**Supplementary Table 1. Change in functional status from baseline to final assessments (N=255)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Baseline CPET** | **Final CPET** | **P-value** |
| Age (years) | 10.6 ± 2.8 | 14.8 ± 2.3 | **<0.01** |
| Height (cm) | 143.7 ± 15.6 | 162.6 ± 12.4 | **<0.01** |
| Weight (Kg) | 38.4 ± 14.5 | 55.1 ± 14.5 | **<0.01** |
| BMI (Kg/m2) | 18.0 ± 3.6 | 20.6 ± 3.9 | **<0.01** |
| Peak heart rate (bpm) | 174±19 | 175±18 | 0.06 |
| RERmax | 1.10±0.10 | 1.21±0.09 | **<0.01** |
| VO2max (ml/Kg/min) | 39.2 ± 7.96 | 33.0 ± 7.5 | **<0.01** |
| VO2max (Z-score) | -0.63 ± 1.22 | -1.21 ± 1.31 | **<0.01** |
| Impaired VO2max (Z-score<1.64) | 55 (22) | 108 (42) | **<0.01** |
| VAT (ml/Kg/min) | 27.2 ± 5.9 | 22.4 ± 5.5 | **<0.01** |
| VAT (Z-score) | -0.60 ± 1.10 | -1.06 ± 1.15 | **<0.01** |
| Impaired VAT (Z-score<1.64) | 45 (18) | 89 (35) | **<0.01** |

Legend: BMI, body mass index; CPET, cardiopulmonary exercise test; RER, respiratory exchange ratio; VAT, ventilatory anaerobic threshold; VO2max, maximum oxygen uptake.

Values are numbers with (%) or means ± standard deviation.

**Supplementary Table 2. Functional status according to Uzark classification**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Functional status** | **Group 1 (a)***N=54* | **Group 2 (b)***N=166* | **Group 3 (c)***N=55* | **Group 4 (d)***N=21* | **P-value** |
| VO2max | Baseline | mL/kg/min | 39.15 ± 7.60 **d** | 39.89 ± 8.11 **c, d** | 36.99 ± 7.63 **b, d** | 32.48 ± 7.91 **a, b, c** | **<0.01** |
|  |  | Z-score value | -0.39 ± 1.01 **c, d** | -0.48 ± 1.14 **c, d** | -1.09 ± 1.35 **a, b, d** | -2.00 ± 1.33 **a, b, c** | **<0.01** |
|  |  | Z-score<-1.64 | 4 (7) **c, d** | 24 (14) **d** | 14 (25) **a, d** | 13 (62) **a, b, c** | **<0.01** |
|  | Final | mL/kg/min | 34.04 ± 8.74 **d** | 33.33 ± 7.36 **c, d** | 30.92 ± 5.69 **b** | 28.02 ± 6.99 **a, b** | **<0.01** |
|  |  | Z-score value | -0.82 ± 1.21 **c, d** | -1.08 ± 1.27 **c, d** | -1.72 ± 1.27 **a, b** | -2.36 ± 1.22 **a, b** | **<0.01** |
|  |  | Z-score<-1.64 | 13/51 (25) **c, d** | 41/143 (29) **c, d** | 22/45 (49) **a, b** | 10/14 (71) **a, b** | **<0.01** |
|   | Relative change in mL/Kg/min\* | (%/year) | -3.45 ± 0.75 | -3.34 ± 0.43 | -2.47 ± 0.74 | -3.67 ± 1.21 | 0.72 |
| VAT | Baseline | mL/kg/min | 27.10 ± 6.40 **d** | 27.37 ± 5.87 **d** | 25.91 ± 5.79 | 22.55 ± 6.75 **a, b** | **<0.01** |
|  |  | Z-score value | -0.43 ± 1.16 **c, d** | -0.51 ± 1.05 **c, d** | -0.90 ± 1.03 **a, b, d** | -1.73 ± 1.26 **a, b, c** | **<0.01** |
|  |  | Z-score<-1.64 | 4 (7) **d** | 20/165 (12) **d** | 11 (20) **d** | 10 (48) **a, b, c** | **<0.01** |
|  | Final | mL/kg/min | 23.18 ± 5.79 NS | 22.51 ± 5.57 NS | 21.20 ± 4.55 NS | 19.79 ± 5.38 NS | **0.03** |
|  |  | Z-score value | -0.70 ± 0.93 **c, d** | -1.01 ± 1.17 **c, d** | -1.42 ± 1.18 **a, b**  | -1.77 ± 1.05 **a, b** | **<0.01** |
|  |  | Z-score<-1.64 | 9/51 (18) **c, d** | 36/143 (25) **d** | 18/45 (40) **a** | 8/14 (57) **a, b** | **<0.01** |
|  | Relative change in mL/Kg/min\* | (%/year) | -3.81 ± 0.83 | -3.76 ± 0.48 | -3.74 ± 0.83 | -2.07 ± 1.34 | 0.68 |

Legend: VAT, ventilatory anaerobic threshold, VO2max, maximum oxygen uptake.

Values are numbers with (%) or mean ± standard deviation. The letters a, b, c, d in superscript represent the four groups (1, 2 ,3 and 4, respectively) and indicate significant group differences within each column. \* Value adjusted on sex and age.

**Supplementary Table 3. Functional status according to Stout classification**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Functional status** | **Group IA (a)***N=23* | **Group IB (b)***N=23* | **Group IIA (c)***N=55* | **Group IIB (d)***N=66* | **Group IIC (e)***N=40* | **Group IIIB (f)***N=51* | **Group IIIC (g)***N=38* | **P-value** |
| VO2max | Baseline | mL/kg/min | 38.16 ± 6.79 | 40.83 ± 7.28 **e,g** | 41.73 ± 8.42 **d,e,g** | 37.77 ± 7.41 **c,f,g** | 35.67 ± 8.83 **b,c,f** | 41.71 ± 6.32 **d,e,g** | 34.04 ± 8.33 **b,c,d,f** | **<0.01** |
|  |  | Z-score value | -0.44 ± 1.21 **e,g** | -0.31 ± 0.89 **e,g** | -0.21 ± 1.13 **d,e,g**  | -0.66 ± 1.09 **c,g** | -1.24 ± 1.26 **a,b,c,f**  | -0.29 ± 0.83 **e,g** | -1.76 ± 1.51 **a,b,c,d,f**  | **<0.01** |
|  |  | Z-score<-1.64 | 3 (13) **g** | 2 (9) **g** | 6 (11) **g** | 12 (18) **f,g** | 11 (28) **f,g** | 0 (0) **d,e,g** | 21 (55) **a,b,c,d,e,f** | **<0.01** |
|  | Final | mL/kg/min | 33.64 ± 7.98 | 33.24 ± 8.24 | 33.58 ± 6.77 **g** | 32.02 ± 6.66 | 31.98 ± 9.14 | 34.83 ± 7.37 **g** | 29.11 ± 6.28 **c,f** | **0.01** |
|  |  | Z-score value | -0.64 ± 1.14 **g** | -1.25 ± 1.39 | -0.96 ± 1.34 **g** | -1.15 ± 1.11 **g** | -1.59 ± 1.46 | -0.95 ± 1.26 **g** | -2.12 ± 1.12 **a,c,d,f** | **<0.01** |
|  |  | Z-score<-1.64 | 4/20 (20) NS | 7/20 (35) NS | 13/50 (26) NS | 17/55 (31) NS | 16/34 (47) NS | 13/46 (28) NS | 16/28 (57) NS | **0.04** |
|  | Relative change in mL/Kg/min\* | (%/year) | -2.33 ± 1.15 | -4.35 ± 1.14 | -4.15 ± 0.74 | -3.11 ± 0.67 | -1.58 ± 0.87 | -3.22 ± 0.78 | -3.68 ± 0.90 | 0.32 |
| VAT | Baseline | mL/kg/min | 26.56 ± 5.30 | 27.65 ± 6.26 | 28.38 ± 6.24 **g** | 26.06 ± 4.76 **f** | 25.06 ± 6.82 **f** | 28.81 ± 6.04 **d,e,g** | 23.78 ± 6.33 **c,f** | **<0.01** |
|  |  | Z-score value | -0.38 ± 1.13 **g**  | -0.50 ± 1.48 **g**  | -0.38 ± 0.97 **e,g** | -0.61 ± 0.91 **g** | -1.00 ± 1.16 **c,f** | -0.35 ± 0.96 **e,g** | -1.45 ± 1.22 **a,b,c,d,f**  | **<0.01** |
|  |  | Z-score<-1.64 | 2 (9) **g** | 3 (13) | 5 (9) **g** | 6 (9) **g** | 10 (25) | 4 (8) **g** | 15 (39) **a,c,d,f** | **<0.01** |
|  | Final | mL/kg/min | 22.53 ± 5.10 | 22.68 ± 6.71 | 22.90 ± 5.98 | 22.17 ± 4.81 | 21.04 ± 5.52 | 23.34 ± 5.42 | 20.37 ± 4.97 | 0.10 |
|  |  | Z-score value | -0.64 ± 0.86 **e,g**  | -1.20 ± 1.38 | -0.86 ±1.31 **e,g**  | -0.91 ± 0.86 **e,g**  | -1.54 ± 1.19 **a,c,d,f** | -0.92 ± 1.16 **e,g** | -1.57 ± 1.00 **a,c,d,f** | **<0.01** |
|  |  | Z-score<-1.64 | 3/20 (15) NS | 6/20 (30) NS | 12/50 (24) NS | 13/55 (24) NS | 17/34 (50) NS | 9/46 (20) NS | 11/28 (39) NS | **0.04** |
|  | Relative change in mL/Kg/min\* | (%/year) | -3.14 ± 1.28 | -4.64 ± 1.27 | -4.31 ± 0.83 | -2.76 ± 0.76 | -3.33 ± 0.98 | -4.08 ± 0.87 | -3.78 ± 1.01 | 0.80 |

Legend: VAT, ventilatory anaerobic threshold, VO2max, maximum oxygen uptake.

Values are numbers with (%) or mean ± standard deviation. The letters a, b, c, d, e, f, g in superscript represent the sub-groups (IA, IB, IIA, IIB, IIC, IIIB and IIIC respectively) and indicate significant group differences within each column. \* Value adjusted on sex and age.

**Supplementary Table 4. Functional status according to Bethesda classification**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Functional status** | **Simple group***N=70* | **Moderate group***N=138* | **Severe group***N=88* | **P-value** |
| VO2max | Baseline | mL/kg/min | 38.76 ± 7.22 | 38.75 ± 8.61 | 38.54 ± 8.14 | 0.98 |
|  |  | Z-score value | -0.46 ±1.05 | -0.66 ± 1.23 | -0.91 ± 1.38 | 0.24 |
|  |  | Z-score<-1.64 | 8 (11) | 26 (19) | 21 (24) | 0.14 |
|  | Final | mL/kg/min | 33.40 ± 7.93 | 32.35 ± 7.31 | 32.48 ± 7.44 | 0.75 |
|  |  | Z-score value | -0.95 ±1.24 | -1.23 ±1.32 | -1.40 ±1.34 | 0.13 |
|  |  | Z-score<-1.64 | 17/62 (27) | 40/118 (34) | 29/73 (40) | 0.32 |
|  | Relative change in mL/Kg/min\* | (%/year) | -3.30 ± 0.66 | -3.09 ± 0.47 | -3.36 ± 0.60 | 0.93 |
| VAT | Baseline | mL/kg/min | 26.82 ± 5.96 | 26.64 ± 5.90 | 26.71 ± 6.64 | 0.98 |
|  |  | Z-score value | -0.46 ± 1.21 | -0.65 ± 1.02 | -0.82 ± 1.21 | 0.13 |
|  |  | Z-score<-1.64 | 7 (10) | 19/137 (14) | 19 (22) | 0.11 |
|  | Final | mL/kg/min | 22.71 ± 5.83 | 21.98 ± 5.35 | 22.12 ± 5.42 | 0.71 |
|  |  | Z-score value | -0.86 ± 1.11 | -1.10 ± 1.16 | -1.17 ± 1.15 | 0.22 |
|  |  | Z-score<-1.64 | 15/62 (24) | 36/118 (31) | 20/73 (27) | 0.66 |
|  | Relative change in mL/Kg/min\* | (%/year) | -3.53 ± 0.73 | -3.57 ± 0.52 | -3.89 ± 0.67 | 0.91 |

Legend: VAT, ventilatory anaerobic threshold, VO2max, maximum oxygen uptake.

Values are numbers with (%) or mean ± standard deviation. \* Value adjusted on sex and age

**Supplementary Table 5. VO2max at baseline according to CHD classifications (N=296)**

|  |  |  |
| --- | --- | --- |
|  | **VO2max impairment (Z-score<-1.64)** | **VO2max - mL/Kg/min** |
| **CHD classification** | **OR [95% CI]** | **P-value** | **cβ [95% CI]** | **P-value** |
| **Bethesda** |  | 0.14 |  | 0.98 |
| Moderate vs simple | 1.80 [0.77 ; 4.21] | 0.18 | -0.02 [-2.37 ; 2.34] | 0.99 |
| Great vs simple | 2.43 [1.00 ; 5.88] | **0.05** | -0.23 [-2.80 ; 2.35] | 0.86 |
| **Uzark** |  | **< 0.01** |  | **< 0.01** |
| Group 2 vs 1 | 2.11 [0.70 ; 6.39] | 0.19 | 0.73 [-1.71 ; 3.17] | 0.56 |
| Group 3 vs 1 | 4.27 [1.30 ; 13.97] | **0.02** | -2.16 [-5.15 ; 0.82] | 0.15 |
| Group 4 vs 1 | 20.31 [5.29 ; 78.08] | **< 0.01** | -6.68 [-10.69 ; -2.67] | **< 0.01** |
| **Stout** |  | **< 0.01** |  | **< 0.01** |
| IB vs IA | 0.68 [0.10 ; 4.21] | 0.64 | 2.67 [-1.81 ; 7.15] | 0.24 |
| IIA vs IA | 0.77 [0.19 ; 3.59] | 0.79 | 3.58 [-0.19 ; 7.35] | 0.06 |
| IIB vs IA | 1.34 [0.38 ; 5.80] | 0.57 | -0.39 [-4.06 ; 3.29] | 0.84 |
| IIC vs IA | 2.28 [0.63 ; 10.23] | 0.19 | -2.49 [-6.46 ; 1.49] | 0.22 |
| IIIB vs IA | 0.06 [0.00 ; 1.19] | 0.06 | 3.55 [-0.26 ; 7.37] | 0.07 |
| IIIC vs IA | 7.20 [1.92 ; 27.01] | **< 0.01** | -4.12 [-8.13 ; -0.11] | **0.04** |

Legend: cβ : Crude β; CHD; congenital heart disease; VO2max, maximum oxygen uptake.