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# Acute Effects of Marathon Running on Lung Function, Lung Mechanics, and Inflammation

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## ABSTRACT

**This study investigated the influence of the marathon on lung function, mechanics, and pulmonary inflammation. Twenty-eight male amateur marathon runners (42.1±6.2 years) were evaluated before and immediately after marathon. Pulmonary function and mechanics were assessed using spirometry and impulse oscillometry, respectively, whereas fatigue of the respiratory muscles by manovacuometry and lung inflammation by fractional exhaled nitric oxide (FeNO). Marathon induced a significant reduction in the lung function as compared to baseline values: FVC (4.81±0.72 vs 4.67±0.62, p=0.0095), VC IN (4.81±0.72 vs 4.67±0.62, p=0.009), FEV1 (3.83±0.62 vs 3.72±0.59, p=0.0232), and FEV6 (4.87±0.68 vs 4.57±0.63, p=0.0006), as well as an impairment in the lung mechanics in comparison to baseline values: reduced pulmonary impedance (Z5Hz; 2.96±1.36 vs 2.67±1.11; p=0.0305), reduced resistance of the whole respiratory system (R5Hz; 2.76±1.27 vs 2.5±1.08; p=0.0388) and pulmonary reactance (X5Hz; -1.05±0.55 vs -0.91±0.36; p=0.0101) and of resistance of proximal airways (R5Hz; 1.26±0.73 vs 1.06±0.86; p= 0.0377). In addition, maximal inspiratory (MIP; 94.14±41.88 vs 72.52±25.50; p=0.0023) and expiratory (MEP; 99.31±31.84 vs 91.29±19.94; p=0.0454) pressures, as well as FeNO levels were lower after the marathon than values pre-marathon (p=0.0359). Marathon running causes an acute disturbance in lung function and mechanics and compromises respiratory muscle strength.**

**Keywords:** impulse oscillometry, inflammation, lung function, lung mechanics, marathon, nitric oxide.

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## I. INTRODUCTION

In healthy individuals, the respiratory system has sufficient capacity to meet the demands of pulmonary ventilation and gas exchange during exercises. However, the physiological demands required by a marathon are extremely higher, harming several systems and organs, including the respiratory system. Concerning the respiratory system, several mechanisms may potentially limit exercise performance, including airflow

limitation, upper airway narrowing/obstruction, and respiratory muscle fatigue (Romer *et al*., 2008, Bussoti *et al*., 2014).

Therefore, a deep knowledge of pulmonary function and mechanics in response to a marathon race is essential to optimize the health and performance of athletes. The assessment of lung function is often performed using spirometry. However, it has been shown that a spirometry-based measurement of the lung function can fail to identify complex dysfunctions of the airways function (Bickel *et al*., 2014). Furthermore, this method of assessment is subject to the influence of inadequate technique for performing the test and to respiratory muscle fatigue during the examination (Miller *et al*., 2005).

Impulse oscillometry system (IOS) is a non-effort-dependent method for assessing lung mechanics, including resistance and elastance of the airways and of peripheral lung tissue. The impulses (from low to high frequencies) generated by the IOS are superimposed on the current respiration and the respiratory impedance is calculated from the pressure and volume changes caused by the impulses during the measurement. Respiratory impedance values are expressed in a range of pulse frequencies that can subsequently allow more accurate detection of the site of airway obstruction (Smith *et al*., 2005). Thus, IOS allows the assessment of lung mechanics in groups of individuals experiencing difficulties with effort-dependent methods. These includes children under five years of age, obese, elderly, critical illnesses, and patients with neuromuscular abnormalities (Scott *et al*., 2014).

So, no study has investigated the effects of marathon running on lung mechanics by using IOS. Therefore, the aim of this study was to evaluate the influence of marathon running on lung function and mechanics, as well as in the levels of pulmonary nitric oxide.

## II. Material and Methods

### *A. Subjects*

Twenty-nine male amateur marathon runners (age 42.1±6.2 years), who participated in the XXV São Paulo International Marathon, held on April 7, 2019, was enrolled in the present study. Volunteers were evaluated 24 hours before and immediately after the marathon race (ranging among 3 to 10 minutes after the marathon). The inclusion criteria were not present cardiorespiratory, metabolic, renal, or inflammatory pathologies, not using any type of drug, not having used any medicine that could compromise the results of the study.

All experimental procedures used in this study were approved by the institutional ethics committee registered under number 2.480.755, in accordance with the Declaration of Helsinki for studies involving human subjects. All subjects were aware of the possible risks involved in the study and provided written informed consent.

### *B. Evaluation of Lung Function by Spirometry*

The spirometer coupled with impulse oscillometer system (IOS) (MasterScreen, Jaeger™, Germany) was used to assess the lung function and mechanics. The lung function parameters measured were forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), Tiffeneau index (FEV1/FVC), forced expiratory flow 25-75% (FEF 25-75%), peak expiratory flow (PEF), FEV3, FEV6 and FEF85%. The measurements were carried out using the forced maneuver pre- and post-action bronchodilator (Salbutamol sulfate 400mcg), as recommended by the American Thoracic Society and European Respiratory Society (King *et al*., 2020) but using the reference values standardized for the Brazilian population (Pereira, 2002). The results were expressed as a percentage of the predicted value.

### *C. Evaluation of Lung Mechanics by Impulse Oscillometry System*

Pulmonary mechanics were assessed using the same IOS cited above, following the procedures: the volunteers, with blocked nostrils, breathe in a tidal volume for 180-200 pulses, which corresponds to approximately 40 seconds, as recommended by the American Thoracic Society and European Respiratory Society (King *et al*., 2020). The parameters analyzed were resistance of the whole respiratory system (R5Hz), resistance of the proximal airways (R20Hz), resistance of the distal airways (R5Hz - R20Hz), the impedance of the respiratory system (Z5Hz), the reactance of the respiratory system (X5Hz) and the resonant frequency (Fres) of the respiratory system. The results obtained both in percentages of the predicted and in absolute values (for the parameters without reference values) (King *et al*., 2020).

### *D. Evaluation of respiratory Muscle Strength*

Respiratory muscle strength was measured by using a manometer (0-300 cmH2O). Maximal inspiratory (MIP) and expiratory (MEP) pressures were obtained as previously and classically published (Do Nascimento *et al*., 2015).

### *E. Determination of Fractional Exhaled Nitric Oxide (FeNO) Levels*

The levels of fractional exhaled nitric oxide were measured using the NOBreath portable nitric oxide monitor (Bedfont Scientific, UK), in which the volunteer must expire for a period of approximately 8 seconds, according to the manufacturer's recommendation. The results were presented in parts per billion (ppb).

### *F. Statistical analysis*

The GraphPad Prism 5.0 software (Graph Pad software, CA, USA) was used to perform a statistical analysis and build the graphs. An analysis of data distribution was performed using the Shapiro-Wilk test, followed by the homogeneity of variance analysis by the Levene test. Paired t-test was used to compare parametric data. And the Wilcoxon test was used to compare non-parametric data. The significance level was set to 5%. The data of spirometry, oscillometry, manuovacuometry and FeNO were presented in mean ± standard deviation.

## III. RESULTS

All twenty-eight marathoners enrolled in the study completed the São Paulo International Marathon and all the steps of this study. The marathon took place in the fall and the day with high humidity, a little drizzle at the start and finish of the race (temperature between 24°C and 22°C and humidity between 94.1% and 69.6%). The demographic and anthropometric characteristics of the volunteers are shown in table 1.

TABLE I: DEMOGRAPHIC CHARACTERISTICS OF MARATHONERS

| Variable | Men Mean ± standard deviation |
|---|---|
| Age | 42,14±6,27 |
| Marathon time (minutes) | 227,53±72,16 |
| Stature (m) | 173,59±6,51 |
| Body Mass (kg) | 70,41±9,44 |
| BMI (kg/m2) | 28,19±2,12 |

### *A. Impact of Marathon on Pulmonary Function of Amateurs Marathoners*

The Figure 1 shows that the marathon running induced a significant reduction in the following spirometry parameters: FVC (Fig. 1A; p=0.0095), VC IN (Fig. 1B; p=0.009), FEV1 (Fig. 1C; p=0. 0232), FEV3 (Fig. 1D; p=0.003) and FEV6 (Fig. 1E; p=0.0006) as compared to baseline values. No significant differences were found in the FEV1/FVC, FEV3, MEF25-75%, MEF85%, and PEF (p>0.05).

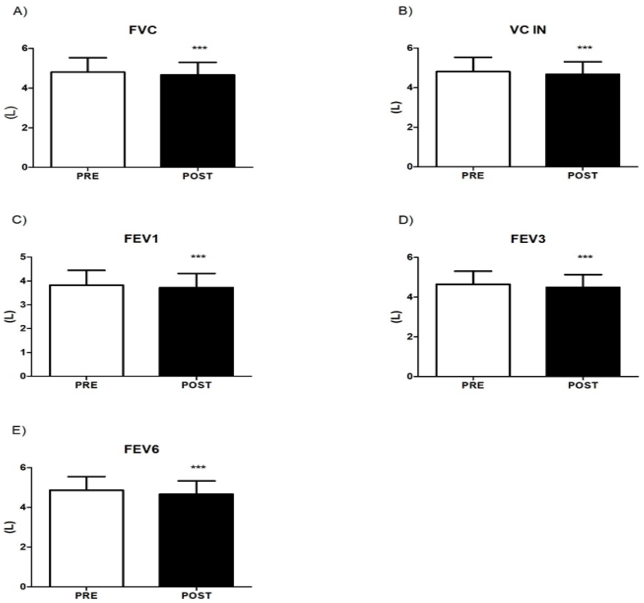


Fig. 1. Lung function of marathoners before and immediately after marathon.

### *B. Impact of Marathon on Pulmonary Function of Amateurs Marathoners*

The Fig. 2 shows that there was a decrease in the following oscillometric parameters: lung impedance (Z5Hz; Fig. 2A; p=0.0305), resistance of the whole respiratory system (R5Hz; Fig. 2B; p=0.0388), reactance of the respiratory system (X5Hz; Fig. 2C; p=0.0101) and of central resistance (RCentral; Fig. 2D; p=0.0377), immediately after the marathon in comparison to the pre-marathon values. No significant differences were found in the resistance of the distal airways (R20Hz), resistance of the distal airways (R5Hz - R20Hz) and the resonant frequency (Fres) of the respiratory system (p>0.05).

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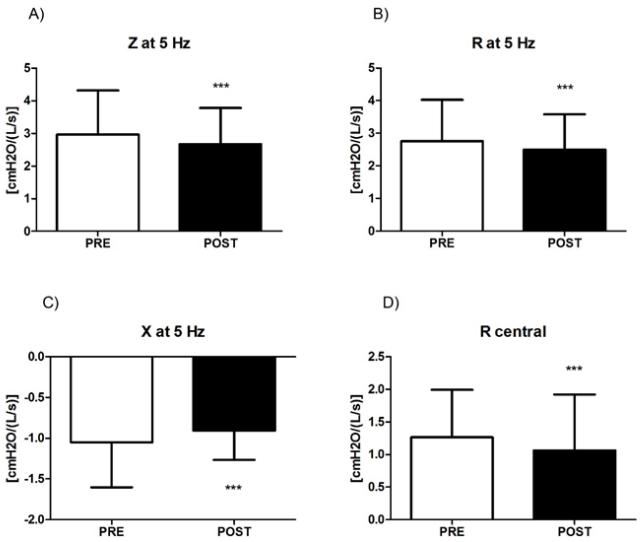


Fig. 2. Lung mechanics of marathoners before and immediately after marathon.

### *C. Changes in Fractional Exhaled Nitric Oxide (FeNO)*

The Fig. 3 demonstrates that there was a decrease in FeNO immediately after the marathon (Fig. 3; p=0.0359) as compared to the baseline values.

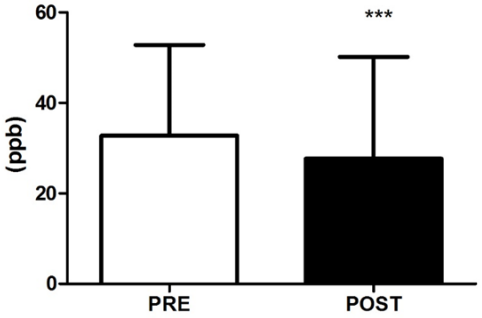


Fig. 3. Values of fractional exhaled nitric oxide (in ppb) obtained before and immediately after marathon race.

### *D. Effects of Marathon on Maximum Expiratory and Inspiratory Pressure*

A reduction in MIP (Fig. 4A; p=0.0023) and MEP (Fig. 4B; p=0.0454) was observed immediately after a marathon in comparison to the baseline values.

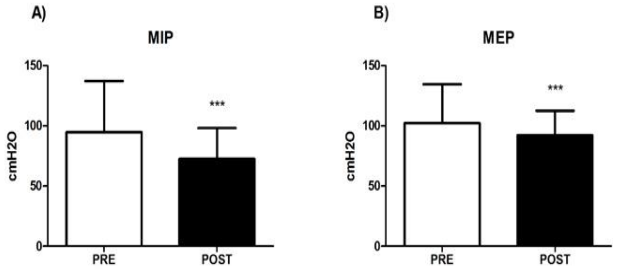


Fig. 4. Effects of Marathon on the Maximum Expiratory and Inspiratory Pressure.

## IV. DISCUSSION

In a general way, our results showed that marathon runners presented not only an acute pulmonary function reduction, demonstrated by a reduction in FVC, VC IN, FEV1, and, but also, for the first time is presented an acute pulmonary mechanical reduction, which denotes an acute impairment of the lung mechanics, demonstrated by a reduction in total respiratory resistance (R5HZ), respiratory impedance (Z5Hz), and respiratory reactance (X5Hz). In addition, we also found lower FeNO levels, as well as MIP and MEP immediately post-marathon race.

It is noteworthy to point out that a novelty in this study was the use of IOS in the marathon context, although the IOS has already been used to assess airway function after bronchoprovocation in athletes

(Oliver *et al*., 2016; Evans *et al*., 2005; Evans *et al*., 2006). Evans *et al*. (2005) found changes in airway function after physical exercise challenges at room temperature and at cold temperature, and only IOS detected such changes, sensibly demonstrating the degree of response between different temperatures, while spirometry did not indicate any difference, suggesting that IOS is a more sensitive method to detect changes in airway function, even in healthy individuals, such as in athletes. In addition, greater sensitivity by IOS for detecting changes in airway function in athletes and physically active people has been demonstrated by other studies (Evans *et al*., 2005; Rundell *et al*., 2005; Oliver *et al*., 2015). IOS is an attractive method for determining the resistance of whole respiratory system (R5Hz), of the proximal airways (R20Hz) and of distal airways (R5Hz-R20Hz), as only a simple tidal breath is required to perform the exam (Scott *et al*., 2014), without the need of forced respiratory maneuvers, which facilitates the assessment of lung function after exercise challenges. Of note, a study has already demonstrated that such acute impairment of pulmonary response after a marathon race occurs due to reduction of bioavailability of nitric oxide, as measured as fractional exhaled nitric oxide (FeNO) (Sierra *et al*., 2019).

FeNO is considered a valuable marker of airway inflammation and hyperresponsiveness, especially in respiratory diseases such as asthma (Mummadi & Hahn, 2016), chronic obstructive pulmonary disease, and idiopathic pulmonary fibrosis (Liu *et al*., 2015; Santini *et al*., 2016). In the present study, a reduction in FeNO was observed again immediately after the marathon, suggesting a reduction in the bioavailability of nitric oxide. In addition, Scott *et al*. (2015) found an acute reduction of FeNO after exercise after moderate exercise on the treadmill in asthmatics, which correlated with increased circulating levels of the anti-inflammatory cytokine, IL-1RA, suggesting an anti-inflammatory pathway involved in such observations.

On the other hand, Sierra *et al*., (2019) verified the acute response of FeNO to marathon and found an acute increase in FeNO immediately after the marathon, which was followed by a strong reduction in the days following the marathon. However, the assessment of FeNO levels after exercise remains controversial and with varying results. Furthermore, few studies have verified changes in FeNO after the marathon.

However, while the lung function is often assessed using only spirometry. This physiological test assesses the competence with which an individual inhales or exhales volumes of air as a function of time, requiring the individual to perform a series of forced vital capacity (FVC) maneuvers in a mouthpiece; is an important tool for tracking overall respiratory health (Miller *et al*., 2005). This test can be done both in the field and in the laboratory, however, it requires a certain degree of training and competence of the individual for valid data to be obtained.

In this way, the present study showed a reduction in lung function, demonstrated by decreased FVC, VC IN, FEV1, FEV3 and FEV6. Studies have shown that marathon may reduce the lung function, which may cause post-race decreases in the range of 10–15% (with or without evidence of airway obstruction) in respiratory function (Sierra *et al*., 2019; Tiller, 2019). Of note, it is well established that when exercise, any type of effort, induces a reduction of at least 10% in the FEV1, this phenomenon is known as exercise-induced bronchospasm (EIB) or exercise-induced bronchoconstriction (EIB) (Abbasi *et al*., 2015). So, although all volunteers of the present study were not asthmatic and not allergic, 62,06% (18 athletes) presented reduction in the VEF1, with only 10,83% (3 athletes) presenting a reduction higher than 10%, which characterizes BIE. In addition, the other 37,93% (11 athletes) presented small increases in the FEV1 after marathon, remaining below the 10%, which would characterize bronchodilatation. Therefore, we point out that a reduction in the FEV1 below 10%, characterizing EIB was present in only 10,83% of the athletes. However, the present study also demonstrated, for the first time, that FEV3 and FEV6 were also reduced. These findings, according to the literature represent airway obstruction of the small airways (Pisi *et al*., 2021), and particularly the reduction in FEV3 and FEV6 represent singly a mild lung injury (Morris *et al*., 2013). Thus, this is the first study to demonstrate that marathon running induces a dysfunction of small airways.

There are several mechanisms by which strenuous endurance exercises can compromise lung and/or respiratory muscle function in healthy individuals. Some of the mechanisms are airway cooling and/or dehydration, increased deposition of air pollutants in the airways, and respiratory fatigue (Tiller, 2019). In addition, respiratory muscle fatigue is a phenomenon in which the inspiratory and/or expiratory muscles have a reduced force-generation capacity in relation to the baseline, usually after high intensity, exhaustive exercises (Romer *et al*., 2007). This phenomenon has the potential to compromise the locomotor blood flow of the limbs, exacerbate dyspnea and compromise the ventilatory capacity of exercise (Romer *et al*., 2007). In the present study, a reduction in MIP and MEP was observed immediately after the marathon. These changes in respiratory pressures generated by the respiratory muscles suggest the development of respiratory muscle fatigue after the marathon. Furthermore, other studies have shown respiratory muscle fatigue using the manovacuometry test (Tiller *et al*., 2019), which can reinforce the findings of the present study.

## V. Conclusion

In conclusion, the present study shows, for the first time, that marathon running induces an acute impairment of the lung function, particularly the small airways, beyond to impair lung mechanics and compromise respiratory muscle strength.

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## Conflict of Interest

Authors declare that they do not have any conflict of interest.

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