

Pulmonary hemodynamic response to exercise in highlanders vs. lowlanders

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Supplementary tables

Supplementary table 1: Baseline characteristics by exploratory subgroups of highlanders according their resting mean pulmonary artery pressure

| | Highlanders mPAP<20mmHg, n=23 | Highlanders mPAP 20-30mmHg, n=24 | Highlanders mPAP >30mmHg, n=5 |
|---|----------------------------------|-------------------------------------|----------------------------------|
| Gender, male/female | 13/10 | 11/13 | 2/3 |
| Age, years | 45.9±9.3 | 47.8±10.6 | 57.4±14.1 |
| Height, cm | 162.8±10.9 | 162.3±7.8 | 158.8±9.9 |
| Weight, kg | 68.8±12.4 | 70.4±15.2 | 75.8±8.1 |
| BMI, kg/m ² | 26.0±3.8 | 26.6±5.3 | 30.2±4.1 |
| Body surface area, m ² | 1.73±0.19 | 1.75±0.20 | 1.78±0.14 |
| Heart rate, bpm | 72±10 | 76±11 | 78±12 |
| Blood pressure systolic, mmHg | 123±21 | 126±21 | 152±26* |
| Blood pressure diastolic, mmHg | 94±11 | 84±13 | 90±8 |
| New York Heart Association functional class I/II/III | 12/8/2 | 11/11/2 | 3/1/1 |
| Max. workload, W | 48±13 | 44±14 | 34±17 |
| SpO ₂ , % | 91±5 | 91±4 | 90±2 |
| Hemoglobin concentration, g/dL | 16.4±2.1 | 15.4±2.5 | 16.6±1.5 |
| Hematocrit, % | 47.8±8.9 | 45.7±6.6 | 48.0±4.6 |
| PaO ₂ , mmHg | 56.9±5.2 | 56.5±7.1 | 52.2±4.9 |
| PaCO ₂ , mmHg | 32.5±2.7 | 32.5±3.1 | 32.8±3.0 |
| Oxygen content, mL O ₂ /dL | 19.7±2.8 | 18.2±3.0 | 19.3±1.5 |
| Pack years | 3.1±5.5 | 4.6±7.1 | 2.8±4.4 |

Values are presented as mean ± SD. *Abbreviations:* BMI: Body mass index; SpO₂: oxygen saturation; PaO₂: Partial pressure of arterial oxygen; PaCO₂: Partial pressure of arterial carbon dioxide. *: significant difference in ANOVA p<0.05

Supplementary table 2: Between subgroups differences of the pressure / flow slope by exploratory subgroups of highlanders according their resting mean pulmonary artery pressure

| | Highlanders mPAP<20mmHg, n=17 | Highlanders mPAP 20- 30mmHg, n=24 | Highlanders mPAP >30mmHg, n=4 | ANOVA |
|--|-------------------------------------|---|-------------------------------------|--------|
| Δ TRPG/ Δ Cardiac index, WU | 5.4 \pm 3.7 | 9.7 \pm 13.6 | 24.5 \pm 4.0 | <0.001 |
| Δ mPAP/ Δ CO | 1.9 \pm 1.3 | 3.4 \pm 4.4 | 8.6 \pm 1.9 | <0.001 |

Values are presented as mean \pm SD. *Abbreviations:* TRPG: tricuspid regurgitation pressure gradient.

Supplementary table 3: Measures during step-wise cycle exercise by exploratory subgroups of highlanders according their resting mean pulmonary artery pressure

| | Highlanders mPAP<20mmHg, n=23 | Highlanders mPAP 20-30mmHg, n=24 | Highlanders mPAP >30mmHg, n=5 | ANOVA |
|---|-------------------------------------|-------------------------------------|----------------------------------|--------|
| SpO ₂ , % BL | 91±3 | 91±2 | 88±2 | 0.139 |
| SpO ₂ , % end exercise | 89±3 | 90±3 | 85±3 | 0.017 |
| SpO ₂ end exercise - BL | -1.7±3.1 | -0.8±2.5 | -3.0±2.7 | 0.611 |
| HR, bpm BL | 80±13 | 82±11 | 87±13 | 0.556 |
| HR, bpm end exercise | 103±18 | 110±11 | 112±6 | 0.914 |
| HR end exercise - BL | 29±15 | 28±10 | 25±11 | 0.127 |
| TRPG, mmHg BL | 20.3±3.9 | 24.4±6.2 | 25.9±4.2 | 0.018 |
| TRPG, mmHg end exercise | 31.0±10.0 | 37.9±10.2 | 54.7±13.6 | <0.001 |
| TRPG end exercise -BL | 10.7±8.6 | 13.5±8.5 | 27.8±16.9 | 0.097 |
| CI l/min/m ² BL | 2.36±0.69 | 2.33±0.55 | 2.56±0.28 | 0.216 |
| CI l/min/m ² end exercise | 4.16±0.72 | 4.16±0.88 | 3.96±0.46 | 0.367 |
| CI endex - BL | 1.80±0.49 | 1.83±0.68 | 1.40±0.64 | 0.410 |
| SVI, l/min BL | 29.9±6.6 | 28.2±7.0 | 31.5±7.4 | 0.948 |
| SVI, l/min end exercise | 38.2±6.3 | 37.6±6.8 | 37.6±4.4 | 0.661 |
| SVI end exercise - BL | 8.2±5.0 | 10.7±8.8 | 6.1±9.1 | 0.079 |
| TAPSE, cm BL | 1.8±0.3 | 2.1±0.4 | 2.0±0.7 | 0.030 |

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|----------------------------|------------|------------|------------|-------|
| TAPSE, cm end | 2.5±0.4 | 2.6±0.5 | 2.4±0.6 | 0.741 |
| exercise | | | | |
| TAPSE end | 0.7±0.4 | 0.6±0.3 | 0.3±0.4 | 0.496 |
| exercise - BL | | | | |
| FAC. % BL | 40.4±8.8 | 42.9±11.9 | 40.7±14.3 | 0.649 |
| FAC. % end | 45.2±12.2 | 43.2±12.0 | 42.6±12.5 | 0.636 |
| exercise | | | | |
| FAC end exercise - | 5.9±15.3 | 2.4±9.2 | 6.2±12.8 | 0.379 |
| BL | | | | |
| RVEDA, cm ² BL | 17.2±3.6 | 17.6±3.2 | 23.1±2.0 | 0.656 |
| RVEDA, cm ² end | 18.9±3.0 | 19.2±3.4 | 22.1±4.5 | 0.542 |
| exercise | | | | |
| RVEDA end | 2.9±4.5 | 1.1±4.2 | 0.8±4.6 | 0.977 |
| exercise - BL | | | | |
| RVESA, cm ² BL | 10.4±3.3 | 10.1±2.3 | 13.7±2.9 | 0.585 |
| RVESA, cm ² end | 10.5±2.2 | 10.9±2.2 | 12.5±2.0 | 0.963 |
| exercise | | | | |
| RVESA end | 0.6±3.5 | 0.1±2.2 | -1.0±5.4 | 0.180 |
| exercise - BL | | | | |
| TAPSE/TRPG, | 0.89±0.25 | 0.96±0.48 | 0.79±0.24 | 0.623 |
| mm/mmHg BL | | | | |
| TAPSE/TRPG, | 0.89±0.33 | 0.76±0.33 | 0.48±0.22 | 0.039 |
| mm/mmHg end | | | | |
| exercise | | | | |
| TAPSE/TRPG end | -0.01±0.34 | -0.19±0.35 | -0.32±0.20 | 0.098 |
| exercise - BL | | | | |
| TAPSE/sPAP, | 0.71±0.17 | 0.77±0.30 | 0.66±0.20 | 0.039 |
| mm/mmHg BL | | | | |
| TAPSE/sPAP, | 0.74±0.25 | 0.66±0.25 | 0.43±0.18 | 0.726 |
| mm/mmHg end- | | | | |

exercise

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|------------------|-----------|------------|-----------|-------|
| TAPSE/sPAP, end- | 0.03±0.25 | -0.10±0.20 | 0.23±0.15 | 0.441 |
|------------------|-----------|------------|-----------|-------|

exercise - BL

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|--------------|--------|--------|--------|-------|
| BPs, mmHg BL | 112±13 | 109±16 | 122±21 | 0.195 |
|--------------|--------|--------|--------|-------|

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|---------------|--------|--------|--------|-------|
| BPs, mmHg end | 128±22 | 133±21 | 156±25 | 0.034 |
|---------------|--------|--------|--------|-------|

exercise

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|--------------------|-------|-------|-------|-------|
| BPs end exercise - | 15±18 | 24±15 | 34±18 | 0.573 |
|--------------------|-------|-------|-------|-------|

BL

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|--------------|------|-------|------|-------|
| BPd, mmHg BL | 76±9 | 76±11 | 87±8 | 0.058 |
|--------------|------|-------|------|-------|

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|---------------|------|-------|-------|-------|
| BPd, mmHg end | 79±9 | 74±13 | 97±18 | 0.008 |
|---------------|------|-------|-------|-------|

exercise

| | | | | |
|--------------------|------|-------|-------|-------|
| BPd end exercise - | 3±11 | -2±13 | 10±12 | 0.782 |
|--------------------|------|-------|-------|-------|

BL

Values are presented as mean ± SD. *Abbreviations:* BL: baseline on cycle ergometer; SpO₂: oxygen saturation; HR: heart rate; TRPG: tricuspid regurgitation pressure gradient; CI cardiac index; SVI: stroke volume index; TAPSE: tricuspid annular plane systolic excursion; FAC: fractional area change; RVEDA: right ventricle end-diastolic area; RVESA: right ventricle end-systolic area; BPs: blood pressure systolic; BPd: blood pressure diastolic.

Supplementary table 4: Linear mixed regression analysis with pressure-flow slope (Δ tricuspid regurgitation pressure gradient / Δ cardiac index) as dependent variable.

| | Coefficient | 95% confidence interval | p-value |
|-----------------|-------------|-------------------------|---------|
| Age | 0.16 | -0.04 to 0.37 | 0.122 |
| Female vs. male | 2.09 | -1.87 to 6.04 | 0.302 |
| Borderline HAPH | 4.73 | 0.52 to 8.93 | 0.028 |
| HAPH | 18.06 | 9.10 to 27.02 | <0.001 |
| Intercept | -4.24 | -14.18 to 5.70 | 0.403 |

Abbreviations: HAPH: high altitude pulmonary hypertension.