**Table 1. Clinical and anamnestic patient characteristics, N (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **HC- group (n = 200)** | **HC+ group (n = 208)** | **P value** |
| Obesity (BMI > 30) | 1 (0.5) | 15 (7.2) | 0.0004 |
| Cardiovascular disorders (EH, CHD, AH) | 17 (8.5) | 39 (18.8) | 0.0037 |
| Past thrombotic events (PE, stroke, DVT) | 7 (3.5) | 10 (4.8) | 0.6228 |
| Chronic venous insufficiency | 17 (8.5) | 23 (11) | 0.4094 |
| Headache (migraine with and without aura) | 10 (5) | 66 (31.7) | < 0.0001 |
| Smoking (> 10 cigarrettes/daily) | 8 (4) | 14 (6.7) | 0.2750 |

AH, arterial hypertension; BMI, body mass index; CHD, coronary heart disease; DVT, deep vein thrombosis of the lower extremities; EH, essential hypertension; HC, hormonal contraception; PE, pulmonary embolism

**Table 2. Association of the integral and local tests for assessment of plasma hemostasis with the risk factors for venous thromboembolic complications (multifactorial covariance analysis)**

|  |  |  |  |
| --- | --- | --- | --- |
| **VTE risk factor** | **Integral test** |  | **Local screening tests** |
| **Factor impact, p** | **Degree of the impact, η2** | **Factor impact, p** | **Degree of the impact, η2** |
| Age | 0.231 | 5.3% | 0.580 | 3.8% |
| Obesity | 0.060 | 6.6% | 0.563 | 4.1% |
| Smoking | 0.096 | 7% | 0.242 | 6% |
| Headache | 0.020 | 9.6% | 0.132 | 7.3% |
| Past TE | 0.135 | 6.4% | < 0.001 | 25.6% |
| CVI | 0.472 | 3.7% | 0.195 | 6.5% |
| CVD | 0.138 | 6.3% | 0.066 | 8.6% |

CVD, cardiovascular disorders; CVI, chronic venous insufficiency; TE, thrombotic events; VTE, venous thromboembolism

**Table 3. Association of the integral test for the assessment of plasma hemostasis and the risk factors for venous thromboembolic complications (univariate multivariable ANCOVA)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Factor** | **V, mcm/min (20–29)** |  | **Tlag, min (0.7–1.5)** |  | **Vi, mcm/min (38–56)** |  | **CS, mcm (800–1200)** |  | **D, units (15000–32000)** |  | **Tsp, min** |
| **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** |
| Age | 0.510 | 0.1 | 0.661 | 0.1 | 0.636 | 0.1 | 0.424 | 0.2 | 0.018 | 3 | 0.485 | 0.2 |
| Obesity | 0.112 | 1.5 | 0.006 | 5.9 | 0.205 | 1.4 | 0.059 | 1.9 | 0.843 | 0.2 | 0.351 | 0.8 |
| Smoking | 0.531 | 0.1 | 0.090 | 1.6 | 0.507 | 0.2 | 0.410 | 0.2 | 0.249 | 0.7 | 0.101 | 1 |
| Headache | < 0.001 | 4.3 | 0.475 | 0.3 | 0.049 | 1.7 | < 0.001 | 4.1 | 0.532 | 0.2 | 0.003 | 3.6 |
| Past TE | 0.144 | 0.7 | 0.777 | 0 | 0.018 | 2.5 | 0.075 | 1.1 | 0.105 | 1.4 | 0.151 | 0.8 |
| CVI | 0.091 | 1 | 0.902 | 0 | 0.431 | 0.3 | 0.039 | 1.4 | 0.515 | 0.2 | 0.120 | 0.9 |
| CVD | 0.008 | 2.5 | 0.690 | 0.1 | 0.083 | 1.3 | 0.002 | 3.2 | 0.618 | 0.1 | 0.036 | 1.7 |

CVD, cardiovascular disorders; CVI, chronic venous insufficiency; TE, thrombotic events

**Table 4. Association of the local tests for the assessment of plasma hemostasis and the risk factors for venous thromboembolic complications (univariate multivariable ANCOVA)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Factor** | **XIIа-fibrinolysis, 5–12 min** |  | **Plg, 80–120%** |  | **vWF, 50–150%** |  | **D dimer, 0–250 ng/mL** |  | **АТ, 75–120%** |  | **FVIII, 70–150%** |
| **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** | **p** | **η2, %** |
| Age | 0.909 | 0 | 0.207 | 0.9 | 0.048 | 2 | 0.399 | 0.3 | 0.809 | 0 | 0.106 | 1.4 |
| Obesity | 0.734 | 0.3 | 0.939 | 0.1 | 0.813 | 0.2 | 0.361 | 0.8 | 0.724 | 0.4 | 0.288 | 1.4 |
| Smoking | 0.054 | 1.6 | 0.845 | 0 | 0.584 | 0.2 | 0.015 | 2.5 | 0.459 | 0.4 | 0.889 | 0 |
| Headache | 0.025 | 2.1 | 0.618 | 0.1 | 0.649 | 0.1 | 0.011 | 2.7 | 0.739 | 0.1 | 0.332 | 0.5 |
| Past TE | 0.019 | 2.3 | 0.555 | 0.2 | 0.008 | 3.7 | 0.001 | 17.8 | 0.605 | 0.2 | 0.002 | 5.3 |
| CVI | 0.069 | 1.4 | 0.735 | 0.1 | 0.625 | 0.1 | 0.459 | 0.2 | 0.041 | 2.7 | 0.619 | 0.1 |
| CVD | 0.298 | 0.5 | 0.113 | 0.7 | 0.982 | 0 | 0.103 | 1.1 | 0.516 | 0.3 | 0.948 | 0 |

CVD, cardiovascular disorders; CVI, chronic venous insufficiency; TE, thrombotic events

**Table 5. Comparative characteristics of the plasma hemostasis parameters in the hormonal contraception users and non-users**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters, units (reference range)** | **HC- group (n = 200)** | **HC+ group (n = 208)** | **P value** |
| V, mcm/min (20–29) | 30.3 [28.0; 33.6] | 36.2 [30.1; 43.6] | < 0.001 |
| Clot size, mcm (800–1200) | 1176 [1110; 1272] | 1318[1178; 1500] | < 0.001 |
| Tsp > 30 min | 173 (89%) | 104 (50%) | < 0.001 |
| XIIа-dependent fibrinolysis, min (5–12) | 6.0 [5.0; 8.0] | 12.8 [8.0; 16.0] | < 0.001 |
| vWF, % (40–158) | 98 [85; 133] | 146 [95; 168] | 0.003 |
| FVIII, % (50–150) | 113 [89; 156] | 150 [107; 180] | 0.015 |
| D dimer, ng/mL (0–255) | 81 [56; 120] | 176 [59; 172] | 0.031 |

Tsp > 30 min, no spontaneous clotting (n values are given for Tsp); HT, hormonal therapy

The values are given as medians (Me) and quartiles [Q25; Q75]

**Table 6. The hemostasis system parameters depending on the presence of individual risk factors in the group of hormonal contraception users**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameters, units (reference range)** | **1 RF (n = 88)** | **2 RF (n = 70)** | **3 RF (n = 25)** | **> 3 RF (n = 25)** | **P value** |
| V, mcm/min (20–29) | 34.5 [29.4; 42.9] | 37.7 [32.0; 44.3] | 38.4 [35.7; 44.7] | 45.6 [37.4; 48.7] | 0.047\* |
| Clot size, mcm (800–1200) | 1315 [1178; 1500] | 1334 [1231; 1546] | 1372 [1300; 1500] | 1500 [1342; 1600] |  |
| XIIа-dependent fibrinolysis, min (5–12) | 10 [7; 16] | 10 [8; 16] | 11 [8; 16] | 17 [13; 19] | 0.011\* |
| vWF, % (40–158) | 115 [95; 145] | 120 [96; 156] | 131 [114; 192] | 180 [156; 214] | 0.002\*0.016\*\*0.003† |
| FVIII, % (50–150) | 128 [100; 159] | 135 [113; 172] | 147 [112; 198] | 175 [162; 198] | 0.007\*0.017† |
| D dimer, ng/mL (0–255) | 99 [56; 162] | 91 [66; 157] | 70 [54; 310] | 120 [86; 360] |  |

RF, risk factor

The values are given as medians (Me) and quartiles [Q25; Q75]

\* The difference between the groups with 1 and > 3 RF

\*\* The difference between the groups with 1 and 3 RF

† The difference between the groups with 2 and > 3 RF

**Table 7. The hemostasis system parameters depending on the presence of individual risk factors in the group of hormonal contraception non-users**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameters, units (reference range)** | **0 RF (n = 95)** | **1 RF (n = 63)** | **2 RF (n = 22)** | **> 2 RF (n = 20)** | **P value** |
| V, mcm/min (20–29) | 29.8 [27.5; 31.7] | 28.9 [26.7; 32.9] | 33.6 [28.0; 35.0] | 32.1 [28.4; 35.0] | 0.007\* |
| Clot size, mcm (800–1200) | 1188 [1100; 1227] | 1136 [1068; 1200] | 1235 [1164; 1289] | 1164 [1156; 1295] | 0.026\*\* |
| XIIа-dependent fibrinolysis, min (5–12) | 6 [5; 6] | 6 [5; 6] | 6.5 [6; 9] | 10 [8; 11] | 0.016\*\* |
| vWF, % (40–158) | 89 [83; 108] | 89 [80; 104] | 120 [90; 155] | 127 [115; 150] | 0.009\*0.035\*\* |
| FVIII, % (50–150) | 96 [85; 120] | 95 [87; 115] | 113 [101; 178] | 140 [110; 154] | 0.002\* |
| D dimer, ng/mL (0–255) | 68 [52; 92] | 56 [50; 101] | 69 [56; 117] | 100 [59; 112] |  |

RF, risk factor

The values are given as medians (Me) and quartiles [Q25; Q75]

\* The difference between the groups with 0 and 2 RF

\*\* The difference between the groups with 0 and > 2 RF

**Table 8. The hemostasis system parameters at baseline and at 3 months after administration of combination oral contraceptives**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters, units (reference range)** | **Before COC (n = 49)** | **At 3 months of therapy (n = 49)** | **P value (Wilcoxon test)** |
| V, mcm/min (20–29) | 28.5 [26.30; 33.0] | 39.0 [32.5; 45.8] | 0.001 |
| Clot size, mcm (800–1200) | 1142 [1093; 1200] | 1392 [12528; 150] | 0.001 |
| Tsp > 30 min | 47 (96%) | 21 (43%) | 0.003 |
| XIIа-fibrinolysis, min (5–12) | 8.0 [6.0; 10.0] | 12.0 [8.0; 16.0] | 0.001 |
| vWF, % (40–158) | 100 [89; 120] | 132 [110; 162] | 0.001 |
| FVIII, % (50–150) | 110 [92; 123] | 143 [114; 168] | 0.005 |
| D dimer, ng/mL (0–255) | 59 [50; 100] | 82 [59; 115] | 0.145 |

COC, combination oral contraceptives

The values are given as medians (Me) and quartiles [Q25; Q75]

Tsp > 30 min, no spontaneous clotting (n values are given for Tsp)