

## Inspiratory muscle strength and walking capacity in patients with COPD

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### ABSTRACT

**Purpose:** It has been suggested that patients with inspiratory muscle weakness could benefit from specific inspiratory muscle training (IMT). We aimed to examine the frequency of patients with inspiratory muscle weakness in a Danish hospital-based outpatient pulmonary rehabilitation program, and to evaluate the association between inspiratory muscle strength and peripheral muscle strength and walking capacity.

**Methods:** Maximal Inspiratory Pressure (MIP) was assessed in 97 patients with COPD (39 men, 58 women, mean age years  $70 \pm 9$ , forced expiratory volume in 1 s ( $FEV_1$ ) =  $35 \pm 10\%$  pred.). The impact of MIP on knee-extension strength, walking distance, and symptom burden was evaluated using multiple linear regression analyses.

**Results:** The MIP of the patients with COPD was 63 (95% CI 59; 67) cmH<sub>2</sub>O and it was significantly reduced compared to gender and age-matched reference values 76 (95% CI 73; 79) cmH<sub>2</sub>O ( $p < 0.001$ ). Seven patients (7.2%) were under the lower limit of normal. MIP was negatively correlated with increasing age, female gender, decreasing knee-extension strength and lower  $FEV_1\%$  pred. Walking distance was associated with knee-extension strength and it was not associated with MIP.

**Conclusion:** Maximal inspiratory pressure was reduced in patients with COPD but only a few patients had a weak MIP. Whilst MIP was associated with leg muscle strength, it was not associated with walking distance or symptoms.

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Maximal inspiratory strength; chronic obstructive pulmonary disease; physiotherapy; quadriceps strength; walking distance

## Introduction


Muscle dysfunction is a serious systemic consequence of chronic obstructive pulmonary disease (COPD), which includes dysfunctions of peripheral muscles as well as the respiratory muscles [1]. The peripheral muscle dysfunction in patients with COPD is associated with reduced walking distance, physical capacity and quality of life, and with elevated health-care use and mortality risk [1]. While the affection of the peripheral muscles is well described, the clinical impact of respiratory muscle dysfunction is less clear. Dyspnea is induced by an imbalance between load on the respiratory system and the capacity of the respiratory muscles. However, dyspnea is also induced by other factors, such as exercise, stimulation of chemoreceptors (hypoxemia, hypercapnia), hyperinflation and an unrewarded neural drive from the brain [2,3].

In Danish hospitals, pulmonary rehabilitation is offered to patients with COPD in the advanced stage, i.e., patients with a low lung function combined with a high burden of symptoms and frequent exacerbations. The pulmonary

rehabilitation includes resistance and endurance training in order to improve the limb muscle function and to increase the walking distance and the physical capacity. It has been suggested that patients with inspiratory muscle weakness could benefit from specific inspiratory muscle training (IMT), as IMT may improve respiratory muscle strength and endurance, and thereby reduce respiratory fatigue and the sensation of dyspnea [4,5]. Maximal inspiratory pressure (MIP) is easily measured in clinical practice using an electronic device with a mouthpiece. The primary goal of an MIP test is to assess the level of inspiratory muscle strength.

The question arises, how many of these severely affected patients in hospital settings have a low MIP and thereby potentially could benefit from IMT, and to what extent that MIP correlates with physical capacity and symptom burden.

The primary aim of this study was to examine the frequency of patients with low MIP in hospital-based outpatient pulmonary rehabilitation settings. The secondary

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aim was to examine the associations between MIP and knee-extension muscle strength, walking distance and symptoms. It was hypothesized that a low MIP was associated with a short walking distance and a reduced knee-extension strength.

## Materials and methods

Patients with severe to very severe COPD (GOLD Stage 3–4, Group B-D) were included in this cross-sectional study. The patients were recruited during the period March 2016 to March 2017 from Nordsjællands Hospital and Hvidovre Hospital, The Capital Region, Denmark. The participants were invited to the study as a part of a pre-test before starting an outpatient pulmonary rehabilitation program.

The inclusion criteria were severe COPD ( $FEV_1/FVC < 0.7$  and  $FEV_1\%$  pred.  $< 50\%$ ) and a high symptom burden (COPD Assessment Test (CAT) score  $> 10$ , Medical Research Council (MRC) score  $\geq 3$ ) or more than two exacerbations within the last year. In addition, patients had to understand Danish, understand instructions, and participate in pulmonary rehabilitation.

The patients provided informed consent prior to participation, and the study was approved by the Danish Data Protection Agency and in accordance with the rules of the Regional Committee on Health Research Ethics (no. H-15001128).

## Assessments

Lung function was assessed using spirometry (presented as  $FEV_1\%$  pred.) (forced expiratory volume in the first second as percentage of predicted values). The score in the CAT-questionnaire (range of 0–40) [6] was registered along with the results of the MRC (range 1–5) [7], body mass index (BMI), self-reported comorbidities, and smoking status. These data in conjunction with a 6 MWT and the Sit-to-Stand test were collected routinely as a part of the pretest before rehabilitation. For this study, MIP and knee-extension strength were added.

### Maximal inspiratory pressure

Respiratory muscle strength was measured as MIP using a POWERbreathe KH2, International Ltd., UK device. The MIP was defined as the largest negative pressure sustained for at least 1 s by each patient. The patients were seated at the test, instructed to use a nose clip and the back of the patient's head was gently supported to avoid movement of the head. The patient was told to slowly exhale maximally (to residual volume), then bring the mouthpiece to the mouth and inhale maximally for approximately 2 s. The

patient was verbally encouraged to perform five inspiratory maneuvers at maximal intensity or as many as necessary to achieve high reliability. A good quality of the test was defined as less than 10 cmH<sub>2</sub>O between the two highest measurements [8].

### Knee-extension strength

Maximal isometric knee-extension strength was measured on the dominant leg using a fixed handheld dynamometer (Power Track II commander, JTechMedical), and strength was expressed in Newtons (N), NewtonMeter (Nm) and in Nm/kg (newtons multiplied by the corresponding lever arm length measured in metres from the lateral epicondyle of the femur to the centre of the transducer, divided by the body weight in kilos) [9]. Each patient was placed on a bench and positioned with the hips and knees in 90 degrees flexions. Their hands were placed on the bench to support. The dynamometer was fixed using a strap surrounding the transducer and the bench. Patients were instructed to press against the transducer and verbally encouraged to perform the test at maximal intensity four times with the dominant leg or as many as necessary to achieve high reliability. The best result was used in the analyses.

### Functional tests

Physical capacity was estimated using the 6 MWT [10]. The patient was asked to walk forth and back on a 30-m aisle for 6 min, and to walk as far as possible. During the test, the patient could pause in a standing position and if the patient was a habitual user of a walker or home oxygen, these were permitted during the test. The distance walked in meters during the 6 min and the corresponding saturation were used in the analyses.

The Sit-To-Stand test required the patient to rise to a full standing position and return to a seated position as frequently as possible within a 30-s time frame, whilst maintaining their arms folded across their chest [11].

### Statistical analyses

Statistical analyses were conducted using SPSS, version 22. The MIP reference values were calculated using the Evans & Whitelaw algorithm [12]: male  $120 - (0.41 \times \text{age})$ ; female  $108 - (0.61 \times \text{age})$  and the lower limit of normal (LLN) male  $62 - (0.15 \times \text{age})$ ; female  $62 - (0.50 \times \text{age})$ . A paired t-test was used to compare the constructed reference value with the patients measured MIP. Weakness of the inspiratory muscles was defined as MIP being below the LLN, as suggested by Evens & Whitelaw [12]. Reference values for knee-extension strength were calculated using the values for

muscle strength normalized against body weight suggested by Bohannon R.W [13]. The values on the dominant side in the 70–79-year-old healthy female (body weight\*0.377) and male (body weight\*0.461) subjects were used [13].

Data (MIP, 6 MWT, knee-extension strength) distributions were tested using histograms and Q-Q-plots and found to be normal. Simple linear regression was used to examine the correlation between MIP and other clinical variables. The same variables were entered in multiple linear regression models to determine their relative contribution to MIP and the walking distance. Independent variables used in multiple regression analyses were: gender, age, knee-extension strength, 6 MWT, desaturation values, FEV<sub>1</sub>% pred., MRC and CAT.

Data are presented as mean ± SD or confidence interval (CI) 95%, numbers and percentages, β and CI 95%. P < 0.05 was considered significant.

## Results

The study included 97 patients with COPD and their characteristics are presented in Table 1. The patients had severe to very severe airway obstruction, 61% of the patients were women and the most frequent reported comorbidity was heart disease.

Of the 97 patients, 16 could not rise from a chair without setting off with the arms and therefore received a zero in the Sit-to-Stand test. Three patients did not complete the maximum knee-extension strength test due to leg wounds, knee osteoarthritis or fatigue, respectively. Data are missing from the 6 MWT in one patient. The results of the strength and functional tests are shown in Table 2.

### Maximal inspiratory pressure

The mean MIP of the patients was 63 (95% CI 59; 67) cmH<sub>2</sub>O with a significant difference between men and

**Table 1.** Characteristics of the patients with COPD, n = 97.

Age (years)	70 ± 9
Gender (male/female)	39/58
FEV <sub>1</sub> % pred.	35 ± 10
COPD Assessment Test	19 ± 6
Body Mass Index (kg/m <sup>2</sup> )	25 ± 6
Current smokers	20 (21)
Medical Research Council	
1	0 (0)
2	3 (3)
3	36 (37)
4	38 (39)
5	16 (16)
Heart disease	37 (38)
Osteoporosis	27 (28)
Hypertension	32 (33)
Diabetes	11 (11)
Depression	8 (8)
Comorbidities > 2	37 (38)

Data are represented as mean ± SD or n (%). FEV<sub>1</sub>%pred.: Forced expiratory volume in the first second as a percentage of predicted values.

**Table 2.** Strength and functional tests.

MIP (cmH <sub>2</sub> O)	63 ± 20
Women, n = 58	58 ± 20
Men, n = 39	71 ± 18
Knee-extension Strength, n = 94 (N)	197 ± 84
Knee-extension Strength, n = 94 (Nm)	76 ± 35
Knee-extension Strength, n = 94 (Nm/kg)	1.1 ± 0.4
Knee-extension Strength, n = 94 (kg)	20.1 ± 8.6
Sit-To-Stand, n = 82 (No.)	8 ± 4.8
Six Minutes Walking Test (m)	330 ± 98
Saturation before test (SpO <sub>2</sub> )	95 ± 2
Saturation after test (SpO <sub>2</sub> )	91 ± 9
Desaturation during test (SpO <sub>2</sub> )	3.9 ± 7

Data are presented as mean ± SD. MIP: Maximal Inspiratory Pressure; N: Newton; Nm/kg: Newton\*meters/body weight in kilos; Desaturation = saturation before test – saturation after test.

women (Table 2). Compared to gender and age-matched reference values in healthy subjects 76 (95% CI 73; 79) cmH<sub>2</sub>O the patients' mean MIP was significantly reduced (p < 0.001). 9.3% of the tested patients had a MIP < 50% of the predicted value. Seven patients (7.2%) were under the lower limit of normal.

76% of the patients had a difference between the highest two measurements less than 10 cmH<sub>2</sub>O. Of the remaining, three patients (3.1%) recorded only one good measurement and had a difference higher than 20 cmH<sub>2</sub>O between the two highest values.

### Knee-extension strength

The mean knee-extension strength is shown in Table 2. The knee-extension strength was significantly reduced in the men 251 ± 85 N, vs. matched reference values from healthy men 371 ± 77 N (p < 0.001), and in the women 159 ± 60 N, vs. the reference values 228 ± 56 N (p < 0.001).

The 6 MWT for men was 335 ± 96 m and for women 327 ± 100 m and in the Sit- to- Stand test the men managed to take 8.2 ± 4 and women 7.7 ± 5 sit- to- stand in 30 s.

### Correlates of maximal inspiratory pressure

Table 3 elucidates the independent impacts of the collected data on MIP in the crude analyses and the relative contributions of the factors on MIP in the adjusted analyses. Contributing factors to a low MIP were high age, female gender, weak knee-extension strength, and low FEV<sub>1</sub>% pred.

The patients' MIP were not associated with their symptom burden measured by CAT nor a desaturation during the 6 MWT. Furthermore, MIP was not associated with dyspnea measured by the MRC (Table 3).

When the 6 MWT was analyzed as the dependent variable it was not influenced by MIP or lung function. The only determinant of the walking distance was the knee-extension strength (Table 4).

**Table 3.** Simple and multiple linear regression analyses of impact factors on inspiratory muscle strength (MIP).

Variables	Crude			Adjusted		
	B	95% CI	P-value	B	95% CI	P-value
6 MWT (m.)	0.1	(0.02, 0.1)	0.002	8.1	(-23, 39.6)	0.6
MRC	-4.6	(-10, 0.8)	0.1	0.1	(-5.7, 5.9)	0.9
CAT	-0.2	(-0.9, 0.5)	0.6	-0.7	(-0.7, 0.6)	0.8
Desaturation	-0.1	(-0.7, 0.6)	0.8	0.2	(-0.4, 0.8)	0.4
FEV <sub>1</sub> % pred.	0.3	(-0.1, 0.7)	0.2	0.6	(0.2, 1.1)	0.01
Knee-extension strength (Nm)	0.3	(0.2, 0.4)	0.00	0.2	(0.03, 0.3)	0.02
Gender (f)	-13.4	(-21.3, -5.4)	0.001	-11.8	(-22.3, -1.3)	0.03
Age	-0.7	(-1.1, 0.3)	0.002	-1.0	(-1.5, -0.5)	0.00

Adjusted R-square 0.36. Maximal Inspiratory Pressure as dependent variable. CI: Confidence Interval. 6 MWT: Six Minutes Walking Test. MRC: Medical Research Council. CAT: COPD Assessment Test. FEV<sub>1</sub>%pred.: Forced expiratory volume in the first second as a percentage of predicted values.

**Table 4.** Simple and multiple linear regression analysis of impact factors on walking distance (6 MWT).

Variables	Crude			Adjusted		
	$\beta$	95% CI	P-value	$\beta$	95% CI	P-value
MIP (cmH <sub>2</sub> O)	1.5	(0.6, 2.5)	0.002	0.3	(-0.9, 1.5)	0.6
MRC	-45.3	(-69.4, -21.1)	0.00	-28.0	(-56.8, 0.7)	0.6
CAT	-2.3	(-5.5, 0.8)	0.1	-0.8	(-4.1, 2.6)	0.1
Desaturation	-1	(-4.1, 2.2)	0.5	0.4	(-2.6, 3.4)	0.7
FEV <sub>1</sub> % pred.	1.1	(-1.0, 3.2)	0.3	1.7	(-0.7, 4.1)	0.8
Knee-extension strength (Nm)	1	(0.4, 1.5)	0.00	0.7	(0.03, 1.4)	0.2
Gender (f)	-8	(-48.8, 32.9)	0.7	28.8	(-25.1, 82.7)	0.04
Age	-2.6	(-4.8, -0.4)	0.02	-2.8	(-5.6, 0.1)	0.3

Adjusted R-square 0.18. Six Minutes Walking Test as dependent variable. CI: Confidence Interval. MIP: Maximal Inspiratory Pressure. MRC: Medical Research Council. CAT: COPD Assessment Test. FEV<sub>1</sub>%pred.: Forced expiratory volume in the first second as percentage of predicted values.

## Discussion

The present study shows that the included patients with severe COPD have a significantly lower MIP compared with reference values from healthy subjects. However, only 7% of the patients have inspiratory muscle weakness defined as being under the LLN. Maximal Inspiratory Pressure is associated with peripheral leg muscle strength, lung function, gender, and age. The study indicates that a low MIP does not explain symptom score, degree of dyspnea, or desaturation during exercise, nor is the low performance in the 6 MWT in this group derived from a weak inspiratory capacity.

In this study of patients with severe COPD, only 7% of the sample had a low MIP. Depending on reference values, the percentage of patients with inspiratory muscle weakness in this study group would vary considerably. We used reference values from Evans & Whitelaw's review [12]. Evans & Whitelaw have specified, that to determine whether a patient has a pathological weakness of respiratory muscles, only the LLN is of interest. However, other studies have used 60 cmH<sub>2</sub>O as a rough cut-off point for a low MIP [4,5] or low MIP < 50% of the predicted normal value [4]. If 60 cmH<sub>2</sub>O was used as the definition of a low MIP, 39% of the patients in this study would have a low MIP, yet again only 9.7% of the patients had a MIP < 50% of predicted normal value. Sixty cmH<sub>2</sub>O is, however,

a very rough cut-off, as a woman above 70 year will have an expected MIP close to 60 cmH<sub>2</sub>O.

In line with other studies [1,14,15], our results showed, that a weak knee-extension strength was associated with a low walking capacity. The patients in the present study performed mean values in knee-extension muscle strength of 197 newton (76 Nm; 1.1 Nm/kg), 330 m in the 6 MWT, and 63 cmH<sub>2</sub>O in the MIP test. Singer and colleagues examined the respiratory and skeletal muscle strength in patients with COPD Gold Stage 4 and reported that the patients as comparison performed a higher knee-extension strength of 250 newtons (56.2 lbs), which was associated with both the 6 MWT of 355 m and a MIP of 56 cmH<sub>2</sub>O in average [14]. Gosselink and colleagues performed the same analysis on 41 patients with moderate to severe airway obstruction [15]. The patients walked 372 m on the 6 MWT, the knee-extension strength was 114 Nm, and their MIP was 65 cmH<sub>2</sub>O. The only two determinants of the 6 MWT were found to be knee-extension strength and MIP. Equally, to these two studies, we found a correlation between peripheral muscle strength and walking distance, however, on the contrary, we found no correlation between MIP and the walking distance after confounder adjustment. The patients in the present study seems to demonstrate a higher MIP compared to the two mentioned studies



when the walking distance and knee-extension strength was taken into account. One such relatively higher MIP could be due to more positive results of smoking history, nutritional status, hypoxemia, numbers of exacerbations or maybe medical treatment. The lack of a significant association between the 6 MWT and MIP in this study indicates that walking distance is more related to the peripheral muscle function than to the respiratory muscles.

Knee-extension strength below 3 Nm/kg increases the risk of impairments [16]. In our study, the average strength was  $1.1 \pm 0.4$  Nm/kg with none of the patients being above 3 Nm/kg. This indicates a seriously weak patient group with muscle dysfunction in the peripheral muscles as well as in the respiratory muscles, although the latter not to the same extent.

In patients with COPD, the high mechanical workload on the respiratory system leads to dyspnea and sometimes hypercapnia, due to an imbalance between the load on the respiratory muscles and their capacity [17]. Patients with chronic hypercapnia will often have a low MIP value, but it is not clear how much the low MIP contributes to the hypercapnia or how much excessive load affects the respiratory muscles, leading to both hypercapnia and a low MIP. Thus, it is not clear whether a low MIP reflects genuine muscle weakness or if it is a mere consequence of a mechanical disadvantage for the respiratory muscles. The underlying reason for reduced MIP is important to know in order to target therapeutic interventions in reversing the respiratory muscle weakness.

We recognize that our study has limitations. Firstly, the variables could have included smoking history, degree of emphysema/hyperinflation, and use of home oxygen. Secondly, a larger number of patients and a series of measurements over time could tell us more about causal correlations and maybe the clinical relevance of measuring MIP routinely as a part of a test-battery in pulmonary rehabilitation.

The study examined the respiratory muscle strength of patients with severe COPD, who receive outpatient pulmonary rehabilitation at the Danish hospitals. It has been suggested that only patients with reduced respiratory strength should be offered inspiratory muscle training as an add-on to rehabilitation as only this group seems to benefit from inspiratory muscle training [5]. However, this benefit has not yet been possible to detect in recent studies [18–20]. Our study indicates that IMT would only concern a small percentage of participants in a Danish pulmonary rehabilitation program, as only seven out of 100 have weak inspiratory muscle strength.

In conclusion, MIP was reduced in the included patients with severe COPD compared to age and gender-

matched normal values. However, only a few patients had an MIP under the lower limit of normal. The patients' knee-extension strength was seriously reduced, a finding that is associated with impairments. Whilst MIP was associated with leg muscle strength, it was not associated with walking distance or symptoms. For the moment, the focus in the Danish pulmonary rehabilitation programs should still be on peripheral muscle strength testing and training.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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## References

- [1] Maltais F, Decramer M, Casaburi R, et al. An official american thoracic society/european respiratory society statement: update on limb muscle dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2014;189:e15–e62.
- [2] Laviolette L, Laveneziana P, ERS Research Seminar Faculty. Dyspnoea: a multidimensional and multidisciplinary approach. *Eur Respir J.* 2014;43:1750–1762.
- [3] Ottenheijm CA, Heunks LM, Dekhuijzen RP. Diaphragm adaptations in patients with COPD. *Respir Res.* 2008;9:12-9921-9-12.
- [4] Charususin N, Gosselink R, Decramer M, et al. Inspiratory muscle training protocol for patients with chronic

- obstructive pulmonary disease (IMTCO study): a multicentre randomised controlled trial. *BMJ Open*. 2013;3:e003101.
- [5] Gosselink R, De Vos J, van den Heuvel SP, et al. Impact of inspiratory muscle training in patients with COPD: what is the evidence? *Eur Respir J*. 2011;37:416–425.
- [6] GlaxoSmithKline group of companies. COPDAssessment Test. updated 2016 Jan 17. Available from: <http://www.catestonline.org/>
- [7] Bestall JC, Paul EA, Garrod R, et al. Usefulness of the medical research council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54:581–586.
- [8] Harik-Khan RI, Wise RA, Fozard JL. Determinants of maximal inspiratory pressure. the baltimore longitudinal study of aging. *Am J Respir Crit Care Med*. 1998;158:1459–1464.
- [9] Arnold CM, Warkentin KD, Chilibeck PD, et al. The reliability and validity of handheld dynamometry for the measurement of lower-extremity muscle strength in older adults. *J Strength Cond Res*. 2010;24:815–824.
- [10] Holland AE, Spruit MA, Troosters T, et al. An official european respiratory society/american thoracic society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J*. 2014;44:1428–1446.
- [11] Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70:113–119.
- [12] Evans JA, Whitelaw WA. The assessment of maximal respiratory mouth pressures in adults. *Respir Care*. 2009;54:1348–1359.
- [13] Bohannon RW. Reference values for knee extension strength obtained by hand-held dynamometry from apparently healthy older adults: a meta-analysis. *J Frailty Aging*. 2017;6:199–201.
- [14] Singer J, Yelin EH, Katz PP, et al. Respiratory and skeletal muscle strength in chronic obstructive pulmonary disease: impact on exercise capacity and lower extremity function. *J Cardiopulm Rehabil Prev*. 2011;31:111–119.
- [15] Gosselink R, Troosters T, Decramer M. Exercise training in COPD patients: the basic questions. *Eur Respir J*. 1997;10:2884–2891.
- [16] Ploutz-Snyder LL, Manini T, Ploutz-Snyder RJ, et al. Functionally relevant thresholds of quadriceps femoris strength. *J Gerontol A Biol Sci Med Sci*. 2002;57:B144–B52.
- [17] Begin P, Grassino A. Inspiratory muscle dysfunction and chronic hypercapnia in chronic obstructive pulmonary disease. *Am Rev Respir Dis*. 1991;143:905–912.
- [18] Charususin N, Gosselink R, Decramer M, et al. Randomised controlled trial of adjunctive inspiratory muscle training for patients with COPD. *Thorax*. 2018;73:942–950.
- [19] Beaumont M, Forget P, Couturaud F, et al. Effects of inspiratory muscle training in COPD patients: a systematic review and meta-analysis. *Clin Respir J*. 2018;12:2178–2188.
- [20] Schultz K, Jelusic D, Wittmann M, et al. Inspiratory muscle training does not improve clinical outcomes in 3-week COPD rehabilitation: results from a randomised controlled trial. *Eur Respir J*. Print. 2018;51:1702000. 2018 Jan.