

## Use of Volumetric Capnography in Submaximal Exercise Test: What Did We Learn?

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### Abstract

Tools that assess the response of the body to exercise activities have been sought in numerous clinical situations. Chronic obstructive pulmonary diseases such as cystic fibrosis (CF) may lead to reduction or limitation in exercise performance by ventilator factors. Consequently, a reduction in lung function can be observed, characterized by decreased respiratory reserve and dynamic hyperinflation during exercise. Various instruments have been developed and studied in the pediatric population in order to evaluate the functional capacity during exercise, being grouped into maximal tests and submaximal tests. The difference between maximal and submaximal tests depends on whether the test is performed in an open area or laboratory, with ergometers or not. In the maximal test, the individual performs the activity to achieve voluntary exhaustion, leading the participant to the fullest of their oxygen uptake and/or estimated (more than 90%) heart rate (HR). In the submaximal tests, the HR is located around 75% to 90% of the maximum estimated HR. In the study, we used a reproducible exercise test protocol in accordance with the pediatric age group. We used the VCap, as an evaluation feature for lung function in children and adolescents with CF and with various degrees of severity of lung disease. We have identified the inhomogeneity of distribution of ventilation in the peripheral airways of patients with normal spirometry. Our findings collaborate with the idea that the VCap is a respiratory assessment tool that is practical, inexpensive and easy to use. The VCap provides information on the pulmonary involvement by the indices and is considered an assessment tool of the degree of regional heterogeneity of the lung for gas exchange. Thus, the VCap is a tool that can be used for analysis of ventilatory efficiency during exercise, providing evidence that the cardiorespiratory response that can be measured non-invasively during exercise testing.

**Keywords:** Capnography; Cystic fibrosis; Exercise; Submaximal test

Physical exercise, including games and other modalities are essential for children and adolescents. These activities allow numerous and unquestioned benefits, maximizing physical, psychological and social development. Tools that assess the response of the body to exercise activities have been sought in numerous clinical situations [1].

Chronic obstructive pulmonary diseases such as cystic fibrosis (CF), asthma, and bronchiolitis obliterans may lead to reduction or limitation in exercise performance by ventilatory factors. Consequently, a reduction in lung function can be observed, characterized by decreased respiratory reserve and dynamic hyperinflation during exercise [1-4].

Various instruments have been developed and studied in the pediatric population in order to evaluate the functional capacity (physical and ventilation functional tests) during exercise, being grouped into maximal tests and submaximal tests. The difference between maximal and submaximal tests depends on whether the test is performed in an open area or laboratory, with ergometers (treadmill) or not. In the maximal test, the individual performs the activity to achieve voluntary exhaustion, leading the participant to the fullest of their oxygen uptake and/or estimated (more than 90%) heart rate (HR). In the submaximal tests, the HR is located around 75% to 90% of the maximum estimated HR [3,5].

The maximal test requires well-defined methodological conditions regarding aspects related to the health expert staff, physical space and adequate equipment, and materials and medications for use in an emergency. The responsible professional must have experience with the test and be able to act in emergencies, so the team must include a medical doctor [5].

Submaximal tests are essential for evaluating physical capacity and ventilator [2]. As activity of daily living (ADL) for children and adolescents is considered mostly sub-maximal, submaximal tests can be representative of the patient's clinical presentation in his routine. Several tests can be modified and reproduced for use in children and adolescents in order to improve the reproducibility and reliability. Among them are: (i) six-minute walk test (6MWT)—the cardiopulmonary test with better reproducibility, which evaluates the interaction between the systems: respiratory, cardiac and muscular; (ii) 3 minute step test, (iii) and recently, Glitre ADL test (T Glitre) [3,6].

In an article published by Parazzi and colleagues [2], we discussed the importance of submaximal exercise with the help of volumetric capnography (VCap) as a tool in the cardiorespiratory evaluation of CF. CF causes physical limitations for patients, minimizing the activities to achieve the maximum effort. The specific equipment for measuring gas exchange is expensive, and requires supervision and technical

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interpretation, and some equipment requires a large physical space. To work around these obstacles, we worked out a submaximal test based on the 6MWT using a treadmill for exercise, with the intention of measuring the gas exchange by VCap. The selected capnography is inexpensive and is easily accessible in hospitals and clinics compared to other equipment. The study confirms the importance of submaximal exercise as a tool for cardiorespiratory evaluation in a clinical setting in CF because CF patients may be unable or unwilling to make a maximum effort. Thus, submaximal exercise, associated with VCap becomes practical, inexpensive and easy to perform, and provides data on pulmonary involvement by indexes, and an evaluation tool for the degree of regional heterogeneity of the lung in relation to gas exchange.

Few studies used the VCap in CF [7-10]. To the best of our knowledge, it is the first and only study comparing the VCap and ventilatory efficacy before, during and after exercise in CF patients (CFG) and healthy subjects (HS). This study provided evidence that cardiorespiratory responses can be measured non-invasively during exercise testing in children, adolescents and young adults with CF [11]. The main objective of the study was achieved by showing the applicability of exercise as an assessment tool, identifying markers of an improvement or a worsening of lung function by VCap.

Among the most relevant results, we note: (i) the volume correlation of forced expiratory volume in one second ( $FEV_1$ ) with the exhaled carbon dioxide production ( $VCO_2$ )—higher  $FEV_1$  values were associated with higher  $CO_2V$  exhaled values during the exercise ( $p < 0.001$ ); (ii)  $VCO_2$ ,  $EV$ (exhaled volume) /  $CO_2V$  and  $PetCO_2$  showed differences between groups at all-time points analyzed, demonstrating that CFG retained  $CO_2$  when compared to HS ( $p < 0.001$ ); (iii) an increased respiratory rate (RR) ( $p \leq 0.001$ ) and HR ( $p \leq 0.001$ ) in CFG, and a decrease in peripheral oxygen saturation ( $SpO_2$ ) during the exercise ( $p \leq 0.001$ ) [2].

The CFG had a greater sensation of dyspnea in relation to HS, before and after exercise, on the Borg scale ( $p < 0.005$ ). We attribute this increase in cardiorespiratory variables in the CFG in relation to HSCG ( $p = 0.002$ ) to lung hyperinflation, which contributed to the increased work of breathing. This event requires the inspiratory muscle works at a mechanical disadvantage. During the exercise, there is an increase in oxygen demand to the muscles, with increased demand for the cardiovascular system [2].

It is known that CF causes progressive deterioration in the ability to perform aerobic exercise and to use oxygen [12]. The reasons for this include: impaired lung function, decreased nutritional status, reduced muscle strength, cardiac dysfunction, high level of inflammation lung and low habitual physical activity and low physical fitness. Therefore, it is important to use equipment and techniques to evaluate functional capacity in these patients, especially those using gas exchange [13,14].

Although there is some standardization in different countries regarding the implementation of tests that evaluate functional capacity, there is no consensus on a gold standard test to meet the needs of evaluating CF patients, at different ages and different degrees of disease severity. The exercise may be associated with adverse effects that can be detected during an exercise test, such as hypoxemia, hypercapnia and cardiac arrhythmias, which cannot be predicted from measurements at rest. Hypoxemia is induced by exercise and is generally limited to patients with  $FEV_1$  below 70% of the predicted level. Arrhythmias triggered by exercise may occur in individuals with preserved lung function. Because physical activity and regular exercise are recommended for CF patients, in most centers, it is prudent to

prescribe a submaximal exercise test in these patients and propose progressive physical conditioning under surveillance and monitoring of a team trained in physical exercise [14,15].

We have detected low fitness in our patients. This has enabled us to prescribe and encourage the practice of physical exercise, and to monitor ventilation and gas exchange, which can assess the aerobic capacity, and to know the factors limiting exercise tolerance in these patients. The test can allow us to monitor patients in the long-term, make comparisons between the reference centers in CF, qualitative and quantitative determination gases exhaled as was done by the VCap, and analyze large databases favoring the clinical records of patients. These procedures should be performed in this order: age, severity of lung function at the time of enrollment, and the *CFTR* genotype. Regarding the use of drugs such as beta-blockers prior to the test, we do not use them because we believe that patients who have used them may have an altered performance; this may lead to an improvement in the patient's performance and can lead to achieving maximum effort. Therefore, these patients were excluded from the previous study because they used the medication in 12 hours, considering that the drug has an influence on the environmental factors (treatment) in the evaluation result for the VCap.

In the study, we used a reproducible exercise test protocol in accordance with the pediatric age group. We used the VCap, first described by Ribeiro et al. [7] as an evaluation feature for lung function in children and adolescents with CF and with various degrees of severity of lung disease. We have identified the inhomogeneity of distribution of ventilation in the peripheral airways of patients with normal spirometry [7]. Our findings collaborate with the idea that the VCap is a respiratory assessment tool that is practical, inexpensive and easy to use. The VCap provides information on the pulmonary involvement by the indices and is considered an assessment tool of the degree of regional heterogeneity of the lung for gas exchange. Thus, the VCap is a tool that can be used for analysis of ventilatory efficiency during exercise, providing evidence that the cardiorespiratory response that can be measured non-invasively during exercise testing.

The continuation of the search for markers of cardiorespiratory changes is necessary, in cross and longitudinal mode, at rest, and during exercise, leading to a greater understanding and monitoring of the deterioration of lung function in CF patients and other lung diseases.

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