# Asthma and chronic obstructive pulmonary disease in the intensive care unit

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## Abstract

There are many pitfalls in the management of patients with asthma or COPD especially when their condition becomes severe enough to warrant intensive care. Mortality in both groups remains significant. Standard principles of oxygen and drug administration and mechanical ventilation technique used for other critically ill patients can all cause problems in this patient group. Recognition of the presence of airflow obstruction, the potential for dynamic hyperinflation and careful adherence to the principles of therapy specific to this group are required to avoid complications. This article addresses the physiological derangements in airflow obstruction, their treatment consequences and how to avoid the management pitfalls that are important contributors to the morbidity and mortality of both conditions.

**Keywords** Asthma; COPD; dynamic hyperinflation; invasive mechanical ventilation; non invasive ventilation

**Royal College of Anaesthetists CPD Matrix**: 1A03, 2C02, 3C00

## Learning objectives

After reading this article, you should be able to:

- outline the medical management of acute exacerbations of COPD and asthma
- list the appropriate initial investigations for a patient with an exacerbation of asthma or COPD, interpret the results, and initiate appropriate interventions such as NIV
- describe the limitations of NIV and the features of patients who are likely to fail treatment with NIV
- list specific complications associated with intubation and mechanical ventilation in patients with these conditions, and describe the appropriate management of these complications if they arise
- describe how to utilize appropriate ventilation strategies to minimize complications commonly associated with ventilating patients with COPD or asthma

## Demographics and medical treatment

Asthma and chronic obstructive pulmonary disease (COPD) are conditions characterized by airflow limitation which, when sufficiently severe, mandate critical care management.

Patients with severe COPD are more commonly admitted to intensive care than patients with severe asthma. Mortality from COPD is increasing worldwide, exacerbations of COPD are triggered by infection (50%) and episodes of heart failure (25%). In others, no obvious cause is identified. COPD also commonly presents as a comorbidity of another illness where mechanical ventilation is required, such as major elective or emergency surgery, or trauma.

There is also an increasing prevalence of asthma amongst populations worldwide, with significant morbidity and impact on quality of life.[1] There are an estimated 346,000 death worldwide per year due to asthma.[1] The prevalence of asthma is highest amongst first world countries.[1] Asthma guidelines and the increased use of inhaled steroids have reduced mortality, as well as hospital and critical care admission rates. However, mortality remains significant, with approximately 1500 (0.3%) deaths per year in England and Wales attributed to acute exacerbations. Acute asthma attacks are attributed to a variety of causes including viral infection, allergen exposure, non-specific irritants (cold air, smoke, pollution), anxiety and unknown factors (up 25% of acute attacks). Two presentations of severe asthma have been described. The most common is an exacerbation on a background of chronic poorly controlled asthma, often viral-triggered. This group of patients require steroids and take many days to respond. Less common is 'hyperacute' or acute asphyxic asthma. This group has a background of hyper-reactivity but minimal or no symptoms until the acute event. The early asthmatic response in allergen-triggered asthma is a classic example. In recent times, ryegrass pollen exposure under unique thunderstorm conditions triggered a massive and rapid (within minutes) bronchospastic epidemic in several thousand susceptible individuals, overwhelming emergency services, and resulting in 35 intensive care admissions and ten deaths.[2] However, those who were able to reach medical care responded quickly to bronchodilators and steroids, and survivors of intensive care admissions only required mechanical ventilation for a relatively brief period. Important risk factors for asthma death include rural location, psychosocial issues, smoking, drug and alcohol dependence, lower socioeconomic status, allergies, respiratory tract infections and delay in seeking help.

Guidelines written and published by various expert bodies (British Thoracic Society [BTS], National Asthma Council of Australia) have been well implemented in primary care, leading to a diminishing burden on acute hospital services. These guidelines can easily be accessed online and are simple to understand and implement. The key components include earlier recognition of asthma severity, more widespread use of inhaled steroids, and pre-set plans to ensure prompt treatment of exacerbations.

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There are comparable and excellent resources guiding the medical management of COPD (Global Initiative for Chronic Obstructive Lung Disease, BTS). In either case it is important that these medical measures are instituted as soon as an exacerbation of either condition is identified.

## Involvement of critical care services and the use of non-invasive ventilation (NIV)

Most referrals to critical care are for consideration of ventilatory support in patients with a severe presentation or who have failed to improve despite optimal medical therapy. Non-invasive ventilation (NIV) has become a care standard in the management of acute exacerbations of COPD, with good evidence proving its role.[3] A large Cochrane meta-analysis[3] demonstrated that NIV significantly reduced mortality and invasive ventilation rates and led to a shortened hospital length of stay. NIV improves respiratory physiology with improvements in both $PaO_2$ and $PaCO_2$.[3] Excellent, concise and specific NIV guidelines exist,[4] focusing on the targeted use of NIV in patients with exacerbations of COPD and concomitant respiratory acidosis, which has failed to respond to optimal medical therapy.

Acute hypercapnic respiratory acidosis may also be triggered or worsened by excess oxygen therapy in a patient subset whose chronic relative hypoxemia is essential for stable ventilatory function. The majority of patients with severe COPD (FEV1 <30% predicted), especially those with pre-existing hypercapnia are at risk of an increasing $PaCO_2$ when oxygen therapy results in $SpO_2$ >95%. This is due to a combination of factors (Figure 1). Improvement may occur with titration of $FiO_2$ to a $SpO_2$ target of 88–92%. If an oxygen-induced rise in $PaCO_2$ has occurred in a patient with an exacerbation of COPD then hypercapnia may improve but not resolve when $FiO_2$ is reduced, such that NIV is often still necessary – hence the need for constant monitoring and regular review (Table 1).

The aims of NIV are to unload respiratory muscles, while augmenting ventilation and oxygenation, and to offset the adverse effects of sleep on ventilation and airway resistance. (Table 2).

Although the use of NIV for asthma has not been definitively established in large randomized trials, there is a growing consensus, supported by a recent meta-analysis,[5] that the judicious use of NIV in a critical care setting for severe acute asthma can reduce fatigue, improve gas exchange, improve airflow obstruction more rapidly and obviate the need for invasive ventilation.

NIV is being increasingly implemented both inside and outside critical care areas including emergency departments and ward areas specializing in this modality. NIV outcomes for COPD appear to be similar whether it is provided in intensive care, dedicated respiratory wards or through a specialized service supporting general wards, as long as experienced staff are involved and can easily escalate care as required. Nevertheless, patients at highest risk should still be admitted to intensive care (Table 2). Despite optimal medical management and the correct usage of NIV, a proportion of patients with COPD and acute asthma will still require endotracheal intubation for severe or increasing respiratory failure (increasing respiratory acidosis,

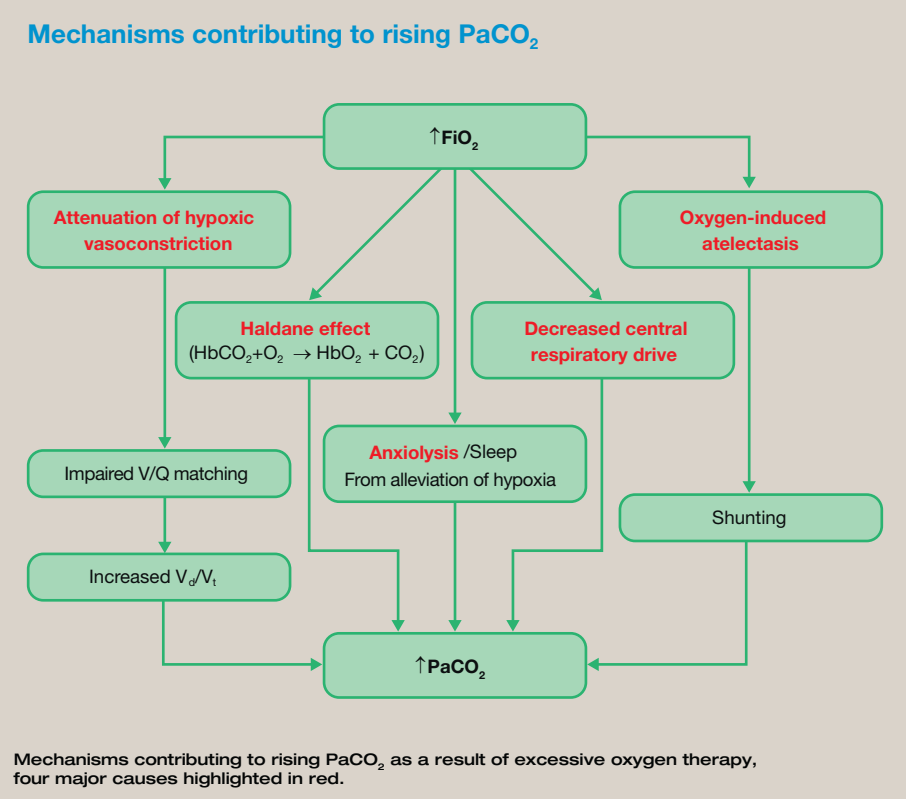


**Figure 1**

## Comparison of medical treatments of exacerbations of COPD and acute severe asthma

| Treatment | Severe COPD | Severe Asthma | |
|---|---|---|---|
| Inhaled B2 agonists | Frequently administered, may need to be driven with air | Driven with oxygen and given "back to back" | MANDATORY |
| Inhaled anticholinergics | Ipratropium bromide 500 mcg qid | Ipratropium bromide 500 mcg qid | |
| Controlled oxygen therapy | Important to titrate $FiO_2$ to $SpO_2$ (aim 88–92%), monitoring of ventilation and $PaCO_2$ important | Usually no adverse effects of high flow $O_2$, hypoxia is a late sign of severe respiratory failure and the impending need for ventilatory support | |
| Glucocorticoids | Hydrocortisone 100–200 mg IV stat then 100 mg qid, to ensure adequate/rapid dosing | Hydrocortisone 100–200 mg IV stat then 100 mg qid, to ensure adequate/rapid dosing | |
| Antibiotics | Majority of sputum cultures negative, but commonly of benefit if features of infective exacerbation (fever, increasing sputum volume, purulent sputum) | Small minority of severe acute asthma triggered by bacterial infection – only indicated if compelling features of infection e.g. fever, neutrophilia, consolidation | OPTIONAL |
| Magnesium infusion | Lacks evidence but unlikely to cause adverse effects | Lacks evidence but unlikely to cause adverse effects | |
| Intravenous theophylline | Effective bronchodilator but side effects close to clinical range and uncertain additional benefit in presence of optimal beta agonists and steroids. Can be tried if bronchospasm refractory to mandatory treatment | Effective bronchodilatorbut side effects close to clinical range and uncertain additional benefit in presence of optimal beta agonists and steroids. Can be tried if bronchospasm refractory to mandatory treatment | |
| Intravenous B2 agonists | Rarely used | Can be used if asthma refractory but evidence lacking and associated with increased risk of lactic acidosis | |
| Advanced care directives | Careful assessment of pre-morbid functional state and patient wishes should be undertaken | Usually not required | |

**Table 1**

exhaustion, hypoxia, reduced conscious level or respiratory arrest). Patients with asthma who fail NIV may deteriorate more precipitously than those with COPD and thus require rapid intubation.

The life expectancy in patients with COPD falls with deteriorating FEV1 and episodes of acute respiratory failure. Of all patients with COPD, those admitted to ICU for invasive ventilatory support have the highest mortality; even those patients who survive to discharge from ICU have a decreased life expectancy in comparison to the general COPD population. Careful assessment of any course of invasive treatment needs to be undertaken in patients who have severe COPD and end-stage lung disease (often in association with significant co-morbidity). This assessment should include age, severity of COPD, the presence of a reversible component and functional status. Functional status prior to the exacerbation is perhaps the most important factor; this often-omitted information should be carefully collected. In patients with severely limited mobility (housebound or worse) and compromised self care (e.g. showering, dressing), limitation of full intensive care management is often appropriate. This limitation is most commonly to provide active non-invasive care including NIV, all drug, fluid, nutritional and physical therapies but not invasive ventilation. It may also include limitations on other life supports systems such as renal replacement therapy and inotropic support.

### Ventilation and dynamic hyperinflation

The primary challenge in the ventilation of patients with COPD or severe asthma is that of dynamic hyperinflation (DHI). Incomplete expiration of inspired gas (gas trapping), due to slow expiratory air flow and airway closure, leads to increased end-expiratory lung volume.[5] Mechanical ventilation can lead to excessive DHI, with compromise of cardiac output, increased the risk of pneumothorax and, when very severe, circulatory collapse.[6,7] The three primary determinants of DHI are: (i) the severity of airflow obstruction (the expiratory time constant); (ii) the volume inspired (Vt); and (iii) the time for expiration (Te), determined by both the respiratory rate and the inspiratory flow (or I:E ratio).

In severe asthma, initial ventilation should target low minute ventilation (<115 ml/kg/min), low tidal volumes (≤6 ml/kg) and low respiratory rate (<14 breaths/minute), high inspiratory flow rates (≥70 L/min, expiratory time of 4 seconds) with volume controlled ventilation in synchronized intermittent mandatory ventilation (SIMV) mode. Externally applied Positive end-expiratory pressure (PEEP), during controlled ventilation

## Indications, complications and contraindications for the application of NIV in COPD

**Indications for NIV in COPD**

Respiratory rate >28/min

PaCO2 >45 mmHg (6KPa) with pH <7.35 ($H^+$ 4.467x$10^{-8}$)— not due to excessive supplemental oxygen therapy

Respiratory distress with impending fatigue

**Cautious Use of NIV i.e. best undertaken in an ICU/Critical care setting**

pH <7.25 (H+ 5.623 x $10^{-8}$)

Mechanical ventilation inappropriate

Drowsiness/reduced conscious level, secondary to respiratory failure

Hypoxaemia — failure is common if in combination with normocapnia or hypocapnia

After extubation - mechanical ventilation to assist in 'stepping down'

**Possible NIV complications**

Pressure ulcers/necrosis from mask — compliance may be improved with full face, helmet or other mask interfaces

Gastric distension/aspiration

Discomfort and intolerance

**Contraindications**

Coma/Severe encephalopathy

Cardiac/Respiratory arrest or severe haemodynamic instability

Facial Surgery/Trauma

Inability to clear secretions, tolerate mask or protect airway

Severe GI bleeding or vomiting

**Table 2**

remains controversial. One study has shown overall worsening of hyperinflation in proportion with the level of external PEEP[8] used suggesting that external PEEP should not be used during controlled mechanical ventilation in this patient group. A subsequent study has shown inconsistent responses to external PEEP in some patients on some on some ventilator settings.[9] If external PEEP is to be used at all, it should only be used if a clear reduction in Pplat occurs when it is applied otherwise 0 PEEP should be used. Significant sedation and, in some patients, intermittent neuro-muscular blockade, may be required to achieve these targets to control DHI. Hypercapnia is not a reason to increase ventilation as this will increase DHI. Although muscle relaxants may be required, their use should be minimized as they have been associated with acute myopathy, which can prolong weaning from ventilation. Reducing high peak inspiratory pressures by decreasing inspiratory flow rate will paradoxically increase the risk of barotrauma by decreasing expiratory time (lower I:E ratio), resulting in worsening DHI and increasing alveolar pressures hidden beneath the decreased peak airway pressure.[5] In severe COPD, the same ventilation principles apply but in this patient group it is usually safe to allow spontaneous ventilation within SIMV mode (e.g. controlled rate <10). When spontaneous breathing is occurring and DHI is not excessive, external PEEP (5—10 $cmH_2O$) may reduce the work of breathing for spontaneous breaths, in both asthma and COPD.

Auto-PEEP or intrinsic PEEP (PEEPi) can be assessed during an end-expiratory pause (0.5 seconds) (Figure 2). This is useful to detect the presence of airflow obstruction, however it underestimates the severity of DHI and is insensitive to change. This is because PEEPi only measures the pressure in lung units still communicating with the central airways at the end of expiration, and cannot measure the pressure in more severely obstructed lung units that have airway closure at higher pressures during expiration. A better measure of DHI is the plateau airway pressure (Pplat) measured during an end-inspiratory pause. This maneuver is best performed after 0.5 seconds of end-inspiratory pause and should target a Pplat <25 $cmH_2O$ (Figure 2). If the application of an end-inspiratory pause reduces the subsequent expiratory time, it is important to avoid applying this pause to sequential breaths as this will worsen DHI. For this reason, most modern ventilators automatically delay the next breath when an end-inspiratory pause is applied.

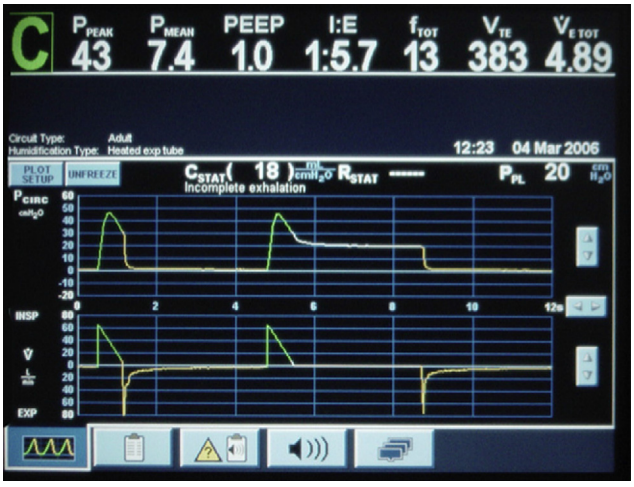


**Figure 2** Ventilator trace during severe airflow limitation. Note the small tidal volume, that high inspiratory flow (Vi) results in high measured peak airway pressures, and that the low respiratory rate in combination with the high Vi results in a long expiratory time. However the ventilatory pattern has resulted in a comfortably safe Pplat during an end-inspiratory pause (white section of pressure curve).

If the Pplat is <25 $cmH_2O$ then the ventilator rate can be increased (provided Pplat remains <25 $cmH_2O$) and, when appropriate, sedation decreased and spontaneous ventilation commenced. If the Pplat is >25 $cmH_2O$ or if there is hypotension present that responds to transient ventilator disconnection then DHI should be reduced by decreasing the respiratory rate, ensuring the inspiratory flow rate is high and accepting the presence of significant respiratory acidosis. The Pplat should be rechecked after these adjustments to ensure it has decreased.

Uncommonly, despite optimal management and profound hypoventilation, some patients with severe asthma may continue to have excessive DHI resulting in refractory hypotension. In this situation, treatments that have no proven role in asthma exacerbations but have anecdotal reports of success may be tried. These include administering intravenous adrenaline and/or intravenous magnesium and/or introducing helium (improved laminar flow of gases) or anaesthetic gases (direct bronchodilatory effect) into the ventilator circuit. Patients in extremis have required extra corporeal membrane oxygenation (ECMO) to achieve adequate gas exchange when even minimal ventilation still results in circulatory failure and/or insufficient gas exchange; however, this requirement is rare and contentious for asthma. Not all centres can offer such specialist intervention and the only practical option may be to tolerate profound hypoventilation with muscle paralysis (Figure 3).

The particular challenges of trying to achieve ventilator targets in the presence of DHI can lead to a constellation of specific problems including myopathy, the risk of barotrauma/pneumothorax and circulatory collapse with pulseless electrical activity (PEA). These in turn may increase the number of days a patient is mechanically ventilated and compromise ventilator weaning.

## Pneumothorax

Though spontaneous pneumothorax occurs more commonly amongst the asthma and COPD populations, it rarely occurs during or as the precipitant of an acute exacerbation. Barotrauma during an exacerbation of asthma or COPD is usually from excessive DHI during mechanical ventilation or needle introduction to the thorax (attempts at gaining central venous access or attempted treatment of suspected tension pneumothorax). Tension pneumothorax is the rule rather than the exception as airflow obstruction itself acts as a valve. This usually presents during mechanical ventilation with a worsening of respiratory state including hypoxia, increased airway pressures, hypotension and sometimes circulatory collapse or even cardiac arrest. Furthermore, a tension pneumothorax on one side can redistribute ventilation to the contralateral lung, worsening DHI within the second lung and risking the development of bilateral pneumothoraces. Thus, when a pneumothorax is suspected and hypotension is absent or mild, the ventilator rate should be decreased (to protect the second lung) and an urgent chest X-ray obtained to ensure a pneumothorax is present before a careful blunt dissection intercostal catheter is inserted. If severe hypotension mandates urgent insertion of a vascular cannula, this should always be followed by an intercostal catheter (again by blunt dissection), as the intravascular cannula will always produce a pneumothorax if it was not already present.

## Pulseless electrical activity (PEA) and cardiac arrest

Tension pneumothorax is a commonly recognized cause of circulatory collapse and cardiac arrest in the ventilated COPD or asthma patient. However DHI, even with very low minute ventilation, can lead to cardiac arrest with PEA, sometimes after

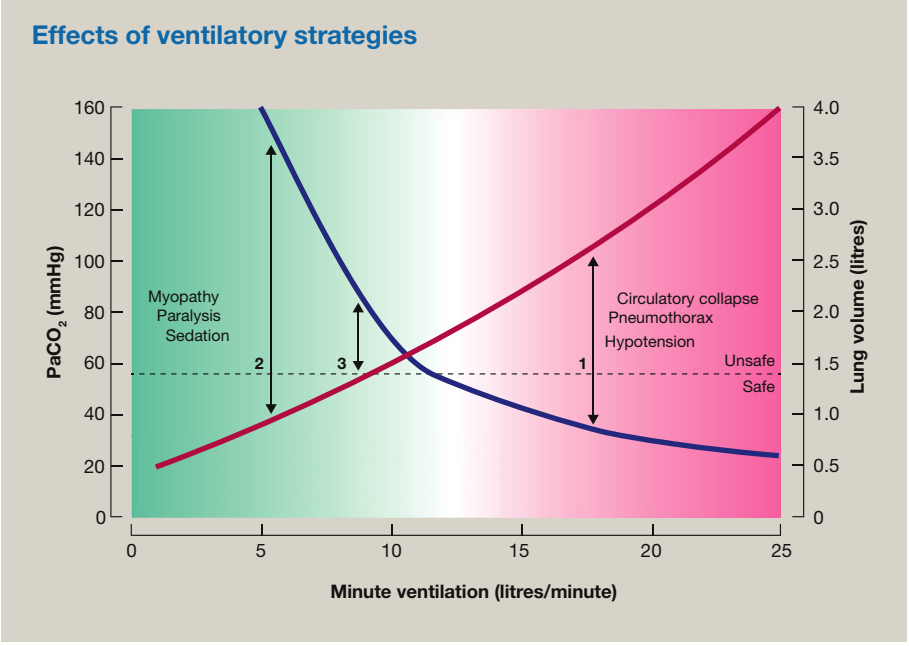


**Figure 3** Strategy 1: Ventilating to a normal $PaCO_2$ (40 mmHg) leads to DHI with dangerous lung volumes and their associated complications (pink shaded area). Strategy 2: Marked hypoventilation eliminates the problems of strategy 1 but leads to severe respiratory acidosis and requires a significant sedation/paralysis associated with complications (green shaded area). Strategy 3: Ventilation just below the safety limit (Pplat 25 cmH2O) results in only mild-moderately elevated $PaCO_2$ and minimizes the complications associated with the alternative strategies.[5]

only a very short period of mechanical ventilation. It is important to recognize to avoid well-intentioned but unnecessary interventions aimed at other causes of PEA (pericardiocentesis, intercostal catheters, etc.), which may complicate the situation further. Disconnecting the ventilator for over one minute or ventilating with fewer than four breaths per minute should be performed in this circumstance. If this maneuver results in spontaneous return of circulation, it is likely that DHI was the underlying cause and ventilation should be resume, but at a much lower rate and tidal volume.

## Myopathy

The combination of hypoventilation, neuromuscular blocking agents and glucocorticoids has been associated with an acute myopathy with EMG changes, increased CK and characteristic biopsy findings.[7] The amount of neuromuscular blocker agents used correlated with the severity of myopathy and suggests the need to avoid excessive sedation and paralysis where possible.

## Lactic acidosis

The use of salbutamol in frequent schedules, high doses or intravenously carries a significant risk of lactic acidosis. Serum lactate levels of 4–12mmol/litre are not uncommon and at these levels significantly add to respiratory distress – infusions should be limited to doses below 10 microgram/min and stat doses to less than 250 micrograms. Ceasing infusions for 4–6 hours will usually lead to resolution of the problem.

## Ventilator management and weaning

When DHI becomes manageable spontaneous ventilation should be encouraged to promote respiratory muscle activity and ventilator support progressively reduced until a trial of extubation can be considered. This usually happens at the commencement of mechanical ventilation in COPD but commonly requires significant improvement in airflow in asthma. The application of NIV immediately following extubation in patients with COPD and persisting hypercapnia reduces the need for reintubation and ongoing mechanical support[10] but is usually not required in asthma except where there is a large irreversible component. In ventilated COPD patients, thickening of the diaphragm on inspiration by more than 30% had a sensitivity and specificity of predicting successful extubation (i.e. $>$ 48 hours) of 88% and 71%, respectively.[11]

Although overfeeding can lead to an increase in $CO_2$ production potentially impairing weaning, the long-term benefits from adequate nutrition are important on COPD and should be given priority.

Tracheostomy is rarely required in patients with asthma but may be required in patients with COPD who are still ventilator dependent after 7–10 days. Extubation to NIV support can be successful and may be worth trying before performing a tracheostomy. A tracheostomy is better tolerated than naso/orotracheal tube with patients requiring less or no sedation. Other benefits include reduction in airway resistance to facilitate weaning, easier upper and lower airway toileting, easier swallowing and speaking, and facilitating ICU discharge.

In a small minority of patients weaning from mechanical ventilation, it may not be possible despite optimization of all reversible factors, in these cases long-term institutional or home ventilation is an option if the service is available. However, the huge impact of such a measure may represent such a poor quality of life that this option may not be desirable.

## Post ICU care

An admission to ICU and the requirement for non-invasive or invasive ventilation represents a life-threatening event in both asthma and COPD with an increased mortality risk in both groups after hospital discharge. It should act as a trigger to review and optimize all aspects of an individual's primary and preventative care. In both asthma and COPD this will usually include regular long-acting bronchodilators and inhaled steroids. In both groups, a plan for early recognition and treatment of future exacerbations should be given to the patient prior to discharge. This plan may include assessment of peak expiratory flow, additional inhaled bronchodilators, and possibly immediate commencement of pre-prescribed oral steroids or antibiotics, and a trigger level and path for medical presentation. In COPD, pulmonary rehabilitation programmes improve physiology, lung function and quality of life while reducing hospitalization rates. Influenza and pneumococcal vaccines should be given to patients with asthma and those with COPD when well. Lung reduction surgery and lung transplantation may also be considered for a select population of those with advanced COPD.

## Prognosis

Survival at 180 days in patients admitted to ICU for COPD exceeds 60%. Importantly, the majority (73%) of these patients reported equivalent or improved quality of life; of survivors, 96% would choose similar treatment again. Features such as organ dysfunction other than respiratory failure, advanced disease with severe respiratory dysfunction and prolonged hospital stay prior to admission to ICU are associated with worse outcomes. In the longer term, outcome data suggest that COPD combined with severe respiratory failure has one and five year survival rates comparable to many solid organ tumours, with studies reporting 21–39% mortality at 1 year and 55–76% mortality at 5 years.[12]

Less than 0.2% of hospital attendances for asthma result in death. Risk factors statistically associated with such a catastrophic outcome are a history of recurrent admissions for asthma and a prior episode of asthma requiring mechanical ventilation.

Recent Australian data indicate that around one third of patients admitted to intensive care with severe asthma require mechanical ventilation. Among these the mortality rate has fallen progressively from 10% to 3% amongst ventilated patients over the 8 years to 2003[13] and a more recent publications shows that mortality has continued to fall since then.[14] Other Australian data have shown that in-hospital mortality rates for hypercapnic COPD patients can be as low as 11%, with all deaths occurring with palliative intent. These results suggest that by recognizing patients with severe airflow limitation and initiating appropriate treatment strategies, improved outcomes are achievable. ◆

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## FURTHER READING/USEFUL RESOURCES


British Thoracic Society - www.brit-thoracic.org.uk.

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