BRIEF COMMUNICATION

Association between respiratory mechanics and autonomic function in morbid obesity[☆]

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Abstract This study aimed to investigate the association between respiratory mechanics and autonomic modulation in morbidly obese patients. We evaluated 10 morbidly obese subjects (BMI = 52.9 ± 11.2 kg/m^2), aged 23−58 years. Assessment of respiratory mechanics was done by the forced oscillation technique (FOT), and cardiovascular autonomic function was recorded by heart rate variability analysis (HRV). The Pearson correlation coefficient was used to test the associations between respiratory mechanics and HRV variables. There were associations between the standard deviation of all RR intervals (SDNN) and airway resistance (Rm) ($r = -0.82$; $p = 0.004$), SDNN and respiratory system resistance (R0) ($r = -0.79$; $p = 0.006$), root mean square of successive differences between adjacent normal RR intervals (rMSSD) and respiratory system resistance (R5) ($r = -0.643$; $p = 0.0451$), rMSSD and R0 ($r = -0.64$; $p = 0.047$), and rMSSD and Rm ($r = -0.658$; $p = 0.039$). We concluded that the airway and respiratory system resistances are negatively associated with parasympathetic activity in patients with morbid obesity.
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Associação entre a mecânica respiratória e função autonómica na obesidade mórbida

Resumo Este estudo teve por objetivo investigar a associação entre mecânica respiratória e modulação autonómica em pacientes com obesidade mórbida. Foram avaliados 10 indivíduos com obesidade mórbida (IMC = 52,9 ± 11,2 kg/m^2), com idade entre 23−58 anos. A avaliação da

Variabilidade da
frequência cardíaca;
Obesidade mórbida

mecânica respiratória foi realizada com a técnica de oscilações forçadas e a função autonómica cardiovascular por meio da variabilidade da frequência cardíaca (VFC). O coeficiente de correlação de Pearson foi utilizado para testar as associações entre a mecânica respiratória e as variáveis de VFC. Houve associações entre o desvio padrão de todos os intervalos RR (SDNN) e a resistência de vias aéreas (Rm) ($r = -0,82$; $p = 0,004$), SDNN e resistência do sistema respiratório (R0) ($r = -0,79$; $p = 0,006$), raiz quadrada média das diferenças sucessivas entre intervalos RR normais adjacentes (rMSSD) e resistência do sistema respiratório (R5) ($r = -0,643$; $p = 0,0451$), rMSSD e R0 ($r = -0,64$; $p = 0,047$), e rMSSD e Rm ($r = -0,658$; $p = 0,039$). Concluímos que a resistência de vias aéreas e do sistema respiratório são negativamente associadas com a atividade parassimpática em pacientes com obesidade mórbida.

Introduction

Overweight contributes to the development of significant cardiorespiratory impairments, including the increase in airway and respiratory system resistance, limited ventilatory capacity, and changes in the cardiovascular autonomic function. As these changes are proportional to the body mass index (BMI), they are more pronounced in patients with morbid obesity.[1,2]

The respiratory system resistance and its components can be determined using the Forced Oscillation Technique (FOT), described by Dubois et al. in 1956 as a non-invasive method for the evaluation of mechanical properties of the respiratory system in different frequencies.[3] Morbidly obese patients also present increased cardiovascular sympathetic discharge and reduced parasympathetic activity.[4] Because heart rate variability is influenced by the autonomic control, the time and frequency-domain analysis of RR intervals has been recognized as an effective and non-invasive method of evaluating the cardiovascular autonomic modulation in obese[4,5] and eutrophic subjects.[6] In time domain methods, the so-called normal-to-normal (NN) intervals (that is all intervals between adjacent QRS complexes resulting from sinus node depolarizations), or the instantaneous heart rate is determined. These NN intervals are statistically processed to calculate its variability.[7] In the frequency domain analysis, the power spectral density provides the basic information of how power (i.e. variance) distributes as a function of frequency.[7]

Although there are many studies on the mechanical cardiopulmonary coupling using HRV,[2,5] we did not find any reports about the possible association between respiratory mechanics and autonomic function in patients with morbid obesity. Thus, in this study we aimed to investigate the association between respiratory mechanics and autonomic modulation in a sample of patients with morbid obesity.

Methods

Sample

We evaluated 10 morbidly obese subjects (four males), aged 23–58 years, followed up by the Bariatric Surgery Program of the University Hospital Clementino Fraga Filho, Federal University of Rio de Janeiro. Patients who had been diagnosed with pulmonary or cardiovascular diseases, spirometric abnormalities, left ventricle ejection fraction <50% and cardiac arrhythmias were excluded from the study. Spirometry and maximal respiratory pressures were assessed in accordance to the recommendations of the American Thoracic Society[8] and the Brazilian Thoracic Society.[9]

The project was approved by the institutional ethics committee and all participants signed an informed consent term.

Respiratory mechanics

Assessment of respiratory mechanics was done by the forced oscillation technique (FOT) by means of an Impulse Oscillometer (Erich Jaeger, Hoechberg, Germany) and its components. After equipment calibration, the patients were seated, kept their heads in a neutral position, their cheeks supported by their hands, and their nostrils were occluded by a nose-clip. Five sequences of 40-s recording of respiratory signals were collected. Signal acceptability criteria included a minimum of 15 s without artifacts and at least 80% of the frequency range used presenting a coherence function equal or superior to 0.9. The following variables were collected: resistance at 5 Hz (R5), resistance extrapolated to 0 Hz (R0), resistance at 20 Hz (R20), mean resistance (Rm), first derivative of resistance as a function of frequency (dR/dF), reactance at 5 Hz (X5), resonant frequency (f0) and integral of the reactance between 5 Hz and f0 (AX). The last three parameters may reflect the shift of the reactance vs frequency curve to the right; this is often associated with increased peripheral resistance or respiratory system elastance.[10]

Autonomic function

The assessment of cardiovascular autonomic function was done by HRV analysis in time and frequency-domains. The subjects were instructed not to have tea, coffee, cola drinks and/or chocolate for at least 6 h before the evaluation, and to avoid physical exercise for 24 h before

the test. The Heart Rate (HR) was recorded using a frequency meter Polar S810 (Oulu, Kempele, Finland). The spectral analysis of HRV RR intervals time series used the software Kubios HRV 2.0 (Kupio, Savonia North, Finland).

The power spectrum was calculated by integrating the function of the power spectral density for the bands of high frequency (HF) and low frequency (LF). Autonomic balance was defined as LF/HF power spectrum.[7]

The variables RR interval and standard deviation RR interval (SDNN) were used to reflect the sympathetic activity. The root mean square of successive differences between adjacent normal RR intervals (rMSSD) and NN50 count divided by the total number of all RR intervals (pNN50) indicated the parasympathetic activity.[7]

Statistical analysis

Statistical analysis used the software SigmaStat 3.1 (Jandel Scientific, San Rafael, CA, USA). As the data were normally distributed (assessed by the Shapiro–Wilk test), the associations between respiratory mechanics and HRV variables were tested with the Pearson correlation coefficient. The significance level was set at 5%.

Results

The 10 patients evaluated were 41.6 ± 10.7 years old. They had a body mass index (BMI) of $52.9 \pm 11.2 \, kg/m^2$, weight of $157.5 \pm 32.3 \, kg$ and height of $1.72 \pm 0.08 \, m$. Their pulmonary function is in Table 1. There were positive correlations between the anthropometric variables and respiratory mechanics: R0 and BMI ($r = 0.65$; $p = 0.04$), Rm and height ($r = -0.71$; $p = 0.019$), R5 and height ($r = -0.67$; $p = 0.032$), X5 and BMI ($r = -0.66$; $p = 0.032$), AX and BMI ($r = 0.63$; $p = 0.046$), X5 ins and height ($r = 0.73$; $p = 0.015$), X5 exp and weight ($r = -0.71$; $p = 0.021$). None of the autonomic function variables correlated with age, weight and BMI. There were associations between SDNN and Rm ($r = -0.82$; $p = 0.004$), SDNN and R0 ($r = -0.79$; $p = 0.006$), rMSSD and R5 ($r = -0.6426$; $p = 0.0451$), rMSSD and R0
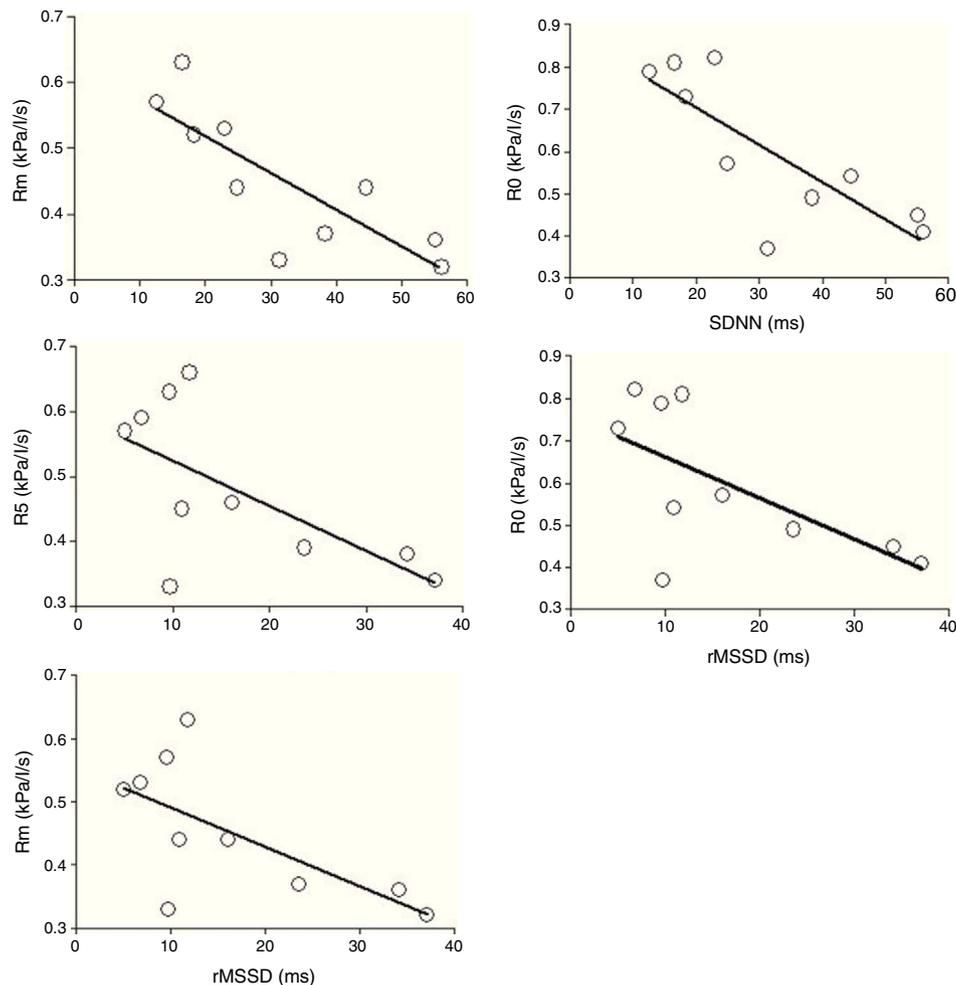
Figure 1 Associations between respiratory mechanics and heart rate variability variables. SDNN: standard deviation of RR intervals; rMSSD: root mean square of successive differences between adjacent normal RR intervals; R0: resistance extrapolated to 0 Hz; R5: resistance at 5 Hz; Rm: mean resistance.

Table 1 Pulmonary function of morbid obesity patients.

Variable	Mean $\pm$ SD ($n = 10$)
FVC (%)	78.7 ± 12.3
FEV_1 (%)	80.5 ± 10.2
FEV_1/FVC	103.4 ± 7.9
MMV (%)	125.8 ± 22.9
MIP (%)	94.5 ± 26.8
MEP (%)	93.9 ± 23.6

FVC: forced vital capacity; FEV_1: forced expiratory volume in the first second; PF: peak flow; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; MVV: maximal voluntary ventilation. Data are mean $\pm$ SD. Predicted values in according to the Brazilian reference equations described by Pereira[11] (spirometry) and Neder[12] (maximal respiratory pressures).

($r = -0.64$; $p = 0.047$), and rMSSD and Rm ($r = -0.6575$; $p = 0.0388$) (Fig. 1).

Discussion

Our results are in agreement with the findings of Zerah et al.,[11] which in a cross-sectional study using FOT, showed an association between airway and respiratory system resistance and BMI in patients with morbid obesity. Because more obese patients present with higher peripheral resistance or respiratory system elastance,[1,2,11] the association between BMI and reactance parameters (AX and X5) found in our study is also an expected result. Conversely, there was no association between R20, which is associated with resistance in central airways or any other anthropometric or autonomic function variable. The association between X5 ins and height may be explained by the proportionality between reactive capacitance and lung size.[10]

Most importantly, we found correlations between respiratory mechanics and autonomic modulation variables. Our results showed that the increase in the airways (Rm) and total resistance of the respiratory system (R5 and R0) are associated with the reduction in parasympathetic activity (rMSSD and SDNN).

At rest the heart rate increases with inspiration and decreases with expiration. This variation, which also depends on tidal volume, is denominated sinus arrhythmia, and results from a vagal biphasic response during the respiratory cycle.[12] The increased airway and respiratory system resistance, associated with reduced total lung capacity make obese patients adopt higher respiratory rates and lower tidal volumes.[2] Although there is no data on the respiratory patterns of our patients, it is likely that the impaired respiratory mechanics led to a higher respiratory rate and, thus increased the number of sinus arrhythmia.[12] Moreover, the higher adrenergic discharge needed to overcome the additional respiratory load found in obese patients could have played a role in the autonomic modulation results observed in our study. New studies with a larger sample size should address the relationship between respiratory mechanics, autonomic modulation, respiratory pattern and ventilatory drive in eutrophic and obese subjects. In conclusion, the airways and respiratory system resistances are negatively associated to the parasympathetic activity in patients with morbid obesity.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data and that all the patients included in the study received sufficient information and gave their written informed consent to participate in the study.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Funding

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