PHILIPS
RESPIRONICS

BiPAP A40 EFL

Evaluating EFL in COPD

Why and when COPD patients should be evaluated (screened) and treated for expiratory flow limitation (EFL)

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Summary

Expiratory flow limitation (EFL) is a feature of Chronic Obstructive Pulmonary Disease (COPD), which can lead to air trapping and breathlessness. In noninvasive ventilation (NIV) users, EFL is best overcome by titrating the level of applied EPAP to overcome EFL, thus relieving air trapping. EFL can be worsened through the night by the effects of posture and, over the medium term, by disease progression or intercurrent inflammation or exacerbation. Next-generation ventilators can measure EFL on a breath-by-breath basis and titrate EPAP to overcome EFL.

Introduction

EFL is the cardinal physiological abnormality in COPD[1] and occurs when the pressure outside the airway exceeds the recoil forces holding the airway open (Figure 1).

Intrinsic pathophysiological processes of inflammation may make this more likely by narrowing airways. Loss of recoil force occurs in COPD because lung destruction (i.e. emphysema) weakens the structures holding the airway open. The point of collapse is termed the choke point (Figure 2).

Although other techniques are available in a research environment (example: negative expiratory pressure), the most clinically practical way of identifying EFL is using FOT.[2] By using the forced oscillation technique (FOT), flow limitation can be measured noninvasively by comparing the difference between inspiratory and expiratory reactance; the underlying principle is that, when the airway is closed, reactance changes dramatically because FOT is then only assessing the airway up to the choke point rather than the entire respiratory system.[2]

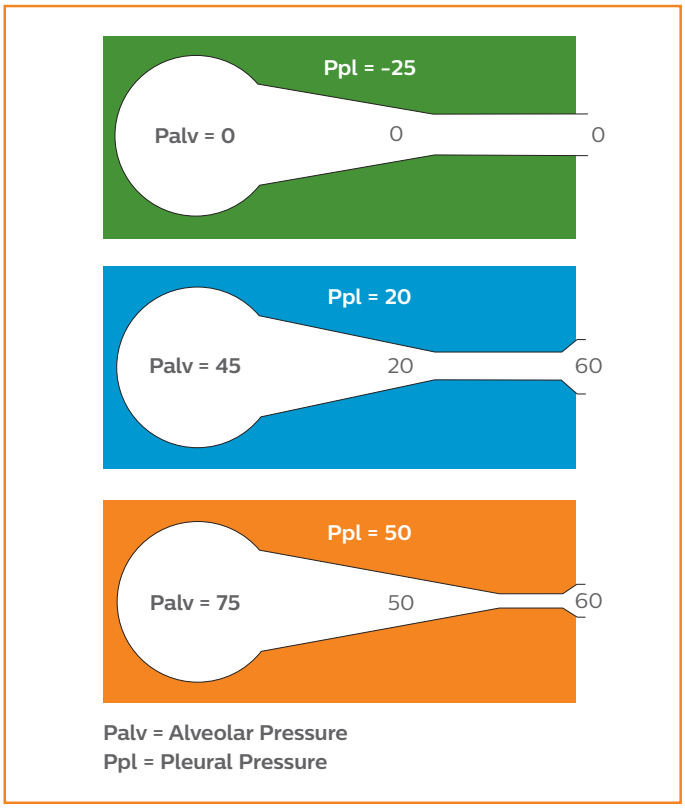


Figure 1

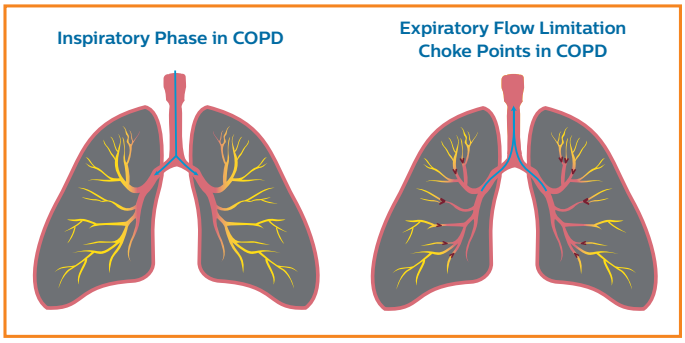


Figure 2

When should you suspect EFL?

In patients with COPD, as might be expected from physiology, EFL is more prevalent in those with more severe disease and those with more extensive emphysema. EFL leads to air trapping whenever minute ventilation is increased, and this has often been studied during exercise and is termed dynamic hyperinflation (Figure 3).

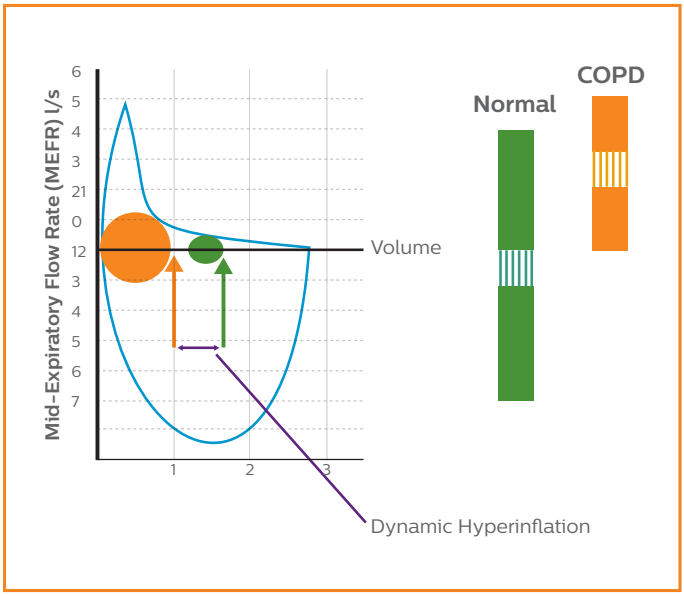


Figure 3

Dynamic hyperinflation is associated with breathlessness in COPD because the increased neural drive is required due to the respiratory system operating closer to total lung capacity where the pressure-volume curve is flatter. This is because the inspiratory muscles are operating at a mechanical disadvantage. Air trapping during sleep may manifest as a sense of hyperinflation, breathlessness or concern of difficulty breathing out. EFL assessment using FOT is more flexible than spirometry since it can evaluate airway obstruction continuously and is, therefore, suitable for use during exercise and sleep.

Clinically the likelihood of EFL being present in an upright patient are increased in those with an FEV_1 less than 50%, mMRC (modified Medical Research Scale) dyspnoea score ≥2 and IC/TLC ratio <0.5. Evidence suggests that patients with EFL are most likely to benefit from interventions, which reduce static or dynamic lung volumes. These are bronchodilators, gases that reduce minute ventilation (e.g. high-flow oxygen, or low-density gases) or patient alterations in their breathing pattern. Although data does not currently exist, such interventions might also include lung volume reduction (whether surgical or bronchoscopic) and the use of ambulatory EPAP.

EFL, BMI and posture

In COPD patients, flow limitation is independently associated with increasing body mass index.[3] EFL is also observed in patients with obesity alone, although the effect is most marked when BMI exceeds 50 kg/m.[2] EFL is worse when in the supine position because, since the effect of gravity of abolishing FRC is lower, it in turn reduces expiratory flow rates. Studies in both obese patients and patients with COPD suggest the prevalence of EFL increases while in the supine position.[4, 5] More data is required to understand the prevalence and or impact of home NIV users (FEV_1 < 50%) where their flow limitation increases when in the supine position.

EFL and disease progression

Acute exacerbation of COPD leads to airway inflammation, which increases airway resistance and thus makes EFL more prevalent. This would lead to a requirement for increased EPAP in ventilator users and, in principle, could be used as a way of detecting exacerbation (Figure 4). However, this proposition would need to be tested in practice since observational data suggests substantial day-to-day variation[3] and, in fact, a home monitoring program, which included home FOT measurement, was not shown to be beneficial in a study of non-ventilator users.[6] Since COPD, due to progressive emphysema, worsens with time, the prevalence tends to increase in a COPD cohort over time. In addition, it is well established that some patients have a frequent exacerbator phenotype and one might expect these to have a wider variation in measures of EFL.

Detecting and Abolishing Expiratory Flow Limitation in Hypercapnic COPD Patients

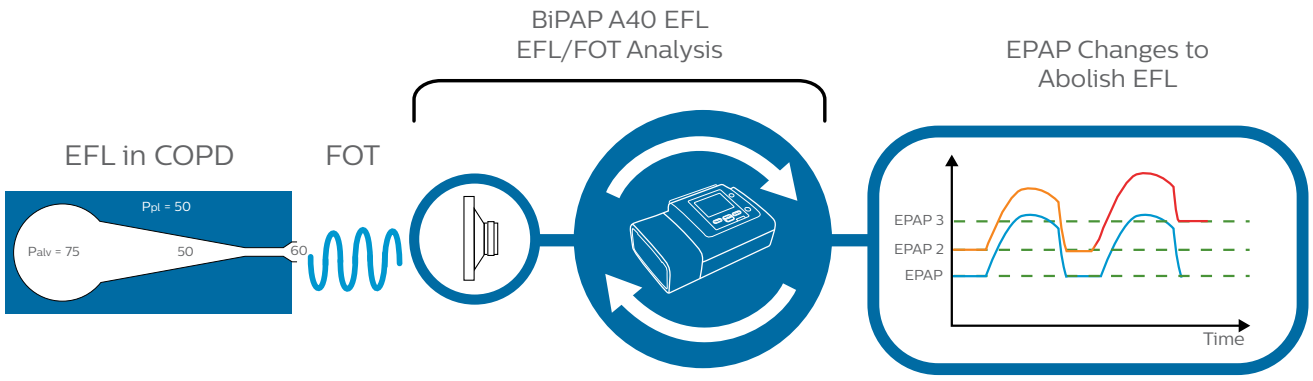


Figure 4

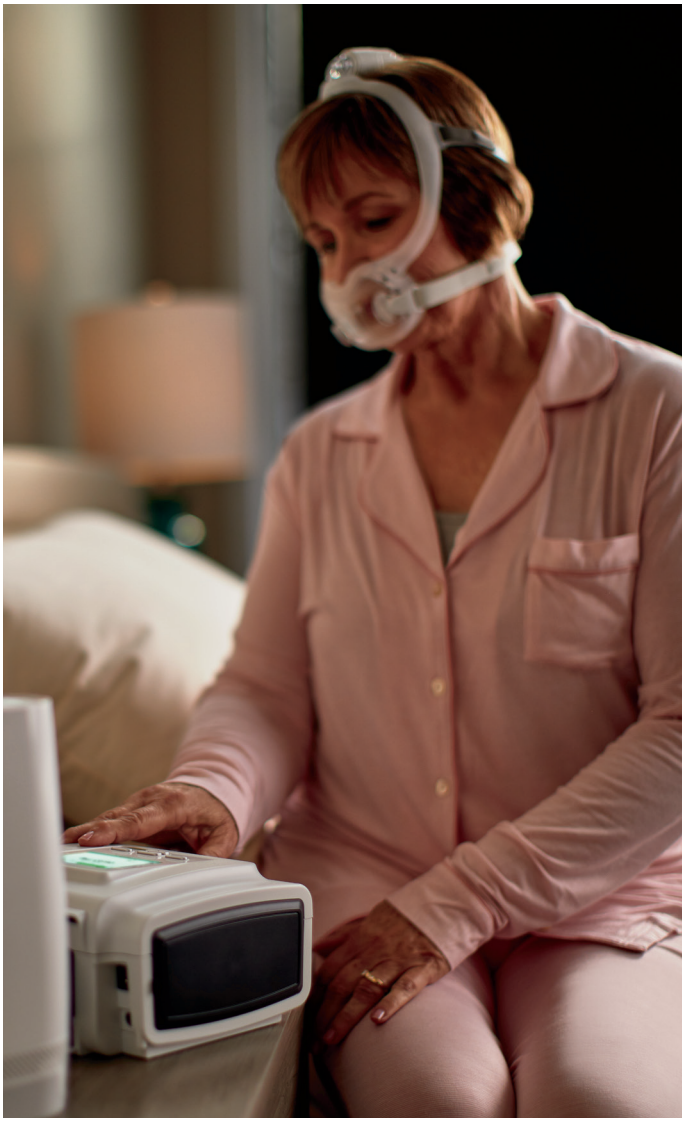
EFL and the COPD patient who uses NIV

A number of circumstances could conceptually change the prevalence or severity of EFL in a COPD patient who uses a ventilator at night. First, data noted above suggest that the likelihood of EFL increases when supine. Second, medicines used for treating bronchoconstriction could wear off during the night. Third, movement of phlegm could change airway dynamics and, fourth, in the presence of co-existent fluid retention, cranial fluid shift might change airway dynamics. Thus a device, like the BiPAP A40 EFL NIV, which can adjust EPAP to differing levels of EFL, may have advantages, although this will need to be confirmed in clinical trials.

Why and when to evaluate COPD patients for EFL

EFL is seldom evaluated in practice although its downstream consequences, such as dynamic hyperinflation, sometimes are. Clinicians tend to be outcome-driven. Therefore, potential indications for investigating the presence of EFL might include:

1. Intolerance of CPAP or NIV where posture-related EFL is suspected to be the cause of the clinician's inability to detect optimal EPAP. FOT can be incorporated into ventilator design and detect EFL.[4] If the ventilator then adjusts EPAP to match the intrinsic PEEP which arises as a result of the EFL, the work of breathing is reduced
2. Disease variation; patients with rapidly progressive disease or those with frequent variation due to exacerbation may develop episodic EFL
3. Where it is desired to use ambulatory pressure support (or CPAP in the case of Excessive Dynamic Airway Collapse (EDAC)) to improve exercise performance or as an adjunct to pulmonary rehabilitation
4. In the selection of patients for lung volume reduction interventions



Studies related to **EFL in COPD**

X5 Reactance measured with FOT and COPD

Reference	Technique	Number studied	Main findings
Crim 2011[7]	FOT	N=2054	Progressive increase in X5 with GOLD stage, reduced with bronchodilators. Poor relationship with CT extent of emphysema.

EFL and COPD severity

Reference	Technique	Number studied	EFL upright	EFL supine	Main findings
Mikamo 2014[8]	FOT	74	37/74	Not done	FL relates Emphysema score, MEF_{25-75}, FRC and whole breath X5.[1]
Aarli 2015[3]	FOT	425	78/4259	Not done	FL per se not analysed but ΔXrs greater with falling FEV1, IC, 6MW and rising SGRQ, RV and BMI
Dean 2017[10]	FOT	147	55/147	Not done	EFL current smokers, lower FEV1, higher RV, FRC, higher SGRQ, symptom scores, lower 6MW **Note:** of those followed up at 2 years 6/20 did not retain FL
Aarli 2017[9]	FOT	425	78/425	Not done	EFL patients had greatest drop in 6MW, more exacerbations (1.6 yr vs 0.7 if NFL), shorter time to AECOPD
Timmins 2012[11]	FOT	26	Not stated	Not done	EFL index related to CT emphysema and FEV_1
Vargas 2009[12]	NEP	35	25/35	Not done	Patients had been recently extubated
Boni 2002[13]	NEP	20	11/35	Not done	No differences (small sample size)

EFL and intervention in COPD (Posture)

Reference	Technique	Number studied	FEV1(% pred)	EFL upright	EFL supine	Main findings
Baydur 2004[14]	NEP	21	39	4/721	3/21	No change with posture in other conditions
Chiari 2014[5]	FOT	40		13/40	27/40	FEV_1, FEV_1/FVC ratio, MEF_{25-75} related to EFL upright and DLCO, KCO, mMRC related to EFL supine
Dellaca 2009[4]	FOT	7	38	43% breaths	78% breathes	Analysed by breath

EFL and intervention in COPD (Exercise)

Reference	Technique	Number studied	Mean FEV_1 (% pred)	Intervention	Main findings
Theodorakopoulou 2017[15]	NEP	42 (16 FL, 26 NFL)	50	PR	6 FL at rest and exercise 26 NFL at rest and exercise 10 FL only during exercise

[1] Whole breath X5 is known to relate to FEV_1

EFL and intervention in COPD (Other)

Reference	Technique	Number studied (patients/controls)	Mean FEV_1 (% pred)	Intervention	Main findings
Chen 2014[16]	NEP	15/13	41	Endurance exercise	No change
Vargas 2009[12]	NEP	25/none	?	Intrapulmonary percussive ventilation (IPV)	Magnitude of EFL reduced in 24 of 25. 3/25 no longer EFL
Ogino 2015[17]	FV loop superimp.	16/16	51	Arm bracing	Substantial reduction in COPD patients, no EFL in controls
Theodorakopoulou 2017[15]	NEP	42 (16 FL, 26 NFL)	50	PR	After rehabilitation only 1/16 FL and then only at peak exercise. Improvement related to breathing pattern change
Dellaca 2009[18]	FOT	42, no control	42	Salbutamol 5mg neb	8 of 20 were not FL after salbutamol
Alvisi 2003[19]	?	10 (8 FL, 2 NFL)	?	Oxygen 30%	2/8 no longer FL
Boni 2002[13]	NET	11 FL, 9 NFL	44	Salbutamol 400µg	Reduced dyspnea and increased IC but no effect in NFL patients
Tantucci 1998[20]	NET	11 FL, 7 NFL	54 NFL, 40 FL	Salbutamol 400µg	No FL patient changed status but only this subgroup increased IC
D'Angelo 2009[21]	NET	13 FL, 13 NFL	49 FL, 64 NFL	Heliox	No clear benefit to Heliox in FL patients but small study

Obesity and EFL

Reference	BMI (kg/m2)	Technique	Main finding
Spyratos 2007[22]	n/a[2]	NEP	14/21 FL before thoracocentesis, 7/21 afterwards
Baydur 2004[14]	42	NEP	No EFL in 9/9
Ferretti 2001[23]	51	NEP	EFL 10/46 upright, 27/46 supine
Pankow 1998[24]	44	NEP	EFL 2/8 upright, 7/8 supine

EFL during exacerbation

Reference	Tests	Patients/controls	Mean FEV_1 (% pred)	Scenario	Main finding
Jetmanali 2015[25]	FOT	29/not studied	31	Recovery AECOPD	Fell during admission in those with FL, no change in those without EFL

[2]Spyratos studied pleural effusion which may be considered a localised form of obesity in this context

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