Oxygen desaturation in healthy subjects undergoing the incremental shuttle walk test*

Dessaturação em individuos saudáveis submetidos ao incremental shuttle walk test

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Abstract

Objective: To determine the probability of oxygen desaturation in healthy individuals undergoing the incremental shuttle walk test (ISWT). Methods: We enrolled 83 healthy subjects: 55 males (including 1 smoker) and 28 females. We determined pre-ISWT FEV1, FEV6, HR and SpO2, as well as post-ISWT HR and SpO2. Results: Mean values overall were as follows: age, 35.05 ± 12.53 years; body mass index, 24.30 ± 3.47 kg/m2; resting HR, 75.12 ± 12.48 bpm; resting SpO2, 97.96 ± 1.02%; FEV1, 3.75 ± 0.81 L; FEV6, 4.45 ± 0.87 L; FEV1/FEV6 ratio, 0.83 ± 0.08 (no restriction or obstruction); incremental shuttle walk distance, 958.30 ± 146.32 m; post-ISWT HR, 162.41 ± 18.24 bpm; and post-ISWT SpO2, 96.27 ± 2.21%. In 11 subjects, post-ISWT SpO2 was higher than was pre-ISWT SpO2. In 17 subjects, there was a 4% decrease in SpO2 after the ISWT. There were no statistically significant differences between the groups with and without post-ISWT oxygen desaturation in terms of age, gender, FEV1, FEV6, FEV1/FEV6, pre-ISWT SpO2, incremental shuttle walk distance, HR, or percentage of maximal HR. In the individuals with post-ISWT oxygen desaturation, the body mass index was higher (p = 0.01) and post-ISWT SpO2 was lower (p = 0.0001). Conclusions: Healthy individuals can present oxygen desaturation after the ISWT. Using the ISWT to predict subtle respiratory abnormalities can be misleading. In healthy subjects, oxygen desaturation is common after the ISWT, as it is during any intense physical activity. Keywords: Heart function tests; Respiratory function tests; Body mass index; Oximetry

Resumo

Objetivo: Determinar a probabilidade de dessaturação arterial em indivíduos saudáveis submetidos ao incremental shuttle walk test (ISWT). Métodos: Foram estudados 83 indivíduos saudáveis, dos quais 55 eram homens (1 deles fumante) e 28 eram mulheres. Foram determinados VEF1 e VEF6 antes da realização do ISWT, assim como FC e SpO2 antes e depois do ISWT. Resultados: As médias gerais foram as seguintes: idade, 35,05 ± 12,53 anos; índice de massa corporal, 24,30 ± 3,47 kg/m2; FC em repouso, 75,12 ± 12,48 bpm; SpO2 em repouso, 97,96 ± 1,02%; VEF1, 3,75 ± 0,81 L; VEF6, 4,45 ± 0,87 L; relação VEF1/VEF6, 0,83 ± 0,08 (sem restrição ou obstrução); distância percorrida no ISWT, 958,30 ± 146,32 m; FC pós-ISWT, 162,41 ± 18,24 bpm e SpO2, pós-ISWT, 96,27 ± 2,21%. Em 11 indivíduos, houve um aumento da SpO2 após o ISWT, ao passo que em 17 houve uma queda de 4%. Não houve diferença estatística entre os grupos com e sem dessaturação após o ISWT no tocante às variáveis idade, gênero, VEF1, VEF6, VEF1/VEF6, SpO2 basal, distância percorrida no ISWT, FC e porcentagem de FC máxima. Nos indivíduos que apresentaram dessaturação, o índice de massa corporal foi maior (p = 0,01) e a SpO2 pós-ISWT foi menor (p = 0,0001). Conclusões: Indivíduos saudáveis podem apresentar dessaturação após o ISWT. O uso do ISWT para prever a presença de problemas respiratórios sutis pode ser enganador. Em indivíduos saudáveis, a dessaturação é um evento comum após o ISWT, assim como o é durante a atividade física intensa. Descritores: Testes de função cardíaca; Testes de função respiratória; Índice de massa corporal; Oximetria.

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Introduction

Although patients with interstitial pulmonary fibrosis or pulmonary arterial hypertension can have normal SpO₂ at rest, some will show oxygen desaturation after submaximal exercise. End-exercise PaO₂ decreases after maximal exercise, and submaximal steady-state exercise was found to be an important measure of disease severity in interstitial pulmonary fibrosis. Lama et al. demonstrated that patients with usual interstitial pneumonia who developed oxygen desaturation during and after a six-minute walk test (6MWT)—a ≥ 4% decrease in oxygen saturation from baseline (Δsat ≥ 4%)—were more than four times more likely to die during follow-up. The abovementioned findings led us to hypothesize that a decrease in oxygen saturation during self-paced walking (a submaximal exercise test) is a meaningful measure of disease status in patients with scleroderma. Our results showed that, in the multiple logistic regression analysis, the variable Δsat ≥ 4% was significantly associated with age, dyspnea, and two other variables related to pulmonary involvement, i.e., FVC < 80% of the predicted value (as assessed by spirometry) and positivity for the Scl-70 antibody, which is a marker of pulmonary disease in scleroderma. However, the statistical model applied to the data did not indicate which of the dependent variables analyzed (Δsat ≥ 4% or the distance walked) was better at predicting pulmonary disease. Nevertheless, Δsat ≥ 4% appeared to be able to provide more information on this issue than did the distance walked.

Another study conducted by our research group and involving patients with systemic lupus erythematosus showed that those with post-6MWT Δsat ≥ 4% (as assessed by pulse oximetry) showed a significant reduction in the six-minute walk distance (6MWD), which was 443 m in the group of patients who developed oxygen desaturation and 497 m in that of those who did not (p = 0.0291). However, both 6MWDs were well above the lower limit of the normal range. In addition, when compared with the patients who did not develop oxygen desaturation, those who did had a higher post-6MWT HR (p = 0.0170), a lower MEP (p = 0.0282), a lower MIP (p = 0.0504), and a restrictive pattern of lung disease (as determined by spirometry). These findings suggest that oxygen desaturation is more sensitive in detecting the presence of respiratory abnormalities in patients with systemic lupus erythematosus than is the 6MWD (unpublished data). Therefore, oxygen desaturation during submaximal exercise seems to be a more sensitive endpoint to detect subtle respiratory abnormalities in pulmonary diseases and in systemic diseases that affect respiration.

Maximal exercise tests, such as cardiopulmonary exercise tests, can provide important information on the integration between the cardiovascular and respiratory systems during exercise. Although cardiopulmonary exercise tests have been extensively used in order to investigate various lung diseases, they are complex tests that require expensive equipment.

The incremental shuttle walk test (ISWT) is a maximal exercise test that provides data that correlate well with measurements made during incremental cardiopulmonary exercise testing, being simpler and less expensive than the latter. The fact that even patients with few symptoms and mild pulmonary involvement can present with a decrease in oxygen saturation in a submaximal test led to us inquire how oxygen saturation would behave during a maximal walk test, such as the ISWT. Could it improve the sensitivity of the 6MWT in detecting respiratory impairment? With the objective of exploring this hypothesis, we decided to perform the ISWT in healthy individuals in order to determine the probability of oxygen desaturation at the end of the test.

Methods

This was a cross-sectional study involving healthy subjects who attended a private fitness center in the city of Campinas, Brazil. All of the enrolled subjects attended the fitness center in order to keep physically active and in good health, and none were professional athletes. They were invited to participate in the study and agreed to perform the tests included in the protocol.

The study was approved by the Research Ethics Committee of the Universidade Estadual de Campinas (Unicamp, State University at Campinas) Hospital de Clínicas, located in the city of Campinas, Brazil, and all participants gave written informed consent.

Subjects were considered ineligible for the ISWT if they had a history of lung or heart disease or any other health condition that might preclude the performance of the ISWT. A standard questionnaire was applied to all participants to ensure that they did not meet any of the exclusion criteria.
A digital peak flow meter (Koko Peak Pro 6; Ferraris Cardiorespiratory PDS Healthcare Products Inc., Louisville, CO, USA) was used in order to determine pre-ISWT FEV$_1$ and FEV$_6$. The FEV$_1$/FEV$_6$ ratio was calculated by the device and was displayed on the screen. Each subject performed at least three forced expiratory maneuvers after maximal inspiratory maneuvers, the best maneuver being automatically chosen by the peak flow meter.

Pre-ISWT HR and oxygen saturation were determined with a pulse oximeter equipped with a finger probe (Nonin Medical, Inc., Plymouth, MN, USA). Fingernail polish, if worn by the subject, was removed before testing. In order to guarantee an accurate assessment of oxygen saturation, the principal investigator checked that the pulse oximeter showed an acceptable pulse signal and that the oximeter light was green and pulsing in synchrony with the HR before the beginning of the tests.

The protocol used for the ISWT was the 12-level version proposed by Singh et al.\textsuperscript{(7)} for functional capacity evaluation in patients with COPD. All participants were tested under standardized conditions by the same investigator. The walking course was level, being 10 m in length. It was delimited by two cones inset 0.5 m from either end to avoid the need for abrupt changes in direction. The speed at which subjects walked was dictated by an audio signal played on a portable microcomputer. Each participant received a standardized explanation (“you should walk at a steady pace, aiming to turn around whenever you hear the signal; you should continue to walk until you feel that you are unable to maintain the required speed”). At the first level of the test, the calculated walking speed was 0.5 m/s and the number of expected shuttles was 3; at the twelfth level, walking speed was 2.37 m/s and 14 shuttles were expected. All subjects were carefully observed during the test so that they would not exceed their exercise limit.

Oxygen saturation was also measured immediately after the end of the ISWT. For the purpose of data analysis, oxygen desaturation was defined as a ≥ 4% decrease in oxygen saturation (SpO$_2$) from baseline ($\Delta$sat = oxygen saturation at rest − oxygen saturation immediately after the ISWT). This 4% decrease in oxygen saturation was validated in studies of exercise-induced hypoxemia during maximal exercise tests in athletes.\textsuperscript{(8)}

Maximum incremental shuttle walk distance (ISWD) was defined as the maximum distance that the subjects were able to walk during the ISWT.

| Variable          | OD (n = 17)       | No OD (n = 66)      | p     |
|-------------------|-------------------|---------------------|-------|
| Age               | 38.65 ± 13.77     | 34.12 ± 12.13       | NS    |
| BMI               | 26.59 ± 3.85      | 23.71 ± 3.14        | 0.01  |
| FEV$_1$           | 3.53 ± 0.67       | 3.80 ± 0.84         | NS    |
| FEV$_6$           | 4.34 ± 0.56       | 4.48 ± 0.93         | NS    |
| FEV$_1$/FEV$_6$   | 0.83 ± 0.11       | 0.84 ± 0.08         | NS    |
| LLN               | 3.95 ± 0.68       | 3.82 ± 0.78         | NS    |
| Initial HR, bpm   | 73.76 ± 10.16     | 75.47 ± 13.06       | NS    |
| Final HR, bpm     | 160.47 ± 20.59    | 162.91 ± 17.72      | NS    |
| Initial SpO$_2$, %| 97.88 ± 0.99      | 97.99 ± 1.03        | NS    |
| Final SpO$_2$, %  | 93.12 ± 1.76      | 97.08 ± 1.46        | 0.0001|
| $\Delta$ SpO$_2$ | 4.77 ± 1.15       | 0.91 ± 1.27         | 0.0001|
| ISWD              | 956.50 ± 127.10   | 958.80 ± 151.80     | NS    |
| Maximal HR, bpm   | 181.53 ± 13.96    | 185.88 ± 12.13      | NS    |
| Maximal HR, %     | 88.29 ± 9.34      | 87.64 ± 9.62        | NS    |
| Recovery HR, %    | 91.24 ± 15.16     | 92.24 ± 17.93       | NS    |
| Recovery SpO$_2$, %| 97.29 ± 0.99    | 97.70 ± 1.07        | NS    |

OD: oxygen desaturation; BMI: body mass index; ISWD: incremental shuttle walk distance; LLN: lower limit of normality; and NS: not significant. *Values expressed as mean ± SD.
A ≥ 4% decrease in oxygen saturation was used in order to divide the study population into two groups. The Anderson–Darling test was applied to the measured variables and the demographic characteristics of the two groups to determine their distribution. Variables with normal distribution were analyzed with the Student’s t-test. Variables with non-normal distribution were analyzed with the Wilcoxon test. Categorical data were compared by the chi-square test or Fisher’s exact test. The statistical analysis was performed with the SAS software, version 8 (SAS Institute, Inc., Cary, NC, USA). Differences were considered significant at p < 0.05.

## Results

Eighty-three individuals who attended a fitness center in the city of Campinas, Brazil, were invited and agreed to participate in the study. Of those, 55 were male and 28 were female. Only 1 was a smoker. The mean age was 35.05 ± 12.53 years, the median being 32 years. The mean body mass index (BMI) was 24.30 ± 3.47 kg/m², the median being 24.5 kg/m². The mean resting HR was 75.12 ± 12.48 bpm, the median being 73 bpm. The mean FEV\(_1\) was 4.45 ± 0.87 L, the median being 4.38 L. The mean FEV\(_1\)/FVC ratio was 0.82. In all enrolled subjects, measured FEV\(_1\) was above the lower limit of the predicted FVC (as determined by the equations devised for the Brazilian population), and all subjects had a FEV\(_1\)/FVC ratio ≥ 0.8. These findings allow the assumption that none of the participants had restrictive or obstructive lung disease (Table 1).

The mean ISWD was 958.30 ± 146.32 m, the median being 1,020 m. The mean post-ISWT HR was 162.41 ± 18.24 bpm, the median being 166 bpm. The mean post-ISWT SpO\(_2\) was 96.27 ± 2.21%. In 11 subjects, post-ISWT oxygen saturation values were higher than pre-ISWT oxygen saturation values. In 17 subjects, oxygen saturation had decreased by ≥ 4% by the end of the test. In 2 subjects, SpO\(_2\) was < 92% (Table 2).

The study population was divided into two groups on the basis of the presence of a post-ISWT oxygen desaturation ≥ 4%. No differences were found between the two groups regarding age, gender, FEV\(_1\), FEV\(_1\)/FVC, initial oxygen saturation (pre-ISWT SpO\(_2\)), ISWD, pre-ISWT HR, post-ISWT HR, or percentage of maximal HR (Table 1). The BMI was significantly higher in those who developed oxygen desaturation (p = 0.01), and post-ISWT SpO\(_2\) was significantly different between the two groups (p < 0.0001).

## Discussion

In 66 subjects, post-ISWT oxygen saturation values were quite similar to pre-ISWT oxygen saturation values, a finding that was expected because of the intensity of the exercise performed. In 11 subjects, post-ISWT SpO\(_2\) values were higher than pre-ISWT SpO\(_2\) values. This finding is not unusual, given that physical activity improves ventilation and alveolar recruitment. However, 17 (20.7%) of the 83 individuals in the study sample showed a significant drop in oxygen saturation during the ISWT (Δsat ≥ 4%). This was an unexpected finding, and there is little information in the literature regarding what happens with oxygen saturation after the ISWT in healthy subjects.

Exercise-induced hypoxemia in athletes is arbitrarily defined as a decrease in PaO\(_2\) of approximately 7.5 mmHg,\(^7\) an SaO\(_2\) below 95%, or both; extreme cases will show an SaO\(_2\) of less than 88%.\(^8\) Oxygen uptake increases during exercise in order to meet the needs imposed by an increased metabolic rate and correlate with work intensity until all subjects achieve maximal oxygen uptake. Each step of oxygen transport from ambient air to the cells can limit whole-body oxygen uptake, and circulation has been considered the most important factor limiting maximal oxygen uptake during large muscle mass exercise.

A decrease in PaO\(_2\) and SaO\(_2\) is quite common during maximal ergometer rowing.\(^\text{11}\) In such subjects, cardiac output can exceed 30 L/min; under such circumstances, the ability to renew alveolar air and maintain high oxygen partial pressures, the diffusion resistance to oxygen at the alveolar-capillary membrane, the reduction in red blood cell transit time in the pulmonary capillary,
and the increased probability of ventilation/perfusion mismatch are critically important to oxygen uptake.\textsuperscript{[12]}

The prevalence of exercise-induced hypoxemia seems to be as high as 50%.\textsuperscript{[13]} Exercise intensity determines the degree of hypoxemia.\textsuperscript{[14]} Oxygen desaturation is also more pronounced during whole-body exercise, such as rowing or running, than during leg exercise, and leg exercise is more capable of inducing hypoxemia than is arm exercise.\textsuperscript{[14]} This suggests that the amount of muscle mass involved in the exercise influences the development of oxygen desaturation.

In 1984, Dempsey et al.\textsuperscript{[15]} studied the incidence of exercise-induced arterial hypoxemia in 16 highly trained healthy runners who were capable of achieving and sustaining very high metabolic rates, including a maximal oxygen uptake of 72 ± 2 mL/kg. Arterial blood gases and acid-base status were determined at each load of a progressive short-term exercise test and repeatedly determined during constant-load treadmill running. Three types of response were encountered and were quite reproducible within subjects: four runners maintained PaO\(_2\) within 10 mmHg of resting values; another four showed a decrease of 10-15 mmHg in PaO\(_2\); and the remaining eight runners showed remarkably decreased PaO\(_2\). The decrease in PaO\(_2\) ranged from 21 mmHg to 35 mmHg, PaO\(_2\) having decreased to less than 75 mmHg in all cases and to less than 60 mmHg in two cases. During constant-load exercise, PaO\(_2\) was often maintained during the initial 30 s, when hyperventilation was greatest; subsequently, hypoxemia occurred, the severity of hypoxemia having either remained the same or worsened over the ensuing 3-4 min in most of the cases. The most severe hypoxemia during heavy exercise was associated with an (estimated) alveolar oxygen tension to a (measured) PaO\(_2\) difference in excess of 40 mmHg. The analysis of all of the variables measured during the investigation led the authors to hypothesize that the observed hypoxemia was attributable to a diffusion limitation secondary to very short red cell transit times in at least a portion of the pulmonary circulation; such short transit times can occur at high metabolic rates. Tidal breathing during heavy exercise can frequently exceed the maximal flow-volume curve, and hyperventilation can be limited by the mechanical load on the chest wall secondary to increased pulmonary impedance, a situation that can also impair the renewal of alveolar air.

Although it has been described as an incremental field walking test that produces a symptom-limited maximal performance, the ISWT cannot be compared with the maximal exercise tests cited above. Nevertheless, 17 healthy subjects showed oxygen desaturation after the ISWT in the present study. The only significant difference between the individuals who developed oxygen desaturation and those who did not was that the BMI was higher in the former. This finding is consistent with the hypothesis that the lungs, during physical activities that cause the HR to get closest to the maximal HR expected for a given subject, are unable to arterialize the fast flowing blood, especially in those subjects whose needs are amplified because of a higher body mass. Although Durand et al.\textsuperscript{[16]} found no differences in height, weight, or lung volume between athletes who developed oxygen desaturation and those who did not, it can be argued that the proportions of those variables are more important than their absolute values.

Our findings and the data from the literature lead to a worrisome possibility: oxygen desaturation during aerobic activity is probably more common than previously thought and can pose a threat to high-performance athletes that has been systematically overlooked. Although the occurrence of oxygen desaturation is acknowledged in studies that date back to the second half of the last century, none of those studies elaborated on the potential harmful effects of such periods of intermittent hypoxemia.

We are unaware of any evaluation protocol for high-performance aerobic training that includes the determination of exercise-induced oxygen desaturation. Given that sudden death is relatively common in athletes, screening for oxygen desaturation seems justified.

Sudden cardiac death (SCD) is considered the leading cause of death in young athletes. The true incidence of SCD is unknown and highly underestimated. The studies reporting the highest incidence estimated that up to 110 deaths occur each year in young athletes, which is equivalent to 1 death every 3 days in the United States.\textsuperscript{[17]} The available evidence points to a structural cardiac abnormality as the underlying cause of SCD. Hypertrophic cardiomyopathy and coronary artery anomalies account for approximately 25% and 14%, respectively, of all SCDs in the
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Brugada syndrome is traditionally thought of as a primary electrical cardiac disease arising in myocardium that is otherwise structurally normal. However, magnetic resonance imaging, positron emission tomography, and pathological evaluation of biopsy specimens have identified structural abnormalities in many patients with a diagnosis of Brugada syndrome, including fibrofatty replacement of the right ventricular free wall and fibrotic disruption of the right bundle branch.

It is established in the literature that Brugada syndrome is the result of an autosomal dominant mutation in the SCN5A gene on chromosome 3, resulting in a loss of function sodium channel abnormality. It has become increasingly clear that ion channel gene expression is highly dynamic and can respond to many environmental stimuli. Hypoxemia is possibly one of these stimuli. Therefore, a genetic predisposition to cardiac arrhythmia does not preclude the superimposition of hypoxemia causing the sudden deaths of young people or athletes.

The data in the present study and the accumulated knowledge regarding oxygen desaturation during physical activity raise the hypothesis that hypoxemia during exercise can be dangerous and suggest that it is advisable to include a screening test for oxygen desaturation in the evaluation protocols for endurance athletes. Further studies are needed in order to explore this hypothesis.

In conclusion, because of the possibility of oxygen desaturation in healthy individuals undergoing the ISWT, the use of the ISWT to predict the presence of subtle respiratory abnormalities undetected by submaximal tests such as the 6MWT can be misleading. The finding that oxygen desaturation is common in healthy subjects undergoing the ISWT adds to the knowledge that oxygen desaturation during intense physical activity is quite common and can have deleterious effects.

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