Running head: In-Exsufflation Pressure Titration

Peak Cough Flow Fails to Detect Upper Airway Collapse during Negative Pressure

Titration for Cough-Assist

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Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosures: none

Clinical Trial Registration: ClinicalTrials.gov [#NCT02137304]

ABSTRACT

Objective: To study the ability of peak cough flow (PCF) and effective cough volume (ECV), defined as the volume exsufflated above 3 L/s, to detect upper airway collapse (UAC) during mechanical insufflation-exsufflation (MI-E) titration in neuromuscular patients.

Design: Prospective observational study

Setting: Rehabilitation hospital

Participants: Twenty-seven patients with neuromuscular disease causing significant impairment of chest wall and/or diaphragmatic movement.

Interventions: The lowest insufflation pressure producing the highest inspiratory capacity was used. Exsufflation pressure was decreased from -20 cmH₂O to -60/-70 cmH₂O, in 10-cmH₂O decrements, until UAC was detected using the reference standard of flow-volume curve analysis (after PCF, abrupt flattening or flow-rate decrease versus previous less negative exsufflation pressure).

Main outcomes: Peak cough flow and ECV profiles during expiration with MI-E.

Results: Upper airway collapse occurred in 10 patients during titration. ECV increased with decreasing expiratory pressure then decreased upon UAC occurrence. PCF continued to increase after UAC occurrence. In 5 other patients, UAC occurred at the initial -20 cmH₂O exsufflation pressure and, during titration, PCF increased and ECV remained unchanged at less than 200 mL. PCF had 0% sensitivity for UAC, whereas ECV had 100% sensitivity and specificity.

Conclusion: Of 27 patients, 15 experienced UAC during MI-E titration. UAC was associated with an ECV decrease or plateau and with increasing PCF. Accordingly ECV, but not PCF, can detect UAC.

24 **Keywords:** cough, mechanical insufflation-exsufflation, neuromuscular disease, exsufflation,
25 upper airway collapse

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28 **List of abbreviations:**

29 ECV : effective cough volume

30 MEP: maximum expiratory pressure

31 MI-E: mechanical insufflation-exsufflation

32 MIP: maximum inspiratory pressure

33 NMD: neuromuscular disease

34 OSA: obstructive sleep apnea

35 PCF: peak cough flow

36 UAC: upper airway collapse

37 VC: vital capacity

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INTRODUCTION

Poor cough efficiency resulting in an inability to clear the airways of secretions is a major risk factor for acute respiratory failure in patients with neuromuscular disease (NMD).^{1,2} Cough-assistance methods include manual and mechanical techniques providing inspiratory and/or expiratory assistance to improve cough efficiency, mobilize and clear the airway secretions, and avoid complications associated with secretion retention.¹⁻⁶ Peak cough flow (PCF) is usually taken as the criterion for determining that airway clearance is effective, the cut-off being 160-180 L/min in adults with NMD.⁷⁻¹³ A baseline PCF<180 L/min (3L/s) is required for reimbursement of secretion-clearance devices by the statutory health insurance systems in Belgium¹⁴ and France.¹¹ Rather than to use a PCF threshold U.S. health insurance companies prefer a clinical evaluation and criteria for MI-E devices (E0482) covering are : 1) a neuromuscular disease (refer to the 10th revision of the “International Statistical Classification of Diseases and Related Health Problems“), and 2) this condition is causing a significant impairment of chest wall and/or diaphragmatic movement, resulting in an inability to clear retained secretions.

Peak cough flow is also the most widely used parameter for assessing the performance of cough-assist techniques in patients with NMD.^{8, 15, 16} Mechanical insufflation-exsufflation (MI-E) is currently considered the technique of choice for the weakest patients with NMD.⁶ The insufflation pressure that achieves the highest PCF is viewed as optimal and is lower than the value providing maximal insufflation.¹⁷ It has been suggested that the optimal exsufflation pressure can also be defined as the value achieving the highest PCF. However, PCF measurement may fail to detect upper airway collapse (UAC) caused by the application of negative pressure. UAC may impair cough effectiveness according to two studies showing evidence of upper airway

obstruction during MI-E.^{18, 19} However, the techniques used in these studies^{18, 19} are not readily applicable to exsufflation pressure titration in everyday practice.

We hypothesized that, when upper airway collapse occurs during titration, the exsufflation pressure achieving the highest volume exhaled at an efficient flow [i.e. above 3 L/min], designated as “effective cough volume” (ECV), is systematically higher (i.e. less negative) than the exsufflation pressure achieving the highest PCF value. The objective of this prospective study in patients with severe respiratory muscle weakness due to NMD was to investigate changes in PCF and ECV during MI-E, particularly upon the occurrence of UAC, as detected by analysis of the flow-volume curve. The performance of PCF and ECV in detecting UAC was quantified.

MATERIAL AND METHODS

Patients

This observational study was approved by the French national ethics committee and registered on ClinicalTrials.gov (#NCT02137304). In 2016 and 2017, we enrolled 27 patients with NMD during their annual follow-up visits to the post-intensive care unit, which routinely included patient education about cough-assist techniques. All 27 patients met the French, Belgium and US criteria required for MI-E coverage. At each visit, the following parameters were recorded: vital capacity (VC),²⁰ unassisted PCF,²⁰ maximum expiratory pressure (MEP), and maximum inspiratory pressure (MIP).^{21, 22} Inclusion criteria were documented NMD, reason for using MI-E, age >18 years, hemodynamic stability, absence of acute bronchial congestion (respiratory tract infection) in the past month, and PCF lower than 4.5 L/s.⁵ Patients gave written informed consent before study inclusion.

Study protocol

Mechanical insufflation-exsufflation was performed using a facemask [Ambu UltraSeal, Ambu, Bordeaux, France] and the Cough-Assist E70 device [JH Emerson Co., Cambridge, MA, USA]. Measurements during maneuvers were obtained with a spirometer (Micro 6000 spirometers; Medissoft, Sorinnes, Belgium) connected to the MI-E circuit and were performed with the study participants seated comfortably in their adapted wheelchair; the experiment was started after a period of quiet breathing. Patients were seated in their own electric wheelchair. Postural adjustments were made following patients' advice for their best respiratory comfort. Degree of tilt, recline or elevation of leg rests were not measured. If possible, the degrees of tilt and recline tried to allow the patient having an overall view on Cough-Assist E70 screen in order to get a visual feedback. The head was on the headrests maintained in the neutral position, when it was possible for the patient, to avoid bias due to effects of position on deep breathing and coughing. Throughout the tests, oxygen saturation and heart rate were monitored using pulse oximetry.

The day before testing, the patients were familiarised with the study cough-assist techniques. The optimal insufflation pressure was determined by starting at 10 cmH₂O, increasing in 5 cmH₂O steps up to 20 cmH₂O, and finally increasing further in 2 cmH₂O steps to a maximum of 40 cmH₂O. Measurements were performed two or three times at each pressure level. The individual pressure titration was stopped when further increase did not lead to additional improvement or if patients did not tolerate higher pressures.¹⁷ Insufflation poor tolerance was defined as an overinflation sensation hindering the compression phase of cough.

Expiratory pressure was titrated on the next day. Three physiotherapists (ML, AB, and LDAC) carried out the MI-E trials. Two physiotherapists participated in each trial: one used the

MI-E device and the other performed the measurements. Great care was taken to avoid leaks around the mask during MI-E. The physiotherapists stimulated the patient's efforts to cough via strong verbal encouragement. MI-E was delivered via a facemask (Ambu UltraSeal^b) using the Cough-Assist E70^c device in automatic mode, as operator-bias might have occurred in manual mode. The duration of insufflation-exsufflation was set at 2.5 s. The optimal insufflation pressure determined on the previous day was used. Exsufflation pressure titration was performed starting at -20 cmH₂O then decreasing in 10 cmH₂O steps to -60 cmH₂O. For those patients expressing the wish to test the limits of the device, the exsufflation pressure was further decreased up to -70 cmH₂O. Each exsufflation pressure was tested at least three times,²³ and the best flow-volume curve was retained for the analysis, which included determination of the highest volume exsufflated at a flow greater than 3L/s (see below).

Individual exsufflation pressure titration was stopped when a further decrease was poorly tolerated by the patient or when an alteration in the flow-volume curve suggested UAC. Exsufflation poor tolerance was defined as an upper airway irritation and/or an UAC sensation limiting expiration and/or a dyspnea increase and/or a desynchronization between the patient and the cough device assistance. Flow-volume curve was considered altered by the physiotherapists on the basis of studies previously described with the negative expiratory pressure technique used to assess upper airway collapsibility during spontaneous breathing to identify patients at risk for obstructive sleep apnea (OSA)²⁴. The spirometer used for the study automatically superimposed successive flow-volume curves (Figure 1). A flow rate decrease occurring abruptly after PCF measurement on at least part of the exhaled volume, compared to the flow rate observed at the previous titration step, was thus taken to indicate UAC. In addition, abrupt flow-volume curve flattening at the beginning of MI-E titration (i.e., at the highest negative exsufflation pressure of -20 cmH₂O) is very typical to UAC but does not allow for comparison to a previous flow-volume

curve. Consequently, in this situation, UAC was diagnosed if further decreasing the negative exsufflation pressure failed to improve the appearance of the flow-volume curve.

The UAC determination by flow-volume curve analysis was checked later by two respiratory physiologists (FL and HP).

Patients could rest between each tested pressure level, and total patient participation did not exceed 40 minutes.

Statistical analysis

Baseline and anthropometric data were described as number (%) for categorical variables, mean $\pm$ SD for normally distributed continuous variables, and median [interquartile range] for skewed continuous variables. Inter-observer reliability of UAC detection based on the flow-volume curve appearance was assessed using Cohen's kappa (κ) statistics. Sensitivity and specificity of PCF and ECV for identifying UAC at the same negative exsufflation pressure during MI-E titration were calculated. A segmented linear mixed-effects regression model was built to assess changes in pressure over flow.

Patients were categorized based on their flow-volume curve patterns. Comparisons across patient categories of relied on ANOVA for normally distributed and homoscedastic quantitative variables and on the Kruskal-Wallis test for non-normally distributed or probably non-homoscedastic quantitative variables. Qualitative variables were compared across patient categories by applying the Mantel-Haenszel chi-square test or, when sample size was <5 , Fisher's exact test.

All tests were two-tailed and P values <0.05 were taken to indicate significant differences. The statistical analyses were carried out with R software version 2.2.0.²⁵

RESULTS

We included 27 patients with advanced muscle weakness due to NMD. Table 1 lists their main characteristics.

Flow-volume curve analysis

Among the 27 patients, 15 exhibited flow-volume curve evidence of UAC during MI-E. For all 15 patients, both observers agreed that the flow-volume curve profile indicated UAC (Cohen's $\kappa=1$).

The changes in flow-volume curve according to exsufflation pressure allowed us to divide the patients into three groups. Figure 2 and Table 2 showed individual characteristics of these 3 groups:

- profile A group [Figure 2, patient #3; Table 2] : In 12 patients, flow-volume curve area improved quasi-systematically as the exsufflation pressure decreased from -20 to -60 or -70 cmH₂O indicating that no UAC occurred. Of these 12 patients, 4 asked to test the -70 cmH₂O exsufflation pressure.
- profile B group [Figure 2, patient #13; Table 2] : In 10 patients, and flow-volume curve improved as the exsufflation pressure decreased, until UAC occurred and induced, after the peak flow, an abnormal abrupt fall in expiratory flow, which was confirmed when comparing these flow-volume loop with those obtained with the previous and less negative exsufflation pressure [profile B in Figure 2]. The exsufflation pressure at which UAC occurred was -70 cmH₂O in 1 patient, -60 cmH₂O in 7 patients, and -50 cmH₂O in 2 patients (Table 2). In one patient, a

decrease in the tolerance characterized by an uninterrupted irritating cough occurred at -50 cmH₂O and was concomitant with occurrence of UAC (patient #8 in Table 2).

- profile C group [Figure 2, patient #17; Table 2]: For the 5 remaining patients, UAC occurred at the beginning of titration. Accordingly the flow-volume curve flattened abruptly starting at the step that immediately followed the initial -20 cmH₂O exsufflation pressure value and did not improve when decreasing expiratory pressure. In 3 patients, titration was stopped before reaching -60 cmH₂O, at -50 cmH₂O in 1 patient and -40 cmH₂O in 2 patients, because of a decrease in the tolerance characterized by clinical sensation of upper airway collapse.

Peak cough flow (PCF)

PCF consistently increased with decreasing exsufflation pressure, regardless of whether UAC did or did not occur. Thus, PCF was always highest at the lowest exsufflation pressure tested. As shown in Figure 3, PCF increased steadily by about 0.32 L/s per 10 cmH₂O from the beginning to the end of titration.

Effective cough volume (ECV)

In the group with profile A, ECV increased steadily from the beginning to the end of titration. In the group with profile B, ECV increased steadily until UAC occurred then consistently decreased. In the group with profile C, ECV remained stable and below 200 mL as the exsufflation pressure decreased.

Comparison between PCF and ECV

The relative changes in PCF and ECV during negative exsufflation pressure titration are reported in Figure 4. In profile A, PCF and ECV increased concomitantly. In profile B, ECV

increased initially with PCF, until UAC occurred, after which ECV decreased while PCF continued to increase. In profile C, PCF increased steadily, while ECV remained below 200 mL. Thus, UAC was always accompanied with an increase in PCF contrasting with either a decrease in EVC or, when UAC occurred at the beginning of titration, a stable ECV value below 200 mL. A decrease in ECV versus earlier value had 100% sensitivity and 100% specificity for detecting UAC, whereas a decrease in PCF versus earlier value had 0% sensitivity and 100% specificity.

Comparison between patient groups with versus without upper airway collapse (UAC)

When we compared patients with versus without UAC diagnosed based on the flow-volume curve (i.e., those with profile A versus those with profile B or C), we found no significant differences in mechanical ventilation duration, VC, MIP, MEP, or baseline PCF ($P=0.78, 0.32, 0.58, 0.12$, and 0.24 , respectively). The distribution of NMD diagnoses differed significantly across the three flow-volume curve profiles (Fisher's exact test, $P=0.03$), chiefly because UAC occurred during titration in all 4 patients with spinal muscular atrophy.

DISCUSSION

We report the first systematic evaluation of flow-volume curve profiles during exsufflation pressure titration for MI-E in patients with NMD. PCF, the parameter generally used to assess cough efficiency, increased consistently as exsufflation pressure decreased. However, despite increasing PCF values, 15 of the 27 patients exhibited flow-volume curve findings indicating UAC and coinciding with a decrease in ECV (defined as the volume coughed at a flow >3 L/s), suggesting impaired cough efficiency. In contrast when the flow-volume curve showed no evidence of UAC, ECV increased steadily as the exsufflation pressure decreased.

The maximum flow achievable during forced expiration or coughing started after maximal or submaximal lung inflation is widely believed to be chiefly effort-dependent.²⁶ However, after the early peak flow, if sufficient expiratory effort is produced to cause dynamic compression of the intrathoracic airways, flow becomes effort-independent (i.e., limited): beyond a given driving pressure, additional force generated by the expiratory muscles does not further increase flow, which diminishes progressively from the early peak until the end of the maneuver.²⁶ This flow limitation is explained by the drop in alveolar pressure along the airways that occurs during expiration, due to airway resistance. The airway pressure may become equal to the intrapleural pressure during forced expiration, i.e., may reach the equal pressure point. When the equal pressure point is reached at the level of the trachea or large bronchi, the presence of hyaline cartilage prevents airway collapse.²⁶ However, due to the decrease in lung volume during forced expiration, the alveolar elastic recoil pressure decreases and the equal pressure point moves upstream towards the alveoli. The equal pressure point may then be reached at the thin-walled bronchioles, which may collapse, inducing a typical depression in the flow-volume curve.²⁶ This phenomenon of intrathoracic airway compression and collapse is critical for the secretion clearance mechanism, as it induces increases in linear velocity and kinetic airstream energy, thereby improving the mobilization and expulsion of material from the bronchial tree.²⁶ Accordingly, sufficient expiratory muscle force is required to reach the flow-limitation threshold. Thus, the greater is the expiratory effort, the earlier is the flow limitation reached during the forced expiratory maneuver and, therefore, the better is the flow-volume curve.

In many patients with NMD, the expiratory muscle weakness limits the production of a satisfactory flow-volume curve. Expiratory muscle weakness does not allow an optimal driving pressure in order to generate a high peak flow and reach the flow-limitation threshold. During the expulsive phase of cough, this weak driving pressure becomes the main cause of expiratory flow

reduction. Accordingly, applying negative pressure during expiration assist expiratory muscle weakness and may increase the peak flow or PCF by increasing the driving pressure and may also improve the second part of the expiratory flow-volume curve by reaching the flow-limitation threshold. This effect of negative exsufflation pressure was seen in our patients with profile A. However, as previously demonstrated in a few patients, if negative pressure induces UAC,^{18, 19} adding further flow limitation, then the flow coming from the lungs may be altered from the beginning to the end of the forced expiration. Moreover, airway collapse may be missed if only peak flow or PCF is measured, as these parameters may be paradoxically increased at the mouth when the collapse causes rapid expulsion of the air contained in the upper airway, although the contribution to airway clearance of airflow from the intrathoracic airways may be reduced by the upper airway obstruction. Our results support this possibility: in profile B seen in 10 of the 27 patients, PCF continued to increase with decreasing negative exsufflation pressure, but the ECV decreased after a threshold, resulting in a flattening of the subsequent part of the flow-volume curve. These results are also concordant with studies that used the negative expiratory pressure technique to assess upper airway collapsibility, as a mean of identifying patients at risk for OSA.²⁴ This technique consists in applying a slightly negative pressure of -5 to -10 cm H₂O at the mouth at the early expiration phase of quiet tidal breathing and comparing the ensuing FV-C with that observed during a control expiration. Negative expiratory pressure application elicits a flow spike, which can exceed 2.5 L/s during passive exhalation, despite the only slightly negative pressure. This spike is ascribed mainly to dynamic airway compression of the compliant oral and neck structures.²⁴ After the spike, flow decreases to a low value, due to an increase in resistance of the oropharyngeal structures, which reflects upper airway collapsibility (extrathoracic expiratory flow limitation).²⁴ It has been demonstrated that this transient spike in expiratory flow correlates with the severity of OSA.²⁴ Compared to those used for the negative expiratory

pressure technique, our conditions of negative pressure application were different: the inspiratory and expiratory efforts during coughing were maximal or submaximal, and the expiratory pressures were considerably lower. Nevertheless, our hypothesis that a high PCF value recorded at the airway opening does not necessarily indicate cough efficiency throughout the bronchial tree is supported by a recent bench study, in which an MI-E device was attached to a lung simulator with and without a collapsible tube.²⁷ PCF values were higher with than without the collapsible tube. The collapsible tube clearly tends to decrease PCF upstream, while increasing PCF downstream due to the additional flow produced by tube wall displacement.

In profile C seen in 5 of the 27 patients and characterized by early UAC, ECV remained below 200 mL. A likely explanation is that a major portion of the ECV in this situation was the volume ejected from the collapsing upper airway previously expanded by the insufflation preceding the exsufflation. Previous studies suggest that upper airway volume may be far less than 200 mL.^{28, 29} Insufflation might result in a larger volume, due to upper airway expansion. However, adduction of laryngeal structures during insufflation has been reported.¹⁸ In addition, upper airway narrowing during exsufflation never results in complete obstruction.¹⁹

We chose ECV, i.e., the volume exhaled above a flow rate of 3 L/s, to assess cough efficiency. The volume exhaled at flow rates above the threshold usually considered to be efficient during coughing,⁶ i.e., 3 L/s, is relevant. In addition, ECV is easy to determine from flow-volume curves in everyday practice.

In our study, the occurrence of suspected UAC during the application of negative exsufflation pressures was not related to the severity of the respiratory muscle dysfunction. However, all 4 patients with spinal muscular atrophy had suspected UAC. This result is not surprising, given that patients with spinal muscular atrophy often exhibit upper airway dysfunction, which may increase the risk of upper airway collapse during MI-E. Thus, studies

have established that the decrease in hypopharyngeal cross-section surface area seen during exsufflation in patients with amyotrophic lateral sclerosis was more marked in the subgroup with bulbar symptoms.¹⁸ Upper airway dysfunction may also be prevalent in spinal muscular atrophy, as chewing and swallowing difficulties have been documented in 28% and 25% of patients with type II disease, respectively.³⁰ Unfortunately, because our study was observational we were unable to modify our standard practice of confining the evaluation to spirometry, which is currently viewed as the reference standard for PCF measurement. Therefore, upper airway function was not routinely investigated. Nevertheless, all 5 patients with profile C, characterized by upper airway collapse starting at the first negative pressure level (-20 cmH₂O), including 3 of the 4 patients with spinal muscular atrophy, reported swallowing difficulties consistent with severe upper airway dysfunction. These results strongly support a need for accurately determining the optimal MI-E negative pressure in patients with NMD and inefficient cough, particularly when bulbar symptoms are present. Flow-volume curve analysis can be an efficient tool for achieving this goal.

Study Limitations

An important limitation of this study is that performance was evaluated only during spirometry. To date, it is unclear whether PCF, ECV, or the flow-volume curve profile is most important for assessing cough efficiency. Nevertheless, a negative exsufflation pressure that decreases ECV may limit cough efficiency. It may be appropriate to discuss the trade-off between improving PCF and keeping the flow-volume curve unaltered. In addition, when the flow-volume curve profile suggests UAC occurring at the beginning of negative exsufflation pressure titration (profile C), further decreasing the exsufflation pressure is unlikely to be beneficial. Thus, in our patients with profile C, decreasing the exsufflation pressure had little effect on ECV, which

remained below 200 mL. Alternative or additional techniques, such as manual assisted coughing, may be beneficial³¹ by increasing airway pressure and possibly preventing UAC during exsufflation, but were not tested in our study. These points should be addressed by future research. In addition, flow-volume curve analysis should be included in guidelines about optimal MI-E titration. We did not test negative exsufflation pressures above -20 cmH₂O, which is the highest initial pressure setting suggested in the literature.¹⁶ Finally, we did not evaluate patient comfort or subjective cough effectiveness. However, in a previous study using various inflation techniques, we found no association of cough performance with subjective impressions.³¹ Finally, patient position may have an important impact on respiratory performances. Postural adjustments were made according to patients' opinion on their best respiratory comfort. We did not describe the position on the wheelchair (degree of tilt, recline or elevating leg rests measures). They might be important to control in future studies.

Conclusions

In conclusion, in some patients with NMD, decreasing the negative exsufflation pressure used for MI-E was associated with a decline in the volume exhaled at a flow rate above 3 L/s (ECV), suggesting UAC. This decline in ECV was accompanied with an increase in PCF, which thus failed to detect UAC. Our findings suggest that analysis of the maximal expiratory flow-volume curve, with ECV measurement, may improve the identification of the negative exsufflation pressure associated with maximal cough efficiency.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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SUPPLIERS

- a. Spirometer: Medisoft, Sorinnes, Belgium
- b. Facemask: Ambu, Bordeaux, France
- c. Mechanical insufflation-exsufflation device: JH Emerson Co., Cambridge, MA, USA

FIGURE LEGENDS

Figure 1

Example of two flow-volume curves obtained during coughing and two different negative pressure applications. The solid line was obtained at a lower pressure than the dotted line and indicated a flow rate decrease for part of the exhaled volume compared to the dotted line, suggesting transient upper airway collapse (UAC). Cough performance was assessed based on the effective cough volume (ECV), defined as the volume exhaled at a flow rate above 3 L/s (180 L/min). See text for details.

Figure 2

Examples of each of the three flow-volume curve profiles (A, B, and C) during titration of the negative exsufflation pressure applied during mechanical in-exsufflation.

A: No upper airway collapse (UAC) : Peak cough flow (PCF) and the effective cough volume (ECV) increase.

B: UAC occurs at a specific exsufflation pressure (in this example at -50 cmH₂O, confirmed at -60 cmH₂O) : PCF increases, ECV decreases.

C: UAC is observed at the beginning of pressure titration: PCF increases, ECV remains stable when expiratory pressure decreases.

See the results section for more details.

Figure 3

Peak cough flow changes according to the level of negative expiratory pressure applied

Figure 4

Individual relationships between peak cough flow (PCF) and effective cough volume (ECV) during negative exsufflation pressure titration in patients with profile A (left panel, n=12) and in those with profile B or C (right panel, n=15). The three profiles are described in Figure 2 and Table 2.

Figure 1 :

Figure 2 :

Figure 3 :

Figure 4 :

Table 1: Baseline characteristics of the 27 patients with neuromuscular disease

Characteristics	Population n=27
Diagnosis, n (%)	
Duchenne Muscular Dystrophy	14 (51)
Limb Girdle Muscular Dystrophy 2C	4 (15)
Spinal Muscular Atrophy	4 (15)
Limb Girdle Muscular Dystrophy 2D	2 (7)
Congenital Myasthenia Gravis	1 (4%)
Charcot Marie-Tooth	1 (4)
Mitochondrial Myopathy	1 (4)
Age, years	30.6 ($\pm$ 9.2)
Male gender, n (%)	16 (59)
MV duration (hour/day)	10.4 ($\pm$ 5.8)
Upright VC, %	20.2 ($\pm$ 11.8)
MIP, cmH ₂ O	20.3 ($\pm$ 13.9)
MEP, cmH ₂ O	18.2 ($\pm$ 10.7)
PCF, Liter/sec	161.4 ($\pm$ 52.6)

The data are mean $\pm$ SD unless specified otherwise. VC, vital capacity as % of the predicted value according to Quanjer et al.²⁰; PCF, peak cough flow; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; MV, mechanical ventilation

Table 2. Characteristics of the 27 patients with neuromuscular disease and chronic respiratory failure

Profile #	Sex/Age	Diagnosis	MV duration	VC seated	MIP/MEP	PCF	Highest IP/EP tested	PCF/ECV at the highest IP/EP	Best ECV and its EP	
	years		h/day	%	cmH ₂ O	L.min ⁻¹	cmH ₂ O	L.min ⁻¹ / L	L/cmH ₂ O	
A	2	M/22	DMD	8	23	32/23	184	24/-70	381/3.70	3.70/-70
A	3	M/32	LGMD2C	8	16	16/16	135	34/-60	344/2.20	2.20/-60
A	4	F/43	CMT	15	23	11/19	178	34/-70	312/0.58	0.58/-70
A	6	M/20	DMD	24	11	21/15	159	38/-70	361/1.20	1.20/-70
A	9	M/40	LGMD2C	10	12	13/13	107	28/-60	332/1.16	1.16/-60
A	12	M/25	DMD	10	32	25/20	236	24/-70	348/0.96	0.96/-70
A	15	M/21	DMD	8	14	19/21	250	28/-60	337/0.60	0.60/-60
A	22	F/26	LGMD2C	0	36	37/30	239	40/-60	327/1.16	1.16/-60
A	23	M/33	DMD	23	11	8/9	119	34/-60	351/1.44	1.44/-60
A	25	M/22	DMD	12	24	9/9	145	34/-60	290/1.08	1.08/-60
A	26	M/26	DMD	8	17	15/25	195	28/-60	337/1.32	1.32/-60
A	27	F/56	MM	12	52	28/55	227	40/-60	284/1.00	1.00/-60
B	5	M/21	DMD	16	9	11/10	160	34/-60	344/0.92	1.44/-50
B	7	M/23	DMD.	12	17	17/19	203	30/-70	342/0.80	1.50/-60
B	8	M/22	DMD	15	10	13/14	154	36/-50	296/0.16	0.50/-40
B	10	M/27	DMD.	18	8	9/5	128	30/-60	349/0.92	0.96/-50
B	11	F/24	DMD	8	24	13/8	215	34/-60	305/1.32	1.60/-50
B	13	F/38	LGMD2D	8	14	11/11	141	34/-60	318/0.40	0.60/-50
B	16	M/23	DMD	9	13	10/11	187	30/-60	316/0.40	0.60/-50
B	18	F/30	SA	0	50	67/37	220	30/-60	272/1.00	1.16/-50
B	20	F/42	LGMD2C	10	12	9/9	130	24/-60	308/1.08	1.32/-50
B	24	F/44	LGMD2D	10	15	7/10	130	30/-50	266/0.32	0.72/-40
C	1	F/37	SA	0	30	40/27	122	34/-40	227/0.12	0.12/-40
C	14	F/25	DMD	9	14	18/29	142	24/-40	259/0.12	0.12/-40
C	17	M/39	SA	8	12	21/15	69	40/-60	231/0.08	0.08/-60
C	19	F/33	SA	12	12	22/14	104	34/-50	248/0.12	0.12/-50
C	21	F/32	CMS	8	33	46/16	179	28/-60	301/0.16	0.16/-60

Abbreviations: MV, mechanical ventilation; F, female; M, male; VC, vital capacity; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; PCF, peak cough flow; IP, insufflation pressure; EP, exsufflation pressure; ECV, effective cough volume; DMD, Duchenne muscular dystrophy; SA, spinal muscular atrophy; CMT, Charcot-Marie-Tooth disease; LGMD2C, limb-girdle muscular dystrophy type 2C; LGMD2D, limb-girdle muscular dystrophy type 2D; CMG, congenital myasthenic syndrome; MM, mitochondrial myopathy; A, B, and C profiles, flow-volume profiles depicted in Figure 2