Six minute walking distance in kyphoscoliosis patients with chronic respiratory failure

Test del cammino di 6 minuti in pazienti con cifoscoliosi ed insufficienza respiratoria cronica

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ABSTRACT

Aim: **To evaluate kyphoscoliosis patients with chronic hypercapnic respiratory failure (CHRF) using the six minute walk test (6MWT) distance (6MWD) and cardio-pulmonary function tests.**

Method: **This prospective cross-sectional study was carried out in a tertiary training and research hospital in Turkey. Kyphoscoliosis patients with CHRF on home mechanical ventilation (HMV) followed in a respiratory intensive care unit (RICU) out-patient clinic were enrolled. Patients' demographics were recorded as well as transthoracic echocardiography (ECHO), 6MWD, spirometry, arterial blood gas (ABG) values and high resolution chest computed tomography. 6MWT results were compared with other parameters.**

Results: **Thirty four patients with kyphoscoliosis and chronic respiratory insufficiency admitted to our outpatient clinic were included in the study but 25 (17 M) patients underwent 6MWT (8 patients walked with oxygen supplement due to PaO_2 < 60 mm Hg). The mean 6MWD was 274.4 ± 76.2 (median 270) m and median 6MWD predicted rate was 43.7% (inter quartile ratio, IQR, 37.6% to 47.7%). Median HMV use was 3 years (IQR 2-4). 6MWD predicted rate, body mass index (BMI), HMV duration were similar in male and female patients. 6MWD correlated well with age, BMI, dyspnea score for baseline 6MWT (r: - 0.59, p < 0.002, r: - 0.58, p < 0.003, r: - 0.55, p < 0.005 respectively) but modestly with forced expiratory volume in one second, pulse rate for baseline 6MWT, pulse saturation rate, fatigue and dyspnea score at end of 6MWT (r: - 0.44, p < 0.048; r: 0.44, p < 0.027; r: - 0.43, p < 0.031; r: - 0.42, p < 0.036; r: - 0.42, p < 0.034 respectively). 6MWD predicted rate was only correlated with dyspnea score at baseline (r: - 0.46, p < 0.022). The systolic pulmonary arterial pressure (PAPs) in 6 (24%) cases was more than 40mmHg, in whom mean PaO_2/FiO_2 was 301.4 ± 55.4 compared to 280.9 ± 50.2 in those with normal PAPs (p > 0.40).**

Conclusion: **The 6MWT is an easy way to evaluate physical performance limitation in kyphoscoliosis patients with chronic hypercapnic respiratory failure using home mechanical ventilation. Nearly 275 m was the mean distance walked in the 6MWT, but rather than distance in meters, the 6MWD predicted rate according to gender and body mass index equation might be a better way for deciding about physical performance of these patients. Dyspnea score at baseline before the 6MWT may be the most important point that affects 6MWD in this patient population.**

Keywords: **Chronic respiratory failure, home mechanical ventilation, kyphoscoliosis, six-minute walk distance.**

RIASSUNTO

Scopo: **Valutare pazienti con cifoscoliosi ed insufficienza respiratoria cronica ipercapnica (CHRF) mediante test del cammino di 6 minuti (6MWT) e prove di funzionalità cardio-respiratoria.**

Metodi: **Studio prospettico traversale effettuato in un centro ospedaliero di training ed insegnamento di terzo livello in Turchia. Sono stati arruolati pazienti con CHRF in ventilazione meccanica domiciliare (HMV) seguiti ambulatorialmente dal reparto di terapia intensiva respiratoria. Sono stati rilevati i dati demografici, l'ecocardiogramma transtoracico (ECHO), la distanza coperta nel 6MWT (6MWD), la spirometria, l'emogasanalisi ed una tomografia assiale computerizzata ad alta risoluzione. I risultati del 6MWT sono stati comparati con gli altri parametri.**

Risultati: **34 pazienti con cifoscoliosi e insufficienza respiratoria cronica sono stati inclusi nello studio, ma solo 25 pazienti (17 M) hanno effettuato il 6MWT (8 pazienti con supplemento di O_2 per PaO_2 <60 mm Hg). La 6MWD media era 274 ± 76 (mediana 270) m, pari al 43% del teorico (IQR 37,6-47,7%). I pazienti erano in HMV da 3 anni (valore mediano, IQR 2-4). I pazienti dei due sessi non differivano per 6MWD teorico, indi-**

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ce di massa corporea, durata della HMV. La 6MWD mostrava una buona correlazione con età, BMI, punteggio della dispnea basale al 6MWT (r: - 0,59, p < 0,002; r: - 0,58, p < 0,003; r: - 0,55, p < 0,005 rispettivamente), più modesta con il volume espiratorio forzato in 1 secondo (FEV_1), frequenza cardiaca basale al 6MWT, frequenza alla pulsossimetria, punteggi di fatica e dispnea al termine del 6MWT (r: - 0,44, p < 0,048; r: 0,44, p < 0,027; r: - 0,43, p < 0,031; r: - 0,42, p < 0,036; r: - 0,42, p < 0,034 rispettivamente). Il valore di 6MWD teorico correlava solo con il punteggio di dispnea prima del test (r: - 0,46, p < 0,022). La pressione polmonare sistolica era superiore a 40 mmHg in 6 casi (24%) che presentavano una PaO_2/FiO_2 di 301 ± 55 mmHg rispetto a 281 ± 50 in coloro che avevano valori normali (p > 0,40).

Conclusioni: **Il 6MWT è un metodo semplice per valutare le limitazioni di performance fisica nei pazienti con cifoscoliosi e insufficienza respiratoria cronica ipercapnica in ventilazione meccanica a lungo termine. La distanza media coperta al 6MWT era circa 275 m, ma più che la distanza assoluta, il teorico della 6MWD corretta per sesso ed indice di massa corporea può essere un metodo più accurato per valutare la performance fisica di questi pazienti. Il punteggio della dispnea prima del 6MWT può essere il miglior predittore della 6WMD in questa popolazione di pazienti.**

Parole chiave: Cifoscoliosi, insufficienza respiratoria cronica, test del cammino di 6 minuti, ventilazione meccanica domiciliare.

INTRODUCTION

Kyphoscoliosis (KS) can lead to chronic respiratory failure (CRF) due to deformity of the chest wall structure. With aging, chest wall compliance decreases [1], and the changing breathing pattern can lead to hypercapnia and hypoxemia [2], although some KS patients have hypoxemia without hypercapnia in moderate to severe disease [2,3]. Exercise limitation is often present in patients with KS although they have a normal breathing pattern response to exercise and a normal maximum tidal volume to vital capacity ratio [4]. Kesten and coworkers [4] showed that exercise intolerance may be a result of physical deconditioning. The 6-minute walking test (6MWT) is a simple exercise test to assess the functional status of patients with obstructive and restrictive diseases [5] and a good predictor of mortality in COPD [6,7], pulmonary hypertension [8] and interstitial lung diseases [9]. To date there is little data available for the 6-minute walk distance (6MWD) in patients with KS-CRF and they do not include a comparison with cardiac function and patients' perception of dyspnea (i.e. Borg scale) [9,10]. However, in few studies were the shuttle walking test or maximal cycle testing used to examine performance in these patients [11,12]. In the present study we aimed to evaluate 6MWD and dyspnea perceptions (modified Borg scale) [13] and cardio-pulmonary function testing in patients with KS-CRF. Some data were presented at the 2009 ERS Congress as an abstract [14].

MATERIALS AND METHODS

This study was performed in accordance with the Helsinki Declaration. Informed consent was obtained from patients enrolled in the study. The study was designed as a prospective cross-sectional study in a large pulmonary diseases-based tertiary training and research hospital in Istanbul, Turkey.

Patients: During a 7-year period (2001–2008) of our program for long-term mechanical ventilation, we prospectively evaluated our 35 patients with idiopathic severe kyphoscoliosis, of whom 25 patients (17 male) underwent the 6MWT and were included in the present study. They had been on mechanical ventilation (non-invasively or invasively via tracheostomy cannula) due to hypercapnia ($PaCO_2 \geq 45$ mm Hg). Patient characteristics, ventilator type, settings (inspiratory, IPAP, and expiratory positive airway pressure, EPAP) were recorded.

Measurements: Arterial blood gases (ABGs) (Bayer Rapidlab 348) were measured in patients at rest, seated, and breathing room air. Patients' oxygenation was defined as a ratio of PaO_2 to fractioned inspired oxygen rate (FiO_2). Spirometry (ZAN-GPI.3.00) was performed according to American Thoracic Society (ATS) guidelines [15]. The 6MWT was measured using the best of two tests performed at least 30 min apart as recommended by ATS guidelines for 6MWT [16]. The test was performed in a 39-meter long corridor under the supervision of a pulmonary physician and results were recorded in meters and in percent of predicted (% pred) as Enright and co-workers suggest [17]. If PaO_2 was 60 mm Hg or resting pulse oxygen saturation (SpO_2) was 90% on room air, patients were not considered eligible for analysis of oxygen desaturation during the 6MWT. In this study, desaturation was defined as a fall in SpO_2 below 90% or as a 4% decrease from the baseline saturation maintaining a SaO_2 from 90 to 94%. Transthoracic echocardiography (ECHO) (Vivid 5 GE Healthcare) was performed by a cardiologist to define pathology of cardiac functions and measure systolic pulmonary arterial pressure (PAPs) indirectly via the presence of tricuspid insufficiency. Lung high resolution computerized tomography (L-HRCT) (Siemens Somatom Spirit) was performed in our hospital to detect pathology in lung parenchyma. We defined "normal L-HRCT" if there was no pathology, and "abnormal L-HRCT" as the presence of bronchiectesis, tuberculosis sequel, or emphysema.

Statistical analysis

Descriptive analysis was performed to define the demographics of the study population. Data are presented as mean ± SD or numbers and percentages when appropriate. Continuous variables were summarized using mean and standard deviation for normal-distributed variables and median for non-normally distributed variables. Spearman's rank correlation test was used to correlate patient characteristics, respiratory functions for 6MWD (meters) and gender-specific regression equations for 6MWD rate [17]. The Mann-Whitney U test was used, dividing patients according to 6MWD value above or below 204 m, to compare patients' characteristics, ABG values and spirometry tests.

Statistical analysis was performed using SPSS version 16.0 and the results were considered statistically significant at a level of $p < 0.05$.

RESULTS

Twenty-five out of 34 patients with severe KS and chronic hypercapnic respiratory failure (CHRF) on home mechanical ventilation (HMV) (17 male) underwent the 6MWT and were followed till the end of study. All patient characteristics, HMV and oxygen devices, usage year, pressure setting levels, ABG values, spirometry parameters, measurement of systolic pulmonary artery pressure (PAPs) greater than 40 mm Hg by transthoracic ECHO results are summarized in Table I.

The median age of patients was 51 years old (interquartile ratio, 44-58) and male gender was predominant (68%). The majority of patients were overweight and obese: 7 patients (28%) with BMI = 25-29 kg/m^2 and 10 patients (40%) with BMI > 30 kg/m^2. Spirometry results showed that the majority of patients (n = 19, 76%) had severe airflow obstruction with restriction. Real time ABGs analysis revealed that 80% (n = 20) of patients were hypercapnic; the remaining five patients were hypercapnic when quitting the HMV device. The majority of patients were hypoxemic; only 8 patients (32%) had PaO_2/FiO_2 greater than 300 and 8 patients (32%) used oxygen supplementation due to PaO_2 < 60 mm Hg or SpO2 < 90%. All patients had HMV devices (68% bi-level PAP/ST, 32% bi-level PAP/S) but 18 (72.0%) KS-CHRF were on long term oxygen devices at home. Follow up duration of patients was 1 to 9 years. Only two patients were ventilated via tracheostomy tube intermittently. Pathology on L-HRCT was observed in 76% (n = 19) of patients (3 TB sequaelae, 5 emphysema, 11 bronchiectasis with emphysema). Six patients (24%) had higher PAPs (> 40 mm Hg) and they all had normal left ventricular function (ejection fraction > 65%). L-HRCT showed no parenchymal abnormalities in half of the patients with PAH without LTOT (n = 3, 50%).

The results of the modified Borg scales [18] before and after 6MWT, and 6MWD results are summarized in Table II.

Mean 6MWD was nearly 275 m (274.4 ± 76.1 m) and all KS had less than half the value of gender-specific regression equations for 6MWD rate [17]. Correlations of patient characteristics, respiratory functions for 6MWD and gender-specific regression equations for 6MWD rate [17] in kyphoscoliosis patients with chronic respiratory failure are summarized in Table III. Body mass index and age were significantly negatively correlated with 6MWD (r: - 0.576, $p < 0.003$; r. - 0.590, $p < 0.002$ respectively). Only forced expiratory volume in one second, liter (FEV_1, L) among spirometry results was weakly negatively correlated with 6MWD (r: - 0.437, $p < 0.048$). ABG values were not correlated with 6MWD. Pulse heart rate for baseline test was weakly significantly correlated with 6MWD (r. 0.442, $p < 0.027$). Pulse oxygen saturation (SpO_2) rate at the end of the 6MWT was negatively weakly correlated with 6MWD (r: - 0.420, $p < 0.036$). Borg

TABLE I: PATIENTS' CHARACTERISTICS AND RESPIRATORY FINDINGS (N = 25)

Variables	Median (inter quartile ratio)
Age, year	51 (44 to 58)
Gender, male/female	17/8
Body mass index, kg/m^2	29 (23 to 31)
HMV duration, year	3 (1.5 to 4.0)
IPAP, cm H_2O	18 (12.0 to 21.0)
EPAP, cm H_2O	6 (5.0 to 6.0)
LTOT, n (%)	18 (72)
FEV_1, L	0.73 (0.7 to 0.85)
FEV_1, % predicted	28.0 (25.0 to 34.0)
FVC, L	0.87 (0.72 to 0.95)
FVC, % predicted	27.0 (24.0 to 34.0)
FEV_1/FVC, %	84.0 (76.0 to 90.5)
Pathologic lung HRCT, n (%)	19 (76)
PaO_2/FiO_2, mm Hg	283.3 (256.8 to 316.4)
PaO_2, mm Hg	60.0 (54.3 to 67.6)
pH	7.39 (7.37 to 7.42)
$PaCO_2$, mm Hg	51.0 (46.5 to 57.8)
HCO_3, mmol/L	30.2 (27.4 to 33.0)
SaO_2, %	91.0 (87.4 to 93.9)
Systolic PAP > 40 mm Hg, n (%)	6 (24)

Definition of abbreviations: EPAP, expiratory positive airway pressure; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; HCO_3, bi-carbonate; HMV, home mechanical ventilation; HRCT, high resolution computerized tomography; IPAP, inspiratory positive airway pressure; LTOT, long term oxygen therapy; PaO_2/FiO_2, partial arterial oxygen pressure over fractionated inspired oxygen; $PaCO_2$, partial arterial carbon dioxide pressure; PAP, pulmonary arterial pressure; SaO_2%, arterial blood oxygen saturation rate.

TABLE II: SIX-MINUTE WALK TEST RESULTS

Variables	Median (inter quartile ratio)
Heart rate/min, baseline	86 (81.5 to 96.0)
Heart rate/min, end of test	123 (116.0 to 136.5)
SpO_2%, baseline	93 (92.0 to 95.5)
SpO_2%, end of test	76 (70.0 to 86.0)
Oxygen supplement during test, n (%)	8(32)
Borg scale score for fatigue, baseline	0 (0 to 1)
Borg scale score for fatigue, end of test	3 (1.5 to 5.5)
Borg scale score for dyspnea, baseline	0 (0 to 0)
Borg scale score for dyspnea, end of test	5 (2.0 to 7.0)
6MWD, m	270 (202 to 330)
6MWD, % predicted	43.7(37.6 to 47.7)
References equation [17] 6MWD, m	630.1 (575.1 to 685.8)
References of lower level limit 6MWD, m	483.9 (427.4 to 541.0)

Definition of abbreviations: 6MWD, six minute walk distance; SpO_2%, pulse oxygen saturation rate.

scale scores for dyspnea at baseline and end of the 6MWT were significantly negatively correlated with 6MWD (r: - 0.548, $p > 0.005$, r: - 0.425, $p < 0.034$ respectively) (Table III). Gender specific equations for 6MWD rate were significantly negatively correlated with Borg dyspnea score at baseline of 6MWT (r: - 0.457, $p < 0.22$).

DISCUSSION

The present study revealed that our patients with severe KS-CHRF walked nearly 270 m in the 6MWT, which was less than half the rate predicted and the sensation of dyspnea at baseline 6MWT was an important symptom that affected the 6MWD.

KS-CHRF is a rare disorder and it is difficult to carry out a prospective study in a large population sample. Our sample size (n = 25) was similar to those of other studies carried out on patients with KS-CHRF (n = 24 to n = 27) [11,12]. Chest wall compliance decreases with age, and work of breathing and risk of respiratory muscle fatigue further increase in elderly patients [1]. Enright and co-workers made an equation for gender, arm span, body weight for 6MWD [17]; we analyzed our results according to both 6MWD (meters) and as a percentage of the 6MWD predicted rate. We showed that age and body mass index were not correlated to the 6MWD predicted rate although both correlated significantly to 6MWD (Table III).

Our patients' spirometry results revealed that nearly all of them had very limited lung function (severe restriction and obstruction) and the severity of lung function did not affect the 6MWD outcome. López-Campos et al. [11] and Cejudo et al. [12] studied the shuttle walking test (SWT) and maximal cycle ergometry test (CET) to assess the functional capacity in patients with KS-CHRF and disease-specific health-related quality of life (HRQoL). The severity of lung function was similar to that of our sample although their patients were older and less hypercapnic, but those authors did not use the 6MWT. The mean 6MWD is well established in patients with severe COPD-CHRF [6] but not in KS-CHRF. In the present study we focused on the 6MWD primarily in that specific patient group. Recently Budweiser and co-workers [10] studied the 6MWT to predict mortality by collecting data retrospectively in 424 patients treated with non invasive ventilation (NIV) due to CHRF (197 COPD, 112 restrictive diseases, 115 obesity hypoventilation syndromes). In that study [10], median 6MWD in patients with restrictive diseases (n = 112, including 77 chest wall diseases, 22 neuromuscular diseases and 15 interstitial lung diseases) was 290 m (quartiles 204 to 362) but the exact number of kyphoscoliosis patients among the group of 77 with chest wall diseases was not clear and their ABG values were slightly better (median $PaCO_2$ 44 mmHg, quartiles 40 to 47 and PaO_2 62 mmHg, quartiles 57 to 68). In the same study the authors claimed that 204 m was

TABLE III: CORRELATIONS OF PATIENT CHARACTERISTICS, RESPIRATORY FUNCTIONS WITH 6MWD AND GENDER-SPECIFIC REGRESSION EQUATIONS FOR 6MWD RATE

Variables	6MWD, m		6MWD pred% [17]	
	R	p	r	P
Body mass index, kg/m^2	-0.576	0.003	-0.266	0.200
Age, year	-0.590	0.002	-0.005	0.981
FEV_1,L	0.134	0.564	0.188	0.413
FEV_1, % pred	-0.437	0.048	0.059	0.800
FVC, L	0.052	0.823	0.171	0.457
FVC, % pred	-0.412	0.063	0.115	0.620
FEV_1/FVC, %	0.163	0.481	-0.096	0.678
PaO_2/FiO_2, mm Hg	0.114	0.587	0.081	0.700
$PaCO_2$, mm Hg	0.012	0.956	-0.132	0.528
Pulse heart rate, baseline	0.442	0.027	0.044	0.836
Pulse heart rate, end of test	0.150	0.475	-0.097	0.644
SpO_2, baseline	-0.278	0.178	-0.286	0.166
SpO_2, end of test	-0.432	0.031	-0.214	0.305
Fatigue score, baseline	-0.256	0.216	-0.291	0.158
Fatigue score, end of test	-0.420	0.036	-0.243	0.242
Dyspnea score, baseline	-0.548	0.005	-0.457	0.022
Dyspnea score, end of test	-0.425	0.034	-0.363	0.074

Spearman's Rank Correlation test was performed.

Definition of abbreviations: 6MWD, six-minute walking distance; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; PaO_2/FiO_2, partial arterial oxygen pressure over fractionated inspired oxygen; $PaCO_2$, partial arterial carbon dioxide pressure; SpO_2, pulse oxygen saturation rate.

a critical value for mortality in patients with restrictive lung diseases [10]. We also further analyzed patients and divided them into two groups according to results of 6MWD above and equal to or below 204 meter. Although patients walking more than 204 m had more obstructive airway functions, they had a better fatigue and dyspnea score at the end of 6MWT (Table IV). More studies are needed to analyze survival and the 6MWT among this specific patient group. A higher dyspnea score at baseline 6MWT may be an important alarm for mortality to physicians.

In the present study, the real time ABGs during the 6MWT and other measurements including cardiac functions were assessed. Our patients, although younger than those of Budweiser's study, walked a shorter distance (median 6MWT distance 270 m, quartiles 202 to 330). Although exercise intolerance may be a result of physical deconditioning [4], the distance walked on the 6MWT can be an easy test for understanding patients' perception of dyspnea and physical performance.

CONCLUSIONS

In conclusion, the 6MWT is an easy way to evaluate physical performance limitation in kyphoscoliosis patients with chronic hypercapnic respiratory failure using home mechanical ventilation. Nearly 275 m was the mean distance walked in the 6MWT, but rather than distance in meters, the 6MWD predicted rate according to gender and body mass index equation might be a better way for deciding about physical performance of these patients. Dyspnea score at baseline before the 6MWT may be the most important point that affects 6MWD in this patient population.

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CONFLICT OF INTEREST STATEMENT: None of the authors has any conflict of interest to declare in relation to the subject matter of this manuscript.

TABLE IV. COMPARISON OF PATIENTS ACCORDING TO 6MWD (ABOVE vs. BELOW 204 METERS)

Variables	Groups according to 6MWD 204 meter median (quartiles 25% to 75%)		p
	204 m and lower, n = 8	205 m and higher, n = 17	
Gender, male/female	3/5	14/3	0.025
Age, year	55 (52 to 65)	46 (42 to 53)	0.013
Body mass index, kg/m^2	32 (32 to 34)	27 (20 to 29)	0.000
FEV_1, L	0.76 (0.58 to 0.98)	0.70 (0.59 to 0.77)	0.447
FEV_1,% pred	35.0 (29.5 to 49.5)	25.0 (22.0 to 32.0)	0.006
FVC, L	0.90 (0.69 to 1.23)	0.82 (0.78 to 0.97)	0.562
FVC, % pred	33.5 (26.5 to 53.5)	26.0 (24.0 to 29.0)	0.038
FEV_1/FVC, %	83.0 (76.0 to 92.0)	84.0 (77.0 to 90.0)	0.856
PaO_2/FiO_2, mm Hg	289 (243 to 319)	279 (258 to 316)	0.816
pH	7.39 (7.37 to 7.40)	7.41 (7.38 to 7.43)	0.218
$PaCO_2$, mm Hg	49.1 (42.8 to 58.4)	51.0 (48.3 to 57.7)	0.382
HCO_3, mmol/L	27.7 (26.8 to 32.0)	30.2 (28.8 to 34.2)	0.165
SaO_2, %	91.8 (85.0 to 93.6)	90.3 (88.6 to 93.7)	0.907
6MWD, meter	190 (180 to 197)	300 (270 to 351)	0.000
6MWD, % predicted	35.1 (30.5 to 42.2)	45.9 (43.3 to 52.7)	0.003
Pulse heart rate/min, baseline	82 (74 to 88)	88 (83 to 100)	0.210
Pulse heart rate/min, end of test	124 (108 to 136)	123 (117 to 132)	0.610
SpO_2%, baseline	94 (92 to 96)	92 (92 to 95)	0.220
SpO_2%, end of test	88 (73 to 93)	73 (70 to 82)	0.061
Fatigue score, baseline	0 (0 to 2)	0 (0 to 0)	0.068
Fatigue score, end of test	6 (3 to 7)	3 (0 to 4)	0.005
Dyspnea score, baseline	1 (0 to 2)	0 (0 to 0)	0.026
Dyspnea score, end of test	7 (6 to 8)	4 (2 to 5)	0.012

Definition of abbreviations: 6MWD, six minute walk distance; SpO_2, pulse oxygen saturation rate.
Mann-Whitney U test, $p < 0.05$ significant.

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