, 20). These official recommendations are based on studies demonstrating that vigorous physical exercise reduces the risk of CVD by tipping the delicate balance between coagulation and fibrinolysis toward an anticoagulant state (44).
Table 1. Baseline characteristics, performance, and clinical chemistry data of 42 premenopausal, obese, but otherwise healthy women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range*</th>
<th>42 Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>41.1 ± 3.8</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>34.4 ± 4.2</td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>92.0 ± 12.1</td>
<td></td>
</tr>
<tr>
<td>Peak VO₂, ml</td>
<td>2,198 ± 147</td>
<td></td>
</tr>
<tr>
<td>Peak VO₂, ml·kg⁻¹·min⁻¹</td>
<td>25.8 ± 3.6</td>
<td></td>
</tr>
<tr>
<td>VT, ml</td>
<td>1,952 ± 145</td>
<td></td>
</tr>
<tr>
<td>VT, % of peak VO₂</td>
<td>88.8 ± 7.5</td>
<td></td>
</tr>
<tr>
<td>70% of peak VO₂, ml</td>
<td>1,539 ± 128</td>
<td></td>
</tr>
<tr>
<td>70% of peak VO₂, % of VT</td>
<td>78.9 ± 6.3</td>
<td></td>
</tr>
<tr>
<td>Performance at 68% peak VO₂, km/h</td>
<td>6 + 7 (±1.77)</td>
<td></td>
</tr>
<tr>
<td>Dummy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical chemistry:

- Glucose, mmol/l: 3.9–6.1 (5.1 ± 1.5)
- Hemoglobin, g/l: 115–155 (128 ± 14)
- Iron, μmol/l: 11–29 (16.8 ± 5.7)
- Ferritin, μg/l: 18–500 (79.9 ± 57.5)
- Cholesterol, mmol/l: <6.35 (5.7 ± 1.33)
- HDL, mmol/l: 0.80–2.35 (1.17 ± 0.28)
- Triglycerides, mmol/l: <1.80 (1.37 ± 0.58)

Data are presented as means ± SD. BMI, body mass index; VO₂, oxygen uptake; VT, ventilatory threshold; HDL, high-density lipoprotein; Pmax, maximum performance; Peak, peak VO₂ performance at 68% peak VO₂ expressed via speed.

*See Ref. 40.

women met the inclusion and exclusion criteria and were enrolled in the study program.

Study design and time schedule. This was a controlled clinical intervention study. All eligibility testing was finalized 4 wk prior to the 30-min walking exercise test. On the morning of the exercise test a standardized breakfast (2–3 h prior to exercise) was provided. The women came to the laboratory to perform the 30-min walking exercise test with an intensity of 70% of individual peak VO₂. All subjects were scheduled between 10 and 20 of the menstrual cycle.

Incremental exercise tests. As part of eligibility testing each woman performed an incremental exercise test on a treadmill ergometer (QUASARmed, HP Cosmos Sports and Medical, Traunstein, Germany) to check heart and circulatory functions and for determination of peak VO₂. Subjects started at 3 km/h on the treadmill for 3 min (0% slope). After 3 min, women walked at 3.2 km/h on the first step for 1 min. Each minute we increased treadmill velocity 0.4 km/h until 6 km/h. From 6 km/h on we did not increase speed anymore (to ensure walking technique/coordination) but increased the slope 1% each minute for women who could maintain performance. Last step and exhaustion were achieved when subjects were no longer able to maintain walking speed/performance. A standard electrocardiogram was recorded during the entire test, which was supervised by a physician. Blood pressure (RR) was measured at the beginning, during, and at the end of the test.

Respiratory gas exchange and heart rate monitoring. Respiratory gas exchange (RGE) variables were measured throughout the incremental exercise tests using a breath-by-breath mode (Metalyzer 3B, Cortex Biophysik, Leipzig, Germany). During these tests, subjects breathed through a facemask. VO₂, carbon dioxide output (VCO₂), minute ventilation (Vt), breathing rate (BR), and tidal volume (Vt) were continuously obtained. Heart rate (HR) was monitored throughout the tests using a commercially available HR monitor (Polar Vantage NV, Polar Electro Finland).

Thirty-minute walking exercise test. For the 30-min aerobic walking exercise tests individual walking speed was adjusted to 70% of individual peak VO₂ for 30 min on the same treadmill ergometer. All exercise tests were carried out 2–3 h after a standardized breakfast. Similar to the maximal test, subjects completed a warm up phase at 3 km/h on the treadmill ergometer for 3 min. Thereafter, exercise was pursued at 3.2 km/h and work rate was increased by 0.4 km/h every minute until the workload at 70% of peak VO₂ was reached, as calculated from the incremental step test. The test stopped after 30 min of defined exercise. Eight weeks later this procedure was repeated on the same treadmill, under standardized room temperature (20°C) and humidity (60%). Electrocardiogram was recorded during the entire test, which was supervised by a physician. Blood pressure (RR) was measured at the beginning, after 10 and 20 min, and at the end of the test.

Collection of WB and preparation of plasma. Each subject had blood collected in the supine position from a medial cubital vein before exercise (Pre) and immediately after exercise (Post). Blood (2.7 ml) was collected into precipitated S-Monovette premarked tubes (3 from each individual) from Sarstedt (Nümbrecht, Germany), containing 300 μl of 0.106 mol/l sodium citrate. The first tube was discarded. The whole blood from the two remaining tubes was pooled and subsequently used for determination of blood cell counts as well as for thrombelastometry and platelet function measurements. The remaining WB was centrifuged at room temperature for 15 min at 1,200 g to obtain PPP for subsequent determination of standard coagulation times, thrombin generation curves, markers of thrombin generation, fibrinolytic parameters, plasma levels of pro- and anticoagulatory factors, and microparticle procoagulant activity.

Blood cell counts. Blood cell counts were determined on a Sysmex KX-21N Automated Hematology Analyzer from Sysmex.

WB tissue factor triggered thrombelastometry assay. The thrombelastometry (TEM) coagulation analysers (ROTEM 05) (Matel Medizin-technik, Graz, Austria) was used to measure coagulation time (CT), the time from initiation of the test to the initial fibrin formation; clot formation time (CFT), the time from the beginning of clot formation until the amplitude of thrombelastogram reaches 20 mm; maximum clot firmness (MCF), the maximum strength in millimeters of the final clot; and alpha, the angle between the line in the middle of the TEM tracing and the line tangential to the developing “body” of the TEM tracing. The alpha angle represents the acceleration (kinetics) of fibrin build up and cross-linking. This method has been described in detail recently (37).

WB platelet aggregation assay. Whole blood aggregation assessments were performed using a Chrono-Log Whole Blood Aggregometer (APTT and PT) PG 500 from Protop and Go (Eidingen, Germany), which is based on the impedance method (30, 32). Impedance aggregometry results are expressed as amplitude (or maximum aggregation) in ohms at 6 min after reagent addition and as lag time (or aggregation time) in seconds, the time interval until the onset of platelet aggregation. The rate of platelet aggregation is expressed as slope in ohms per minute. Collagen was used as platelet agonist, as previously described (11).

WB platelet adhesion assay. Platelet adhesion was assessed using a Cone and Platelet Analyzer (CPA) (DiaMed, Linz, Austria). The method has been described previously (41). Briefly, 130 μl of citrated WB is placed in polystyrene tubes and allowed to flow (1,300 s) for 2 min using a rotating Teflon cone. The cells were washed with phosphate-buffered saline, stained with May–Grünwald solution and analyzed with an image analysis system. The three platelet function variables, i.e., surface coverage (SC), average size (AS), and number of adhering objects (objects), were evaluated. SC is expressed as the percentage of total area covered by platelets. Average size is defined as the average size of the surface bound objects (28).

APTT and PT. Both APTT and PT were measured on the optomechanical Behring Fibrinometer (Behring Diagnostics, Marburg, Germany) coagulation analyzer. PT results are reported as international normalized ratio (INR).

Automated fluorometric measurement of the thrombin generation. Thrombin generation curves were monitored using calibrated automated thrombography (CAT) (Thrombinoscope BV, Maastricht, the Netherlands) (22). The ability of a given plasma sample to generate thrombin was assessed with respect to lag time preceding the thrombin burst (Lag
Markers of thrombin generation. Plasma levels of prothrombin fragment 1+2 (F 1+2) and thrombin-antithrombin complexes (TAT) were determined using ELISA kits from Behring Diagnostics (Marburg, Germany).

Fibrinolytic values. Plasma levels of tissue-plasminogen activator (t-PA) and plasminogen activator inhibitor-I (PAI-I) were determined using the assays IMUBIND tPA ELISA kit and IMUBIND PAI-I Plasma ELISA, respectively, from American Diagnostica (Pfungstadt, Germany).

Procoagulatory factors. Plasma levels of prothrombin (FII), FVIII, and FXa were determined using the IMUBIND tPA ELISA kit and IMUBIND PAI-I Plasma ELISA, respectively, from American Diagnostica (Pfungstadt, Germany). Plasma levels of prothrombin (FII), FVII, FVIII, and FXa were determined using the assays IMUBIND tPA ELISA kit and IMUBIND PAI-I Plasma ELISA, respectively, from American Diagnostica (Pfungstadt, Germany).

Anticoagulatory factors. Plasma levels of tissue factor pathway inhibitor (TFPI) were determined using the ACTICHROME Tissue Factor ELISA kit from American Diagnostica.

Statistical analyses. All statistical analyses were performed using SPSS for Windows software, version 19.0. Data are shown in Table 2. Statistical significances concerning CT and MCF. CTs and CFTs in both pre- and postexercise were compared pre- and postexercise with respect to amplitude, slope, and lag time. These parameters were not affected by this model of exercise. Platelet aggregation in terms of amplitude and slope was slightly less pronounced in the obese women compared with apparently healthy women (37). Data are shown in Table 2.

**RESULTS**

Thirty-minute controlled walking exercise. The postexercise analyses revealed that women performed de facto at 68.2 ± 3.1% of individual peak VO2 (which was determined 4 wk before). This demonstrates that the women could hold the preset intensity at 70% of peak VO2 over 30 min accurately. The average walking speed was 6 ± 0.59 km/h at this exercise intensity. Performance and clinical chemistry data are shown in Table 1.

Blood cell counts pre- vs. postexercise. WBC count increased significantly from pre- to postexercise (P = 0.045), indicating a mild exercise-induced leukocytosis (18). IL-6 and TNF-alpha remained unchanged (data not shown). Red blood cell count did not change, although there was a trend to increased hematocrit and hemoglobin (P = 0.077 and 0.072 respectively). Data are shown in Table 2.

Platelet aggregation values pre- vs. postexercise. WB platelet aggregation values were compared pre- and postexercise with respect to amplitude, slope, and lag time. These parameters were not affected by this model of exercise. Platelet aggregation in terms of amplitude and slope was slightly less pronounced in the obese women compared with apparently healthy women (37). Data are shown in Table 2.

**Table 2. Coagulation values in WB samples prior and after the 30-min aerobic walking exercise test**

<table>
<thead>
<tr>
<th>Blood cell counts</th>
<th>Preexercise (Mean ± SD)</th>
<th>Postexercise (Mean ± SD)</th>
<th>Reference Values Mean (95% Range) or Mean ± SD</th>
<th>Significance (Pre vs. Post)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC, ×10⁹ µl⁻¹</td>
<td>6.7 ± 1.8</td>
<td>7.5 ± 1.9</td>
<td>7.0 (4.3–10.0)a</td>
<td>0.045</td>
</tr>
<tr>
<td>RBC, ×10⁶ ml⁻¹</td>
<td>4.1 ± 0.3</td>
<td>4.2 ± 0.4</td>
<td>4.5 (3.5–5.5)a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>12.6 ± 0.8</td>
<td>12.9 ± 0.8</td>
<td>13.5 (12–15)a</td>
<td>0.072</td>
</tr>
<tr>
<td>Hct, %</td>
<td>38.3 ± 1.8</td>
<td>39.0 ± 1.8</td>
<td>42 (36–48)a</td>
<td>0.077</td>
</tr>
<tr>
<td>Platelets, ×10⁹ ml⁻¹</td>
<td>239 ± 56</td>
<td>257 ± 64</td>
<td>250 (125–318)a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Thrombelastometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT, s</td>
<td>382 ± 86</td>
<td>398 ± 83</td>
<td>322 ± 55b</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>CFT, s</td>
<td>142 ± 31</td>
<td>165 ± 47</td>
<td>119 ± 28b</td>
<td>0.037</td>
</tr>
<tr>
<td>MCF, mm</td>
<td>60.9 ± 3.6</td>
<td>61.6 ± 4.2</td>
<td>61.3 ± 5b</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Alpha, °</td>
<td>63.2 ± 6.2</td>
<td>59.8 ± 7.7</td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>Platelet aggregation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lag time, s</td>
<td>133.1 ± 95.1</td>
<td>131.6 ± 84.4</td>
<td>58.6 ± 9.7a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Slope, ohms/min</td>
<td>9.6 ± 4.8</td>
<td>10.2 ± 4.4</td>
<td>8.4 ± 2.0a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Amplitude, ohms</td>
<td>12.1 ± 3.1</td>
<td>12.9 ± 3.2</td>
<td>13.6 ± 1.4a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Platelet adhesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surface coverage, %</td>
<td>12.5 ± 3.9</td>
<td>12.8 ± 4.1</td>
<td>14.9 ± 2.5a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Average size, µm²</td>
<td>41.7 ± 16.9</td>
<td>38.1 ± 14.0</td>
<td>39.4 ± 5.2a</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Objects, counts</td>
<td>1,853 ± 415</td>
<td>2,002 ± 512</td>
<td>1,380f</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

WB, whole blood; WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Hct, hematocrit; CT, coagulation time; CFT, clot formation time; MCF, maximum clot firmness; Pre, preexercise; Post, postexercise. See text for definition of alpha angle. aSee Ref. 21; bsee Ref. 11; csee Ref. 10; dsee Ref. 15; esee Ref. 25. Boldface indicates significant difference, Pre vs. Post.
healthy adults; lag times were markedly prolonged compared with healthy adults (11). Data are shown in Table 2.

**WB platelet adhesion pre- vs. postexercise.** WB platelet adhesion values were compared pre- and postexercise with respect to SC, AS, and number of objects. No differences were found for these parameters. Platelet adhesion in terms of SC and AS was comparable to that of healthy adults; number of objects was higher in the obese women. Data are shown in Table 2.

**APTT and PT (INR) pre- vs. postexercise.** No statistically significant differences were found between pre- and postexercise. Data are shown in Table 3.

**Thrombin generation values pre- vs. postexercise.** Thrombin generation was compared pre- and postexercise with respect to Lag Time, tPeak, Peak, ETP, and StartTail. In the postexercise PPP samples, ETP was significantly decreased \((P = 0.039)\) and thrombin formation ceased earlier, reflected in shortened StartTail \((P = 0.046)\). Lag Time, tPeak, and Peak remained unaffected by exercise. Data are shown in Table 3.

**Markers of thrombin generation pre- vs. postexercise.** Plasma levels of F1+2 as well as of TAT were not affected by the model of exercise. F1+2 levels were above normal in both pre- and postexercise PPP samples. Data are shown in Table 3.

**Fibrinolytic values pre- vs. postexercise.** Significantly elevated t-PA levels \((P = 0.001)\) postexercise indicated an exercise-induced activation of the fibrinolytic system. Levels of PAI-1 were not affected by the model of exercise. Data are shown in Table 3.

**Levels of procoagulatory factors pre- vs. postexercise.** Plasma levels of FII and FVII were not affected by exercise. However, both markers were distinctly above normal in both pre- and postexercise samples. FVIII levels exceeded 168% in both pre- and postexercise samples. No exercise-induced increase in plasma levels of TF was observed. Data are shown in Table 3.

**Microparticle procoagulant activity pre- vs. postexercise.** Microparticle procoagulant activity, evaluated by means of enzyme-linked immunosorbent assay, was not affected by the model of exercise. However, the values were distinctly above normal in both pre- and postexercise PPP samples. Data are shown in Table 3.

**Concentration of anticoagulatory factors pre- vs. postexercise.** Exercise did not cause significant changes in plasma levels of TFPI. Levels of TFPI were lower than normal in both pre- and postexercise PPP samples. Data are shown in Table 3.

**DISCUSSION**

Numerous studies, undertaken to examine the effects of physical activity on hemostasis, report on both pre- as well as on anticoagulant effects of exercise. A field synopsis leads to the assumption that the hemostatic response to exercise is mainly influenced by the intensity of exercise (26, 27, 39). Heavy exercise (83% VO\(_{2}\)\(_\text{max}\)) activates both the coagulation and the fibrinolysis system (43) whereas vigorous exercise (68% VO\(_{2}\)\(_\text{max}\)) is associated with an enhancement of fibrinolysis without a concomitant increase in markers of blood coagulation (44). Wang et al. (42) have shown that platelet adhesiveness and aggregation are upregulated by strenuous but not by vigorous exercise.

In this study the aim was to investigate whether otherwise healthy obese women, assumed to be at an elevated risk for thrombotic events, might show a hemostatic benefit from a controlled bout of vigorous exercise.

Hemostatic profiling of the preexercise PPP, but not of the WB samples, suggests that, in accordance with the above-

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**Table 3. Coagulation values in PPP samples prior and after the 30-min aerobic walking exercise test**

<table>
<thead>
<tr>
<th>Coagulation times</th>
<th>Preexercise Mean ± SD</th>
<th>Postexercise Mean ± SD</th>
<th>Reference Range</th>
<th>Significance (Pre vs. Post)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTT, s</td>
<td>35.2 ± 4.0</td>
<td>36.1 ± 4.7</td>
<td>30–40</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>INR</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Thrombin generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lag time, min</td>
<td>2.07 ± 0.5</td>
<td>2.1 ± 0.3</td>
<td>3.1 ± 1.4*</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>ETP, nmol·L(^{-1})·min(^{-1})</td>
<td>1,981 ± 311</td>
<td>1,640 ± 304</td>
<td>1,879 ± 284*</td>
<td>0.039</td>
</tr>
<tr>
<td>Peak, nmol/l</td>
<td>479 ± 56</td>
<td>463 ± 59</td>
<td>458 ± 60*</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Time to peak, min</td>
<td>3.8 ± 0.7</td>
<td>3.7 ± 0.6</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Starttail, min</td>
<td>19.2 ± 2.0</td>
<td>18.4 ± 2.1</td>
<td>0.046</td>
<td></td>
</tr>
<tr>
<td>Markers of thrombin generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F1+2, pmol/l</td>
<td>247.9 ± 97.0</td>
<td>268.2 ± 107.0</td>
<td>69–229*</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>TAT, μg/l</td>
<td>6.26 ± 10.7</td>
<td>3.1 ± 1.2</td>
<td>1.0–4.1*</td>
<td>0.064</td>
</tr>
<tr>
<td>Fibrinolytic values</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-PA Ag, ng/ml</td>
<td>6.4 ± 2.2</td>
<td>8.6 ± 3.1</td>
<td>1.4–8.4*</td>
<td>0.001</td>
</tr>
<tr>
<td>PAI-1 Ag, ng/ml</td>
<td>16.5 ± 13.9</td>
<td>15.1 ± 11.6</td>
<td>3–40*</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Procoagulatory factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F II, %</td>
<td>145.1 ± 24.6</td>
<td>148.1 ± 22.0</td>
<td>70–120</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>F VII, %</td>
<td>143.0 ± 34.9</td>
<td>142.6 ± 35.2</td>
<td>70–120</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>F VIII, %</td>
<td>&gt;168</td>
<td>&gt;168</td>
<td>70–120</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>TF, pg/ml</td>
<td>187 ± 59</td>
<td>195 ± 64</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>MP procoagulant activity, nmol/l</td>
<td>19.1 ± 13.1</td>
<td>21.9 ± 15.2</td>
<td>9.2 ± 2.8*</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Anticoagulatory factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TFPI, μg/l</td>
<td>49.8 ± 17.1</td>
<td>49.5 ± 16.3</td>
<td>60–180*</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

PPP, platelet-poor plasma; APTT, activated partial thromboplastin time; INR, international normalized ratio; ETP, endogenous thrombin potential; F 1+2, prothrombin fragment 1+2; TAT, thrombin-antithrombin complex; t-PA, tissue-plasminogen activator; PAI-1, plasminogen activator inhibitor I; TF, tissue factor; MP, microparticles; TFPI, tissue factor pathway inhibitor. *See Ref. 17; †according to Dade Behring (unpublished observations); ‡see Ref. 9; ‡‡see Ref. 30; ‡‡‡see Ref. 3. Boldface indicates significant difference, Pre vs. Post.
Exercise and Coagulation in Obese Women • Lamprecht M et al.

mentioned assumption, these women were in a hypercoagu-
able state compared with healthy, nonobese subjects. Preexer-
cise plasma levels of F 1+2 were markedly higher than those of healthy nonobese subjects, indicating elevated formation of
thrombin. Moreover, preexercise plasma levels of FII, FVII, and FVIII were markedly higher than normal. Elevated plasma
levels of these three coagulation factors have been shown to be associated with an increased readiness to form thrombin (4, 7, 22). Further evidence of a hypercoagulable state in these obese
women was the low level of TFPI. Low levels of TFPI have been shown to have a procoagulant effect by facilitating the initiation of
thrombin generation (1, 4). Evidently, these obese women were
apparently in a hypercoagulable state prior to exercise due to a markedly elevated procoagulant activity of microparticles com-
pared with healthy young men (38). These results emphasize the
importance of an antithrombotic prophylaxis/treatment of obese
women.

The data show that regular vigorous exercise might be a
suitable tool to shift the hemostatic system of obese women
toward an anticoagulant state. 1) The fibrinolytic system was
significantly activated; and both the 2) clot-forming capacity as
well as the 3) thrombin-forming capacity were significantly
decreased in the postexercise samples.

1) Obesity-related atherothrombotic risk has been shown to be
associated with an impaired capability of endothelial cells to
release t-PA, the pivotal enzyme initiating the endogenous
fibrinolytic response (5, 40). The present study showed, in
accordance with others, significantly elevated t-PA levels in
the postexercise PPP samples (29, 36, 45). We conclude that
particularly obese women, known to be at an elevated risk for
thromboembolic complications, might benefit from the exer-
cise-induced high plasma levels of t-PA known to enhance the
efficacy of endogenous fibrinolysis (23).

2) TEM measurements revealed an impaired clot-formation
capacity of the postexercise WB samples. CFTs were signific-
antly prolonged and alpha angles were significantly lower in
the postexercise compared with the preexercise WB samples,
indicating impaired fibrin build up and cross-linking (37).
Presumably, this impaired clot formation is attributable, at least
in part, to the exercise-induced increase of t-PA. Several
groups have reported impaired clot development in the pres-
ence of increasing amounts of t-PA. Nielsen et al. (31) have
shown significantly decreased TTP (total thrombus generation
in the presence of increasing amounts of t-PA. Ploppa et al.
(33) have shown significantly impaired clot formation in a
patient with a massive pulmonary embolism after administr-
ation of recombinant t-PA, and D’Amico et al. (14) have shown
reduced MCFs and prolonged CTs in the presence of recom-
binant t-PA (1 μg/ml).

3) CAT measurements revealed an impaired thrombin-forming
capacity after vigorous exercise. Free thrombin was gen-
erated in significantly lower amounts (reflected by lower ETP
values) and disappeared significantly earlier (reflected by
shorter StartTails) in the postexercise PPP samples stimulated
by addition of TF. The underlying mechanisms leading to this
diminished capability of the postexercise PPP samples to
generate thrombin remain to be elucidated. The two most
reasonable explanations, decreased plasma levels of prothrom-
bin and/or decreased plasma levels of TF, do not apply. It has
been shown that thrombin generation dose dependently de-
creases in the presence of decreasing amounts of prothrombin
(2) as well as of TF (2, 22). However, in the present study, both
prothrombin and TF levels were virtually the same in the pre-
and postexercise samples. Another explanation for the dimin-
ished capability of the postexercise PPP samples to generate
thrombin might be exercise-induced elevated levels of antith-
rombin (AT) or alpha 2-macroglobulin (a2-M), the two most
efficient inhibitors of thrombin (4). A dose-dependent decrease
of ETP in the presence of increasing amounts of AT and a2-M
has been shown previously (13). In the present study AT and
a2-M plasma levels were not determined. However, it is
unlikely that the vigorous exercise applied here resulted in
significantly elevated plasma levels of these two inhibitors.
Huisveld et al. (23) have shown elevated AT and a2-M levels
after exhaustive exercise, but that increase was completely
attributable to hemoconcentration, and Cerneca et al. (6) have
shown modest, yet significant, increases in AT levels after
exhaustive exercise in trained but not in untrained individuals.
Despite this, plasma levels of AT as well as of a2-M remain to
be monitored in future studies dealing with exercise and
coagulation.

In a similar study, Beltan et al. (2a) have shown a decrease
of APTT in healthy subjects after a 15 min duration exercise
conducted at almost the same intensity as in the present study
indicating no such decrease. It has been suggested that the
decrease of APTT is, at least partially, attributable to an
exercise-induced increase of FVIII coagulant activity. In con-
trast to the study of Beltan et al. (2a), our subjects were already
in a hypercoagulable state prior to testing, reflected by, e.g.,
increased levels of FVIII. Thus an exercise-induced increase of
already elevated FVIII levels apparently does not result in
shortened APTT. This assumption is supported by the findings
of van Veen et al. (47). They have shown that the procoagulant
action of FVIII dose dependently increases (by measuring
thrombin generation curves) within a range of 1 to 100% of
normal value and reaches a plateau at ~150%.

Presumably, the anticoagulant effect of vigorous exercise
might be dampened by leukocytosis. In agreement with various
other studies this work showed significantly elevated WBC
counts (by ~12%) in the postexercise WB samples (35). Leuko-
cyte procoagulant activity and the capability of leuko-
cyte products to augment the ability of endothelial cells to
activate coagulation have been shown previously (17). How-
ever, this leukocytosis-induced procoagulant effect is modest
in this vigorous exercise experiment, although it might be of
importance in studies dealing with intense exercise (19).

At this time it is unknown how long the effect of a single
exercise bout on blood coagulation persists. Further research is
required to estimate the effects of standardized chronic exer-
cise programs over several weeks or months on hemostasis in
obese women.

In conclusion, these findings demonstrate that a single bout
of vigorous aerobic exercise is clearly associated with an
activation of the fibrinolytic system and with a decreased
readiness of the postexercise samples to form a clot and to
generate thrombin, the pivotal enzyme of hemostasis.

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No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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