PHILIPS
RESPIRONICS

BiPAP A40 EFL

Detect and abolish EFL in COPD

Expiratory flow limitation (EFL): overview, detection and an application to abolish EFL

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EFL

In patients with chronic obstructive diseases, airflow obstruction requires developing greater respiratory pressures to produce pulmonary ventilation and, therefore, these patients experience respiratory muscle fatigue and, in most severe conditions, respiratory failure. Because of the mechanical and structural arrangements of the mammalians' respiratory system, humans can increase their airway caliber by increasing their operating lung volume, taking advantage of the elastic nature of the parenchymal tissues, which transmit the elastic recoil pressure from the pleurae to the external structures of the airways. Therefore, by increasing lung volumes, a patient can reduce airway resistance and increase respiratory flows.

Breathing at increased lung volumes is an abnormal operating condition and it is commonly referred to as "dynamic hyperinflation" (DH). DH is commonly detected and quantified by measuring the increase of the end-expiratory lung volume (EELV) compared to the mechanical resting volume (i.e. the functional residual capacity, FRC). In COPD, dynamic hyperinflation occurs as a result of a combination of reduced expiratory flows and expiratory time. In this situation, patients start an inspiration before their respiratory system reaches FRC at the end of the preceding exhalation. DH is promoted by the presence of tidal expiratory flow limitation (EFL),[10] i.e. the inability to increase expiratory flows by increasing alveolar pressure. This occurs when the recorded tidal expiratory flow-volume loop reaches the maximal expiration and requires the patient to breathe at higher lung volumes to produce larger expiratory flow.

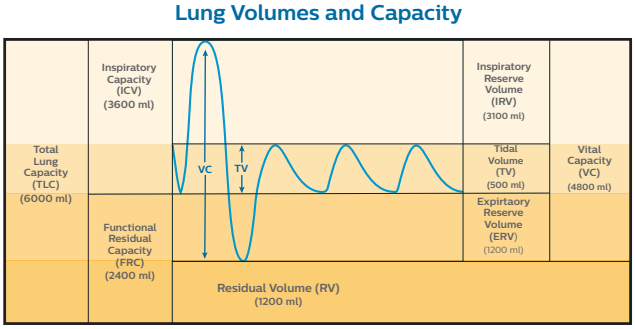


Figure 1

When a patient begins inspiration before reaching FRC, the inspiratory muscles have to overcome an additional threshold pressure load, called intrinsic positive end expiratory pressure (PEEPi or intrinsic PEEP), before being able to develop the inspiratory flow. PEEPi is the increase in the expiratory recoil pressure of the total respiratory system at the end of expiration compared to the pressure in resting condition at the end of a prolongued relaxed expiration (FRC).

In obstructed patients who experience DH and, therefore, have PEEPi, the additional threshold mechanical load is counterbalanced by the force developed by the respiratory muscles that are in charge of accounting for this extra load on top of the one needed to face the increased airway resistance and lower compliance. In these patients, the inspiratory efforts required may be excessive, with PEEPi accounting for up to more than 50% of the disease-related increases in work of breathing,[3,5] leading to respiratory failure. It has been shown, both in physiologic and clinical studies, that the application of an external PEEP (sometimes indicated also as extrinsic PEEP, PEEPe or expiratory positive airway pressure, (EPAP)) by means of mechanical ventilators or CPAP devices reduces the work of breathing, normalises the breathing pattern, improves blood gases and reduces patient-ventilator asynchrony.[2,11,14]

The positive effects of the application of PEEP depend on careful tailoring of this parameter, with external or extrinsic PEEP to be set identical to PEEPi. If the applied PEEP is lower than PEEPi, it is not able to abolish the threshold load, therefore providing limited improvements to patients. Alternatively, if the externally applied PEEP is greater than the PEEPi, it results in an externally induced hyperinflation (further increase of EELV on top of patient's DH), resulting in the patient breathing at increased lung volumes, where the respiratory system compliance is lower and with disadvantageous arrangements of respiratory muscle geometry (flattened diaphragmatic dome, reduced muscle length, etc.). In these conditions, the excessively applied PEEP yields to an additional increase, instead of a decrease, of the patient's work of breathing. Moreover, the increased mean intra-thoracic pressure promotes adverse effects on hemodynamics (the dynamics of blood flow), as it may severely decrease venous return and cardiac output, depending upon intravascular volume status, myocardial function and other factors.[1,2,4]

The appropriate application of a PEEP to overcome EFL requires the accurate tailoring of pressure for each individual patient. Such tailoring would require taking into account that DH is a condition that may present considerable changes with time[15] as it is not only influenced by the disease severity but also by changes in body posture (from seated to supine or from supine to one's side) and breathing patterns that commonly happen during sleep.

The forced oscillation technique (FOT) and its application to detect tidal EFL

Forced oscillation technique (FOT) is a simple and minimally invasive method used to study the mechanical properties of the respiratory system by measuring its response to an externally applied oscillatory forcing signal.[13] With FOT, the mechanical behavior of the respiratory system is characterised by computing its impedance (Z), defined as the ratio between pressure applied to the airway opening (P) and the resulting volumetric flow rate (V) computed only at the frequencies (f) contained in the forcing signal (Z(f) = P(f)/ V(f)). This requires that all the pressure sources embedded in the system are under analysis (i.e. the respiratory muscles) and are not contributing to creating flow at the forcing frequencies. In a typical FOT measurement, this last condition is obtained by forcing the respiratory system (and, therefore, computing Z (f)) at frequencies greater than 4 Hz, that are higher than the maximum frequency contribution of spontaneous breathing in adult humans. In this way, the pressure developed by the respiratory muscles during breathing cannot interfere with the estimation of Z (f) and, therefore, the subject is allowed to breathe spontaneously during the measurement, without needing to perform any kind of respiratory maneuver. In most FOT configurations, an oscillatory pressure is applied at the mouth of the subject, where the flow is also measured. In this situation, the measured impedance is called "total respiratory system input impedance", Zrs, and reflects the mechanical properties of the overall respiratory system, including upper and lower airways as well as lung and chest wall tissues.

Total respiratory input impedance represents how difficult it is for an oscillatory pressure applied at the airway opening to produce an oscillatory flow.

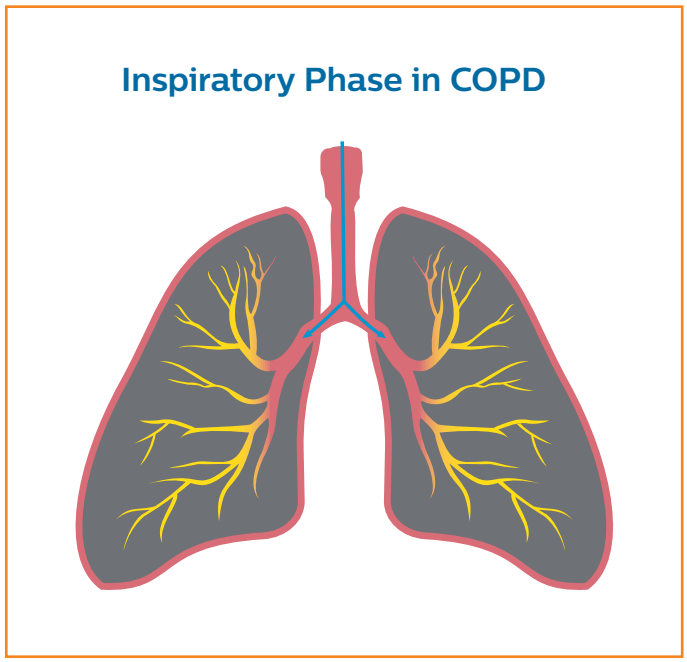
As impedance is lowered, the flow produced increases as a consequence of the same driving pressure. However, as the mechanical properties of the respiratory system are a combination of dissipative (resistive) and conservative (elastic and inertial) components, the response of the respiratory system to an external oscillatory forcing is determined not only in terms of amplitude but also by the phase shift (the delay) between the pressure and the resulting flows. In order to capture both features of the mechanical properties of the system, for a given frequency two numbers, the resistance (Rrs)(f) and the reactance (Xrs)(f), commonly expressed as "f" or the respiratory imedance, are used to oscillate the system. Rrs represents the frictional loss within the system resulting from airway and tissue resistances and Xrs represents the contribution of the elastic (respiratory system compliance, C) and inertial forces. In presence of a purely elastic or resistive and elastic load, Xrs measured at the frequency "f" is related to "C" by the following equation:

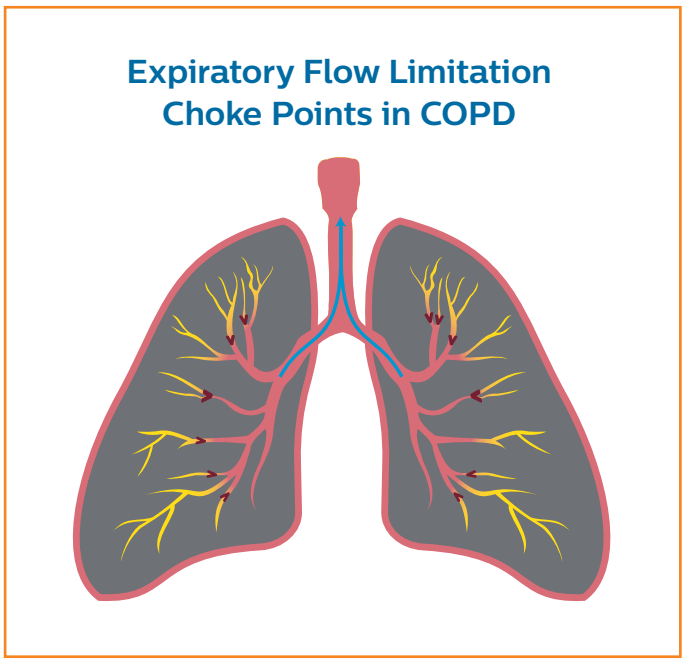
$$Xrs = I2\pi f - \frac{1}{2\pi fC}$$

(Equation 1)

Where 'I' is the inertance (measure of the pressure difference in a fluid required to cause a unit change in the rate of change of volumetric flow-rate with time) of the respiratory system, "C" is compliance and "f" is the forcing frequency.

In adult healthy humans, Xrs measured at 5 Hz is approximately zero, as inertial and elastic forces equilibrate; therefore, if the respiratory system becomes less compliant (i.e. if C reduces), Xrs assumes larger negative values, which represents the absence of EFL.





As the reactance reflects the elastic and inertial properties of the entire respiratory system, in healthy subjects, in normal conditions, its values are stable within the breathing cycle (i.e. similar values are measured during the inspiratory and expiratory phases). When tidal EFL is present, during expiration the linear velocity of the gas passing through regions of dynamic airways compression (i.e., choke points) equals the local speed of pressure wave propagation[6] and the expiratory flow becomes independent from the driving pressure. As a consequence, a choke point prevents the propagation of pressure oscillations across it[16] toward the lung periphery and, therefore, when tidal EFL is present, the oscillatory impedance measured during expiration can measure exclusively the mechanical properties of the respiratory structures downstream of the choke points (i.e. from choke points to airway opening) (Figure 2).

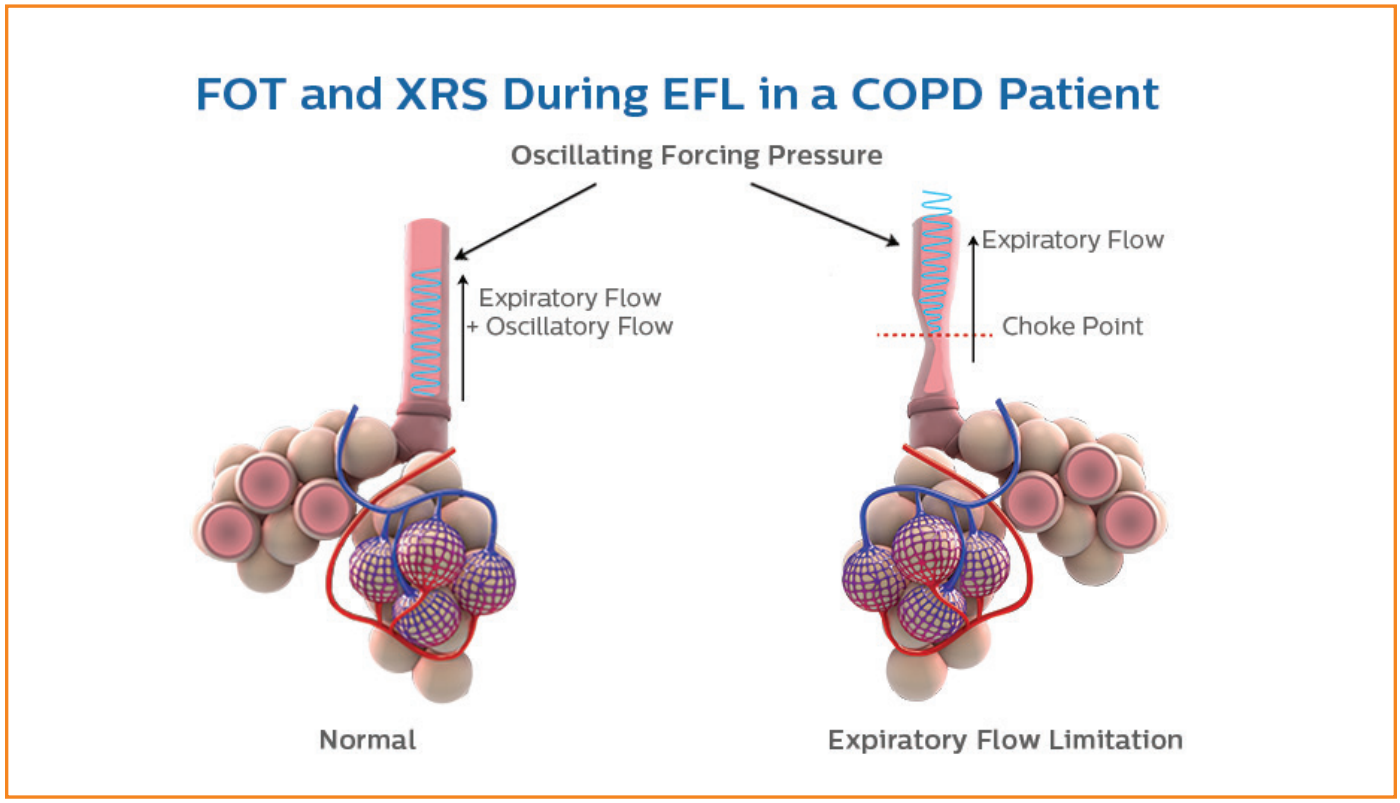


Figure 2

These structures, which are essentially central and upper airways, are much stiffer (less compliant) than the lung periphery and, therefore, associated with a decreased (i.e. a more negative) Xrs. For this reason, the development of choke points (and, therefore, tidal EFL) results in the appearance of a negative swing of Xrs during expiration compared to the values measured during inspiration. In Figure 2, within-breath variations of Xrs are shown from a representative healthy subject (left), a COPD patient without tidal EFL (middle panel), and a COPD patient with tidal EFL (right panel). Tidal EFL was independently confirmed by the analysis of esophageal pressure.[9]

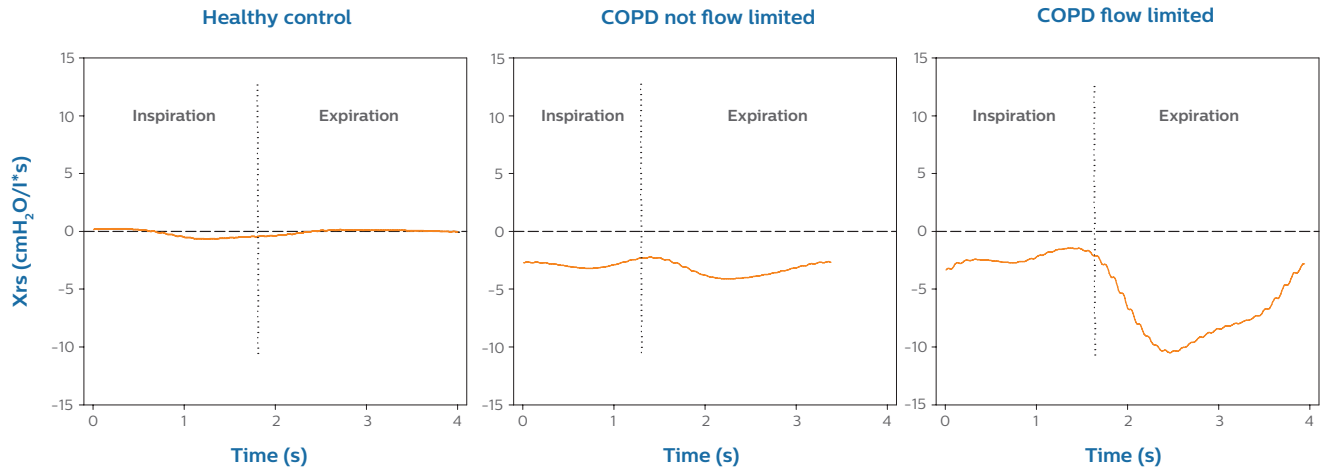


Figure 3

As the development of choke points results in intra-tidal changes in Xrs, this feature can be used for defining a quantitative index for detecting the presence of tidal EFL (Figure 4).

Several validation studies compared the accuracy of using different indices to quantify intra-tidal changes of Xrs to detect EFL as compared to the gold standard Mead and Whittenberger method, which is based on the invasive measurement of transpulmonary pressure by esophageal catheters.[1,2] They found that the difference between the average inspiratory Xrs and the average expiratory Xrs measured over one breath (namely ΔXrs) can detect the presence of tidal EFL with high specificity and sensitivity during quiet breathing,[7,9] when this method was applied during CPAP[8] and noninvasive ventilation (NIV) using nasal masks.[8]

The ΔXrs index represents the difference of reactance measured during inspiration (therefore reporting the compliance of the whole respiratory system) and the one measured during expiration which, in case of developments of choke points, reflects the lower compliance of only airway walls and other structures downstream of choke points. For this reason, its absolute value has different meanings depending on the underlying physiological mechanisms. When ΔXrs is between approximately zero (no choke points developing during expiration) and the threshold value of 2.8 cmH_2O*s/L experimentally identified for determining the presence of fully developed tidal EFL, i.e. when all lung periphery is choked,[9] it means that there are parts of the lung periphery which are choked and parts which are not. In this condition of "partially developed" EFL, the amplitude of ΔXrs is related to the amount of lung periphery that the forced oscillations cannot reach because of the choke points, i.e. the amount of choked lung periphery. Once a full tidal EFL has established (i.e. all lung periphery are connected to the airway opening through choked airways), ΔXrs overcomes the threshold and the Xrs measured during expiration represents the mechanical properties of upper airways (including soft tissue shunt, such as the one provided by the cheeks) and the central airways downstream of the choke points. In this condition, larger ΔXrs are associated with more centrally choked lung while smaller ΔXrs are indicative either of a more peripheral location of the choke points.

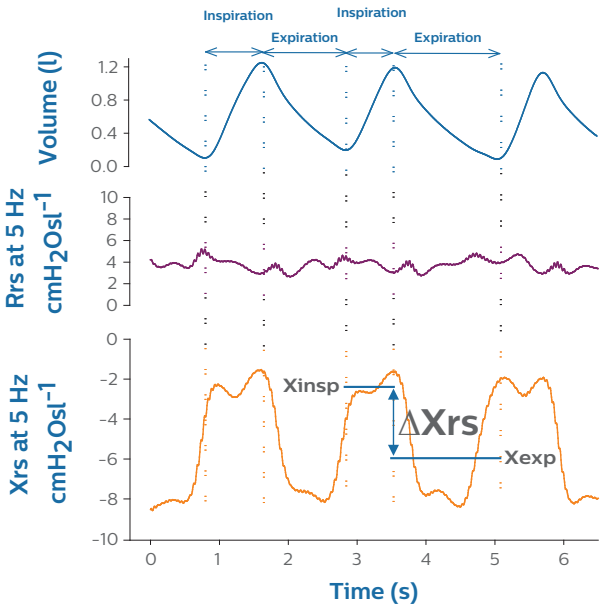


Figure 4

It is worthwhile to underline that large leak or large shunt loads (such as poor control of the cheeks or very large volume and compliant masks during NIV) can affect the measurement of Xrs. If leaks are not properly estimated and corrected, they can lead to the underestimation of Xrs and, therefore, to smaller or lower ΔXrs, with possible false negative errors (i.e. breaths with tidal EFL misclassified as not flow limited) resulting from the test.

Applications of FOT for detecting tidal EFL in noninvasive mechanical ventilation

One of the most important advantages of ΔXrs for detecting tidal EFL is that, compared to other available techniques, this test is suitable for continuous and automatic monitoring during NIV, opening new perspectives for the real-time automatic adjustment of PEEP during this therapy. To this aim, an automatic algorithm based on the continuous monitoring of tidal EFL by ΔXrs can be implemented in mechanical ventilators. According to the presence of tidal flow-limitation (ΔXrs equal to 2.8 $cmH_2O/s/L$ or greater), a new Philips ventilator (BiPAP A40 EFL with ExpiraFlow technology) automatically adjusts EPAP by increasing it if the patient has EFL and decreasing it otherwise, resulting in the continuous application of the minimum EPAP needed to abolish tidal EFL. In Figure 5, an example of the activity of the system is depicted.

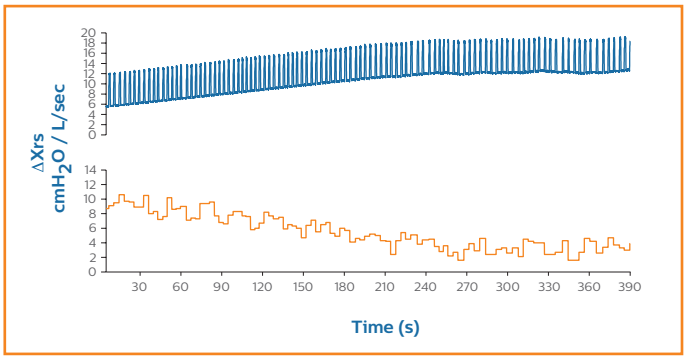


Figure 5

In this example, the auto-adjusting ventilator was connected to a COPD patient with the initial EPAP set to 5 cmH_2O. The system started the evaluation of ΔXrs for every single breath and identified the presence of tidal EFL (Xrs >2.8$cmH_2O/s/L$), therefore it started increasing EPAP slowly. By increasing EPAP, ΔXrs decreased to the threshold of 2.8 $cmH_2O/s/L$, approximately 260 seconds after the beginning of the trial, when EPAP approached 10 cmH_2O. Subsequently to this point, the system continuously adjusted EPAP to keep ΔXrs around the threshold for EFL.

The Philips auto-adjusting EPAP ventilator is able to react in real-time to changes in patient conditions, such as the Xrs fluctuations resulting from changing posture from supine to one's side, by continuously adjusting EPAP accordingly. In a currently active and preliminary study, twelve hypercapnic COPD patients were studied over two nights. During one night the setting of EPAP prescribed by the physician was used (standard or usual care); during the other night the ventilator was allowed to auto-adjust EPAP in real-time depending on ΔXrs values. The self-tailoring system was well tolerated by all patients. During the auto-adjusted EPAP night, patients received a highly variable EPAP that resulted in a reduced number of ineffective ventilation triggering efforts and, most importantly, improved blood gasses, especially $PaCO_2$, even if the average pressure support delivered over the night was constant. Pressure and transcutaneous CO_2 from a representative patient are reported in Figure 6 with the fixed PEEP setting night (standard care) in blue and the automatic system night in orange.

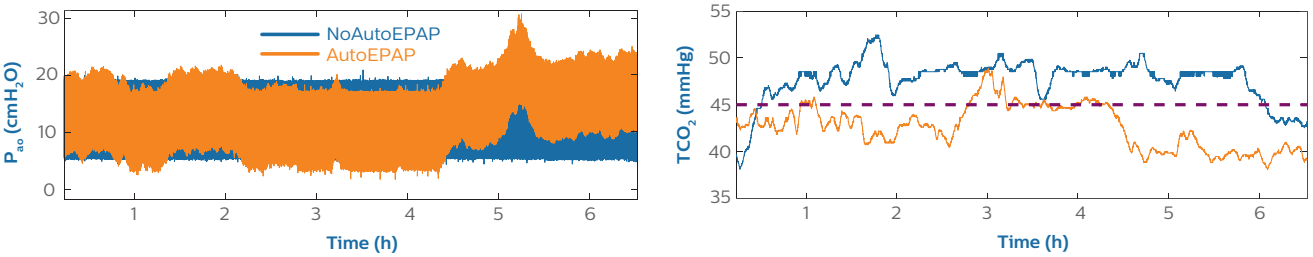


Figure 6

In a current clinical overnight comparative observational trial, (M. Vitacca et al. - pending publication) twelve hypercapnic COPD patients were subject to an auto-adjusting EPAP ventilation method to abolish EFL compared to their current standard of care. The overnight auto-adjusting EPAP ventilation method to abolish EFL reflected a nightly reduction of $TcCO_2$ by 21% or 10.9 mmHg, while participants experienced 17.1% fewer desaturation events (events less than SpO_2 < 92%) compared to their standard or usual care of prescribed nightly ventilation.

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