

Evaluation of respiratory muscle strength and functional capacity in patients with cystic fibrosis

Cássio Magalhães da Silva e Silva¹, Adriele Mascarenhas Araujo², Anna Lúcia Lima Diniz da Silva³, Valdívnia Alves de Sousa³, Mansueto Gomes Neto⁴, Micheli Bernadone Saquetto¹

ABSTRACT

Objective: To correlate the respiratory muscle strength and functional capacity in patients with CF. **Method:** Cross-sectional study in adults with cystic fibrosis. Sampling data were cataloged in Microsoft Office Excel 2007 and the variables analyzed by SPSS version 20.0 using the Student t test and the Spearman coefficient. The level of significance adopted was $p < 0.05$. **Results:** We assessed 35 patients with cystic fibrosis (44.6 ± 19.0 years), the great majority of patients in FC ($n=22$) did not present weakness of the inspiratory muscles ($MIP -90,7 \pm 27.4$ cmH₂O). It was not found statistically significant differences only between the adult and elderly patients. There was a positive correlation between MIP and MEP and a six-minute walk test (6MWT) in participants with respiratory muscle weakness and in the elderly. There was statistically significant difference between the averages of the distance covered on the 6MWT and the maximal respiratory pressures with the average of what was envisaged for these variables. **Conclusion:** All groups presented limitation of respiratory strength and functional capacity. The correlations between the respiratory pressures with the 6MWT were low and small in adults and individuals without respiratory muscle weakness; moderate to high in the elderly; small to moderate in women; small and negative in men; and high in patients with respiratory muscle weakness.

Keywords: Cystic Fibrosis, Respiratory Muscles, Exercise Tolerance

¹ Physiotherapist, Assistant Professor, Federal University of Bahia – UFBA.

² Physiotherapist, Emergency and Intensive Care Unit Physiotherapy Resident of Octávio Mangabeira Specialized Hospital – SESAB.

³ Physiotherapist, Octávio Mangabeira Specialized Hospital – SESAB.

⁴ Physiotherapist, Adjunct Professor, Federal University of Bahia – UFBA.

Mailing address:
Instituto de Ciências da Saúde – ICS
Cássio Magalhães da Silva e Silva
Av. Reitor Miguel Calmon, s/n
Salvador – BA
CEP 40110-100
E-mail: cassioms@ufba.br

Received on June 17, 2016.

Accepted on November 28, 2016.

DOI: 10.5935/0104-7795.20160035

INTRODUCTION

During the last three decades, due mainly to early diagnosis, the implementation of treatment programs and the creation of specialized centers, the life expectancy of patients with cystic fibrosis (CF) born in developed countries has increased.¹ However, life expectancy of these patients is related to the severity and evolution of lung impairment associated with this disease.²

Respiratory changes of CF consist of pneumothorax, hemoptysis, nasal polyps and progressive chronic obstructive pulmonary disease, whose progression is the main cause of morbidity and mortality in patients with CF.²⁻⁵ The most relevant functional alterations include airflow obstruction, air trapping, and ventilatory deficiency. The evolution pattern of these alterations is characterized by a predominance of obstructive ventilatory disorder with early reduction of small airway flows and late impairment of forced vital capacity (FVC), whereas the total pulmonary capacity (TPC) is usually slightly increased, normal or reduced.⁵⁻⁷

Due to the respiratory conditions, the evaluation of respiratory muscle strength is an important parameter in clinical and functional respiratory practice, since respiratory muscles are responsible for the proper functioning of the respiratory system, and they maintain the adequate ventilation for gas exchange and consequent maintenance of activities of daily life.

The assessment of exercise tolerance and physical fitness of patients with CF is a sensitive measure to analyze the impact of this disease on daily activities, particularly in individuals at severe stages of the pathology.⁸

The 6-minute walk test (6MWT) assesses the functional capacity of healthy individuals or those with chronic diseases who cannot perform an ergometric. The 6MWT is a submaximal test that allows the assessment of the respiratory, cardiac and metabolic tracts, that is widely applied in physical rehabilitation programs and in treatment of patients with cardiopulmonary diseases.⁹⁻¹⁴

In patients with CF, muscle weakness and functional impairment associated with malnutrition are factors that limit physical capacity.¹⁵⁻¹⁷

OBJECTIVE

The objective of the study was to analyze respiratory muscle strength and functional capacity of patients with cystic fibrosis.

METHODS

Participants

Thirty-five patients were recruited from a convenience sample by consecutive sampling to participate in a cross-sectional study, which was conducted between August and October 2014 at the CF referral center of a specialized and public hospital, in the city of Salvador, Bahia, Brazil. Individuals of both sexes, older than 18 years, with diagnosis of CF who participated in the physiotherapy program and who signed the free and informed consent form were included. Patients with cognitive alterations, hearing and visual disabilities, orthopedic limitations, and lack of interest in participating in the study and who did not sign the informed consent form were excluded.

This study was approved by the Research Ethics Committee of the Faculty of Medicine of the Federal University of Bahia - UFBA, and received the registration number 731.684. The ethical principles of the Helsinki Declaration were fulfilled.¹⁸

Materials

At the beginning of data collection, the socio-demographic status (age, sex, marital status, profession, race) was recorded on an evaluation form. Weight was measured by a digital scale (Magna 150kg, G-Life, CA4000, São Paulo, Brazil), and height by a measuring tape of 150cm. Measurements of maximum respiratory pressures and the required rest variables to perform the 6MWT were also recorded.

The maximum respiratory pressure was measured by an analogue manovacuometer (WIKA, model 611.10, São Paulo, Brazil), with 10 cmH₂O sensitivity interval and a range -150 to +150 cmH₂O. To measure the maximum inspiratory pressure (MIP), the patient sat and was instructed to slowly exhale and, when in residual volume, a mouthpiece was connected between their lips, the nasal cavity was simultaneously closed by a clip, and the patient was requested to try his most intense and deepest inspiration out of the manovacuometer. To measure maximum expiratory pressure (MEP), the patient remained in the sitting position, and was requested to slowly inhale until total pulmonary capacity (TPC) was reached. Immediately after TPC, the manovacuometry mouthpiece was connected between the patient's lips and the nasal passage was occluded with a clip, so that the patient could try a rapid and intense expiration. Both pressures were alternately measured three times with two minutes of rest between each

measurement. A variation of 10% was accepted and only the highest value was analyzed, even though all measurements were recorded in the evaluation form. In between the MIP and MEP measurements, there was an interval of five minutes.¹⁹ The reference values of MIP and MEP for the Brazilian population are approximately 100 cmH₂O and 110 cmH₂O, respectively.²⁰

The evaluator then recorded the patient's heart rate (HR, bpm) and peripheral oxygen saturation (SpO₂,%) values with a portable pulse oximeter (Contec MED CMS-50D, Commercial Society, Hebei, China), blood pressure (BP, mmHg) with an automatic arm pressure device (OMRON, model HEM-7113, Dalian, China), respiratory rate (RR, ipm) and degree of dyspnea and fatigue with a modified Borg scale. Then the participant was taken to an outdoor 30-meter length flat corridor, with marks every 3 meters, to perform the 6MWT.

Before the beginning of the 6MWT, the participant was instructed to walk, and not to jump or run and, if he felt any discomfort, the test could be interrupted, but the test time would continue. The researcher stayed at one end of the corridor, where every minute he signaled the time remaining to the end of the test, as well as offering a verbal encouragement in a neutral voice ("You're doing well!" and "Carry on!"). After six minutes, counted by a chronometer, the patient was instructed to stop and the total distance from the starting to the stopping point was measured.²¹ At the end of the test and three minutes later, the values of the HR, FR, SpO₂, PA and modified Borg scale variables were measured, the evaluator again checked the same variables.¹⁵ The mean distance of the 6MWT is 576m for men and 494m for women.¹⁶

Statistical analysis

The statistical analysis was performed with the complete sample of patients, as well as with subgroups as male and female, patients older and younger than 60 years of age. All variables were evaluated as means and standard deviations. The sample data were compiled in Microsoft Office Excel 2007 and the variables were analyzed by the statistical package SPSS version 20.0. Student's t-test was used for the subgroup comparisons. The Spearman coefficient was used to test the correlations between MIP and MEP, MIP and 6MWT, and MEP and 6MWT of patients above and below 60 years of age, and female and male patients. These correlations were interpreted as very weak ("r" up to 0.25), weak ("r" between 0.26-0.49), moderate ("r" between

0.50-0.69), strong ("r" Between 0.70-0.89) and very strong ("r"above 0.90), according to the reference values described by Domholdt.²² The established level of significance was $p < 0.05$.

RESULTS

35 patients were included and evaluated, and their sociodemographic data is described in table 1.

The comparison between the values of respiratory pressures and the distance of the 6MWT of those younger and older than 60 years of age, there was no statistically significant difference, as shown in Table 2.

When the values of respiratory pressures and distance walked on the 6MWT are compared between the female and the male patients, a statistically significant difference was found, as shown in Table 3.

Mean of the distance covered in the 6MWT (480.7 ± 74.3) by the patients with cystic fibrosis was lower than the mean of the predicted distance (625.3 ± 115.5) for these individuals, with a statistically significant difference between them ($p < 0.001$). It also occurred with respiratory pressures, where the mean values of MIP ($79 \text{ cmH}_2\text{O}$) and MEP ($79 \text{ cmH}_2\text{O}$) were lower than the predicted values ($95 \text{ cmH}_2\text{O}$ and $98 \text{ cmH}_2\text{O}$, respectively), whose comparison yielded statistically significant differences of MIP ($p = 0.005$) and MEP ($p = 0.002$).

Among the adults (up to 60 years of age), a weak correlation was found between MIP and MEP ($r = 0.403 / p = 0.057$), MIP and 6MWT ($r = 0.383 / p = 0.720$), and MEP and 6MWT ($r = 0.213 / p = 0.847$). However, among the elderlies (above 60 years of age), there was positive and statistically significant correlation between MIP and MEP ($r = 0.617 / p = 0.04$), MIP and 6MWT ($r = 0.767 / p = 0.014$), and MEP and 6MWT ($r = 0.707 / p = 0.013$).

Regarding the genders, the best correlation was evidenced among females, for whom moderate correlation was found between MIP and MEP ($r = 0.536 / p = 0.002$), weak correlation between MIP and 6MWT ($r = 0.406 / p = 0.768$), and weak correlation between PEM and 6MWT ($r = 0.215 / p = 0.969$). Among the male population, the correlations were very weak and negative between MIP and MEP ($r = -0.254 / p = 0.08$), MIP and 6MWT ($r = -0.229 / p = 0.87$), and MEP and 6MWT ($r = -0.297 / p = 0.277$).

Table 1. Sociodemographic data of patients with CF

Sociodemographic data	(n=35)
Age, years \pm SD	44.6 \pm 19.0
Gender, male/female (%)	9 (26%) / 26 (74%)
Marital status	
Without a partner	20 (57%)
With a partner	15 (43%)
Ethnic	
White	10 (28%)
Black	7 (20%)
Brown	18 (52%)
BMI, kg/m ²	
Under weight (17 – 18.49)	7 (20%)
Normal weight (18.5 – 24.99)	20 (57%)
Overweight / pre obese (25 – 29.99)	7 (20%)
Obesity class I (30 – 34.99)	1 (3%)

SD, standard deviation; BMI, body mass index.

Table 2. Values of maximum respiratory pressures and distance walked on the 6MWT of patients younger and older than 60 years of age

	Younger than 60 N=25	Older than 60 N=10	p
Age (years)	34.9 \pm 12.8*	68.7 \pm 4.4*	
MIP (cmH ₂ O)	76 \pm 29.1*	-87 \pm 35.9*	0.403
MEP (cmH ₂ O)	77.6 \pm 26.1*	84.5 \pm 29.4*	0.528
Total distance (m)	493.1 \pm 75.4*	449.9 \pm 65.1*	0.107

MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; * Mean and standard deviation; ** Statistically significant ($p < 0.05$).

Table 3. Values of the maximum respiratory pressures and distance of the 6MWT of female and male patients

	Female N=26	Male N=9	p
Age (years)	44.7 \pm 18.6*	44.2 \pm 21.4*	
MIP (cmH ₂ O)	-71.5 \pm 26.6*	-101.1 \pm 34*	0.036**
Predicted MIP (cmH ₂ O)	-88.9	-120.1	
MEP (cmH ₂ O)	74.4 \pm 27.9*	94.4 \pm 17.4*	0.020**
Predicted MEP (cmH ₂ O)	88.8	139.7	
Total distance (m)	450.5 \pm 56.5*	568.2 \pm 44*	0.000**
Predicted distance (m)	620.1	644.6	

MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; * Mean and standard deviation; ** Statistically significant ($p < 0.05$).

DISCUSSION

All patients with CF has limitations of functional capacity and of respiratory muscle strength for those with MIP lower than $60 \text{ cmH}_2\text{O}$.¹⁹ There was a statistically significant difference between the mean distance covered in the 6MWT and the mean predicted dis-

tance for these individuals, as well as between the mean and predicted values of respiratory pressures. When respiratory pressures were correlated one to another and to the 6MWT, adults (younger than 60 years of age) and individuals without respiratory muscle weakness had low and small correlations, whereas the elderlies (older than 60 years of age) the cor-

relation ranged from moderate to strong. The women had weak to moderate correlations, whereas men had negative and weak correlations. And participants with respiratory muscle weakness had strong correlations.

The performance of any muscle can be analyzed by its strength, endurance and resistance to fatigue. The measurement of these characteristics makes it possible to obtain significant information for the functional evaluation of respiratory muscles. MIP and MEP produced in the mouth during static and forced respiration are considered a surrogate measure of respiratory muscle strength.²⁰

The age related muscular changes affect the respiratory muscles function, with an important reduction of about 25% in the strength of the diaphragm of the elderly, when compared to young adults, which can lead to respiratory fatigue during exercise.²³ Vasconcellos et al.²⁴ measured the respiratory muscle strength and functional capacity of sedentary elderly women and showed a positive and significant correlation between the walk distance (443.5 ± 49.6 m) and inspiratory muscle strength (-55.6 ± 21.0 cmH₂O). In our research, as well as the authors cited, we observed a significant correlation between 6MWT and MIP, but, opposed to their findings, we observed a positive correlation between the walk distance of the 6MWT and expiratory muscle strength for all the elderly population.

The MIP measured in females over 60 years of age was higher than the inspiratory muscle strength of the sedentary elderly women in the study by Vasconcellos et al.²⁴, if the only parameter is the walk distance of the 6MWT. This can be explained since the patients with CF in our sample attend physical therapy sessions and, some of them, Pilates.

Both genders had shorter distances of the 6MWT than the predicted reference values of CF patients, what certain consequences on low functional capacity and limitation for performing activities of daily life. Similarly, Ziegler et al.²⁵ found that 73.2% of the 41 adolescent and adult patients with CF of their sample walked shorter 6MWT distances than the normal distance predicted. However, unlike our study, Chetta et al.²⁶ analyzed 25 adult patients (15 women, aged 18-39 years) diagnosed with CF, have shown normal exercise capacity in the walk distance of the 6MWT (629 ± 49 m).

It was observed that the male and female patients presented low MIP and MEP values when compared to the reference value for this population ($p < 0.05$), and there was a positive correlation between these variables only at the women group. The predicted values were

obtained from the MIP and MEP reference equation for men and women, based on their mean age.²⁰

Nonetheless, it was observed that the MIP measured on both genders was high, what could not determine respiratory muscle weakness, even though these values are below the reference value for males (84.1% of the predicted value) and females (80, 4% of the predicted value) with cystic fibrosis. Accordingly, Zanchet et al.²⁷ showed mean values of respiratory pressures above the reference values for individuals with cystic fibrosis and his justification is that 55% of their sample had not yet presented pulmonary function impairment.

It is expected that, given men have greater respiratory muscle strength, they have better functional capacity than women.^{28,29} This was observed in our study, once the male subjects presented higher mean values for all variables when compared to the female subjects, confirming the findings of the literature for MIP, MEP and walk distance. However, there was no significant correlation between the 6MWT and the gender. Similarly, Pereira et al.,¹⁵ who compared functional performance during the 6MWT of 55 patients with cystic fibrosis with 115 healthy individuals, with a mean age of 12.2 ± 4.3 years and 11.3 ± 4.3 years respectively, found that sex has no influence on walk distance of the 6MWT, whose correlations occur only with age, weight and height.

A high MIP (> 80 cmH₂O) or a high MEP (> 90 cmH₂O) exclude significant inspiratory or expiratory weakness, in which the evidence that a person has a low MIP, this value should be less than 60% of the predicted value, which in turn must be based on variables such as gender, age, body weight and height; values above 60 cmH₂O clinically exclude the possibility of respiratory muscle weakness.⁷ In our study, the most patients had MIP above 60 cmH₂O, what excluding the possibility of respiratory muscle weakness. However, in the individual analysis of the sample, 9 patients had MIP lower than or equal to 60 cmH₂O, for whom there was statistically significant differences between the MIP, MEP and 6MWT variables.

Regarding functional capacity, the gradual reduction of physical fitness associated with inactivity begins a vicious cycle in which the worsening of dyspnea is related to increasingly smaller physical efforts, seriously impairing the quality of life.²⁴ Therefore, a widely used test for assessing submaximal exercise capacity in patients with pulmonary disease and heart failure has been the 6MWT which is also indicated for the assessment of recovery after therapeutic interventions.²¹

Enright and Sherrill²¹ emphasized that the walk distance of the 6MWT is an important predictor of morbidity and mortality of patients with pulmonary and / or cardiovascular diseases, especially those who have walked less than 300 meters. However, although a few participants needed to stop and rest to complete the test, and the distances the patients in our study walked were lower than the reference value, all these individuals walked more than 300m in the 6MWT, showing that in our study sample, patients did not present an increased risk of morbidity and mortality due to cystic fibrosis.

Ziegler et al.,²⁵ whose sample consisted of individuals with cystic fibrosis with a mean age of 23.7 ± 6.5 years, observed that the walk distance of the 6MWT did not significantly correlate with BMI, age, MEP, MIP, SpO₂ at rest, dyspnea at the start of the test, and dyspnea at the end of the test. However, in our study, there was a positive correlation between the 6MWT with MIP and MEP for elderly individuals and those with MIP less than 60 cmH₂O.

The limitation of this study is the lack of evidence in the literature to be used as background to the discussion of the sample we studied.

CONCLUSION

In this context, we conclude that respiratory muscle weakness was evident only in the group with MIP < 60 cmH₂O of the studied population, but all groups presented limitation of respiratory muscle strength and functional capacity.

Regarding the comparisons between the means of the walk distance of the 6MWT and the maximum respiratory pressures with the mean of the predicted values for these variables, it was observed that there was a statistically significant difference.

The correlations among respiratory pressures and the correlations between these pressures with the 6MWT were low and weak in adults and individuals without respiratory muscle weakness, moderate to strong in the elderly population, weak to moderate in women, weak and negative in men, and strong in those with respiratory muscle weakness.

ACKNOWLEDGMENTS

We acknowledge the help and assistance of all participants with cystic fibrosis of the HEOM referral hospital.

REFERENCES

1. Farias L, Rosario Filho NA, Kovalhuk L, Miasaki N, Chaves SM, Recco RAC, et al. Aspectos clínicos da fibrose cística: experiência no Hospital de Clínicas da UFPR, 1980-1996. *Pediatria (São Paulo)*. 1997;19(4):241-8.
2. Prado ST. O Papel da fisioterapia na fibrose cística. *Rev Hosp Universitário Pedro Ernesto*. 2011;10(4):118-25.
3. Costa ASM, Britto MCA, Nóbrega SM, Vasconcelos MGL, Lima LS. Vivências de familiares de crianças e adolescentes com fibrose cística. *Rev Bras Crescimento Desenvolvimento Hum*. 2010;20(2):217-27.
4. Lemos ACM, Matos E, Franco R, Santana P, Santana MA. Fibrose cística em adultos: aspectos clínicos e espirométricos. *J Bras Pneumol*. 2004;30(1):9-13. DOI: <http://dx.doi.org/10.1590/S1806-37132004000100004>
5. Muramatu LH, Stirbulov R, Forte WCN. Características funcionais pulmonares e uso de broncodilatador em pacientes com fibrose cística. *J Bras Pneumol*. 2013;39(1):48-55. DOI: <http://dx.doi.org/10.1590/S1806-37132013000100007>
6. Fernandes AK, Mallmann F, John AB, Faccin CS, Dalcin PTR, Barreto SSM. Relação entre alterações funcionais e radiológicas em pacientes com fibrose cística. *J Pneumol*. 2003;29(4):196-201. DOI: <http://dx.doi.org/10.1590/S0102-35862003000400006>
7. Capone D, Salles REB, Freitas MR, Azevedo L, Lucas R, Montessi O, Junqueira C. A radiologia do tórax na fibrose cística. *Rev Hosp Universitário Pedro Ernesto*. 2011;10(4):66-72.
8. Coelho CC, Aquino ES, Almeida DC, Oliveira GC, Pinto RC, Rezende IMO, et al. Análise comparativa e reprodutibilidade do teste de caminhada com carga progressiva (modificado) em crianças normais e em portadoras de fibrose cística. *J Bras Pneumol*. 2007;33(2):168-74. DOI: <http://dx.doi.org/10.1590/S1806-37132007000200011>
9. Annoni R, Silva WR, Mariano MS. Análise de parâmetros funcionais pulmonares e da qualidade de vida na revascularização do miocárdio. *Fisioter Mov*. 2013;26(3):525-36. DOI: <http://dx.doi.org/10.1590/S0103-51502013000300006>
10. Blanhir JEM, Vidal CDP, Romero MJR, Castro MMG, Villegas AL, Zamboni M. Teste de caminhada de seis minutos: uma ferramenta valiosa na avaliação do comprometimento pulmonar. *J Bras Pneumol*. 2001;37(1):110-7. DOI: <http://dx.doi.org/10.1590/S1806-37132011000100016>
11. Gomes ELFD, Silva, DS, Costa, D. Testes de avaliação da capacidade física em pediatria. *Rev Fisioter Bras*. 2012;13(6):470-6.
12. Luz Neto TA, Suzuki FS, Trindade GRGN, Oliveira Filho A, Trindade BO. Teste de 6 minutos. Possíveis parâmetros para elaboração de um programa de caminhada para idosos. *Col Pesq Edu Fis*. 2009;8(5):103-8.
13. Rocha RM, Santo EPE, Gouveia EP, Bittencourt MI, Dowsley R, Meirelles LR, et al. Correlação entre o teste de caminhada de 6 minutos e as variáveis do teste ergométrico em pacientes com insuficiência cardíaca: estudo piloto. *Rev SOCERJ*. 2006;19(6):482-6.
14. Rosa FW, Camelier A, Mayer A, Jardim, JR. Avaliação da capacidade de exercício em portadores de doença pulmonar obstrutiva crônica: comparação do teste de caminhada com carga progressiva com o teste de caminhada com acompanhamento. *J Bras Pneumol*. 2006;32(2):106-13. DOI: <http://dx.doi.org/10.1590/S1806-37132006000200005>
15. Pereira FM, Ribeiro MA, Ribeiro AF, Toro AA, Hessel G, Ribeiro JD. Functional performance on the six-minute walk test in patients with cystic fibrosis. *J Bras Pneumol*. 2011;37(6):735-44. DOI: <http://dx.doi.org/10.1590/S1806-37132011000600006>
16. Schindel CS, Donadio MVF. Efeitos de programas de exercício físico em pacientes com fibrose cística. *Scientia Med (Porto Alegre)* 2013;23(3):187-90.
17. Haack A, Novaes MRG. Exercício físico e fibrose cística: uma revisão bibliográfica. *Com Cienc Saúde*. 2013;24(2):145-54.
18. Associação Médica Brasileira. Declaração de Helsinque [texto na Internet]. São Paulo: AMB [citado 2016 jun 17]. Disponível em: http://www.amb.org.br/_arquivos/_downloads/491535001395167888_DoHBrazilianPortugueseVersionRev.pdf
19. Rocha CBJ, Araújo S. Avaliação das pressões respiratórias máximas em pacientes renais crônicos nos momentos pré e pós hemodiálise. *J Bras Nefrol*. 2010;32(1):107-13. DOI: <http://dx.doi.org/10.1590/S0101-28002010000100017>
20. Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res*. 1999;32(6):719-27. DOI: <http://dx.doi.org/10.1590/S0100-879X1999000600007>
21. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998 158(5 Pt 1): 1384-7. DOI: <http://dx.doi.org/10.1164/ajrccm.158.5.9710086>
22. Domholdt E. Physical therapy research: principles and applications. 2nd ed. Philadelphia: WB Saunders; 2000.
23. Simões LA, Dias JMD, Marinho KC, Pinto CLLR, Britto RR. Relação da função muscular respiratória e de membros inferiores de idosos comunitários com a capacidade funcional avaliada por teste de caminhada. *Rev Bras Fisioter*. 2010; 14(1):24-30. DOI: <http://dx.doi.org/10.1590/S1413-3552010000100005>
24. Vasconcellos JAC, Britto RR, Parreira VF, Cury AC, Ramiro SM. Pressões respiratórias máximas e capacidade funcional em idosos assintomáticos. *Fisioter Mov*. 2007;20(3):93-100.
25. Ziegler B, Rovedder PME, Lukrafka JL, Oliveira CL, Menna-Barreto SS, Dalcin PTR. Submaximal exercise capacity in adolescent and adult patients with cystic fibrosis. *J Bras Pneumol*. 2007; 33(3):263-9. DOI: <http://dx.doi.org/10.1590/S1806-37132007000300006>
26. Chetta A, Pisi G, Zanini A, Foresi A, Grzincich GL, Aiello M, et al. Six-minute walking test in cystic fibrosis adults with mild to moderate lung disease: comparison to healthy subjects. *Respir Med*. 2001;95(12):986-91. DOI: <http://dx.doi.org/10.1053/rmed.2001.1194>
27. Zanchet RC, Chagas AM, Melo JS, Watanabe PY, Simões-Barbosa A, Feijo G. Influence of the technique of re-educating thoracic and abdominal muscles on respiratory muscle strength in patients with cystic fibrosis. *J Bras Pneumol*. 2006;32(2):123-9. DOI: <http://dx.doi.org/10.1590/S1806-37132006000200007>
28. Chaves CRMM, Oliveira CQ, Britto JAA, Elsas MIGG. Exercício aeróbico, treinamento de força muscular e testes de aptidão física para adolescentes com fibrose cística: revisão de literatura. *Rev Bras Saúde Matern Infant*. 2007;7(3):245-50. DOI: <http://dx.doi.org/10.1590/S1519-38292007000300003>
29. Dourado V, Vidotto MC, Guerra RLF. Equações de referência para os testes de caminhada de campo em adultos saudáveis. *J Bras Pneumol*. 2011;37(5):607-14. DOI: <http://dx.doi.org/10.1590/S1806-37132011000500007>