Table. 1. Influence of an acute exercise bout on biomarkers of thrombogenicity.

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| **Subject characteristics** | **Exercise mode // duration // intensity** | **Biochemical markers of blood homeostasis: Post** **vs. pre acute** **exercise** | **Reference**  |
| **Males and Females** **(grouped)**21 Males & 3 FemalesAge: 26 ± 7 yr.VO2max (ml kg min-1): 35.6 ± 7.3 | Semi-recumbent bike ergometer // 5 min (submaximal) & ~12 min (maximal) //Submaximal Exercise (5 watts)Maximal Exercise (peak power 269 ± 48 watts) | (arrows indicate **vs. pre** resting plasma markers)

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| **Submaximal** Exercise↔ df↔ TGP↔ GGP↔ PT↔ APTT↔ Clauss↔ Fibrinogen↔ D-dimer↔ Factor VIII:C↔ vWF Antigen↔ PAI-1 Antigen | **Maximal** Exercise↑ df↓ TGP↑ GGP↔ PT↓ APTT↔ Clauss↔ Fibrinogen↔ D-dimer↔ Factor VIII:C↔ vWF Antigen↑ PAI-1 Antigen |

 | (Davies et al., 2016) (n=24) |
| **Male only**Age: 25 ± 3 yr.VO2peak (ml kg min-1): 43.1 ± 5.2  | Bike-ergometer // 60 min // Moderate Exercise (57 ± 9 % VO2Peak) Strenuous Exercise (69 ± 10 % VO2Peak) | (arrows indicate **vs. pre** resting plasma markers; double arrow **vs. moderately** exercise in addition)

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| **Moderate** Exercise:↑ D-dimer↑ Factor VIII↑ Plasmin–a2–antiplasmin complex↑ t-PA Activator↑ t-PA Antigen↓ APTT↔ PT ↔ Post exercise Lactate ↑ Epinephrine ↑ Norepinephrine | **Strenuous** Exercise:↓ D-dimer↑↑ Factor VIII↑↑ Plasmin–a2–antiplasmin complex↑↑ t-PA Activator↑↑ t-PA Antigen↓ APTT↔ PT ↑ Post exercise Lactate↑ Epinephrine↑↑ Norepinephrine |

 | (Menzel and Hilberg, 2011)(n=20) |
| **Males Only**Age: 23.4 ± 2.8 yr.VO2max (ml kg min-1): 47.8 ± 5.4 | Walk // 30 min 1.93 km h-1Run // 30 min 70–75% VO2max (Moderate intensity)  | (arrows indicate **vs. pre** resting plasma markers)

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| **Walk**:↔ APTT↔ D-dimer↔ Factor VIII↔ t-PA  | **Run:**↓ APTT↑ D-dimer↑ Factor VIII↑ t-PA  |

 | (Hegde et al., 2001)(n=10) |
| **Males Only**Age: 22.9 ± 3.4 yr.VO2max (ml kg min-1): 41.4 ± 3.9Blood taken immediately before ceasing of exercise. | Bike-ergometer // 20 min // ½ of lactate threshold, lactate threshold and 4 mmol/L.  | (arrows indicate **vs. pre** resting plasma markers)

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| **½ lactate threshold:**↔ t-PA Antigen↔ t-PA Activator↔ PT↔ APTT↔ PAI-1 Antigen↔ Plasminogen | **lactate threshold:**↔ t-PA Antigen↔ t-PA Activator↔ PT↓ APTT↔ PAI-1 Antigen↔ Plasminogen  | **4 mmol/L:**↑ t-PA Antigen↑ t-PA Activator↔ PT↓ APTT↔ PAI-1 Antigen↑ Plasminogen |

 | (Handa et al., 1992)(n=10) |
| **Males only** Age: 28.0 yr. (P25 23/P75 32)VO2peak (ml kg min-1): 47.62 ± (P25 45,21/P75 52,27)(medians and P25/75 – percentiles) | Bike ergometer // Sprints 30sec // Wingate-testing (Maximal intensity) | (arrows indicate **vs. pre** resting plasma markers; double arrow **vs. 30 min post** in addition)

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| **2 min post**:↑↑ D-dimer↑↑ Factor VIII↑↑ Fibrinogen↑↑ PT↑↑ t-PA↓ PTT | **9 min post**:↑ D-dimer↑↑ Factor VIII↑↑ Fibrinogen↑↑ PT↑↑ t-PA↓ PTT | **30 min post:**↑ D-dimer↑ Factor VIII↑ Fibrinogen↑ PT↑ t-PA↓ PTT |

 | (Gunga et al., 2002)(n=15) |
| **Males only**Age:31.8 yr.“Well-trained healthy male” | Marathon running finnish // 2:44:30 ± NA | (arrows indicate **vs. pre** resting plasma markers; double arrow **vs. 22 hours post** exercise in addition)

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| **Immediately post**:↑↑ Factor VIII↔ Fibrinogen↔ PT↓ PTT | **60 min post**:↑↑ Factor VIII↔ Fibrinogen↔ PT↓ PTT | **22 hours post:**↑ Factor VIII↔ Fibrinogen↔ PT↔ PTT |

 | (Röcker et al., 1986)(n=16) |
| **Males only** Untrained (n=13) Age: 52.5 ± 5.4 yr. VO2max (ml kg min-1): 34.5 ± 4.3 Moderately trained (n=15)Age: 52.0 ± 5.4 yr.VO2max (ml kg min-1): 46.6 ± 3.9Highly trained (n=14) Age: 50.1 ± 5.6 yr.VO2max (ml kg min-1): 60.0 ± 6.0 | Dynamic one-leg knee-extension // 10 min & 10 min // 40% watt max:17 ± 7.2 Untrained23 ± 7.7 moderately trained32 ± 3.7 highly trained | **Resting:** (one arrow indicates **vs. untrained** resting platelet reactivity; double arrow **vs. moderately** trained in addition)

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|  | **Moderately trained:****platelet reactivity induced by:**↔ Collagen ↔ Adrenaline | **Highly trained:****platelet reactivity induced by:**↓↓ Collagen ↓↓ Adrenaline |

**12 Watt:** (arrows indicate **vs. inherent** resting platelet reactivity)

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| --- | --- | --- |
| **Sedentary:**↔ Adrenaline induced platelet aggregation | **Moderately trained:**↓ Adrenaline induced platelet aggregation | **Highly trained:**↓ Adrenaline induced platelet aggregation |

**40% Wattmax:** (arrows indicate **vs. inherent** resting reactivity)

|  |  |  |
| --- | --- | --- |
| **Sedentary:**↑ Adrenaline induced platelet aggregation | **Moderately trained:**↔ Adrenaline induced platelet aggregation | **Highly trained:**↔ Adrenaline induced platelet aggregation |

 | (Lundberg Slingsby et al., 2018) (n=42) |
| **Female only** 14 completedAge: 20.1 ± 1.4 yr.VO2max (ml kg min-1): 30.4 ± 3.2Menstrual phase confirmed by plasma progesterone levels:* **Late follicular**
* **Midluteal**
 | Bike-ergometer // 15 min // Moderate intensity (75% HRmax) | **Pre-exercise:** (arrows indicate **vs. other** menstrual phase)

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| Late follicular:↔ Thromboxane B2 levels**platelet reactivity induced by:**↔ ADP ↔ Collagen  | Midluteal:↑ Thromboxane B2 levels**platelet reactivity induced by:**↔ ADP ↔ Collagen  |

**Post-exercise:** (arrows indicate **vs. pre**-exercise values)

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| --- | --- |
| Late follicular:↑ Thromboxane B2 levels**platelet reactivity induced by:**↔ ADP ↑ Collagen | Midluteal:↔ Thromboxane B2 levels**platelet reactivity induced by:**↔ ADP ↑ Collagen  |

 | (Ersöz et al., 2002)(n=16) |

Values are Mean ± SD unless stated otherwise.

Table 2. The effect of different training protocols on biomarkers of thrombogenicity.

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| **Subject characteristics** | **Exercise mode // duration // intensity** | **Biochemical markers of blood homeostasis: Post vs. pre**- **exercise training** | **Reference**  |
| **Males only**Training (n=26)Age: 30 to 49 yr. VO2max (ml kg min-1): 38.4 beforeVO2max (ml kg min-1): n.s . afterControl (n=27)Age: 30 to 49 yr.VO2max (ml kg min-1): 36.1 beforeVO2max (ml kg min-1): n.s. after | Brisk walking + slow jogging // 3 months - 45 to 60 min, 5 x week // moderate/low-intensity | (arrows indicate **vs. pre** training resting platelet reactivity)

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| --- | --- |
| **Training** ↓ ADP induced platelet aggregation | **Control**  ↔ ADP induced platelet aggregation |

 | (Rauramaa et al., 1986) (n=53) |
| **Males only** Control (n=12)Age: 21.7 ± 2.2 yr. VO2max (ml kg min-1): ~34 beforeVO2max (ml kg min-1): ~44 afterTraining (n=11)Age: 21.0 ± 2.3 yr.VO2max (ml kg min-1): ~34.5 beforeVO2max (ml kg min-1): n.s. after | Bike-ergometer // 2 months – 30min, 5 x week // moderate-intensity | (arrows indicate **vs. pre** training platelet reactivity after acute maximal exercise)

|  |  |
| --- | --- |
| **Training** ↓ ADP induced platelet aggregation | **Control** ↔ ADP induced platelet aggregation |

 | (Wang et al., 1995)(n=21) |
| **Females only**Training (n=8)Age: 22 ± 1.3 yr. VO2max (ml kg min-1): ~26 beforeVO2max (ml kg min-1): ~36 afterControl (n=8)Age: 21.3 ± 0.8 yr.VO2max (ml kg min-1): ~25 beforeVO2max (ml kg min-1): n.s. after | Bike-ergometer // 2 menstrual cycles – 30min, 5 x week // moderate-intensity | (arrows indicate **vs. pre** training platelet reactivity after acute maximal exercise)

|  |  |
| --- | --- |
| **Training**↓ ADP induced platelet aggregation | **Control** ↔ ADP induced platelet aggregation |

 | (Wang et al., 1997)(n=16) |
| **Males and Females (grouped)**Exercise (7M/6F) Age: 32.1 ± 6.4 yr. VO2max (ml kg min-1): 42.9 ± 2.3 beforeVO2max (ml kg min-1): 47.8 ± 2.7 afterControl (6M/6F) Age: 33.4 ± 5.4 yr.VO2max (ml kg min-1): 43.5 ± 0.4 beforeVO2max (ml kg min-1): 44.0 ± 2.8 after | Bike-ergometer // 3 months - 30 min, 3 x week // moderate-intensity |  (arrows indicate **vs. pre** training plasma markers at rest and after acute maximal exercise)

|  |  |
| --- | --- |
| **Training**↔ APTT↔ Factor VIII antigen  | **Control**↔ APTT↔ Factor VIII antigen  |

 | (El-Sayed et al., 1995)(n=25) |
| **Males only** Age: 26 ± 3.6 yr. (n=13) VO2max (ml kg min-1): 48.4 ± 5.8 beforeVO2max (ml kg min-1): 56.5 ± 6.1 afterAge: 40 ± 3.6 yr. (n=13) VO2max (ml kg min-1): 41.2 ± 6.1 beforeVO2max (ml kg min-1): 47.2 ± 6.9 afterAge: 54 ± 3.6 yr. (n=13)VO2max (ml kg min-1): 31.2 ± 4.0 beforeVO2max (ml kg min-1): 36.6 ± 5.1 after | Bike-ergometer // 3 months - 60 min, 2 x week // moderate-intensity | (arrows indicate **vs. pre** training plasma markers immediately after acute maximal exercise)

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| **Age 20-30:**↑ t-PA Activator↑ t-PA Antigen↑ Factor VIII:C↓ APTT↑ vWF Activity↔ D-dimer | **Age 35-45**:↑ t-PA Activator↑ t-PA Antigen↑ Factor VIII:C↓ APTT↑ vWF Activity ↔ D-dimer | **Age 50-60:**↑ t-PA Activator↑ t-PA Antigen↑ Factor VIII:C↓ APTT↔ vWF Activity↔ D-dimer |

 | (van den Burg et al., 2000)(n=39) |
| **Females only**Pre-menopausal (n=13)Age: 49.1 ± 1.4 yr. VO2max (ml kg min-1): 31.5 ± 2.2 beforeVO2max (ml kg min-1): 34.8 ± 3.2 afterPost-menopausal (n=14) Age: 53.7 ± 2.2 yr.VO2max (ml kg min-1): 30.4 ± 3.4 beforeVO2max (ml kg min-1): 33.5 ± 4.1 after | Bike-ergometer // 3 months - 1h, 3 x week // high-intensity | (arrows indicate **vs. pre** training resting platelet reactivity)

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| **Pre**-menopausal**platelet reactivity induced by:**← TRAP-6 ↓ ADP↓ Collagen | **Post**-menopausal**platelet reactivity induced by:**← TRAP-6 ↔ ADP↔ Collagen |

 | (Lundberg Slingsby et al., 2017) (n=27) |

Values are Mean ± SD unless stated otherwise.

Table 3. Influence of an acute exercise bout on biomarkers of thrombogenicity in patient groups compared to healthy controls.

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| --- | --- | --- | --- |
| **Subject characteristics** | **Exercise mode // duration // intensity** | **Biochemical markers of blood homeostasis: Post** **vs. pre acute** **exercise** | **Reference**  |
| **Males and Females** **(grouped)**Control 11 Males & 9 FemalesAge: 63 ± 10 yr. Ankle brachial pressureindex: 1.14 ± 0.10Patients with intermittent claudication**\*** 16 Males & 4 FemalesAge: 68 ± 8 yr.Ankle brachial pressureindex: 0.62 ± 0.13 | Treadmill (speed 3.5 km h-1, incline 5°) // maximum walking distance or corresponding average for control (3min, 20sec) \* medicated with 75mg aspirin; 40 mg of simvastatin or pravastatin and 10 mg of atorvastin | (arrows indicate **patient vs. control** plasma markers)

|  |  |  |
| --- | --- | --- |
| **Before:**↑ soluble P-selectin ↔ vWF**Platelet reactivity induced by:**↓ TRAP ↓ COX | **Immediately post:**↑ soluble P-selectin ↔ vWF**Platelet reactivity induced by:**↓ TRAP ↓ COX | **1 hour post:**↑ soluble P-selectin ↔ vWF |

 | (Collins et al., 2006)(n=40) |
| **Males and Females (grouped)**Control 15 Males & 3 Females Age: 33.9 ± 6.2 yr. BMI (kg m-2): 23.54 ± 2.66Hypertensives# 22 Males & 4 FemalesAge: 38.1 ± 6 yr.BMI (kg m-2): 28.35 ± 2.57 Coronary artery disease patients\* 13 Males & 3 Females Age: 40.9 ± 3.9 yr.BMI (kg m-2): 29.07 ± 4.26 | Treadmill exercise test by modified protocol by Bruce (increased gradually from2.7 km/h (1.7 mph) and 10% grade incline every three minutes)  // 5 stages (15 min)# not using antihypertensive medication\* Medication of CAD group were paused for at least one week. The use of aspirin, non-steroid anti-inflammatory drugs or other drugs that interfere with platelet function was prohibited for two weeks prior to experiment. | **Pre-exercise:** (one arrow indicates **vs. Control** resting platelet reactivity)

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| --- | --- | --- |
|  | Hypertensive:↔ Thromboxane B2 levels↑ Epinephrine ↑ Norepinephrine | Coronary artery disease:↔ Thromboxane B2 levels↑ Epinephrine ↑ Norepinephrine |

**15 min treadmill:** (arrows indicate **vs. inherent** pre-exercise platelet reactivity and plasma markers; double arrow **vs. Control** in addition)

|  |  |  |
| --- | --- | --- |
| Control:↔ Thromboxane B2 ↑ Epinephrine ↑ Norepinephrine**Platelet reactivity induced by:**↓ Collagen ↓ ADP | Hypertensive:↔ Thromboxane B2 levels↑↑ Epinephrine ↑↑ Norepinephrine**Platelet reactivity induced by:**↓ Collagen ↓ ADP | Coronary artery disease:↔ Thromboxane B2 levels↑↑ Epinephrine ↑↑ Norepinephrine**Platelet reactivity induced by:**↓ Collagen ↓ ADP |

**10 min post:** (arrows indicate **vs. inherent** resting platelet reactivity and plasma markers; double arrow **vs. Control** in addition)

|  |  |  |
| --- | --- | --- |
| Control↔ Thromboxane B2 levels↑ Epinephrine ↑ Norepinephrine **Platelet reactivity induced by:**↓ Collagen ↓ ADP | Hypertensives**:**↔ Thromboxane B2 levels↑↑ Epinephrine ↑ ↑ Norepinephrine**Platelet reactivity induced by:**↔ Collagen ↔ ADP | Coronary artery disease:↔ Thromboxane B2 levels↑↑ Epinephrine ↑↑ Norepinephrine**Platelet reactivity induced by:**↔ Collagen ↔ ADP  |

 | (Petidis et al., 2008)(n=60) |
| **Males and Females (grouped)**Control\* 17 Males & 14 Females Age: 35.2 ± 9.4 yr.VO2peak (ml kg min-1): 37.84 ± 8.66 Hypertensives\* 12 Males & 7 FemalesAge: 46.8 ± 7.5 yr.VO2peak (ml kg min-1): 31.04 ± 10.55  | Treadmill // 20 min // Moderate intensity (65–70% VO2peak) \*no medication 1 week prior toexercise | (arrows indicate **Hypertensives vs. control** plasma markers)

|  |  |  |
| --- | --- | --- |
| **Before:**↔ Epinephrine ↔ Norepinephrine **Platelet reactivity by:**↔ Unstimulated↔ ADP | **Immediately post:**↔ Epinephrine ↔ Norepinephrine **Platelet reactivity by:**↔ Unstimulated↔ ADP | **25 min post:**↔ Epinephrine ↔ Norepinephrine **Platelet reactivity by:**↑ Unstimulated↔ ADP |

 | (Hong et al., 2009)(n=50) |
| **Males and Females (grouped)**Control 16 Males & 4 Females Age: 51 ± 7 yr.Coronary artery disease patients\* 46 Males & 16 FemalesAge: 54 ± 8 yr. | Treadmill exercise test by modified protocol by Bruce (increased gradually from 2.7 km/h (1.7 mph) and 10% grade incline every three minutes) // 7.2 ± 1.3 min in patient group // till onset of symptoms\* Experiment 6 to 13 months (mean 8) after percutaneous revascularization | (arrows indicate **patient vs. control** plasma markers)

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| --- | --- |
| **Pre**:**Platelet reactivity by:**NA collagen/epinephrineNA collagen/ADP | **1 min post:****Platelet reactivity by:**↑ collagen/epinephrine↔ collagen/ADP |

 | (Pamukcu et al., 2005)(n=82) |
| **Males only** **Acute coronary syndrome patients undergoing cardiac rehabilitation** Moderate-intensity continuous training (MICT) (n=42) Age: 61.7 ± 9.8 yr.VO2max (ml kg min-1): 23.2 ± 5.4high-intensity interval training (HIIT) + MICT (n=40)Age: 60.0 ± 9.4 yr.VO2max (ml kg min-1): 23.1 ± 5.0 | Bike-ergometer // 3 months – 20-60 min, 4 x week // MICT: 4x/week moderate intensity trainingHIIT + MICT: 2x/week high-intensity training (>90% HRpeak) + 2x/week moderate intensity trainingExercise test: Bike-ergometer // incremental increase (1 min step-protocol) // Maximal intensity | **Pre training** (arrows indicate **changes in HIIT + MICT** **vs. MICT** training platelet reactivity before (rest) and after acute maximal exercise)

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| --- | --- |
| **Rest**↔ Soluble P-selectin **Platelet reactivity by:**↔ TRAP-6 | **Immediately post:**↔ Soluble P-selectin **Platelet reactivity by:**↔ TRAP-6 |

**6-week training period:** (arrows indicate **vs. MICT** resting reactivity)

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| **Rest**↔ Soluble P-selectin **Platelet reactivity by:**↓ TRAP-6 | **Immediately post:**↔ Soluble P-selectin **Platelet reactivity by:**↓ TRAP-6 |

**12-week training period:** (arrows indicate **vs. MICT** resting reactivity)

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| --- | --- |
| **Rest**↔ Soluble P-selectin **Platelet reactivity by:**↓ TRAP-6 | **Immediately post:**↔ Soluble P-selectin **Platelet reactivity by:**↓ TRAP-6 |

 | (Heber et al., 2020)(n=82) |

Values are Mean ± SD unless stated otherwise.

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