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Non-invasive detection of expiratory flow limitation in COPD patients during nasal CPAP

Raffaele L. Dellacà[1], Mar Rotger[2], Andrea Aliverti[1], Daniel Navajas[2], Antonio Pedotti[1] and Ramon Farre'[2].

[1] TBM Lab, Dipartimento di Bioingegneria, Politecnico di Milano University, Milano, Italy

[2] Unitat de Biofísica i Bioenginyeria, Facultat de Medicina, Universidad de Barcelona-IDIBAPS, Barcelona, Spain

Correspondence: Raffaele L. Dellaca'
Dipartimento di Bioingegneria
Politecnico di Milano
Piazza Leonardo da Vinci 32
I-20133 Milano Italy
Tel: +39 (02) 2399 9005
Fax: +39 (02) 2399 9000
E-Mail: raffaele.dellaca@polimi.it

Running head: Automatic detection of EFL during CPAP by FOT

Abstract

The difference between inspiratory and expiratory respiratory reactance (ΔXrs) measured by forced oscillation technique (FOT) at 5Hz allows the detection of expiratory flow limitation (EFL) in COPD patients breathing spontaneously. This study was aimed to evaluate whether this approach can be applied to COPD patients during non-invasive pressure support.

ΔXrs was measured in 7 COPD patients subjected to nasal continuous positive airway pressure (CPAP) at 0, 4, 8 and 12 cmH_2O in sitting and supine positions. Simultaneous recording of esophageal pressure and the Mead and Whittenberger (M-W) method provided a reference to score each breath as flow-limited (FL), non-flow-limited (NFL) or indeterminate (I). For each patient, we analysed 6 consecutive breaths for each posture and CPAP level.

According to M-W scoring, 47 breaths were FL, 166 NFL and 51 I. EFL scoring by FOT coincided with M-W in 94.8% of the breaths. In the 4 patients that were FL in at least one condition, ΔXrs was reduced with increasing CPAP.

These data suggest that FOT may be useful in COPD patients on nasal pressure support by identifying CPAP levels that support breathing without increasing lung volume which in turn increase the work of breathing and reduce muscle effectiveness and efficiency.

Abstract word count: 200

Keywords: within-breath impedance, non-invasive mechanical ventilation, respiratory system reactance, forced oscillation technique.

Introduction

Dynamic hyperinflation caused by expiratory flow limitation (EFL) has been identified as one of the main causes of dyspnea in patients with COPD(1;2). The increase of a subject's operating volumes at a given ventilatory rate increases the passive pressure load to be overcome by the inspiratory muscles and therefore the work of inspiration. It has been shown in both physiologic and clinical studies that application of nasal ventilatory support and particularly positive end expiratory pressure (PEEP) reduces the inspiratory load at any given volume, and therefore reduces this increase in work load, normalizes the pattern of breathing, improves blood gases and reduces patient-ventilator asynchrony (3-5) However, CPAP may have harmful effects on hemodynamics, in particular by increasing intrathoracic pressure in one or more phases of the respiratory cycle and thereby reducing venous return (6-8). CPAP may also impair the function of the inspiratory muscles if it increases operating volumes above the levels imposed by EFL, in particular if operating volumes increase to levels where the respiratory system is stiffer (increased elastance), or where the inspiratory muscles operate at disadvantageously shorter lengths or less favorable mechanical advantage. Any such increase in elastance increases the pressure and work loads on the inspiratory muscles, and shorter muscle lengths or less favorable mechanical advantage may decrease their effectiveness and energetic efficiency independent of any increase in work load.

The optimized application of end expiratory pressure would require tailoring the applied pressure value to each individual patient. Specifically, the optimal end-expiratory pressure should be a trade-off between being high enough to avoid EFL andlow enough to limit unnecessary patient discomfort, embarrassment of hemodynamics, and increase of lung volume. . Such tailoring would require taking into account that EFL is a condition that may change considerably with time (9), and particularly from night to day, owing to the change in body posture and breathing pattern during sleep. Therefore, a noninvasive tool to continuously assess EFL during application of ventilatory support through a nasal mask should be quite useful.

A new noninvasive method to continuously detect EFL has been recently proposed and evaluated in both normals and COPD patients during spontaneous breathing (10). The method is based on measuring the within-breath change in respiratory reactance (Xrs) measured by a single frequency forced oscillation at 5 Hz. Given that forced oscillation can be easily applied during noninvasive nasal ventilatory support(11;12), the method described could be applicable during routine noninvasive ventilation. The method, and in particular the suitability of the threshold value of reactance change used to detect EFL, has not been evaluated when the patient is subjected to different levels of nasal pressure and with changes in posture.

Accordingly, the aim of this work was to evaluate the effectiveness of the forced oscillation technique (FOT) method to detect EFL in patients with different levels of nasal PEEP in sitting and supine postures. We analysed data from a previous study where forced oscillations were applied for a different reason from the one in this work(11). To test the sensitivity and specificity of the method the study was conducted in patients with either COPD or with chest wall restrictive diseases. The Mead and Whittenberger method (M-W) to detect EFL based on the analysis of the flow and transpulmonary pressure signals was used as reference(13).

Methods

Patients

This study was carried out by analyzing the data collected in a previous study(11) on 11 patients with severe chronic respiratory disease, 7 with COPD and 4 with restrictive ventilatory defect due to chest wall diseases (Table 1). All the patients were in stable condition at time of the study and avoided bronchodilators for at least 24 hours before the measurements.

The institutional Ethics Committee approved the study and written informed consent was obtained from the patients.

Measurements

Patients were studied while receiving continuous positive airway pressure (CPAP) through a nasal mask. Nasal pressure (Pn) was measured by a pressure transducer (MP-45,±20 cmH_2O; Validyne, Northridge, CA, USA) connected to the mask and nasal flow ($\dot{V}n$) by a Fleisch-type pneumotachograph (resistance of 0.35 cmH_2O.s/L) and a pressure transducer (MP-45,±2 cmH_2O; Validyne). Esophageal pressure (Pes) was measured by a transducer (MP-45,±50 cmH_2O Validyne) connected to a standard balloon-catheter system placed in the lower esophagus. Its position was tested by the occlusion method(14). Transpulmonary pressure (P_L) was obtained as P_L=Pn-Pes. All the signals were low-pass filtered at 16 Hz by anti-aliasing filters (Butterworth, 8-poles) and sampled at 100Hz by a data acquisition board (CODAS; DATAQ Instruments Inc, Akron, OH, USA).

The patients were studied by applying a FOT sinusoidal pressure at the mask (5Hz, ~1.5cmH_2O amplitude) generated by a loudspeaker (JBL-800 GTI, JBL, Vitoria, Spain) connected in parallel to a conventional CPAP device (CP90, Taema, Airliquide, France) (Figure 1). A 2L chamber closed the rear part of the loudspeaker to withstand continuous positive pressures generated by the CPAP device(15).

Protocol

Each subject was studied in both the seated and the supine positions while receiving CPAP at 0, 4, 8 and 12 cmH_2O. Posture and CPAP levels were changed in random order and maintained for about 10 min to allow patient adaptation. Data were recorded for all the duration of the test (approx. 80 min). See ref.(11) for further details. Three COPD patients were not able to either maintain the supine position at the lowest CPAP or to adapt to the CPAP in one ore more levels in supine position. Thus we only have data for them in the seated position. We did not study semi-recumbent positions.

Data analysis

For each patient and measuring condition we selected the latest six consecutive breaths where the breathing pattern was stable with no swallowing, oesophageal spasms or other transient reflexes, according to flow, esophageal pressure and impedance recordings. All six breaths were analyzed by both FOT and M-W.

FOT: Within-breath Xrs was computed for each breath from Pn and $\dot{V}n$ as described in ref. (10). The mean values of Xrs during inspiration ($\overline{Xinsp}$) and expiration ($\overline{Xexp}$) were computed. Their difference ($\overline{\Delta Xrs} = \overline{Xinsp} - \overline{Xexp}$) was used to detect EFL. A breath was considered flow-limited (FL) if $\overline{\Delta Xrs}$ was greater than a threshold of 2.8 $cmH_2O{\cdot}s/L$, a value that in our previous study(10) was able to identify FL breaths with 100% sensitivity and specificity when compared to M-W.

M-W: Our reference for the detection of EFL breath-by-breath during tidal ventilation was based on the M-W (13) method of measuring pulmonary resistance. Briefly, the flow-resistive pressure drop (Pfr) was estimated by subtracting from P_L the elastic recoil pressure of the lung. When the Pfr-$\dot{V}n$ plot showed a loop during the expiration where flow decreased during expiration while Pfr increased, the breath was classified as FL; if the expiratory phase was characterized by a quasi-linear dependence between Pfr and flow with little or no loop, the breath was classified as not FL (10). When the inspiratory pressure-flow curve was looped (possible errors in elastic recoil pressure estimation) or when the expiratory pressure flow curve showed a loop characterized by a phase in which flow decreased but Pfr did not simultaneously increase, the breath was classified as 'indeterminate' (I). Examples of flow-limited, not flow-limited and indeterminate breaths are reported in Figure 2.

Results

Experimental tracings for a representative COPD patient in the supine position are shown in Figure 3. In this subject, Xrs showed an inspiratory mean value similar for all the CPAP levels. Conversely, during expiration Xrs reached much more negative values at CPAP=0 cmH_2O than in all the other CPAP levels, suggesting that EFL was present only in this condition. For all the breaths at CPAP=0 cmH_2O the values of $\overline{\Delta Xrs}$ were above the threshold for EFL, while at the other CPAP levels it was below the threshold in all the breaths except one breath at CPAP=4 cmH_2O. The study of the M-W graphs confirmed that this patient was FL only at CPAP=0 cmH_2O.

The average values of $\overline{Xinsp}$, $\overline{Xexp}$ and $\overline{\Delta Xrs}$ in the different CPAP and postures are reported in Table 2. In COPD patients $\overline{Xinsp}$ was always less negative than $\overline{Xexp}$, it showed less variability and it was only slightly affected by increasing CPAP. Conversely, $\overline{Xexp}$ was more negative and, consequently, $\overline{\Delta Xrs}$ was greater at CPAP=0 cmH_2O than at CPAP=12 cmH_2O. They also presented high variability at low CPAP (as indicated by the high SD in table 2), suggesting that some patients were EFL at low CPAP levels and that EFL reduced or disappeared increasing CPAP. Restricted patients showed high variability also in $\overline{Xinsp}$, mainly at low CPAP levels, where its average value was even greater than $\overline{Xexp}$. The mean value of $\overline{\Delta Xrs}$ was very small at all CPAP levels for all the restricted patients, suggesting the absence of EFL.

The breaths classification by M-W technique in all the patients and all conditions is reported in Table 3. Altogether, 213 breaths from the COPD patients were classified as FL or not FL on the 264 studied. The remaining 51 breaths (19% of the total) were classified as indeterminate according to the criteria indicated in the methods section. In the COPD patients, the $\overline{\Delta Xrs}$ index computed from the FOT signal was able to correctly classify as FL or NFL 94.8% of the breaths, as shown in Table 3, providing a sensitivity and specificity of 95% and 98%, respectively. The restricted patients never showed breaths with EFL by the M-W technique. For these patients the classified breaths were 161 on 192 (Table 3), with three breaths misclassified by $\overline{\Delta Xrs}$ as false positive (1.9% of the analyzed breaths).

In all the patients (COPD and restricted) but one, the misclassification was present in a maximum of one for the six selected breaths for each condition. Therefore the majority of the analyzed breaths were classified in the same way by the two techniques in all cases but one (patient 3 at CPAP 4).

To evaluate if the threshold of 2.8 $cmH_2O{\cdot}s/L$ defined in our previous study was appropriate for the experimental conditions of the present study, in Figure 4 we plotted the sensitivity and specificity of $\overline{\Delta Xrs}$ as a function of the threshold value and we superimposed to this plot the one obtained in our previous study. The two plots are very similar and identify very comparable optimal thresholds (2.8 $cmH_2O{\cdot}s/L$ for the previous study, 2.61 $cmH_2O{\cdot}s/L$ for the present one).

Figure 5 shows the relationship between $\overline{\Delta Xrs}$ and CPAP level in the four COPD patients that were able to perform the experiment in both sitting and supine postures. In general $\overline{\Delta Xrs}$ was higher in supine than in sitting, reflecting the fact that the decrease in elastic recoil in the supine posture promotes the development of EFL in COPD patients(16;17). When the patients were flow limited at CPAP=0 cmH_2O, the increase in CPAP resulted in a progressive decrease in $\overline{\Delta Xrs}$. When the patients were not flow-limited, increasing CPAP did not modify $\overline{\Delta Xrs}$.

Figure 6 illustrates how our approach could be used to continuously monitor the development of EFL in clinical practice. The computation of $\overline{\Delta Xrs}$ for all the breaths in the tracing recorded in a representative patient throughout the whole protocol was done automatically without manual elimination of swallows or other abnormalities. We implemented a filtering procedure to exclude abnormal impedance measurements. First outlier breaths with $\overline{\Delta Xrs}$ greater than 9 or smaller than –1 $cmH_2O{\cdot}s/l$ were rejected, as we excluded all the $\overline{\Delta Xrs}$ measurements not included in the range of values found in our previous study performed in optimal conditions (10). Second, a moving average filter with a window of 12 breaths was applied on $\overline{\Delta Xrs}$ time series. The example in Figure 5 shows that the filtered $\overline{\Delta Xrs}$ signal provides a real-time index of EFL indicating how EFL is modified by the application of different CPAP values and/or by changing posture.

Discussion

The main purpose of this study was to assess whether our method of detecting EFL based on FOT is applicable to COPD patients during non-invasive pressure support delivered by a nasal mask. In this condition it can be difficult to obtain accurate measurements of the patient impedance because of the possible leakages around the nasal mask (that constitutes a parallel pathway that affects the measurements of both resistance and reactance) and because of the high patient impedance offered by the nasal pathway (that increases the effects of shunt pathway and reduces the signal-to-noise ratio of the measurement). For this reason we evaluated the sensitivity and specificity of our technique in COPD and restricted patients during CPAP in a typical clinical setting. We found that also in this condition $\overline{\Delta Xrs}$ provides a robust method for detecting EFL when compared to the invasive M-W, as both sensitivity and specificity were very high (>95%) regardless of the demanding experimental conditions.

Figure 4 shows that the sensitivity and specificity values of $\overline{\Delta Xrs}$ obtained from our previous study(10) are very similar to the ones obtained in the present study. This confirms that $\overline{\Delta Xrs}$ is very sensitive to the development of EFL but largely independent from patients' characteristics (anthropometric and spirometric values), experimental conditions (quiet breathing or during CPAP, mouth or nasal impedance), posture (sitting or supine) and equipments, allowing the definition of a unique constant threshold value. It is also remarkable that the method provides similar results in two studies where patient impedance was considerably different (the patient impedance in our COPD patients was on average 14 $cmH_2O{\cdot}s/L$, approximately 3 times larger than in our previous study(10)).

As our technique is based on the analysis of within-breath variations of Xrs, a measurement that reflects elastic and inertial mechanical properties of the respiratory system, we also assessed if a reduction in static chest wall compliance, such as in restrictive chest wall diseases, may induce false positive measurements. Therefore, we analyzed four patients with restrictive chest wall diseases and we found that the percentage of misclassified breaths was not different from COPD patients (Table 3). In particular, patient #10 showed a $\overline{Xinsp}$ value of less than –12 cmH_2O•s/L for all CPAP levels, much more negative than any $\overline{Xinsp}$ value from our COPD patients. However, the $\overline{Xexp}$ value was of the same order of magnitude, allowing for very small $\overline{\Delta Xrs}$ values and suggesting the absence of EFL, confirmed by M-W analysis.

The slightly lower specificity and sensitivity found in the present study (95% and 98%) compared to the previous one (100% for both) may be attributed to the presence of a higher level of noise and variability in the Xrs time courses. Our previous study was conducted under laboratory conditions, allowing the patient to relax and to repeat the measurements if required. By contrast, the data from the present study were obtained from untrained patients in body positions and with CPAP values that were felt as very uncomfortable in some cases. This resulted in the presence of spikes in the Xrs tracing that affect the computation of mean inspiratory or mean expiratory values, resulting in $\overline{\Delta Xrs}$ values that can misclassify the breath, as occurred in the fifth breath at CPAP=4 cmH_2O in Figure 3. Interestingly, most of the misclassifications were false positive (13 out of 14, Table 2) and in all but one cases $\overline{\Delta Xrs}$ was increased above the threshold because the $\overline{Xinsp}$ became less negative compared to the previous and the following breaths. This supports the hypothesis that the false positive misclassifications are the results of noise in the recorded signals. However, as the majority of the breaths were classified in the same way by FOT and M-W in all the cases but one (patient #3, supine, at CPAP=4 cmH_2O), it is possible to automatically exclude abnormal values by considering the average of at least 5-10 consecutive breaths to improve sensitivity and specificity. As shown in Figure 6, the use of a very simple moving average filter on $\overline{\Delta Xrs}$ data provided a very effective tool for the real-time monitoring of EFL in a given patient submitted to noninvasive mechanical ventilation.

This method has also a physiological basis. The impedance measured by FOT in absence of EFL reflects the mechanical properties of the whole respiratory system. Conversely, during EFL, the impedance measured by FOT is only a measure of the mechanical properties of airways downstream from the choke points. This is because a change in pressure cannot be transmitted upstream through the choke points and thus only the downstream airways are oscillated (18). We found that the threshold is independent of subject size and severity of the disease. This suggests that the differences in the mechanical properties of the airways downstream of choke points (measured by Zin during expiration if the patient is FL) vs. the mechanical properties of the whole respiratory system (measured by Zin during inspiration) must be much greater than any possible inter-subjects variability of airway wall mechanics and location of choke points. The progressive reduction of $\overline{\Delta Xrs}$ observed in the flow-limited COPD patients with increasing CPAP values (Figure 4) suggests that $\overline{\Delta Xrs}$ not only detects EFL but also indirectly quantifies how far a subject is from being not flow-limited. This hypothesis is supported by the higher values of $\overline{\Delta Xrs}$ showed by EFL patients in the supine position compared to the sitting.

This may also explain the only case (COPD patient #3 in the supine position at CPAP=4 cmH_2O) in which the majority of the breaths (five/six) were misclassified. We found that that patient was FL at CPAP=0 cmH_2O but not at CPAP=8 cmH_2O by both the M-W and the $\overline{\Delta Xrs}$ techniques. This suggests that CPAP=4 cmH_2O positioned the patient in a condition of transition between FL and non FL: in this case it is possible that the number of choke points developed during expiration was sufficient to lower Xrs below the threshold but that few non-choked pathways were able to slightly increase the expiratory flow by increasing alveolar pressure, keeping the M-W loop substantially closed during the breath. If this was the case, when passing from EFL to non-EFL and vice-versa there could be a short transition phase in which the two methods give different results. However, our data show that this is unlikely to occur frequently and, moreover, $\overline{\Delta Xrs}$ indications during this transition phase between EFL and non-EFL might better reflect the overall condition of the lung than the M-W.

A typical problem encountered when measuring impedance during noninvasive mechanical ventilation is the presence of unavoidable leakages around the nasal mask. The leakages introduce a shunt pathway in parallel with the subject that affects the measured impedance. A leak with a resistance comparable to that of the respiratory system decreases the magnitude of both the measured resistance and reactance. In particular, the higher the respiratory system resistance and reactance, the greater their reduction. Therefore, the within-breath change in reactance (i.e. $\overline{\Delta Xrs}$) is also reduced. In this study the nasal mask was carefully fitted to the patients and the leakages were monitored before starting the experiment. Nevertheless, we found that during the recording throughout our study an average leak flow of 35, 66 and 105 ml/s was present at CPAP values of 4, 8 and 12 cmH_2O, respectively. These figures correspond to an average leak resistance of 117 $cmH_2O{\cdot}s/L$, with individual values ranging from 45 to 281 $cmH_2O{\cdot}s/L$, values normally encountered during clinical nasal CPAP treatments (19). In our study we found only one false negative misclassification out of the 372 analyzed breaths, suggesting that leakages may have negligible effects on the detection of EFL by FOT. Moreover, as the pneumotachograph can easily measure leakages (20), the presence of abnormally large leaks can be automatically identified indicating the possible loss in reliability in detecting EFL.

The possible application of our method is the identification of minimum CPAP or PEEP values required to minimize the development of EFL in mechanically ventilated COPD patients. This information may guide the clinician's choice of CPAP so as to eliminate unnecessary effects on hemodynamics and impairment of inspiratory muscle function by increase of operating volumes. Moreover, as FOT has already been proved to be very well tolerated by patients when combined with noninvasive mechanical ventilation(21) (22), it may be useful to include this measurement into mechanical ventilators able to continuously optimize the PEEP level to changes in patient posture, conditions, lung volumes and breathing pattern.

Identification of EFL by FOT may guide the clinician's choice of CPAP so as to eliminate unnecessary effects on hemodynamics and impairment of inspiratory muscle function by increase of operating volumes.

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Figure legend

Figure 1 – Experimental set-up for oscillatory impedance measurement during CPAP.

Figure 2 - Examples of breaths classification by the Mead and Wittenberger graphs. Upper panels: non flow-limited (left) and flow-limited (right) breaths. Lower panels: examples of breaths classified as indeterminate because expiration showed a loop characterized by a phase in which flow decreased but the flow-resistive pressure drop (Pfr) did not simultaneously increase (left) or because the graphs showed an opening of the inspiratory loop suggesting that the estimation of the elastic recoil pressure of the lung was not correct (right).

Figure 3 – Experimental tracing from a representative patient. From top to bottom: flow at the nasal mask (positive when inspiratory), nasal pressure, esophageal pressure, total respiratory input reactance (Xrs) at 5Hz and difference between mean inspiratory ($\overline{Xinsp}$) and mean expiratory reactance ($\overline{\Delta Xrs}$) for each breath at the four considered CPAP values of 0, 4, 8 and 12 cmH_2O (from left to right).

Figure 4 - Sensitivity (the number of detected FL breaths divided by the total number of FL breaths, dashed lines) and specificity (the number of detected NFL breaths divided by the total number of NFL breaths, continuous lines) expressed as percentage of all the classified breaths are plotted versus the threshold values for the data from mouth impedance (from Ref. 10, thin lines) and for the data from nasal impedance analyzed in the present study (thick lines).

Figure 5 – Mean value and SD of $\overline{\Delta Xrs}$ determined on the group of six consecutive breaths considered for the validation study at each CPAP level in the seated (open symbols) or in the supine

(closed symbols) positions for the four COPD patients able to maintain the supine position at all CPAP levels.

Figure 6 – Example of EFL monitoring during the whole protocol from a representative subject (subject #3). Upper panel: nasal pressure tracing. Lower panel: $\overline{\Delta Xrs}$ values. The dashed line indicates the threshold for EFL. $\overline{\Delta Xrs}$ data were filtered with a moving average filter by using a window of 12 breaths. See text for details.

Table 1: Patients characteristics

Patient #	Sex	Age Years	Weight Kg	Height cm	FEV1 L	FEV1 %Pred	FEV1/FVC %	TLC L	TLC %Pred	Supine
COPD										
#1	M	63	66	162	0.850	29	34			no
#2	M	48	58	156	2.370	69	51			yes
#3	M	76	60	163	0.560	21	40			yes
#4	M	78	81	167	1.300	46	62			yes
#5	M	71	65	174	1.080	32	37			yes
#6	M	73	49	158	0.930	37	67			no
#7	M	72	78	159	0.730	28	41			no
mean		**68.7**	**65.3**	**162.7**	**1.117**	**37.4**	**47.4**			
SD		**10.3**	**11.2**	**6.2**	**0.602**	**16.0**	**12.9**			
Restricted										
#8	F	63	40	158	0.390	18	81	2.32	44	yes
#9	F	68	48	147	1.070	61	76	2.81	57	yes
#10	M	56	70	171	2.040	58	75	5.43	74	yes
#11	F	62	51	151	0.830	42	86	2.31	48	yes
mean		**62.3**	**52.3**	**156.8**	**1.1**	**44.8**	**79.5**	**3.2**	**55.8**	
SD		**4.9**	**12.7**	**10.5**	**0.7**	**19.7**	**5.1**	**1.5**	**13.3**	

Table 2: Mean inspiratory ($\overline{Xinsp}$), mean expiratory ($\overline{Xexp}$) reactance and their difference ($\overline{\Delta Xrs}$, all expressed in $cmH_2O{\cdot}s/L$) at the considered CPAP values (expressed in cmH_2O) for COPD and Restricted patients in the seated and supine position.

COPD

CPAP pressure (cmH_2O)	Seated $\overline{Xinsp}$	Seated $\overline{Xexp}$	Seated $\overline{\Delta Xrs}$	Supine $\overline{Xinsp}$	Supine $\overline{Xexp}$	Supine $\overline{\Delta Xrs}$
0	-3.70 ± 1.96	-6.30 ± 2.86	2.60 ± 3.04	-4.42 ± 1.54	-9.56 ± 4.32	5.14 ± 3.13
(min÷max)	(-6.92 ÷ -1.36)	(-9.01 ÷ -1.78)	(-1.01 ÷ 5.5)	(-5.86 ÷ -2.24)	(-13.47 ÷ -3.39)	(1.15 ÷ 8.79)
4	-3.77 ± 1.64	-4.55 ± 2.79	0.78 ± 1.56	-4.16 ± 1.75	-6.92 ± 3.87	2.77 ± 2.29
(min÷max)	(-5.19 ÷ -0.87)	(-8.5 ÷ -0.42)	(-0.96 ÷ 3.88)	(-5.36 ÷ -1.55)	(-10.63 ÷ -1.64)	(0.09 ÷ 5.27)
8	-3.71 ± 2.03	-4.21 ± 2.19	0.51 ± 0.92	-3.62 ± 1.74	-4.99 ± 2.57	1.37 ± 1.10
(min÷max)	(-5.75 ÷ -1.09)	(-7.27 ÷ -1.34)	(-0.22 ÷ 1.47)	(-5.67 ÷ -1.42)	(-7.28 ÷ -1.44)	(0.02 ÷ 2.68)
12	-3.41 ± 1.46	-4.36 ± 3.41	0.95 ± 2.86	-3.20 ± 1.40	-3.92 ± 1.96	0.72 ± 0.63
(min÷max)	(-5.6 ÷ -1.07)	(-11.05 ÷ -0.76)	(-1.05 ÷ 7.10)	(-4.46 ÷ -1.26)	(-5.89 ÷ -1.21)	(-0.05 ÷ 1.43)

Restricted

CPAP pressure (cmH_2O)	Seated $\overline{Xinsp}$	Seated $\overline{Xexp}$	Seated $\overline{\Delta Xrs}$	Supine $\overline{Xinsp}$	Supine $\overline{Xexp}$	Supine $\overline{\Delta Xrs}$
0	-5.66 ± 3.72	-4.66 ± 0.58	-0.89 ± 3.56	-4.13 ± 5.51	-3.31 ± 3.50	-0.39 ± 5.31
(min÷max)	(-11.14 ÷ -3.09)	(-5.39 ÷ -4.01)	(-8.22 ÷ 1.05)	(-12.02 ÷ -3.7)	(-12.86 ÷ -2.71)	(-8.26 ÷ 2.63)
4	-2.84 ± 0.79	-3.37 ± 0.69	0.52 ± 0.86	-2.23 ± 3.08	-2.55 ± 3.33	0.66 ± 0.87
(min÷max)	(-3.52 ÷ -1.99)	(-3.95 ÷ -2.57)	(-0.5 ÷ 1.59)	(-13.51 ÷ -1.95)	(-12.61 ÷ -1.7)	(-0.89 ÷ 1.59)
8	-3.81 ± 1.42	-3.66 ± 0.87	-0.15 ± 0.60	-3.02 ± 3.23	-2.75 ± 3.23	0.20 ± 0.82
(min÷max)	(-4.92 ÷ -1.79)	(-4.37 ÷ -2.51)	(-0.64 ÷ 0.72)	(-12 ÷ -1.73)	(-9.57 ÷ -1.77)	(-2.43 ÷ 0.04)
12	-3.32 ± 0.75	-3.15 ± 1.13	-0.16 ± 0.60	-2.12 ± 3.21	-2.54 ± 3.19	0.78 ± 1.17
(min÷max)	(-3.91 ÷ -2.28)	(-4.55 ÷ -1.79)	(-0.6 ÷ 0.71)	(-12 ÷ -1.26)	(-8.78 ÷ -0.84)	(-3.22 ÷ 0.71)

Table 3: Summary of breaths classification. FP: false positive. FN: false negative. FL, NFL and I are for flow-limited, non flow-limited and indeterminate, respectively.

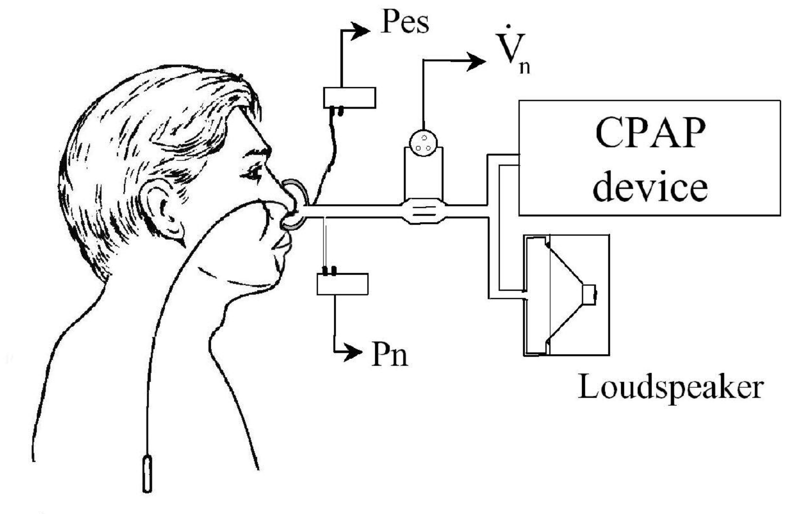
COPD

CPAP pressure (cmH_2O)	Seated FL	Seated NFL	Seated I	Seated Total	Seated Class. Err.	Supine FL	Supine NFL	Supine I	Supine Total	Supine Class. Err.
0	16	21	5	42	2 (FP)	14	4	6	24	0
4	6	32	4	42	1 (FN)	5	13	6	24	5 (FP)
8	0	30	12	42	0	0	19	5	24	2 (FP)
12	6	26	10	42	1 (FP)	0	21	3	24	0
Total	**28**	**109**	**31**	**168**	**4**	**19**	**57**	**20**	**96**	**7**

Restricted

CPAP pressure (cmH_2O)	Seated FL	Seated NFL	Seated I	Seated Total	Seated Class. Err.	Supine FL	Supine NFL	Supine I	Supine Total	Supine Class. Err.
0	0	20	4	24	1 (FP)	0	16	8	24	2 (FP)
4	0	19	5	24	0	0	19	5	24	0
8	0	22	2	24	0	0	21	3	24	0
12	0	21	3	24	0	0	23	1	24	0
Total	**0**	**82**	**14**	**96**	**1**	**0**	**79**	**17**	**96**	**2**

Figure 1



376x296mm (120 x 120 DPI)

Figure 2

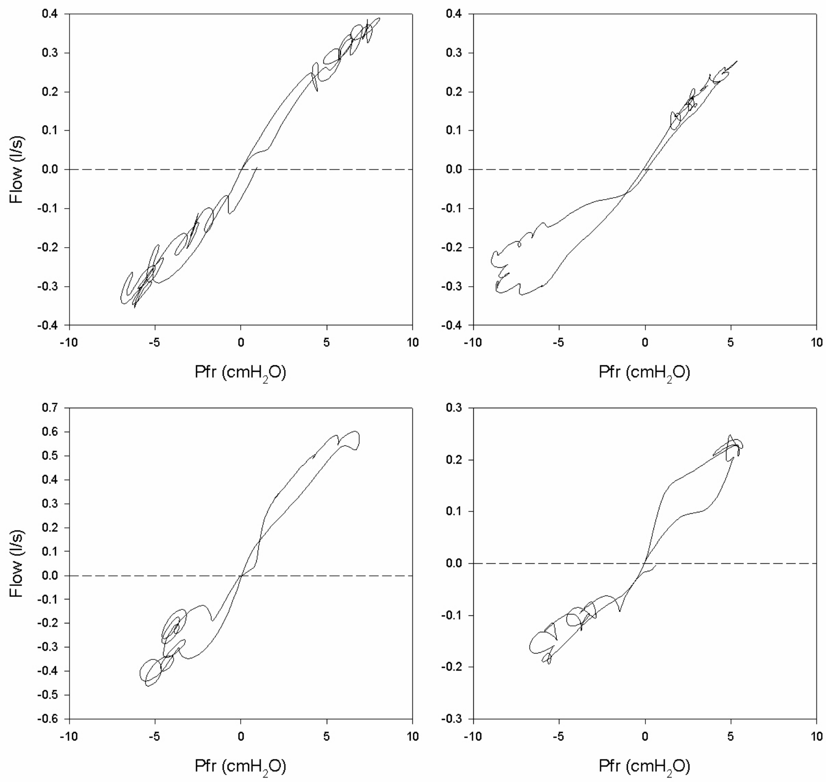


Figure 3

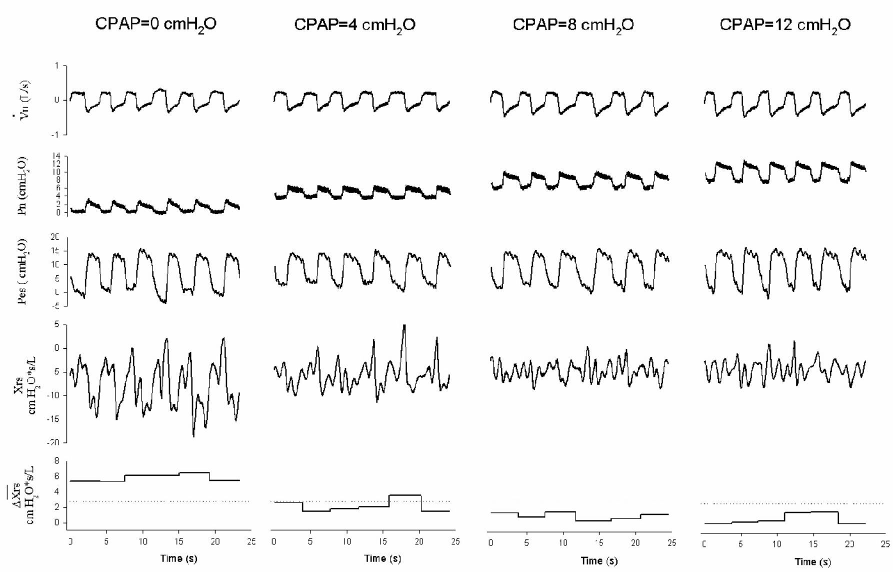


Figure 4

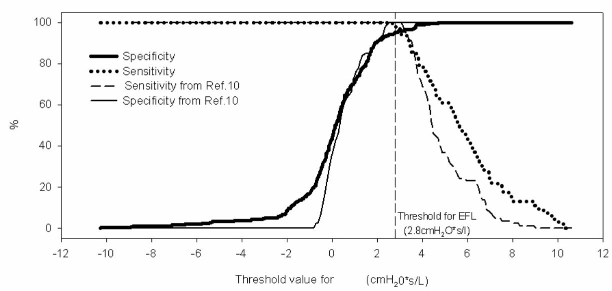

Specificity
Sensitivity
Sensitivity from Ref.10
Specificity from Ref.10
100
80
60
40
20
0
%
Threshold for EFL
(2.8cmH2O*s/l)
-12
-10
-8
-6
-4
-2
0
2
4
6
8
10
12
Threshold value for (cmH20*s/L)

Figure 5

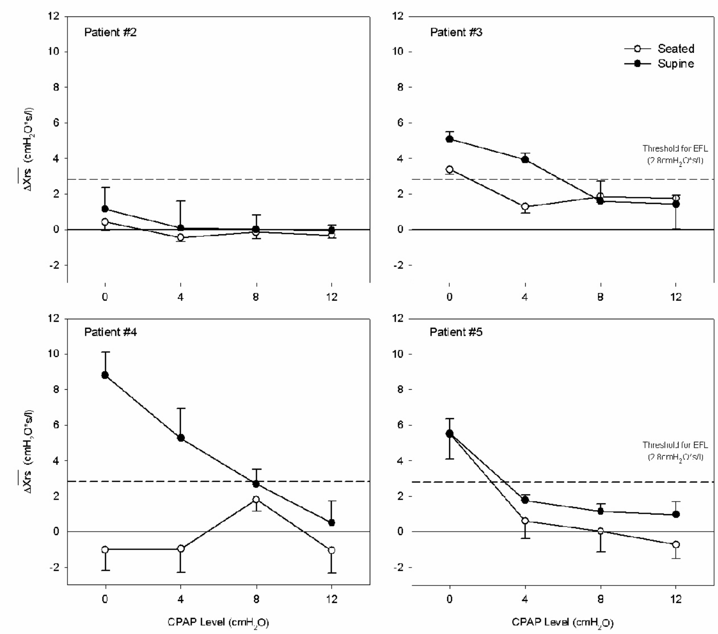
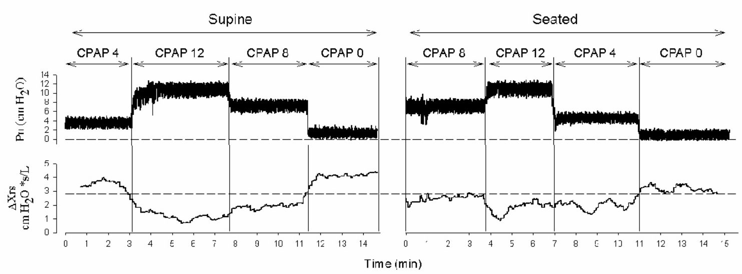

Patient #2
Patient #3
Patient #4
Patient #5
Seated
Supine
Threshold for EFL
ΔXrs (cmH2O*s/l)
CPAP Level (cmH2O)

Figure 6


Supine
Seated
CPAP 4
CPAP 12
CPAP 8
CPAP 0
CPAP 8
CPAP 12
CPAP 4
CPAP 0
Time (min)