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Correlation of anthropometric index and cardiopulmonary exercise testing in children with pectus excavatum

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ABSTRACT

Background: Cardiopulmonary exercise testing (CPET) is a method used to evaluate functional impairment of patients with various diseases.
Objective: The objective was to use CPET to estimate the usability of anthropometric index (AI) in patients with pectus excavatum (PE) as a marker of functional impairment caused by chest deformity.
Methods: The study included 32 paediatric patients (28 males) with PE. Patients underwent CPET using a breath-by-breath exhaled gas analysis method and continuous monitoring of cardiac parameters.
Results: In both groups, two (overall four) patients met criteria for cardiogenic limitation (low VO_2 and low O_2Pulse). Mean VO_2/WR was below two standard deviations (2SD) in patients with less severe PE; other observed parameters were within normal limits (Z-score ± 2 SD). The AI had no observed correlation with peak ventilation, VO_2peak and peak workload.
Conclusion: The obtained CPET data do not correlate well with the severity of chest deformity expressed with AI. There were similar physical activity limitations in both examined groups of patients and they did not depend on the severity of the deformity.

1. Introduction

Cardiopulmonary exercise testing (CPET) is a method that helps clinicians understand the root of cardiorespiratory impairment in various diseases. The use of breath-by-breath analysis of exhaled air in a stress test helps clinicians understand the cause and pathophysiology of pathological patterns causing clinical symptomatology. Pectus excavatum (PE) is a congenital deformity of the chest of unknown aetiology, in which an abnormal formation of bone-cartilaginous joints of the ribs and sternum occurs, creating a concave depression of the chest wall (Jaroszewski et al., 2010). Frequently present symptoms are lack of endurance, shortness of breath during exercise and chest pain (Rowland and American College of Sports Medicine, 2017). Symptoms often vary in severity and their effect on normal daily activities (Krystofová et al., 2011). The severity of the deformity does not necessarily correlate with the severity of the symptoms. Many patients are asymptomatic at a younger age but begin to experience the first symptoms during puberty and adolescence. This can be caused by a growth spurt or an increase in physical activity. The most common symptoms are dyspnoea during exercise and loss of stamina (Krystofová et al., 2011). In addition to somatic problems, patients with PE often have psychological problems based on the perception of physical deformity. Exercise intolerance might be a secondary sequela to psychologically escalated fear of physical activity to which the body might be exposed (showering, changing clothes), and so it might be manifested by subsequent hypoactivity (Kelly et al., 2008).

Examination of patients with PE includes a careful anatomical description, evaluation of the extent of cardiac compression, measurement of lung function and echocardiography (ECG) to detect the presence of mitral valve prolapse or reduced right ventricular volume. The extent of the chest deformity is based on chest computed tomography (CT) and determination of the so-called Haller index (HI; Jaroszewski

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et al., 2010). Indications for surgical treatment include two or more of the following: severe symptomatic deformity; deformity progression; paradoxical chest movement with breathing; HI greater than 3.25; cardiac compression and/or pulmonary compression; finding a restrictive ventilation disorder; mitral valve prolapse, right bundle branch block; or other cardiological pathology secondary to cardiac compression (Kelly, 2008).

To monitor non-invasively patients with PE who are not candidates for surgery, a proposal was submitted to assess the severity of PE, the so-called anthropometric index (AI). For PE, this index is defined as the B measurement divided by the A measurement (AI = B/A) (Rebeis et al., 2007). The A and B clinical measurements are carried out with the patient in a horizontal supine position on a flat table parallel to the floor during deep inhalation. The A measurement is defined as the largest anteroposterior diameter at the level of the distal third of the sternum, and the B measurement is the greatest depth at the same level (Rebeis et al., 2007). A cut-off value for determining the severity of PE was determined to be 0.12 based on measurements and comparisons with the HI. Patients with a value greater than 0.12 are those in whom surgery is indicated in the presence of the auxiliary criteria listed above (Saxena, 2017).

Patients without the need for surgery or not wanting to undergo surgery are treated conservatively with physiotherapy and suitable candidates are also treated with vacuum bell. In those patients, measuring the HI is an unnecessary risk and the search for a non-invasive, X-ray-free measurement is ongoing. Because it has only been proved that the HI correlates with the physical abilities of patients with PE, and it appears that the HI correlates with the AI, we hypothesise that the AI is a suitable observatory index for patients not undergoing surgery due to its low cost, repeatability and lack of X-ray.

2. Methods

The study was performed from December 2017 to December 2020 and included children aged 8–19 years with a diagnosis of PE. The project protocol was approved by the Ethics Committee of the Jessenius Faculty of Medicine in Martin. All patients and their legal representatives were informed of the nature and purpose of the examination and had signed informed consent. The work was carried out at the Centre for the Diagnosis of Functional Disorders in Childhood at the Clinic for Children and Adolescents, Jessenius Medical Faculty, University Hospital Martin. The study included paediatric patients and adolescents with PE who were referred from the Pediatric Surgery Clinic and were candidates for conservative therapy (with vacuum bell) or surgical treatment. Only patients who were not undergoing vacuum bell treatment at the time of testing and did not undergo corrective surgery were included in the cohort of the patients. Chest CT with the determination of the HI was not required. Assessing physical activity over an entire week in the studied patients with PE was necessary to match their results with appropriate normal values (Malek et al., 2006). To correct for the large body size and body mass diversity amongst children and adolescences, we used age-, sex- and mass-adjusted reference values based on multivariate regression models with corrections for overweight and obesity. Every measured parameter was compared to reference values and Z-scores was estimated, considering an interval of two standard deviations (SD) as a normal value (Blanchard et al., 2018).

After basic examinations (12-lead ECG, spirometry), CPET on treadmill (RAM Clinical 870A, Belgium) was performed using the breath-by-breath analysis of expired gas (Geratherm Respiratory, Germany). An individualised load protocol was used to achieve the maximum tolerated load between 8 and 12 min. Prior to the exercise, a manoeuvre was performed to determine the inspiratory capacity during calm breathing, and subsequently the inspiratory capacity was paired with the tidal volume. The patient was monitored during exercise with a continuously recorded 12-lead ECG. During exercise, respiratory parameters (minute ventilation [VE], breathing reserve [BR], breathing rate [BF]), oxygen consumption parameters (O_2Pulse, VO_2), cardiovascular parameters (ECG, heart rate [HR]) and respiratory exchange ratio (RER) were recorded and then ventilation efficiency parameters (VE/VCO_2) and oxygen extraction efficiencies (VO_2/WR) were calculated. Anaerobic threshold (AT) was calculated using the V-slope method. All examinations were performed in the morning and the patients were instructed to rest at least 24 h before the examination and come sufficiently hydrated.

Analysis of the obtained data was performed in Systat 13 (Systat Software Inc., 2011). Student's T-test was used to compare the equality of population averages (for parametric data). Pearson's correlation coefficients were used to express the correlation of the monitored parameters. When plotting the dependent variables, we used direct linear regression of the obtained data to linearly predict future values. The prediction is expressed as x + 30 % (where x is the maximum of the values obtained).

Table 1
Baseline characteristics of all patients and groups of patients based on the anthropometric index (AI).

	All patients		AI < 0.12		AI ≥ 0.12		
	n = 32 (28 males)		n = 17 (15 males)		n = 15 (13 males)		
	Mean	SD	Mean	SD	Mean	SD	p
AI (1)	0.13	0.06	0.09	0.02	0.17	0.05	
Height (cm)	176.7	14.6	178.43	13.04	175.21	15.77	> 0.05
Weight (kg)	59.6	13.6	62.77	13.79	56.84	12.72	> 0.05
BMI (kg/m^2)	18.8	2.4	19.32	2.70	18.26	1.94	> 0.05
Age (years)	15.3	2.9	15.53	2.59	15.11	3.21	> 0.05

BMI, body mass index; SD, standard deviation.

Table 2
The results of cardiopulmonary exercise testing in all patients (n = 32) with pectus excavatum (expressed as mean Z-scores).

Parameter	Mean	SD	r
AI	0.13	0.06	
WR/kg	−0.07	1.82	0.07
VO_2peak	−1.51	1.11	−0.02
HR peak	−0.82	1.58	0.14
HRR 1	−0.94	1.58	0.25
HRR 2	−0.74	1.61	0.18
O_2Pulse	−1.21	1.10	−0.06
VE	−0.61	1.41	0.18
RER	−0.23	1.68	0.18
VO_2/WR	−1.51	2.61	−0.03
VE/VCO_2	0.19	1.28	0.38
BR (% MVV)	34.59	12.54	−0.36
AT (% of VO_2)	58.2	10.69	0.01

The r value represents Pearson's correlation coefficient of the AI and the measured parameter. The Z-score calculator for cardiopulmonary exercise testing in children is based on Blanchard et al. (2018). AI, anthropometric index; WR/kg, maximum tolerated load per kilogram of weight; VO_2peak, peak oxygen consumption; HRpeak, maximum heart rate; HRR 1, heart rate at 1 min after exercise; HRR 2, heart rate at 2 min after exercise; RER, respiratory exchange ratio; VO_2/WR, oxygen consumption related to workload; VE/VCO_2, ventilation efficiency; BR, breathing reserve, AT, anaerobic threshold; SD, standard deviation.

3. Results

We included 32 patients (28 males) in our study. Based on the severity of the deformity, the patients in our cohort were divided into two groups: a group of patients with PE and an AI < 0.12 and a group of patients with PE and an AI ≥ 0.12. A total of 17 patients (15 males) were enrolled in the AI < 0.12 group, with a mean AI of 0.09 ± 0.02. A total of 15 patients (13 males) were enrolled in the AI ≥ 0.12 group, with a mean AI of 0.17 ± 0.05. There were no statistically significant

Table 3
The results of cardiopulmonary exercise testing in patients divided according to the anthropometric index.

	AI < 0.12			AI ≥ 0.12			
	Mean	SD	r	Mean	SD	r	p
AI	0.09	0.02		0.17	0.05		
WRpeak	0.03	0.02	−0.14	−0.15	1.23	0.07	> 0.05
VO_2peak	−1.47	1.25	−0.32	−1.54	0.96	−0.14	> 0.05
HR peak	−1.13	1.41	−0.34	−0.54	1.67	0.01	> 0.05
HRR 1	−1.16	1.39	−0.47	−0.75	1.71	0.11	> 0.05
HRR 2	−1.00	1.28	−0.30	−0.52	1.82	0.07	> 0.05
O_2Pulse	−1.07	1.23	−0.58	−0.75	1.71	−0.20	> 0.05
VE	−0.93	1.35	−0.64	−0.33	1.40	−0.09	> 0.05
RER	−0.37	1.87	−0.24	−0.12	1.47	0.20	> 0.05
VO_2/WR	−2.13	1.68	−0.10	−0.96	3.11	−0.21	> 0.05
VE/VCO_2	−0.33	0.85	−0.09	0.65	1.40	0.07	< 0.05
BR (%MVV)	39.10	14.13	0.29	30.60	9.24	−0.02	< 0.05
AT (% of VO_2)	56.05	12.54	−0.36	59.77	8.68	0.02	< 0.05

The r value represents Pearson's correlation coefficient of the AI and the measured parameter. The Z-score calculator for cardiopulmonary exercise testing in children is based on Blanchard et al. (2018). AI, anthropometric index; WRmax/kg, maximum tolerated load per kilogram of weight; VO_2peak, peak oxygen consumption; HRpeak, maximum heart rate; HRR 1, heart rate at 1 min after exercise; HRR 2, heart rate at 2 min after exercise; RER, respiratory exchange ratio; VO_2/WR, oxygen consumption related to workload; VE/VCO_2, ventilation efficiency; BR, breathing reserve, AT, anaerobic threshold; SD, standard deviation.

differences in the observed height, weight, body mass index (BMI) and age. Baseline characteristics of all patients and patients in groups based on their AI are presented in Table 1.

Based on interviews with parents of the studied children, we estimated that none of the studied subjects partake in extracurricular physical activity more than three times a week nor are they competitive athletes. No patient had subjectively perceived dyspnoea at rest, and 6/32 patients (three boys) stated they had lower stamina compared with their peers. No patient had been diagnosed with cardiological or other problems that might prohibit them from exercising.

All patients finished the examination and met the criteria for the maximal test (RER > 1.1; breathing rate > 40/min; plateau in VO_2; heart rate > 85 % of predicted).

The results obtained by examination of all patients with PE are summarised in Table 2. One patient with an AI of 0.23 had a BR of 8% at peak exercise but VO_2peak and WRpeak were within normal limits; thus, they did not meet the criteria for respiratory limitation. Two patients in the AI < 0.12 group and two patients in the AI ≥ 0.12 group had low VO_2max, low WRpeak and low O_2Pulse; thus, they had a cardiogenic limitation to exercise. However, none of them perceived unusual fatigue, palpitation, chest pain or any other unexpected symptoms at peak load, nor did they have any pathological ECG changes.

The mean values of all observed parameters in patients with PE considered as one group were within the limit of Z-score ± 2 SD. There were no observed significant differences in WRpeak, VO_2peak, VE, O_2Pulse and RER between the studied groups (Table 3). The mean %VO_2 at AT was achieved in both groups under physiological circumstances (within the limit of 40 %–60 % VO_2peak). Only two patients (both in the AI < 0.12 group) achieved AT with less than 40 % VO_2 (35.8 % and 39.6 %) but had WRpeak and VO_2peak within normal limits. There was no correlation between AI and WRpeak in the entire study population (r = 0.068, $p > 0.05$) as well as no correlation between AI and VO_2peak (r = -0.018, $p > 0.05$). Patients with less severe deformity had lower VE/VCO_2, and this measure was mildly correlated with severity of the deformity (r = 0.38, $p < 0.05$). Patients in the AI < 0.12 group had a higher BR at peak load and the BR was mildly negatively correlated with AI (r = -0.36, $p < 0.05$). There were weak correlations between the observed performance parameters and the AI in the patients with less severe PE (VO_2peak for the AI < 0.12 group: r = - 0.32). The same observation was true for O_2Pulse (r = -0.58) and VE (r = -0.64) in patients in the AI < 0.12 group, although the correlations were stronger. These observations, however, were only made in group of patients with less severe PE; they were not applicable to the patients with the more severe form of PE (Table 3), in which patients with more severe PE (higher AI) did not display worse performance results.

4. Discussion

The most objective method to measure exercise capacity is CPET, which measures peak oxygen consumption (Leclerc, 2017). Non-invasive examination methods without exposure to radiation are preferred in assessing the health status of paediatric patients (Jurko et al., 2016). PE is the most common deformity of the child's chest; it can have a major impact on the quality of life of the child not only by reducing physical condition, but also by the psychological effect that hinders their full development. Current therapeutic options are based on a quality functional assessment of the health condition of a patient with PE, on the basis of which surgeons decide on the suitability of a surgical or conservative procedure in the treatment of chest deformity. Static examination methods (imaging and functional) have long been used to monitor patients with PE. By their nature, these methods do not directly evaluate the functional capacities of the child's body, as their results correspond to resting capacities and do not reflect functional changes during exercise (both normal daily and peak) (Malek et al., 2006). Clinical evaluations aim to obtain clinically relevant data on patients related to their functional capacity using methodologies that do not evaluate the affected organ systems independently, but comprehensively, in the context of a real clinical burden (Jesenak et al., 2020). By analysing the exhaled air using continuous monitoring of the cardiovascular system under load, it is possible to evaluate the functional capacity of the cardiovascular, pulmonary and musculoskeletal systems in one session (Wasserman et al., 2011).

The relationship between deformity severity and performance parameters in patients with PE has most often been evaluated on the basis of the HI. Disadvantages of this method are the need for radiation exposure (CT), high cost and/or low availability (magnetic resonance imaging). To monitor noninvasively patients with PE who are not candidates for surgery, a proposal was submitted to assess the severity of PE, the so-called AI (Saxena, 2017). The use of an AI in the context of evaluating the functional capacity of a person with PE has not yet been published.

It is assumed that increased respiratory work arising from the partial restriction of chest movements in PE plays a role in limiting physical activity (Rowland and American College of Sports Medicine, 2017). According to Malek et al. (2006) sternal compression reduces the sternum volume, leading to a reduction in maximal oxygen consumption during exercise, exercise tolerance, tidal volume and vital capacity, all of which reduce body endurance and cause dyspnoea and compensatory tachypnoea during exercise. BR, expressed as a percentage of peak ventilation to maximum voluntary ventilation (VE/MVV), is a parameter evaluating the total respiratory reserve of the organism at the peak of exercise and in practice is used to discriminate patients with respiratory limitation (Kelly et al., 2008). In our study, we demonstrated a mild negative relationship between deformity severity and BR (r = - 0.36, $p < 0.05$).

Reduced oxygen supply to the working muscle as a consequence of reduced venous return to the right atrium also contributes to the reduced physical fitness of patients with PE (Jaroszewski, 2010). In patients whose right side of the heart is in contact with the sternum, a decrease in maximal O_2Pulse is expected as a result of limited right ventricular filling at maximal load (Rowland and American College of Sports Medicine, 2017). The relationship between the chest deformity and the position of the heart leads to a reduction in the stroke volume of the heart, severe deformities and a consequent decrease in cardiac output, which results in compensatory tachycardia and accelerated fatigue

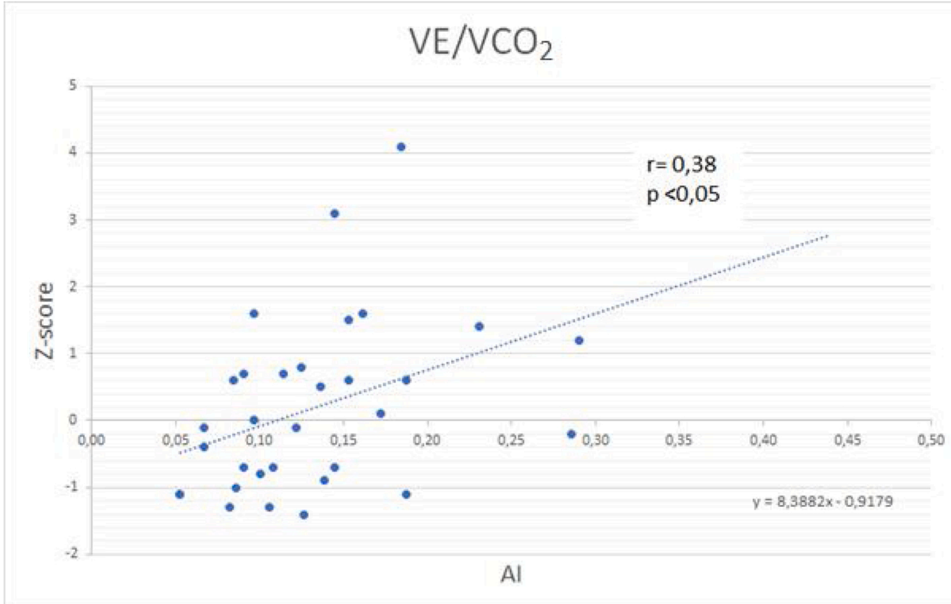

Fig. 1. Correlation of the ventilation efficiency (VE/VCO_2) with the severity of the deformity (based on the anthropometric index [AI]). The dotted line represents a linear regression of all data with a 30 % prediction.

(Guntheroth and Spiers, 2007). Oxygen consumption values (VO_2Max, VO_2Peak) may be significantly lower in patients with PE than the predicted values based on the patient's height and weight (Colombani, 2009). We confirmed the presence of cardiogenic limitation in four patients (two from each group) with low O_2Pulse and low VO_2max. Overall, however, we did not demonstrate lower mean values of O_2Pulse and VO_2max, nor did we confirm the correlation of the deformity severity expressed as the AI with those parameters. The peak heart rate (HRpeak) did correlate negatively with the severity of the deformity in the AI < 0.12 group ($r = -0.34$, $p > 0.05$). Once the AI reached the cut-off value of 0.12, the correlation was not apparent.

The VO_2/WR assessment can express the efficiency with which a person's muscles use the supplied oxygen (Wynn et al., 1990). In studies evaluating this parameter in patients with PE before and after surgery, the authors did not show that correction of deformity would lead to an improvement (increase) in this efficacy (Kelly et al., 2008; Quigley et al., 1996; Wynn et al., 1990). By correlating the severity of the deformity with VO_2/WR, we did not demonstrate the dependence of VO_2/WR on AI in the general PE population ($r = -0.03$, $p > 0.05$).

The VE/VCO_2 parameter (the steepness of its rise) is a parameter determining the efficiency of pulmonary perfusion, respiration and ventilation pairing and thus the efficiency of the entire process of ventilation (Takken et al., 2017). In patients with PE there have been no hypotheses regarding the effect of deformity on this parameter. In our study, we observed a lower VE/VCO_2 (slope) in patients with less severe deformity compared with patients with more severe deformity (Fig. 1) and confirmed a mild correlation with AI ($r = 0.38$, $p < 0.05$).

5. Conclusion

CPET is a valid, accessible, non-invasive and easily repeatable method of functional diagnostics that is applicable in childhood to determine the functional capacity of the subject and to detect the causes of reduced exercise tolerance. PE is a frequent deformity of the chest (especially in the male population) and the functional obstacles in the tolerance of physical exertion are frequently attributed to people with this deformity. Understanding the pathophysiological context in patients with PE should lead to the discovery of the real impact of the deformity on the overall health of the patient and should guide the decision on therapeutic interventions. According to our findings, the AI might be a suitable parameter to follow long-term aesthetic changes, but it does not correlate well with the functional parameters of the affected children.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Jessenius Medical Faculty in Martin, Commenius University, Bratislava, Slovakia. Written informed consent to participate in this study was provided by the patient's legal guardian or next to kin.

Author contributions

OF, SB, PD, MG, KT, MM and MD managed the patients and contributed to the conception of the study. OF, SB, AD and KT drafted the manuscript. All authors have read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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