Predictors of oxygen desaturation during the six-minute walk test in patients with cystic fibrosis*

Preditores da dessaturação do oxigênio no teste da caminhada de seis minutos em pacientes com fibrose cística

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Abstract

Objective: To identify the predictive factors of oxygen desaturation during the six-minute walk test (6MWT) in patients with cystic fibrosis (CF). **Methods:** Prospective cross-sectional study involving clinically stable patients with CF aged ≥ 10 years. The patients were submitted to nutritional evaluations, oral glucose tolerance tests, pulmonary function tests, chest X-rays and 6MWTs. **Results:** The study included 88 patients (43 females and 45 males; mean age, 19.9 ± 7.2 years; mean FEV_1, 65.4 ± 28.4%). We observed oxygen desaturation in 13 patients (OD+ group) and no oxygen desaturation in 75 (OD– group). In comparison with OD– group patients, OD+ group patients presented higher mean age ($p = 0.004$), worse clinical score ($p < 0.001$), worse radiological score ($p < 0.001$), higher incidence of glucose intolerance ($p = 0.004$), lower incidence of methicillin-sensitive *Staphylococcus aureus* infection ($p < 0.001$), higher incidence of methicillin-resistant *S. aureus* infection ($p = 0.016$), higher incidence of *Pseudomonas aeruginosa* infection ($p = 0.008$), lower mean resting SpO_2 ($p < 0.001$) and lower mean FEV_1 ($p < 0.001$). In the logistic regression analysis, oxygen desaturation during the 6MWT correlated with resting SpO_2 (OR = 0.305, $p < 0.001$) and FEV_1 (OR = 0.882, $p = 0.025$). The parameters maximizing the predictive value for oxygen desaturation were resting $SpO_2 < 96\%$ and $FEV_1 < 40\%$. In this sample, 15% of the patients with CF aged ≥ 10 years presented oxygen desaturation during the 6MWT. **Conclusions:** Resting $SpO_2 < 96\%$ and $FEV_1 < 40\%$ can predict oxygen desaturation during the 6MWT.

Keywords: Cystic fibrosis; Respiratory function tests; Exercise tolerance.

Resumo

Objetivo: Identificar os fatores preditores de dessaturação de oxigênio durante o teste de caminhada de seis minutos (TC6) em pacientes com fibrose cística (FC). **Métodos:** Estudo transversal e prospectivo em pacientes com FC clinicamente estáveis com idade superior a 10 anos. Os pacientes foram submetidos à avaliação nutricional, teste oral de tolerância à glicose, testes de função pulmonar, exame radiológico do tórax e TC6. **Resultados:** Foram incluídos 88 pacientes (43 femininos e 45 masculinos) com média de idade de 19,9 ± 7,2 anos e média de VEF_1 de 65,4 ± 28,4%. Observamos que 75 pacientes apresentaram-se sem dessaturação de oxigênio (SD) e 13 com dessaturação (CD). Os pacientes do grupo CD apresentaram maior média de idade ($p = 0,004$), pior escore clínico ($p < 0,001$), pior escore radiológico ($p < 0,001$), maior frequência de intolerância à glicose ($p = 0,004$), menor frequência de infecção bacteriana por *Staphylococcus aureus* sensível à meticilina ($p < 0,001$), maior frequência de infecção por *S. aureus* resistente à meticilina ($p = 0,016$) e por *Pseudomonas aeruginosa* ($p = 0,008$) e menor valor médio de SpO_2 em repouso ($p < 0,001$) e de VEF_1 ($p < 0,001$) do que os pacientes do grupo SD. Na análise de regressão logística, SpO_2 em repouso (OR = 0,305, $p < 0,001$) e VEF_1 (OR = 0,882, $p = 0,025$) se associaram com a dessaturação de oxigênio no TC6. Os parâmetros que maximizaram o valor preditivo para dessaturação de oxigênio foram SpO_2 em repouso < 96% e $VEF_1 < 40\%$. Nessa amostra, 15% dos pacientes com FC com mais de 10 anos apresentaram dessaturação de oxigênio no TC6. **Conclusões:** Os parâmetros SpO_2 em repouso < 96% e $VEF_1 < 40\%$ contribuem como preditores de dessaturação no TC6.

Descritores: Fibrose cística; Testes de função respiratória; Tolerância ao exercício.

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Introduction

In individuals with cystic fibrosis (CF), pulmonary involvement is the leading cause of morbidity and mortality and is often accompanied by inability to engage in physical activity, progressing to inability to perform activities of daily living.[1]

The ability to perform activities of daily living is mentioned as the major determinant of quality of life in CF.[2] Physical activity is recommended as a therapeutic measure in patients with CF and provides significant benefits.[3]

Exercise limitation alone has also been considered a determinant of mortality in patients with CF, regardless of age or pulmonary function. Exercise performance can be affected by many factors, such as progression of the pulmonary disease, dynamic hyperinflation, nutritional depletion and increased energy demands.[4]

The six-minute walk test (6MWT) is a submaximal exercise test that can be performed by patients who do not tolerate maximal exercise tests. The test is simple, requires low-cost equipment and is reproducible. In addition, it is considered safe because patients set their own limits during the exercise. The ability to walk a certain distance reflects the quality of life of patients and their ability to perform activities of daily living.[5]

One group of authors[6] evaluated 34 patients with primary pulmonary hypertension in order to correlate six-minute walk distance (6MWD), oxygen desaturation during the 6MWT and mortality. In conclusion, it was demonstrated that these parameters are useful in screening patients for inclusion on the transplant waiting list. Another study involving 197 patients with idiopathic pulmonary fibrosis demonstrated that oxygen desaturation during the 6MWT is associated with increased mortality.[7]

A previous study[8] evaluated submaximal exercise capacity in 41 patients with CF (mean age, 23.7 years) using the 6MWT. It was observed that, although 6MWD was not significantly associated with pulmonary function impairment ($p = 0.07$), oxygen desaturation during the test was significantly higher in the patients with greater pulmonary function impairment ($p = 0.039$). The test would be useful in identifying patients with oxygen desaturation and submaximal exercise limitation. However, the factors that can lead to oxygen desaturation in patients with CF during the 6MWT have yet to be described in the literature.

The objective of the present study was to determine the predictive factors of oxygen desaturation during the 6MWT in patients with CF.

Methods

This was a prospective cross-sectional study carried out at a single center. The study sequentially included patient volunteers treated via the Pediatric Program or via the Program for Adults with CF of the *Hospital de Clínicas de Porto Alegre* (HCPA, Porto Alegre *Hospital de Clínicas*). All patients were submitted to nutritional evaluations, oral glucose tolerance tests (OGTTs), pulmonary function tests, chest X-rays and 6MWTs. The study protocol was approved by the HCPA Research Ethics Committee, and all participants gave written informed consent.

The study included patients with CF aged 10 years or older. The diagnosis was confirmed in accordance with the criteria established in the Cystic Fibrosis Foundation Consensus statement.[9] All patients should be clinically stable (as defined in the consensus statement), without any change in medication within the last 30 days and with an interval of at least 30 days since the end of the last course of i.v. or p.o. antibiotics for the treatment of pulmonary exacerbation. Patients who refused to participate in the study were excluded, as were pregnant women and individuals with heart disease, orthopedic disorders or trauma-related injury, as well as patients who presented any other clinical condition that prevented the performance of the tests used in the study.

All evaluations and tests used in the study were performed within a maximum period of one week.

The clinical score was determined by a member of the team of physicians of the Program for Adults with Cystic Fibrosis, using the Shwachman-Kulczycki scoring system.[10]

Nutritional status was assessed using the body mass index (BMI) and the BMI percentile. The patients were classified by nutritional status into three groups: normal nutritional status, BMI > 20 kg/m^2 (patients aged 18 or older) or BMI percentile > 25 (patients younger than 18 years); at nutritional risk, BMI between 18.5 and 20.0 kg/m^2 (patients aged 18 or older)

or BMI percentile between 10 and 25 (patients younger than 18 years); and impaired nutritional status, BMI < 18.5 kg/m^2 (patients aged 18 or older) or BMI percentile < 10 (patients younger than 18 years).[11,12]

All patients underwent 2-h OGTTs, with the exception of those previously diagnosed with diabetes mellitus based on fasting glycemia. After fasting the previous night, the individuals ingested glucose solution (1.75 g/kg of body weight; maximum, 75 g) in less than 5 min, in accordance with the American Diabetes Association guidelines.[13] Blood samples were collected at 0 and at 120 min for the measurement of serum glucose levels. The patients were classified by glucose tolerance as follows: normal glucose tolerance, serum glucose levels after 2 h < 140 mg/dL; glucose intolerance, serum glucose levels after 2 h between 140 and 200 mg/dL; CF-related diabetes mellitus, serum glucose levels after 2 h > 200 mg/dL or two fasting measurements of serum glucose levels > 126 mg/dL.

All patients underwent conventional chest X-rays. The radiographic score was calculated by a radiologist who was blinded to the clinical condition and the identification of the patients. The Brasfield scoring system was used.[14]

The bacteriological tests on sputum performed in the HCPA Department of Microbiology were reviewed. The following pathogens were identified: *Staphylococcus aureus*; *Pseudomonas aeruginosa*; and *Burkholderia cepacia*. Each pathogen considered should have been identified at least twice in sputum samples collected during routine clinical visits within the 12 months preceding the study.

Spirometry was performed using a Jaeger spirometer (v4.31a; Jaeger, Würzburg, Germany). The values of FVC, FEV_1 and the FEV_1/FVC ratio were recorded. The test was performed in accordance with the acceptance and reproducibility criteria established by the Brazilian Thoracic Association.[15] All parameters were expressed as percentage of predicted for age, height and gender.[16]

Maximal static respiratory pressures were measured using a digital vacuum manometer (MVD –300/+300, version 1.0; Microhard, Porto Alegre, Brazil). The MIP was measured at RV, whereas the MEP was measured at TLC. The MIP and MEP values were expressed as % of predicted. For children and adolescents, the predicted values were obtained from the study by Wilson et al.,[17] whereas, for adults, the predicted values were obtained from the study by Neder et al..[18]

The 6MWT was performed in accordance with the American Thoracic Society guidelines.[5] The distance that the patient was able to walk in a period of 6 min was determined in a 30-m corridor. The total distance walked in 6 min was measured in meters and as % of predicted. The predicted distance was calculated using normality equations for adults[19] and children.[20] Resting and post-6MWT SpO_2 was measured using a pulse oximeter (NPB-40; Nellcor Puritan Bennett; Pleasanton, CA, USA). Resting and post-6MWT HR, RR and dyspnea perception were recorded using the Borg scale, as were pre- and post-6MWT perception of lower limb fatigue.[21]

Based on the 6MWT results, the patients were classified into two groups: oxygen desaturation group (OD+ group) and no oxygen desaturation group (OD– group). Individuals whose difference between post-6MWT SpO_2 and resting SpO_2 was

Table 1 - General characteristics of the patients with cystic fibrosis in the sample.

Variable	Patients (n = 88)
Gender, male/ female	45 (51.1)/ 43 (48.9)
Oxygen desaturation/ No oxygen desaturation	13 (14.8)/ 75 (85.2)
White, yes/ no	84 (95.5)/ 4 (4.5)
Age, years	19.9 ± 7.2
Age at diagnosis, years[a]	2.5 (11.0)
BMI, kg/m^2	19.7 ± 2.4
Nutritional status	
Normal	59 (67.0)
At risk	15 (17.0)
Impaired	14 (15.9)
S-K score, points[a]	75 (25)
Brasfield score, points[a]	17 (8)
FEV_1, % of predicted	65.4 ± 28.4
FVC, % of predicted	74.6 ± 23.7
FEV_1/FVC, % of predicted	84.0 ± 17.2

BMI: body mass index; and S-K: Shwachman-Kulczycki. Results expressed as n (%) or as mean ± SD, except where indicated. [a]Results expressed as median (interquartile range).

lower than or equal to 4% were considered to belong to the OD– group, whereas individuals whose difference was greater than 4% were considered to belong to the OD+ group.[22]

Data were expressed as number of cases (proportion), as mean ± SD, or as median (interquartile range). Categorical variables were compared using the chi-square test with adjusted standardized residuals, and Yates' correction or Fisher's exact test was used when necessary. The independent sample t-test was used to compare the two groups in terms of continuous variables with normal distribution. The Mann-Whitney U test was used to compare the two groups in terms of ordinal variables or continuous variables without normal distribution. The non-collinear variables that reached significance ($p < 0.01$) in the univariate analysis, adjusted for gender and age, were included in a binary logistic regression model using the forward conditional method. The most significant variable of this multivariate analysis was correlated with the outcome (oxygen desaturation or no oxygen desaturation) and submitted to the ROC curve to determine the cut-off point maximizing the predictive value. The sensitivity, specificity, positive predictive value and negative predictive value of the predictive index were calculated.

Data were analyzed using the program Statistical Package for the Social Sciences, version 15.0 (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $p < 0.05$. All statistical tests used were two-tailed.

Results

Between March of 2007 and August of 2008, 107 patients with CF were evaluated. Of those, 10 refused to participate in the study and 9 were excluded because they did not complete all the tests required by the protocol. Therefore, 88 patients completed the study.

Table 1 presents the general characteristics of the patients with CF. The mean age was 19.9 ± 7.2 years (range, 10-49 years). Regarding gender, 45 patients were male and

Table 2 - Characteristics of the patients with cystic fibrosis by presence of oxygen desaturation during the six-minute walk test.

Variable	Oxygen desaturation (n = 13)	No oxygen desaturation (n = 75)	p
Gender, male/female	7/6	38/37	0.832
Age, years	25.1 ± 8.6	19.0 ± 6.6	0.004
White	12 (92.3)	72 (96.0)	0.479
Age at diagnosis, years[a]	2.8 (12)	2.0 (11)	0.511
S-K clinical score, points[a]	60 (10)	80 (21)	< 0.001
Brasfield score, points[a]	10 (7)	18 (7)	< 0.001
Nutritional status			
Normal	8 (61.5)	51 (68.0)	0.746
At risk	2 (15.4)	13 (17.3)	
Impaired	3 (23.1)	11 (14.7)	
Pancreatic insufficiency	12 (92.3)	60 (80.0)	0.448
Glucose tolerance			
Normal	4 (30.8)*	55 (73.3)*	0.004
Intolerance	6 (46.2)*	9 (12.0)*	
Diabetes mellitus	3 (23.1)	11 (14.7)	
Bacterial infection			
MRSA	6 (46.2)	11 (14.7)	0.016
MSSA	3 (23.1)	57 (76.0)	< 0.001o1
Pseudomonas aeruginosa	13 (100.0)	48 (64.0)	0.008
Burkholderia cepacia	5 (38.5)	11 (14.7)	0.055

S-K: Shwachman-Kulczycki; MRSA: methicillin-sensitive *Staphylococcus aureus*, and MSSA: methicillin-sensitive *S. aureus.* Results expressed as n (%) or as mean ± SD, except where indicated. [a]Results expressed as median (interquartile range). The chi-square test was used for categorical variables; *adjusted standardized residual > 1.96 or < –1.96 (implies significantly different percentages). The t-test or the Mann-Whitney U test was used for quantitative data.

43 were female. Most of the patients (84) were White (4 were non-White). The mean BMI was 19.7 ± 2.4 kg/m² (range, 13.3-26.1 kg/m²). In our sample, 67% of the patients were classified as well-nourished, 17% were classified as being at nutritional risk and 16% were classified as malnourished. The mean FEV_1 was 65.4 ± 28.4%.

In this sample of patients, 75 (85%) were classified as belonging to the OD− group and 13 (15%) were classified as belonging to the OD+ group. Table 2 shows the characteristics of the patients with CF by presence of oxygen desaturation during the 6MWT. In comparison with OD− group patients, OD+ group patients presented higher mean age (p = 0.004), worse clinical score (p < 0.001), worse radiological score (p < 0.001), higher incidence of glucose intolerance (p = 0.004), lower incidence of methicillin-sensitive *S. aureus* infection (MSSA, p < 0.001), higher incidence of methicillin-resistant *S. aureus* infection (MRSA, p = 0.016) and higher incidence of *Pseudomonas aeruginosa* infection (p = 0.008). There were no significant associations between the groups in terms of age at diagnosis (p = 0.511), gender (p = 0.832), nutritional status (p = 0.746), incidence of pancreatic insufficiency (p = 0.448) or incidence of *B. cepacia* infection (p = 0.055).

Table 3 summarizes the results of the 6MWTs and the pulmonary function tests by the presence of oxygen desaturation. In comparison with OD− group patients, OD+ group patients presented significantly shorter 6MWD (p = 0.005), significantly lower resting SpO_2 (p < 0.001) and post-6MWT SpO_2 (p < 0.001), as well as significantly lower FEV_1 (p < 0.001), FVC in % of predicted (p < 0.001) and FEV_1/FVC in % of predicted (p < 0.001). In addition, OD+ group patients presented significantly higher post-6MWT RR (p = 0.005) and post-6MWT Borg dyspnea score (p < 0.001).

Among the variables included in the binary logistic regression, the following were excluded from the final equation: age (p = 0.996); clinical score (p = 0.076); *B. cepacia* infection (p = 0.533); *P. aeruginosa* infection (p = 0.229); MSSA infection (p = 0.084); MRSA infection (p = 0.582); and the presence of glucose intolerance (p = 0.404). Two equation models were

Table 3 - Results of the six-minute walk tests and the pulmonary function tests by presence of oxygen desaturation in patients with cystic fibrosis.

Variable	Oxygen desaturation (n = 13)	No oxygen desaturation (n = 75)	p
6MWT			
6MWD, m	524.7 ± 114.6	595.4 ± 75.5	0.005
6MWD, % of predicted	70.9 ± 15.6	78.0 ± 9.3	0.025
Resting SpO_2, %	93.7 ± 2.4	97.5 ± 1.3	< 0.001
Post-6MWT SpO_2, %	81.3 ± 6.2	97.2 ± 2.0	< 0.001
Resting HR, bpm	96.5 ± 16.4	90.5 ± 13.0	0.148
Post-6MWT HR, bpm	150.2 ± 13.8	140.1 ± 73.4	0.624
Resting RR, breaths/min	20.6 ± 4.8	19.3 ± 4.0	0.312
Post-6MWT RR, breaths/min	30.5 ± 6.6	25.7 ± 5.2	0.005
Resting Borg dyspnea score, mean (II)	0 (0.9)	0 (0)	0.400
Post-6MWT Borg dyspnea score, mean (II)	3.5 (4)	0.5 (2)	0.001
Resting Borg fatigue score MMII, mean (II)	0 (0)	0 (1)	0.558
Post-6MWT Borg fatigue score MMII, mean (II)	2 (4)	1 (3)	0.013
FEV_1, % of predicted	27.1 ± 8.2	72.2 ± 25.1	< 0.001
FVC, % of predicted	41.9 ± 12.2	80.3 ± 20.3	< 0.001
FEV_1/FVC, % of predicted	65.3 ± 13.2	87.3 ± 15.7	< 0.001
MIP, % of predicted	103.7 ± 41.2	112.7 ± 34.1	0.129
MEP, % of predicted	108.6 ± 33.1	104.2 ± 28.4	0.613

6MWT: six-minute walk test; 6MWD: six-minute walk distance; and MMII: lower limbs. Results expressed as mean ± SD or as median (interquartile range). The t-test or the Mann-Whitney U test was used for quantitative data.

generated. In the first model, the variable that was significantly and independently associated with oxygen desaturation during the 6MWT was resting SpO_2 ($\beta = -1.187$; $p < 0.001$; OR = 0.305; 95% CI: 0.172-0.542). In the second model, the variable that was significantly associated with oxygen desaturation during the 6MWT was FEV_1 ($\beta = -0.126$; $p = 0.025$; OR = 0.882; 95% CI: 0.790-0.984).

When resting SpO_2 was submitted to the ROC curve, the area under the curve was 0.91 ($p < 0.01$) and the cut-off point maximizing the predictive value for the outcome post-6MWT oxygen desaturation was 96% (sensitivity, 96%; specificity, 77%; positive predictive value, 96%; and negative predictive value, 77%).

When FEV_1 was submitted to the ROC curve, the area under the curve was 0.97 ($p < 0.001$) and the cut-off point maximizing the predictive value for the outcome post-6MWT oxygen desaturation was 96% (sensitivity, 100%; specificity, 89%; positive predictive value, 62%; and negative predictive value, 100%).

The combination of resting $SpO_2 < 96\%$ and $FEV_1 < 40\%$ to predict the outcome post-6MWT oxygen desaturation obtained a sensitivity of 96%, a specificity of 83%, a positive predictive value of 97% and a negative predictive value of 77%.

Discussion

The principal finding of this prospective cross-sectional study was the fact that 15% of the patients with CF aged 10 years or older presented significant oxygen desaturation during the 6MWT. The variables that were independently associated with oxygen desaturation were resting SpO_2 and FEV_1. In addition, resting $SpO_2 < 96\%$ and $FEV_1 < 40\%$ maximized the identification of patients who were likely to present oxygen desaturation during the 6MWT.

In the present study, we observed that the 6MWD was significantly shorter in the OD+ group. One group of authors[23] studied 25 adult patients with CF (mean age, 25 ± 5 years; FEV_1, 69 ± 23% of predicted; and BMI, 21 ± 2 kg/m^2). Those authors observed that 9 of the 25 patients presented post-6MWT oxygen desaturation ($SpO_2 < 90\%$). Although oxygen desaturation was significantly associated with lower resting FEV_1, higher resting RV and lower resting SpO_2, the OD+ group and the OD− group did not differ significantly in terms of 6MWD. A possible explanation for the fact that the two groups did not differ in terms of 6MWD is that the study included only patients with mild to moderate disease, with a small number of patients. Another group of authors[24] conducted a study involving 42 patients with COPD and 28 patients with severe chronic asthma. The patients with COPD and the asthma patients, respectively, had a mean age of 62.3 ± 9.1 and 57.4 ± 12.9 years, as well as FEV_1 of 40,3 ± 21.6 and 56.7 ± 20.6 (% of predicted). Despite the higher age bracket and the greater functional severity of the patients included, oxygen desaturation was not found to be associated with 6MWD.

The identification of oxygen desaturation during the 6MWT seems to have significant clinical and prognostic value over the course of the disease. One group of authors[6] conducted a study involving 34 patients with primary pulmonary hypertension (mean age, 44.3 ± 11.9 years). That study demonstrated that 6MWD and post-6MWT oxygen desaturation could be useful in screening patients for inclusion on the lung transplant list. Another important study[22] involving 536 patients in the preoperative period of pulmonary resection demonstrated that oxygen desaturation during a submaximal step climbing test is an important predictor of postoperative complications.

The prognostic value of the 6MWT was demonstrated in a study involving 197 patients with idiopathic pulmonary fibrosis.[7] That study demonstrated that, when patients were stratified by presence of oxygen desaturation, OD+ group patients were older, as well as having greater pulmonary function impairment, lower DLCO and a shorter 6MWD. Six months after the initial evaluation, it was found that oxygen desaturation could predict which patients would be at greater risk of mortality, which was not determined by 6MWD.

One group of authors[25] conducted a study involving 20 patients with COPD who presented oxygen desaturation (mean FEV_1, 61.1 ± 3.2% of predicted). The objective of that study was to assess the effect of rehabilitation on post-6MWT oxygen desaturation. In conclusion, that study demonstrated that an exercise program can act on oxygen desaturation. Although 13 patients continued to present oxygen desaturation after the exercise program, there was a reduction

in dyspnea and an increase in 6MWD in those patients.

The pathophysiological mechanism of oxygen desaturation, as well as its predictive factors, needs to be better understood in many pulmonary and cardiac diseases. One group of authors[26] conducted a study with the objective of determining the predictors of oxygen desaturation during a submaximal exercise test in 8,000 patients aged 35 years or older and presenting different types of pulmonary disease. Those authors observed that the risk of oxygen desaturation was greater in the patients with low DLCO. However, we did not evaluate this factor in our study.

Airway bacterial infection is an important factor related to mortality and morbidity in patients with CF. Patients with CF who are infected with *P. aeruginosa* or *B. cepacia* can suffer a rapid decline in pulmonary function or worsening of their clinical status.[27,28] In contrast, glucose tolerance can play an important role in the decline in clinical status.[29,30] In our study, MRSA bacterial infection, *P. aeruginosa* bacterial infection and glucose tolerance impairment were associated with oxygen desaturation during the 6MWT, probably expressing the greater clinical severity related to these factors. Infection with *B. cepacia* was of borderline significance in the association with oxygen desaturation, suggesting a greater severity in patients infected with this bacterium, but the small number of patients infected with this bacterium in our sample affects this analysis. In contrast, MSSA infection was more frequent in OD– group patients, suggesting that the presence of this bacterium is a marker of lower pulmonary severity. However, these factors did not reach significance in the logistic regression analysis.

This study has some limitations. The study design was cross-sectional, which does not provide sufficient evidence to establish the temporal sequence of the association between oxygen desaturation during the 6MWT and FEV_1, nor does it allow determination of the prognostic importance of this finding. In addition, although we excluded most of the patients aged 10 years or older who were treated at our facility, the number of events in the OD+ group was low (13 patients).

The clinical importance of the present study involves the identification of patients with CF who present oxygen desaturation during exercise and might require oxygen therapy during physical activity. We showed that resting $SpO_2 < 96\%$ and $FEV_1 < 40\%$ were useful parameters in this screening. Another aspect to be examined in future cohort studies is whether oxygen desaturation is a more sensitive predictive factor of mortality than is 6MWD.

In conclusion, it was demonstrated that 15% of the patients with CF aged 10 years or older presented significant oxygen desaturation during the 6MWT and that the variables independently associated with this desaturation were resting SpO_2 and FEV_1. The cut-off point of 96% for resting SpO_2 and of 40% for FEV_1 in % of predicted maximized the predictive value for the outcome post-6MWT oxygen desaturation.

This population of patients should be prospectively monitored in order to obtain more complete estimates of the prognostic value of oxygen desaturation during the 6MWT and to determine the implications of treatment of this alteration on clinical status, exercise capacity, pulmonary hypertension and mortality in such patients.

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