

# Maximum oxygen uptake in children with congenital heart diseases: a multicenter comparative study

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**Background:** Cardiopulmonary exercise test (CPET) is recommended in the follow-up of adults with congenital heart diseases (CHD) but not yet in CHD children.

**Objectives:** We aimed to compare the maximum oxygen uptake ( $VO_{2max}$ ) of a large cohort of CHD children to that of a control population. We also intended to identify clinical characteristics that most impacted  $VO_{2max}$  in this population.

**Methods:** From 2010 to 2015, we included healthy and CHD children who performed a complete CPET. Children with no chronic disease, no treatment and normal physical examination were included in the control group. The impact of clinical characteristics on  $VO_{2max}$  was studied with multivariate analysis.

**Results:** 798 children (496 CHD and 302 controls) were included. Mean  $VO_{2max}$  in the CHD group and control represented respectively  $93\pm 20\%$  and  $107\pm 17\%$  of predicted values.  $VO_{2max}$  was significantly lower in the CHD group, overall ( $37.8\pm 0.3$  vs  $42.6\pm 0.4$  ml/kg/min,  $p<0.0001$ ) and for each group ( $p<0.05$ ). Mean  $VO_{2max}$  decline per year was significantly higher in CHD than in controls overall ( $-0.85\pm 0.10$  vs  $-0.34\pm 0.17$  ml/kg/min/year,  $p<0.01$ ), for males ( $-0.72\pm 0.14$  vs  $0.11\pm 0.19$  ml/kg/min/year,  $p<0.01$ ) and for females ( $-1.00\pm 0.13$  vs  $-0.55\pm 0.21$  ml/kg/min/year,  $p=0.05$ ).  $VO_{2max}$  was impacted by age, gender, body mass index, restrictive ventilatory disorder, tricuspid regurgitation, number of cardiac catheter or surgery procedures and presence of a genetic anomaly.

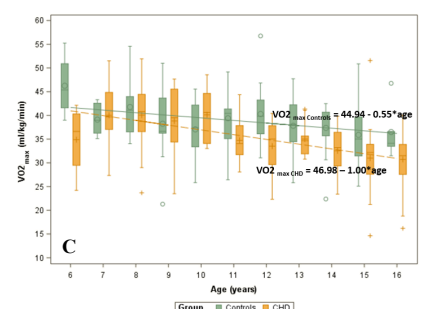
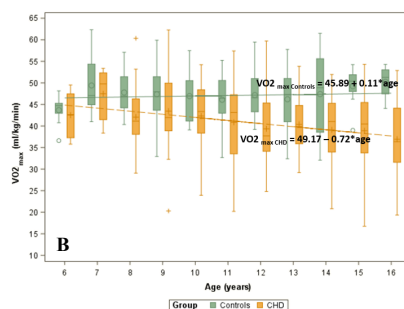
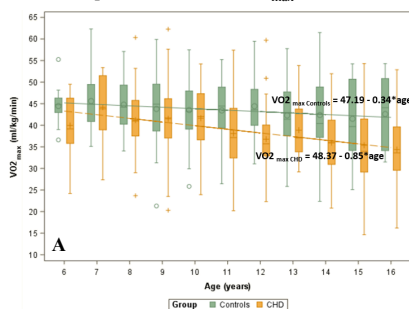
VO <sub>2max</sub> explanatory variables in the CHD group			
Variables	Description	Univariate analysis	Multivariate analysis (AIC selection model) (N=391)
		r	p-value
Age (years)		-0.35	<.0001
BMI (kg/m <sup>2</sup> )		-0.51	<.0001
	Mean VO <sub>2max</sub> ±SD	p-value	p-value
Gender	Girls	34.7±6.8	<.0001
	Boys	40.5±8.1	<.0001
Restrictive ventilatory disorder	No	38.4±8.0	0.02
	Yes	36.1±8.1	<.0001
Obstructive ventilatory disorder	No	38.0±8.0	<.01
	Yes	28.0±5.9	-
Altered systolic ejection fraction	No	37.9±8.2	0.06
	Yes	33.4±3.6	-
Right ventricle systolic hypertension	No	38.0±8.2	0.10
	Yes	36.2±7.7	-
Right outflow tract obstacle	No	37.5±8.1	0.14
	Yes	39.4±8.0	-
Left outflow tract obstacle	No	37.9±8.2	0.36
	Yes	36.5±6.8	-
Aortic regurgitation	No	38.0±8.2	0.08
	Yes	37.5±7.0	-
Tricuspid regurgitation	No	37.9±8.0	0.12
	Yes	34.9±10.1	0.01
Pulmonary regurgitation	No	37.8±8.3	0.86
	Yes	37.6±7.4	-
Genetic anomalies	No	38.1±8.0	<.0001
	Yes	32.1±7.9	0.08
Number of cardiac surgical procedures	0	38.7±8.0	<.01
	1	38.7±8.2	<.01
	2	35.4±7.6	<.0001
Number of cardiac catheter procedure	0	38.3±8.2	0.01
	1	38.5±7.8	<.01
	2	33.5±7.3	<.0001
Beta blockers	No	38.3±8.1	<.01
	Yes	35.3±7.7	<.0001

VO <sub>2max</sub> in CHD and controls									
	N <sub>CHD</sub> / N <sub>Controls</sub>	VO <sub>2max</sub> (ml/kg/min) Mean ± SD		p *	% of predicted VO <sub>2max</sub> Mean ± SD		p *	VO <sub>2max</sub> variation according age (ml/kg/min/year) § β coeff ± SDβ	
		CHD	Controls		CHD	Controls		CHD	Controls
Total	496 / 302	38.1±8.1	43.5±7.5	<.0001	93±20	107±17	<.0001	-0.85±0.10 †	-0.34±0.17 ‡
Gender									
Male	290 / 172	40.5±8.1	47.1±6.3	-	91±22	106±16	-	-0.72±0.14 †	0.11±0.19
Female	206 / 130	34.7±6.8	38.7±6.4	-	96±16	108±17	-	-1.00±0.13 †	-0.55±0.21 ‡
P <sub>male vs female</sub>		<.0001	<.0001	-	<.0001	0.23	-		
ACC-CHD group	N <sub>CHD</sub> / N <sub>Controls</sub>	CHD	Controls	p †	CHD	Controls	p †	CHD	Controls
1	3 / 36	42.6±4.9	44.6±7.3	0.65	101±16	104±17	0.68	-	-
2	13 / 147	39.4±6.3	45.6±7.0	<.01	97±18	107±17	0.03	-1.02±0.35 †	-0.19±0.24
3	29 / 194	37.9±6.6	41.8±7.5	<.01	98±18	108±16	<.01	-0.38±0.41	-0.55±0.22 ‡
4	27 / 185	35.4±9.4	43.6±7.3	<.0001	88±23	106±16	<.0001	-1.85±0.44 †	0.41±0.22
5	5 / 64	33.5±5.2	42.2±7.9	<.01	80±20	104±17	<.01	-	-
6	25 / 221	32.3±7.2	45.0±7.4	<.0001	76±16	106±17	<.0001	-0.56±0.42	-0.39±0.19 ‡
7	46 / 259	38.2±7.5	43.6±7.6	<.0001	92±16	106±17	<.0001	-0.25±0.38	-0.21±0.21
8.1	72 / 261	40.5±7.7	44.2±7.5	<.0001	93±20	106±17	<.0001	-0.81±0.26 †	-0.14±0.18
8.2	93 / 286	36.7±7.7	43.4±7.5	<.0001	91±20	107±16	<.0001	-0.70±0.22 †	-0.32±0.17
8.5	52 / 285	36.7±8.0	43.6±7.5	<.0001	92±19	106±16	<.0001	-0.92±0.33 †	-0.31±0.17
8.6	49 / 281	40.2±7.6	43.8±7.5	<.01	102±15	107±17	0.03	-0.86±0.33 †	-0.47±0.18 ‡
9	76 / 289	39.9±8.8	43.4±7.6	<.0001	95±21	107±17	<.0001	-0.93±0.29 †	-0.37±0.19 ‡
10	6 / 135	36.4±11.8	42.6±8.2	0.07	93±30	106±17	0.09	-	-

\* Comparisons of  $VO_{2max}$  (ml/kg/min) between CHD and controls after adjustment on age and gender.  
 † Comparisons of  $VO_{2max}$  (ml/kg/min) between CHD and controls matching on age and gender (random cluster).  
 ‡ Significant  $VO_{2max}$  variation (β coefficient different of 0) according to age ( $p<0.05$ ).  
 § Interaction age\*group being significant, regression coefficient were reported for a variation of 1 year of age by group.

## Box plots of $VO_{2max}$ as a function of age (years)

A. Global population. B. Males. C. Females. The bottom and top of the box represent the first and third quartiles, the band inside the box represent the median, whiskers represent the minimum and maximum values, mean and data not included between the whiskers (outliers) were plotted with small circles (controls) and crosses (CHD), the linear curves represent the mean  $VO_{2max}$  variation with age



**Conclusion:**  $VO_{2max}$  among children with CHD, as opposed to adults, was weakly altered but remained significantly lower than normal children. We recommend performing CPET in routine follow-up of these patients. We should now focus on pediatric cardiac rehabilitation among selected CHD children.