Acute effects of air stacking maneuver and posture on cardiac autonomic function in patients with spinal muscular atrophy types II and III

Efeitos agudos da manobra de empilhamento de ar e postura na função autonômica cardíaca em pacientes com atrofia muscular espinhal tipos II e III

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Abstract

Background: Respiratory dysfunction is the major cause of morbidity and mortality in patients with spinal muscular atrophy. Air stacking is a clearance airway technique frequently used but its effects on cardiac autonomic function in patients with spinal muscle atrophy is not clear. Objective: To evaluate the acute effect of air stacking and posture on cardiac autonomic function in patients with spinal muscular atrophy types II and III. Methods: Nine patients with spinal muscle atrophy type II and III were recruited. Electrocardiogram signals were recorded for analyses of heart rate variability during air stacking in supine and sitting position. Data were collected before, during and after air stacking and were compared using Anova Repeated Measures or Kruskal-Wallis Anova on Ranks, followed by Tukey test. The relationship between heart rate variability indexes and age was evaluated by Pearson correlation. Significant level was set at 5%. Results: During air stacking, STDRR, LF and SD2 significantly increased in supine and sitting positions. In supine, air stacking significantly reduced LF and increased both LF/HF and SD2. In sitting position, RMSSD and SD1 were significantly lower reduced in pre period and air stacking led to significant increase in STDHR and RMSSD. MeanRR and Mean HR correlated with age in sitting position. MeanRR was significantly lower and MeanHR was significantly higher in both positions in all moments. Conclusion: Patients with spinal muscle atrophy types II and III present alterations on heart rate variability during postural change and air stacking maneuver is suggestive of cardiac autonomic control integrity.

Keywords: Spinal muscular atrophy; Physical therapy modalities; Air stacking; Autonomic nervous system.

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Resumo

Introdução: A disfunção respiratória é a maior causa de morbidade e mortalidade em pacientes com atrofia muscular espinal. O empilhamento de ar (air stacking) é uma técnica de higiene brônquica frequentemente utilizada, no entanto, seus efeitos na função autonômica cardíaca de pacientes com atrofia muscular espinal não são claros. Objetivo: Avaliar o efeito agudo da manobra de empilhamento de ar e de posturas na função autonômica cardíaca em pacientes com atrofia muscular espinal tipos II e III. Métodos: Nove pacientes com atrofia muscular espinal tipos II e III foram recrutados. Sinais de eletrocardiograma foram registrados para as análises da variabilidade da frequência cardíaca durante a manobra de empilhamento de ar nas posições supina e sentado. Os dados foram coletados antes, durante e após a manobra de empilhamento de ar e foram comparados utilizando o teste de Anova de Medidas Repetidas ou Kruskal-Wallis Anova on Ranks, com o respectivo teste de Tukey. A relação entre os índices da variabilidade da frequência cardíaca e idade foram analisados por meio do coeficiente de correlação de Pearson. A significância estatística foi determinada em 5%. Resultados: Durante a manobra de empilhamento de ar, STDrr, LF e SD2 aumentaram significativamente na posição supina e sentada. Na posição supina, a manobra de empilhamento de ar reduziu significantemente LF e aumentou o LF/HF e o SD2. Na posição sentada, RMSSD e SD1 foram significativamente menores no período pré, e a manobra de empilhamento de ar aumentou significativamente o STDHR e o RMSSD. MeanRR e MeanHR correlacionaram com a idade na posição sentada. MeanRR foi significativamente menor e MeanHR foi significativamente maior nas duas posições em todos os momentos. Conclusão: Pacientes com atrofia muscular espinal tipos II e III apresentam alterações na variabilidade da frequência cardíaca durante as mudanças de postura e a manobra de empilhamento de ar, o que é sugestivo de integridade do controle autonômico cardíaco.

Palavras-chave: Atrofia muscular espinal; Modalidades de fisioterapia; Empilhamento de ar; sistema nervoso autônomo.

Introduction

Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disorder characterized by progressive muscular weakness and atrophy secondary to degeneration of spinal cord and bulbar (in the most severely affected patients) motor neurons. SMA is the most common genetic cause of infant mortality after cystic fibrosis (1-4) with an estimated incidence of 1:6,000 to 1:10,000 live births (2).

Respiratory dysfunction is the major cause of morbidity and mortality in patients with SMA type I and II and may occur in small proportion in SMA type III (1-4). Forced vital capacity (FVC) and sniff nasal inspiratory pressure (SNIP) are important respiratory parameters which showed lower values at younger age in patients with SMA type 2 when compared to patients with SMA type 3. However, the rate of decline of FVC and SNIP could be comparable between type 2 and type 3 SMA (4). Additionally, these patients present higher adiposity and lower chest wall expansion (5). Because of the severity of muscle weakness these patients present reduced cough peak flow (CPF) and limited capacities to remove secretion of lower airways. SMA patients need to be treated with airway clearance methods such as manual assisted cough (air stacking to approach maximum insufflation capacity associated to an expiratory-timed abdominal thrust) and mechanical insufflator/exsufflator device (6).

In addition to deconditioning and the common occurrence of right ventricular hypertension to maintain lung ventilation, neurologic disorders can also affect the heart’s electrical system in patients with SMA. A growing number of SMA case studies suggested that both cardiac and autonomic complications might either be associated with SMA or be uncovered, as patient survival is extended by improved medical intervention (7-9).
The ANS influences cardiovascular variables such as blood pressure, peripheral vascular resistance and cardiac output, and thus great attention has been directed to spontaneous fluctuations in heart rate, generically called heart rate variability (HRV) (10). From HRV analysis, it is possible to obtain indirect information about disorders of the autonomic cardiac modulation (11). Alterations in HRV patterns provide a sensitive and anticipated indicator of health conditions, since the reduction of HRV is considered a risk factor for global mortality and arrhythmic events (12).

The effects of air stacking maneuver on cardiac autonomic control in patients with SMA are unknown, thus the aim of this study was to evaluate the acute effect of air stacking and posture on cardiac autonomic function in patients with spinal muscular atrophy types II and III.

Materials and Methods

Patients

Nine patients, aged between 6 and 22 years, with clinical diagnosis of SMA types II and III confirmed by laboratory exam were prospectively recruited in Martagão Gesteira Institute of Child Care and Pediatrics (IPPMG) at the Rio de Janeiro Federal University from April to October 2011. This study protocol was approved by the Research Ethics Committee of Augusto Motta University Center (27/2011-CAAE: 0028.0.307.000-11) and written informed consent was obtained from all participants’ parents before the admission in this study. Once air-stacking maneuver is commonly used in these patients, there are no additional risks related to this technique and this study can give some information regarding the safety of this method related to cardiac function.

Inclusion criteria for participation in the study protocol were done according to the following criteria: diagnosis of SMA types II and III, absence of acute respiratory disease in the last two weeks, agreement to participate in the study, according to the written informed consent and at least 5 years old.

Experimental Protocol and Measurements

This observational study was developed for evaluation and comparison of HRV during the air stacking maneuver in type II and III SMA patients in both supine and sitting position. Data acquisition and analysis were carried out in the Laboratory of Cardiovascular and Respiratory Systems Analysis of Augusto Motta University Center – RJ – Brazil. All data were collected and analyzed by the same physiotherapist.

Air stacking maneuver was done using a manual resuscitator (ambu’), with overpressure relief value of 40 cmH₂O, adapted to a mouth piece to deliver volumes of air that are consecutively held by glottis closure until no more air can be retained. The maximum lung volume that can be held by air stacking is the maximum insufflation capacity (MIC) (1,6). A Wright® ventilometer (British Oxygen Company; London, England) was properly attached to ambu’, allowing to measure MIC (13,14).

All patients had a period of 5 minutes to adapt to air stacking maneuver, before starting electrocardiogram (EKG) signal record and performing the techniques in supine and sitting position. All data were collected during the afternoon, with 15 minutes of interval between each protocol. EKG records were obtained in three consecutive periods, for both protocols (supine and sitting): 1) before intervention at a quiet and spontaneous breathing by 15 minutes, 2) during air stacking by 15 minutes, and 3) after intervention in spontaneous breathing by 15 minutes. Each air stacking
maneuver achieved the MIC as registered by ventilometer. Peripheral oxygen saturation (SpO₂) (Pulse Oximeter, 2500A, Nonin Medical Inc Model, Plymouth, MN, USA) was recorded before, during and after the intervention.

EKG signals were continuously recorded using WinCardio 6.003 software (Micromed, Brazil), and stored in a personal computer for posterior analysis. HRV was analyzed by mathematical and linear statistical models in the time and frequency domains, and by nonlinear models through Kubios HRV Analysis software (MATLAB, version 2 beta, Kuopio, Finland). In the time domain, mean R-R interval (MeanRR), the standard deviation of all R-R interval in ms (STDRR), mean heart frequency (MeanHR), standard deviation of heart frequency (STDHR) which are an estimate of overall HRV and the square root of the mean squared differences of successive RR intervals (RMSSD) and the percentage of differences between adjacent RR intervals that are >50msec (pNN50) representative of parasympathetic activity were analyzed (11,15,16).

In the frequency domain analysis, the components of the power spectrum were analyzed using the Fast Fourier Transform in the following components: low frequency (LF), representative of sympathetic activity; high frequency (HF) representative of parasympathetic activity; and LF/HF ratio, representative of sympathovagal balance. In nonlinear analysis, were used Poincaré plot measure indexes SD1 and SD2 (the standard deviation of the Poincaré plot perpendicular and along the line of identity, respectively), representative of parasympathetic autonomic activity and total HRV, respectively (11,15,16).

Statistical Analysis

Statistical analysis was performed on SigmaStat® Program for Windows (version 3.0, Jandel Scientific, San Rafael, CA). The normality of the data (Kolmogorov-Smirnov test with Lilliefors’ correction) and the homogeneity of variances (Levene median test) were tested. Then, the data were compared using One Way Anova Repeated Measures or Kruskal-Wallis Anova on Ranks, followed by Tukey test as appropriate. Correlation analysis was performed by Pearson Correlation. The results were expressed as mean±standard deviation and the level of significance considered was 5%.

Results

All patients completed the protocol and there were no reports of respiratory adverse effects, as well as any episode of hemodynamic instability during the procedures. Demographic and clinical data from patients are listed in Table 1. SpO₂ showed normal values with no significant changes during the protocol. Most of them (seven) were using albuterol at the dose of 2 mg/5mL, 3 times per day for more than one year by the time of their evaluation (Table 1).
Time Domain Analysis

During the air stacking maneuver, there was a significant increase in STDRR both in supine (56.14±38.36 vs 83.30±34.59; p=0.024) and sitting (43.73±20.15 vs 73.04±35.24; p=0.012) positions, in comparison to pre-intervention period (Table 2).

In sitting position, during the air stacking maneuver, there was a significant increase in STDHR (6.38±2.32 vs 11.68±6.52; p<0.001) and RMSSD (38.82±29.38 vs 59.12±34.71; p=0.005), in comparison to pre-intervention period (Table 2).

MeanRR was significantly lower in sitting position in the pre-intervention period (617.20±75.83 vs 666.08±80.47; p=0.002), during air stacking (624.24±72.16 vs 662.80±80.54; p=0.024) and in the post-intervention period (622.10±82.52 vs 666.98±77.91; p=0.006) in comparison to supine position (Table 2).

MeanHR was significantly higher in sitting position in the pre-intervention period (98.03±12.46 vs 92.48±11.73; p=0.04), during air stacking (98.61±10.05 vs 93.04±10.25; p=0.04) and in the post-intervention period (99.26±12.90 vs 90.95±11.89; p<0.001) in comparison to supine position (Table 2).

Additionally, in the pre-intervention period, RMSSD (38.82±29.38 vs 59.32±25.15; p=0.005) were significantly lower in sitting position in comparison to supine (Table 2).

### Tabela 1 | Demographic and clinical data.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Gender</th>
<th>SMA (Type)</th>
<th>Age (years)</th>
<th>SpO₂ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pre</td>
<td>Air Stacking</td>
</tr>
<tr>
<td>1*</td>
<td>M</td>
<td>II</td>
<td>9</td>
<td>98</td>
</tr>
<tr>
<td>2*</td>
<td>F</td>
<td>II</td>
<td>8</td>
<td>98</td>
</tr>
<tr>
<td>3*</td>
<td>M</td>
<td>II</td>
<td>9</td>
<td>99</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>III</td>
<td>12</td>
<td>98</td>
</tr>
<tr>
<td>5*</td>
<td>M</td>
<td>III</td>
<td>13</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>III</td>
<td>6</td>
<td>98</td>
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<tr>
<td>7*</td>
<td>M</td>
<td>II</td>
<td>8</td>
<td>98</td>
</tr>
<tr>
<td>8*</td>
<td>M</td>
<td>II</td>
<td>22</td>
<td>96</td>
</tr>
<tr>
<td>9*</td>
<td>M</td>
<td>II</td>
<td>21</td>
<td>98</td>
</tr>
</tbody>
</table>

M: male; F: female; peripheral oxygen saturation (SpO₂) corresponding to values registered in the sitting position. *Patients who were using albuterol.
In sitting position, during air stacking, there was a significant correlation between MeanRR ($r=0.69; p=0.03$) (Figure 1) and MeanHR ($r=-0.70; p=0.03$) with patients age.

Tabela 2 | Heart Rate Variability Values in Time Domain.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre</th>
<th>Air Stacking</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supine Position</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeanRR (ms)</td>
<td>666.08 ± 80.47</td>
<td>662.80 ± 80.54</td>
<td>666.98 ± 77.91</td>
</tr>
<tr>
<td>STD RR</td>
<td>56.14 ± 38.36</td>
<td>83.30 ± 34.59*</td>
<td>53.77 ± 26.62†</td>
</tr>
<tr>
<td>MeanHR</td>
<td>92.48 ± 11.73</td>
<td>93.04 ± 10.25</td>
<td>90.95 ± 11.89</td>
</tr>
<tr>
<td>STD HR</td>
<td>9.57 ± 10.84</td>
<td>10.67 ± 2.86</td>
<td>6.72 ± 2.42†</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>59.32 ± 48.51</td>
<td>66.91 ± 41.55</td>
<td>51.13 ± 40.76</td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>28.36 ± 25.15</td>
<td>27.34 ± 18.82</td>
<td>23.62 ± 23.64</td>
</tr>
<tr>
<td><strong>Sitting Position</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeanRR (ms)</td>
<td>617.20 ± 75.83†</td>
<td>624.24 ± 72.16‡</td>
<td>622.10 ± 82.52‡</td>
</tr>
<tr>
<td>STDRR</td>
<td>43.73 ± 20.15</td>
<td>73.04 ± 35.24*</td>
<td>57.40 ± 31.56</td>
</tr>
<tr>
<td>MeanHR</td>
<td>98.03 ± 12.46†</td>
<td>98.61 ± 10.05‡</td>
<td>99.26 ± 12.90‡</td>
</tr>
<tr>
<td>STDHR</td>
<td>6.38 ± 2.32</td>
<td>11.68 ± 6.52*</td>
<td>11.20 ± 11.01</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>38.82 ± 29.38‡</td>
<td>59.12 ± 34.71*</td>
<td>48.49 ± 34.79</td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>17.78 ± 20.40</td>
<td>23.30 ± 16.50</td>
<td>20.09 ± 19.31</td>
</tr>
</tbody>
</table>

The values correspond to the mean ± SD of 9 patients. †Significantly different from the pre period. ‡Significantly different from supine. MeanRR = mean R-R interval; STDRR = standard deviation of all R-R interval, MeanHR = mean heart frequency, STDHR = standard deviation of heart frequency; RMSSD = square root of the mean squared differences of successive RR intervals; pNN50 = the percentage of differences between adjacent RR intervals that are >50msec.
Frequency Domain Analysis

During air stacking, there was a significant increase in LF both in supine (32.50±8.91 vs 56.17±21.62; p<0.001) and sitting (28.91±8.39 vs 57.07±17.33; p<0.001) positions in comparison to pre-intervention period (Table 3).

In supine, air stacking lead to significant reduction in HF (33.50±18.08 vs 17.42±16.77; p=0.03) and significant increment in LF/HF (1.62±1.71 vs 7.76±7.73; p=0.005) (Table 3).
During air stacking, there was a significant increase in SD2 both in supine (66.60±43.44 vs 106.53±42.66; p=0.004) and sitting (54.34±22.59 vs 93.68±45.31; p=0.005) positions (Table 4).

In the pre-intervention period, SD1 was significantly lower in sitting position in comparison to supine (27.48±20.79 vs 41.99±34.35; p=0.009) (Table 4).

In all analysis, HRV indexes returned to pre-intervention values after the interruption of air stacking maneuver in both positions (Tables 2, 3 and 4).

### Tabela 4 | Heart Rate Variability Values in Nonlinear Analysis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre</th>
<th>Air Stacking</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supine Position</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD1</td>
<td>41.99 ± 34.35</td>
<td>47.36 ± 29.41</td>
<td>36.19 ± 28.85</td>
</tr>
<tr>
<td>SD2</td>
<td>66.60 ± 43.44</td>
<td>106.53 ± 42.66*</td>
<td>65.43 ± 28.39†</td>
</tr>
<tr>
<td>SD1/SD2</td>
<td>0.58 ± 0.21</td>
<td>0.44 ± 0.19</td>
<td>0.52 ± 0.25</td>
</tr>
<tr>
<td><strong>Sitting Position</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD1</td>
<td>27.48 ± 20.79*</td>
<td>41.86 ± 24.56</td>
<td>43.32 ± 28.73</td>
</tr>
<tr>
<td>SD2</td>
<td>54.34 ± 22.59</td>
<td>93.68 ± 45.31*</td>
<td>72.50 ± 39.48</td>
</tr>
<tr>
<td>SD1/SD2</td>
<td>0.46 ± 0.24</td>
<td>0.46 ± 0.17</td>
<td>0.63 ± 0.45</td>
</tr>
</tbody>
</table>

The values correspond to the mean ± SD of 9 patients. *Significantly different from the pre period. †Significantly different from air stacking. ‡Significantly different from supine. SD1 and SD2 = the standard deviation of the Poincaré plot perpendicular and along the line of identity, respectively.

### Nonlinear Analysis

During air stacking, there was a significant increase in SD2 both in supine (66.60±43.44 vs 106.53±42.66; p=0.004) and sitting (54.34±22.59 vs 93.68±45.31; p=0.005) positions (Table 4).

In the pre-intervention period, SD1 was significantly lower in sitting position in comparison to supine (27.48±20.79 vs 41.99±34.35; p=0.009) (Table 4).

In all analysis, HRV indexes returned to pre-intervention values after the interruption of air stacking maneuver in both positions (Tables 2, 3 and 4).
Discussion

This study showed that air stacking maneuver and postural changes lead to autonomic cardiac adaptations in patients with SMA types II and III. These results are suggestive of heart autonomic control integrity. Previous studies have reported that a reduced HRV is associated with a poorer prognosis for a wide range of clinical conditions, conversely, periodic changes in R-R interval are often a hallmark of health (11,17). The rhythmic changes in heart rate reflect the complex interaction between sympathetic nerve (increase heart rate), parasympathetic nerve (decrease heart rate) and mechanical and other factors on the pacemaker cells in sinoatrial node (17).

Arrhythmias can be developed from either autonomic nervous system (ANS) defects or from cardiomyopathies. ANS symptoms such as hyperhidrosis and poor circulation have been casually observed in SMA patients (7,8). In this context, previous studies have described vascular perfusion abnormalities with digital necrosis (7,9) and vascular thrombosis (9) in patients with severe SMA type I. Previously, Arai and colleagues (2005) showed, by finger cold-induced vasodilatation and analysis of R-R interval variation, that some patients with SMA have an imbalance in sympathetic and parasympathetic nervous functions, especially sympathetic nerve hyperactivity (18). This increment in sympathetic activity was also described by Hachiya and co-workers (2005) in two patients with SMA type I and the involvement of central autonomic network was speculated (19). It has been hypothesized that autonomic dysfunction is the primary source of these vascular abnormalities (7,9,18).

In present study, it was observed that MeanRR, RMSSD and SD1 were significantly higher and MeanHR was significantly lower in supine in comparison to sitting position, suggesting a reduction...
in sympathetic tonus and an increment in HRV in supine. In this context, Zuttin and colleagues (2008), analyzing autonomic heart control in young sedentary male subjects, observed that RMSSD, pNN50 and HF were higher and LF and LF/HF were lower in supine than in sitting position (20). A study of Rajendra and coworkers (2005) also showed higher values of RMSSD and pNN50 and lower values of LF/HF index in supine position in comparison to sitting position (21). Both study data are in accordance with our study. The adjustments of heart rate modulation from supine to sitting position are related to the hydrostatic deviation caused by gravitational displacement of blood to the dependent regions of the body, leading to a reduction on cardiac output, systemic arterial pressure and activation of arterial and cardiopulmonary receptors (20,22).

The shift from parasympathetic to sympathetic modulation in response to environmental or physiologic stimuli is considered the basis of normal cardiac autonomic functioning, and postural change is one such stimulus used in clinical practice to elicit this shift. HRV response to these stimuli has been considered a more sensitive measure of cardiac autonomic modulation (23). It is important to emphasize that HRV provides an indirect evaluation of cardiac autonomic control and does not provide a direct measurement of either cardiac parasympathetic or sympathetic nerve activity. Thus, a low or high amount of HRV may reflect a decreased or an increased cardiac autonomic regulation, but it does not represent a quantification of the actual cardiac nerve firing rate (17).

It is important to mention that either salbutamol or albuterol, which were used for more than one year in most of the patients in this case series, are short-acting β2-adrenergic receptor agonist. The most common side effects of this drug are fine tremor, anxiety, headache, muscle cramps, dry mouth and palpitation. Most of these are related to its sympathetic action.

In the present study it was also observed a significant correlation between MeanHR and MeanRR with patient age in the sitting position. Previous studies have shown that there are significant age-related changes in HRV in healthy children (24-28) and also, a possible gender influence (28). Children present a significantly higher heart rate in comparison to adolescents and adults (24). In this context, Massin and von Bernuth, evaluating HRV in 210 infants and children aged from 3 days to 14 years, have shown a positive correlation between all HRV parameters and age (25). The significant negative correlation (MeanHR vs age) and positive correlation (MeanRR and age) observed in our study are in accordance with these previous data and suggest a progressive maturation of the autonomic nervous system in patients with SMA type II and III as noted in healthy children.

To our knowledge no previous studies have evaluated HRV in patients with SMA. A study by Mochizuki and colleagues, evaluating HRV in patients with Duchenne muscular dystrophy (DMD), has shown that the coefficient of the R-R interval variation (CvRR) was negatively correlated with PaCO2 and that low CvRR is one of the signs of respiratory insufficiency in DMD patients (29).

Because of respiratory complications observed in patients with SMA, it is necessary to include physiotherapeutic techniques to improve ventilation and to assist cough. Air stacking is a technique used in patients who are able to close glottis, to provide maximum lung insufflations, and the primary objectives of this technique are to increase the MIC, to maximize cough peak flow, to maintain or improve pulmonary and chest wall compliance or eliminate atelectasis and to master noninvasive positive pressure ventilation (1,30). In our study, air stacking was provided by a manual resuscitator with a 40 cmH2O pressure relief valve and each maneuver achieved the MIC recorded by a ventilometer. To promote maximum lung expansion, air stacking permits greater lung distention, voice volume and CPF and, consequently, can decrease atelectasis and loss of pulmonary compliance and it helps
to maintain chest wall mobility (1,6,30). High inspiratory volume is essential to the effectiveness of cough and maintaining the lung at high volumes during the air stacking maneuver could improve collateral ventilation and open previously collapsed areas (1,14,30). Prolonged maintenance of high lung volume during air stacking could lead to a reduction in venous return and cardiac output and in blood pressure due to an increment in intrathoracic pressure (14,31). However, our patients did not present hemodynamic instability during air stacking.

In the present study, air stacking led to significant increment in STDRR, LF and SD2 indexes both in supine and sitting positions. Additionally, there were, in supine position, significant reduction in HF and significant increase in LF/HF suggesting a higher sympathetic activation in this position during the air stacking maneuver. The elevation of sympathetic activity increases the vulnerability of the heart and, consequently, the risk of cardiovascular events (32). Sympathetic nerve dysfunction has been described in patients with SMA, and autonomic dysfunction can affect quality of life and the life expectancy of patients with SMA (18). However, the HRV data of the present study cannot predict the risk of cardiac complications of air stacking.

Respiratory parameters can deeply alter heart rate and R-R interval variability independent of changes in cardiac autonomic regulation. It is well established that increases in respiratory frequency reduce the amplitude of heart rate oscillations while increases in tidal or static lung volumes provoke increases in the R-R interval variability (17). It is important to consider that the increase in HRV observed during air stacking in the present study could be attributed to the higher inspiratory volume achieved.

The present study has some limitations, such as the relative small number of patients and the use of albuterol that could influence the hemodynamic and autonomic responses. In this context, there are some controversies regarding albuterol effects on cardiac autonomic function. Eryonucu and colleagues showed that albuterol increases sympathetic modulation in the cardiac activity in adult asthmatic patients (33). On the contrary, according Kaya et al, albuterol did not affect HRV parameters both at rest and during exercise in healthy subjects (34).

**Conclusion**

In conclusion, this study showed that patients with SMA types II and III present alterations on heart rate variability during air stacking maneuver and postural changes suggesting a possible integrity of cardiac autonomic control.

**References**


27. Heragu NP, Scott WA. Heart rate variability in healthy children and in those with congenital heart disease both before and after operation. Am J Cardiol. 1999 Jun;83(12):1654-7.


