**Table 1. Clinical characteristics of the patients**

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| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Total sample (n = 90)** | **Off-line group (n = 30)** | **Online group (n = 30)** | **Control group (n = 30)** | **p value** |
| Age, years | 49.0 [46.0; 56.0] | 51.5 [47.0; 56.0] | 48.5 [45.0; 54.0] | 49.0 [46.0; 56.0] | 0.541 |
| Breast cancer characteristics and anti-tumor treatments |
| Stage, n (%): |  |  |  |  | 0.633 |
| I | 13 (14.4) | 6 (20.0) | 2 (6.7) | 5 (16.7) |  |
| II | 43 (47.8) | 14 (46.7) | 16 (53.3) | 13 (43.3) |  |
| III | 34 (37.8) | 10 (33.3) | 12 (40.0) | 12 (40.0) |  |
| Anthracycline-based CT, n (%) | 90 (100) | 30 (100) | 30 (100) | 30 (100) | 1 |
| Anti-HER2 agents, n (%) | 27 (30.0) | 6 (20.0) | 8 (26.7) | 13 (43.3) | 0.194 |
| Hormonal therapy, n (%) | 57 (63.3) | 20 (66.7) | 17 (56.7) | 20 (66.7) | 0.652 |
| Surgery, n (%) | 90 (100) | 30 (100) | 30 (100) | 30 (100) | 1 |
| Radiation therapy, n (%) | 68 (75.6) | 18 (60.0) | 26 (86.7) | 24 (80.0) | 0.024 |
| Cardiovascular disorders and conventional cardiovascular risk factors |
| AH, n (%) | 42 (46.7) | 14 (46.7) | 13 (43.3) | 15 (50.0) | 0.881 |
| Dyslipidemia, n (%) | 70 (77.8) | 24 (80.0) | 24 (80.0) | 22 (73.3) | 0.773 |
| Smokers, n (%): |  |  |  |  | 0.384 |
| current | 9 (10.0) | 2 (6.7) | 4 (13.3) | 3 (10.0) |  |
| past | 32 (35.6) | 10 (33.3) | 12 (40) | 10 (33.3) |  |
| Obesity, n (%) | 26 (28.9) | 9 (30.0) | 7 (23.3) | 10 (33.3) | 0.691 |
| Total level of PA, n (%): |  |  |  |  | 0.293 |
| low | 16 (17.8) | 4 (13.3) | 3 (10.0) | 9 (30.0) |  |
| moderate | 56 (62.2) | 20 (66.7) | 21 (70.0) | 15 (50.0) |  |
| high | 18 (20.0) | 6 (20.0) | 6 (20.0) | 6 (20.0) |  |
| DM, n (%) | 6 (6.7) | 2 (6.7) | 2 (6.7) | 2 (6.7) | 1 |
| CHF, n (%) | 11 (12.2) | 5 (16.7) | 2 (6.7) | 4 (13.3) | 0.493 |
| IHD, n (%) | 1 (1.1) | 1 (3.3) | 0 (0.0) | 0 (0.0) | 0.364 |
| CV risk, n (%): |  |  |  |  | 0.719 |
| low / moderate | 34 (37.8) | 11 (36.7) | 13 (43.3) | 10 (33.3) |  |
| high / very high | 56 (62.2) | 19 (63.3) | 17 (56.7) | 20 (66.7) |  |
| Echocardiographic parameters |
| LAIV, mL/m2 | 26.9 [24.0; 29.3] | 26.9 [24.4; 29.5] | 25.8 [22.7; 29.2] | 27.8 [24.4; 29.4] | 0.360 |
| LV EDIV, mL/m2 | 43.7 [39.5; 49.6] | 44.0 [40.6; 46.3] | 43.5 [37.3; 49.7] | 43.7 [40.9; 52.8] | 0.490 |
| LV EF, % | 59.0 [56.0; 60.0] | 58.0 [55.0; 60.0] | 59.0 [56.0; 61.0] | 59.0 [56.0; 60.0] | 0.102 |
| Е/е´ | 6.7 [6.0; 7.7] | 6.9 [6.2; 8.9] | 6.6 [6.0; 7.6] | 6.6 [5.9; 7.5] | 0.548 |
| Exercise testing results |
| МЕТ | 5.90 [5.00; 6.90] | 5.70 [5.00; 6.40] | 5.90 [5.40; 6.90] | 6.40 [4.60; 7.20] | 0.369 |
| VO2peak, mL/min/kg | 16,2 [13,1; 18,2] | 16,0 [13,4; 18,6] | 16,5 [12,7; 18,1] | 15,8 [12,3; 19,2] | 0,918 |
| Psychological status |
| AS, n (%): |  |  |  |  |  |
| total | 45 (50.0) | 16 (53.3) | 15 (50.0) | 14 (46.7) | 0.876 |
| subclinical | 27 (30.0) | 10 (33.3) | 11 (36.7) | 6 (20.0) | 0.329 |
| clinically overt | 18 (20.0) | 6 (20.0) | 4 (13.3) | 8 (26.7) | 0.435 |
| DS, n (%): |  |  |  |  |  |
| total | 16 (17.8) | 6 (20.0) | 2 (6.6) | 8 (26.7) | 0.120 |
| subclinical | 11 (12.2) | 4 (13.3) | 1 (3.3) | 6 (20.0) | 0.140 |
| clinically overt | 5 (5.6) | 2 (6.7) | 1 (3.3) | 2 (6.7) | 0.429 |
| High stress level, n (%) | 51 (56.7) | 18 (60.0) | 18 (60.0) | 15 (50.0) | 0.603 |
| Sleep quality, cognitive functions, social status |
| Poor sleep quality, n (%) | 80 (89.0) | 29 (96.7) | 27 (90.0) | 24 (80.0) | 0.118 |
| Cognitive impairment, n (%) | 11 (12.4) | 5 (17.2) | 4 (13.3) | 2 (6.7) | 0.458 |
| Married, n (%) | 64 (71.9) | 19 (63.3) | 24 (80.0) | 21 (70.0) | 0.358 |
| Higher education, n (%) | 80 (88.9) | 27 (90.0) | 26 (86.7) | 27 (90.0) | 0.894 |
| Treatment with psychopharmacological agents, n (%) | 6 (6.7) | 3 (10) | 1 (3.3) | 2 (6.7) | 0.586 |

AH, arterial hypertension; AS, anxiety symptoms; CHF, chrоnic heart failure; CT, chemotherapy; CV, cardiovascular; DM, diabetes mellitus; DS, depressive symptoms; Е/е´, the ratio of early mitral velocity to an increase of left ventricular base in the early diastole; HER2, human epidermal growth factor receptor 2; IHD, ischemic heart disease; LAIV, left atrial indexed volume; LV EDIV, left ventricular indexed end diastolic volume; LV EF, left ventricular ejection fraction; МЕТ, metabolic equivalent of task; PA, physical activity; VO2peak – peak oxygen uptake

The values are given as absolute patient numbers (n) and their proportions (%); quantitative parameters are given as medians and lower and upper interquartile range [25%; 75%]

**Table 2. Associations between psychological status parameters, sleep quality, cognitive function and physical activity level**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters** | **AS, score** | **DS, score** | **Stress, points** |
| AS, score | – | r = 0.53395% CI: 0.336, 0.685р < 0.001 | r = 0.56595% CI: 0.376, 0.709р < 0.001 |
| DS, score | r = 0.53395% CI: 0.336, 0.685p < 0.001 | – | r = 0.45495% CI: 0.240, 0.626p < 0.001 |
| Stress, points | r = 0.56595% CI: 0.376, 0.709p < 0.001 | r = 0.45495% CI: 0.240, 0.626p < 0.001 | – |
| Sleep quality index, score | r = 0.45495% CI: 0.241, 0.626р < 0.001 | r = 0.45195% CI: 0.237, 0.624р < 0.001 | r = 0.31395% CI: 0.112, 0.490р = 0.003 |
| Cognitive functions, score | r = -0.31595% CI: -0.518, -0.079р = 0.010 | r = -0.33395% CI: -0.532, -0.099р = 0.006 | NS |
| PA, МЕТ/min weekly | r = -0.33295% CI: -0.504, -0.134р = 0.002 | r = -0.27995% CI: -0.480, -0.030р = 0.029 | NS |

AS, anxiety symptoms; CI, confidence interval, DS, depressive symptoms; МЕТ, metabolic equivalent of task; NS, non-significant; PA, physical activity

**Table 3. Changes over time in psychological status parameters, sleep quality and cognitive functions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Off-line group (n = 20)** | **On-line group (n = 23)** | **Control group (n = 24)** | **р between the groups** |
| HADS-A, scores: |  |  |  |  |
| Baseline | 8.5 [6.0; 10.0] | 7.0 [5.0; 8.0] | 6.0 [4.5; 9.0] | 0.434 |
| At 6 months | 6.0 [4.0; 9.5] | 5.0 [3.0; 8.0] | 7.0 [3.5; 9.5] | 0.621 |
| Difference of the median values (95% CI) | -1.5 (-3.0, -0.5) | -2.0 (-3.0, -0.5) | -0.5 (-2.0, 0.5) |  |
| р for the difference compared to baseline values | 0.026 | 0.018 | 0.181 |  |
| HADS-D, scores: |  |  |  |  |
| Baseline | 5.0 [4.0; 7.0] | 4.0 [1.3; 5.0] | 4.5 [3.0; 8.0] | 0.067 |
| At 6 months | 4.0 [2.5; 5.5] | 3.0 [2.0; 5.0] | 5.0 [2.5; 7.5] | 0.189 |
| Difference of the median values (95% CI) | -1.5 (-3.0, 0.5) | -0.5 (-1.0, 0.0) | 0.5 (-1.0, 1.5) |  |
| р for the difference compared to baseline values | 0.099 | 0.263 | 0.571 |  |
| Stress levels, points: |  |  |  |  |
| Baseline | 8.0 [5.0; 9.0] | 7.0 [6.0; 8.0] | 6.0 [3.5; 8.0] | 0.162 |
| At 6 months | 7.0 [4.0; 8.0] | 5.0 [4.0; 6.8] | 6.0 [3.0; 8.0] | 0.318 |
| Difference of the median values (95% CI) | -1.5 (-2.0, 0.0) | -1.5 (-2.5, -0.5) | 0.0 (-1.0, 1.0) |  |
| р for the difference compared to baseline values | 0.050 | 0.003 | 0.974 |  |
| Sleep quality index: |  |  |  |  |
| Baseline | 11.0 [8.0; 13.0] | 8.0 [7.0; 12.0] | 9.5 [7.0; 12.0] | 0.386 |
| At 6 months | 8.5 [7.0; 11.5] | 9.0 [5.3; 11.0] | 8.0 [6.0; 11.0] | 0.825 |
| Difference of the median values (95% CI) | -1.3 (-3.5, 0.0) | 0.0 (-1.5, 1.0) | -0.5 (-2.0, 1.0) |  |
| р for the difference compared to baseline values | 0.153 | 0.784 | 0.390 |  |
| Cognitive functions, score: |  |  |  |  |
| Baseline | 28.0 [27.0; 29.0] | 29.0 [27.3; 29.8] | 28.5 [27.0; 29.0] | 0.587 |
| At 6 months, score | 28.5 [27.0; 30.0] | 29.0 [29.0; 30.0] | 29.0 [27.5; 29.5] | 0.294 |
| Difference of the median values (95% CI) | 0.5 (-0.5, 2.0) | 0.5 (0.0, 1.0) | 0.5 (-0.5, 1.0) |  |
| р for the difference compared to baseline values | 0.135 | 0.021 | 0.369 |  |

CI, confidence interval; HADS, Hospital Anxiety and Depression Scale

Quantitative parameters are given as medians and lower and upper interquartile range [25%; 75%]

**Table 4. Comparison of the changes over time in anxiety symptoms and stress levels depending on their baseline severity**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Off-line + online groups (n = 43)** | **Difference of the medians (95% CI)** | **р between the subgroups** | **Control group (n = 24)** | **Difference of the medians (95% CI)** | **р between the subgroups** |
| Baseline anxiety levels | HADS-А ≥ 8 scores (n = 24) | HADS-А < 8 scores (n = 19) |  | HADS-А ≥ 8 scores (n = 10) | HADS-А < 8 scores (n = 14) |  |
| Δ HADS-А, scores | -3.0 [-4.0; -0.5] | -1.0 [-2.0; 1.0] | 2.0 (0.0, 4.0) | 0.017 | -2.5 [-4.0; 1.0] | 0.0 [-1.0; 1.0] | 2.0 (0.0, 5.0) | 0.060 |
| Baseline stress levels | High (n = 27) | Not high (n = 16) |  | High (n = 11) | Not high (n = 13) |  |
| Δ VAS, points | -2.0 [-3.0; -1.0] | 0.0 [-1.0; 2.0] | 3.0 (1.0, 4.0) | < 0.001 | 0.0 [-2.8; 1.0]\* | 1 [-1.3; 3.3] | 2.0 (-1.0, 3.0) | 0.168 |

CI, confidence interval; VAS, visual analogous scale

Quantitative parameters are given as medians and lower and upper interquartile range [25%; 75%]

\* р = 0.020, the difference of the medians: -2.0 (95% CI: -3.0, 0.0) between the two merged groups of cardio-oncology rehabilitation and the control group (patients with a high baseline stress level)