Chronic obstructive pulmonary disease and anaesthesia

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Key points

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory condition resulting in expiratory airflow limitation.

Treatment involves smoking cessation, inhaled therapy, pulmonary rehabilitation, and appropriate and timely treatment of exacerbations.

Patients with COPD are at increased risk of developing perioperative complications and have an increased mortality.

Anaesthetic management centres on preoperative optimization and the use of regional techniques wherever possible.

If general anaesthesia is used, then artificial ventilation is challenging because of the development of intrinsic positive end-expiratory pressure.

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Chronic obstructive pulmonary disease (COPD) is a commonly encountered respiratory disorder. Patients with COPD pose a challenge to the anaesthetist because intraoperative and post-operative complications occur more commonly than in those without the disease, and can lead to prolonged hospital stay and increased mortality. This article provides an overview of COPD and discusses implications for the anaesthetic management of patients with the disease.

Pathophysiology

COPD is a chronic and progressive inflammatory condition affecting central and peripheral airways, lung parenchyma, and pulmonary vasculature. This leads to poorly reversible narrowing of the airways, remodelling of airway smooth muscle, increased numbers of goblet cells and mucus-secreting glands, and pulmonary vasculature changes resulting in pulmonary hypertension.

It is widely accepted that cigarette smoking is the key noxious stimulus leading to the development of COPD. However, more recently it has been suggested that genetic factors are also implicated, with the finding that a genetic variant (FAM13A) is associated with the development of COPD in the COPDGene study.[1]

COPD is characterized by expiratory airflow limitation because of a combination of small airway inflammation (obstructive bronchiolitis) and parenchymal destruction (emphysema). In the former, inflammation in the small airways causes obstruction and air trapping, leading to dynamic hyperinflation, which adversely affects both ventilation/perfusion (V/Q) matching and the mechanics of the respiratory muscles. In emphysema the end result of inflammation is elastin breakdown and subsequent loss of alveolar structural integrity leading to decreased gas transfer, reduction in the pulmonary capillary bed, and further worsening of V/Q matching. Further airflow limitation results from reduced

parenchymal support of small airways. Often it is not possible to make clear distinctions between the two subtypes and the relative contribution of each varies from patient to patient. In patients with advanced COPD, the combination of V/Q mismatch, decreased gas transfer, and alveolar hypoventilation ultimately leads to respiratory failure.

COPD is often associated with a number of coexisting diseases that may complicate the anaesthetic management of these patients. A high proportion of patients with COPD are smokers, hence the disease is associated with the development of lung cancer. Pulmonary hypertension is prevalent in a third of patients with COPD and has been shown to be an indicator of poor long-term survival. Inflammatory processes in the lung not only cause pulmonary effects but also contribute to the extrapulmonary effects of the disease. The origin of this systemic inflammation is unclear and probably multifactorial, but results in weight loss, skeletal muscle dysfunction (with further adverse effects on respiratory muscle function), cardiovascular disease, depression, and osteoporosis. Weight loss occurs in 50% of patients with severe COPD and indicates a poor prognosis.

Clinical features

Epidemiology

It has been estimated that 3 million people have COPD in the UK, two-thirds of these being undiagnosed. Diagnosis is most common in the sixth decade of life.

COPD confers increased risk of hospitalization in general, and in the critically ill it has been shown to increase mortality both in those with ventilator-associated pneumonia and in those with non-exacerbated disease. The long-term survival of patients with severe COPD undergoing surgery is poor, with postoperative pulmonary complications being common. A recent study identified COPD as an independent

1

predictor of the development of hypoxaemia requiring intubation within 3 days of surgery.[2] This unanticipated early intubation was identified as an independent predictor of 30-day mortality.

Diagnosis and assessment

Both the National Institute for Clinical Excellence (NICE) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) offer guidelines for the diagnosis and assessment of COPD.[3,4]

A diagnosis of COPD should be considered in smokers over the age of 35 presenting with exertional breathlessness, a chronic cough, regular sputum production, and frequent winter bronchitis or wheeze. Spirometry should be used both at the time of diagnosis and also to reconsider the diagnosis if patients show an exceptionally good response to treatment. Airflow obstruction defined by a ratio of forced expired volume in 1 s to forced vital capacity (FEV_1/FVC) of <0.7 is used to diagnose COPD. If FEV_1 is $>80\%$ of the predicted value, then a diagnosis of COPD should only be made in the presence of respiratory symptoms. Reversibility testing with bronchodilators or corticosteroids is not necessary for diagnosis, and clinical features should be used to differentiate COPD from asthma.

While it is important to assess disease severity in COPD to guide therapy and predict prognosis, no single measure correlates exactly with true severity in an individual patient. Comprehensive assessment thus includes measurement of the degree of airflow obstruction, level of disability, the frequency of exacerbations and factors such as FEV_1, carbon monoxide transfer factor (TL_{CO}), degree of breathlessness, exercise capacity, and body mass index.

Airflow obstruction should be assessed according to the reduction in FEV_1, as shown in Table 1.[3–5]

Treatment

Cessation of smoking is vital. Even at a late stage of the disease this may slow down the rate of deterioration and prolong the time before disability and death occurs.

Inhaled therapy

Inhaled therapy provides the mainstay of day-to-day treatment. Short-acting bronchodilators are used initially for the relief of breathlessness and exercise limitation. With persistent breathlessness, treatment should be stepped up to include either a long-acting muscarinic antagonist (LAMA), or a long-acting β_2 agonist (LABA), which may be combined with an inhaled corticosteroid (ICS). In more severe cases, patients may be maintained on a LABA and ICS in a combination inhaler plus a LAMA. The majority of patients will administer their medication via hand-held inhalers, with nebulizers being reserved for those with distressing or disabling breathlessness despite maximum therapy with inhalers.

Oral therapy

Maintenance use of oral corticosteroid therapy in COPD is not usually recommended, but may become necessary in advanced COPD. These patients are therefore at risk of osteoporosis, immunosuppression, hyperglycaemia, peptic ulcer disease, impaired wound healing, and acute adrenal insufficiency at times of stress, such as when undergoing surgery.

Oral theophylline is occasionally used in the treatment of severe COPD or in those unable to use inhaled therapy. Co-administration of drugs that inhibit hepatic cytochrome P450 (e.g. cimetidine, erythromycin, or ciprofloxacin) tend to delay the elimination of theophylline and a reduction in dose is recommended. Drugs that induce hepatic cytochrome P450 (e.g. phenytoin, carbamazepine, or barbiturates) increase theophylline clearance and the dose may need to be increased. It has a narrow therapeutic index and monitoring of plasma levels is necessary to avoid toxicity, which may manifest as tachyarrythmias, seizures, nausea and vomiting, or rhabdomyolysis.

Oral mucolytic therapy (for example carbocysteine) is occasionally used in patients with a chronic productive cough and should be continued if there is symptomatic improvement. These agents may reduce rates of exacerbation in certain individuals, but there is little evidence to demonstrate superiority to standard maximal therapy. Mucolytics have no significant adverse effects but must be continued long-term in responsive patients.

Oxygen therapy

Long-term oxygen therapy to reduce pulmonary arterial pressure has been shown to prolong life when used to maintain oxygen saturations $>90\%$ for large proportions of the day and night. It is indicated in patients with a Pa_{O_2} of <7.3 kPa when stable, or <8 kPa when stable and with polycythaemia, nocturnal hypoxaemia, peripheral oedema, or pulmonary hypertension. Supplemental oxygen needs to be breathed for at least 15 h day^{-1} to improve mortality.

Pulmonary rehabilitation

This should be offered to all suitable COPD patients, including those recently hospitalized for an exacerbation and those who

Table 1 Classification of severity of airflow limitation in COPD. Reproduced from NICE guideline 101.[3] FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; NICE, National Institute for Health and Clinical Excellence; ATS, American Thoracic Society; ERS, European Respiratory Society; GOLD, Global initiative for chronic Obstructive Lung Disease. *Symptoms should be present to diagnose COPD in patients with mild airflow obstruction. [†]Or $FEV_1 <50\%$ with respiratory failure.

FEV_1/FVC (post bronchodilator)	$FEV_1\%$ predicted	NICE 2004	ATS/ERS 2004[5]	GOLD 2008[4]	NICE 2010[3]
<0.7	$>80\%$		Mild	Stage 1—mild	Stage 1—mild*
<0.7	50–79%	Mild	Moderate	Stage 2—moderate	Stage 2—moderate
<0.7	30–49%	Moderate	Severe	Stage 3—severe	Stage 3—severe
<0.7	$<30\%$	Severe	Very severe	Stage 4—very severe[†]	Stage 4—very severe[†]

consider themselves functionally disabled by COPD. It is unsuitable for those who cannot walk or who have unstable cardiac conditions.

Non-invasive positive pressure ventilation

Non-invasive positive pressure ventilation (NPPV) is now widely used in the management of respiratory failure secondary to COPD, and a meta-analysis has concluded that NPPV should be the first-line intervention in addition to usual medical care in all suitable patients.[6] It should be tried early in the course of respiratory failure to reduce mortality, avoid tracheal intubation, and decrease treatment failures.

Management of exacerbations

Repeated exacerbations of COPD result in an accelerated deterioration in lung function and general health, poorer quality of life, and an increased mortality rate. Comprehensive and effective management therefore relies both on the prevention of exacerbations by strict adherence to the treatment regime and on the prompt recognition and treatment of exacerbations when they do occur. Timely institution of antibiotics and oral steroids, in addition to early use of NPPV, is vital in these situations.

A recent randomized controlled trial explored whether providing self-help management to patients with COPD could reduce hospital admission and mortality.[7] Patients in the intervention group were educated to recognize the early signs of an exacerbation and commence early oral antibiotics and steroids. Despite not being able to show an overall benefit in the self-help group, a subset group who were deemed 'effective self-managers' did have significantly lower admission and mortality rates.

Preoperative evaluation and medical optimization

The patient with COPD requires a comprehensive preoperative evaluation, which ideally should commence well in advance of the proposed surgical intervention to allow adequate time for additional investigations and treatment to be instigated.

Preoperative evaluation

A full history is a useful clinical assessment of COPD severity and should focus on exercise tolerance. This is frequently unreliable when self-reported and so it is useful to question relatives if available. It is also helpful to be specific when enquiring about the maximal level of exertion attainable, for example 'are you breathless when dressing?' or 'how many stairs can you climb before needing to rest?' The frequency of exacerbations, timing of the most recent course of antibiotics or steroids, hospital admissions, and previous requirements for invasive and non-invasive ventilation should be identified, and any co-morbid conditions identified.

In addition to the routine preoperative blood tests, patients with COPD require an electrocardiogram to look for any evidence of right-sided heart disease or concomitant ischaemic heart disease.

In accordance with recommendations from NICE, a chest X-ray is not mandatory and may add little value. It should be considered if there is clinical evidence of current infection or recent deterioration in symptoms to exclude lower respiratory tract infection or occult malignancy. The presence of extensive bullous disease on a chest X-ray highlights the risk of pneumothorax. Spirometry is useful to confirm the diagnosis and to assess the severity of COPD as outlined in Table 1. Not surprisingly, more severe disease is associated with increased risk of postoperative complications.

It is important to consider assessment of the functional status of patients, with simple and safe tests such as stair climbing and the 6-min walk test correlating well with more formal exercise testing. Of course this is not possible in everyone. A baseline arterial blood gas measurement may be useful in predicting high-risk patients, with both $Pa_{CO_2} > 5.9$ kPa and $Pa_{O_2} < 7.9$ kPa predicting a worse outcome.

Nutritional status should be routinely assessed, as patients with both high and low body mass index have increased risk. Poor nutritional status with a serum albumin level <35 mg litre^{-1} is a strong predictor of postoperative pulmonary complications. It may be beneficial to consider preoperative nutritional supplementation in such patients, particularly in those undergoing thoracic surgery where it has been shown to reduce overall complications.

All patients with COPD require a preoperative examination, as decreased breath sounds, prolonged expiration, wheeze, and rhonchi are predictive of postoperative pulmonary complications. Preoperative wheezing warrants aggressive treatment with bronchodilators and possibly steroids before surgery. Signs of active respiratory infection such as pyrexia, purulent sputum, worsening cough, or dyspnoea should be sought, and if identified surgery should, if possible, be postponed and appropriate treatment instituted.

Preoperative interventions

Smoking history is important as current smoking increases the risk of postoperative pulmonary complications, with smokers having an increased risk of pneumonia, length of stay in intensive care, and requirement for mechanical ventilation. Smoking cessation has been shown to slow the deterioration of lung function, although the timing of this in the preoperative period is controversial. Maximum benefit is obtained if smoking is stopped at least 8 weeks before surgery with some studies suggesting that cessation <8 weeks before surgery is associated with increased risk of postoperative complications. However, these data are largely from observational studies in cardiac surgery, and studies in other surgical specialities have failed to confirm the findings. Most centres therefore now advocate stopping smoking regardless of the interval before surgery. The preoperative visit is an emotional time for patients where perceived risk and individual mortality are being considered in detail. It represents a 'teachable moment' when patients may be particularly receptive to education and advice about stopping smoking.[8] Patients should be urged to seek help with this as new cessation treatment methods have resulted in greatly improved success rates. In addition

to nicotine replacement therapy, varenicline or amfebutamone are options for motivated patients, but should only be prescribed alongside behavioural support. Varenicline (Champix) is a partial agonist at the α4β2 neuronal nicotinic acetylcholine receptor and has been shown to reduce withdrawal and craving by preventing nicotine binding to the receptor.

Patients with large volumes of sputum should be identified and referred for preoperative physiotherapy in an attempt to reduce the incidence of intraoperative bronchial plugging or pneumonitis. Pulmonary rehabilitation in the form of patient education, exercise training, and behavioural interventions does not currently have a routine place in the preoperative period, but this may become commonplace in the near future.

Conduct of anaesthesia

Regional anaesthesia

It is accepted that general anaesthesia, and in particular tracheal intubation and intermittent positive pressure ventilation (IPPV), is associated with adverse outcomes in patients with COPD. Such patients are prone to laryngospasm, bronchospasm, cardiovascular instability, barotraumas, and hypoxaemia, and have increased the rates of postoperative pulmonary complications. It is perhaps unsurprising therefore that there is now increasing evidence to support the use of regional techniques in cases traditionally thought possible only under general anaesthesia. One study found a 50% reduction in the risk of postoperative pneumonia in COPD patients when surgery was conducted with epidural anaesthesia alone.[9] The inability of some patients to lie flat may limit the use of this technique. However, by using a combination of reassurance and sedation, along with a degree of surgical flexibility with respect to table position, it may be possible to avoid a general anaesthetic in many patients. The use of non-invasive ventilation intra-operatively may also be used to ameliorate the respiratory effects of laying flat.

Controversy remains over the use of interscalene brachial plexus block in patients with COPD. Concerns about diminished respiratory function as a result of phrenic nerve palsy from anterior spread of local anaesthetic have led some to suggest that this should be avoided in patients with COPD. Conversely, there are reports of the use of such blocks as the sole anaesthetic technique to avoid the need for a general anaesthetic in patients with severe COPD.[10] It is possible that better use of ultrasound guidance will minimize the volume of local anaesthetic required and so may reduce the incidence of phrenic nerve involvement.

## General anaesthesia

Pre-induction

A patient with COPD requiring a general anaesthetic is likely to be at risk of haemodynamic compromise on induction of anaesthesia and initiation of IPPV. Placement of an arterial catheter should be considered for both beat-to-beat blood pressure monitoring and for repeated blood gas analysis.

Preoxygenation should be used in any patient who is hypoxic on air before induction. In patients with severe COPD and hypoxia, CPAP during induction may be used to improve the efficacy of pre-oxygenation and reduce the development of atelectasis.

Ventilatory management

Most of the difficulties encountered when anaesthetizing patients with COPD can be explained by the occurrence of increased intrathoracic pressure when using IPPV. Limited expiratory flow rate because of airway narrowing results in the next inhalation occurring before expiration of the previous breath is complete, and leads to 'breath stacking' or 'air trapping' and the development of intrinsic positive end-expiratory pressure (PEEPi) (Fig. 1). The elevation of intrathoracic pressure results in decreased systemic venous return and may be transmitted to the pulmonary artery, raising pulmonary vascular resistance, and leading to right heart strain. Along with direct pressure exerted on the heart by hyper-inflated lungs, this explains the cardiovascular instability that commonly occurs. Other potential harmful effects of air trapping include pulmonary barotrauma or volutrauma, hypercapnia, and acidosis.

One of the first indicators of air trapping may be the slow filling of the manual ventilator bag during induction of anaesthesia. Once mechanical ventilation has begun, air trapping may be suggested by a capnography trace that does not reach a plateau, indicating continuing admixture of air from the dead space reducing end-expired CO_2 concentration. It may also be possible to identify air trapping using the ventilator to show that expiratory flow has not reached zero, or by measurement of PEEPi.
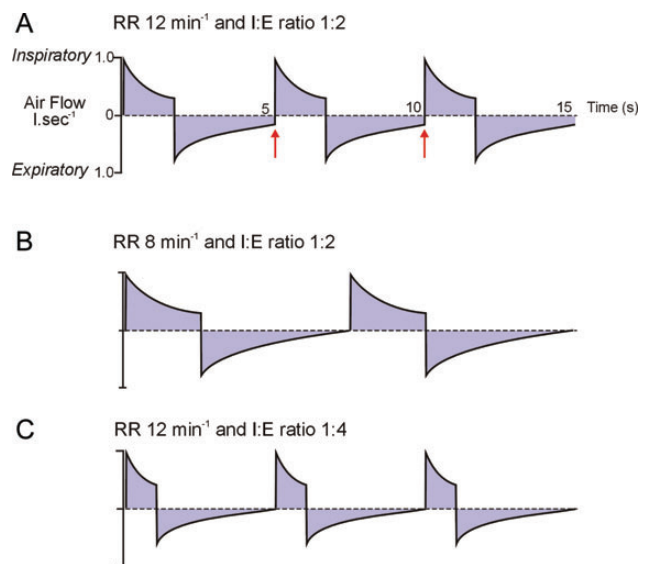
Fig 1 Air trapping during intermittent positive pressure ventilation in a patient with COPD. (A) Standard ventilator settings leading to incomplete expiration before the onset of the next inspiration (red arrows). This may be prevented by increasing expiratory time, either by slowing respiratory rate (B) or increasing the I:E ratio (C), both of which will reduce minute ventilation and so risk the development of hypercapnia.

When considering ways to reduce the harmful effects of air trapping, there are three approaches to consider:

1. Allowing more time for exhalation. Reducing the respiratory rate or the I:E ratio (typically to 1:3–1:5) allows more time for exhalation thus reducing the likelihood of breath stacking (Fig. 1B and C). However, this will inevitably result in reduced minute volume, leading to hypercapnia, hypoxia, or acidosis, which may elevate pulmonary vascular resistance and worsen haemodynamic instability. If this is a concern, it may be preferable to increase the inspiratory flow rate and tolerate higher peak pressures, which risks pulmonary barotrauma.

2. Application of PEEP. The use of external PEEP in ventilated patients with COPD has theoretical benefits by keeping small airways open during late exhalation, so potentially reducing PEEPi. It has been suggested that if the values of applied PEEP are kept below PEEPi there should be no significant increase in alveolar pressure and so no worsening of the cardiovascular effects while hopefully attenuating PEEPi. Clinical studies addressing this topic are inconclusive, partly because measurement of PEEPi is difficult, but also because patient responses to extrinsic PEEP have been found to be unpredictable, particularly in terms of improving gas exchange.[11]

3. Treatment of bronchospasm. Gas flow in small airways may be severely compromised by bronchospasm, which commonly occurs at induction of anaesthesia or during airway instrumentation. It should be treated promptly either by inhaled bronchodilators or by deepening anaesthesia with propofol or increased concentrations of inhalation anaesthetics.

Satisfactory ventilation of patients with COPD is therefore often a matter of compromising between the conflicting requirements for oxygenation, normocapnia, and cardiovascular stability. In severe COPD it may be necessary to accept some derangement of all these physiological aims to facilitate the anaesthetic and surgery.

Extubation

Before extubation, it is important to optimize the patient's condition. The neuromuscular blocking agent should be fully reversed and the patient warm, well oxygenated, and with a Pa_{CO_2} close to the normal preoperative value for the patient. Peri-extubation bronchodilator treatment may be helpful. Extubation of the high-risk patient directly to non-invasive ventilation may reduce the work of breathing and air trapping and has been shown to reduce the need for reintubation in the postoperative period after major surgery.

Postoperative care

Respiratory support

After operation, patients with severe COPD need close monitoring to avoid respiratory failure or postoperative chest infections. Patients should be assessed before operation for their likelihood of requiring postoperative respiratory support. Those with severe disease or significant co-morbid conditions, particularly those undergoing major surgery, should be managed in a high dependency setting capable of regular monitoring of arterial blood gases and providing non-invasive ventilation if required.

Hypoventilation as a result of residual anaesthesia or opioids should be avoided as this may lead to hypercarbia and hypoxia. Use of saline nebulization, suctioning, and physiotherapy are useful to avoid sputum plugging and ventilatory failure.

Analgesia

Effective analgesia is a significant determinant of postoperative pulmonary function. Epidural analgesia is a particularly attractive option as it reduces the risk of respiratory failure because of excessive sedation from opioids. It should therefore be considered if appropriate to the surgical procedure.

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Please see multiple choice questions 1–4.