Relationship of obstructive sleep apnea with oxygen consumption, physical activity, and diet

Relação da apneia obstrutiva do sono com consumo de oxigênio, atividade física e alimentação

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ABSTRACT

Objective: To evaluate the maximum oxygen consumption (VO\textsubscript{2max}), physical activity level, food consumption and quality of life in patients with obstructive sleep apnea (OSA). Methods: Descriptive qualitative and quantitative study with cross-sectional analysis based on the application of structured questionnaires, carried out in a private clinic at Petrolina, PE, Brazil. Quality of life was assessed by the WHOQOL-bref, food consumption using the form of food consumption markers contained in the SISVAN Protocol, and the level of physical activity by the IPAQ short version. Results: Of the 16 included patients, 6 had no OSA, 4 had mild OSA, 2 had moderate OSA, and 4 had severe OSA. Sedentary lifestyle was prevalent in 20% of the patients with mild OSA, in 50% of those with moderate OSA and in 75% of those with severe OSA. Healthy food consumption prevailed in all groups, with a higher consumption of unhealthy foods in the severe OSA group. A predominance of regular quality of life was identified in all groups, especially needing to improve the physical domain of all of them. Both VO\textsubscript{2max} and the anaerobic threshold showed reduced values as the severity of the disease increased, with lower values in patients with the most severe form of the disease. Conclusion: An inverse relationship was found between more severe OSA with VO\textsubscript{2max} and the levels of physical activity of the patients analyzed. There is a greater consumption of unhealthy foods with poor diet and sedentary behavior that are important risk factors for the development and worsening of the disease.

Keywords: food consumption; exercise; quality of life; sleep obstructive apnea; sedentary behavior.

RESUMO

Objetivo: Avaliar o consumo máximo de oxigênio (VO\textsubscript{2max}), nível de atividade física, consumo alimentar e qualidade de vida em pacientes com apneia obstrutiva do sono (AOS). Métodos: Estudo descritivo qualitativo e quantitativo com análise transversal a partir da aplicação de questionários estruturados, realizado em uma clínica privada de Petrolina/PE. A qualidade de vida foi avaliada pelo WHOQOL-bref, o consumo alimentar pelo formulário de marcas do consumo alimentar que consta no Protocolo do SISVAN e o nível de atividade física pela versão curta do IPAQ. Resultados: Dos 16 pacientes incluídos, 6 não tinham AOS, 4 tinham AOS leves, 2 tinham AOS moderada e 4 tinham AOS graves. O sedentarismo foi prevalente em 20% dos pacientes com AOS leve, em 50% dos com AOS moderada e em 75% dos com AOS grave. O consumo alimentar saudável prevaleceu em todos os grupos, com maior consumo de alimentos não saudáveis por pacientes com AOS grave. Foram identificados predomínio de qualidade de vida regular em todos os grupos, precisando melhorar especialmente o domínio físico de todos eles. Tanto VO\textsubscript{2max} quanto o limiar anaeróbico apresentaram valores reduzidos à medida que a gravidade da doença aumentava, sendo menores os valores nas pacientes com a forma mais grave da doença. Conclusão: Houve constatação de relação inversa entre AOS mais grave com o VO\textsubscript{2max} e os níveis de atividade física dos pacientes analisados. Há um maior consumo de alimentos não saudáveis com má alimentação e comportamento sedentário que constituem importantes fatores de risco para o desenvolvimento e agravamento da doença.

Palavras-chave: consumo de alimentos; exercício físico; qualidade de vida; apneia obstrutiva do sono; comportamento sedentário.
Introduction

Obstructive sleep apnea (OSA) is characterized by repeated upper airway obstructions [1,2]. This disorder is highly prevalent and has a considerable influence on the morbidity and mortality of the Brazilian population [2,3]. OSA may be associated with the development of type II diabetes mellitus [2]. It is also a risk factor for systemic arterial hypertension, stroke, depression, insomnia, anxiety, and cardiovascular diseases [1,3]. Besides, it is known that the drowsiness characteristic of this disorder is the cause of many traffic and work accidents [1].

Advancing age is the principal risk factor associated with OSA [4]. Also, sleep disorders are correlated with decreased fiber intake, increased carbohydrate intake, and increased fat consumption [5]. Obese patients are more likely to have a positive OSA diagnosis, mainly due to the increased fat deposition in the neck region. This increases the circumference of the cervical region and makes the upper airways narrower, which leads to collapse during sleep [6].

The diagnosis and severity of OSA are assessed using the apnea-hypopnea index (AHI) using polysomnography. AHI is calculated by dividing the total number of apneas and hypopneas by the number of hours of sleep. AHI is considered normal when less than 5 events per hour occur, mild OSA between 5 and 14 events/hour, moderate OSA between 15 and 29 events/hour, and severe OSA ≥ 30 events/hour [7,8].

As a result of insomnia (morning headache, increased drowsiness, and fatigue) caused by recurrent sleepless nights, patients with OSA tend to have multifactorial changes in functional capacity, maximum oxygen consumption (VO_{2max}), and in their activities of daily living (ADLS) [9]. This favors an increased risk for the onset of diseases and chronic conditions such as diabetes, obesity, cardiovascular disease, and depression [10].

This work is justified by the gaps concerning the study of OSA, mainly about data from populations in the interior of the Brazilian Northeast. Thus, this study aims to describe VO_{2max}, level of physical activity, food consumption, and quality of life in patients with OSA in the Vale do São Francisco region.

Methods

Study design

It is a qualitative and quantitative analytical study using mixed methods of investigation through the retrospective description of secondary data, obtained through the medical records of the patients included in the study and cross-sectional analysis using structured questionnaires. The research was approved by the Research Ethics Committee of the Federal University of Vale do São Francisco (UNIVASF), with a certificate of presentation for ethical appreciation (CAAE) number 65947617.2.0000.5196.
Scenario
The study was carried out between July 2015 and November 2017 in a private clinic at Petrolina, PE, Brazil. Participants were invited to the place where the study was carried out, where the informed consent form (ICF) was read in conjunction with the researchers, and the questionnaires were properly applied. At another time, data was collected from the medical records of patients who adhered to the study.

Inclusion and exclusion criteria
The study included patients who underwent polysomnography exams with ApneaLink (Resmed, Sydney, Australia) and ergospirometry, using Ergostik (Geratech, Bad Kissingen, Germany), during the period analyzed at the clinic. Patients with medical records who presented incomplete data and those who did not have a polysomnography report were excluded.

Data collection
Data collection took place through the sample of patients at risk for OSA who underwent polysomnography. This population was divided into groups according to the AHI: Normal (≤ 5 events/hour), Mild (5-14 events/hour), Moderate (15-29 events/hour), and Severe (≥ 30 events/hour), which will serve as a basis for correlations with secondary data [7,8].

Thus, the application of questionnaires to analyze the quality of life (QoL), physical activity level (PAL), and food consumption was performed with patients who underwent the cardiopulmonary stress test (CPET) within the diagnosed population. The parameters analyzed in CPET were VO2max and the anaerobic threshold (AT). The sample that composed this study was obtained for convenience.

Quality of life assessment
QoL was assessed using the World Health Organization Quality of Life Instrument Bref questionnaire (WHOQOL-bref) translated and validated by the World Health Organization (WHO) in Brazil, being considered an instrument that is easy to apply and understand for the adult population. The WHOQOL-bref is the short version of the WHOQOL 100 and consists of 26 questions. Two questions are about the general quality of life, and 24 represent each of the 24 facets that make up the original instrument. This instrument consists of four domains of quality of life. Each of them aims to analyze, respectively, physical capacity, psychological well-being, social relationships, and the environment where the individual is inserted and is also composed of a domain that investigates the global quality of life. Each field is composed of questions, whose response scores vary between 1 and 5. The final scores for each domain are calculated using a syntax, which considers the answers for each question that makes up the domain, resulting in final scores on a scale of 1 to 5. Depending on the score, the QoL of the population can be classified into four categories: needs improvement (1 to 2.9), regular (3 to 3.9), good (4 to 4.9), or very good (5) [11].
**Physical activity level assessment**

The PAL evaluation was performed using the International Physical Activity Questionnaire (IPAQ) in its short version, translated and validated for Brazil [12]. Its questions are related to the time spent by the subject performing physical activities in the last week, including the activities he did at his workplace, to go from one place to another, for leisure and sports. The analysis of the results is performed following the criteria of frequency, duration, and intensity, classifying the individual as active, insufficiently active, or sedentary. An individual is considered active if they reach the following criteria: a) vigorous physical activity with a frequency equal to or greater than three days per week with a duration equal to or greater than 20 minutes per session; b) moderate physical activity or walking with a frequency equal to or greater than five days/week and duration equal to or greater than 30 minutes/session; c) any physical activity whose added frequency is equal to or greater than five days/week and with a duration equal to or greater than 150 minutes/week. The subjects who did not reach the criteria were classified as insufficiently active or sedentary according to the IPAQ standardization [12].

**Food consumption assessment**

For the assessment of food consumption, the form of food consumption markers for individuals older than five years of age was used, which appears in the Protocol of the Food and Nutrition Surveillance System (SISVAN). This instrument seeks to portray the usual food intake, which is a type of retrospective record of the frequency of consumption of some foods and drinks in the last seven days of the evaluation. The instrument is related both to a healthy diet (for example, daily consumption of beans, fruits, and vegetables) and to practices that are not recommended (frequent consumption of fried foods and sweets, for instance) [13]. This form aims to identify the dietary pattern of the individual broadly, not intending to quantify the diet in terms of calories and nutrients, but rather to indicate the quality of the food in its positive and negative characteristics [14].

**Statistical analysis**

Statistical analysis was performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA, Release 16.0.2, 2008). The normality and homoscedasticity of the data were verified using a histogram following Bartlett’s criteria. Continuous variables are presented as mean ± standard deviation, while categorical variables are presented using absolute and relative frequencies. One-way analysis of variance (ANOVA) was used to compare the results obtained between the groups studied. All analyzes performed were two-tailed, with the exact values of P calculated at a significance level of 5%.
Results

Of the 446 individuals who underwent polysomnography from July 2015 to November 2017, 58 underwent CPET. Of these, 42 were excluded after applying the exclusion criteria. The total sample of this study consisted of 16 individuals, of which 25% (n = 4) of the patients had severe OSA, 12.5% (n = 2) moderate OSA, 25% (n = 4) mild OSA and 37.5% (n = 6) normal results (without OSA). Table I presents the general characterization of the sample.

Table I - Sample characterization

<table>
<thead>
<tr>
<th>Variables</th>
<th>without OSA (n = 6)</th>
<th>Mild OSA (n = 4)</th>
<th>Moderate OSA (n = 2)</th>
<th>Severe OSA (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AH1 (events/hour)</td>
<td>1.83 ± 1.32</td>
<td>8.5 ± 3</td>
<td>19.5 ± 4.94</td>
<td>43 ± 9.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.83 ± 11.17</td>
<td>54 ± 11.97</td>
<td>55.5 ± 4.94</td>
<td>59.66 ± 12.09</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.46 ± 5.60</td>
<td>31.8 ± 1.85</td>
<td>34.15 ± 2.05</td>
<td>34.1 ± 3.66</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>05 (83%)</td>
<td>03 (75%)</td>
<td>1 (50%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Male</td>
<td>01 (17%)</td>
<td>01 (15%)</td>
<td>1 (50%)</td>
<td>2 (50%)</td>
</tr>
</tbody>
</table>

AH1 = apnea-hypopnea index; BMI = body mass index

Table II shows the average values of VO₂max and AT, relative to the total body mass of each individual, stratified according to the severity of the disease. The analysis of the ergospirometric data showed that the average VO₂max of the group without OSA was 19.9 ml/kg/min, this average being reduced as the disease severity increased. The same happened with the AT, which presented an average value of 12.2 ml/kg/min in the group without OSA and was lower in patients who had the most severe forms of the disease.

Table II - Mean value of VO₂max and AT

<table>
<thead>
<tr>
<th>Variables</th>
<th>without OSA (n = 6)</th>
<th>Mild OSA (n = 4)</th>
<th>Moderate OSA (n = 2)</th>
<th>Severe OSA (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂max (ml/kg/min)</td>
<td>19.86 ± 6.72</td>
<td>17.58 ± 9.21</td>
<td>17.93 ± 6.34</td>
<td>12.16 ± 7.66</td>
</tr>
<tr>
<td>AT (ml/kg/min)</td>
<td>12.23 ± 3.42</td>
<td>13.34 ± 8.11</td>
<td>8.17 ± 2.29</td>
<td>7.03 ± 5.74</td>
</tr>
</tbody>
</table>

VO₂max = maximum oxygen consumption; AT: anaerobic threshold

The data related to PAL are shown in table III, showing sedentary behavior that is more prevalent in groups with moderate and severe OSA.

Table III - Classification of physical activity level

<table>
<thead>
<tr>
<th>Classification</th>
<th>without OSA (n = 6)</th>
<th>Mild OSA (n = 4)</th>
<th>Moderate OSA (n = 2)</th>
<th>Severe OSA (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active, n (%)</td>
<td>0 (0%)</td>
<td>1 (20%)</td>
<td>1 (50%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Insufficiently active, n (%)</td>
<td>5 (80%)</td>
<td>2 (60%)</td>
<td>0 (0%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Sedentary, n (%)</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>1 (50%)</td>
<td>3 (75%)</td>
</tr>
</tbody>
</table>
The analysis of the QoL domains is described in table IV, in which in general is observed a worsening of QoL as the severity of OSA increases.

**Tabela IV - Classification of the level of quality of life**

<table>
<thead>
<tr>
<th>Domains of quality of life</th>
<th>without OSA (n = 6)</th>
<th>Mild OSA (n = 4)</th>
<th>Moderate OSA (n = 2)</th>
<th>Severe OSA (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical capacity</td>
<td>VG = 1</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 1</td>
</tr>
<tr>
<td>G = 1</td>
<td>G = 1</td>
<td>G = 0</td>
<td>G = 1</td>
<td></td>
</tr>
<tr>
<td>R = 3</td>
<td>R = 1</td>
<td>R = 2</td>
<td>R = 0</td>
<td></td>
</tr>
<tr>
<td>NI = 1</td>
<td>NI = 2</td>
<td>NI = 0</td>
<td>NI = 2</td>
<td></td>
</tr>
<tr>
<td>Psychological well-being</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 0</td>
</tr>
<tr>
<td>G = 1</td>
<td>G = 1</td>
<td>G = 0</td>
<td>G = 2</td>
<td></td>
</tr>
<tr>
<td>R = 5</td>
<td>R = 3</td>
<td>R = 2</td>
<td>R = 1</td>
<td></td>
</tr>
<tr>
<td>NI = 0</td>
<td>NI = 0</td>
<td>NI = 0</td>
<td>NI = 1</td>
<td></td>
</tr>
<tr>
<td>Social relationships</td>
<td>VG = 1</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 0</td>
</tr>
<tr>
<td>G = 3</td>
<td>G = 1</td>
<td>G = 2</td>
<td>G = 2</td>
<td></td>
</tr>
<tr>
<td>R = 2</td>
<td>R = 3</td>
<td>R = 0</td>
<td>R = 2</td>
<td></td>
</tr>
<tr>
<td>NI = 0</td>
<td>NI = 0</td>
<td>NI = 0</td>
<td>NI = 0</td>
<td></td>
</tr>
<tr>
<td>Environment</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 0</td>
<td>VG = 0</td>
</tr>
<tr>
<td>G = 3</td>
<td>G = 0</td>
<td>G = 0</td>
<td>G = 1</td>
<td></td>
</tr>
<tr>
<td>R = 2</td>
<td>R = 3</td>
<td>R = 2</td>
<td>R = 2</td>
<td></td>
</tr>
<tr>
<td>NI = 1</td>
<td>NI = 1</td>
<td>NI = 0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VG = Very good; G = Good; R = Regular; NI = Needs improvement

The results regarding the analysis of the consumption of foods considered healthy or not are shown in Graph 1. The group without OSA showed higher consumption of healthy foods when compared to the other groups.

**Graph 1 - Frequency of eating healthy and unhealthy foods**
Discussion

It was observed in the present study that patients with a higher level of OSA severity have lower VO\(_{2\text{max}}\) when compared to the reference group (without OSA), in the same way that these patients also present a higher frequency of sedentary behavior and lower values of individual AT.

The results found can be explained for several reasons. Initially, the lower VO\(_{2\text{max}}\) in the groups with OSA is possibly due to the decline in lung volume, which can decrease tracheal traction forces [15]. Besides, the low PAL of patients with OSA can also contribute to the reduced values of VO\(_{2\text{max}}\) [16]. Low PAL is associated with a higher degree of obesity that provides the accumulation of fat in the cervical region and narrows the upper airways, worsening OSA [15]. Therefore, the reduced values of the AT in the groups with OSA are explained both by the reduced PAL itself and by the cardiovascular comorbidities of these patients, mainly heart failure [17]. The low PAL observed in groups with OSA is mainly due to obesity and the low quality of sleep that causes daytime sleepiness [1,15].

It has also been described, in the literature, that individuals with reduced VO\(_{2\text{max}}\) tend to have less physical and functional capacity [1,3,17]. This will directly impact the ADLs of these individuals, as VO\(_{2\text{max}}\) is an indicator of cardiorespiratory resistance capacity and an important predictive parameter of morbidities associated with OSA, such as heart failure, stroke, among others that have been reported in similar studies [18]. Lin et al. [18] analyzed, in a case-control study using CPET, 20 overweight patients who had OSA and found that VO\(_{2\text{max}}\) and performance during the test were significantly lower (P < 0.05) in individuals who had OSA (21.6 ml/kg/min) compared to the control group (30.2 ml/kg/min).

However, the evidence in the literature has shown conflicting results. More recent studies have not shown a significant difference in VO\(_{2\text{max}}\) in patients with and without OSA. Fernandez et al. [19] in a randomized clinical trial that included 46 obese patients, 31 with OSA (mean AHI of 43.6 events/hour) and 15 who did not have the disease, found no difference in VO\(_{2\text{peak}}\) of the groups with OSA (25.0 ml/kg/min) and without OSA (25.3 ml/kg/min), as well as there was no difference in AT (56.5 l/min vs. 56.1 l/min, respectively). In short, it is not clear whether obesity or OSA can decrease individuals’ maximum oxygen consumption. Current findings suggest that OSA does not impair individuals’ functional capacity in terms of VO\(_{2\text{max}}\) values.

Regarding the level of physical activity analyzed using the IPAQ, it was seen that only 12.5% of patients in the entire sample were considered active and 75% of patients with severe OSA were considered sedentary, which corroborates the findings regarding the VO\(_{2\text{max}}\) of this study, since individuals in the severe OSA group, in addition to having a low PAL, also obtained reduced values of VO\(_{2\text{max}}\). In this sense, PAL demonstrates its importance as a VO\(_{2\text{max}}\) prediction parameter. The less active the individual is, the lower their VO\(_{2\text{max}}\) values tend to be [16,20]. These results are in line with other studies that claim that sedentary and obese individuals have a greater
propensity for a positive diagnosis of the disease, with physical inactivity constituting one of the main risk factors for its development, with physical exercise being a fundamental integral in the treatment of OSA. Physical exercise has a range of varieties and can be practiced even by diabetic individuals [21].

Aiello et al. [22], in a meta-analysis, found that physical exercise was effective both in improving OSA and in reducing the severity of the disease. However, the mechanisms that lead to physical exercise to reduce the disease symptoms are still not well understood. However, it is known that physical activity modulates the secretion of a series of fundamental cytokines for body homeostasis [23]. Iftikhar et al. [24] demonstrated that the effects of physical exercise on sleep apnea are independent of a reduction in BMI and body weight.

When analyzing the domains of the QoL questionnaire of patients who presented OSA, a greater predominance of regular QoL is found. Improvements are needed, especially in the physical domain, which includes questions related to pain and discomfort, energy and fatigue, sleep and rest, mobility, activities of daily living, dependence on medication or medical treatment, and work capacity. In the present study, patients with OSA had lower scores when compared to patients without OSA in this domain. This fact has as aggravating factor a low PAL in this population, a situation that possibly impacted on the functional capacity of these individuals, as well as may have been responsible for the reduction in performance during the performance of ADLs and that certainly contributed to the decrease in the QoL of this group. Yosunkaya et al. [25] analyzed the QoL of 200 patients with suspected OSA and found that overall health, life satisfaction, energy, and vitality in those diagnosed with OSA were worse than those whose diagnosis was negative. According to the authors, these factors are related to a reduction in the quantity and quality of sleep during the night, mainly in the period of a deep sleep, due to the frequent interruptions caused by OSA.

In the sample of this study, it was also observed that the impairment of QoL was not proportional to the severity of OSA, since patients with mild OSA reported the same or greater impairment in some domains of the WHOQOL-bref than those who had the most severe form of the disease. This corroborates some studies described in the literature, such as that of D’Ambrosio et al. [26], in which the QoL of 29 patients with OSA was assessed and identified that the disease had an impact on the QoL of individuals in several ways. However, some of these patients with mild OSA reported the same degree of impairment in the QoL domains, as those with severe OSA, with no association, as in this study, between the decrease in QoL scores and the severity of the disease.

When dealing with the eating habits of the population studied, there was a higher prevalence in all groups of consumption of foods considered healthy when compared to unhealthy ones. However, the group that presented the most severe form of the disease consumed less healthy foods (49%) when compared to the group without OSA (78%), a factor that directly contributes to the pathophysiology of OSA. Since the increase in the consumption of processed foods, which contains a high
caloric density, associated with physical inactivity are predisposing factors for the development of obesity, hypertension, and, consequently, OSA due to the increased distribution of fat in the body and increased deposition of fat in the neck area. Trakada et al. [27], in a recent study, through the evaluation of 19 patients with OSA, demonstrated that apneas increased significantly on the second night after eating a high-fat diet. Besides, recent studies such as Smith et al. [28] demonstrated that sleep restriction and interruption can increase ghrelin levels and reduce leptin, hormones responsible for regulating appetite and satiety. Thus, individuals with OSA have an increased appetite and a greater propensity to consume food with high-fat content. These aspects are associated with the fact that individuals with OSA stay more awake provide more time for eating at night. This will possibly contribute to the increase in obesity and, consequently, the severity of the disease. It is necessary to adopt a healthy lifestyle with a diet rich in nutrients in this population so that together with the association of physical activities, disease control is carried out, a fact that has a direct impact on the health and well-being of these individuals [28].

In this study, we consider the small sample size as the main limitation, mainly due to the small number of patients who underwent CPET. Therefore, the sample size did not allow the identification of statistically significant differences between the groups. Still, the results suggest that OSA leads to changes in VO$_{2\text{max}}$, PAL, QoL, and food consumption of these individuals. Given this, the present study will continue following to adapt to this limitation and, possibly, improve comparisons and results of the work.

**Conclusion**

According to the results found, we suggest the existence of an inverse relationship between the most severe levels of obstructive sleep apnea (moderate and severe) with the maximum oxygen consumption and with the levels of physical activity. Higher consumption of unhealthy foods, showing poor diet, and sedentary behavior are important risk factors for the development and worsening of obstructive sleep apnea.

**Conflict of interest**
No conflicts of interest have been reported for this article.

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Conception and design of the research: Brito EZA, Fernandes DSS, Schwingel PA, Mesquita FOS. Data collection: Brito EZA, Guimarães MP, Fernandes DSS, Neves VR, Gambassi BB, Schwingel PA, Mesquita FOS. Analysis and interpretation of data: Brito EZA, Guimarães MP, Fernandes DSS, Neves VR, Gambassi BB, Schwingel PA, Mesquita FOS. Statistical analysis: Schwingel PA. Writing of the manuscript: Brito EZA, Guimarães MP, Fernandes DSS, Neves VR, Gambassi BB, Schwingel PA, Mesquita FOS. Critical revision of the manuscript for important intellectual content: Neves VR, Gambassi BB, Schwingel PA, Mesquita FOS.

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