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# Cardiopulmonary fitness in children with asthma versus healthy children

Johan Moreau,<sup>1,2</sup> Floriane Socchi,<sup>1,3</sup> Marie Catherine Renoux,<sup>1</sup> Anne Requirand,<sup>1</sup> Hamouda Abassi,<sup>1,2</sup> Sophie Guillaumont,<sup>1,3</sup> Stefan Matecki,<sup>1,2</sup> Helena Huguet,<sup>4</sup> Martina Avesanni,<sup>5</sup> Marie-Christine Picot,<sup>4,6</sup> Pascal Amedro<sup>5,7</sup>.

## Correspondence to

Professor Pascal Amedro, Service de Cardiologie Pédiatrique et Congénitale, CRMR M3C, Hôpital Cardiologique du Haut-Lévêque, CHU de Bordeaux, Pessac, France; pascal.amedro@chu-bordeaux.fr

JM and FS contributed equally.

## ABSTRACT

**Objectives** To evaluate, with a cardiopulmonary exercise test (CPET), the cardiopulmonary fitness of children with asthma, in comparison to healthy controls, and to identify the clinical and CPET parameters associated with the maximum oxygen uptake ( $VO_{2max}$ ) in childhood asthma.

**Design** This cross-sectional controlled study was carried out in CPET laboratories from two tertiary care paediatric centres. The predictors of  $VO_{2max}$  were determined using a multivariable analysis.

**Results** A total of 446 children (144 in the asthma group and 302 healthy subjects) underwent a complete CPET. Mean  $VO_{2max}$  was significantly lower in children with asthma than in controls ( $38.6 \pm 8.6$  vs  $43.5 \pm 7.5$  mL/kg/min; absolute difference (abs. diff.) of  $-4.9$  mL/kg/min; 95% CI of  $(-6.5$  to  $-3.3)$  mL/kg/min;  $p < 0.01$ ) and represented  $94\% \pm 9\%$  and  $107\% \pm 17\%$  of predicted values, respectively (abs. diff.  $-13\%$ ; 95% CI  $(-17$  to  $-9)\%$ ;  $p < 0.01$ ). The proportion of children with an impaired  $VO_{2max}$  was four times higher in the asthma group (24% vs 6%,  $p < 0.01$ ). Impaired ventilatory efficiency with increased  $VE/VCO_2$  slope and low breathing reserve (BR) were more marked in the asthma group. The proportion of children with a decreased ventilatory anaerobic threshold (VAT), indicative of physical deconditioning, was three times higher in the asthma group (31% vs 11%,  $p < 0.01$ ). Impaired  $VO_{2max}$  was associated with female gender, high body mass index (BMI), FEV<sub>1</sub>, low VAT and high BR.

**Conclusion** Cardiopulmonary fitness in children with asthma was moderately but significantly altered compared with healthy children. A decreased  $VO_{2max}$  was associated with female gender, high BMI and the pulmonary function.

**Trial registration number** NCT04650464.

## INTRODUCTION

Asthma is the most common paediatric chronic disease worldwide, leading to frequent hospital admissions and school absenteeism.<sup>1</sup> Paediatric asthma has become a serious public health issue and current management mainly relies on symptom

control in order to ensure to children with asthma a normal quality of life.<sup>2</sup> Asthma is characterised by chronic inflammation of lower airways, marked by expiratory airflow limitation and repeated respiratory symptoms, including wheezing, shortness of breath, chest tightness and cough.<sup>3</sup> Asthma symptoms, associated with patient's fear of exertional dyspnoea, may limit the ability to be physically active, leading to a sedentary lifestyle, and ultimately affect child's quality of life.<sup>4</sup>

In 1980, the WHO stated that functional capacity explorations best reflected the impact of chronic disease on health-related quality of life.<sup>5</sup> Therefore, cardiopulmonary exercise test (CPET) with maximum oxygen uptake ( $VO_{2max}$ ) assessment has become the reference functional examination in cardiorespiratory diseases,<sup>6</sup> first in adult population, and more recently in paediatric population. Indeed, in children,  $VO_{2max}$  is associated with patient-reported outcomes, such as health-related quality of life.<sup>7</sup> The existence of an impaired cardiopulmonary fitness in children may be related to various limiting factors, such as cardiac limitation, ventilatory limitation, physical deconditioning or even psychological barriers to physical activity.<sup>8</sup>

Most paediatric studies on cardiopulmonary fitness have enrolled healthy children, children with cardiac conditions<sup>9</sup> or children with cystic fibrosis.<sup>10</sup> By contrast, the level of  $VO_{2max}$  in children with asthma from large paediatric CPET cohorts has been scarcely reported, especially in comparison with healthy children.<sup>11-14</sup> Previous reports suggested that ventilatory exercise limitations could be related to the severity of bronchial obstruction,<sup>15-16</sup> but the predictors of  $VO_{2max}$  and the level of physical deconditioning in children with asthma remain unclear.<sup>17-18</sup>

In this study, we aimed to evaluate the cardiopulmonary fitness, assessed by a CPET, in a large cohort of children with asthma, and to compare the results to healthy controls. We also intended to identify the predictors of  $VO_{2max}$  in children with asthma.

## **METHODS**

### **Study design and population**

This cross-sectional controlled study was carried out from January 2015 to December 2019 in two tertiary care paediatric centres (Montpellier University Hospital and Saint-Pierre- Institute, France). Children aged 5-18 years old, and measuring at least 120 cm, were recruited in two paediatric CPET laboratories. Children with absolute contraindications for CPET were not eligible.<sup>9</sup>

Two groups were identified: children with asthma and healthy control children.

The asthma group consisted of children followed up for asthma and referred to one of the two centres by paediatricians, pulmonologist or general practitioners. The level of asthma severity was assessed by the therapeutic burden from the Global Initiative for Asthma (GINA) classification.<sup>3</sup> From patients' interviews, the absence of any physical activity, apart from physical education at school, was indicative of sedentary lifestyle. Also, exercise-related symptoms (chest pain or excessive dyspnoea) were reported.

As in our previous similar CPET controlled paediatric studies, the control group consisted of children referred for non-severe functional symptoms linked to exercise (murmur, palpitation or dyspnoea) or for medical sports certificate.<sup>9-19-20</sup> These children were classified as controls after a completely normal check-up, including physical examination, ECG, echocardiography and spirometry. Children with any chronic disease, medical condition (cardiac, neurologic, respiratory, muscular or renal), or medical treatment, and those requiring any further specialized medical consultation were not eligible.

### **Paediatric laboratory functional tests: spirometry and CPET**

Functional tests procedures in both centres were harmonized before the study started. We used the Quark CPET calibrated gas analyser (Cosmed Srl., Pavonna di Albano, Italy).

Spirometry tests were repeated at least three times to ensure reproducibility,<sup>21</sup> and the results of FEV1, FVC and FEV1/FVC ratio (FEV1/FVC%) were expressed in Z-scores.<sup>22</sup>

Both centres used the same CPET paediatric cycle ergometer protocol to obtain a homogeneous incremental overall duration between 8 and 12 min. Whenever the  $VO_{2max}$  did not reach a plateau, which is common in children, the peak  $VO_2$  was collected.<sup>8</sup>  $VO_{2max}$  values were normalised as percentage of the predicted  $VO_{2max}$ .<sup>23</sup> A  $VO_{2max}<80\%$  of predicted values indicated impaired cardiopulmonary fitness.<sup>24</sup>

The ventilatory anaerobic threshold (VAT) was measured using the V-slope method.<sup>25</sup> A decreased VAT  $<55\%$  of predicted  $VO_{2max}$  values was in favour of physical deconditioning.<sup>9</sup> <sup>26</sup> The ventilatory efficiency (VE/ $VCO_2$  slope) was measured from the maximum exercise.<sup>27</sup> A VE/ $VCO_2$  slope  $>30$  indicated impaired ventilatory efficiency.<sup>27</sup> The maximal voluntary ventilation, the breathing reserve (BR), the oxygen pulse, the oxygen uptake efficiency slope (OUES)<sup>28</sup> and the main respiratory variables at maximal exercise were collected (detailed CPET protocol and parameters available in online supplemental material).

## Statistical analysis

The study population was described using means and SD or median and interquartiles (Q1-Q3) for quantitative variables, and with frequencies for categorical variables. The continuous variable distributions were tested using the Shapiro-Wilk test. Quantitative variables were compared using Student's t-test when the distribution was Gaussian and using the Mann-Whitney test otherwise. For qualitative variables, groups were compared using the  $\chi^2$  test or Fisher's exact test.

Depending on the distribution of variables, correlations were performed using Pearson's or Spearman's coefficients.

We compared CPET parameters between asthma and control groups with generalised linear models adjusted on gender, age and body mass index (BMI).

A linear model was used to compare the variation of  $VO_{2max}$  per year between asthma and control groups. This analysis was stratified on gender because the interaction between age and gender was significant ( $p<0.01$ ). The results were illustrated with a scatter plot and their regression line for each group. On these figures, the p value represented the slope comparison between asthma and control groups.

A multiple linear regression was used to identify the explanatory factors for  $VO_{2max}$  in the asthma group. The clinically relevant variables (such as the BR to explore ventilatory limitation, the VAT to reflect muscular deconditioning and usual spirometric parameters), some clinically relevant interactions (such FEV1\*BMI or VAT\*BMI and BR\*BMI) and the variables with a p value  $\leq 0.2$  in the univariate analysis were included in the model. The final model was obtained using an upward selection based on the corrected Akaike information criterion and with an exit threshold of 0.10. The normality of residuals in the final model was tested using the Shapiro-Wilk test.

The statistical significance was set at 0.05 and analyses were performed using Statistical Analysis Systems Enterprise Guide V.4.3 (SAS Institute).

## Ethics

The study was conducted in compliance with the Good Clinical Practices protocol and Declaration of Helsinki principles. Informed consent was obtained from all parents or legal guardians.

## RESULTS

### Population

A total of 446 children were included in the study (centre 1, n=236; centre 2, n=210): 144 in the asthma group and 302 in the control group. No family refused to participate.

<b>Demographic data</b>				
<b>Variables</b>	<b>Asthma (N=144)</b>	<b>Controls (N=302)</b>	<b>Abs. diff. (95% CI)</b>	<b>P value</b>
Age (years)	11.4±2.8	11.1±2.6	0.3 (-0.2 to 0.8)	0.41
Height (cm)	149.5±14.7	150.0±16.0	-0.4 (-3.5 to 2.7)	0.80
Weight (kg)	44.1±15.0	42.2±13.3	1.9 (-0.8 to 4.7)	0.32
BMI (kg/m <sup>2</sup> )	19.3±4.0	18.3±2.9	1.0 (0.3 to 1.7)	0.05
Male	88 (61)	172 (57)	4.2 (-5.6 to 13.9)	0.41
<b>Spirometry data</b>				
FEV1 (Z-score)	-0.7±1.4	0.5±1.1	-1.2 (-1.4 to -0.9)	< 0.01
FVC (Z-score)	-0.2±1.4	0.5±1.3	-0.8 (-1.0 to -0.5)	< 0.01
FEV1/FVC (Z-score)	-0.7±1.4	0.0±1.2	-0.7 (-1.0 to -0.4)	< 0.01
<b>Clinical data</b>				
Regular controller treatment	101 (70)			
<b>Step GINA</b>				
1	43 (30)	-		-
2	11 (8)	-		-
3	41 (28)	-		-
4	44 (31)	-		-
5	5 (3)	-		-
Step GINA: severe (4-5)	49 (34)	-		-
Associated pathology	21 (15)	-		-
Sedentary lifestyle	44 (33)	-		-
Symptoms during daily exercise	110 (76)	-		-
Values are mean±SD or N (%).				
Abs. diff., absolute difference; BMI, body mass index.				

There was no difference between the two centres in terms of demographic data and asthma severity assessed by the therapeutic burden from the GINA classification (p=0.35). Moreover, asthmatic and control children were similar, except for anthropometric and spirometry data (table 1). No adverse events were reported during the exercise tests.

In the asthma group, 70% of patients had a specific asthma treatment and one-third was classified in the step 4 or 5 of GIN classification. FEV1, FVC and ratio FEV1/FVC were significantly lower in the asthma group. Most patients with asthma felt chest pain or excessive dyspnoea during daily exercise, and one-third had a sedentary lifestyle.

## CPET results

All enrolled children performed a maximal exercise test and both groups were similar in terms of maximum load. In the control group, the mean  $\dot{V}O_{2max}$  per body weight was normal ( $43.5 \pm 7.5$  mL/kg/min), representing  $107\% \pm 17\%$  of the predicted values. In the asthma group, the mean  $\dot{V}O_{2max}$  per body weight was good, overall ( $38.6 \pm 8.6$  mL/kg/min), representing  $94\% \pm 19\%$  of the predicted values, but was significantly lower than in healthy controls, with an absolute difference of  $-4.9$  mL/kg/min and a 95% CI of  $(-6.5$  to  $-3.3)$  mL/kg/min (p<0.01).

Expressed in  $\dot{V}O_{2max}$  percent-predicts, this represented an absolute difference of  $-13\%$  (95% CI  $(-17$  to  $-9)\%$ ; p<0.01). We found similar results after adjustment on age, gender and BMI. The proportion of children with an impaired  $\dot{V}O_{2max}$  was four times higher in the asthma group than in the control group (24% vs 6%, p<0.01, respectively). The VAT was significantly lower in the asthma group ( $26.7 \pm 6.9$  vs  $29.1 \pm 6.4$  mL/kg/min), with an absolute difference of  $-2.4$  mL/kg/min (95% CI  $(-3.7$  to  $-1.1)$  mL/kg/min; p<0.01).

Expressed in  $\dot{V}O_{2max}$  percent-predicts, this represented  $65\% \pm 16\%$  of predicted  $\dot{V}O_{2max}$  and an absolute difference of  $-6\%$  (95% CI  $(-9$  to  $-3)\%$ ; p<0.01). The proportion of children with a decreased VAT <55% was three times higher in the asthma group (31% vs 11%, p<0.01).

In the asthma group, the VE/VCO<sub>2</sub> slope, the proportion of children with an impaired ventilatory efficiency and the PetCO<sub>2</sub> were higher. The BR, Vt and oxygen pulse values were significantly lower in

the asthma group. No significant differences were observed for respiratory rate, ventilatory equivalents and OUES values.

After adjustment of CPET parameters on age, gender and BMI, similar differences between asthma and control groups were observed for VO<sub>2max</sub>, VAT, VE/VCO<sub>2</sub> slope and BR (table 2). In female children, VO<sub>2max</sub> decreased significantly faster with age in the asthma group than in controls (-1.36 mL/kg/min per year, 95% CI (-1.87 to -0.84) vs -0.55 mL/kg/min per year, 95% CI (-0.96 to -0.15), p=0.02, respectively) (figure 1). We observed a decrease of 1.95% of predicted VO<sub>2max</sub> per year of age in girls with asthma. No difference was observed in male subjects (-0.36 mL/kg/min per year, 95% CI (-1.04 to 0.33) vs 0.10 mL/kg/min per year, 95% CI (-0.27 to 0.48), p=0.20, respectively, for asthma and control groups) (figure 2).

## Predictors of VO<sub>2max</sub> in the asthma group

A lower VO<sub>2max</sub> was associated with female gender, high BMI, low FEV<sub>1</sub>, low VAT and high BR, in both univariate and multivariable analyses (table 3). However, no association was found between VO<sub>2max</sub> and the level of asthma severity from the GINA classification. There was no significant interaction between BMI with FEV<sub>1</sub>, VAT and BR. The final multivariate model explained 82% of the variability of VO<sub>2max</sub> in the asthma group.

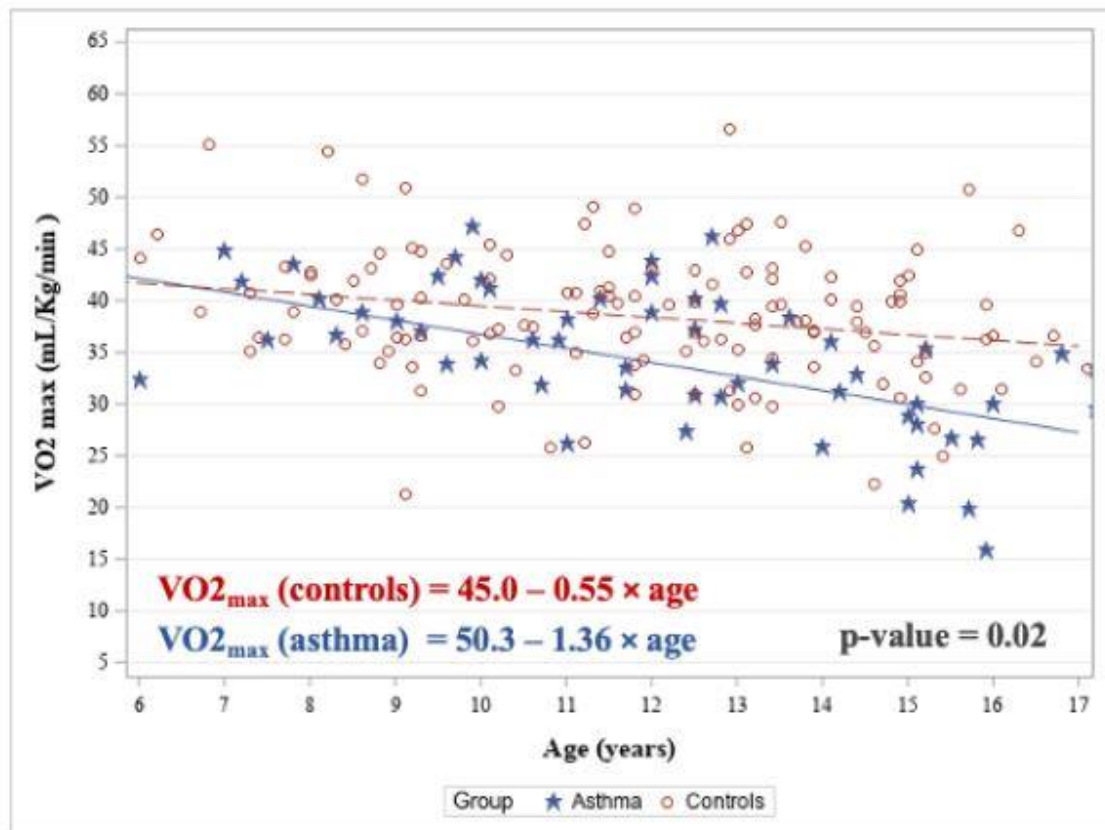
Variables	Raw CPET values				Adjusted CPET values*			
	Asthma	Controls	Abs. diff.(95% CI)†	P value	Asthma	Controls	Abs. diff. (95% CI)	P value
VO <sub>2max</sub> (mL/kg/min)	38.6±8.6	43.5±7.5	-4.9 (-6.5 to -3.3)	<0.01	38.5±5.9	42.6±5.9	-4.1 (-5.2 to -2.9)	<0.001
Percent-predicted VO <sub>2max</sub> (%)	94±19	107±17	-13 (-17 to -9)	<0.01	96±15	106±15	-10 (-13 to -7)	<0.001
Low VO <sub>2max</sub> <80%	35 (24)	19 (6)	18 (10 to 26)	<0.01	-	-	-	-
Maximal load (watt)	115 (95-155)	120 (75-160)	0(-10 to 20)	0.54	120.0±42.0	112.2±41.7	7.8 (-0.5 to 16.1)	0.06
VAT (mL/kg/min)	26.7±6.9	29.1±6.4	-2.4 (-3.7 to -1.1)	<0.01	26.8±5.1	28.4±5.1	-1.6 (-2.7 to -0.6)	<0.01
Percent-predicted VAT (%)	65±16	71±14	-6 (-9 to -3)	<0.01	67±13	71±13	-4 (-6 to -1)	<0.01
Low VAT <55%	44 (31)	34 (11)	19 (11 to 28)	<0.01	-	-	-	-
BR (%)	23 (11-34)	30 (19-39)	-7 (-10 to -4)	<0.01	22.0±15.8	29.3±15.7	-7.2 (-10.4 to -4.1)	<0.001
Vt (mL/kg)	28.8±7.2	30.4±5.9	-1.6(-2.9 to -0.2)	0.02	29.0±5.4	30.0±5.3	-1.0 (-2.0 to 0.1)	0.08
Respiratory rate (breaths/min)	50.5±10.2	52.0±10.2	-1.6 (-3.6 to 0.5)	0.13	50.4±10.0	51.9±9.9	-1.5 (-3.5 to 0.5)	0.14
PetCO <sub>2</sub> (mm Hg)	34.8 (32.0-38.0)	33.5 (31.0-35.8)	1.4 (0.5 to 2.2)	<0.01	34.8±4.3	33.6±4.3	1.3 (0.4 to 2.1)	<0.01
VEQ <sub>O<sub>2</sub></sub>	34.4 (31.3-39.1)	34.9 (31.1-38.5)	0.0 (-1.2 to 1.1)	0.98	35.6±5.7	35.4±5.6	0.2 (-0.9 to 1.3)	0.73
VEQCO <sub>2</sub>	30.1 (27.9-33.5)	31.2 (29.0-33.7)	-0.8 (-1.5 to 0.0)	0.05	30.9±3.9	31.5±3.8	-0.6 (-1.4 to 0.1)	0.10
Peak heart rate (beats/min)	185 (178-191)	187 (181-193)	-3 (-5 to -1)	<0.01	183.9±11.1	187.5±11.1	-3.6 (-5.8 to -1.4)	<0.01
Percent-predicted peak HR (%)	84 (81-87)	90 (87-93)	-6 (-7 to -5)	<0.01	84±5	90±5	-6 (-7 to -5)	<0.001
Peak oxygen pulse (mL/beat)	8.5 (7.2-10.2)	9.1 (7.4-11.0)	-0.5 (-1.0 to -0.0)	0.04	8.5±1.9	9.6±1.9	-1.2 (-1.6 to -0.8)	<0.001
RER	1.2 (1.1-1.2)	1.1 (1.1-1.2)	0.0 (0.0 to 0.1)	<0.01	1.2±0.1	1.1±0.1	0.1 (0.0 to 0.1)	<0.01
VE/VCO <sub>2</sub> slope	30.8 (28.7-33.3)	29.6 (26.6-32.1)	1.5 (0.7 to 2.2)	<0.01	31.1±3.9	29.6±3.8	1.5 (0.7,2.3)	<0.001
VE/VCO <sub>2</sub> slope >30	90 (63)	136 (45)	17 (8 to 27)	<0.01	-	-	-	-
OUES	1840.0 (1488.5-2225.0)	1739.5 (1383.0-2225.0)	82.0 (-50.0 to 215.0)	0.22	1772.7±438.4	1852.1±433.3	-79.4 (-181.1 to 22.3)	0.13
OUES/kg	43.5 (37.1-52.9)	44.1 (38.6-50.1)	0.2 (-2.4 to 2.7)	0.91	44.7±8.6	43.9±8.5	0.8 (-1.1 to 2.8)	0.41

Values are mean±SD or median (Q1-Q3) or N (%).  
Significant values are marked in bold.  
\*Adjusted on age, gender and BMI.  
†Hodges-Lehmann method was used to calculate the absolute difference of the median with its CI.  
Abs. diff., absolute difference; BR, breath reserve; HR, heart rate; OUES, oxygen uptake efficiency slope; PetCO<sub>2</sub>, partial pressure of end tidal CO<sub>2</sub>; Oxygen pulse, VO<sub>2</sub> ÷ heart rate; RER, respiratory exchange ratio (VCO<sub>2</sub> ÷ VO<sub>2</sub>); VE/VCO<sub>2</sub> slope, the minute ventilation/carbon dioxide production slope; VAT, ventilatory anaerobic threshold; VEQCO<sub>2</sub>, ventilatory equivalent for carbon dioxide: ratio of the volume of air ventilating the lungs to the volume of carbon dioxide produced; VEQO<sub>2</sub>, ventilatory equivalent for oxygen: ratio of the volume of gas expired per minute to the volume of oxygen consumed per minute; VO<sub>2max</sub>, maximum oxygen uptake; Vt, tidal volume.

## DISCUSSION

From a paediatric cohort of 446 subjects, this multicentre controlled study provided values and predictors of cardiopulmonary fitness in 144 children with asthma compared with 302 healthy controls.

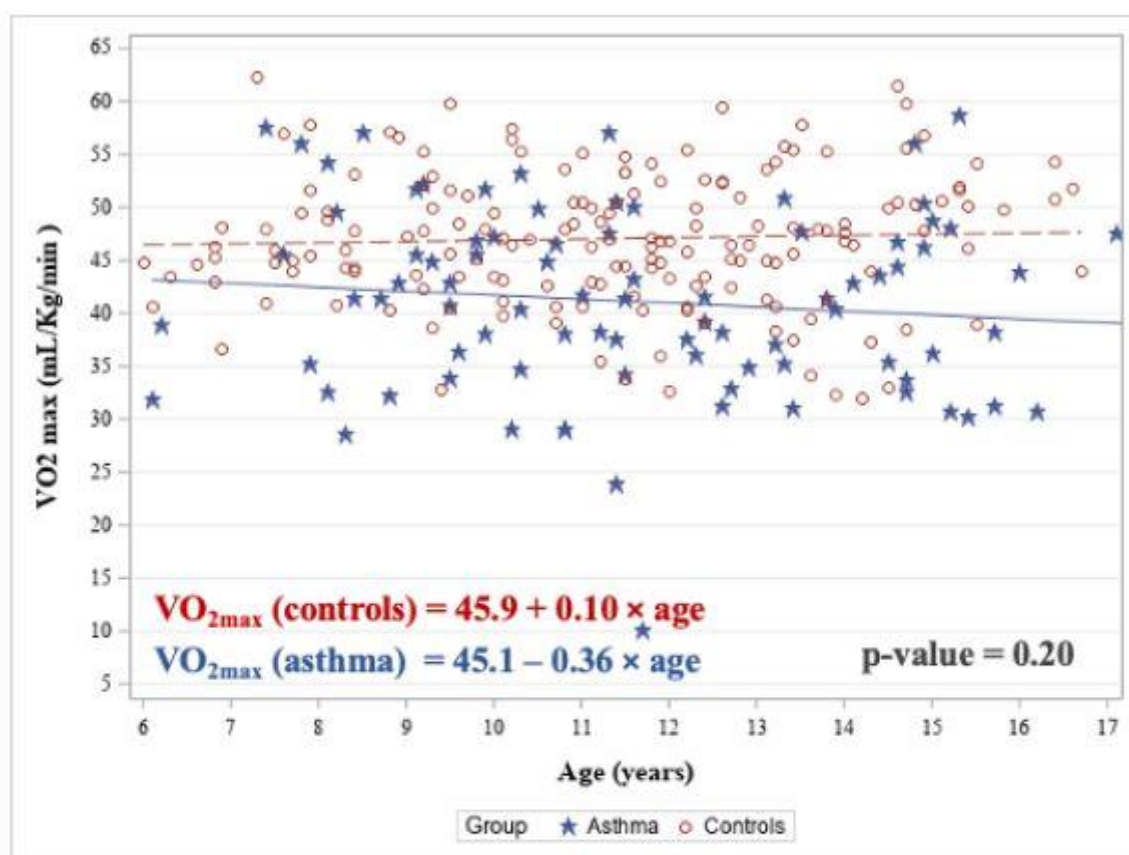
Overall, the cardiopulmonary fitness of children with asthma was good ( $VO_{2max} > 90\%$ ). However, their  $VO_{2max}$  was lower than that of healthy subjects, with a mean difference of 13% between their respective percent-predict values. Moreover, the  $VO_{2max}$  was impaired in nearly one-fourth of children with asthma, which was four times higher than in healthy subjects. The  $VO_{2max}$  decrease was associated with lower FEV1.



**Figure 1** Relationship between age and  $VO_{2max}$  in female subjects. Equations of the  $VO_{2max}$  models according to age for asthma and control groups were reported. The p value illustrates the comparison between the two slopes.

Previous reports on cardiopulmonary fitness in children with asthma are controversial,<sup>29</sup> as some studies found  $VO_{2max}$  values similar to healthy controls,<sup>13 14</sup> whereas others found lower  $VO_{2max}$  values in children with asthma.<sup>12 30</sup> However, those studies enrolled small numbers of subjects and used heterogeneous CPET protocols. Unsurprisingly, the  $VO_{2max}$  was lower in children with high BMI, as adipose tissue does not consume oxygen, as well as in girls, reflecting the well-known gender differences in muscle mass and adipose tissue.<sup>9 31</sup> Exercise-induced symptoms may be associated with misdiagnosis of asthma in overweight subjects.<sup>32</sup>

Therefore, in this study, CPET parameters' comparisons used generalised linear models adjusted not only on gender and age, but also on BMI, in order to determine the impact of paediatric asthma on aerobic fitness. Interestingly, the results of this study suggest the existence of an early onset of physical deconditioning in childhood asthma. Indeed, the VAT was a predictor of  $VO_{2max}$  and nearly one-third of children with asthma had low VAT values, which was three times higher than in healthy controls. Moreover, asthma severity, as assessed by the GINA classification, was not associated with  $VO_{2max}$ .



**Figure 2** Relationship between age and  $VO_{2max}$  in male subjects. Equations of the  $VO_{2max}$  models according to age for asthma and control groups were reported. The p value illustrates the comparison between the two slopes.

Nevertheless, few subjects with severe asthmatic forms were included in this study. In this cohort, most children with asthma felt chest pain or excessive dyspnoea during daily exercise, and one-third had a sedentary lifestyle. In the literature, barriers to physical activity in children with asthma have been mainly related to an altered self-perception of physical capacity<sup>16 18</sup> and, to a lesser extent, to insufficient asthma control, dynamic hyperinflation and air trapping during effort, or exercise-induced bronchoconstriction.<sup>33 34</sup>

Indeed, some children may limit their activities for fear of experiencing symptoms during exercise.<sup>35</sup> They gradually adopt a sedentary lifestyle, responsible for increased symptoms during exercise, which will ultimately aggravate the vicious circle of physical deconditioning. This is supported in this study by the  $VO_{2max}$  decrease over time in the asthma group (1.36 mL/kg/min/ year in girls and 0.36 mL/kg/min/year in boys).

Furthermore, this study provided original data on ventilatory parameters during exercise in childhood asthma. Previous studies failed to identify any significant differences in exercise ventilatory parameters between children with and without asthma.<sup>15 36</sup> Globally, children with asthma were prone to some degree of ventilatory inefficiency, as reflected by the  $VE/VCO_2$  slope. Previous reports have described the hyperventilation syndrome<sup>37</sup> as indicative of ventilatory limitation in children with asthma,<sup>38</sup> but this has not been observed in our study, where higher  $PetCO_2$  values at the end of exercise have been observed. Interestingly, in children with asthma from our cohort, a higher BR was a predictor of a lower  $VO_{2max}$ , suggesting that exercise limitation in childhood asthma does not only rely on the respiratory impairment but also includes a certain degree of physical deconditioning.



As a result, the use of CPET in childhood asthma follow-up provides a comprehensive assessment of cardiopulmonary fitness and evaluates the impact of the obstructive lung disease on physical capacity. Ultimately, the CPET identifies the patients most at risk of physical deconditioning in this population, and therefore could be the first step of exercise rehabilitation in childhood asthma. Unfortunately, cardiopulmonary rehabilitation programmes in asthma have been scarcely developed, despite preliminary positive results in small studies focused on physical training.<sup>39</sup> Nevertheless, previous studies have highlighted the benefits of regular physical activity in asthma in terms of disease control, lung function and mental health.<sup>30</sup> Moreover, regular physical activity is highly recommended by GINA in the global management of asthma.<sup>3</sup> In a near future, evaluation and promotion of physical activity in children with asthma and impaired physical fitness could therefore be supported by structured rehabilitation programmes, including both exercise training and patient education, as recently reported in other paediatric conditions.<sup>40</sup>

**Table 3** Clinical determinants of  $VO_{2max}$  in the asthma group (linear regression)

Variables				Univariate analysis		Multivariable analysis (N=144)	
		N	r	$\beta$ (95% CI)	P value	$\beta$ (95% CI)	P value
Age (years)*		144	-0.3	-0.85 (-1.34 to -0.36)	<0.001	-	-
BMI (%)*		144	-0.52	-0.13 (-0.17 to -0.09)	<0.0001	-0.07 (-0.09 to -0.05)	<0.0001
FEV1 (Z-score)*		144	0.15	0.91 (-0.08 to 1.90)	0.07	0.86 (0.39 to 1.32)	<0.001
FVC (Z-score)*		144	0.18	1.09 (0.08 to 2.10)	0.04	-	-
FEV1/FVC (Z-score)		144	-0.03	-0.20 (-1.20 to 0.80)	0.69	-	-
VAT (mL/kg/min)*		144	0.86	1.08 (0.97 to 1.18)	<0.0001	0.87 (0.76 to 0.98)	<0.0001
BR (%)*		144	-0.18	-0.09 (-0.17 to -0.01)	0.04	-0.08 (-0.12 to -0.05)	<0.0001
		<b>N</b>	<b>Mean±SD</b>				
Gender*	Female	56	34.6±6.9	-6.44 (-9.17 to -3.72)	<0.0001	-2.11 (-3.50 to -0.73)	<0.01
	Male	88	41.1±8.8	-		-	
Regular controller treatment	No	43	38.3±8.4	-0.38 (-3.50 to 2.74)	0.81	-	-
	Yes	101	38.7±8.8	-		-	-
Step GINA severe	No	95	38.9±8.9	1.08 (-1.93 to 4.08)	0.48	-	-
	Yes	49	37.8±8.1	-		-	-
Montelukast treatment	No	116	38.5±9.1	-0.40 (-4.01 to 3.20)	0.83	-	-
	Yes	28	38.9±6.7	-		-	-
Sedentary lifestyle*	No	88	40.1±8.7	4.97 (1.84 to 8.10)	<0.01	-	-
	Yes	44	35.2±8.3	-		-	-
Symptoms during daily exercise	No	34	37.7±8.8	-1.09 (-4.44 to 2.27)	0.52	-	-
	Yes	110	38.8±8.6	-		-	-
Associated pathology	No	123	38.7±8.7	1.11 (-2.92 to 5.15)	0.59	-	-
	Yes	21	37.6±8.1	-		-	-

Values are correlation coefficients (r) or means ± SD.  
 \*Candidate variables for multivariable analysis. Variables associated with  $VO_{2max}$  in both univariate and multivariable analyses are marked in bold.  
 $\beta$ , adjusted  $\beta$ ; BMI, body mass index; BR, breath reserve;  $\beta$ , crude  $\beta$ ; FEV1/FVC, Tiffeneau index; VAT, ventilatory anaerobic threshold;  $VO_{2max}$ , maximum oxygen uptake.

## Study limitations

This study was performed in tertiary care centres, therefore, children with more severe asthma status may have been enrolled, which may not represent asthmatic children in the general population.

Data on asthma control were not available but would have been of great interest in the perspective of further patients' education. Moreover, further work should be carried out to evaluate the impact of exercise-induced bronchospasm and dynamic hyperinflation on cardiopulmonary fitness in paediatric asthma.

## CONCLUSION

Cardiopulmonary fitness in children with asthma was moderately but significantly altered, in comparison with healthy children, and  $VO_{2max}$  was impaired in one-fourth of children with asthma. A decreased  $VO_{2max}$  was associated with female gender, high BMI, low VAT and low FEV1. Nearly one-third of children with asthma had low VAT values, suggesting an early onset of physical deconditioning. Children with asthma were prone to ventilatory inefficiency during exercise. The use of CPET in the follow-up of paediatric asthma evaluates the impact of the obstructive lung disease on

cardiopulmonary fitness and identifies the children most at risk of physical deconditioning. Further work will have to determine the interest of CPET in promotion of physical activity and cardiopulmonary rehabilitation for childhood asthma.

#### Author affiliations

<sup>1</sup>Unit of Paediatric Pulmonology and Cardiology, Department of Paediatrics, Montpellier University Hospital, Montpellier, France

<sup>2</sup>PhyMedExp, INSERM 1046, University of Montpellier, Montpellier, France

<sup>3</sup>Paediatric Cardiopulmonary Rehabilitation Centre, Saint-Pierre Institute, Palavas-les-ots, France

<sup>4</sup>Department of Epidemiology and Biostatistics, Montpellier University Hospital, Montpellier, France

<sup>5</sup>Paediatric and Congenital Cardiology Department, M3C National CHD Reference Centre, Bordeaux University Hospital, Bordeaux, France

<sup>6</sup>CIC 1411, INSERM, University of Montpellier, Montpellier, France

<sup>7</sup>IHU Liryc, INSERM 1045, University of Bordeaux, Bordeaux, France

**Twitter** Pascal Amedro @Pascal\_Amedro

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