

Being ambulatory does not secure respiratory functions of Duchenne patients

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Abstract

Aim: The aim of this work was to assess the respiratory functions of ambulatory Duchenne patients and to propose an earlier time period for intervention. **Materials and Methods:** Lung functions and North Star Ambulatory Assessment (NSAA) scores of Duchenne patients were evaluated simultaneously. **Results:** Thirty ambulatory Duchenne patients were included in this study. NSAA scores of the patients were directly correlated with arm abduction, arm adduction, and shoulder flexion strengths. Forced expiratory volume in 1 second percent predicted and forced vital capacity (FVC) percent predicted correlated inversely to age and to the NSAA score. Twelve of 13 patients with FVC values lower than 80% of predicted had NSAA scores below 24 points. None of the patients who were younger than 7 years had FVC values lower than 80% of predicted. **Conclusion:** Annual spirometry is necessary for Duchenne patients older than 6 years regardless of the ambulatory status.

Key Words

Duchenne muscular dystrophy, north star ambulatory assessment, respiratory functions

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Introduction

Duchenne muscular dystrophy (DMD) is a severe X-linked neuromuscular disease. It is characterized by progressive muscular weakness leading to wheelchair dependence and death from cardiorespiratory complications.^[1] Life quality and expectancy of DMD patients are poor due to limited treatment options. Several targeted therapies are now in progress that aim to correct the DMD genetic defect at the molecular level.^[2,3] Early recognition of functional loss of patients and intervention are important in saving time until decisive therapy. Loss of ambulation and scoliosis are considered red flags for respiratory failure and referral to a pulmonologist. This study aims to assess the respiratory functions of ambulatory Duchenne patients and to propose an earlier intervention time period.

Materials and Methods

This study was conducted at the outpatient clinic of the

Pediatric Neurology Department of Istanbul Medical Faculty between November 2009 and June 2010. Ambulatory DMD patients on regular follow-up were enrolled in this study. Lung function was measured by maximum expiratory flow-volume loops. The subjects breathed through a silicon mouthpiece placed between the teeth, with a rim inserted between the teeth and lips to ensure that no leaks occurred during forced expiration. Optimum of the three consecutive trials were valued. Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were the lung function parameters chosen for assessment. FEV1 and FVC were corrected for age, height, and weight in order to calculate the percentage of predicted values. Three patients who could not cooperate with spirometry were excluded from this study.

During the North Star Ambulatory Assessment (NSAA) tests, the same physiotherapist (F.B.) recorded the time elapsed while rising from floor (from supine position), walking 10 m and climbing four steps as well as upper limb strength (arm abduction, arm adduction, and shoulder flexion). The NSAA scale consists of 17 items (stand up from chair, stand on one leg, climb box step, etc.) that allow to assess the abilities that are necessary to remain functionally ambulant. Each item can be scored on a 3-point scale using simple criteria: 2, "Normal" – achieves goal without any assistance; 1, Modified method but achieves goal independent of physical assistance from another; and 0 – Unable to achieve

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independently. The total score is achieved by adding together the scores for all the individual items.

Statistical Package for the Social Science 15.0 for Windows was used for data analysis. Bivariate correlation analyses were performed using Pearson's correlation coefficient. The study was approved by the medical ethics committee, and verbal consent was given by the parents of the children included in this study.

Results

Thirty ambulatory genetically proven Duchenne patients were included in this study. The mean patient age was 88 months (60–122 months). None had chronic respiratory disease or scoliosis. FEV1% predicted and FVC% predicted correlated inversely to age ($P = 0.007$; $P = 0.003$) and the NSAA score ($P = 0.020$; $P = 0.014$). Twelve of the 13 patients with FVC values lower than 80% of predicted had NSAA scores below 24 points [Figure 1]. None of patients who were younger than 7 years had FVC values lower than 80% of predicted [Figure 2]. Fourteen of 18 patients over 7 years old had FVC values lower than 80% of predicted. FVC correlated inversely with the time elapsed while climbing four steps ($P = 0.026$) and standing up from supine position ($P = 0.010$). Lung function tests did not correlate to upper limb muscle strength.

The NSAA scores of the patients were directly correlated with arm abduction, arm adduction, and shoulder flexion strengths. NSAA scores correlated inversely with the time elapsed while climbing four steps ($P = 0.00$) and standing up from supine position ($P = 0.00$), but no significant correlation was found with time elapsed while walking 10 m.

Discussion

Various aspects of respiratory function have been assessed in relation to DMD, including measuring maximum inspiratory and expiratory pressures in order to detect respiratory muscle weakness and measuring lung volumes.^[4] FVC has proven to be the best parameter reflecting lung function in DMD patients.^[5]

A FVC of <40%–50% of predicted or <1 L are associated with nocturnal hypoventilation and the need for noninvasive ventilation, independent of clinical symptoms.^[6]

According to an American Thoracic Society consensus statement, "patients should visit a physician specializing in pediatric respiratory care twice yearly after confinement to a wheelchair, fall in vital capacity below 80% predicted, and/or age 12 years old. Children should have at least 1 visit with a physician who specializes in pediatric respiratory care early in the course of disease (4–6 years of age) and before confinement to a wheelchair to have baseline pulmonary function testing performed."^[7] The consensus also recommends annual testing of lung function. In our study, we found that a significant part of ambulatory patients had a vital capacity below 80% of predicted. Age was the parameter most strongly correlated with vital capacity. We have concluded that being over 7 years of age is a risk factor for lower vital capacity. These patients must be evaluated by a pulmonologist for the quality of cough, elimination of sputum, and necessity of more intensive respiratory physiotherapy. As FVC does not directly correlate with the quality of cough, it is necessary to measure the maximal expiratory pressure in these patients.^[8]

We have not demonstrated any correlation between FVC and upper limb muscular function. However, significant negative correlation between FEV1% predicted and the muscular function score of the upper limbs has previously been described by Tangsrud *et al.*^[9] in a cohort with advanced disease. We connect this inconsistency to the design of our study, namely, our patients all being at an earlier stage of the disease.

The NSAA was specifically designed for ambulant children with DMD.^[10] The reliability and feasibility of the scale have already been reported in a UK study that has also shown how the NSAA can detect changes over time in DMD patients.^[11] Our results show that patients who have scored under 24 points must be evaluated for respiratory functions. As far as our knowledge goes, the NSAA and its correlation with FVC has been demonstrated for the first time in this study.

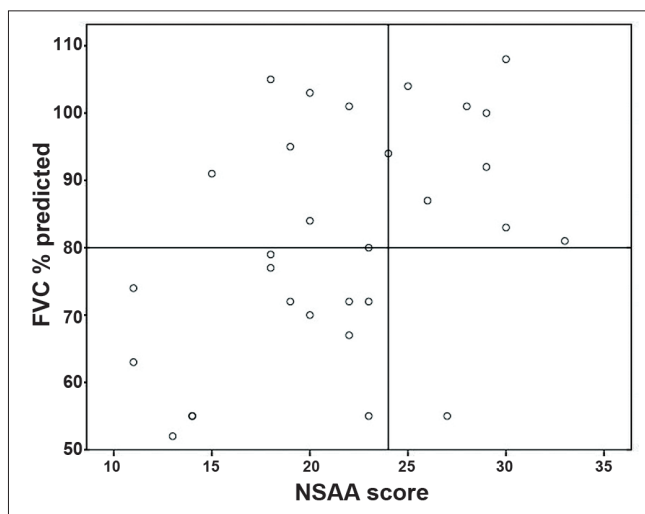


Figure 1: Scatterplot of FVC percent predicted values versus NSAA scores

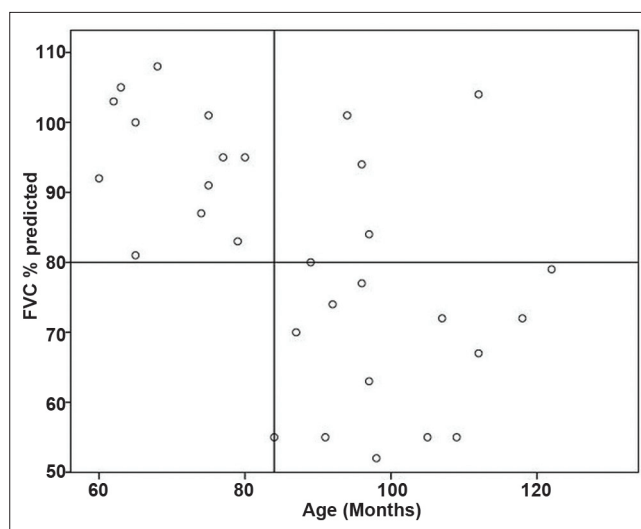


Figure 2: Scatterplot of FVC percent predicted values versus age

Previous studies of nonambulatory patients have found that FVC declines rapidly when standing ceases. Percent FVC was found to be the parameter of pulmonary function that was most strongly correlated with age and scoliosis measurements.^[12] Contrary to expectations from scoliosis surgery, a longitudinal study found that spinal stabilisation in DMD did not alter the decline in pulmonary function.^[13]

In conclusion, being ambulatory does not secure respiratory functions in Duchenne patients. Annual spirometry is necessary for Duchenne patients older than 6 years. These patients can have FVC values lower than 80% of predicted as early as 7 years of age.

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