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Review Article

Postoperative pulmonary complications

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Abstract

Postoperative pulmonary complications (PPCs) are common, costly, and increase patient mortality. Changes to the respiratory system occur immediately on induction of general anaesthesia: respiratory drive and muscle function are altered, lung volumes reduced, and atelectasis develops in > 75% of patients receiving a neuromuscular blocking drug. The respiratory system may take 6 weeks to return to its preoperative state after general anaesthesia for major surgery. Risk factors for PPC development are numerous, and clinicians should be aware of non-modifiable and modifiable factors in order to recognize those at risk and optimize their care. Many validated risk prediction models are described. These have been useful for improving our understanding of PPC development, but there remains inadequate consensus for them to be useful clinically. Preventative measures include preoperative optimization of co-morbidities, smoking cessation, and correction of anaemia, in addition to intraoperative protective ventilation strategies and appropriate management of neuromuscular blocking drugs. Protective ventilation includes low tidal volumes, which must be calculated according to the patient's ideal body weight. Further evidence for the most beneficial level of PEEP is required, and on-going randomized trials will hopefully provide more information. When PEEP is used, it may be useful to precede this with a recruitment manoeuvre if atelectasis is suspected. For high-risk patients, surgical time should be minimized. After surgery, nasogastric tubes should be avoided and analgesia optimized. A postoperative mobilization, chest physiotherapy, and oral hygiene bundle reduces PPCs.

Key words: complication, postoperative; risk factors; ventilation, mechanical

The term postoperative pulmonary complication (PPC) encompasses almost any complication affecting the respiratory system after anaesthesia and surgery. These complications are defined heterogeneously, occur commonly, have major adverse effects on patients, and are difficult to predict. This paper reviews the current literature regarding PPCs to enable readers to understand better why they occur, identify at-risk patients, and to suggest strategies to reduce their occurrence. This is a narrative rather than systematic review, and because of the amount of literature on the topic of PPCs it has not been possible to include all relevant papers, so we have focused on those which are, in our opinion, most relevant to clinical practice.

Definition and impact of PPCs

Postoperative pulmonary complications can be considered as a composite outcome measure. In 2015, a European joint taskforce published guidelines for perioperative clinical outcome (EPCO) definitions.[1] The EPCO-recommended definitions for PPCs are shown in Table 1 alongside other published definitions to demonstrate the variability in the literature. The taskforce considered respiratory infection, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonitis to be the composite measures and defined pneumonia, acute respiratory distress syndrome (ARDS), and

Table 1 European Perioperative Clinical Outcome definitions[1] for postoperative pulmonary complications and other defined outcome measures, shown to highlight the variation of definitions in the literature; in particular, respiratory failure and pneumonia. International statistical classification of diseases and related health problems, ninth revision (ICD-9) codes have also been used to define PPCs.[2 3] ARDS, acute respiratory distress syndrome; CXR, chest radiograph; EPCO, European Perioperative Clinical Outcome; FI_{O_2}, fraction of inspired oxygen; NIV, non-invasive ventilation; Pa_{O_2}, partial pressure of oxygen in arterial blood; PPC, postoperative pulmonary complication

Outcome measure	EPCO definitions (identical set used by Canet and colleagues[4] and subsequent studies)[5 6]	Other published definitions
Respiratory infection	Antibiotics for suspected infection with one or more of the following: new or changed sputum, new or changed lung opacities, fever, white blood cell count $>12 \times 10^9$ litre^{-1}	Two or more of the following for >48 h: new cough/sputum production, physical findings compatible with pneumonia, fever >38 °C, and new infiltrate on CXR[7]
Respiratory failure	Postoperative Pa_{O_2} <8 kPa (60 mm Hg) on room air, a Pa_{O_2}:FI_{O_2} ratio <40 kPa (300 mm Hg), or arterial oxyhaemoglobin saturation measured with pulse oximetry <90% and requiring oxygen therapy	Ventilator dependence for >1 postoperative day or re-intubation[8 9] Need for postoperative mechanical ventilation >48 h[10–13] Unplanned re-intubation because of respiratory distress, hypoxia, hypercarbia, or respiratory acidosis within 30 days of surgery[10 11 13–15] Re-intubation within 3 days requiring mechanical ventilation[16] Postoperative acute lung injury[17] ARDS[17–19] Requiring mechanical ventilation within 7 days of surgery[20 21] Requiring NIV[22]
Pleural effusion	CXR with blunting of costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, displacement of adjacent anatomical structures, or (in supine position) hazy opacity in one hemithorax with preserved vascular shadows	Pleural effusion requiring thoracocentesis[8 9 20]
Atelectasis	Lung opacification with mediastinal shift, hilum or hemidiaphragm shift towards the affected area, with compensatory hyperinflation in adjacent non-atelectatic lung	Requiring bronchoscopic intervention[20] Major atelectasis (one or more pulmonary segments)[23]
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura	Pneumothorax requiring thoracocentesis[20 22]
Bronchospasm	Newly detected expiratory wheeze treated with bronchodilators	Clinical diagnosis resulting in change in therapy[89] Refractory wheeze requiring parenteral drugs in addition to preoperative regimen[24]
Aspiration pneumonitis	Acute lung injury after inhalation of regurgitated gastric contents	
Pneumonia	CXR with at least one of the following: infiltrate, consolidation, cavitation;plus at least one of the following: fever >38 °C with no other cause, white cell count <4 or > 12×10^9 litre^{-1}, >70 yr of age with altered mental status with no other cause;-plus at least two of the following: new purulent/changed sputum, increased secretions/suctioning, new/worse cough/dyspnoea/tachypnoea, rales/bronchial breath sounds, worsening gas exchange	Radiographic change and antibiotics[89] Antibiotics with new/changed sputum or radiographic change or fever or increased white cell count >12 000 μl^{-1} [4] Two or more of the following for ≥2 consecutive days: new cough/sputum production, examination compatible with pneumonia, temperature >38 °C, and radiographic change[7 23] New or progressive infiltrate on CXR or crackles or dullness on percussion and any of the following: new purulent/changed sputum, positive blood cultures, isolation of pathogen from sputum[20 25] Positive sputum culture or infiltrate on CXR, and diagnosis of pneumonia or pneumonitis[18] New infiltrate on CXR plus fever, leucocytosis, and positive sputum Gram stain/culture[24]
ARDS		Ventilated, bilateral infiltrates on CXR, Pa_{O_2}:FI_{O_2} ≤300, minimal evidence of left atrial fluid overload within 7 days of surgery[19]
Tracheobronchitis		Purulent sputum with normal chest radiograph, no i.v. antibiotics[8 9]

Continued

Table 1 Continued

Outcome measure	EPCO definitions (identical set used by Canet and colleagues[4] and subsequent studies)[5 6]	Other published definitions
Pulmonary oedema		Pulmonary congestion/hypostasis, acute oedema of lung, congestive heart failure, fluid overload[2 3]
Exacerbation of pre-existing lung disease[23]		Not further defined
Pulmonary embolism[23]		Not further defined
Death[24 26]		

pulmonary embolus as individual adverse outcomes. Studies evaluating PPCs also use different combinations of these individual outcomes. A systematic review for the American College of Physicians showed almost 60% of 16 studies used a combination of pneumonia and respiratory failure to define PPCs.[27]

Incidence

It has been estimated that worldwide >230 million major operations occur annually.[28] The incidence of PPCs in major surgery ranges from <1 to 23%.[45 78 12 17 20 22 23 29] Several studies have shown pulmonary complications to be more common than cardiac complications,[8 30 31] and postoperative respiratory failure is the most common PPC.[6 29] Table 2 shows major studies from the last 16 yr, focusing on the varying incidences and mortality, which differ depending on the PPC definitions.[47 8 12 20 23 29] Table 2 clearly illustrates the wide variation in incidence and mortality rate, mostly caused by a combination of differing definitions (Table 1) and different patient populations, in particular the surgical specialty (see 'Surgery type' section below).

Impact

Mortality is increased in both the short and long term in patients who develop a PPC. One in five patients (14–30%) who have a PPC will die within 30 days of major surgery compared with 0.2–3% without a PPC.[46 15 17 23 20 35] The 90 day mortality has been shown to be significantly increased in those with a PPC: 24.4 *vs* 1.2%.[4] An observational study of two large databases shows long-term significant differences in mortality rates with and without PPCs: 45.9 *vs* 8.7% at 1 yr or 71.4 *vs* 41.1% at 5 yr.[35]

Morbidity is also increased by PPCs. Length of hospital stay (LOS) has been shown to be prolonged by 13–17 days.[8 23 36] For example, postoperative respiratory failure requiring unplanned re-intubation (mostly occurring within 72 h of surgery)[15 21] has been shown to be associated with a considerable increase in morbidity and LOS.[15 36]

Developing a PPC also increases health-care costs, primarily as a result of increased LOS.[22] For example, pneumonia or respiratory failure in a Canadian tertiary hospital resulted in a 41 and 47% increase in cost, respectively.[30] The most recent study to evaluate the additional expenditure attributable to PPCs found an incremental cost of $25 498 per admission after gastrointestinal surgery.[37] In times of increasing financial restrictions, particularly in the UK, PPCs represent a significant potential source of cost-savings. Anaesthetists and surgeons should therefore be aware of those at risk and adopt preventative measures that may reduce morbidity, mortality, and the cost of a surgical procedure.

Pathophysiology leading to PPCs

Intraoperative changes to the respiratory system

Adverse respiratory effects of general anaesthesia (GA) begin as soon as the patient loses consciousness.[38] Central respiratory drive is depressed, causing prolonged apnoea followed by a return of spontaneous ventilation with a dose-dependent reduction in minute ventilation. The ventilatory responses to hypercapnia and hypoxia are significantly impaired even at low doses of anaesthetic drugs.[39] As a result, hypercapnia is the norm unless artificial ventilation is used, and severe hypoxaemia occurs if ventilation is challenged by, for example, airway obstruction.

Respiratory muscle function changes immediately after induction. Airway obstruction occurs, there is increased curvature of the spine, cephalad diaphragm displacement in dependent areas, and a reduced cross-sectional area of the chest wall. These changes in end-expiratory muscle tone occur irrespective of whether or not the patient receives a neuromuscular blocking drug (NMBD) and lead to a reduction of functional residual capacity (FRC) of 15–20% compared with the subject's awake, supine volume.[38] The reduced FRC, along with abnormal regional distribution of ventilation during intermittent positive pressure ventilation and reduced cardiac output, leads to altered ventilation perfusion ($\dot{V}/\dot{Q}$) relationships. Although overall ventilation and perfusion are not particularly abnormal, there are increased areas of both high and low $\dot{V}/\dot{Q}$ ratios. The former contribute to alveolar deadspace and a further impairment of carbon dioxide elimination, whereas the latter contribute to impaired oxygenation.

A more significant effect of reduced lung volume with regard to PPCs is the development of atelectasis. This occurs in more than three-quarters of patients receiving GA involving a NMBD,[40] and is easily seen on computerized tomography (CT) scans in the dependent areas of the lung irrespective of the patient's position (Fig. 1). Physiological factors contributing to formation of atelectasis include direct compression of lung tissue, for instance by the displaced diaphragm, airway closure when FRC reduces below closing volume, and rapid absorption of gases from alveoli in lung regions where the airways are narrowed or closed. The last of these factors is exacerbated by the use of high fractional inspired oxygen (FI_{O_2}), particularly at values of 1.0. For example, preoxygenation with an FI_{O_2} of 1.0, 0.8, or 0.6 results in 5.6, 1.3, and 0.2% atelectasis, respectively, on

Table 2 Incidence and mortality rates of major studies evaluating postoperative pulmonary complications since the year 2000. Prospective studies are followed by retrospective studies in reverse chronological order. Where more than three surgical specialties are included, the term 'multi-specialty' is used. Where risk prediction model papers include a training set and a validation set, data from the validation set have been used. AAA, open abdominal aortic aneurysm; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; CXR, chest radiograph; EPCO, European Perioperative Clinical Outcome definition (Table 1); EVAR, endovascular aneurysm repair; PE, pulmonary embolus; PERISCOPE, Prospective Evaluation of a RIsk Score for postoperative pulmonary COmPlications in Europe; PPC, postoperative pulmonary complication; RF, respiratory failure; Sp_{O_2}, peripheral oxygen saturation; UPI, unplanned intubation

Study	Year	Design	PPCs	Sample size	PPC incidence (%)	Mortality rate with PPC (%)	Operative specialty
Canet and colleagues[29]	2015	Secondary analysis of 'PERISCOPE' Prospective multi-centre cohort; evaluating PPCs	RF	5384	4.2	10.3 (in hospital)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Mazo and colleagues[6]	2014	'PERISCOPE' Prospective multicentre cohort; external validation of 'ARISCAT'	As per EPCO	5099	7.9	8.3 (in hospital)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Canet and colleagues[4]	2010	'ARISCAT' Prospective multicentre cohort	As per EPCO	2464	5.0	19.5 (30 day) 24.4 (90 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Scholes and colleagues[32]	2009	Prospective multi-centre cohort	More than four of the following: i. collapse/consolidation on CXR; ii. Sp_{O_2} <90%; iii. abnormal sputum production; iv. positive sputum culture; v. leucocytosis; vi. abnormal auscultation; or vii. physician's diagnosis	268	13.0	Not stated	Upper abdominal
McAlister and colleagues[20]	2005	Prospective single-centre cohort	RF, pneumonia, atelectasis, pneumothorax, pleural effusion	1055	2.7	Not stated	Multi-specialty (non-thoracic) elective, including abdominal
Yang and colleagues[12]	2015	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	Pneumonia, UPI, or RF	165 196	5.8	Not stated	Elective major abdominal (non-vascular)
Jeong and colleagues[5]	2014	Retrospective single-centre analysis of prospectively collected cohort regarding PPC risk	As per EPCO	2059	6.8	Not stated	Multi-specialty elective and emergency, including abdominal (open and laparoscopic), vascular, cardiac, and thoracic
Blum and colleagues[19]	2013	Retrospective single-centre cohort	ARDS	50 367	0.2	27.0 (90 day)	Multi-specialty (non-cardiothoracic) elective and emergency, including abdominal
Brueckmann and colleagues[16]	2013	Retrospective single-centre cohort	UPI	33 769	0.43	16.0	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Gupta and colleagues[13]	2013	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	Pneumonia	211 410	1.8	17.0 (30 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic

Li and colleagues[18]	2013	Retrospective single-centre cohort	Pneumonia, pulmonary oedema, atelectasis, ARDS, pleural effusion	316	18.9	Not specific to PPC	Elective and emergency infrarenal AAA
Hua and colleagues[14]	2012	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	UPI	231 548	1.9	28.0 (30 day)	Multi-specialty elective and emergency, including major abdominal, vascular (open and EVAR) cardiac, and thoracic
Kor and colleagues[17]	2011	Retrospective analysis of prospective single-centre cohort evaluating intraoperative ventilator settings and ALI	ALI/ARDS	4366	2.6	14.2	Multi-specialty elective, including abdominal (open and laparoscopic), vascular, cardiac, and thoracic
Gupta and colleagues[11]	2011	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	RF, UPI	211 410	2.6	25.6 (30 day)	Multi-specialty elective and emergency, including abdominal, vascular, cardiac, and thoracic
Ramachandran and colleagues[15]	2011	Retrospective analysis of multi-centre prospective cohort (not specific to PPCs)	UPI	222 094	0.9	9.7 (low-risk group), 30.6 (high-risk group)	Elective multi-specialty (non-cardiac)
Smith and colleagues[23]	2010	Retrospective single-centre cohort	Pneumonia, acute bronchitis, atelectasis, exacerbation of pre-existing lung disease, RF, PE	329	7.0	16.0 (30 day)	Elective and emergency laparotomy, including AAA
Johnson and colleagues[33]	2007	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	RF, UPI	180 359	3.0	26.5 (30 day)	Elective and emergency major vascular and general
Arozullah and colleagues[25]	2001	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	Pneumonia	160 805	1.5	21 (30 day)	Multi-specialty (non-cardiac), including abdominal, vascular, and thoracic
Arozullah and colleagues[34]	2000	Retrospective analysis of multi-centre prospective cohort (non-specific to PPCs)	RF	81 719	3.4	27 (30 day)	Multi-specialty (non-cardiac), including abdominal, vascular, and thoracic

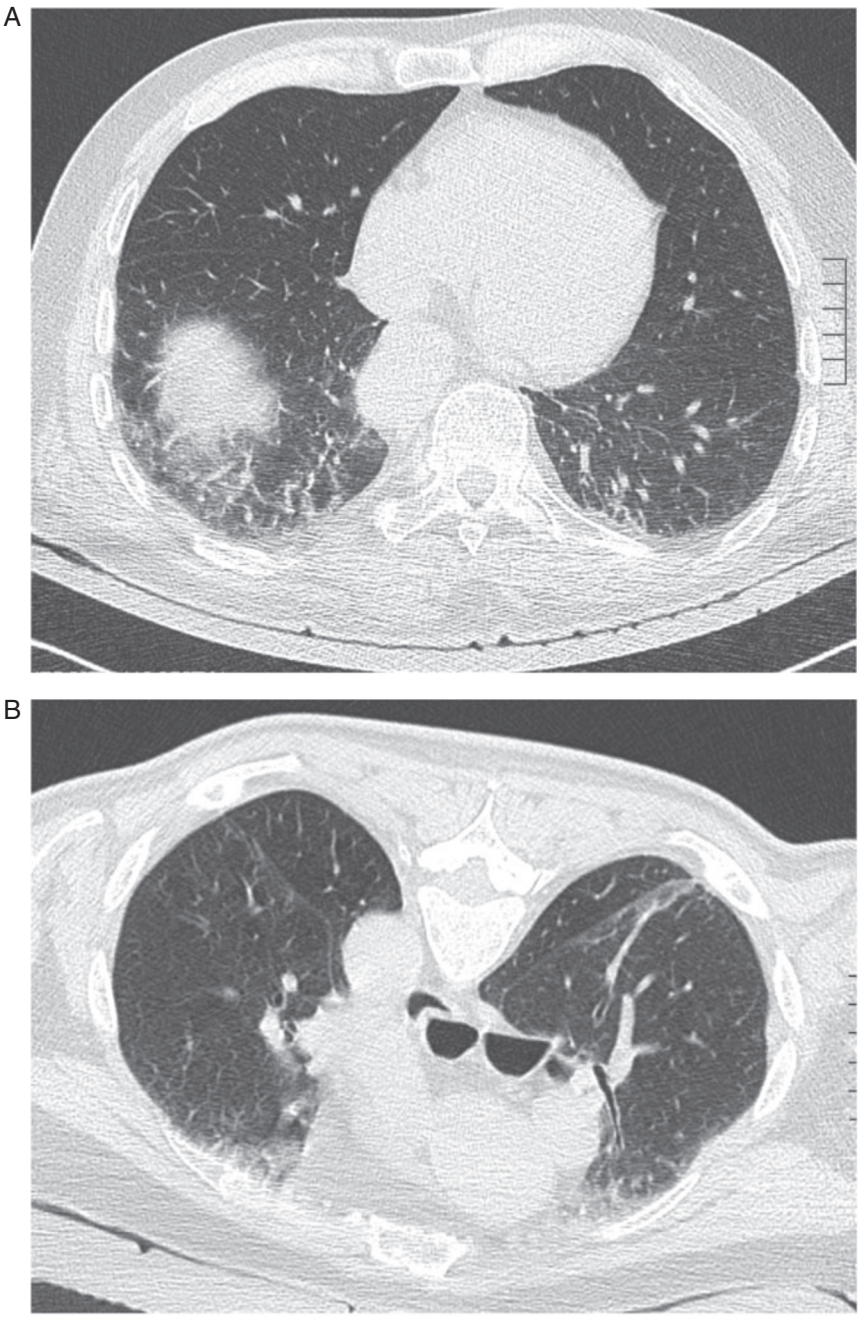

Fig 1 Computerised tomography scans of the chest in two patients during general anaesthesia in the supine (A) and prone (B) positions. Both scans are taken just cephalad of the right diaphragm, and show atelectasis in dependent lung regions irrespective of patient position.

cross-sectional area of a CT scan a few minutes after induction.[41] Despite these dramatic differences at induction, there is no evidence that use of 'hyperoxia' (normally FI_{O_2} of 0.8) throughout a GA with the aim of reducing surgical site infection results in more atelectasis after surgery.[42] This suggests that even 20% nitrogen in inspired gas is helpful in preventing alveolar collapse. Strategies that may be used to minimize atelectasis involve avoiding the use of 100% oxygen and maintaining moderate levels of positive airway pressure during expiration to maintain airway patency. Once atelectasis has occurred, recruitment manoeuvres (RMs) are required to re-expand it.[43 44]

These multiple and universal physiological changes to respiratory function are, in most instances, easily managed during routine GA, with the majority of patients having no

respiratory problems beyond a few hours after emergence. Although poorly researched in comparison with intraoperative changes, it is, however, likely that the changes developing in the early stages of the anaesthetic form the pathophysiological basis for subsequent PPCs in at-risk patients, such as older patients with cardiorespiratory co-morbidity undergoing prolonged major surgery.

Postoperative respiratory pathophysiology

Postanaesthesia care unit changes

Hypoxia is common in the postanaesthesia care unit (PACU) and classified by some studies as a PPC in its own right.[21] Multiple interacting factors contribute to episodes of desaturation.

(i) Airway obstruction occurs in many patients, exacerbated by the factors below.
(ii) Continued sedation from residual anaesthetic and opioid drugs, or from hypercapnia attributable to continuing central respiratory depression.
(iii) Residual effects of NMBDs. Even when conventional clinical and quantitative neuromuscular junction monitoring indicate adequate recovery, NMBDs may still impair respiratory function. There is impairment of the normal phasic activity of genioglossus, making airway obstruction or increased resistance more likely.[45] Co-ordination of pharyngeal and upper oesophageal muscles is abnormal, increasing the risk of aspiration. This has been elegantly demonstrated in healthy awake volunteers given small doses of NMBDs to train-of-four (TOF) ratios of 0.6–0.9,[46] the last of these being generally regarded as clinically recovered from a NMBD. At all levels of NMBD block there were significant numbers of subjects with pharyngeal dysfunction, and videofluoroscopy of a swallow found a high incidence of misdirected swallowing and penetration of contrast onto the vocal cords, even with a TOF ratio of 0.9. These events are likely to be much worse in a patent in the PACU who is also sedated. These changes do not result from muscle weakness *per se*, but illustrate how small changes in the speed and fine control of muscle responses cause failure of crucial reflexes.
(iv) Impairment of ventilatory responses to hypercapnia and hypoxia. Experimental studies in isocapnic subjects show that the hypoxic response is significantly impaired at low doses of anaesthetic drugs (e.g. 0.2 minimal alveolar concentration), but there is wide variation between different agents and experimental conditions.[47] In hypercapnic conditions, which are most likely in the clinical situation, the response may be at least partly preserved, but that is not to say that an obstructed patient in the PACU will generate a normal ventilatory response to hypoxia during an episode of airway obstruction.

The reduced FRC and impaired oxygenation normally seen during anaesthesia usually return to normal within a few hours after minor operations, but this is not the case after major surgery. Atelectasis is still present in patients in the PACU. In a small study of 30 patients having peripheral surgery under GA, CT scans were performed 20 min after extubation and showed significant areas of atelectasis still to be present,[48] and this was significantly worse if the patient had received 100% oxygen during emergence. A further small study of patients having either inguinal hernia or open cholecystectomy procedures showed CT evidence of atelectasis in nine of 10 subjects at 1 h and in five of 10 at 24 h after surgery.[49] Atelectasis on CT scans 24 h after surgery is also more common in morbidly obese patients.[50] Although involving only small numbers owing to the challenges of performing chest CT in patients recovering from a recent GA, these studies still suggest that expansion of atelectasis does not reliably occur after surgery. Further indirect evidence of atelectasis in the PACU can be obtained by measuring oxygenation, most easily done with alveolar-to-arterial oxygen difference, which remains substantially elevated 1 h after extubation in patients having major surgery,[51] indicating significant venous admixture.

Residual effects of NMBDs may contribute to the inability to re-expand atelectasis in the first few hours after major surgery. Unsurprisingly, residual NMBD activity after GA, defined as a TOF ratio <0.9, is associated with significantly lower values for forced vital capacity (FVC) and peak expiratory flow rate.[52] Of more potential relevance to re-expanding atelectasis is a finding in healthy awake volunteers that inspiratory respiratory manoeuvres are more sensitive to NMBD effects than the more usually measured expiratory ones.[53] This means that after a dose of a NMBD it takes longer for a patient to recover inspiratory respiratory strength and coordination than to recover normal expiratory activity as demonstrated with FVC or forced expiratory volume in 1 s (FEV_1). A TOF ratio of >0.95 was required for a normal forced *inspiratory* volume in one second, which is the respiratory muscle activity most useful for lung re-expansion.

Respiratory changes beyond the PACU

After major surgery, the restoration of a normal alveolar-to-arterial oxygen difference may take some days, and episodes of hypoxaemia are common. After upper abdominal surgery, FRC usually reaches its lowest value 1–2 days after surgery, before slowly returning to normal values after 5–7 days.[54–56] As described above, atelectasis seen on CT scans during anaesthesia persists for at least 24 h in most patients having major surgery. One review of postoperative atelectasis in a heterogeneous group of non-thoracic patients found radiological evidence of atelectasis in 539 of 944 (57%) patients,[57] with this incidence showing little sign of improving on postoperative day 3. The presence of atelectasis was not associated with a fever, indicating the difficulty in diagnosing this particular PPC without radiography.

Effort-dependent lung function tests, such as FVC, FEV_1, and peak expiratory flow rate, are all reduced significantly after surgery, particularly if the patient has pain.[56] The normal activity of most respiratory muscle groups is impaired after major surgery, including the airway muscles, abdominal muscles, and diaphragm.[58] Factors contributing to this dysfunction include anaesthetic agents and NMBDs, postoperative analgesic drugs (particularly opioids), pain, disturbed sleep patterns, and the inflammatory response to surgery. The aetiology is more complex than simple muscle weakness and also involves poor coordination between muscle groups along with failure of the normal physiological reflexes and control mechanisms on which their activity depends.[58]

Respiratory control may be abnormal for some weeks after anaesthesia and surgery,[59] with, for example, reduced ventilatory responses to hypercapnia and hypoxia. This has major implications for overcoming airway obstruction when asleep and probably explains the particular challenges faced by patients with obstructive sleep apnoea (OSA) in the postoperative period. In one study, the responses were still slightly impaired 6 weeks after surgery, at a time when inflammation, pain, and analgesic use were absent.[59] These results suggest plasticity in the

respiratory control mechanisms at the time of surgery that takes some time to return to normal.

Sputum retention is common after surgery. General anaesthesia, particularly with a tracheal tube, causes impairment of mucociliary transport in the airways,[60] an effect that may persist into the postoperative period.

This combination of reduced FRC, residual atelectasis, an ineffective cough, and abnormal respiratory control, forms an ideal situation for PPCs to develop.

Preoperative risk stratification

Risk prediction models can be used to identify patients at high risk of complications and so may enable more informed consent and optimal perioperative management. Many prediction models for PPCs have been published in the last 5 yr, most of which have limitations as a result of being developed from retrospective databases,[5 10 11 13 14 19 25] focused on a single adverse outcome (e.g. pneumonia,[13 25] respiratory failure,[11 29] unplanned re-intubation,[10 14] or acute lung injury/ARDS),[17 19] or from a lack of inclusion of intraoperative risk factors. There is therefore no 'one size fits all' model for PPC risk stratification.

Here, we describe three related risk prediction models, which were prospective, multicentre trials, using EPCO definitions for composite outcomes. ARISCAT (**a**ssess **r**espiratory **r**isk in **s**urgical patients in **Cat**alonia) developed a seven-variable regression model, stratifying patients into low-, intermediate-, and high-risk groups. Respective incidences of PPC development in their validation group were 1.6, 13.3, and 42.1%. The independent variables are low preoperative peripheral oxygen saturation (Sp_{O_2}; <96%), respiratory infection in the last month, age, preoperative anaemia (<100 g dl^{-1}), intrathoracic/upper abdominal surgery, duration of procedure (>2 h), and emergency surgery.[4] Definition of a PPC was the development of at least one of the outcomes subsequently defined by EPCO (Table 1).

PERISCOPE (**p**rospective **e**valuation of a **r**isk **s**core for postoperative pulmonary **co**m**p**lications in **E**urope) externally validated ARISCAT with good discrimination; *c*-statistic 0.80 [confidence interval (CI) 0.78–0.82].[6] In 2015, secondary analysis of these data (sample size 5384) was used to develop and validate a score to predict postoperative respiratory failure (PRF). The incidence of PRF was 4.2%, and seven factors were used to stratify patients into low-, intermediate-, and high-risk groups, with incidences of PRF of 1.1, 4.6, and 18.8%, respectively. However, the independent variables differ slightly from those found in ARISCAT: low preoperative Sp_{O_2}, at least one preoperative respiratory symptom, chronic liver disease, congestive heart failure, intrathoracic/upper abdominal surgery, procedure >2 h, and emergency surgery.[29]

One other prospective multicentre cohort study, with a small sample size of 268, focused specifically on risk-stratifying patients with upper abdominal incisions.[32] They defined PPCs as shown for Scholes and colleagues[32] in Table 2. Five independent risk factors were identified in the regression model, including duration of anaesthesia, surgical category, respiratory comorbidity, current smoker, and predicted maximal oxygen uptake. A score of 2.02 or less derived from a clinical prediction rule was associated with a high risk of PPCs [odds ratio (OR) (CI) 8.41 (3.33–21.26)]. This model requires external validation before clinical implementation. Further risk prediction models have been summarized in Table 2.

These studies highlight the complexity of choosing an appropriate risk prediction model. Although they have undoubtedly furthered our understanding of which patient groups are susceptible to PPCs, the lack of agreement between studies and the complexity of the scoring systems currently make them impractical for routine clinical use.

Who gets postoperative pulmonary complications?

The numerous published non-modifiable and modifiable risk factors that may predict the development of a PPC are shown in Table 3. They can be considered as patient related, procedure related, or laboratory testing risk factors, as categorized by Smetana and colleagues.[27] Only the more clinically significant and independent factors are discussed in more detail in this review. These factors are reproducible in multiple studies, and we believe them to be the most clinically relevant.

Non-modifiable risk factors

Age

Advancing age, even when adjusted for co-morbidity, is predictive of PPCs. Multiple studies have found age >60 or 65 yr to be a risk factor.[7 18 20 33] More detailed age stratification shows an increased risk of a PPC as age increases. Compared with patients <60 yr, the OR (95% CI) for a PPC for 60- to 69-yr-olds is 2.1 (1.7–2.6) and for 70- to 79-yr-olds 3.1 (2.1–4.4).[27] Above 80 yr of age, the risk increases further to an OR of 5.1 (1.9–13.3) compared with patients <50 yr old.[4] These studies have not considered frailty when adjusting for age. Older patients are more likely to be frail, and frailty has also been shown to be associated with PPCs, even when adjusted for age.[81] Interest in frailty is increasing, and the results of further studies of PPC occurrence in age-matched frail and non-frail patients will be interesting.

Surgery type

Patients are at high risk of developing PPCs after certain types of surgery.[16 25] Compared with 'other types of surgery', the incidence of pneumonia is significantly higher after abdominal aortic aneurysm repair [OR (CI) 4.29 (3.34–5.50)], thoracic [3.92 (3.36–4.57)], upper abdominal [2.68 (2.38–3.03)], or neck surgery [2.30 (1.73–3.05)], neurosurgery [2.14 (1.66–2.75)], and major vascular surgery [1.29 (1.10–1.52)].[25] 'Other types of surgery' included ear, nose, and throat, lower abdominal, urological, peripheral vascular, and spinal surgery as a collective comparator.

Abdominal and vascular procedures have repeatedly been shown to be high risk for development of PPCs.[47] Laparotomy with an upper abdominal incision may have up to 15 times the risk of a PPC compared with a lower abdominal incision.[7 23] Yang and colleagues[12] confirmed this finding, with a higher incidence of PPCs with oesophagectomy and other upper abdominal procedures compared with colectomy, but did not comment on whether procedures were laparoscopic or open. Emergency surgery compared with elective surgery confers a two- to six-fold increased risk for a PPC.[4 16 23 33] Several multivariate analyses have identified reoperation to result in a four- to seven-fold increase in PPCs compared with one procedure.[23 26] Although the surgery type is non-modifiable itself, laparoscopic surgery for both upper and lower gastrointestinal procedures results in fewer PPCs compared with open procedures.[26 77–79]

Preoperative investigations

Preoperative spirometry and arterial blood gases (ABGs) have traditionally been cited as useful for PPC prediction. However, a

Table 3 Published risk factors for developing a postoperative pulmonary complication, categorized into patient factors, procedure factors, and laboratory testing (as defined by Smetana and colleagues),[27] further divided into non-modifiable and modifiable. Risk factors with strong evidence in the literature are discussed in more detail in the main text. AAA, abdominal aortic aneurysm; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CXR, chest X-ray; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GA, general anaesthesia; GORD, gastro-oesophageal reflux disease; NMBDs, neuromuscular blocking drugs; OSA, obstructive sleep apnoea; PACU, postanaesthesia care unit; 'Positive cough test', patient takes a deep breath and coughs once, and a positive test=ongoing coughing after the initial cough; TOF, train of four

Patient factors	Procedure factors	Laboratory testing
Non-modifiable	**Non-modifiable**	Urea >7.5 mmol litre^{-1} [10 25]
Age[4–7 10 13 14 18 20 24 25 27 33 36]	Type of surgery:[4–7 10–13 15–18 23 25 27 29]	Increased creatinine[33]
Male sex[12 19 33]	• upper abdominal	Abnormal liver function tests[15]
ASA ≥II[5 11–14 16 19 27 33]	• AAA	Low preoperative oxygen saturation[4 6 29]
Functional dependence (frailty)[10–13 25 27 34 36]	• Thoracic	'Positive cough test'[20]
Acute respiratory infection (within 1 month)[4 6]	• Neurosurgery	Abnormal preoperative CXR[9 27]
Impaired cognition[7]	• head and neck	Preoperative anaemia (<100 g litre^{-1})[4 6]
Impaired sensorium[25]	• vascular	Low albumin[5 10 27]
Cerebrovascular accident[25]	Emergency (*vs* elective)[4–6 10 11 16 18 19 23 25 29 33 36]	Predicted maximal oxygen uptake[32]
Malignancy[7 15]	Duration of procedure[6 12 14 20 22 27 29 32]	FEV_1:FVC <0.7 and FEV_1 <80% of predicted[5]
Weight loss >10% (within 6 months)[15 25]	Re-operation[18 23 36]	
Long-term steroid use[25]	Multiple GA during admission[19]	
Prolonged hospitalization[15]	**Modifiable**	
Modifiable	Mechanical ventilation strategy[3 19 63–71]	
Smoking[57 12 13 15 25 32 33 61]	GA (*vs* regional)[4 25 27 72]	
COPD[10 12 13 15–19 24 25 27 32 33 36]	Long-acting NMBDs and TOF ratio <0.7 in PACU[73]	
Asthma[20 32]	Residual neuromuscular block	
CHF[15 16 18 27 29 33]	Intermediate-acting NMBDs with surgical time <2 h (not antagonized)[21]	
OSA[62]	Neostigmine[21 74]	
BMI <18.5 or >40 kg m^{-2} [15]	Sugammadex with supraglottic airway[75 76]	
BMI >27 kg m^{-2} [7]	Failure to use peripheral nerve stimulator[21 74]	
Hypertension[15]	Open abdominal surgery (*vs* laparoscopic)[5 26 77–79]	
Chronic liver disease[29]	Perioperative nasogastric tube[18 20 22 23 25 80]	
Renal failure[19]	Intraoperative blood transfusion[19 25 36]	
Ascites[12]		
Diabetes mellitus[15 17]		
Alcohol[17 25]		
GORD[17]		
Preoperative sepsis[13–15 33]		
Preoperative shock[12]		

systematic review in 2002 found four out of five studies of spirometry values not to be predictive of PPCs.[22] The fifth study, in patients undergoing head and neck surgery, found spirometry to be predictive of PPCs only in a univariate analysis. This did not extrapolate in multivariate analysis, suggesting that overall, spirometry results are not a useful predictor for PPC development.[82] Three studies evaluated the predictive value of preoperative ABGs; none found hypercarbia to be independently associated with PPCs.[22] A later systematic review concluded that patients deemed high risk from spirometry results could easily be identified by clinical assessment alone, and that the evidence is not robust for risk stratification for PPCs with spirometry or ABG for non-cardiothoracic surgery.[27] The usefulness of a preoperative chest X-ray (CXR) has likewise had inconsistent results. McAlister and colleagues[20] found that patients having a CXR performed at the discretion of a clinician did not have more frequent PPCs, whereas Lawrence and colleagues[9] found that having an abnormal preoperative CXR (compared with normal CXR) resulted in an OR (CI) of 3.2 (1.1–9.4) for a PPC. Again, an abnormal CXR is likely to be predictable by clinical assessment, but once an abnormal CXR has been found it is predictive of a PPC.[27] The National Institute for Health and Care Excellence (NICE) advises that spirometry and ABGs should be performed only at the request of a senior anaesthetist for ASA score III or IV patients with confirmed or suspected respiratory disease, and that CXRs should not be offered routinely before elective surgery.[83]

Most recently, low preoperative Sp_{O_2} (assessed when supine, breathing room air) was found to be a significant independent risk factor for PPCs. Compared with $Sp_{O_2} \geq 96\%$, patients with preoperative Sp_{O_2} 91–95% were twice as likely to get a PPC and those with $Sp_{O_2} \leq 90\%$ 10 times more likely.[4] This simple test comes at minimal cost and has been externally validated as part of two further PPC prediction models.[6 29]

Modifiable risk factors and their management

Co-morbidity

An ASA score of II or higher or a diagnosis of chronic obstructive pulmonary disease (COPD), congestive heart failure, or chronic liver disease are independent risk factors for PPCs.[16 18 24 27 29 33] A recent meta-analysis has shown that patients with OSA are more than twice as likely as those without OSA to develop acute respiratory failure after non-cardiac surgery.[62]

Co-morbidities are modifiable to a certain extent in that preoperative medical optimization is possible. Chronic obstructive pulmonary disease and asthma should be optimally treated with bronchodilators and inhaled or oral steroids. A respiratory infection in the last month is associated more chance of developing a PPC,[6] and so elective surgery should be postponed until symptoms and lung function tests are back to baseline,[84] unless the surgery is urgent, in which case an individual patient decision must be made, balancing the risks of developing a PPC *vs* delaying surgery. Perioperative steroid replacement for those on high-dose oral steroids should be considered according to local guidelines as there is a paucity of research evidence to guide this practice.[85] Congestive heart failure can be pharmacologically optimized by a cardiologist with the aim of minimizing symptoms and maximizing functional capacity. European Society of Cardiology guidelines for treatment of congestive heart failure have been updated in 2016.[86] Patients with severe OSA undergoing elective surgery should be commenced on continuous positive airway pressure (CPAP) treatment and assessed for compliance before elective surgery.[87]

Smoking

Smoking is a risk factor for PPCs.[7 12 15 25 61] A meta-analysis comparing current and ex-smokers (for >4 weeks) showed a statistically significant decrease in PPCs for ex-smokers [relative risk (RR) 0.81, CI 0.70–0.93].[88] Four large retrospective cohort studies have used the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database to collate information on postoperative complications in current, previous (cessation >1 yr), and never smokers undergoing major surgery. Current smokers were more likely to have a PPC compared with ex-smokers, who were in turn more likely than those who had never smoked,[88–90] particularly if they had smoked for >10 pack-yr.[91] In active smokers, PPC incidence increases incrementally with the number of pack-year smoked,[92] significantly so for >20 pack-yr; the adjusted OR (CI) compared with non-smokers was 1.20 (1.05–1.38) for <20 pack-yr, 1.57 (1.45–1.70) for 41–60 pack-yr, and 1.82 (1.70–1.94) for >60 pack-yr.[90] Mortality (<30 days after surgery) is increased in current smokers with an OR (CI) of 1.17 (1.10–1.24), but not in non- and ex-smokers, defined as those who have not smoked for 1 yr before surgery.[92] In contrast to increased morbidity, ex-smokers do not appear to have increased 30 day mortality, whether there is a 10 or 50 pack-yr history.[92]

Smoking cessation before major surgery reduces postoperative morbidity.[88 89 93] In 2013, NICE published perioperative smoking cessation recommendations, focusing on pharmacological and behavioural support to aid cessation in the preoperative assessment phase.[94] Intervention commenced at this stage of the surgical pathway has been shown to be effective in reducing smoking rates on admission and achieving a 30 day postoperative abstinence, especially in a day-surgery setting.[95] Patients are almost three times more likely to remain smoke free at 12 months if they have received intensive compared with minimal cessation support.[96] Several small studies have looked at the effectiveness of preoperative smoking cessation programmes in terms of reducing postoperative complications, but have not been adequately powered to show reductions in PPCs specifically.[97–99] However, once pooled, data show a significant reduction in PPCs [RR (CI) 0.81 (0.70–0.93].[88]

Timing of smoking cessation is of interest. Cessation for >4 weeks reduces PPCs by 23%, and for >8 weeks by 47%,[93] suggesting that maximizing the preoperative smoking cessation period minimizes PPCs.[88] Concerns regarding increased sputum production after smoking cessation resulting in increased pulmonary complications have been refuted.[100] Further research is required to evaluate any benefit of smoking cessation 1–2 weeks before surgery. Patients undergoing major surgery have been shown to have a spontaneously high rate of permanent smoking cessation, and Shi and Warner[101] stated that having surgery should be regarded by all clinicians involved as a 'teachable moment' for smokers.

Preoperative anaemia

Approximately one-third of European patients presenting to preassessment clinics are anaemic.[102] Patients with preoperative anaemia (haemoglobin <100 g litre^{-1}) undergoing any type of surgery have a three-fold increase in the risk of a PPC.[4] Autologous blood transfusion itself has also been shown to be independently associated with PPCs,[25 36] and therefore alternative means of treating preoperative anaemia should be considered. The cause of anaemia should be established. Treatment options include dietary supplements, such as vitamin B_{12}, folate, and oral or i.v. iron therapy (if oral intolerant or <4 weeks before surgery) for iron-deficiency anaemia.[103] Erythropoietin is also an option but is itself associated with perioperative complications.[104] Recent UK national guidelines have been published for the management of preoperative anaemia.[105] Identification and treatment may diagnose disease, reduce autologous blood transfusion, conserve supplies, reduce PPCs, and avoid other potentially harmful effects of both anaemia and transfusion.

General anaesthesia

General anaesthesia disturbs many aspects of respiratory function, and it may therefore seem obvious that the incidence of PPCs is reduced in patients who have central or peripheral regional anaesthesia (RA) instead. The nature of surgical procedures that necessitate GA is similar to those listed above as being high risk for developing a PPC, which one may think would account for a proportion of the increased risk of GA *vs* RA. However, studies have shown that even for the same procedure, GA is an independent risk factor for PPCs compared with RA. For example, an overview of Cochrane systematic reviews showed a significant reduction in postoperative pneumonia [RR (CI) 0.45 (0.26–0.79)] although there was no difference in 30 day mortality.[72] Likewise, a study including >200 000 veterans undergoing major non-cardiac surgery demonstrated an OR (CI) of 1.56 (1.36–1.80) for GA compared with RA.[25] Canet and colleagues[4] demonstrated an incidence of 7.5 *vs* 2.0% of developing at least one PPC with and without GA in their prospective multicentre study of 2464 patients.

A duration of surgery and anaesthesia of >2 h is independently associated with PPC development.[4 20] The OR (CI) increased further with increasing operation time, being 4.9 (2.4–10.1) with >2 h and 9.7 (4.7–19.9) when >3 h.[4] The authors state that this risk factor could, to some extent, be controlled by the surgeons;[4] they do not suggest how, but it seems reasonable that those at high risk of a PPC should have a senior surgeon to minimize operative time.

Intraoperative ventilation strategies

Mechanical ventilation under GA plays a large role in development of PPCs. The benefits of lung-protective artificial ventilation in patients with ARDS are well established.[106] Good evidence now exists that the incidence of PPC is significantly reduced when protective ventilation strategies are used in patients with non-injured lungs (i.e. during surgery). Protective ventilation involves consideration of tidal volume (VT), level of PEEP, and use of RMs. There is robust evidence that low VT is protective against PPCs; however, the ideal level of PEEP is more controversial, as many studies do not evaluate PEEP independently from low tidal volumes,[65–68] and there are concerns over haemodynamic compromise with high PEEP levels. Also, PEEP is most effective for optimizing lung function when a RM is performed before application of PEEP,[107] but RMs have not been evaluated independently of the level of PEEP, and the definition of RM varies between studies (Table 4). In the non-obese patient with healthy lungs, a plateau 'opening pressure' of 40 cm H_2O for 7–8 s effectively opens all alveoli.[44]

Studies with the highest quality evidence focus on open abdominal surgery. The most current expert recommendation (for non-obese patients with normal lungs) is initially to use a low VT (6–8 ml kg^{-1}) with PEEP $\leq$ 2cm H_2O, FI_{O_2} 0.4 if oxygen saturations are $\geq$92%, and respiratory rate titrated to maintain normocarbia.[69] In the event of inadequate oxygenation, an algorithm is suggested.[69]

Evidence continues to be evaluated. A further meta-analysis in 2016 demonstrated reduced lung infection with low VT alone, but when PEEP with RM were performed in combination with low VT, lung infection, atelectasis, and acute lung injury were also reduced.[71] PROBESE,[110] IPROVE,[111] and LAS VEGAS[112] are three studies in the recruitment, data collection, and manuscript preparation phases, respectively, which will provide more evidence for protective perioperative ventilation strategies. Additional trials are required to evaluate the role of individualized, higher PEEP levels in the prevention of PPCs in other types of surgery.

Low tidal volume

A recent meta-analysis of 15 randomized controlled trials (RCTs) including 2127 patients undergoing general surgery showed a significant reduction in PPCs between low (< 8 ml kg^{-1}) and high (>8 ml kg^{-1}) VT ventilation, regardless of the PEEP level used.[63] A large multicentre observational study from 2006 showed that 18% of patients still received a VT >10 ml kg^{-1} despite evidence at the time that high VT promoted an inflammatory response and contributed to acute lung injury.[113 114] It does, however, appear that there has been a trend for reduced VT over time, probably influenced by evidence from ARDS ventilation strategies. Levin and colleagues[64] noted a significant reduction from 9 to 8.3 ml kg^{-1} (P=0.01) between 2008 and 2011, and a prospective study of 406 patients in the UK in 2016 showed median tidal volumes of 8.4 ml kg^{-1} predicted body weight.[115] Extremes of weight and female sex are risk factors for inadvertent high-volume ventilation.[113 116] It must be emphasized that VT in these studies is always set based on predicted or ideal body weight rather than real weight. Previously described calculations for predicted body weight used by the ARDS network are as follows:[106]

Men: 50+0.91(centimetres of height−152.4)
Women: 45.5+0.91(centimetres of height−152.4)

Evidence for moderate to high PEEP

Several RCTs and a meta-analysis have shown reduced PPCs with low VT and moderate PEEP levels.[65–67] Severgnini and colleagues[65] compared 9 ml kg^{-1} VT, zero PEEP, and no RMs (standard ventilation) with 7 ml kg^{-1}, 10 cm H_2O PEEP, and an RM after induction, disconnection, and before extubation (protective ventilation). This study evaluated 56 patients undergoing open abdominal surgery of >2 h duration. Pulmonary function (FVC and FEV_1) and arterial oxygenation in air were improved, atelectasis on CXR reduced, and the 'Clinical Pulmonary Infection Score' reduced in the protective ventilation group. No haemodynamic compromise occurred in the protective ventilation group in this small study.[65] Futier and colleagues[66] compared 10–12 ml kg^{-1} and zero PEEP (standard) with 6–8 ml kg^{-1} and 6–8 cm H_2O PEEP with a RM every 30 min (protective), in 400 patients undergoing major open or laparoscopic abdominal surgery. The RR (CI) for PPC development in the protective arm was 0.29 (0.14–0.61). Neither study, as mentioned above, differentiates between low VT and higher PEEP as the beneficial component.

An observational study (>29 000 patients) showed an increased 30 day mortality in patients ventilated with low VT (6–8 ml kg^{-1}) and low PEEP [median (range) 4.0 (2.2–5.0) cm H_2O], suggesting that low VT may be beneficial only when used with

Table 4 Different recruitment manoeuvres used in individual studies of intraoperative ventilation strategies; described by Güldner and colleagues[69] as three different techniques: 'bag-squeezing', 'stepwise increase in tidal volume', and 'stepwise increase in PEEP'. CPAP, continuous positive airway pressure; IBW, ideal body weight (see main text for calculation); I:E, inspiratory to expiratory ratio; RM, recruitment manoeuvre; RR, respiratory rate; VT, tidal volume

Study	Technique
Severgnini and colleagues (2013)[65]	Initial setting: 7 ml kg^{-1} IBW, RR 6 min^{-1}, PEEP 10 cm H_2O, I:E ratio 3:1 VT increased in steps of 4 ml kg^{-1} IBW until plateau pressure 30 cm H_2O for three breaths Settings returned to original, with PEEP maintained at 10 cm H_2O
Futier and colleagues (2013)[66]	CPAP 30 cm H_2O for 30 s
Treschan and colleagues (2012)[108]	Three manual bag ventilations with a maximal pressure of 40 cm H_2O before extubation
Weingarten and colleagues (2010)[109]	Three-step increase in PEEP: 4–10 cm H_2O for three breaths 10–15 cm H_2O for three breaths 15–20 cm H_2O for 10 breaths PEEP reduced and maintained at 12 cm H_2O Repeated 30 and 60 min after the first RM and hourly thereafter

an appropriate level of PEEP.[64] Secondary analysis of a recent larger retrospective study of 64 000 ventilated patients undergoing non-cardiac surgery showed zero PEEP to be harmful, and a PEEP of 5 cm H_2O with plateau pressures ≤16 cm H_2O to be protective against developing PPCs. Interestingly, low VT (<10 ml kg^{-1}) was not protective in this retrospective study.[3] Another small observational study of ear, nose, and throat patients showed a PEEP of 5 cm H_2O to be insufficient to prevent atelectasis, but PPCs were not evaluated.[117] This group suggests that compliance should be monitored during surgery and PEEP set accordingly. Whether this prevents PPCs is questionable.[118]

Evidence against high PEEP

High PEEP (>10 cm H_2O) may not be as important as low VT in protecting against PPCs and may, in fact, be harmful. The above-mentioned low tidal volume meta-analysis[63] showed a non-significant risk reduction towards a low PEEP level, a finding that was supported by the PROVHILO study.[70] PROVHILO is a large RCT and is the first to compare low VT with high PEEP (12 cm H_2O) with RM *vs* low VT with low PEEP (≤2 cm H_2O) without RM. Postoperative pulmonary complications occurred in 40% of the high PEEP group and 39% of the low-PEEP group [RR (CI) 1.01 (0.86–1.20)]. Furthermore, haemodynamic compromise occurred significantly more commonly in the high-PEEP group requiring more fluid and vasopressors. However, fluid loading before RM and high PEEP reduces cardiovascular compromise in obese patients,[119] and PROVHILO does not mention the use of fluid loading before RM in the high-PEEP group.[70] Hong and colleagues[120] demonstrated significantly increased bronchiolar inflammatory markers in pigs exposed to high PEEP levels in comparison to the low-PEEP group, after 8 h of low-volume ventilation without surgery, suggesting that lung injury might result from high PEEP.

Protective ventilation for obese patients

There is mixed evidence as to whether obese patients, as an individual cohort, are at increased risk of PPCs. However, because of altered respiratory physiology in obesity, especially during GA, a specific protective ventilation strategy is recommended, primarily to reduce atelectasis.[121] Tidal volume should be 6–8 ml kg^{-1} based on predicted body weight, along with PEEP ≥5 cm H_2O with the use of appropriate RMs. These patients may require a higher opening pressure of up to 55 cm H_2O.[107] Respiratory rate should be used to control carbon dioxide concentrations and maintain normal pH.[121]

Inevitably, with such a mass of often conflicting evidence, the ideal ventilator settings during surgery depend on the individual patient. The authors' opinion is that a small VT of 6–8 ml kg^{-1}, based on ideal body weight, should be used in all patients, and in patients with healthy lungs having open or peripheral surgery, PEEP of >2 cm H_2O is unlikely to be required.[69] However, many patients have additional respiratory challenges, such as obesity, pneumoperitoneum, or existing lung disease (including current smokers), and more protective ventilation components are then likely to be required.[70] Initially, greater levels of PEEP may be used in an attempt to prevent atelectasis and $\dot{V}/\dot{Q}$ mismatch developing to such an extent that oxygenation becomes impaired even with modestly increased FI_{O_2} (up to 0.6). Finally, when the PEEP level reaches that associated with cardiovascular problems (≥10 cm H_2O),[70] an RM should be performed before increasing FI_{O_2} or PEEP further.

Postoperative respiratory support with CPAP and nasal high-flow oxygen

A Cochrane review published in 2014 evaluated 10 studies (1981–2007) with 709 patients.[122] It concluded that there was insufficient evidence to confirm a benefit of postoperative CPAP after major abdominal surgery, with regard to reducing mortality or major respiratory complications. A meta-analysis, published in 2012, demonstrated non-invasive ventilation to be beneficial in the postoperative period after major surgery (reduced LOS, re-intubation, and pneumonia rates).[123] However, the postoperative data from this meta-analysis are heavily weighted by one RCT focusing on cardiac surgery,[124] and otherwise evaluate the same studies as the Cochrane review.[124] Post-cardiac surgery prophylactic CPAP (10 cm H_2O for 6 h) has been shown to reduce PPCs, but did not shorten LOS.[124] A recent meta-analysis showed a reduction in respiratory complications [RR (CI) 0.33 (0.16–0.66)] with pre- and postoperative non-invasive ventilation in obese patients, but only a trend towards a reduction in unplanned re-intubation and intensive care admission.[125] Further large, high-quality RCTs are required.

Nasal high-flow oxygen is becoming a popular form of well-tolerated non-invasive ventilation for respiratory failure and is being studied for its place in prevention of PPCs. Prophylactic nasal high-flow oxygen may benefit high-risk cardiac patients with respiratory co-morbidity; a trial is in the pre-recruitment phase to determine this.[126] However, it does not improve oxygenation or respiratory function or reduce complications after uncomplicated coronary artery bypass graft surgery.[127] The results from an RCT comparing nasal high-flow oxygen with standard treatment to prevent hypoxaemia after abdominal surgery are awaited.[128]

Neuromuscular blocking drugs and their reversal

It is well known that postoperative residual paralysis causes respiratory compromise. The link between NMBDs and PPCs was first described in an audit of 600 000 patients in 1954, showing a mortality rate of 1:370 in patients who received curare *vs* 1:2100 in those who did not, with 63% of the deaths having a respiratory component.[129] More recent studies confirmed this observation. For example, the use of long-duration NMBDs, such as pancuronium, with a TOF ratio <0.7 after extubation is a risk factor for developing a PPC.[73] The same study demonstrated that the occurrence of PPCs was not higher with the use of pancuronium when residual block was avoided, or with atracurium and vecuronium, even in the presence of residual block. In contrast, a recent large observational study showed that using intermediate-duration NMBDs is associated with greater likelihood of desaturation in the PACU and unplanned re-intubation, especially if the duration of surgery was <2 h.[21] The control cohort in this study underwent similar major surgical procedures, such as cardiac, thoracic, and abdominal surgery, apparently without the use of a NMBD, highlighting the limitation of retrospective analysis of database information. Another group have shown there to be a dose-dependent increase in PPC development with the use of intermediate-duration NMBDs, but the strength of this relationship was lessened by correct management of NMBD reversal.[2]

Neostigmine, particularly if given to patients whose NMBD activity is low, has respiratory effects of its own, probably resulting from excess acetylcholine causing weakness. When neostigmine is administered without a NMBD, there is impairment of genioglossus function and pharyngeal muscle coordination,[130] and decreases in TOF ratio in peripheral muscles.[131 132] These changes may translate into clinical problems. Recent

evidence suggests that neostigmine is independently associated with PPCs, ascribed by the study authors either to excess acetylcholine or the duration of action of neostigmine being less than the elimination time of the NMBD in certain conditions.[21] The odds of developing postoperative pulmonary oedema and re-intubation are increased when neostigmine is used without neuromuscular monitoring.[74]

Use of peripheral nerve stimulation in conjunction with neostigmine to guide reversal of NMBDs can reduce residual block and therefore PPCs.[21 74] There have been recent calls in both the USA and UK to increase the use of mandatory quantitative monitoring of neuromuscular function whenever NMBDs are administered.[133 134]

Choice of reversal agent is currently limited by cost in the UK; however, the use of sugammadex is becoming increasingly popular for reversal of rocuronium and vecuronium, with the advantage that it can counteract profound neuromuscular block. Sugammadex use has, however, already been linked to adverse outcomes, such as laryngospasm and negative pressure pulmonary oedema with early administration in the presence of a supraglottic airway.[75 76] Prospective evidence is conflicting as to whether sugammadex reduces postoperative residual curarization as a direct cause for reducing PPCs.[135 136] A small RCT demonstrated reduced PPCs with sugammadex,[137] and in a larger retrospective study comparing sugammadex with neostigmine or no reversal, the authors suggest that PPCs may be reduced with the use of sugammadex.[138] A trial is currently recruiting to evaluate PPCs after major abdominal surgery, comparing sugammadex and neostigmine.[139]

These associations between management of NMBDs and PPCs at first seem surprising. The pharmacokinetics of modern NMBDs suggest that they should be having little clinical effect a few hours after emergence, yet PPCs occur more frequently for several days in patients receiving them. In addition to the failure to re-expand intraoperative atelectasis, there are other possible mechanisms by which events early in recovery might influence longer-term respiratory outcomes. These include inadequate clearance of the airway secretions normally associated with manipulation of the airway at emergence, and aspiration of pharyngeal or gastric secretions, the mechanisms of which are described in the above pathophysiology section.

Nasogastric tube

Several of the above-mentioned studies have identified nasogastric tube (NGT) placement as a risk factor for PPCs. Patients undergoing abdominal surgery are five to eight times more likely to have a PPC if an NGT is used in the perioperative period.[20 22 23] A meta-analysis showed increased rates of atelectasis and pneumonia with routine use of NGTs.[80] They are traditionally left *in situ* after abdominal surgery to speed return of bowel function, reduce distension, reduce risk of aspiration, and protect anastomoses. Two meta-analyses have shown no benefit in routine NGT placement after elective or emergency open abdominal surgery.[80 140] Considering their association with PPCs as described above, their use should therefore be reserved only for symptom relief or specific surgical reasons.

Other preventative measures

Preoperative physiotherapy

A systematic review of 12 controlled trials showed that preoperative aerobic exercise and inspiratory muscle training (IMT) reduced PPCs and LOS in patients undergoing cardiac and abdominal surgery but not joint replacement surgery.[141] The RR (CI) for PPCs was 0.4 (0.23–0.72). The authors recommended targeting patients at high risk of developing a PPC in order to instigate preoperative IMT.[141] A more recent meta-analysis included additional controlled trials and showed similar outcomes with IMT, with PPCs almost halved [RR (CI) 0.48 (0.26–0.89)] when compared with 'sham' or no IMT in patients having cardiac and abdominal surgery.[142] A 2015 Cochrane review confirmed a reduction in postoperative atelectasis and pneumonia after cardiac and major abdominal surgery with preoperative IMT compared with none. However, it is emphasized that the quality of evidence is low to moderate because of unavoidable inadequate blinding in the studies.[143] These techniques are time consuming and expensive, normally requiring repeated direct supervision of the patient by a physiotherapist, so until the evidence for their use is more robust they should be reserved for only those patients at very high risk of PPCs.

Postoperative physiotherapy and mobilization

I COUGH is a postoperative respiratory care programme that reduces rates of pneumonia and unplanned re-intubation in general and vascular patients.[144] The programme starts before surgery, with education in leaflet and video format. Incentive spirometry is prescribed 10 times each hour (three to five efforts each set) during waking hours until discharge, with the device always being in reach and after preoperative technique practice. Four-hourly documentation of incentive spirometry volumes occurs. Patients deep breathe and cough every 2 h. Ideally, patients are sat in a chair, or the head of the bed is elevated >30°, with mobilization three times a day. Oral hygiene is maintained with twice daily teeth brushing and mouthwash. Incentive spirometry alone has not been shown to reduce PPCs after thoracic, cardiac, or abdominal surgery.[145 146] A combination of physiotherapy, mobilization, and oral hygiene seems to be more beneficial.

Analgesia

Addition of epidural analgesia to GA significantly reduces the risk of postoperative pneumonia in the general surgical population when compared with systemic opioids alone.[72 147] It is especially beneficial for patients with severe COPD having major abdominal surgery, presumably as a result of improved analgesia and reduced opioid consumption. Epidural analgesia improves respiratory function and reduces rates of pneumonia, postoperative ventilation, and unplanned re-intubation.[148 149]

Obese patients are more likely to have OSA, and those with OSA are at risk of respiratory depression after surgery because of increased sensitivity to opioids and sedatives.[121 150] Reduced doses of opioids should therefore be administered to some patients with known or suspected OSA, because opioid dose is correlated with postoperative increases in OSA and therefore the potential for PPCs.[150]

Conclusion

Postoperative pulmonary complications are common, and although many scoring systems exist to quantify PPC risk, there is no consensus on the best one to use, and they remain too complex to use clinically. Preoperative investigations, with the exception of Sp_{O_2} while breathing air, are poor predictors of developing a PPC. Modifiable risk factors include most cardiorespiratory co-morbidities, and these should be optimized before surgery if time allows. Preoperative smoking cessation interventions before surgery reduce PPC incidence, and more

intensive cessation support increases their success. Correction of severe preoperative anaemia also improves PPC risk. In the intraoperative period, avoidance of GA in favour of RA will reduce PPC risk. In those receiving a GA, 'protective ventilation' should be used, particularly a small VT of 6–8 ml kg^{-1} of ideal body weight, supplemented with RMs and PEEP if required. The ideal level of PEEP remains controversial, with <5 cm H_2O being acceptable in low-risk patients, but higher levels will be required in more challenging patients. The use of NMBDs is associated with PPCs, so these should be avoided if possible, and when used, they should be monitored quantitatively and antagonized with neostigmine only when required. Postoperative non-invasive ventilation may be useful in a small group of high-risk patients, but otherwise avoidance of PPCs after major surgery requires good analgesia and a care bundle of physiotherapy, mobilization, and good oral hygiene. It is our hope that as these strategies become more widely adopted, the incidence of PPCs and their associated morbidity and mortality will reduce.

Authors' contributions

A.M. and A.L. contributed equally to development, drafting, and final approval of the version to be published, and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of interest

None declared.

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