How Respiratory Muscle Strength Correlates with Cough Capacity in Patients with Respiratory Muscle Weakness

Jung Hyun Park,[1] Seong-Woong Kang,[2] Sang Chul Lee,[3] Won Ah Choi,[2] and Dong Hyun Kim[2]

[1]Department of Rehabilitation Medicine, Eulji University Hospital, Daejeon;
[2]Department of Rehabilitation Medicine and Rehabilitation Institute of Muscular Disease, Yonsei University College of Medicine, Seoul;
[3]Department of Physical Medicine and Rehabilitation, Myongji Hospital, Kwandong University College of Medicine, Seoul, Korea.

Purpose: The purpose of this study is to investigate how respiratory muscle strength correlates to cough capacity in patients with respiratory muscle weakness. **Materials and Methods:** Forty-five patients with amyotrophic lateral sclerosis (ALS), 43 with cervical spinal cord injury (SCI), and 42 with Duchenne muscular dystrophy (DMD) were recruited. Pulmonary function tests including forced vital capacity (FVC) and respiratory muscle strength (maximal expiratory pressure, MEP; maximal inspiratory pressure, MIP) were performed. The correlation between respiratory muscle strength and cough capacity was analyzed. **Results:** In the SCI group, FVC in a supine position (2,597 ± 648 mL) was significantly higher than FVC in a sitting position (2,304 ± 564 mL, $p < 0.01$). Conversely, in the ALS group, FVC sitting (1,370 ± 604 mL) was significantly higher than in supine (1,168 ± 599 mL, $p < 0.01$). In the DMD group, there was no statistically significant difference between FVC while sitting (1,342 ± 506 mL) and FVC while supine (1,304 ± 500 mL). In addition, the MEP and MIP of all three groups showed a significant correlation with peak cough flow (PCF) ($p < 0.01$, Pearson's correlation analysis). In the SCI group, MIP was more closely correlated with PCF, while in the ALS and DMD groups, MEP was more closely correlated with PCF ($p < 0.01$, multiple regression analysis). **Conclusion:** To generate cough flow, inspiratory muscle strength is significantly more important for SCI patients, while expiratory muscle function is significantly more important for ALS and DMD patients.

Key Words: Amyotrophic lateral sclerosis, muscular dystrophy, duchenne, respiratory function tests, spinal cord injuries

INTRODUCTION

An effective cough is an important host defense mechanism to clear the airway.[1] The phases of cough are classified as 1) inspiratory, 2) compressive, and 3) expiratory.[1-4] During the inspiration phase, normal subjects have pre-cough volumes that are about 85% to 90% of their inspiratory capacity and have a total cough volume of about 2.3 L to obtain optimal cough flows.[5] After enough air volume is inhaled, the glottis automatically closes and prevents any outflow of inhaled air.[6,7] The contraction of the expiratory muscles while the glottis is open initiates the

expulsion phase during which air from the lungs is forcibly expelled.[4] An effective cough cannot be obtained if one of these phases fails.

Respiratory muscle weakness and decreased cough capacity are the main causes of pulmonary complications that result in morbidity and mortality in patients with neuromuscular disorders (NMDs) and in tetraplegics. To prevent pulmonary complications in these patients, it is necessary to understand the mechanics of the respiratory system and to accurately evaluate pulmonary function.

In patients with Duchenne muscular dystrophy (DMD), diaphragmatic function is relatively well preserved despite generalized muscle dysfunction.[8] However, patients with amyotrophic lateral sclerosis (ALS) experience profound diaphragm weakness, early in the disease process.[9-11] Finally, in many patients with spinal cord injury (SCI) if injured at high cervical levels, the functions of intercostal and abdominal muscles are impaired, while diaphragm function is preserved.[8-10,12,13]

Previous studies have examined respiratory function in patients with NMDs by analyzing the differences between vital capacity measured while patients are in various positions.[8-10,13] Several researchers have also studied the correlation between expiratory muscle strength and cough.[4,14] However, the relationship between cough capacity and differential respiratory muscle weakness patterns has rarely been discussed. Although expiratory muscle function is crucial for an effective cough, the lung volume attained before expiratory muscle contraction also plays an important role. If insufficient pre-cough volume is obtained due to inspiratory muscle weakness, cough capacity decreases in spite of functional expiratory muscles.[15] As a result, a lack of deep breathing leads to atelectasis, where the lung and chest walls lose their elasticity and compliance in the chronic stage.[16-18] In addition, a loss of lung compliance may exacerbate cough weakness by restricting dynamic airway compression.[15]

The correlation between cough capacity and the inspiratory muscle strength necessary to obtain adequate lung volume has rarely been studied.[19,20] For this reason, we studied patients with clinically common diseases that accompany restrictive lung disease (RLD) to establish how weakened respiratory muscles affect cough capacity. We evaluated patients with ALS, cervical SCI, and DMD that had different but well-defined patterns of respiratory muscles weakness.

MATERIALS AND METHODS

Subjects

Forty-two patients with DMD were involved in this study; DMD diagnosis was established according to an internatio-

nally accepted criteria[21]: progressive muscular weakness, increased plasma muscle enzymes, muscle biopsy showing fiber degeneration and the absence of the dystrophin protein, and alterations in the dystrophin gene (e.g., deletions). Forty-five patients with probable or definitive ALS according to El Escorial criteria[22] were also included in the study. Finally, 43 patients with traumatic cervical SCI, who sustained complete motor injuries as defined by the American Spinal Injury Association (ASIA) criteria, were also included. The recruitment period was from February 2000 to May 2007. Patients who had concomitant intrinsic lung diseases, who could not hold breaths due to vocal cord paralysis, who were intubated or had a tracheostomy, and who took medications that affect pulmonary function were excluded.

The institutional review board of our institute approved our study. Informed consent was obtained from all subjects.

Measurements

Forced vital capacity (FVC)
Forced vital capacity (FVC) was measured in sitting and supine positions using a spirometer (Wright spirometer; Ferraris Development & Engineering Co. Ltd., London, England). This process was repeated at least three times; the highest value was selected as the FVC. We calculated predicted FVC values (FVCpre) based on age, height, and weight.[23] Relative FVC values were reported as FVC/FVCpre (%).

Respiratory muscle strength
Maximal respiratory pressure and reflecting respiratory muscle strength was measured by mouth pressure-meter (MicroRPM; Micro Medical Ltd., Rochester, England) in a sitting position. To measure maximal expiratory pressure (MEP), subjects performed maximal expiratory effort after maximal inspiration. Maximal inspiratory pressure (MIP) was measured by exerting maximal inspiratory effort after maximal expiration. To measure these pressures, effort was maintained for at least 1 second. The highest positive MEP value and the lowest negative MIP value in three or more attempts were chosen. We calculated predicted MEP (MEPpre) and MIP (MIPpre) values based on age, height, and weight.[23] Relative MEP and MIP values were presented as MEP/MEPpre (%) and MIP/MIPpre (%).

Peak cough flow (PCF)
Peak cough flow (PCF) was measured by a peak flow-meter (ASSESS®; Health Scan Products Inc., Cedar Grove, NJ, USA). Unassisted PCF was measured by having the patient cough as much as possible through a peak flow-meter. The highest value in each test was used by running at least three trials. Cough capacity, defined as the ability to clear

airway secretion, can be represented as PCF.[2,14,19]

Statistical analysis

A paired t-test was used to compare the FVC in sitting and supine positions of patients with ALS, cervical SCI, and DMD. The relationships between MIP and PCF and between MEP and PCF were analyzed in each patient group using Pearson's correlation and multiple regression analysis. All data were analyzed using Statistical Package for the Social Sciences (SPSS) 12.0 (SPSS, Inc; Chicago, IL, USA).

RESULTS

Table 1 lists patient characteristics. All 43 SCI patients showed complete motor paralysis at the cervical level; 32 were classified as having ASIA-A. Twenty-one of these patients were injured at C6, six patients were injured at C7,

and five patients were injured at C8. Eleven patients had ASIA-B tetraplegia; seven of these patients had levels of injury at C6, three patients were injured at C7, and one patient was injured at C8.

Table 2 shows that in the cervical SCI group, FVC and %FVC while supine was significantly greater than FVC and %FVC while sitting ($p < 0.01$). In the ALS group, however, FVC and %FVC while sitting was significantly greater than while supine ($p < 0.01$). In the DMD group, there was no statistically significant difference between the mean FVCs while sitting or supine. The mean PCF and %FVC is also noted in Table 2.

The SCI group had a relative MIP value much greater than the relative MEP value ($p < 0.01$) (Table 3). In the ALS group, the relative MEP value was lower than the relative MIP value, but there was no significant difference between the two values (Table 3). In DMD patients, the relative MIP value was significantly higher than the relative MEP value ($p < 0.01$) (Table 3).

Table 1. Subject Characteristics

		SCI (n = 43)	ALS (n = 45)	DMD (n = 42)
Sex	Men	35	35	42
	Women	8	10	0
Age (yr)		35.0 ± 12.6	54.4 ± 11.1	16.1 ± 4.0
Height (cm)		107.4 ± 7.7	165.9 ± 10.7	152.5 ± 11.4
Body weight (kg)		62.3 ± 9.2	54.9 ± 9.1	42.7 ± 12.7

SCI, spinal cord injury; ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy.
Data presented as mean ± SD.

Table 2. Pulmonary Function Test Results

	SCI (n = 43)	ALS (n = 45)	DMD (n = 42)
FVCsit (mL)	2,304 ± 564*	1,370 ± 604*	1,342 ± 506
(%FVCsit = FVCsit / FVCpre)	(48.3 ± 10.0%)*	(34.5 ± 15.6%)*	(43.0 ± 19.3%)
FVCsup (mL)	2,597 ± 648*	1,168 ± 599*	1,304 ± 500
(%FVCsup = FVCsup / FVCpre)	(54.2 ± 10.4%)*	(29.2 ± 14.93%)*	(41.9 ± 18.9%)
PCF (L/min)	261 ± 72	193 ± 63	205 ± 57

FVCsit, forced vital capacity in sitting position; FVCpre, predicted value of forced vital capacity; FVCsup, forced vital capacity in supine position; PCF, peak cough flow; SCI, spinal cord injury; ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy.
Data presented as mean ± SD.
*Paired t-test, $p < 0.01$.

Table 3. Comparison between MIP and MEP

	SCI (n = 43)	ALS (n = 45)	DMD (n = 42)
MIP (cmH$_2$O)	63.8 ± 25.0*	24.3 ± 10.6	32.4 ± 11.3*
(%MIP = MIP / MIPpre)	(63.8 ± 21.3%)*	(30.1 ± 13.6%)	(40.2 ± 16.7%)*
MEP (cmH$_2$O)	36.2 ± 17.2*	31.6 ± 15.2	28.3 ± 10.4*
(%MEP = MEP / MEPpre)	(26.4 ± 11.4%)*	(26.9 ± 13.1%)	(23.8 ± 10.1%)*
%MIP / %MEP	2.42	1.12	1.69

MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; MIPpre, predicted maximum inspiratory pressure; MEPpre, predicted maximum expiratory pressure; SCI, spinal cord injury; ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy.
Data presented as mean ± SD.
*Paired t-test, $p < 0.01$.

Table 4. Correlation between PCF and MIP, MEP

		SCI (n = 43)		ALS (n = 45)		DMD (n = 42)	
		MIP	MEP	MIP	MEP	MIP	MEP
PCF	r	0.609	0.534	0.339	0.528	0.637	0.742
	p	< 0.01	< 0.01	0.023	< 0.01	< 0.01	< 0.01

PCF, peak cough flow; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; SCI, spinal cord injury; ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy; r, Pearson correlation coefficient.

Table 5. Results of Multiple Regression Analysis

Group	Calculated PCF (L/min)	*p* value
SCI	$144.415 + 1.290 \times MIP + 1.013 \times MEP$	MIP: $p = 0.007$ MEP: $p = 0.132$
ALS	$127.311 - 0.344 \times MIP + 2.335 \times MEP$	MIP: $p = 0.751$ MEP: $p = 0.003$
DMD	$71.707 + 1.364 \times MIP + 3.131 \times MEP$	MIP: $p = 0.051$ MEP: $p = 0.000$

PCF, peak cough flow; SCI, spinal cord injury; ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure.

Respiratory muscle strength and PCF were significantly correlated in all three groups. In the SCI group, both MEP (Pearson's coefficient of correlation r = 0.534, *p* < 0.01) and MIP (r = 0.609, *p* < 0.01) (Table 4) were significantly correlated with PCF, but MIP (*p* = 0.007) was more strongly correlated than MEP (*p* = 0.132) (Table 5) with PCF. The results of the ALS group were somewhat different: again, both MEP (r = 0.528, *p* < 0.01) and MIP (r = 0.339, *p* < 0.05) (Table 4) were significantly correlated with PCF, but in this group, MEP (*p* = 0.003) was more strongly correlated than MIP (*p* = 0.751) (Table 5). The DMD group showed similar results to the ALS group: MEP (r = 0.742, *p* < 0.01) and MIP (r = 0.637, *p* < 0.01) (Table 4) were significantly correlated with PCF, but MEP (*p* = 0.000) was more strongly correlated than MIP (*p* = 0.051) (Table 5).

DISCUSSION

In this study, we compared the FVC of subjects in both sitting and supine positions. In the SCI group, the FVC was larger in the supine position than in the sitting position, which reflects preserved diaphragmatic function but impaired function of the intercostal and abdominal muscles. However, in ALS patients the FVC in the supine position was much smaller than that in the sitting position, suggesting both rapidly progressing muscle weakness with profound diaphragm weakness. In contrast, because in DMD patients the diaphragm retains its function as the primary inspiratory muscle, there is scant difference in vital capacity when the patient's position changes. These results are similar to those of previous studies.[8-13,24] We confirmed that measuring FVC in different positions is important to fully understand the weakness patterns of inspiratory and expiratory muscles in patients with RLD.

In this study, the cervical SCI group showed markedly decreased MEP, moderately decreased MIP, and high %MIP/%MEP (2.42) (Table 3), indicating expiratory muscle weakness as the predominant respiratory dysfunction in the SCI group. In the ALS group, both MIP and MEP were markedly decreased, in addition to a lower %MIP/%MEP value (1.12) (Table 3), which suggests that the inspiratory and expiratory muscles had similar and profound levels of weakness. In the DMD group, both MIP and MEP were low, but the ratio of %MIP/%MEP (1.67) (Table 3) was midway between that of the SCI and ALS groups. This indicates that the DMD group exhibited both inspiratory and expiratory muscle weakness, but retained more inspiratory muscle function than the ALS group.

In our correlation study, both MIP and MEP showed significant correlations with PCF in all three groups. However, in the SCI group, multiple regression analysis showed that MIP (*p* = 0.007) was more highly correlated with PCF than MEP (*p* = 0.132) (Table 5). This may indicate that inspiratory muscles are more important for cough production in motor complete cervical SCI patients who have lost a large percentage of expiratory muscle power. Conversely, in the ALS group, MEP (*p* = 0.003) was more highly correlated with PCF than MIP (*p* = 0.751) (Table 5). Due to the inspiratory and bulbar muscle weakness in patients with ALS, it is difficult to attain sufficient pre-cough volume and to hold the breath just before coughing. Thus, in ALS patients, cough may depend predominantly on expiratory muscle strength. Finally, in the DMD group, MEP (*p* = 0.000) was more highly correlated with PCF than MIP (*p* = 0.051) (Table 5). This indicates that although patients with

DMD retain more of their inspiratory muscle strength, both inspiratory and expiratory muscle weakness are profound. Because inspiratory muscle strength is insufficient to generate enough pre-cough volume, cough in patients with DMD depends more upon expiratory muscle strength than in patients with SCI.

It is easily understood that coughing is a kind of exhalation process, which leads to the conclusion that expiratory muscle strength is more strongly correlated than inspiratory muscle strength with cough capacity. In light of our results, however, this assumption can be misleading, depending on the disease process and its effects on respiratory muscle weakness. Like the SCI cases in this study, inspiratory muscle strength can correlate more strongly with cough capacity. Thus, we conclude that both expiratory and inspiratory muscle function are important to build an effective cough. Given this assertion, it is difficult to achieve a sufficiently strong cough by assisting only expiratory muscles without assisting inspiratory muscles in RLD patients whose pre-cough volumes decrease.[15] Therefore, an adequate cough can be generated by not only expiratory phase assistance, but also by pre-cough volume support.[25,26]

This study has several limitations. We think it is worthy to note that inspiratory muscle strength may be important for producing an effective cough in patients with predominantly expiratory muscle dysfunction, in light of the fact that inspiratory muscle strength is one of the determinants of pre-cough lung volume. However, we were unable to determine the pre-cough lung volume directly. We believe that the functional residual capacity (FRC) is an indicator of pre-cough lung volume, but our study would be strengthened by obtaining additional lung volume data (total lung capacity, functional residual capacity, residual volume, etc.). With this information, the correlation between FRC and PCF could be analyzed in detail. However, in our hospital, those parameters are not included in routine pulmonary evaluation of patients with severe respiratory compromise.

In conclusion, 1) inspiratory muscle strength is important for producing an effective cough in certain patients with respiratory muscle dysfunction, even though coughing is a type of exhalation process; and 2) pre-cough lung volume may play an important role in establishing an effective cough in patients with respiratory muscle dysfunction whose expiratory muscles are highly impaired.

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