Exercise stress echocardiography of the pulmonary circulation and right ventricular-arterial coupling in healthy adolescents

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Aims
To explore the effects of age and sex in adolescents vs. young or middle-aged adults on pulmonary vascular function and right ventricular-arterial (RV-PA) coupling as assessed by exercise stress echocardiography.

Methods and results
Forty healthy adolescents aged 12–15 years were compared with 40 young adults aged 17–22 years and 40 middle-aged adults aged 30–50 years. Sex distribution was equal in the three groups. All the subjects underwent an exercise stress echocardiography. A pulmonary vascular distensibility coefficient $a$ was determined from multipoint pulmonary vascular pressure–flow relationships. RV-PA coupling was assessed by the tricuspid annular plane systolic excursion (TAPSE) to systolic pulmonary artery pressure (PASP) ratio, who has been previously validated by invasive study. While cardiac index and mean PAP were not different, adolescents compared to young and middle-aged adults, respectively had higher pulmonary vascular distensibility coefficients $a$ (1.60 ± 0.31%/mmHg vs. 1.39 ± 0.29%/mmHg vs. 1.20 ± 0.35%/mmHg, $P<0.00001$). Adolescents and young adults compared to middle-aged adults, respectively had higher TAPSE/PASP ratios at rest (1.24 ± 0.18 mm/mmHg and 1.22 ± 0.17 mm/mmHg vs. 1.07 ± 0.18 mm/mmHg, $P<0.008$) and during exercise (0.86 ± 0.24, 0.80 ± 0.15 and 0.72 ± 0.15 mm/mmHg, $P<0.04$). The TAPSE/PASP ratio decreased with exercise. There were no sex differences in $a$ or TAPSE/PASP.

Conclusion
Compared to adults, adolescents present with a sex-independent more distensible pulmonary circulation. Resting and exercise RV-PA coupling is decreased in middle-aged adults.

Keywords
pulmonary vascular resistance • growth • children • VO2max • TAPSE

Introduction
Pulmonary vascular pressure–flow relationships are slightly curvilinear, rather than strictly linear as assumed by the pulmonary vascular resistance (PVR) equation, and this is explained by the natural distensibility of pulmonary resistive vessels. Accordingly, the PVR equation can be improved by the incorporation of a resistive vessel distensibility coefficient $a$ so that $PAMP = [(1 + aLAP)^5 + 5aR_0CO)^{1/5} - 1]/a$, where PAMP is pulmonary artery mean pressure, LAP left atrial pressure, CO cardiac output, and $R_0$ PAMP/CO at rest. An interesting application of this equation is that $a$ can be calculated from the best fit of PAMP, LAP (or wedged PAP, PAWP), and CO measurements obtained during exercise to increase cardiac output. Invasive and non-invasive studies have shown that a so calculated index of distensibility $a$ is normally between 1 and 2%/mmHg, higher in young healthy women, and decreased with aging or chronic hypoxic exposure. Exercise haemodynamic studies have shown that the distensibility coefficient $a$ is decreased in early or latent pulmonary vascular disease and in heart failure. In the latter study, the $a$ coefficient was positively correlated to right ventricular ejection fraction (RVEF) and independently predicted peak oxygen uptake (VO2) suggesting RV afterload limitation of maximum...
CO. There has been no report of α coefficient determinations in children.

The coupling of RV function to the pulmonary circulation is best defined by a ratio of end-systolic to arterial elastances (Ees/Ea). Gold-standard measurements of Ees/Ea require sophisticated high-fidelity micromanometer-tipped conductance catheter technology to generate pressure–volume relationships. This is not practical for bedside and even less so for exercise studies. Therefore, echocardiographic surrogates have been developed. It has been recently suggested that the best echocardiographic estimate of RV Ees/Ea is the tricuspid annular plane systolic excursion (TAPSE) to systolic PAP (PASP) ratio. The TAPSE/PASP is a potent predictor of outcome in heart failure and in pulmonary hypertension. The TAPSE/PASP decreases with aging and with exercise. However, there has been no report of TAPSE/PASP ratio measurements in children.

In this study, we evaluated the RV and the pulmonary circulation during exercise in adolescent children as compared to young and middle-aged adults.

### Methods

#### Study population

The study included 120 healthy Caucasian subjects from 12 to 50 years old, divided into three age-groups: 12–15, 17–22, and 30–50 years old (Table 1). Sex distribution was equal in the three groups. All the subjects were Caucasians, naturally conceived, non-smoker, and declared themselves in good health. They led a healthy lifestyle, with 2–4 h physical activity per week. None of them was engaged in competitive sports. Their physical examination and resting electrocardiogram were normal. Twenty-one subjects with insufficient quality resting echocardiography had been excluded in the screening phase of the study. The subjects (and parents of the adolescents) gave an informed consent to the study, which was approved by the local Institutional Ethics Committee (reference B406201422389).

#### Experimental protocol

Each subject reported to the laboratory on two occasions within a week. On the first visit, the participant underwent a clinical examination and a standard resting echocardiographic examination followed by an incremental stress echocardiography. The exercise echocardiography was performed on a semi-recumbent position as previously reported with an incremental workload increase of 20 W/2 min until exhaustion. The second visit consisted of a standard incremental cardiopulmonary exercise test (CPET) on a cycle ergometer to measure ventilation (V̇e), carbon dioxide output (VCO2), and oxygen uptake (VO2). Maximum VO2 (VO2max) was considered to be achieved when two of the following criteria were met: an increase in VO2 of <100 ml/min with a further increase in workload, a respiratory exchange ratio (RER) greater than 1.1 or achievement of age-predicted maximal heart rate (HR).

#### Cardiopulmonary exercise testing

The CPET were performed as previously reported with breath by breath measurements of VO2, VCO2, and VE on a cycle ergometer at progressively increased workload (HypoAir; Medisoft; Dinant, Belgium) of 10–30 W/min until volitional fatigue for an optimal test duration between 10 and 12 min for all subjects. SpO2 and HR were measured continuously. BP was measured every minute. The ventilatory threshold (VT1) was measured by the V-slope method on the VCO2 vs. VO2 relationship and V̇e/V̇CO2 ratio was then recorded. Oxygen pulse was calculated as VO2/HR.

#### Statistics

Results are presented as mean ± SD. The statistical analysis consisted of repeated measures analysis of variance calculations. When the F ratio of

### Table 1 Baseline characteristics of adolescents and young and middle-aged adults

<table>
<thead>
<tr>
<th></th>
<th>Adolescents</th>
<th>Young adults</th>
<th>Middle-age adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13 ± 1</td>
<td>18 ± 2</td>
<td>39 ± 8***</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164 ± 9</td>
<td>171 ± 9*</td>
<td>173 ± 9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>52 ± 8</td>
<td>64 ± 9</td>
<td>67 ± 10</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.3 ± 3.0</td>
<td>21.9 ± 2.6*</td>
<td>22.3 ± 2.0*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.85 ± 0.18</td>
<td>2.09 ± 0.19*</td>
<td>2.14 ± 0.21*</td>
</tr>
</tbody>
</table>

BMI, body mass index; BSA, body surface area.

*P < 0.001 vs. adolescents.

**P < 0.001 middle-age adults vs. young adults.
the analysis of variance reached a $P < 0.05$ critical value, Student’s $t$-tests were applied for age group comparisons and exercise vs. rest comparisons. Correlations were calculated by Pearson’s linear regression analysis. $P$ values $< 0.05$ were considered significant.

## Results

### Anthropomorphic data

Height, weight, body mass index (BMI), and BSA regardless of sex increased during adolescence until the end of growth (Table 1). Height, weight, and BSA were higher in adult men compared to adult women with no sex-related differences in BMI (not shown).

### Haemodynamics

As shown in Table 2, at rest there were no between-group differences for BP, CI, PAMP, and indexed TPR (TPRI), while SV was lower and HR higher in adolescents. At maximal exercise, adolescents showed identical CI but lower BP, SV, CO compared to adults. Middle-aged adults had lower maximal HR and higher maximal SV, TPRI, and PAMP as compared to young adults.

The PAMP-CI slope was lower in adolescents and increased with age (Figure 1). The CO-workload relationships were not different in the three age groups (all $0.06 \pm 0.01$ L/min/W). The PAMP-CO slopes were increased in the middle-aged adults compared to the two other age groups (Table 2) and so were the PASP-W slopes which were of $0.13 \pm 0.04$, $0.13 \pm 0.03$, and $0.22 \pm 0.06$ mmHg/mmHg, respectively ($P < 0.001$ compared to adolescent and young adult groups. The pulmonary vascular distensibility factor $\alpha$ was higher in adolescents and decreased with age (Figure 2). The limits of normal of $\alpha$ estimated as mean - 2SD to mean + 2SD would be $0.9–1.6$, $0.9–1.6$, and $0.7–1.4$ mm/mmHg, respectively at rest, and $0.4–1.3$, $0.5–1.1$, and $0.4–1.0$ mm/mmHg, respectively at maximal exercise. The effects of age on $S'/PASP$ at rest and during exercise are shown in Figures 3 and 6, respectively. The limits of normal of $S'/PASP$ in adolescents, young adults, and middle age adults would be $0.4–0.9$, $0.4–0.8$, and $0.4–0.8$, respectively at rest, and $0.3–0.8$, $0.4–0.7$, and $0.3–0.6$, respectively at exercise.

### Cardiopulmonary exercise testing

As shown in Table 4, workload (W), RER, $O_2$ pulse, and absolute $VO_2$ at maximal exercise were lower, while $V_{E}/V_{CO_2}$ was increased in the adolescents. $VO_2$max corrected for body weight and VT were not different between the age groups. As shown in the Supplementary data on line, Table S2, $VO_2$max, $O_2$ pulse, workload, were higher in men independently of age. $V_{E}/V_{CO_2}$ was higher in young and middle-aged adult women.

## Discussion

The present results show that healthy adolescents have a higher pulmonary vascular distensibility than young or middle-aged adults, and better coupling of the RV to the pulmonary circulation at rest and at exercise than middle-aged adults. Our observations offer insight into age-related limits of normal of these measurements from late childhood to early adult life.

Even though available validation against invasive measurements is only indirect, exercise stress echocardiography of the pulmonary circulation to generate PAMP-flow relationships and resistive vessel distensibility calculations has been shown to be feasible and has allowed to disclose age-, sex-, environmental-related, and early stage disease alterations. The distensibility factor $\alpha$ has been shown to be higher in pre-menopausal women and lower in aging adults, lower in young adult men of Sub-Saharan African ascendance lower with chronic but not acute hypoxic exposure or diesel exhaust exposure, and lower in adolescents born by in vitro fertilization. $\alpha$ has been reported to be decreased in patients with borderline hypertension, early or latent pulmonary vascular disease, and heart failure. A decreased pulmonary vascular distensibility results in higher PA pressures during exercise, which may be associated with insufficient RV function adaptation, RV-PA uncoupling and decreased aerobic exercise capacity, in healthy subjects, and more so in heart failure patients. In this study, the pulmonary circulation was more distensible in adolescents compared to adults. Even though this was associated with a better RV-PA coupling as assessed by TAPSE/PASP and $S'/PASP$ ratios, aerobic exercise measured by $VO_2$max corrected for body weight was not different. This is likely related to other growth and maturation factors with more impact than RV function adaptation to afterload.

The RV basically adapts to afterload by an increased contractility to preserve its coupling to the pulmonary circulation and flow output adapted to metabolic demand. The matching of RV function to afterload in exercising healthy subjects, has been demonstrated to be well preserved by invasive measurements of $Ees$ and $Ea$ ($Ees/Ea$). The TAPSE/PASP was recently shown to be superior to other echocardiographic estimates of the $Ees/Ea$ ratio for the quantification of RV-PA coupling. In those studies, the tricuspid annular systolic velocity $S'$ was not assessed. In this study, TAPSE and $S'$ increased during exercise in all age groups, in keeping with previously
demonstrated increase in contractility to preserve RV-PA coupling. Yet the ratios of TAPSE or S’ to PASP decreased with exercise, though less so in adolescents. Why the TAPSE/PASP or the S'/PASP decrease during exercise while the Ees/Ea does not is unclear. We may speculate that during exercise, as opposed to resting condition, RV systolic function might rely more on transverse rather than longitudinal shortening. It also may be that TAPSE as a measure of Ees and PASP as a measure of Ea lack specificity and proportional change in numbers compared to those of elastance measurements. This study nevertheless suggests that RV-PA coupling is better maintained in

Table 2  Haemodynamics at rest and at maximum exercise in adolescents and in young and middle-aged adults

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adolescents</th>
<th>Young adults</th>
<th>Middle-age adults</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>mBP (mmHg)</td>
<td>Rest 82 ± 9</td>
<td>83 ± 9</td>
<td>86 ± 10</td>
<td>1.5</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>Max 102 ± 14</td>
<td>111 ± 17**</td>
<td>112 ± 13**</td>
<td>5.3</td>
<td>0.0062</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>Rest 91 ± 13</td>
<td>84 ± 12**</td>
<td>85 ± 15**</td>
<td>4.9</td>
<td>0.0096</td>
</tr>
<tr>
<td></td>
<td>Max 194 ± 12</td>
<td>190 ± 11</td>
<td>174 ± 12**</td>
<td>32.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>Rest 55 ± 10</td>
<td>66 ± 17**</td>
<td>64 ± 18**</td>
<td>5.9</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Max 71 ± 19</td>
<td>85 ± 16**</td>
<td>97 ± 25**</td>
<td>12.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>Rest 4.9 ± 0.8</td>
<td>5.4 ± 1.3</td>
<td>5.1 ± 1.2</td>
<td>2.3</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Max 13.7 ± 3.2</td>
<td>16.1 ± 3.2**</td>
<td>16.6 ± 5.0**</td>
<td>6.3</td>
<td>0.002</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>Rest 2.7 ± 0.4</td>
<td>2.6 ± 0.8</td>
<td>2.7 ± 0.8</td>
<td>0.01</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>Max 7.4 ± 1.6</td>
<td>7.7 ± 1.5</td>
<td>7.7 ± 2.2</td>
<td>0.4</td>
<td>0.64</td>
</tr>
<tr>
<td>PAMP (mmHg)</td>
<td>Rest 16.1 ± 1.6</td>
<td>16.0 ± 1.6</td>
<td>16.8 ± 2.6</td>
<td>1.4</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>Max 28.2 ± 4.1</td>
<td>29.8 ± 3.5</td>
<td>37.3 ± 8.7$$ $$ $$</td>
<td>25.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>TPRI (Wood units/m²)</td>
<td>Rest 6.2 ± 1.1</td>
<td>6.4 ± 1.4</td>
<td>6.7 ± 2.0</td>
<td>1.4</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>Max 3.8 ± 0.7</td>
<td>4.0 ± 0.7</td>
<td>5.0 ± 0.9$$ $$ $$</td>
<td>24.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>PAMP-CO slope (mmHg/L/min)</td>
<td>Total 1.4 ± 0.4</td>
<td>1.4 ± 0.4</td>
<td>1.6 ± 0.4$$ $$ $$</td>
<td>6.2</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>PAMP-CI slope(mmHg/L/min/m²)</td>
<td>2.5 ± 0.7</td>
<td>2.8 ± 0.8$$ $$ $$</td>
<td>3.4</td>
<td>0.08$$ $$ $$ $$</td>
</tr>
<tr>
<td>α (%/mmHg)</td>
<td>Total 1.60 ± 0.31</td>
<td>1.39 ± 0.29$$ $$ $$</td>
<td>1.20 ± 0.35$$ $$ $$</td>
<td>15.3</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

All variables were significantly increased or decreased at maximum exercise.

CI, cardiac index; CO, cardiac output; HR, heart rate; mBP, mean blood pressure; PAMP, mean pulmonary arterial pressure; SV, stroke volume; TPRI, indexed total pulmonary vascular resistance.

*: P < 0.05 vs. adolescents.
**: P < 0.01 vs. adolescents.
***: P < 0.001 vs. adolescents.
$: P < 0.05 young vs. middle-age adults.
$$: P < 0.01 young vs. middle-age adults.
$$$: P < 0.001 young vs. middle-age adults.

Figure 1  Influence of age on PAMP-CI slope. PAMP-CI slopes in adolescents (circles), young adults (squares), and middle-aged adults (triangles). Horizontal bars indicate the group means. The slope of the pressure–flow relationship increased with aging. *P < 0.05, **P < 0.01, and ***P < 0.001.

Figure 2  Influence of age on distensibility factor α. Pulmonary vascular distensibility factor α in adolescents (circles), young adults (squares), and middle-aged adults (triangles). Horizontal bars indicate the means. Pulmonary vascular distensibility decreased with aging. *P < 0.05, **P < 0.01, and ***P < 0.001.
adolescents, possibly in relation to more distensible pulmonary circulation.

A previous large-scale study on 1168 healthy subjects aged from 16 to 93 years showed that the TAPSE/PASP decreases with aging, but significantly so only after 60 years. In that study, the TAPSE/PASP was on average higher in men compared to women on average by 0.2 mm/mmHg. In this study, there were no significant male vs. female differences in the TAPSE/PASP, which was, however, decreased in the middle-aged adults. In a smaller size study on 90 healthy adults aged from 19 to 63 years, the TAPSE/PASP decreased with aging following the equation TAPSE/PASP = -0.013 × age + 1.83. While in this study, TAPSE/PASP was similar to previously reported, the prediction equation over-estimated the measurements in adolescents, young, and middle-age adults by an average of 0.75, 0.38, and 0.23 mm/mmHg, respectively.

This study did not evaluate other indices of RV-PA coupling derived from 2D measurements as previously reported. Several such indices have been shown to be inferior to the TAPSE/PASP in predicting Ees/Ea. Exercise-induced changes in S’ in the present study were quantitatively the same as exercise-induced changes in TAPSE, suggesting that the S’/PASP could be used as alternative or an internal control to assess RV-PA coupling. However, the S’/PASP in the present study was not affected by aging at rest, which indirectly suggests inferior sensibility compared to TAPSE/PASP.

The present results confirm that aerobic exercise capacity increases gradually with age during childhood and adolescence. The kinetics of this evolution are different in girls and boys related to pubertal hormonal changes reaching a peak in VO2max earlier in girls compared to boys. However, VO2max in children is not age-dependent when corrected by body weight. On the other hand, the maximal workload, endurance time, maximum average running...
speed increase continuously with age in relation to increased body dimensions and mechanical efficiency of muscle work.\(^{31}\) Higher VE/VCO\(_2\) has also been previously reported in children,\(^ {26}\) and in pre-menopausal women vs. adult men.\(^ {31}\) These differences are explained by higher chemosensitivity in children and in adult women, the latter being related to progesterone secretion.

A limitation of this study is in the exclusive use of echocardiographic measurements without validation against other imaging modalities or invasive measurements. Non-invasive exercise stress testing of the pulmonary circulation using Doppler echocardiography has been previously indirectly validated by good agreement with invasive measurements in healthy subjects\(^ {3,4,29}\) and in PH patients,\(^ {32}\) but this has been rigorously demonstrated for all the components of the PVR equation only in resting conditions.\(^ {33}\) Echocardiographic estimates of PAP from the maximum velocity of tricuspid regurgitation during exercise have recently been shown to be associated with only minimal bias at Bland and Altman analysis, demonstrating acceptable accuracy, but limits of agreement were wide indicating limited precision.\(^ {34}\) Nineteen percent of the subjects were excluded at preliminary screening for insufficient quality of tricuspid regurgitation signals to estimate PAP. This is higher than 16% reported in previous studies in our laboratory.\(^ {19}\) Even higher rates of insufficient quality exercise echocardiographies in healthy volunteers have been reported by others,\(^ {34}\) showing that the estimation of PAP from tricuspid regurgitant velocities requires expertise. Whether the excluded subjects might have influenced the reported results is not known. The TAPSE/PASP ratio has been validated by uni- and multivariable analysis of predictors of E\(_{es}/E_a\) among usual echocardiographic assessments of the RV.\(^ {10}\) In general imaging estimates of the PVR equation or RV-PA coupling, though accurate, may suffer from insufficient precision to allow for individual clinical decisions.

This study did not include children aged <12 years, which is another limitation to the definition of still needed exhaustive paediatric limits of normal for the pulmonary circulation and RV function.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adolescents</th>
<th>Young adults</th>
<th>Middle-age adults</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPSE (mm)</td>
<td>Rest 24 ± 3</td>
<td>25 ± 3</td>
<td>24 ± 3</td>
<td>3.0</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>Max 33 ± 4</td>
<td>34 ± 3</td>
<td>33 ± 4</td>
<td>1.4</td>
<td>0.26</td>
</tr>
<tr>
<td>TAPSE/PASP (mm/mmHg)</td>
<td>Rest 1.24 ± 0.18</td>
<td>1.22 ± 0.17</td>
<td>1.07 ± 0.18(^ {**})</td>
<td>5.2</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Max 0.86 ± 0.24</td>
<td>0.80 ± 0.15</td>
<td>0.72 ± 0.15(^ {**})</td>
<td>3.7</td>
<td>0.04</td>
</tr>
<tr>
<td>S’ (cm/s)</td>
<td>Rest 15 ± 2</td>
<td>14 ± 2</td>
<td>13 ± 2</td>
<td>2.5</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Max 26 ± 5</td>
<td>27 ± 4</td>
<td>21 ± 3(^ {*<strong>}),(^ {</strong>})</td>
<td>11.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>S'/PASP (cm/s/mmHg)</td>
<td>Rest 0.64 ± 0.12</td>
<td>0.63 ± 0.11</td>
<td>0.62 ± 0.09</td>
<td>0.3</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>Max 0.58 ± 0.12</td>
<td>0.58 ± 0.08</td>
<td>0.45 ± 0.08(^ {*<strong>}),(^ {</strong>})</td>
<td>10.9</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

All variables were significantly increased or decreased at maximum exercise.

PASP, systolic pulmonary arterial pressure; S’, tricuspid annular systolic velocity; TAPSE, tricuspid annular plane systolic excursion.

\(^ {**}\)P < 0.01 vs. adolescents.

\(^ {***}\)P < 0.001 vs. adolescents.

\(^ {**}\)P < 0.01 young vs. middle-age adults.

\(^ {**}\)P < 0.001 young vs. middle-age adults.

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Table 4  Cardiopulmonary exercise testing

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adolescents</th>
<th>Young adults</th>
<th>Middle-age adults</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO(_2)max (L/min)</td>
<td>2.3 ± 0.4</td>
<td>2.8 ± 0.7(^ {**})</td>
<td>3.0 ± 0.9(^ {***})</td>
<td>10.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>VO(_2)max (mL/kg/min)</td>
<td>45 ± 8</td>
<td>43 ± 7</td>
<td>44 ± 11</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Workload max (W)</td>
<td>163 ± 31</td>
<td>206 ± 53(^ {**})</td>
<td>260 ± 100(^ {*<strong>}),(^ {</strong>})</td>
<td>20.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>RER max</td>
<td>1.14 ± 0.07</td>
<td>1.18 ± 0.09(^ *)</td>
<td>1.21 ± 0.10(^ {**})</td>
<td>5.3</td>
<td>0.006</td>
</tr>
<tr>
<td>O(_2) pulse max (mL/beat)</td>
<td>11.9 ± 2.7</td>
<td>14.7 ± 3.4(^ {**})</td>
<td>18.7 ± 5.8(^ {*<strong>}),(^ {</strong>})</td>
<td>24.0</td>
<td>0.006</td>
</tr>
<tr>
<td>VO(_2) (% VO(_2)max)</td>
<td>66 ± 8</td>
<td>64 ± 8</td>
<td>64 ± 9</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>V(_e)/VCO(_2)</td>
<td>31 ± 3</td>
<td>30 ± 3(^ *)</td>
<td>29 ± 3(^ *)</td>
<td>3.2</td>
<td>0.04</td>
</tr>
</tbody>
</table>

RER, respiratory exchange ratio; VCO\(_2\), carbon dioxide output; V\(_e\), ventilation; VO\(_2\)max, maximum oxygen uptake.

\(^ {*}\)P < 0.05 vs. adolescents.

\(^ {**}\)P < 0.01 vs. adolescents.

\(^ {***}\)P < 0.001 vs. adolescents.

\(^ {**}\)P < 0.01 young vs. middle-age adults.

\(^ {**}\)P < 0.001 young vs. middle-age adults.
However, this would require another study with adapted technology and study design. A final limitation is that CPET and exercise stress echocardiography were performed on different days, which could have increased the variability in the measurements. However, simultaneous echocardiography and CPET is technically very difficult because of multiplicity of operators, connections, and measurements which could be another potential cause of variability in the results. In conclusion, adolescents compared to young or middle-aged adults have a more distensible pulmonary circulation and better indices of RV-PA coupling but of insufficient magnitude to allow for body-size-corrected aerobic exercise capacity.

Supplementary data

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

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References