

Limits of Effective Cough-Augmentation Techniques in Patients With Neuromuscular Disease

Michel Toussaint PT PhD, Louis J Boitano MSc RRT, Vincent Gathot MSc PT, Marc Steens MSc PT, and Philippe Soudon MD

BACKGROUND: Manual and mechanical cough-augmentation techniques can improve peak cough flow (PCF) in patients with respiratory insufficiency caused by neuromuscular disease. **METHODS:** We studied cough-augmentation techniques in 179 clinically stable patients with various neuromuscular diseases. We measured vital capacity (VC), maximum expiratory pressure (MEP), and PCF, with and without 3 cough-augmentation techniques: manually assisted cough (MAC); breath-stacking (in a subgroup of 60 patients receiving noninvasive mechanical ventilation); and breath-stacking in combination with MAC (also in the 60-patient subgroup). We analyzed the data with the receiver operating characteristic (ROC), to predict the lower limits (assisted PCF \geq 180 L/min) and upper limits (assisted PCF < unassisted PCF) of effectiveness of the 3 cough-augmentation techniques. **RESULTS:** The lower limit of effective assisted cough with MAC, breath-stacking, and breath-stacking plus MAC was best predicted by VC > 1,030 mL (ROC 0.86, $P < .001$), VC > 558 mL (ROC 0.92, $P < .001$), and VC > 340 mL (ROC 0.90, $P < .001$). The upper limit of effective MAC was best predicted by MEP > 34 cm H₂O (ROC 0.89, $P < .001$), whereas the ROC prediction of the upper limit of effective cough with breath-stacking and with breath-stacking plus MAC was not better than random. With each of the cough-augmentation techniques the benefits decreased linearly with increasing MEP and VC ($P < .001$). Compared to MAC and breath-stacking alone, breath-stacking plus MAC best improved unassisted PCF ($P < .001$). **CONCLUSIONS:** In clinically stable patients with neuromuscular diseases, the effectiveness of cough-augmentation techniques can be predicted with measurements of maximum respiratory capacity. Patients with VC > 340 mL and MEP < 34 cm H₂O would optimally benefit from the combination of breath-stacking plus manually assisted cough to improve PCF to > 180 L/min. *Key words:* breath-stacking, airway clearance, chest physiotherapy, cough, cough augmentation, hyperinflation, neuromuscular, noninvasive ventilation, mucus clearance. [Respir Care 2009;54(3):359–366. © 2009 Daedalus Enterprises]

Introduction

In the last decade, quality of life and survival have substantially increased among patients with neuromuscular disease receiving home mechanical ventilation.¹⁻³ These patients typically have cough impairment due to respiratory muscle weakness. Cough-augmentation techniques have contributed to the success of noninvasive ventilation (NIV) in these patients.^{4,5} Cough-augmentation techniques

include inspiratory muscle aids, expiratory muscle aids, and combined inspiratory and expiratory muscle aids.

Effective Cough

An effective cough depends on the capacity to produce adequate peak cough flow (PCF).⁶ Three phases of cough combine to produce PCF. The first phase, inspiration, consists of a variable inhalation volume of air. In the second

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This research was partly supported by Société Française de Kinésithérapie.

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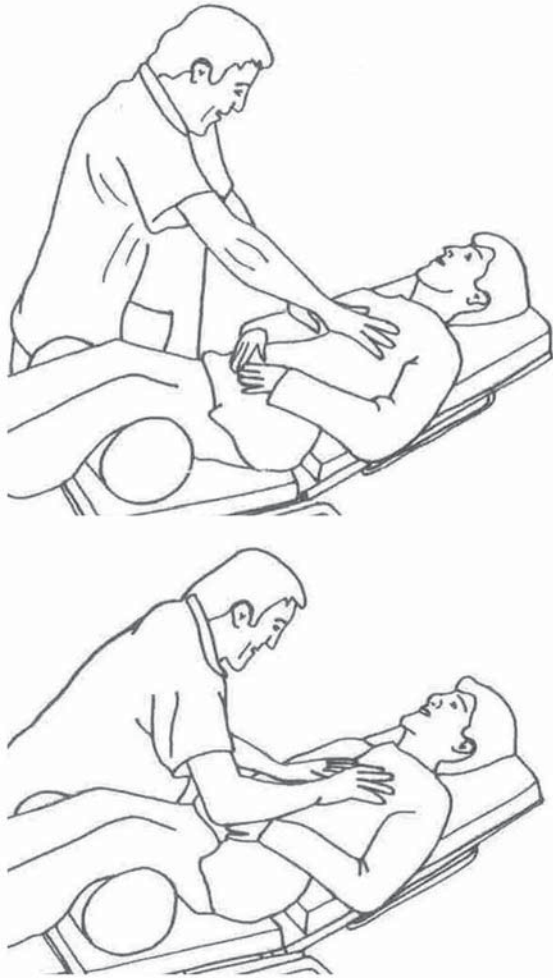


Fig. 1. Manually assisted cough via thoracic compression.



Fig. 2. Manually assisted cough via abdominal-thoracic compression.

phase, compression, the air volume is compressed in the lungs by expiratory muscle force against a closed glottis. In the third phase, expiration, PCF occurs after the glottis quickly opens and releases the compressed gas volume, under continued expiratory muscle force. PCF depends on the amplitude of the inspiratory phase (ie, the inhaled volume, which depends on the inspiratory muscle strength), and on the expiratory muscle strength and glottic function. In normal subjects, PCF is generally > 500 L/min.⁷ A PCF range of 160–180 L/min has been found to provide effective airway clearance in adult patients with stable neuromuscular disease who still have bulbar function.^{4,8-11} In the present study we considered 180 L/min the threshold PCF, above which cough was considered effective. In Belgium, PCF < 180 L/min is mandatory to obtain reimbursement for secretion-clearance devices (Belgian Agreement for Home Mechanical Ventilation, and the 1994 Belgian law on mandatory insurance on health care and indemnities). In France, PCF of 180 L/min was recently proposed as the threshold value for effective cough.¹⁰

Cough in Neuromuscular Diseases

Patients with neuromuscular disease can have moderate to severe weakness of both inspiratory and expiratory muscles. Cough-augmentation techniques were developed to compensate for that muscle weakness. There are inspiratory aids,¹² such as hyperinflation via breath-stacking, and expiratory aids,¹³ such as manually assisted cough (MAC). In breath-stacking the patient inhales a volume of air from the ventilator, retains that volume by closing the glottis, then inhales another volume of air, then again closes the glottis. Additional volumes can be inhaled (“stacked”), depending on the set tidal volume and the patient’s ability to perform the breath-stacking maneuver. When maximally insufflated, the patient quickly releases the air by coughing. Pulmonary and chest wall elastance alone can expel the gas with sufficient flow to clear secretions.

Inspiratory and expiratory aids improve cough clearance,¹²⁻¹⁴ and the greatest benefit is obtained by combin-

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Table 1. Subject Demographics and Pulmonary Capacity Values ($n = 179$)

	Duchenne or Becker Muscular Dystrophy	Type-2 Spinal Muscular Atrophy	Other Neuromuscular Diseases
Male/female	127/0	14/12	18/8
Age (mean \pm SD y)	22.2 \pm 7.1	26.4 \pm 9	33 \pm 15
BMI (mean \pm SD kg/m ²)	17.2 \pm 5	19.6 \pm 7.6	18 \pm 3.9
VC (mean \pm SD mL)	1,191 \pm 890	1,644 \pm 1,005	1,348 \pm 719
VC (mean \pm SD % predicted)	24 \pm 17	38 \pm 22	29 \pm 15
MEP (mean \pm SD cm H ₂ O)	26 \pm 18	39 \pm 16	42 \pm 20
Unassisted PCF (mean \pm SD L/min)	163 \pm 81	198 \pm 78	199 \pm 84
PCF with thoracic MAC (mean \pm SD L/min)	209 \pm 71*	225 \pm 73*	197 \pm 78
PCF with abdominal-thoracic MAC (mean \pm SD L/min)	210 \pm 70*	245 \pm 73*†	197 \pm 85

*Assisted peak cough flow (PCF) was significantly greater than unassisted PCF ($P < .001$ via paired t test).

† PCF was greater with abdominal-thoracic manually assisted cough (MAC) than with thoracic MAC ($P < .001$ via paired t test).

BMI = body mass index

VC = vital capacity

MEP = maximum expiratory pressure

ing inspiratory and expiratory aids.¹⁵ Mechanical insufflation-exsufflation (with the Cough-Assist In-exsufflator, Respironics, Murrysville, Pennsylvania) combines inspiratory and expiratory aids, but in-exsufflation is expensive and not generally available in countries with limited health-care resources. In-exsufflation may be useful when MAC and breath-stacking are no longer effective in weak or fatigued neuromuscular patients who still have bulbar function.¹⁶⁻¹⁸ The most appropriate cough-assistance technique is partly based on the limits of effectiveness of MAC, breath-stacking, and breath-stacking plus MAC, which at present are unknown in clinically stable or unstable neuromuscular patients.

We tested cough-assistance techniques based on maximum respiratory capacity measurements in clinically stable neuromuscular patients. We hypothesized that the vital capacity (VC), maximum expiratory pressure (MEP), and unassisted PCF would predict the lower limit of effective assisted cough (PCF $>$ 180 L/min) and the upper limit of effective assisted cough (assisted PCF $<$ unassisted PCF) in patients with neuromuscular disease. Our aim was to identify easily measurable predictors of which patients will benefit from which cough-augmentation techniques.

Methods

Study Design

This prospective cross-sectional study compared 3 cough-augmentation techniques: manually assisted cough (MAC) (with either thoracic MAC [Fig. 1] or abdominal-thoracic MAC [Fig. 2]); breath-stacking; and the combination of breath-stacking plus MAC. Our institution's ethics committee approved the study, and informed consent was obtained from all patients.

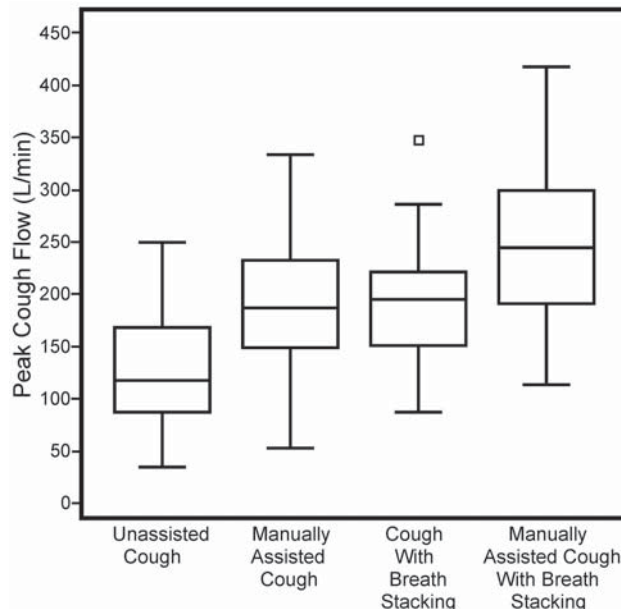


Fig. 3. Peak cough flow with and without manually assisted cough, and with and without breath-stacking in mechanically ventilated patients with neuromuscular disease. (Data in box-and-whisker presentation.)

Patients

During 2002 through 2006, all patients with stable neuromuscular disease who were referred to our center were considered for study inclusion. Exclusion criteria included tracheostomy, age $<$ 8 years, inability to follow directions during lung-function testing, respiratory tract infection, bulbar impairment, and history of pneumothorax or symptomatic low cardiac output syndrome. MAC was measured with 179 patients. Breath-stacking, and breath-stacking plus

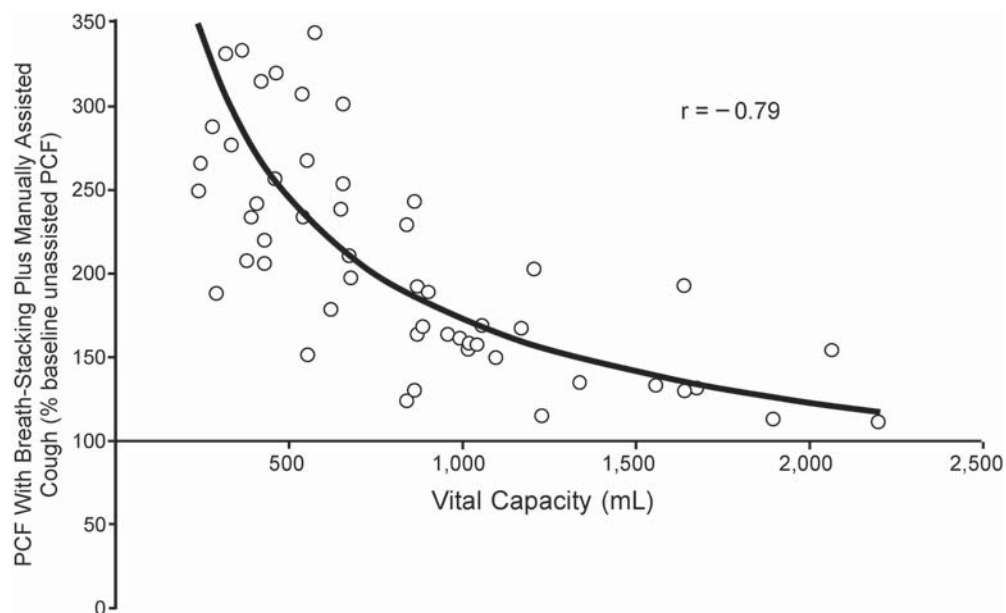


Fig. 4. Peak cough flow (PCF) versus vital capacity. With increasing vital capacity, the PCF benefit from breath-stacking plus manually assisted cough decreases.

MAC were measured in a subgroup of 60 patients who were on NIV.

Measurements

VC and unassisted PCF were measured with a portable spirometer (5410, Datex-Ohmeda, Louisville, Kentucky). Maximum inspiratory pressure (MIP) and MEP were measured with the method described by Black and Hyatt,¹⁹ with a manometer (Microloop, Micro Medical, Rochester, United Kingdom). The best of 3 VC, MIP, MEP, and unassisted PCF values were retained for analysis. VC, MIP, and MEP were measured with the patient sitting. Unassisted and assisted PCF were measured with the patient supine. In clinical practice we assist cough in sitting patients when there is little airway encumbrance. In patients with more severe encumbrance we use the supine position because it provides a more powerful chest squeezing (see Figs. 1 and 2),¹⁸ so in the present study we used the supine position as the reference position for cough measurements. Predicted VC values were calculated with reference values from the European Respiratory Society.²⁰

Assisted PCF was recorded by experienced therapists (MT and MS). For the breath-stacking maneuvers the breaths were delivered via volume-controlled ventilator and nasal mask. The effectiveness of breath-stacking was assessed based on the patient's capacity to store a > 10% higher air volume than his or her best unassisted expiratory VC. After 2 min of training, the patient was asked to stack breaths, then to perform a cough maneuver with forced expiration, and we measured PCF from that ma-

neuver. Since the PCF depends on the breath-stacking technique,²¹ prior to each study we assessed the number of stacked breaths that achieved the highest PCF.

The lower limit of cough effectiveness was defined as PCF of 180 L/min. The upper limit of cough effectiveness was defined as the ratio of assisted PCF to unassisted PCF less than 1.

Analysis

With statistics software (MedCalc, MedCalc Software, Mariakerke, Belgium) we computed the sensitivity, specificity, and area-under-the-curve of the receiver operating characteristic (ROC) to determine each respiratory variable's power to predict the limits of effective cough. The cut-off value represented the best compromise between sensitivity and specificity. An ROC area of 1 would indicate a perfect predictor of the limit. An ROC area of 0.5 indicates a weak predictor (a 50% chance of error). In this context the *P* value is the probability that the ROC area is equal to 0.5. We used the paired *t* test for paired comparisons. Differences were considered significant when *P* < .05.

Results

Table 1 reports the characteristics of the 179 patients included in the study: 127 had dystrophinopathies (117 with Duchenne muscular dystrophy, and 10 with Becker muscular dystrophy), 26 had intermediate type-2 spinal muscular atrophy, and 26 had miscellaneous neuromuscu-

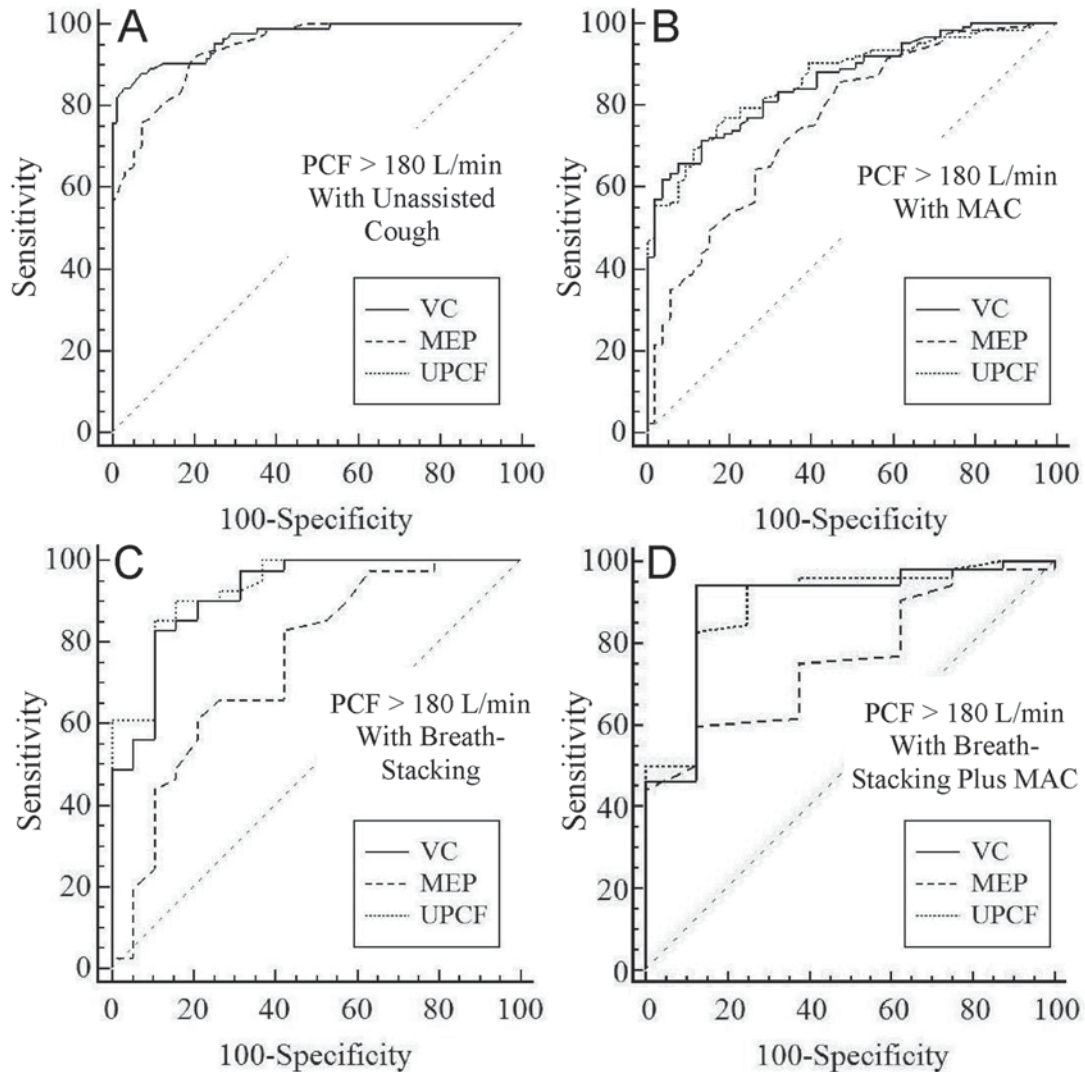


Fig. 5. Predictors of the lower limits of effective cough (peak cough flow [PCF] > 180 L/min). See Table 2 for the receiver operating characteristic (ROC) curve, sensitivity, and specificity values. A: Unassisted cough. B: Manually assisted cough (MAC). C: Breath-stacking. D: Breath-stacking plus MAC. VC = vital capacity. MEP = maximum expiratory pressure. UPCF = unassisted peak cough flow.

lar diseases (9 with congenital muscular dystrophy, 8 with limb girdle dystrophy, 3 with Steinert dystrophy, 2 with amyotrophic lateral sclerosis, 1 with Landouzy-Dejerine dystrophy, 1 with Pompe disease, 1 with Charcot Marie-Tooth disease, and 1 with metabolic dystrophy). A subgroup of 60 patients were on NIV: 38% only at night, 62% day and night.

Compared to unassisted PCF, MAC improved PCF in the patients with Duchenne/Becker muscular dystrophy and type-2 spinal muscular atrophy (see Table 1). The best performance with thoracic or abdominal-thoracic MAC was not related to MEP or body mass index. The patients with type-2 spinal muscular atrophy had higher assisted PCF with abdominal-thoracic MAC (245 L/min) than with thoracic MAC (225 L/min, $P < .001$). In

the 60 patients on NIV, the PCF values with MAC, breath-stacking, and breath-stacking plus MAC were 49%, 53%, and 98% higher, respectively, than unassisted PCF (Fig. 3). The benefit from breath-stacking, MAC, and breath-stacking plus MAC was inversely related to MEP and VC ($P < .001$). Figure 4 shows that with increasing VC there was decreasing benefit from breath-stacking plus MAC ($r = -0.79$, $P < .001$).

Figure 5 and Table 2 report the ROC predictions of the lower limits of effective assisted and unassisted cough, as assessed relative to PCF > 180 L/min. VC and MEP were sensitive and specific predictors of effective unassisted cough (see Fig. 5A). VC and unassisted PCF were better than MEP in predicting PCF > 180 L/min (see Fig. 5B, 5C, and 5D).

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Table 2. Predictors of the Lower Limits of Effective Unassisted and Assisted Cough

Predictor	ROC Area	Sensitivity	Specificity	<i>P</i>
PCF > 180 L/min with unassisted cough*				
VC > 1,180 mL	0.97	84	97	< .001
MEP > 24 cm H ₂ O	0.94	92	80	< .001
PCF > 180 L/min with MAC†				
VC > 1,030 mL	0.86	66	93	< .001
Unassisted PCF > 140 L/min	0.86	71	87	< .001
MEP > 14 cm H ₂ O	0.76	86	53	< .001
PCF > 180 L/min with breath-stacking‡				
Unassisted PCF > 110 L/min	0.93	85	90	< .001
VC > 558 mL	0.92	83	90	< .001
MEP > 11 cm H ₂ O	0.75	83	58	.001
PCF > 180 L/min with breath-stacking and MAC§				
VC > 340 mL	0.90	94	88	< .001
Unassisted PCF > 90 L/min	0.89	83	88	< .001
MEP > 14 cm H ₂ O	0.76	60	88	< .001

* The receiver operating characteristic (ROC) areas for vital capacity (VC) and maximum expiratory pressure (MEP) were not significantly different ($P = .17$).

† The ROC areas of VC and unassisted PCF were similar ($P = .57$), and both were higher than MEP ($P < .001$).

‡ The ROC areas of VC and unassisted PCF were similar ($P = .58$), and both were higher than MEP ($P = .001$).

§ The ROC areas of VC and unassisted PCF were similar ($P = .92$), and VC and unassisted PCF were higher than MEP ($P = .05$ and $.03$, respectively).

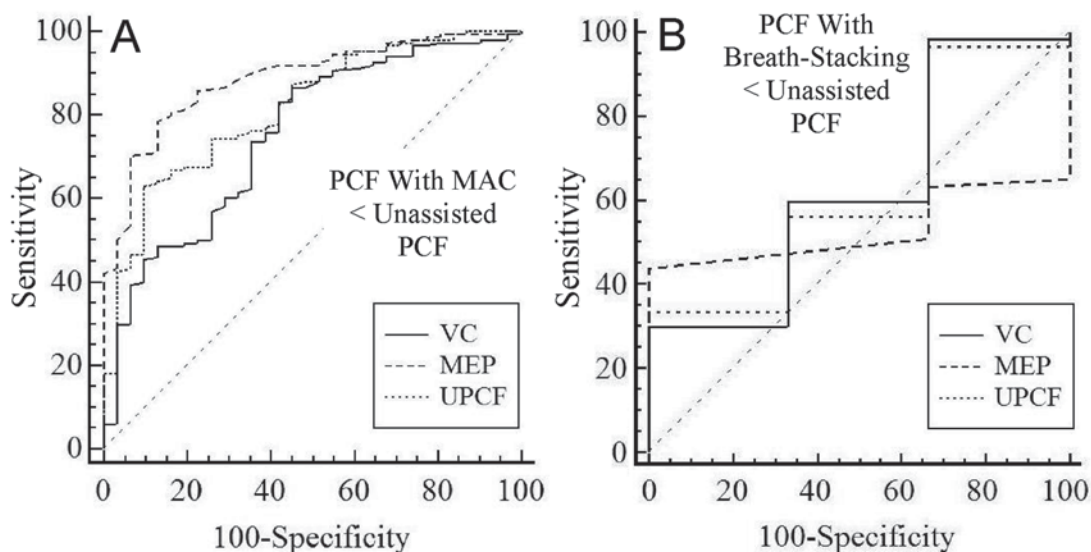


Fig. 6. Predictors of the upper limits of effectiveness of assisted cough (assisted peak cough flow [PCF] < unassisted PCF). See Table 3 for the receiver operating characteristic (ROC) curve, sensitivity, and specificity values. A: Manually assisted cough (MAC). B: Breath-stacking. VC = vital capacity. MEP = maximum expiratory pressure. UPCF = unassisted peak cough flow.

Figure 6 and Table 3 report the ROC predictions of the upper limits of effective assisted cough (assisted PCF/unassisted PCF < 1). MEP > 34 cm H₂O predicted no further cough improvement with MAC (see Fig. 6A). VC, unassisted PCF, and MEP were not better than random in predicting cough improvement with breath-stacking alone (Fig. 6B). No marker of the upper limit of effectiveness of breath-stacking plus MAC was identified. Table 4 sum-

marizes the range of respiratory muscle strength for effective cough-augmentation techniques in patients with neuromuscular disease.

Discussion

Our main findings suggest limits to the effectiveness of cough-augmentation techniques and when these techniques

Table 3. Predictors of the Upper Limits of Effective Assisted Cough

Predictor	ROC Area	Sensitivity	Specificity	P
Assisted < unassisted PCF with MAC*				
MEP > 34 cm H ₂ O	0.89	78	87	< .001
Unassisted PCF > 178 L/min	0.82	78	87	< .001
VC > 1,910 mL	0.75	87	55	< .001
Assisted < unassisted PCF with breath-stacking				
VC > 1,900 mL	0.63	98	33	.48
Unassisted PCF > 92 L/min	0.62	33	100	.50
MEP > 13 cm H ₂ O	0.53	44	100	.87

* For maximum expiratory pressure (MEP) > unassisted peak cough flow (PCF), $P = .05$.
For unassisted PCF > vital capacity (VC), $P = .006$.
ROC = receiver operating characteristic

Table 4. Range of Respiratory Muscle Capacity for Effective Assisted Cough

	MAC	Cough With Breath-Stacking	Cough With Breath-Stacking Plus MAC
VC (mL)	1,030*–1,910	558–no limit	340*–no limit
MEP (cm H ₂ O)	14–34*	11–no limit	14–no limit
Unassisted PCF (L/min)	140–178	110*–no limit	90–no limit

* Best receiver operating characteristic (ROC) predictor of the limit of cough effectiveness among vital capacity (VC), maximum expiratory pressure (MEP), and unassisted peak cough flow (PCF).

No limit = no limit identified with ROC analysis
MAC = manually assisted cough

are ineffective in patients with neuromuscular disease. MAC should benefit patients whose VC range is 1,030–1,910 mL (MEP 14–34 cm H₂O). Under and above those limits, MAC may not be effective. Breath-stacking alone, and breath-stacking with MAC may provide PCF > 180 L/min in patients with VC > 558 mL and VC > 340 mL, respectively. The absence of an upper limit of effectiveness suggests that breath-stacking and breath-stacking plus MAC may benefit all patients with neuromuscular disease; however, the benefits of cough-augmentation appear to decrease linearly with increasing VC and MEP.

Our results suggest that lung function testing can serve as baseline predictor of which cough-augmentation techniques will benefit patients with stable neuromuscular disease. These predictors may overestimate the cough capacity of patients with neuromuscular disease who have an unstable respiratory status.⁹ We suggest the following categories for the potential benefit of cough-augmentation in stable patients with neuromuscular disease:

Category 1: Patients with MEP > 34 cm H₂O or VC > 1,910 mL. In these patients, manual chest compression may not augment cough clearance. As shown in Figure 4, breath-stacking alone or combined with MAC is possible, but the benefit decreases with increasing VC and MEP.

Category 2: Patients with VC of 340–1,910 mL or MEP 14–34 cm H₂O. In these patients, unassisted cough may be effective when VC is > 1,180 mL. Assisted cough may be effective with expiratory cough-augmentation alone, inspiratory cough-augmentation alone, or in combination when VC is > 1,030 mL, > 560 mL, or > 340 mL, respectively.

Category 3: Patients with VC < 340 mL. These patients are not likely to receive adequate support from breath-stacking plus MAC. Without an in-exsufflation device these patients are at high risk of cough-assistance failure.

The above definition of Category 1 patients is consistent with previous studies. With a physiologic approach,²² PCF did not change with increasing MEP if the subjects had MEP > 50 cm H₂O. Others²³ observed that PCF was preserved in patients with MEP > 45 cm H₂O. Interestingly, Sivasothy et al²¹ found a negative impact on cough from an expiratory aid in a group of patients with mean MEP of 51 cm H₂O, but they found a positive impact in another group with mean MEP of 22 cm H₂O. Despite potential bias from the presence of scoliosis, which might limit the ability to administer effective MAC, the cut-off value to determine negative and positive impact on cough from expiratory aid was expected to be between 22 cm H₂O and 51 cm H₂O.²¹ In the present study this MEP cut-off value was 34 cm H₂O. Our findings indicate that patients with MEP > 34 cm H₂O should cough better unassisted than with MAC. To our knowledge, this is the first time that a limit of effectiveness has been reported with MAC, which is a widely used cough-augmentation technique.

We also compared the thoracic and abdominal-thoracic MAC techniques. Patients with type-2 spinal muscular atrophy had greater benefit from abdominal-thoracic MAC, which may be explained by the fact that in type-2 spinal muscular atrophy the expiratory muscles are usually affected earlier than the inspiratory muscles. In all the other patient groups, abdominal-thoracic MAC was often better in patients who were cooperative and did not experience abdominal pain from the MAC. In abdominal-thoracic MAC (see Fig. 2) the therapist bends over the patient. Abdominal MAC is applied while the upper forearm splints the patient's sternum during cough. We were not able to predict the best MAC by comparing the thoracic and abdominal-thoracic maneuvers to improve cough in each patient. This suggests that regular trials are required to determine which MAC technique is best for each patient, and to maximize MAC effectiveness in case of infection.

The present study also confirmed that combining breath-stacking with MAC increases the benefit.^{15,21,24} Bach¹⁵

found cough-augmentation effective in patients with neuromuscular disease who had cough insufficiency. Unassisted PCF, PCF with breath-stacking, and PCF with breath-stacking plus MAC were 108 L/min, 202 L/min, and 256 L/min, respectively. In patients with a mean unassisted PCF of 104 L/min, Sivasothy et al²¹ found that assisted PCF was 185 L/min, 156 L/min, and 248 L/min with MAC, breath-stacking, and breath-stacking plus MAC, respectively. In contrast, our PCF values with breath-stacking were not lower than those with MAC. Sivasothy et al²¹ administered only one pressure-limited (20 cm H₂O) insufflation volume, whereas we used volume-controlled ventilation to stack multiple inhalations and maximize the inspired volume.

Conclusions

Markers of maximum respiratory capacity may predict unassisted and assisted PCF > 180 L/min in clinically stable patients with neuromuscular disease. The best cough improvement results from a combination of breath-stacking plus MAC. But if VC is < 340 mL, breath-stacking plus MAC may be insufficient to produce a PCF > 180 L/min. The upper limits of PCF improvement with breath-stacking alone or breath-stacking plus MAC are not predictable. MAC seems to interfere with spontaneous cough in patients with stronger cough and MEP > 34 cm H₂O.

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