Correlation of Anthropometric Index and Cardiopulmonary Exercise Testing Parameters in Patients with Pectus Excavatum

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Abstract

Introduction : Cardiopulmonary exercise testing (CPET) is a method used to diagnose and stratify patients with known disease. The use of breath-by-breath analysis of exhaled air in a stress test helps us to understand the root cause and pathophysiology of pathological patterns causing clinical symptomatology. Aim : Using CPET to elucidate the role of chest deformity on human physical abilities, to determine the correlation of the measured parameters with the anthropometric index (AI) evaluating the severity of the deformity in patients with pectus excavatum (PE). Methods : The study included 30 paediatric patients with PE. According to AI, patients were divided into two groups, to patients with AI below 0.12 and patients with AI 0.12 and more. Patients underwent CPET using a breath-by-breath exhaled gas analysis method and continuous monitoring of cardiac parameters. Ventilation and cardiac parameters were statistically processed, the severity of the deformity was correlated with the results using the Pearson index. Results : The severity of the deformity according to AI had no effect on peak ventilation, VO2peak and WRpeak. By graphical representation and prognosis of the data, we demonstrated the relationship between the severity of the deformity and the efficiency of ventilation, OUES and O2Pulse at the peak of the exercise. Ventilation efficiency expressed as the slope of the VE/VCO2 curve also had a graphically dependent trend without statistical significance. Conclusion : CPET data obtained suggest that physical fitness parameters in patients with PE have a correlation with the severity of the deformity expressed by AI. The OUES parameter is a promising parameter for assessing the overall physical fitness of these patients and a parameter with potential use in deciding on the appropriateness of a therapeutic intervention.

Key words : cardiopulmonary exercise testing, pectus excavatum, exercise tolerance

Correlation of Anthropometric Index and Cardiopulmonary Exercise Testing in Patients with Pectus Excavatum

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Ethics Statement

The studies involving human participants were reviewed and approved by the Ethics Committee of University hospital Martin. 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 managed the patients and contributed to the conception of the study. OF, SB, PB, AD drafted the manuscript. All authors have read and approved the final manuscript.

Conflict of 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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Abstract

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Aim : Using CPET to elucidate the role of chest deformity on human physical abilities, to determine the correlation of the measured parameters with the anthropometric index (AI) evaluating the severity of the deformity in patients with pectus excavatum (PE).

Methods : The study included 30 paediatric patients with PE. According to AI, patients were divided into two groups, to patients with AI below 0.12 and patients with AI 0.12 and more. Patients underwent CPET using a breath-by-breath exhaled gas analysis method and continuous monitoring of cardiac parameters. Ventilation and cardiac parameters were statistically processed, the severity of the deformity was correlated with the results using the Pearson index.

Results : The severity of the deformity according to AI had no effect on peak ventilation, VO2peak and WRpeak. By graphical representation and prognosis of the data, we demonstrated the relationship between the severity of the deformity and the efficiency of ventilation, OUES and O2Pulse at the peak of the exercise. Ventilation efficiency expressed as the slope of the VE/VCO2 curve also had a graphically dependent trend without statistical significance.

Conclusion : CPET data obtained suggest that physical fitness parameters in patients with PE have a correlation with the severity of the deformity expressed by AI. The OUES parameter is a promising parameter for assessing the overall physical fitness of these patients and a parameter with potential use in deciding on the appropriateness of a therapeutic intervention.

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Introduction

Cardiopulmonary exercise testing (CPET) is a method used to diagnose and stratify patients with known disease. The use of breath-after-breath analysis of exhaled air in a stress test helps us to understand the root cause and pathophysiology of pathological patterns causing clinical symptomatology. Pectus excavatum (PE) is a congenital deformity of the chest of unknown etiology, in which an abnormal formation of bone-cartilaginous joints of the ribs and sternum occurs, creating a concave depression of the chest wall [1]. Frequently present symptoms are lack of endurance, shortness of breath during exercise or chest pain [2]. Although pectus excavatum may be part of some less common syndromes, patients are usually healthy.

Examination of patients with PE should include a careful anatomical description, chest CT and determination of the so-called Haller index in case of planned surgical intervention, evaluation of the extent of cardiac compression, measurement of lung function and echocardiography in order to detect the presence of mitral valve prolapse (in 15%) or reduced right ventricular volume. Indications for surgical treatment include two or more of the following: severe symptomatic deformity; deformity progression; paradoxical chest movement when breathing; Haller index greater than 3.25; cardiac compression and / or pulmonary compression; finding a restrictive ventilation disorder; mitral valve prolapse, Tawar's shoulder block, or other cardiological pathology secondary to cardiac compression [3].

In order to non-invasively monitor patients with PE who are not indicated for surgery, a proposal was submitted to assess the severity of pectus excavatum, the so-called anthropometric index (AI). AI for PE is defined as the B measurement divided by the A measurement (AI = B/A)[4]. 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 was the largest depth at the same level [4]. A cut-off value for determining the severity of PE was determined to be 0.12 based on measurements and comparisons with the Haller index. Patients with a value greater than 0.12 are patients in whom, similar to Haller's index, surgery is indicated in the presence of the auxiliary criteria listed above[5].

Patients with PE may have various subjectively perceived symptoms. Symptoms often vary in severity and their effect on normal daily activities [6]. 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 highlighting of the growth spurt error or an increase in physical activity. The most common symptoms are dyspnoea during exercise and loss of endurance [6].

Anatomical abnormalities (decreased chest volume, heart compression) are a possible cause of the patient's subjective symptoms. The increased respiratory work arising from the partial restriction of chest movements in PE and the reduced oxygen supply to the working muscle as a consequence of the reduced venous return to the right atrium probably also play a role [7]. Compression of the sternum results in a reduced sternum volume, which leads to a reduction in maximal oxygen consumption during exercise, a reduction in exercise tolerance, a reduction in tidal volume, vital capacity, which reduces body endurance and causes dyspnoea and compensatory tachypnoea during exercise[9].

In addition to somatic problems, patients with PE often have psychological problems based on the perception of physical deformity. Exercise intolerance can also be a manifestation of somatization of psychologically escalating fear of physical activity, which could lead to the discovery of the body (showering, changing clothes) and also a manifestation of exercise, which is based on hypoactivity[10].

Stress test by CPET is a suitable examination to reveal the cause and pathophysiology of performance decline in patients with PE[7]. O2Pulse, VE (minute ventilation) and maximum oxygen consumption (VO2Max, VO2Peak) values may be significantly lower in patients with PE than predicted values for patient height and weight[7]. Lesbo et al. demonstrated in a sample of 49 adolescents, using the method of repeated breathing of inert gases, that PE significantly reduces exercise tolerance, has an effect on the values of maximum oxygen consumption and cardiac output [11]. The study by Rowland et al. confirmed the finding of impaired cardiac function in patients with PE using exercise echocardiography, where patients with PE had a significantly lower cardiac index compared to healthy controls [12]. The lower limit of the norm and subnormal values in the exercise examination suggest that the patient requires intervention (surgical, non-surgical). Postoperative measurement of CPET parameters in most cases of symptomatic patients reveals improvement or adjustment of cardiorespiratory parameters[13].

Methods

The study was done from December 2017 to December 2020 and included children aged 8-19 with a diagnosis of pectus excavatum. 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, JLF UK and UNM in Martin. The study included pediatric patients and adolescents with PE who were referred from the Pediatric Surgery Clinic and were candidates for conservative therapy (with vacuum bell) or the surgical treatment. Only patients who were without vacuum bell treatment at the time of testing and did not undergo corrective surgery were included in the cohort of the patients. Chest CT study with the determination of the Haller index was not required.

After basic examinations (12-lead ECG, spirometry), CPET on treadmill (RAM Clinical 870A, Belgium) was performed using the breath-by-breath analysis of exspired gas (Geratherm Respiratory, Germany). An individualized load protocol was used to achieve the maximum tolerated load between 8 and 12 minutes. 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 (tidal volum - Vt, minute ventilation - VE, breathing reserve - BR, breathing rate - BF, end-tidal CO2 - PETCO2, end-tidal O2PETO2), oxygen consumption parameters (O2Pulse, VO2), cardiovascular parameters (ECG, heart rate - HR), respiratory exchange ratio (RER) were recorded and then ventilation efficiency parameters (VE/VO2, VE/VCO2) and oxygen extraction efficiencies (VO2/WR, oxygen uptake efficacy slope - OUES) were calculated. All examinations were performed in the morning and the patients were instructed on the need for at least 24 hours of rest and sufficient hydration before the examination.

Analysis of the obtained data was performed in Systat 13 (Systat Software Inc.). Student's T-test was used to compare the equality of population averages (for parametric data). Pearson's test was 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 was expressed as x + 30% (where x is the maximum of the values obtained).

Results

Based on the severity of the deformity, the patients in our cohort were divided into two groups - a group of patients with PE with AI below 0.12 and a group of patients with PE with AI 0.12 and more. A total of 15 patients were enrolled in the below 0.12 group and the mean AI was 0.09 ± 0.02 and in the 0.12 and more group, 15 patients were enrolled, and the mean AI was 0.17 ± 0.05. No statistically significant differences were found in the observed height, weight, BMI and age. The basic characteristics of examined patients are displayed in Table 1.

The results obtained by protocol examination of patients with PE are summarized in Table 2. Patients with less severe deformity achieved AT at higher load, but the severity of deformity did not correlate with the level of this load or with VO2 at the time of achieving AT. The peak load was insignificantly higher in patients with milder deformity (4.35 vs 4.16 W / kg; $p > 0.05$). Peak oxygen consumption expressed as VO2peak/kg did not correlate with AI and no statistically significant changes were observed in the comparison groups (39.71 vs 40.07 ml / kg / min; $p > 0.05$) (Graph 1). O2Pulse was statistically insignificantly higher in patients with milder deformity (13.84 vs 12.88 ml/beat; $p > 0.05$). Ventilation efficiency was higher in patients with milder deformity (27.29 vs 29.78; $p > 0.05$) (Graph 2). No statistically significant differences in respiratory rate, tidal volume, respiratory reserve, and expiratory flow limitation were observed between patients based on the severity of the deformity. A weak correlation was observed between the severity of the deformity and the OUES parameter ($r = -0.33$; $p > 0.05$) (Graph 3).

Discussion

The most objective method to measure exercise capacity is cardiopulmonary exercise test which measures peak oxygen consumption[14]. Non-invasive examination methods without exposure to radiation exposure are the preferred options in assessing the health status of pediatric patients [15]. PE is the most common deformity of the child's chest, which 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 the full development of the child. 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 in the monitoring of patients with PE, which by their nature do not directly tell about 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)[9]. It is the effort of clinical workplaces to obtain clinically relevant data on patients related to the functional capacity of the organism using examination methodologies that do not evaluate the affected organ systems independently, but comprehensively, in the context of real clinical burden.

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 [16]. For such an assessment, it is necessary to know the physiology of these systems under load and the pathophysiological mechanisms that are the essence of clinical difficulties.

The relationship between deformity severity and performance parameters in patients with PE has so far been evaluated in published works most often on the basis of the Haller index, which, however, carries with it the need for radiation exposure (computed tomography) or high cost and low availability (magnetic resonance imaging). In order to non-invasively monitor patients with PE who are not indicated for surgery, a proposal was submitted to assess the severity of pectus excavatum, the so-called anthropometric index (AI) [5]. The use of an anthropometric index in the context of evaluating the functional capacity of an organism with PE has not yet been published. In our work, we evaluate the correlation of individual monitored parameters with the severity of chest deformity using the Pearson index.

It is assumed that increased respiratory work arising from the partial restriction of chest movements in PE appears to play a role in limiting physical activity [2]. This assumption should be supported by the finding of an increased maximum respiratory rate, a decreased tidal volume at peak load, and a high respiratory reserve. We did not show a dependence of the severity of the deformity on the maximum respiratory rate ($r = 0.05$). According to Malek et al. sternal compression results in a reduced sternum volume, leading to a reduction in maximal oxygen consumption during exercise, a reduction in exercise tolerance, a reduction in tidal volume, vital capacity, which reduces body endurance and causes dyspnoea and compensatory tachypnoea during exercise [9]. Comparison of tidal volume alone at the peak of load between individual groups is not possible due to the dependence of VT on anthropometric parameters of the patient. The ratio of tidal volume to FVC (Max VT/FVC) is comparable to each other. In this parameter, the severity of the deformity did not have a statistically demonstrable effect on Max VT/FVC, but the linear prognosis (taking into account all data) shows a declining trend and a direct dependence of the severity of the deformity on the maximum tidal volume Respiratory reserve (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 load limitation [9]. In our study, we did not demonstrate a relationship between deformity severity and BR ($r = -0.08$).

Reduced oxygen supply to the working muscle as a consequence of reduced venous return to the right atrium also contributes to reduced physical fitness of patients with PE [1]. In patients whose right side of the heart is in contact with the sternum, a decrease in maximal O2Pulse is expected as a result of limited right ventricular filling at maximal load [2]. The relationship of the chest deformity to the position of the heart leads to a reduction in the ejection volume of the heart and in severe deformities to a decrease in cardiac output, which results in compensatory tachycardia and consequently accelerated fatigue [17]. We did not demonstrate the relationship of O2Pulse to chest deformity ($r = -0.26$; $p > 0.05$), but the graph of linear dependence using the forecast shows a decreasing trend (graph 4). Maximum peak heart rate (HRpeak) did not correlate with the severity of the deformity ($r = 0.04$, $p > 0.05$) and thus we did not confirm the presence of compensatory tachycardia, which should compensate for insufficient cardiac output during exercise.

Oxygen consumption values (VO2Max, VO2Peak) may be significantly lower in patients with PE than the predicted values for patient height and weight [7]. However, other studies have provided conflicting information because in the study by Quigley et al. patients with PE had higher VO2peak scores than controls [18] but in a study by Wynn et al. these results were reversed[19]. Due to the discrepancy of these data, a meta-analysis of CPET data was performed in 2006, where cardiovascular and respiratory parameters before and after surgical correction of PE were evaluated. The finding of this study was that after the operation itself, in the period from 9 to 12 months after its operation, there was no significant increase in VO2 in the monitored patients[9]. As an explanation for this condition, it is stated that deformity alone would not lead to reduced aerobic capacity of the body and physical deconditioning of patients after surgery had a greater effect on VO2 than the limitations resulting from deformity[9,10]. By correlating the measured values of oxygen consumption, we did not show that the severity of the deformity correlates with the measured oxygen consumption ($r = -0.09$; $p > 0.05$) or with exercise tolerance ($r = -0.07$, $p > 0.05$). The VO2/WR assessment can express the efficiency with which the person's muscles use the supplied oxygen[20]. In studies evaluating this efficacy in patients with PE before and after surgery, they did not show that correction of deformity would lead to an improvement (increase) in this efficacy[10]. By correlating the severity of the deformity with VO2/WR, we did not demonstrate the dependence of VO2/WR on AI ($r = 0.20$; $p > 0.05$). The VE/VCO2 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 whole act of ventilation [21]. In patients with PE there has not been hypotheses of the effect of deformity on this parameter postulated. In our study, we observed a lower VE/VCO2 (slope) value in patients with less severe deformity compared to patients with more severe deformity (27.29 vs 29.78; $p > 0.05$).

A rather novel parameter that has not yet been evaluated in patients with PE is the oxygen uptake efficacy slope. Its use to evaluate the effectiveness of a patient's use of oxygen under increasing load was suggested in an electronic commentary on the evaluation of cardiorespiratory parameters before and after surgery in adult patients with PE [22.23]. The advantage of using this parameter is that it is independent of effort and motivation, easily reproducible and is obtained without the need for a maximum stress test (even without meeting the criteria for maximum test). The disadvantage is lack of standardized reference data both for children and in general for patients with non-cardiovascular diseases. In our work, we obtained the parameter by automatic recalculation of all submaximal data in the Bluecherry software (Geratherm Respiratory, Germany). In patients, we demonstrated a slight dependence of OUES on the severity of the deformity ($r = -0.33$; $p = 0.05$). Linear regression and the created trend line indicate a negative correlation of OUES with the severity of the deformity, which is an interesting observation, given that it may be a suitable parameter that indicates the body's overall ability to efficiently obtain and use oxygen from the atmosphere (Graph 3). Since the parameter is independent of the effort, it can be used in less cooperative or motivated patients.

Learning points:

- Patients with pectus excavatum showed no signs of direct cardiopulmonary impairment.
- Severity of the chest deformity expressed with anthropometric index does not statistically correlate well with cardiopulmonary exercise data (such as VO2, O2Pulse or VO2/WR) but graphically expressed relations show dependence and correlation.
- OUES is new perspective parameter showing negative correlation with deformity severity.

Conclusion

CPET is a valid, accessible, non-invasive and easily repeatable method of functional diagnostics, which is applicable in childhood to determine the functional capacity of the organism of the subject and to detect the causes of reduced exercise tolerance. Pectus excavatum 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 persons 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. When conducting future studies in patients with PE, it is appropriate to compare their CPET parameters with equally active healthy controls to distinguish changes that are attributable to deformity and those that are due to other physical activity. The appropriateness of using the OUES parameter to assess the relationship of deformity to physical condition and performance should be supported by other independent observations as well as observations in patients with PE with respect to normal weekly physical activity. In order to develop knowledge of the body's adaptation to stress and the impact of this adaptation on CPET parameters, it is necessary to evaluate in the future not only performance parameters but also regeneration parameters (e.g. pulse regeneration, respiratory regeneration) and also focus on new parameters such as respiratory patterns or the character of flow limitation.

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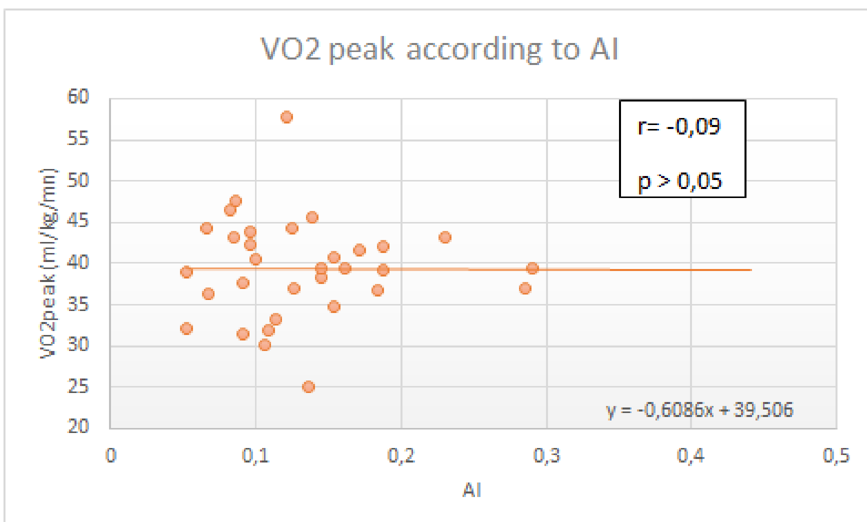

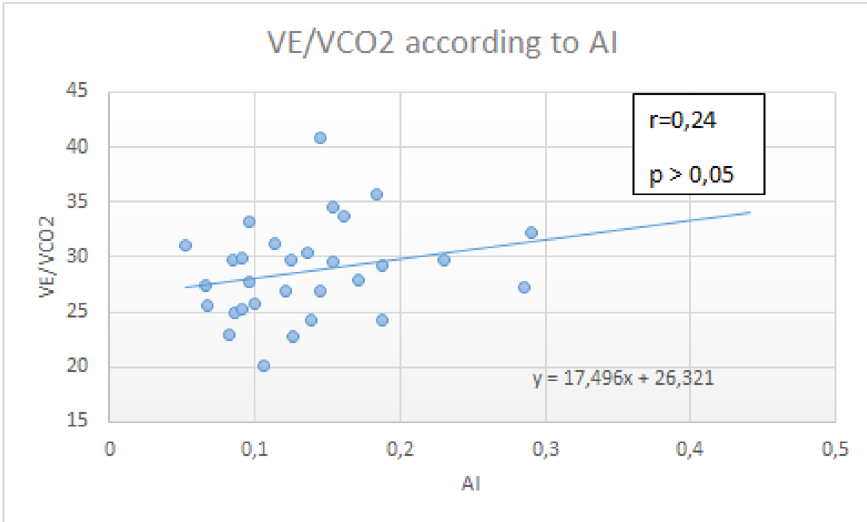
VE/VCO2 according to AI
r=0,24
p > 0,05
y = 17,496x + 26,321
VE/VCO2
AI
45
40
35
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20
15
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0,1
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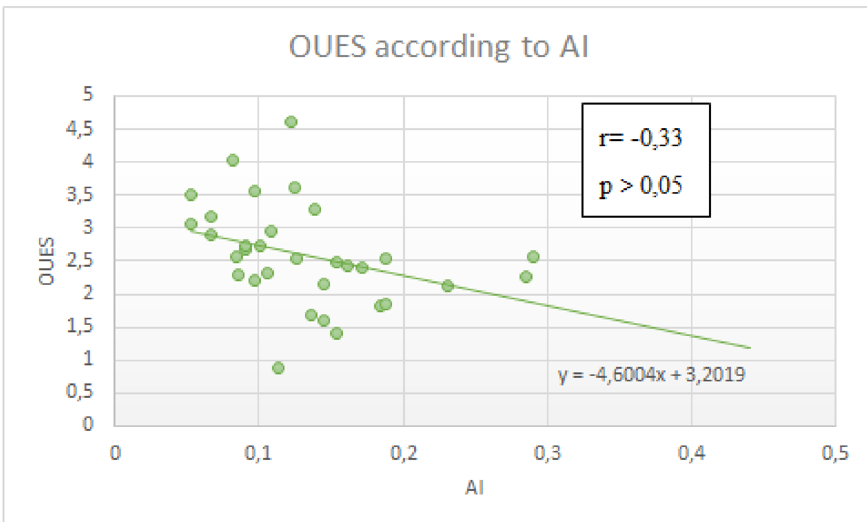
OUES according to AI
r= -0,33
p > 0,05
y = -4,6004x + 3,2019
OUES
AI
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4
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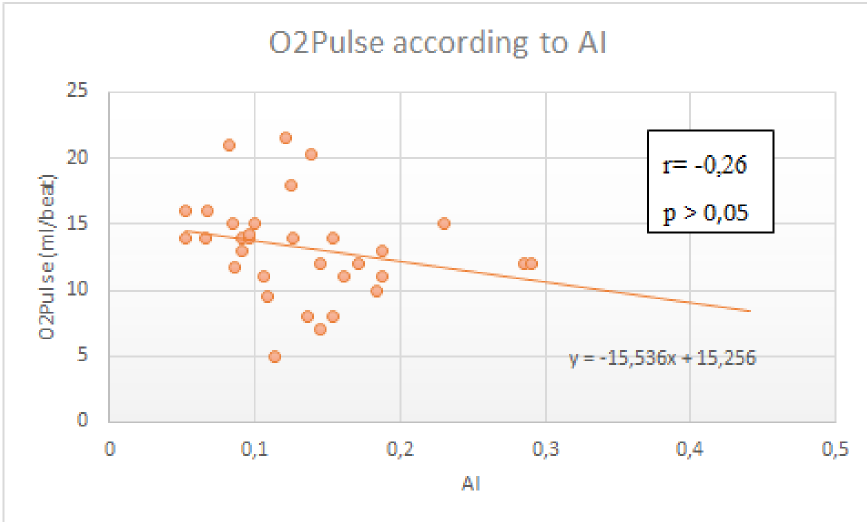
O2Pulse according to AI
r= -0,26
p > 0,05
y = -15,536x + 15,256
O2Pulse (ml/beat)
AI
0
5
10
15
20
25
0
0,1
0,2
0,3
0,4
0,5