TITLE PAGE

Postoperative pulmonary complications: **understanding** definitions and risk assessment

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ABSTRACT

Postoperative pulmonary complications (PPCs) can have severe consequences and their incidence is high. In recent years PPCs have been the subject of numerous studies and articles, which have provided a huge amount of information that is beneficial but can cause confusion on a practical level. This review will focus on three main points: 1) the definitions of PPCs, which are heterogeneous and often vary from one report to another, though consensus is emerging; 2) the risk as reflected in the pool of PPC predictors, of which every study has identified some in a myriad of combinations; and 3) the many PPC prediction scores proposed, each with its strengths and limitations. We will attempt to clarify the practical and research implications of the current situation.

Key words:

Cohort Studies

Lung Diseases

Postoperative Complications

Predictive Value of Tests

Prospective Studies

Quality Control

Respiratory Tract Infections

Risk Assessment

Risk Factors

Introduction

Postoperative pulmonary complications (PPCs) are a major problem because of their incidence is high and their potential consequences can be serious. PPCs develop in an estimated 5–8% of general surgical populations and associated mortality ranges from 8–24%.[1, 2] Detecting patients at risk is a main goal for anaesthesiologists, who must focus special attention on these patients, setting up strategies for prevention during surgery and afterwards.

In the last 15 years, many studies [1, 3-13] have analysed PPC risk factors on which to base clinical scores that can quickly predict high-risk. Results have differed considerably from study to study, however, because of variation in populations of interest, inclusion and exclusion criteria, candidate variables, outcome definitions and study designs. The vast and heterogeneous information produced by this research is not easy to process and can unfortunately lead to confusion.

In this review we will describe the PPC definitions used to date and emerging ones, discuss evidence for the main PPC risk factors, and analyse the PPC prediction scores designed for clinical use thus far.

Definitions of postoperative pulmonary complications

PPCs are many and they are defined in various ways. Studies of PPC risk have sometimes used specific outcomes, such as pneumonia, acute respiratory distress syndrome (ARDS) or postoperative respiratory failure (PRF). Some have well established definitions, while others do not. For example, the diagnosis of postoperative pneumonia has long been guided by the definition of the US Centers for Disease Control and Prevention[14] and ARDS can be diagnosed according to the recent Berlin definition.[15] In contrast, the story of PRF is different. PRF has been variously identified by surrogates, such as the need for mechanical ventilation,

prolonged ventilation, or unexpected reintubation,[5, 7-9, 11] and has also been equated with ARDS.[16] We have argued elsewhere that the most accurate and clinically useful definition of PRF is hypoxaemia of new onset (appearing in the first few postoperative days) with or without hypercapnia,[3, 16] following West's well-established textbook[17] and in keeping with new recommendations.[18] Hypoxaemia is objective (based on a measurement), precise (as a diagnosis of gas exchange impairment) and clinically useful (revealing a clinical problem that may not yet have led to other symptoms). It is probably more sensitive than surrogate definitions of PPC risk, such as postoperative intubation, since a patient can be treated with NIV without intubation. And it is also more specific, since a surrogate event like postoperative intubation could be related to non-respiratory complications such as stroke or cardiac arrest.

In the interest of reaching consensus on diagnostic criteria, a combined task force of the European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM) recently proposed standardised definitions of outcome measures.[18] Table 1 shows their proposals for PPC definitions, which we think should be applied in future studies.

Many researchers have defined composite PPC outcomes,[1, 12] a debated approach in which several complications, any of which contributes to a diagnosis of PPC for the researchers' purpose, are grouped together in clinically defensible ways. One result is that the rate of events is usefully increased for risk analysers, increasing power. There are benefits for the clinicians who ultimately use the resulting risk scales, as it is probably easier in most clinical conditions to apply a score that groups all foreseeable PPCs than to apply multiple scores for several specific complications (ARDS, pneumonia, postoperative intubation, etc.) The point of preoperative risk assessment, however, is to trigger an anaesthetist's vigilance by warning that some threat is a strong possibility, and a high score for a PPC composite will do that quickly.

Once predictors of composite risk have been identified, further research can focus on specific outcomes for some clinical contexts, since the pathophysiology and time course of single PPCs are different.

Risk for developing PPCs

In studies on PPC risk that started to appear about 15 years ago, around 50 risk factors have been identified and discussed in reviews.[16, 19, 20] The weights of these factors are assigned variously in different studies, so that many potential combinations of them might be inferred. We agree with the approach of most authors to direct attention toward predictors that can be identified in the preoperative period, the moment when patients and clinical teams have time and resources to devote to attenuating risk.[21] The sooner predictors are identified, the more likely they are to be modifiable.

The present review focuses attention on the main predictors, according to their weight in risk models, the evidence that supports them, and their apparent modifiability. We will also discuss the hypothetical mechanisms that might explain why these variables have emerged as predictors. Although risk analysis studies are observational and do not usually attempt to provide explanatory models, hypotheses about possible causal relationships are relevant because they speak to plausibility as well as the clinician and patient's motivation to act on them.

The starting point for any exploration of risk and strategies to reduce PPCs is the American College of Physicians' (ACP) 2006 guidelines, based on systematic review by the group of Smetana and co-workers[19, 22]. The evidence for risk factors available at that time is summarised in Table 2. Some, but not all, of the ACP-listed factors were further corroborated in later studies, and other new risk factors have been found since then.[1, 6-11, 13] Below, we list the ones that are relevant at this time,

classified traditionally as patient- or procedure-related, and comment on the level of evidence supporting their inclusion in risk scores.

Patient-related risk factors

Advanced age, one of the most frequently described risk factors for PPC,[19] is characterised by comorbidity, disability and frailty.[23] Although comorbidity and disability (the latter evaluated as functional dependence) are conventionally recorded in studies of risk and in clinical practice, age **itself** can be designated a surrogate factor in scores, without resort to these related variables, **which require more effort to record**.

Frailty, defined as increased vulnerability to stressors,[24] refers to a state that compromises the individual's ability to recover after surgery. Components of frailty are weakness and decreased functional reserve, which are candidates to target for improvement in prehabilitation interventions.[23-25]

Functional dependence is most often related to advanced age and, like frailty, it indicates a weakened state. About 30% of subjects older than 70 years have some degree of disability, which is a predictor of poor outcome in these patients.[26] Prehabilitation may be useful for reducing complications, but the effect on surgical outcome is not clearly defined.[27]

American Society of Anesthesiologists (ASA) class, which can be estimated quickly and is used worldwide, has also been frequently reported as a risk factor for **PPCs and it is certainly useful to predict overall risk in populations in spite of reports of inter-observer inconsistency.[28, 29] It is important to stress that ASA class absorbs a great deal** of clinical information about the patient along with data from laboratory tests and imaging studies as well as other risk scores; **additionally, the way** clinicians score this long-established variable is constantly being reinvented as new knowledge and technologies enter routine practice. **The score's subjectivity and change in meaning over time is balanced** against its power to reflect all available information about the

1 patient, a strength that unfortunately means it will always be identified as a risk factor
2 for any type of complication. Because this score usually earns an odds ratio (OR) that
3 is much higher than that of other predictors (Table 3), modellers of risk will find that it
4 overwhelms other variables without offering specificity to the clinician.[20] Therefore,
5 attention will not be drawn to other more specific variables that could conceivably be
6 acted upon to lower PPC (or other specific) risk; the presence of ASA class can cause
7 other relevant variables to drop out given that only a limited number of predictors can
8 enter the model.
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11 **Chronic obstructive pulmonary disease (COPD)**, was the most commonly
12 reported risk factor when the ACP guidelines were compiled,[19] and it was also
13 identified in later studies.[4-6, 9-11, 13, 30] COPD is probably the most worrying
14 comorbidity, even though its associated OR in models is often lower than that of other
15 predictors (Tables 3 and 4). We hypothesise that the ORs are lower than expected
16 because the patients have often been classified in hospital records as having COPD
17 based on heterogeneous criteria (clinical, spirometric, or self-reports) . In addition,
18 COPD is often included merely as a dichotomous variable (yes or no) even though it
19 can be stratified from mild to very severe.[1, 2, 4-13] Including COPD stage diagnoses
20 for patients in prospective risk studies might improve the weight of this predictor.
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22 **Smoking** leads progressively to COPD, and some clinicians erroneously put
23 smokers and COPD patients in the same boat, assuming that both carry the same level
24 of risk. However, young smokers do not have symptoms because the effects of
25 smoking increase over time as spirometric parameters decrease until gas exchange is
26 eventually impaired.[31] This interpretation is consistent with the lower ORs reported
27 for smoking in comparison with COPD, which in turn has lower ORs than respiratory
28 symptoms or low oxygen saturation[1] (Table 3).
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30 **Respiratory symptoms** that are relevant to risk are cough, sputum production,
31 dyspnoea, and wheezing.[32] In COPD patients, though symptoms increase
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progressively, they also increase more markedly when disease is exacerbated.[31] **The clinical course of this disease** probably explains why the weight of respiratory symptoms exceeded that of COPD itself when it is recorded as a dichotomous variable in some PPC prediction models.[1, 3]

The cough test, which asks the patient to take a deep breath and cough once, is positive if the patient continues to cough.[12] This easy clinical test **was linked to PPCs** in one prospective cohort study,[12] but in a study by our group it did not survive multivariable regression modelling.[1] Still, the cough test is clinically simple and we think it is worthwhile to continue to include it as a candidate predictor in future risk studies.

Low oxygen saturation. Preoperative arterial hypoxaemia was found to confer risk for PPCs in 2000,[33] but a simple way to score this variable did not emerge until a low pulse oximetry estimation (SpO₂) **was confirmed to predict composite PPC risk[1] as well as PRF risk[3] in population-based studies. Moreover, low SpO₂ specifically has also been linked to mortality in a general nonsurgical population.[34] Elsewhere, we have contended that this variable deserves further prospective study,[20] given that pulse oximetry can now be used inexpensively and routinely immediately before surgery in many practice settings, and it has been described as a stronger predictor than a non-stratified diagnosis of COPD[1, 3], probably because only severe COPD patients show desaturation.**

Respiratory infection in the last month as a variable has only been included **to date** in the study to develop the ARISCAT score[1] and in the **PERISCOPE study[2] (an external validation of the ARISCAT score), although sputum production had been linked to PPCs in the 1990s.[35, 36]** However, when the PERISCOPE database was used to build a new score to specifically predict PRF,[3] recent respiratory infection did not survive multivariable modelling because the weight of respiratory symptoms was

higher. A recent respiratory infection would justify delaying surgery in patients mainly if other major risk factors (abdominal surgery, age, etc) were also present.

Congestive heart failure (CHF) is a strong, evidence-based predictor of PPCs,[19] with ORs for mortality of around 2.[37] Level of risk is related to CHF severity, provided pure cardiac failure is excluded as the cause of dyspnoea, rales or other respiratory problems.[3]

Low serum albumin (< 30 g/L) had good evidentiary support according to the ACP guidelines,[19] but only one of the later risk studies[30] included it. It is possible that low serum albumin is ignored because it is not routinely measured; thus its possible relevance would not be detected in retrospective studies. Nonetheless, albumin level predicts postoperative mortality,[38] probably because it is a sign of malnutrition and warns of anastomotic leakage.[39, 40] It may merit study in some clinical or disease settings.

Weight loss[4] or a low body mass index (BMI),[9] like serum albumin level, would be a candidate when assessing risk because it is related to malnutrition.

Anaemia, defined by a haemoglobin concentration of < 10 g/dL, was reported to be a strong predictor in a recent large prospective cohort,[1] in which its association with PPCs was independent of transfusion, another risk factor we will discuss under procedure-related risks.

Sepsis was identified in several studies as a predictor of pneumonia[13] and PRF.[7-9] Sepsis has been found to be the cause of more than half of ARDS cases.[41]

Renal failure was reported as increasing risk on the basis of fair evidence in the ACP guidelines,[19] but only a single retrospective study offered confirmation.[6] Fluid overloading and comorbidity, which are usually observed in renal failure,[42] might account for the relationship between acute renal failure and PPCs.

Chronic liver disease, not reported in the ACP guidelines in 2006,[19] was identified as a risk factor in 2 later studies.[3, 9] Cirrhosis was independently

1 associated with mortality after noncardiac surgery in a prospective cohort study in 28
2 European countries.[37]

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4 **Obesity**, according to the ACP guidelines,[19] does not indicate PPC risk (good
5 evidence). Only a single later study found that morbid obesity (BMI > 40 kg/m²)
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7 predicted a specific PPC (unanticipated postoperative intubation). If BMI were routinely
8
9 measured, however, extreme obesity might emerge more often as a predictor.

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11 **Obstructive sleep apnoea (OSA)** was not supported by sufficient evidence to be
12 considered a risk factor by the compilers of the ACP guidelines in 2006.[19] The
13 situation now is not much changed. As we suggested in another review,[20] authors
14 have reported conflicting results regarding the relevance of OSA to PPC risk, and as a
15 result, this clinical condition continues to receive attention. For example, a large
16 retrospective study was recently unable to identify sleep-disordered breathing as a
17 preoperative predictor of mortality.[43] We think the explanation for the findings in this,
18 and perhaps other cases where OSA does not confer risk, can probably be found in
19 two aspects of these studies: 1) the impreciseness of the diagnosis of OSA in routine
20 clinical practice and 2) differences in postoperative management in these patients.
21 When OSA is appropriately managed with positive airway pressure, it is unsurprising to
22 find no evidence of risk. This hypothesis requires confirmation, however.

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24 **Alcohol use** is often registered as a dichotomous (yes/no) variable in studies
25 that consider it. As a result, the information for individuals drinking 25 g/day is mixed
26 with that of others who have acquired alcohol-related diseases.[4, 5, 9, 10] In other
27 words, in the absence of categorisation, light alcohol users are mixed in with heavy
28 drinkers. Probably for this reason the ACP guidelines[19] found only fair evidence
29 supporting risk from alcohol even though its effects on the immune system have been
30 found to increase susceptibility to respiratory infections[44] and alcohol-related
31 neurologic disorders can favour the aspiration of gastric contents.

Diabetes mellitus was discarded as a risk factor in the ACP guidelines,[19] but 2 later studies[9, 10] identified this **diagnosis as a predictor**. Diabetes has been analysed in most PPC risk studies,[1, 3-8] but it is often discarded from the final models, suggesting it is probably a secondary predictor.

Impaired sensorium or previous stroke was linked to risk (fair evidence) in the ACP guidelines[19] but has not been **singled out** in later studies (Table 3). Pneumonia[4] and PRF[5] were the complications linked to neurologic problems, probably related to airway disorders and aspiration of gastric contents.

Corticosteroid use had insufficient evidence to be a potential predictor of PPC in the 2006 guidelines-[19] **and no new information has emerged**.

Finally, four **new candidates** that have been suggested since 2006 are also unsupported by much evidence thus far, as they have emerged only in single prognostic modelling studies. They are cancer,[9] gastroesophageal reflux disease,[10] male sex,[6] and hypertension.[9]

Procedure-related factors

Factors that are present because the patient is undergoing a procedure and that leads to higher PPC risk can be grouped under 3 headings 1) surgical procedures, 2) second-hit factors[45], and 3) general anaesthesia.

Surgical procedures

Surgery close to the diaphragm or other respiratory muscles, such as cardiac, thoracic or upper abdominal surgeries, are major risk factors for PPCs according to good evidence.[19] Complications would develop in relation to **three** factors:-tissue injury, pain and diaphragm dysfunction.

Tissue injury in cardiac and thoracic surgery usually affects the lung, intercostal muscles and chest wall, although the airways themselves, the diaphragm or the

phrenic nerve might also be injured. Upper abdominal surgery can induce atelectasis on posterior and caudal areas of the lung[46-48] that can last for several days.[48, 49]

Pain is triggered by respiration. After thoracotomy, inspiration moves both the skin and the intercostal muscles around the incision. Patients can be trained in diaphragmatic breathing to reduce the use of the external intercostal muscles, but the internal intercostals are still necessary for coughing. Given that sternotomy leads to considerably less pain than thoracotomy,[50] because the intercostal muscles are not directly injured in sternotomy, surgical approach can sometimes be taken into consideration. However, coughing involves the entire chest wall, including the sternum, and at least 3 studies in the last decade have observed moderate to severe pain at rest and increased pain with coughing.[51] After upper abdominal surgery, the diaphragm and the external intercostals are not directly injured, but diaphragmatic breathing still causes pain when the abdominal wall is moved. To avoid this discomfort, the patient can shift from diaphragmatic (abdominal) breathing to external intercostal (thoracic) breathing. However, as thoracic breathing is less forceful and deep breaths will be less effective, atelectasis, if it develops, will be more difficult to reverse. Coughing will be painful because the incision will be moved when the abdominal muscles are recruited. These events are unavoidable and certainly painful.

Diaphragm dysfunction after upper abdominal laparotomy has been reported.[52] but the mechanism remains to be determined and an association with pain has not been clearly demonstrated.. Studies on muscle dysfunction after laparoscopy have reported inconsistent findings.[53, 54] Mild postoperative pain was reported only by some patients.

Vascular surgery also confers risk for PPCs according to good evidence.[19] Open surgery to repair an abdominal aortic aneurysm is the procedure associated with higher risk than any other procedure.[19] Vascular procedures have often been grouped without distinction between abdominal or peripheral surgeries,[4, 5, 11] but

when Ramachandran et al[9] did so, they were able to distinguish the moderate risk for PPCs conferred by peripheral vascular procedures from the high risk associated with iliac arterial surgery. Nonetheless, peripheral vascular surgery appears to be riskier than other peripheral procedures, probably due to the high rate of comorbid conditions in patients requiring these interventions.

Neurosurgery and head and neck surgeries were named as risk settings in the ACP guidelines[19] on the basis of good evidence and this assessment is supported by the findings of later studies (Table 4). Relevant studies have usually looked at surrogate outcomes (e.g., need for intubation or mechanical ventilation).[5, 9, 11] A PPCs in these patients would be related to problems involving sensorial, upper airway, or swallowing problems.

Prolonged surgery was judged a major risk factor based on good evidence in 2006.[19] Recent studies even confirmed that risk for PPCs was higher after prolonged surgery than after surgery near the diaphragm[1, 3] (Table 4). This should be taken into account in the scheduling of major invasive operations, to ensure that specialists are experienced, for example, or to avoid multiple simultaneous prolonged procedures, particularly when other risk factors are associated.

Emergency surgery was supported as a risk factor by good evidence in 2006[19] and was also identified in later studies(Table 4). The explanation can probably be found in the severity of the surgical problems encountered, the experience of teams, and comorbid conditions present. The clinical question is whether postponing surgery would improve the outcome or not. Focused trials are needed and, in the meantime, individualised management should be considered.

Second-hit factors

ARDS and ventilator associated lung injury can be triggered by additional factors under the multiple-hit hypothesis.[20, 45] In this theory, patients have experienced a

first hit (sepsis, trauma) that is one of the main reasons they are scheduled for surgery.

The impact of first hits cannot be changed by the time risk is being assessed. However, a second hit that appears with treatment and management might be modifiable if anticipated. These second-hit factors would be as follows:

Transfusion is related to infection and adverse outcomes.[55-57] However, risk from transfusion was supported only by fair evidence in the ACP guidelines[19] and only one later **retrospective study**.[6] Anaemia, however, did emerge as a strong risk factor **in a prospective study**.[1] At this time, there are several questions: Can risk for PPCs be reduced by transfusing **anaemic** patients or will transfusion further increase their risk for PPCs? Can we identify a threshold for preoperative anaemia that requires treatment in order to decrease the risk of PPCs? What role could blood salvage or other management strategies[58] play in preventing PPCs?

Fluid overdose predicts postoperative ARDS.[6] The current trend toward restricted hydration probably reduces risk, but the role of colloids and their effects on postoperative outcomes needs further study.[59, 60]

Atelectrauma[61] is caused by the constant tendency of the anaesthetised lung to develop atelectasis.[46, 47] Positive end-expiratory pressure (PEEP) support is a preventive measure and its generalised use is widely supported.[62] The PROVHILO (PROtective Ventilation using High versus LOw PEEP) study, however, found no differences between low or high levels of PEEP.[63]

Volutrauma[61, 62] is caused by alveolar overdistension, which in turn is a product of high intraoperative drive pressure, which has been recently described as the variable with the strongest association with survival in patients with ARDS. [64]

Surgical patients at risk for lung injury should be under protective ventilation with low tidal volumes and PEEP.[62] This strategy is probably not needed in surgical patients not at risk of lung injury.[65]

Hyperoxia related to a high fraction of inspired oxygen was reported as a predictor for ARDS,[6] but like drive pressure, it is difficult to decide whether hyperoxia is **a cause or a consequence**.[66] The debate on the effects of hyperoxia remains open[67-70] and there is not enough information to support scoring it as a PPC risk factor at this time. Hyperoxia was also ruled out as a risk factor for atelectasis in a recent meta-analysis.[71]

Prolonged mechanical ventilation leads to an inflammatory response in the lung. In association with prolonged surgery and other second-hit factors, it can promote PPCs.[62, 72, 73]

Delayed resuscitation and inappropriate antibiotics can promote the development of sepsis[41] and would probably favour the development of PPCs.

General anaesthesia

Finally, general anaesthesia was reported to confer risk on the basis of good evidence in the 2006 ACP guidelines.[19] However, randomised, controlled trials had not consistently **found** an effect of anaesthetic technique on PPCs at that time, and **later** studies did not **confirm** general anaesthesia as a predictor. We think that improvements in anaesthetic management with new drugs and monitoring have probably decreased the previously hypothesised risk related to general anaesthesia.

PPC prediction studies and scores

Reported risk factors need to be weighted if they are to be useful in clinical decision-making. **The clinician wants to know how accurately complications can be predicted for an individual. To that end, PPC prognostic scores based on well-designed modelling studies are developed and should then be adequately validated internally as**

well as externally.[74] Several recent reports and editorials[20, 21, 74-76] have stressed this, allowing us to list the characteristics of ideal, or optimal, predictive models according to current thinking. We summarise them as follows:

- **A clear description of the model's development.** Unfortunately, the account of the modelling process is often too vague for the reader to assess.[74, 75] Authors should follow (and readers should be aware of) the criteria in the relevant reporting guidelines (STROBE –Strengthening the Reporting of Observational Studies in Epidemiology; and the very recent TRIPOD – Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis). Key aspects to report include patient selection to support the appropriate use of the score under clinical conditions; sample size to allow for a ratio of less than 10 between the number of events and the number of candidate factors to be tested[75, 77]; and a relevant range of variables (because a variable that is not recorded will never be recognised as a risk factor).
- **Accuracy.** This characteristic is defined as the level of agreement between predicted and recorded outcomes.[78] The higher a model's accuracy, the more precisely it will foresee real outcomes. Accuracy has two components: calibration and discrimination. Calibration indicates the match between the predicted probability and the observed data for a population and can be illustrated by plotting predicted versus observed outcomes.[78] Discrimination refers to the ability to distinguish a patient with the outcome of interest from another patient without that outcome.[75, 78] Discrimination, which is usually measured with the area under the receiver-operating characteristic curve, ranges from 0.5 (no discrimination) to 1.0 (perfect discrimination).[78]
- **Generalisability.** A model has this quality only if it can accurately predict the outcome in a new population of patients. In other words, external validation must show that a score is both reproducible (valid for new samples from the same

underlying population) and transportable (mainly, valid in future patients from that population as well as those in different locations).[78] Further validation studies of a score should be prospective, multisite, independent and done at different time points.[78]

- **Population appropriateness.** A score can be designed for a general population or for a highly selected one (patients undergoing the same procedure for example).

Research on a general surgical population will provide a practical and widely applicable score, **although** heterogeneity will also probably lower the score's accuracy.[76] Two arguments lead us to tend to favour more general populations. One is the difficulty of enrolling an adequately large sample to model risk prospectively in specific procedures. Another is the heterogeneity of practice in large health systems: clinicians would need numerous scores for numerous procedures, even though the separate scores would probably share similar predictors.

Clinicians adopt a score not simply because it is methodologically sound, but mainly because it is **practical and seems reliable** in routine practice: it should be easy to score and it must distinguish those with a high probability of developing complications. For example, the score from Arozullah et al[5] **could** identify patients with a 30% likelihood of PRF in the group with the highest risk, making this tool useful for guiding decisions. In contrast, **a score developed by other researchers[9] could** predict **only 3.7% of** unanticipated early postoperative tracheal intubation, a surrogate for PRF, in the highest-risk group. **At this level, a clinician would be left** wondering if **clinical routines should or should not be changed.**

With these criteria for excellence in mind, we will now discuss the relative merits of recent studies on PPC prediction.

The pioneers in risk assessment in 2000 and 2001 were the group of Arozullah et al.[4, 5] Their scores for predicting PRF[5] and pneumonia[4] were based on properly

designed and clearly reported studies of huge samples from a voluntary case registry, the database of the National Surgical Quality Improvement Program (NSQIP) of the American College of Surgeons. The dataset had high rates of the predicted outcomes in higher-risk patients. Seven predictors for PRF and 14 for pneumonia were identified. However, the populations were almost exclusively male veterans and neither score has yet been externally validated in other populations.

The later ARISCAT study[1] took a different approach, modelling risk in a prospective, multicentre design that randomly sampled a highly representative general surgical population. This study also achieved a high incidence of the predicted outcome in the highest-risk patients, and to date and to our knowledge, it is the only study to bring together all these characteristics. The ARISCAT score's inclusion of new easy-to-obtain predictors (e.g., low oxygen saturation, preoperative anaemia [haemoglobin < 10 g/dL] and respiratory infection in the last month) that were not present in previous studies, mainly because they had not previously been recorded for consideration. A limitation of the development study[1] was that its sample size of 2464 patients obliged the use of a bootstrapping technique for internal validation. However, this score underwent successful external validation in a larger cohort (the PERISCOPE study).[2]

A secondary analysis of the PERISCOPE dataset built a score for predicting PRF.[3] Seven variables, some of which were not included among the ARISCAT predictors, were identified. The PERISCOPE-PRF study underlined the greater interest of scoring preoperative SpO₂ and clinical symptoms over the scoring of COPD, and it identified the relevance of chronic liver disease as a PRF predictor.

Blum et al[6] determined predictors of ARDS in a general surgical population, using retrospectively obtained data from a single centre. These authors identified 10 risk factors (Tables 3 and 4) without developing a score. One problem with the model is that predictors that could be either the cause or the consequence of ARDS were included; examples are driving pressure and the fraction of inspired oxygen.[66].

In another single-centre study of data from several electronic sources, Brueckmann et al[11] developed a score for predicting postoperative respiratory complications [SPORC], using a surrogate outcome: unplanned postoperative reintubation. The relevant factors identified were ASA ≥ 3 , emergency surgery, CHF, a high-risk surgical intervention, and COPD. Although patients in the most vulnerable group had only a 6% higher risk for the outcome, this score has been judged potentially useful for screening for a complication that increases mortality and costs.[76]

Since the 2 pioneering studies of Arozullah et al[4, 5] other researchers have used the NSQIP data to develop at least 4 more clinical tools to predict various PPCs. Ramachandran et al[9] proposed 14 equally weighted factors to predict unplanned postoperative intubation; for patients in the worst scenario, the predicted risk was 4%. However, when Hua et al[8] built a score to predict the same outcome with 4 variables (age, ASA, sepsis, and operative time) rather than 14, the predicted risk for patients in the worst scenario was around 16%. A limitation is that the score includes variables that are highly dependent on the outcome, such as sepsis and ASA class.[21] Online calculators have been prepared for some of these scores (e.g., for PRF[7] and postoperative pneumonia[13]) (available from <http://www.surgicalriskcalculator.com/>). These calculators facilitate use, but the scores retain the limitation inherent to their development in a voluntarily compiled retrospective database. Prospective external validation, however, might obviate that limitation.

Kor et al[10] undertook a secondary analysis of a cohort at a single centre. Many candidate predictors identified in other studies were not considered, probably explaining why weak predictors like diabetes and alcohol use entered their model. In our opinion, the main contribution of this study was that it called attention to gastroesophageal reflux disease as a predictor.

Finally, Jeong et al[30] based a score on a single-centre retrospective study. Because the sample was obtained from outpatient visits to respiratory physicians, the

selection of patients could be biased. This study called attention to the relevance of an elevated serum albumin concentration, a risk factor supported by good evidence but ignored in most of studies.

Summary

PPCs group together several disorders or states under a single heading. The recent standards for defining postoperative outcome measures, published after a working group consensus process by the ESA and the ESICM,[18] have brought PPC definitions up to date. The authors have clearly identified the main risk factors for PPCs, and any new predictors that might be proposed need to be backed by evidence for their relevance and practical utility. Studies on PPC risk typically start with the same pool of variables, so that the same information is repeatedly emerging in slightly varying combinations of traditional variables. New predictors are still needed if we are to improve our ability to predict PPCs with easy-to-record variables early enough to intervene or plan.

Concerning the many risk scores that have been proposed for various settings, we emphasise that most still need to be externally validated. We therefore counsel against starting new retrospective studies. Risk researchers should focus on evaluating the clinical use of previously described scores or on new original prospective research into new variables that might resolve the limitations of other scores.

Practice points

- Definitions of postoperative pulmonary complications were updated in a recent consensus process led by the European Society of Anaesthesiologists.[18]
- Future studies should apply these definitions when comparing results.
- Patient-related factors account for about 50% of risk for PPCs. Procedure-related factors account for the remaining risk.
- Recently described predictors need further study so we can assess the level of evidence that supports them.
- Most of the predictive scores developed so far still need to be externally validated.

Research agenda

- To promote large, prospective, population-based studies on **well selected** outcomes
- To look for new easy-to-assess, objective risk factors with strong predictive value
- To agree on predictive scores for PPCs that have been rigorously validated in new populations (external validation)
- To undertake controlled studies in high-risk patients to evaluate perioperative measures to reduce PPC risk

Conflicts of interest: none

Acknowledgements: Mary Ellen Kerans advised on English usage in a version of this manuscript.

Funding source: None

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Table 1. Definitions of postoperative pulmonary complications ^a	
Complication	Definition
Respiratory infection	<ul style="list-style-type: none">• Patient has received antibiotics for a suspected respiratory infection and• Presence of one or more of the following:<ul style="list-style-type: none">• new or changed sputum• new or changed lung opacities• fever• white blood cell count > 12 000
Respiratory failure	<ul style="list-style-type: none">• Postoperative PaO₂ < 8 kPa (60 mmHg) on room air, or• PaO₂:FIO₂ ratio <40 kPa (300 mmHg) or• SpO₂ < 90% and requiring oxygen therapy
Pleural effusion	Chest radiograph demonstrating <ul style="list-style-type: none">• blunting of the costophrenic angle,• loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position,• evidence of displacement of adjacent anatomical structures, or• (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows
Atelectasis	<ul style="list-style-type: none">• Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and• compensatory over-inflation in the adjacent non-atelectatic lung
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura
Bronchospasm	Newly detected expiratory wheezing treated with bronchodilators
Aspiration pneumonitis	Acute lung injury after the inhalation of regurgitated gastric contents
^a adapted from Jammer et al[18] Abbreviations: FIO ₂ , fraction of inspired oxygen; PaO ₂ , oxygen saturation in arterial blood; SpO ₂ , oxygen saturation in arterial blood measured with pulse oximetry.	

Table 2. Risk Factors for Postoperative Pulmonary Complications ^a				
	Level of certainty	Patient-related factors	Procedure-related factors	Preoperative Testing
ACP guidelines[19]	Good evidence	Congestive heart failure ASA class ≥ 2 Advanced age COPD Functional dependence	Aortic aneurysm Thoracic Abdominal Upper abdominal Neurosurgery Prolonged surgery Head and neck Emergency Vascular General anaesthesia	Albumin < 30 g/L
	Fair evidence	Weight loss Impaired sensorium Smoking Alcohol use	Transfusion	Chest X-ray BUN > 21 mg/dL)
Recently identified risk factors or conflicting results	Insufficient evidence	Respiratory infection in the last month Respiratory symptoms GERD Diabetes mellitus Weight loss BMI ≥ 40 kg/m ² Obstructive sleep apnoea Liver disease Sepsis		Positive cough test SpO ₂ <96% Hb < 10 g/dL
^a Adapted from Canet et al[20] Abbreviations: ACP, American College of Physicians; ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; ; Hb, haemoglobin; SpO ₂ , oxygen saturation measured by pulse oximetry.				

Table 3. Patient- related Risk Factors for PPC, by Odds Ratios												
	PPC Risk Studies											
Patient risk factors	Arozullah et al[5]	Arozullah et al[4]	Blum et al[6]	Brueckmann et al[11]	Canet et al[1]	Canet et al[3]	Gupta et al[7]	Gupta et al[13]	Hua et al[8]	Jeong et al[30]	Kor et al[10]	Ramachandran et al[9]
	PPC Outcome Studied											
	PRF	Pneumonia	ARDS	Unplanned intubation	Composite	PRF	Mechanical ventilation	Pneumonia	Unplanned intubation	Composite	ARDS	Unplanned intubation
Age (cut-off points)												
>80	1.91	5.63			5.1			1.015 x yr	3.93	2.03		
70-80	1.91	3.58			1.4				3.33	2.03		
60-70	1.51	2.38			1.4				2.67			
50-60		1.49			1.4				2.016			
40-50									1.47			
ASA												
4-5			18.96	5.32			1.28 ^a	1.01 ^a	7.34	1.59		
3			18.96	5.32					3.46	1.59		
2										1.59		
Male sex			1.65									
Albumin	2.53 ^b									1.49 ^c		
Renal failure	2.29	1.41	2.19									
Partially dependent	1.92	1.83					2.16	2.15				
Totally dependent	1.92	2.83					4.07	2.56				
COPD	1.81	1.72	2.16	1.74				1.58		1.75	2.14	1.6
Weight loss/low BMI		1.92										1.5
CHF				2.36							Exc	1.6
NYHA ≥ II						5.9						

NYHA I						2.2						
Impaired sensorium		1.51										
Sepsis			Exc				1.32	0.92	2.81		Exc	1.5
Septic shock							2.47	1.11				
Previous stroke		1.47										
Steroids		1.33										
Smoking		1.28								1.62		1.5
Alcohol		1.24									2.86	1.4
Basal SpO2												
< 90					10.7	7.4						
91-95					2.2	3.4						
Recent Respiratory infection					5.5							
Anaemia (Hb<10 g/dL)					3.0							
Respiratory symptoms						4.3						1.6 ^c
Diabetes											1.8	1.3
GERD											1.86	
Cough test												
Morbid obesity												1.3
Liver disease						2.6						1.4
Hypertension												1.4
Cancer												1.5

^a Reference group, ASA 5

^b Albumin concentration, <3 g/dL

^c Albumin concentration, < 4 g/dL

Abbreviations: ARDS, acute respiratory distress syndrome; ASA, American Society of Anesthesiologists; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; **Exc, excluded**; GERD, gastroesophageal reflux disease; NYHA, New York Heart Association; PPC, postoperative pulmonary complications; PRF, postoperative respiratory failure; SpO₂, oxygen saturation measured by pulse oximetry; Hb, haemoglobin.

Figure

Table 4. Procedure-related risk factors for PPC												
Procedure risk factors	PPC Risk Studies											
	Arozullah et al[5]	Arozullah et al[4]	Blum et al[6]	Brueckmann et al[11]	Canet et al[1]	Canet et al[3]	Gupta et al[7]	Gupta et al[13]	Hua et al[8]	Jeong et al[30]	Kor et al[10]	Ramachandran et al[9]
	PPC Outcome Studied											
	PRF	Pneumonia	ARDS	Unplanned intubation	Composite	PRF	Mechanical ventilation ^c	Pneumonia ^c	Unplanned intubation ^d	Composite	ARDS	Unplanned intubation
Cardiac	Exc	Exc	Exc	3.06 ^a	11.4	8.4	1.32	1.15		7.02	1.85	Exc
Thoracic	8.14	3.92	Exc	3.06 ^a	11.4	8.4	1.96	2.44			1.49	5.3 ^c
AAA	14.3	4.29	Exc				2.94	2.05		7.02	3.3 ^b	5.3 ^e
Upper abdominal	4.21	2.68			4.4	3.2 ^b	2.64	2.9		7.02		5.3 ^e
Neurosurgery	4.21	2.14		3.06 ^a			2.08	1.98				5.3 ^e
Closed intrathoracic/ upper abdominal						1.5						
Abdominal										7.02		
Vascular	4.21	1.29	Exc	3.06 ^a								2.2 ^e
Transplant			Exc	3.06 ^a	Exc	Exc			Exc			
Neck	3.10	2.30						1.08 ^c				
General				3.06 ^a								
Burns				3.06 ^a								2.2 ^e
Emergency	3.12	1.33	9.34	4.21	2.2	2.6	1.78 ^c			2.16	Exc	Exc
General anaesthesia		1.56										
Duration of surgery (h)												
≥ 6h									4			
>3					4.9	3.9			2.7			
2-3					9.7	2			1.6			