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## SPECIAL ARTICLE

# Preoperative evaluation of the patient with pulmonary disease<sup>☆</sup>

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Evaluation;  
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### Abstract

**Background and objectives:** In daily clinical practice, pulmonary complications related to surgical procedure are common, increasing the morbidity and mortality of patients. Assessment of the risk of pulmonary complications is an important step in the preoperative evaluation. Thus, we review the most relevant aspects of preoperative assessment of the patient with lung disease.

**Content:** Pulmonary risk stratification depends on clinical symptoms and patient's physical status. Age, preexisting respiratory diseases, nutritional status, and continued medical treatment are usually more important than additional tests. Pulmonary function tests are of great relevance when high abdominal or thoracic procedures are scheduled, particularly when lung resection are considered.

**Conclusion:** Understanding the perioperative evaluation of the potential risk for developing pulmonary complication allows the medical team to choose the adequate anesthetic technique and surgical and clinical care required by each patient, thereby reducing adverse respiratory outcomes.

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## Introduction

Postoperative complication is the occurrence of an unexpected change that affects the patient's welfare or deviates from the expected outcome after a surgical procedure. Postoperative pulmonary complications (PPCs) occur within

thirty days after the surgical procedure, alter the clinical picture of the patient, and may require drug therapy intervention.

It is known that most surgical procedures is related to pulmonary function changes,<sup>1–3</sup> usually mild or moderate, but occasionally severe.<sup>4</sup> Pulmonary complications are important causes of perioperative morbidity.<sup>5,6</sup> It has been reported in 1%–2% of all patients undergoing minor or mid-size surgery and may reach 10%–20% in those undergoing upper abdominal or thoracic surgery.<sup>5,6</sup> There are reports that acute lung injury (ALI) occurred in 3% of patients after elective surgery, a major cause of postoperative respiratory failure.<sup>4</sup>

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Pulmonary complications may be classified according to their potential for death as major (respiratory failure, mechanical ventilation and/or intubation for more than 48 h, and pneumonia) or minor (purulent tracheobronchitis, atelectasis with clinical and bronchospasm).

The achievement of adequate preoperative evaluation of pulmonary risk allows the institution of measures to reduce such complications and consequently the perioperative morbidity and hospital stay. As a rule, it is recommended that patients with previous respiratory disease are evaluated by a pulmonologist.

Several predictors were identified for PPCs and are related to previous clinical conditions and characteristics of the anesthetic-surgical procedure. Age over 60 years, pre-existing lung disease, smoking, and previous spirometric changes ( $FEV_1 < 1$  L) are associated with high pulmonary risk. Similarly, duration of anesthesia (>3 h), head and neck surgeries, chest and upper abdomen surgeries, and use of nasogastric tube preoperatively increase the incidence of respiratory events.

Because pulmonary complications are associated with worsening of the postoperative outcome,<sup>7</sup> in this article we will discuss the main clinical factors and strategies in order to reduce perioperative pulmonary complications of the surgical patient.

## Preoperative evaluation of the candidate for general surgical procedures

There are no validated models of pulmonary risk stratification. We present here a suggestion for initial evaluation based on the guidelines of the American College of Physicians<sup>8</sup> and on the outpatient experience of preoperative evaluation of the disciplines of Pneumology and Anesthesiology, Pain and Intensive Care Medicine of the Escola Paulista de Medicina (EPM-Unifesp).

All assessment depends crucially on the history and physical examination, considering the additional tests retrospectively, which will be requested in a targeted manner. Risk factors will be discussed in a systematic way below.

## Surgery-related aspects

Usually, in surgical procedures with no cavity opening or airway manipulation, the risk for PPCs is low. Intra-cavity procedures induce major changes in the respiratory system compared to peripheral procedures. Thoracic and abdominal surgeries (especially with upper abdomen incisions) are the non-cardiac procedures with a higher risk of pulmonary complications.<sup>8-10</sup> The laparoscopic approach may minimize these changes, but it does not eliminate the risk of PPCs.

Heart surgery has a peculiar risk for PPCs. In myocardial revascularization, dissection of the internal thoracic artery may predispose to temporary or perennial phrenic nerve injury. After cardiopulmonary bypass (CPB), pulmonary dysfunction is well described but poorly understood.<sup>11</sup> Although the incidence of acute respiratory distress syndrome (ARDS) after CPB is low (<2%), mortality is high (>50%).<sup>12</sup> During CPB, both lungs are kept collapsed. If measures are not taken immediately after the end of CPB, the lungs will be slowly recruited and more than half of the lungs can

remain atelectatic one to two days after surgery, with intrapulmonary shunt around 20%–30% of cardiac output.<sup>13</sup> CPB duration is directly related to the incidence of postoperative respiratory complications,<sup>14</sup> as well as the intensity of pulmonary interstitial edema.<sup>15</sup> Severe pulmonary changes with interstitial and alveolar edema may occur when the period of CPB exceed 150 min.<sup>14</sup>

A surgical time greater than 3 h is an independent risk factor for the occurrence of postoperative pulmonary complications. Emergency surgeries are also associated with higher incidence of PPCs, as there is no time to stabilize the underlying diseases and properly prepare for the procedure.<sup>8</sup>

## Anesthesia-related aspects

General anesthesia is reported in several studies as a risk factor for PPCs. The use of neuromuscular blocking agents for adequate surgical relaxation may be an important cause of respiratory complications and development of postoperative hypoxemia. This is primarily due to the presence of residual neuromuscular block.<sup>16</sup> The use of long-term neuromuscular blocking increases this effect by depressing the cough reflex and allowing the microaspiration of gastric contents.<sup>17</sup> Prolonged exposure to general anesthetics may promote changes in gas exchange and temporary immunosuppression due to reduced production of surfactant, increased alveolar–capillary permeability, impaired alveolar macrophage function, and slow mucociliary clearance.

During general anesthesia, the supine position and invasive ventilation promote changes in ventilatory mechanics because it impairs the diaphragm action, resulting in reduced volumes and lung capacities. As a result, up to 90% of anesthetized patients present with atelectasis, which promote disturbances in ventilation-perfusion ( $V_A/Q$ ), impair lung compliance, and explain the onset of hypoxemia. Persistent atelectasis postoperatively, associated with transient respiratory muscle dysfunction and eventual ventilation-dependent pain after thoracic and/or abdominal procedures result in increased work of breathing<sup>11</sup> (Table 1).

In regional anesthesia, the ventilatory effects will depend on the type and extent of motor blockade. In epidural or subarachnoid extensive anesthesia, with the blockade of basic thoracic segments, there is a reduction in inspiratory capacity and expiratory reserve volume from 20% to 0%.<sup>18</sup> The diaphragmatic function, however, is usually spared, even in cases of inadvertent extension of neuraxial block to cervical levels.<sup>19</sup> Usually, gas exchange is minimally altered by regional anesthesia.

Thus, blood oxygenation and carbon dioxide elimination during epidural and spinal anesthesia are preserved. This corroborates the fact that there is a reduction in functional residual capacity and change in the ratio  $V_A/Q$  during epidural anesthesia. Exception occurs with morbidly obese patients in which blockade of the abdominal muscles causes a reduction of up to 25% in forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC), in addition to interfering with the ability to cough and eliminate tracheobronchial secretions.<sup>20</sup> Epidural anesthesia has the

**Table 1** Effects of anesthesia on respiratory system.

1	<b>Lung parenchyma</b> Decreased lung volume and vital capacity Increased closing volume Decreased lung compliance Increased ventilatory work
2	<b>Airways</b> Bronchodilation (inhaled anesthetics) Bronchoconstriction Decreased mucociliary clearance
3	<b>Ventilatory control</b> Reduced ventilatory response to hypercapnia, hypoxia, and acidosis
4	<b>Pulmonary circulation</b> Reduced reflex vasoconstriction to hypoxia (inhalation anesthetics)
5	<b>Gas exchange</b> Increased alveolar–arterial O <sub>2</sub> gradient secondary to change in V <sub>A</sub> /Q ratio
6	<b>Immune function</b> Decreased bactericidal activity of alveolar and bronchial macrophages Increased release of proinflammatory cytokines

additional advantages of reducing the need for opioids and contributes to adequate postoperative analgesia.

Interscalene brachial plexus block is often associated with ipsilateral phrenic nerve block<sup>21,22</sup> due to cephalad spread of anesthesia and the nerve bundle proximity, which originates in the cervical roots C3–C5. After interscalene block, the incidence of hemidiaphragmatic paralysis reaches 100%.<sup>21,23–26</sup> Thus, changes in lung mechanics occur, which are potentially harmful to patients with limited respiratory reserve. Reducing the volume of local anesthetic from 20 to 5 mL through brachial plexus block guided by ultrasound lowered the incidence of diaphragmatic paralysis from 100% to 45%.<sup>27</sup>

In healthy patients, diaphragmatic paralysis associated with brachial plexus block usually has no symptoms. This block, however, is not recommended in patients with severe pulmonary disease.<sup>28</sup> Urmev and McDonald<sup>23</sup> contraindicate interscalene block in patients who cannot tolerate 25% reduction in lung function.

Altintas et al.<sup>29</sup> reported that interscalene block with bupivacaine is associated with a greater decrease of FVC, FEV<sub>1</sub>, and peak expiratory flow (PEF) than those found in patients anesthetized with ropivacaine. Regarding analgesia, equipotent doses of ropivacaine produces less motor block and greater ability to blockade the A-delta and C fibers than bupivacaine.<sup>30</sup>

### Patient-related aspects

Advanced age is associated with increased risk of developing PPCs, even when adjusted for comorbidities. This risk increases significantly with each decade of life after 60 years.<sup>8</sup> The partial or total dependence to perform daily

and instrumental activities is also associated with increased risk of PPCs.<sup>8</sup>

Cigarette smoking is an independent risk factor for the occurrence of PPCs, even without concomitant chronic lung disease. The impact is greater in patients with a 20 pack-year smoking history and those who persisted smoking before surgery.<sup>8,31</sup>

The detrimental effect of smoking in the postoperative period is multifactorial and influenced by carbon monoxide, nicotine, and other elements capable of inducing inflammation and oxidative stress. The proinflammatory effects of cigarette smoke increases the incidence of cardiovascular and infectious complications and hinders the surgical wound healing, in addition to being associated with longer hospital and intensive care unit stays.<sup>32</sup>

Patients with BMI  $\geq 40$  kg m<sup>-2</sup> have 30% chance of developing atelectasis and/or pneumonia after abdominal surgery. Additionally, these patients have an increased risk of thromboembolism and wound infection compared to normal individuals.<sup>33</sup> Similarly, patients who evolve with acute weight loss and/or malnutrition with hypoalbuminemia (serum albumin  $<3.5$  g L<sup>-1</sup>) also have a higher incidence of PPCs.<sup>8</sup>

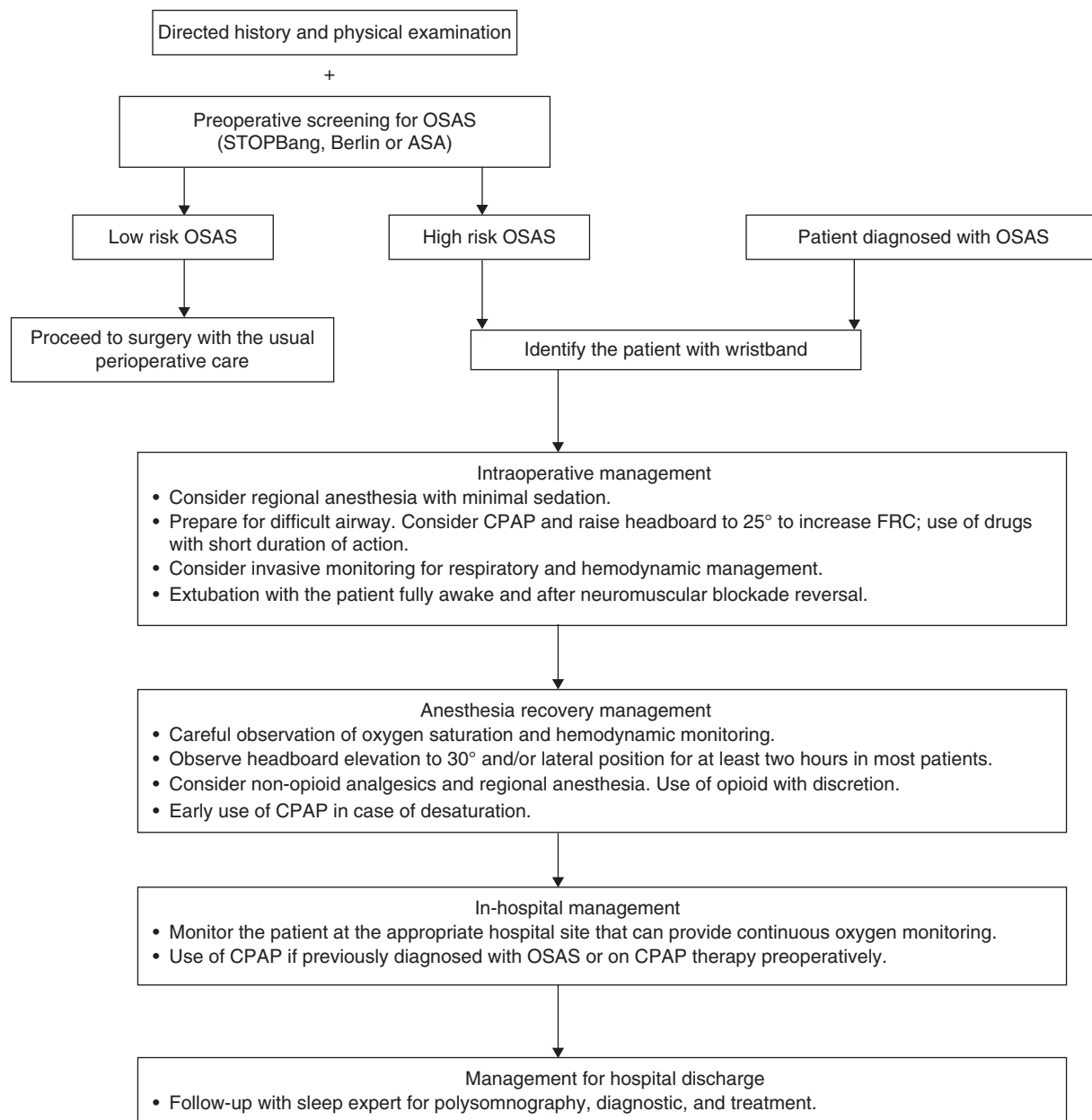
Patients with preexisting chronic lung disease, such as chronic obstructive pulmonary disease (COPD), even clinically stable and with controlled disease, have substantially increased risk of PPCs. Airway management in these patients may lead to exacerbation of bronchial inflammation with worsening of hyperactivity and increased risk of bronchospasm. Airway chronic bacterial colonization associated with temporary immunosuppression induced by surgical procedure and increased work of breathing also contributes to increase complications.<sup>32</sup> The risk and severity of postoperative complications are generally proportional to the degree of clinical impairment and preoperative spirometry (FEV<sub>1</sub>—moderate if between 50% and 80% and severe if  $<50\%$ ). Prognosis is worse in patients who present with pulmonary hypertension and need for home oxygen therapy.<sup>34,35</sup>

Although restrictive lung diseases appear to be associated with adverse respiratory events, the literature still presents controversial results. General anesthesia and mechanical ventilation may increase the risk of exacerbating the inflammatory process of parenchymal fibrotic diseases and promote the adult respiratory distress syndrome.<sup>36</sup>

Similarly, there is a decrease of up to 60% of spirometric variables in scoliosis correction surgery, and many of these patients already have severe restrictive lung disease, which contributes to greater delay in extubation. The peak fall in lung volumes occurs on the third day after surgery, and recovery to baseline levels may take up to two months.<sup>37</sup>

Additionally to identifying the presence of chronic lung diseases, it is also necessary to assess the degree of symptom control with the specific treatment used at that time. Patients often tend to overestimate their lung condition, so it is recommended that the physician actively ask about respiratory symptoms, preferably with the use of standardized questionnaires.

Obstructive sleep apnea syndrome (OSAS) is present in up to 22% of the adult population undergoing surgical treatment, but almost 70% of them have no diagnosis prior to preoperative assessment.<sup>38</sup> Thus, the active investigation



**Figure 1** Suggested steps for management of OSA patients undergoing elective surgery.

of symptoms, such as snoring, episodes of apnea observed by the caregiver, and non-restorative sleep with excessive daytime sleepiness should be routinely included in the preoperative medical history. The observed characteristics predisposing to the existence of OSAS include male gender, age over 50 years, BMI  $>30 \text{ kg m}^{-2}$ , neck circumference  $>40 \text{ cm}$ , deviated septum, tonsillar hypertrophy, laryngomalacia, tracheomalacia, Down syndrome, micrognathia, achondroplasia, acromegaly, and macroglossia. There are validated questionnaires to screen for OSAS in the perioperative period, such as the Berlin questionnaire,<sup>39</sup> ASA OSA scoring checklist,<sup>40</sup> and STOP-Bang<sup>41</sup> (Table 2). Fig. 1 shows the steps suggested for managing patients with OSAS undergoing elective surgery.<sup>42</sup>

On the first postoperative day, there is fragmentation and decreased total sleep time, with suppressed REM sleep.

In subsequent days, REM sleep rebound and the consequent worsening of sleep apnea have been associated with the occurrence of PPCs and cardiovascular complications. The use of sedatives and analgesics (especially opioids and benzodiazepines) also contributes by decreasing pharyngeal tone. The presence of OSAS increases the length of stay and the chances of hypoxemia and reintubation in the postoperative period, besides being associated with greater incidence of arrhythmias, acute coronary syndrome, and sudden death.<sup>42</sup>

Patients with clinically controlled diseases (physical status P II) are known to have lower perioperative mortality (0.2%).<sup>8</sup> Thus, patients with inadequate clinical control of symptoms (P III and IV) must first receive maximized therapy before undergoing anesthesia and surgical procedures, except in emergency surgery.

**Table 2** STOP-Bang score used as OSAS screening in preoperative evaluation.

	Analyzed variable	Question to be asked/examination findings
S	Snoring	Do you Snore Loudly? Louder than talking or loud enough to be heard through a closed door?
T	Tiredness	Do you often feel Tired? Do you sleep during the daytime?
O	Observed apnea	Has anyone observed you stop breathing during sleep?
P	Pressure	Do you have high blood pressure?
B	BMI	BMI > 35 kg m <sup>-2</sup>
A	Age	Over 50 years
N	Neck	Circumference >40 cm
G	Gender	Male

High risk for OSAS:  $\geq 3$  positive responses.

Low risk for OSAS: <3 positive responses.

Chronic alcoholism with more than 60 g dia<sup>-1</sup> ethanol consumption increases up to twice the risk of perioperative acute lung injury in candidates for lung resection surgery,<sup>43</sup> in addition to predisposing to infections and bleeding. Acute sensory changes, delirium, previous stroke, and chronic use of corticosteroids are also independent risk factors for PPCs.

### Role of additional medical tests in pulmonary risk evaluation

Medical history and physical examination are in most cases sufficient to determine the pulmonary risk involved in general surgery. Blood tests, chest X-ray and pulmonary function test should only be ordered when the results actually involve changing the strategy planned for the initial evaluation. Preoperative arterial blood gases should not be required routinely, except in patients with chronic lung disease and moderate to severe airway obstruction on spirometry.

Multicenter prospective studies showed that urea dosage above 21 mg dL<sup>-1</sup> and serum albumin below 3.5 g dL<sup>-1</sup> were predictors of PPCs, particularly pneumonia and acute respiratory failure in postoperative noncardiac surgery.<sup>8</sup> Perioperative mortality was also higher in patients with serum creatinine greater than 1.5 g dL<sup>-1</sup>, due to both pulmonary and infectious and cardiovascular and hemorrhagic adverse events.<sup>44</sup>

Although chest X-ray is frequently ordered in the preoperative evaluation, its importance is questioned. In up to 23% of these tests, an abnormal finding is seen, but in only 0.1%–3% of cases, the pre-established medical approach is changed.<sup>45</sup> Chest X-ray is more important in patients with prior cardiopulmonary disease, those older than 40 years or who will undergo medium and major surgeries, particularly thoracic and abdominal or surgical correction of aortic aneurysm.<sup>46</sup>

Among the recognized tests to assess lung function, spirometry is universally known and most requested during preoperative evaluation. However, as a predictor of pulmonary adverse events in the postoperative period, it is not as good as the clinical evaluation. Its use in intra-abdominal

and thoracic procedures without pulmonary resection has been considered in the following situations: patients with known chronic lung disease, smokers or exposed to inhalants long enough to cause structural lung injury, and those with chronic respiratory symptoms or findings on physical or radiological examination suggestive of chronic pulmonary disease.<sup>47</sup>

Other situations in which spirometry is considered are: candidates for bariatric surgery, patients with kyphoscoliosis undergoing general anesthesia, chronic lung disease undergoing neurosurgery, and neuromuscular patients undergoing general anesthesia. In patients with neuromuscular disease or kyphoscoliosis, measurements of maximal inspiratory and expiratory pressures should also be ordered. FVC below 40% of the predicted value and/or maximum pressures below 30 cm H<sub>2</sub>O significantly increases the risk of extubation failure in postoperative period.<sup>45,47</sup> Contrary to what occurs in lung resection surgery, there are no FEV<sub>1</sub> prohibitive limits for performing general surgeries.

In patients with pulmonary arterial hypertension (PAH), preoperative evaluation should include electrocardiogram at rest and echocardiography, in addition to 6-min walk test (6MWT). The presence of right atrial pressure >77 mm Hg at the last hemodynamic assessment before surgery, 6MWT distance walked <399 m, greater clinical severity, and emergency surgery are indicative of greater postoperative morbidity and mortality.<sup>48</sup> Cardiopulmonary exercise testing is routinely used in the clinical evaluation of patients with PAH to establish prognosis and assess therapeutic response. However, although it may help to stratify the severity of disease, its role in predicting the surgical risk for these patients is still limited.

### Risk stratification of postoperative pulmonary complications

Currently, there are no validated stratification models of pulmonary risk in general surgery. However, the American College of Physicians adopted some scales for assessing the risk of specific respiratory complications,<sup>9,10</sup> such as acute respiratory failure (Table 3) and pneumonia (Table 4). The American Society of Anesthesiologists has developed a risk score for prediction of respiratory complications in patients with OSAS<sup>40</sup> (Table 5).

### Particularities of the preoperative evaluation for lung resection surgery

There is a clear association between the extent of pulmonary resection and perioperative morbidity and mortality. Mortality rate after pneumonectomy is up to two-fold higher than that of lobectomy. Similarly, the mortality rates of segmentectomy and lumpectomy are inferior to that of lobectomy, especially if performed by thoracoscopy.<sup>49</sup>

Unlike general surgery, preoperative evaluation of patients scheduled for pulmonary resection requires spirometry testing and, if necessary, cardiopulmonary exercise testing (CPET). For a complete assessment, it is necessary to combine functional imaging data from computed tomography, pulmonary perfusion scintigraphy, and bronchoscopy. These tests aim to assess whether the area to be resected

**Table 3** Risk factors for acute respiratory failure in postoperative period of general non-cardiac surgery.

Risk factor	Score
Abdominal aortic aneurysm repair	27
Thoracic	14
Upper abdominal, peripheral or vascular neurosurgery	21
Neck	11
Emergency surgery	11
Albumin <3.0 mg dL <sup>-1</sup>	9
Plasma urea >30 mg dL <sup>-1</sup>	8
Totally or partly dependent functional status	7
COPD	6
Age ≥70 years	6
Age 60–69 years	4

Class	Score	%Risk
1	≤10	0.5
2	11–19	1.8
3	20–27	4.2
4	28–40	10.1
5	≥40	26.6

Risk assessment for acute respiratory failure in postoperative general non-cardiac surgery.

still participates in pulmonary gas exchange, and the final calculation should be done to estimate the residual values of pulmonary function after the scheduled resection. FEV<sub>1</sub> is the spirometric parameter used most often for this purpose, followed by carbon monoxide diffusion (DLCO) or maximal oxygen uptake (VO<sub>2</sub>max) obtained in CPET. The ppo designation is added to indicate that the estimated parameter refers to the late postoperative period; i.e., three to six months after the surgical procedure (FEV<sub>1</sub>-ppo, DLCO-ppo, and VO<sub>2</sub>max-ppo).

The simplest calculation uses the number of functioning lung segments (right upper lobe = 3, middle lobe = 2, right lower lobe = 5, left upper lobe = 3 of the upper division + 2 of the lingula and left lower lobe = 4) and assumes that all segments contribute equally to gas exchange, which is rarely true in unhealthy lungs.<sup>50</sup> This method is used to estimate the function after lobectomy and the following formulas may be applied:

$$\text{Mode 1: ppo value} = \left( \frac{\text{preoperative value}}{T} \right) \times R$$

$T = 19$  – number of obstructed segments;  $R = T$  – number of functioning segments to be resected.

$$\text{Mode 2: ppo value} = \text{preoperative value} \times \left( 1 - \frac{a}{b} \right)$$

$a$  = number of non-obstructed segments to be resected;  $b$  = total number of non-obstructed segments.

For pneumonectomy, the calculation should be made using the results of perfusion scintigraphy or pulmonary ventilation. Perfusion examination is the most commonly used method for this purpose. In this case, the formula

**Table 4** Risk factors for postoperative pneumonia in general non-cardiac surgery.

Risk factor	Score
<i>Type of surgery</i>	
Abdominal aortic aneurysm repair	15
High thoracic	14
High abdominal	10
Neck or neurosurgery	08
Vascular	03
<i>Age (years)</i>	
≥80	17
70–79	13
60–69	09
50–59	04
<i>Functional status</i>	
Totally dependent	10
Partially dependent	6
<i>Weight loss over 10% in the last 6 months</i>	7
<i>COPD</i>	5
<i>General anesthesia</i>	4
<i>Altered sensorium</i>	4
<i>Prior stroke</i>	4
<i>Urea (mg dL<sup>-1</sup>)</i>	
<8	4
22–30	2
≥30	3
<i>Blood transfusion greater than 4 units</i>	3
<i>Emergency surgery</i>	3
<i>Chronic use of corticosteroids</i>	3
<i>Smoking in the last year</i>	3
<i>Alcohol intake &gt;2 doses in the previous 2 weeks</i>	2

Class	Score	%Risk
1	0–15	0.24
2	16–25	1.2
3	26–40	4.0
4	41–55	9.4
5	>55	15.8

Risk assessment for postoperative pneumonia in general non-cardiac surgery.

used for the calculation is: ppo value = preoperative value × (1 – perfusion fraction of the lung to be resected).

Traditionally, the estimated postoperative values of FEV<sub>1</sub> and/or DLCO less than 30% were considered absolute contraindications for lung resection due to the high incidence of cardiorespiratory complications and death in the postoperative period. Likewise, values between 30% and 40% frequently imposed more risks than the anticipated benefits of surgery; therefore, cardiopulmonary exercise testing (CPET) is mandatory in this group of patients.<sup>51</sup>

However, the advent of minimally invasive surgical techniques, such as video-assisted thoracic surgery (VATS), and the possibility of performing viable lung parenchyma sparing resections have allowed patients with ppo FEV<sub>1</sub> and/or DLCO <40% to undergo these procedures with morbidity rates relatively low (15–25%) and postoperative mortality

**Table 5** The American Society of Anesthesiologists score for postoperative complication assessment in patients with OSAS.

**A: Severity of sleep apnea based on sleep study (or clinical indicators if sleep study not available)**

None = 0, mild = 1, moderate = 2, severe = 3  
 Subtract 1 point in patients using CPAP or BiPAP  
 Add 1 point for patients with PaCO<sub>2</sub> >50 mm Hg

**B: Surgery and anesthesia**

Superficial surgery under local anesthesia or peripheral nerve block = 0  
 Superficial surgery with moderate sedation or general anesthesia or peripheral surgery with epidural anesthesia (up to moderate sedation) = 1  
 Peripheral surgery with general anesthesia or airway surgery with moderate sedation = 2  
 Major surgery or airway surgery with general anesthesia = 3

**C: Requirement for postoperative opioids**

None = 0, low oral dose = 1, high oral dose or parenteral or neuroaxial = 3

**D: Estimation of perioperative risk**

Global risk = A score + greater score for B or C  
 Patients with global risk  $\geq 4$  may be at increased perioperative risk for OSAS  
 Patients with global risk  $\geq 5$  may be at significantly increased risk for OSAS

ranging from 1% to 15%, reported in the literature.<sup>52-54</sup> In these patients, surgery to treat lung cancer in stage I, even with minor resections (sublobar resections) result in increased survival compared to patients who did not undergo the procedure.<sup>55</sup> Moreover, tumor resection in patients with severe COPD may have a reduced functional impact in two situations: (1) tumor is located in the upper lobe, which is also the site of major involvement of centrilobular emphysema and, therefore, with less functional loss; (2) if there is the possibility of combining tumor resection with lung volume reduction surgery, if the patient is a candidate for this procedure.<sup>56-60</sup>

Accordingly, it became necessary to develop a broader method of preoperative evaluation for lung resection surgery, allowing risk stratification less focused on simple lung function parameters and more related to the individual's ability to perform his daily activities. The flowchart recently developed and published on the guidelines for lung cancer from the American College of Chest Physicians (Fig. 2) is based on this concept.<sup>61</sup> Under the new guidelines, patients with ppo FEV<sub>1</sub> and/or DLCO >60% are considered at low risk for surgery, with an estimated mortality rate <1%, and do not require additional pulmonary evaluation. Patients with ppo FEV<sub>1</sub> and/or DLCO between 30% and 60% should undergo simple exercise tolerance test as a screening method. Those who reach a walk distance >400 m on the shuttle walk test or are able to climb >22 m on the stair climbing test are also considered at low risk and do not require additional pulmonary evaluation. On the other hand, if these cut-off values are not achieved, CPET should be

compulsorily performed for surgical risk stratification. Likewise, patients with ppo VEF<sub>1</sub> and/or DLCO <30% also have absolute indication to perform the CPET.

Portable spirometry has very limited availability in clinical practice, but it is an important tool for preoperative evaluation of individuals scheduled for lung resection surgery. VO<sub>2</sub>max values (oxygen uptake at peak exercise) above 20 mL kg<sup>-1</sup> min<sup>-1</sup> or 75% higher than expected ensure a safe surgical approach (low risk).<sup>62</sup> This value indicates that the patient's functional reserve is sufficient to withstand the stress of surgery and perform daily activities in the late postoperative period. Patients with VO<sub>2</sub>max between 10 and 20 mL kg<sup>-1</sup> min<sup>-1</sup> or between 35% and 75% of the expected value are at moderate risk for perioperative complications, but these values are not prohibitive, provided that the benefit of surgery is considered to outweigh the risks.<sup>63</sup> Values below mL kg<sup>-1</sup> min<sup>-1</sup> or <35% of the expected mean high risk and are generally considered a contraindication to surgery due to the high mortality rate (>10%).<sup>64</sup>

CPET provides data on cardiovascular performance during exercise, which have prognostic importance and may directly or indirectly influence risk stratification. For example, this is the case of parameters such as aerobic efficiency (VO<sub>2</sub>/W), oxygen pulse (VO<sub>2</sub>/HR), and the ratio minute-volume/CO<sub>2</sub> production (VE/VCO<sub>2</sub>). Based on the foregoing, the adoption of cardiac risk as an indication for performing CPET was included in the new protocol for functional assessment of lung resection surgery. Patients with Thoracic Revised Cardiac Risk Index (ThRCRI)<sup>65,66</sup>  $\geq 2$ , who are unable to climb two flights of stairs or have heart disease requiring medication or newly diagnosed, should be initially evaluated by a cardiologist and undergo diagnostic tests and treatments according to protocols for perioperative evaluation of the cardiology societies. After this initial step, all patients considered at high cardiac risk should undergo a CPET (Fig. 2).

## Perioperative strategies to reduce the risk of postoperative pulmonary complications

The ultimate goal of preoperative evaluation and risk assessment for PPCs lies in the individualization of perioperative strategies able to reduce the calculated risk. In some high-risk situations without strategies to decrease it, special attention should be paid to early diagnosis of PPCs, and aggressive treatment should be done to reduce mortality. Didactically, we tried to group strategies into preoperative, intraoperative, and postoperative.

### Preoperative strategies

Specific therapy should be optimized to ensure that the patient achieves the best possible clinical and functional condition. If there is evidence of exacerbations, the use of corticosteroids alone or combined with antibiotics may be necessary and, in such cases, it is recommended that surgery be postponed for at least 30 days after the process resolution.

In stable patients, the recommendation is that the medication should not be discontinued even on the day of surgery. In symptomatic patients, even with optimal medication

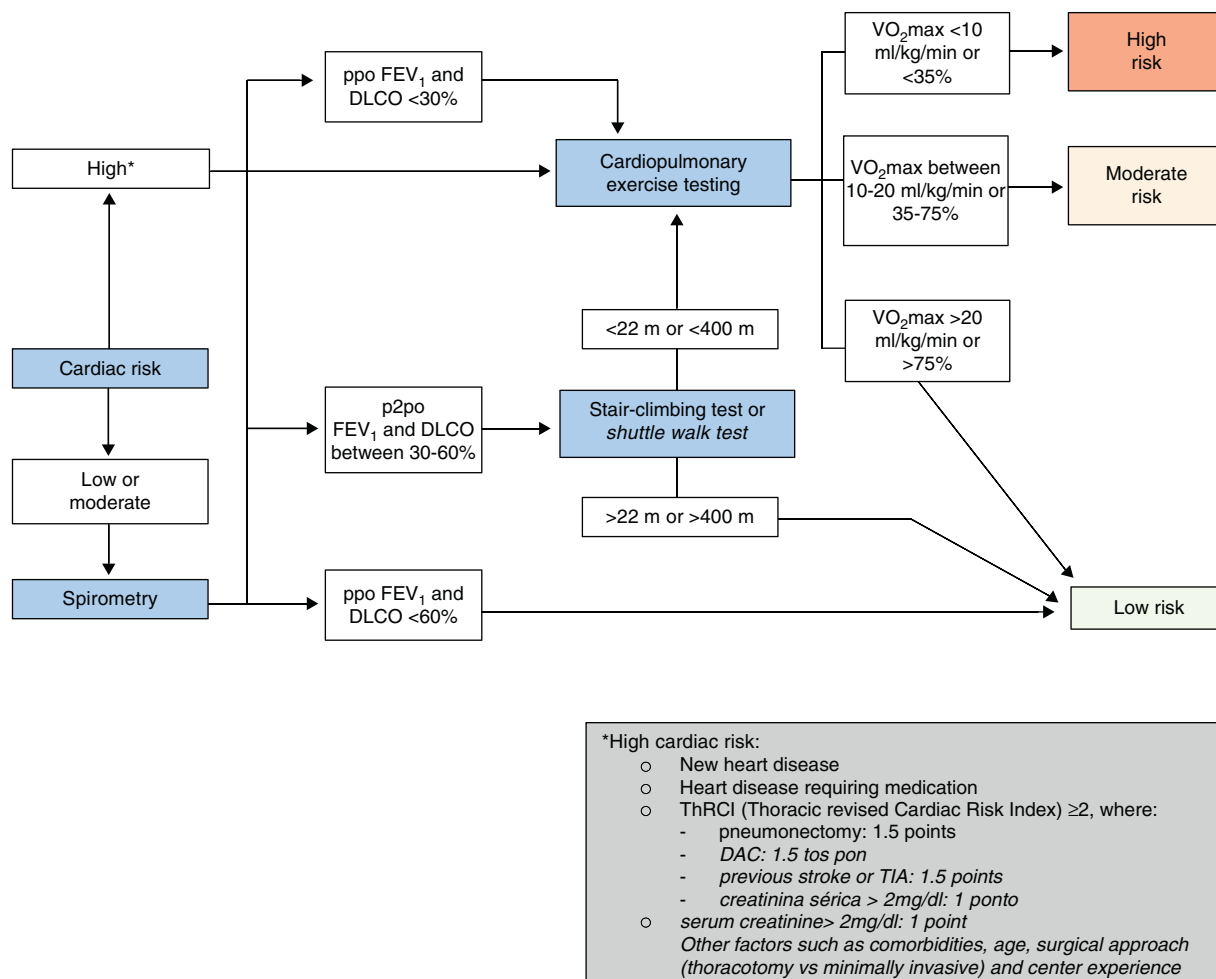


Figure 2 Evaluation of the patient undergoing pulmonary resection.

and undergoing major or midsize elective surgery, the hospitalization three to five days before the procedure may be beneficial because it allows the administration of intravenous corticosteroids and fast action inhaled bronchodilators on a fixed schedule, in addition to respiratory therapy. In patients with uncontrolled persistent cough receiving corticosteroids and bronchodilators, the use of cough suppressants may be useful.

In the patient with bronchial hyperreactivity undergoing general anesthesia with endotracheal intubation, starting with systemic steroids orally five days before the procedure is recommended. Moreover, immediately before surgery, the patient should receive short duration inhaled beta-2 and full doses of anticholinergics associated with intravenous corticosteroids.<sup>67-69</sup>

Patients with lung disease are often chronic users of corticosteroids, either as maintenance or prescribed treatment at exacerbation times. Thus, those using doses of prednisone >7.5 mg or equivalent for more than 30 days or >20 mg for more than two weeks in the past year are considered at risk for developing postoperative adrenal insufficiency.<sup>46</sup> Patients treated with radiotherapy to the pituitary region, with autoimmune diseases or a clinical diagnosis suggestive of adrenal insufficiency, are also considered at risk. Ideally, they should undergo diagnostic evaluation prior to surgery;

however, if there is not enough time for the investigation, empirical corticosteroid supplementation is recommended, depending on the size of surgery.<sup>46</sup>

- **Mild surgical stress:** double or triple the daily dose of corticosteroids used for patients with a previous diagnosis of adrenal insufficiency or chronic corticosteroid users. In case of fasting, prescribe hydrocortisone (50 mg) immediately before surgery with 25 mg maintenance every 12 h for up to 24 h after the procedure.
- **Moderate surgical stress:** parenteral hydrocortisone (25 mg every 8 h), beginning on the morning of surgery and with dose reduction of 50%/day postoperatively up to suspension or achieving the regular dose.
- **High surgical stress:** parenteral hydrocortisone (50 mg every 6 h), beginning on the morning of surgery and with dose reduction of 50%/day postoperatively up to suspension or achieving the regular dose.

Cigarette smoking increases the risk of perioperative cardiac and pulmonary complications. Smoking abstinence can reduce the rate of such complications.<sup>70</sup> However, the preoperative period of abstinence required for this benefit is not established. Some experts suggest that abstinence for a brief period before surgery (often defined as less than eight



weeks) may have an increased risk of PPCs. The supposed mechanism for this increased risk is a transient increase in cough and mucous production after abstinence. However, there are several studies that found no relationship between increased risk and a short period of abstinence.<sup>71</sup> Recent meta-analysis concluded that the available evidence does not support the association between short period of abstinence and increased postoperative risk.<sup>72</sup> In outpatients, smoking cessation is not associated with increased cough or sputum production,<sup>73</sup> and sputum production during surgery is not increased in recent ex-smokers (abstinence eight weeks before surgery) compared to those who continued smoking.<sup>74</sup> Thereby: (1) there is no study reporting that abstinence from smoking in a short interval preoperatively significantly increases pulmonary risk; (2) meta-analysis of available studies showed no significant increased risk; (3) there is no support for the supposed underlying mechanism that contributes to the risk; (4) there is no evidence of reduced PPCs in subjects undergoing surgery after a period of four weeks abstinence.<sup>75</sup> Thus, preoperative evaluation should be considered an important measure to encourage smoking cessation, regardless of the period in which it has been made.

Cognitive-behavioral strategies, associated with specific drugs or not so (nicotine replacement therapy,<sup>76</sup> bupropion,<sup>76</sup> varenicline<sup>77</sup>), are effective in smoking cessation and may be used both pre- and postoperatively. The choice of drug treatment should take into account individual patient contraindications and not be changed by the type of surgery. Nicotine patches may be used even in the immediate postoperative period.<sup>46</sup>

Respiratory physiotherapy is crucial for reducing the risk of perioperative pulmonary complications. It can be started before surgery and maintained throughout hospitalization in order to maximize lung function and minimize respiratory symptoms. Preoperative respiratory muscle training can reduce the incidence of atelectasis and increase by 10% the mean value of postoperative maximum inspiratory pressure.<sup>78</sup>

The strategies that can be applied by physiotherapists are varied and include: incentive spirometer, sustained deep breathing exercises, assisted coughing, postural drainage, percussion and vibration, and use of intermittent noninvasive ventilation (CPAP or BiPAP). Meta-analysis showed a 50% reduction of perioperative complications with the use of incentive spirometer and deep breathing exercises, but so far, there is no evidence of superiority of one strategy over the other.

### Intraoperative strategies

Anesthesia causes respiratory impairment, whether the patient is maintained on spontaneous or mechanical ventilation. This impairment prevents the adequacy of alveolar ventilation and perfusion and, consequently, blood oxygenation. An important factor for respiratory impairment during general anesthesia with the patient in spontaneous ventilation is the reduction of CO<sub>2</sub> sensitivity caused by inhaled anesthetics,<sup>79</sup> barbiturates,<sup>80</sup> and opioids.<sup>81</sup> The response is dose dependent and there is a direct relationship between ventilation reduction and anesthetic depth. This does not

preclude the use of spontaneous ventilation during inhalational anesthesia in children<sup>82</sup> and adults,<sup>83</sup> performed under monitoring and appropriate adjustment.

The use of neuromuscular blockers for adequate surgical relaxation intraoperatively may be an important cause of respiratory complications and onset of postoperative hypoxemia. This is primarily because of the presence of residual neuromuscular block.<sup>16</sup> Thus, the evaluation of patients with the use of quantitative neuromuscular blockade monitors should be considered<sup>17,84–88</sup>, particularly when long-acting blockers such as pancuronium are used.

There is evidence that inhaled anesthetics, such as isoflurane<sup>89</sup> and sevoflurane,<sup>90</sup> may reduce the ventilation-induced lung injury (VILI). Preconditioning with isoflurane in the lungs and other organs mimics the cardioprotective effect of ischemic preconditioning<sup>91</sup> through the activation of adenosine receptors<sup>92</sup> and ATP-sensitive potassium channels.<sup>93</sup> Isoflurane induces protective effects during ischemia–reperfusion<sup>94</sup> and lung injury induced by endotoxin<sup>95</sup> or zymosan.<sup>96</sup> There are also benefits in reducing cytokine release caused by mechanical ventilation,<sup>97</sup> in addition to a protective effect against lung injury by avoiding pro-inflammatory responses.<sup>89</sup>

Balanced anesthesia should be used in patients with obstructive lung diseases due to the action of inhaled bronchodilator. Desflurane should be used sparingly due to the effect of coughing, laryngospasm, bronchospasm, and bronchial hypersecretion.<sup>98,99</sup>

In regional anesthesia for upper limb surgery, interscalene brachial plexus block with large volume of local anesthetic should be avoided in severe chronic lung disease patients, as there is a risk of ipsilateral diaphragmatic paralysis. Preferably, plexus block should be performed under direct visualization with ultrasound and minimum local anesthetic volumes.<sup>100</sup>

In the intra- and postoperative periods, fluid replacement should be made with caution and excessive administration of fluids and positive fluid balance avoided. The excessive intravascular volume leads to extravasation of fluid into the interstitium and predisposes to acute lung injury and respiratory failure,<sup>101</sup> wound infection, anastomotic dehiscence, and postoperative ileus. Moreover, positive balance often generates extubation difficulties, resulting in longer intubation time and ICU stay. Thus, fluid replacement should preferably be based on macro and micro-hemodynamic parameters.<sup>102</sup>

The use of a nasogastric tube (NGT) increases the risk of microaspirations and, consequently, pulmonary infections in the postoperative period. Thus, its routine use should be abandoned and the passage of NGT restricted to patients with a clear indication.<sup>103</sup>

### Postoperative strategies

The decision to request that the first post-operative care of a patient be made in the ICU depends on the size of the surgery, severity of the patient's condition, and risk of perioperative complications. Thus, the recommendation should be made judiciously from careful preoperative evaluation.

Analgesics that depress the respiratory system should be avoided whenever possible. In OSA patients, the use of

systemic opioids is known to worsen the airway obstruction and increase the incidence of postoperative complications. Therefore, the use of simple analgesics (dipyrone, paracetamol) and hormonal or non-hormonal anti-inflammatory drugs is recommended for cases of mild pain. For moderate to severe pain, ketamine or dexmedetomidine can reduce opioid requirements.<sup>104</sup> In cases of regional anesthesia, maintaining catheters for postoperative local analgesia is recommended.

Postoperatively, patients with spontaneous breathing should be evaluated regarding the need for supplemental oxygen by facemask or catheter through blood gas analysis and pulse oximetry. Especially in patients with COPD, OSAS and/or heart failure, the use of noninvasive ventilation if respiratory distress occurs may avoid reintubation. OSA patients have higher risk of developing hypoxemia and hypercapnia postoperatively and should be handled with CPAP routinely as soon as they are admitted to the ICU or ward.

Patients on invasive mechanical ventilation should be immediately included in weaning protocols and, whenever possible, ventilated in pressure support mode. Deep sedation and analgesia should be avoided, aiming at scores of 2 or 3 on the Ramsay scale, and respecting the sedation protocol of daily interruption. Respiratory therapy and endurance workouts also help to reduce the time of intubation.

Except in cases of contraindication due to the surgical procedure nature, the head should be kept at 30° inclination. This measure not only helps prevent airway obstruction in patients with spontaneous ventilation, but has also proven to reduce the incidence of ventilator-associated pneumonia.

## Conclusions

Preoperative evaluation of patients with respiratory diseases should be made in candidates to elective or emergency surgery, as there is the possibility of establishing measures that reduce the risk of complications during intra- and postoperative periods. In any of these situations, the initial assessment is clinical, and complementary examinations should be requested based on this assessment. In elective procedure, the goals of preoperative assessment can be more widely attained; namely, clinical stabilization of lung disease, maximizing lung function, smoking cessation, and early institution of preoperative respiratory therapy.

Finally, lung disease patients often present with other comorbidities and should be globally assessed for cardiovascular, metabolic, renal, and venous thromboembolism risks involved in the anesthetic-surgical procedure to be performed.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

- Hedenstierna G, Edmark L. Mechanisms of atelectasis in the perioperative period. *Best Pract Res Clin Anaesthesiol.* 2010;24:157–69.
- Valenza F, Chevillard G, Fossali T, Salice V, Pizzocri M, Gattinoni L. Management of mechanical ventilation during laparoscopic surgery. *Best Pract Res Clin Anaesthesiol.* 2010;24:227–41.
- Duggan M, Kavanagh BP. Perioperative modifications of respiratory function. *Best Pract Res Clin Anaesthesiol.* 2010;24:145–55.
- Fernandez-Perez ER, Sprung J, Afessa B, et al. Intraoperative ventilator settings and acute lung injury after elective surgery: a nested case control study. *Thorax.* 2009;64:121–7.
- Kroenke K, Lawrence VA, Theroux JF, Tuley MR, Hilsenbeck S. Postoperative complications after thoracic and major abdominal surgery in patients with and without obstructive lung disease. *Chest.* 1993;104:1445–51.
- Licker M, Diaper J, Villiger Y, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. *Crit Care.* 2009;13:R41.
- Lawrence VA, Hilsenbeck SG, Mulrow CD, Dhanda R, Sapp J, Page CP. Incidence and hospital stay for cardiac and pulmonary complications after abdominal surgery. *J Gen Intern Med.* 1995;10:671–8.
- Smetana GW, Lawrence VA, Cornell JE. Preoperative pulmonary risk stratification for noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med.* 2006;144:581–95.
- Arozullah AM, Daley J, Henderson WG, Khuri SF. Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. *Ann Surg.* 2000;232:242–53.
- Arozullah AM, Khuri SF, Henderson WG, Daley J. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. *Ann Intern Med.* 2001;135:847–57.
- Apostolakis EE, Koletsis EN, Baikoussis NG, Siminelakis SN, Papadopoulos GS. Strategies to prevent intraoperative lung injury during cardiopulmonary bypass. *J Cardiothorac Surg.* 2010;5:1.
- Ng CS, Wan S, Yim AP, Arifi AA. Pulmonary dysfunction after cardiac surgery. *Chest.* 2002;121:1269–77.
- Tenling A, Hachenberg T, Tyden H, Wegenius G, Hedenstierna G. Atelectasis and gas exchange after cardiac surgery. *Anesthesiology.* 1998;89:371–8.
- Hachenberg T, Tenling A, Hansson HE, Tyden H, Hedenstierna G. The ventilation–perfusion relation and gas exchange in mitral valve disease and coronary artery disease. Implications for anesthesia, extracorporeal circulation, and cardiac surgery. *Anesthesiology.* 1997;86:809–17.
- Ratliff NB, Young Jr WG, Hackel DB, Mikat E, Wilson JW. Pulmonary injury secondary to extracorporeal circulation. An ultrastructural study. *J Thorac Cardiovasc Surg.* 1973;65:425–32.
- Sauer M, Stahn A, Soltesz S, Noeldge-Schomburg G, Mencke T. The influence of residual neuromuscular block on the incidence of critical respiratory events. A randomised, prospective, placebo-controlled trial. *Eur J Anaesthesiol.* 2011;28:842–8.
- Berg H, Roed J, Viby-Mogensen J, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. A prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. *Acta Anaesthesiol Scand.* 1997;41:1095–103.
- Yamakage M, Namiki A, Tsuchida H, Iwasaki H. Changes in ventilatory pattern and arterial oxygen saturation during spinal anaesthesia in man. *Acta Anaesthesiol Scand.* 1992;36:569–71.
- Warner DO, Warner MA, Ritman EL. Human chest wall function during epidural anesthesia. *Anesthesiology.* 1996;85:761–73.

20. Regli A, von Ungern-Sternberg BS, Reber A, Schneider MC. Impact of spinal anaesthesia on peri-operative lung volumes in obese and morbidly obese female patients. *Anaesthesia*. 2006;61:215–21.
21. Urmev WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498–503.
22. Casati A, Fanelli G, Cedrati V, Berti M, Aldegheri G, Torri G. Pulmonary function changes after interscalene brachial plexus anesthesia with 0.5% and 0.75% ropivacaine: a double-blinded comparison with 2% mepivacaine. *Anesth Analg*. 1999;88:587–92.
23. Urmev WF, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:352–7.
24. Al-Kaisy A, McGuire G, Chan VW, et al. Analgesic effect of interscalene block using low-dose bupivacaine for outpatient arthroscopic shoulder surgery. *Reg Anesth Pain Med*. 1998;23:469–73.
25. Singelyn FJ, Seguy S, Gouverneur JM. Interscalene brachial plexus analgesia after open shoulder surgery: continuous versus patient-controlled infusion. *Anesth Analg*. 1999;89:1216–20.
26. Urmev WF, Gloeggler PJ. Pulmonary function changes during interscalene brachial plexus block: effects of decreasing local anesthetic injection volume. *Reg Anesth*. 1993;18:244–9.
27. Riaz S, Carmichael N, Awad I, Holtby RM, McCartney CJ. Effect of local anaesthetic volume (20 vs 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. *Br J Anaesth*. 2008;101:549–56.
28. Gottardis M, Luger T, Florl C, et al. Spirometry, blood gas analysis and ultrasonography of the diaphragm after Winnie's interscalene brachial plexus block. *Eur J Anaesthesiol*. 1993;10:367–9.
29. Altintas F, Gumus F, Kaya G, et al. Interscalene brachial plexus block with bupivacaine and ropivacaine in patients with chronic renal failure: diaphragmatic excursion and pulmonary function changes. *Anesth Analg*. 2005;100:1166–71.
30. Heavner JE. Cardiac toxicity of local anesthetics in the intact isolated heart model: a review. *Reg Anesth Pain Med*. 2002;27:545–55.
31. Warner MA, Divertie MB, Tinker JH. Preoperative cessation of smoking and pulmonary complications in coronary artery bypass patients. *Anesthesiology*. 1984;60:380–3.
32. Licker M, Schweizer A, Ellenberger C, Tschopp JM, Diaper J, Clergue F. Perioperative medical management of patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2007;2:493–515.
33. Von Ungern-Sternberg BS, Regli A, Schneider MC, Kunz F, Reber A. Effect of obesity and site of surgery on perioperative lung volumes. *Br J Anaesth*. 2004;92:202–7.
34. Jaber S, Delay JM, Chanques G, et al. Outcomes of patients with acute respiratory failure after abdominal surgery treated with noninvasive positive pressure ventilation. *Chest*. 2005;128:2688–95.
35. Ramakrishna G, Sprung J, Ravi BS, Chandrasekaran K, McGoon MD. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. *J Am Coll Cardiol*. 2005;45:1691–9.
36. Honma K, Tango Y, Isomoto H. Perioperative management of severe interstitial pneumonia for rectal surgery: a case report. *Kurume Med J*. 2007;54:85–8.
37. Yuan N, Fraire JA, Margetis MM, Skaggs DL, Tolo VT, Keens TG. The effect of scoliosis surgery on lung function in the immediate postoperative period. *Spine (Phila Pa 1976)*. 2005;30:2182–5.
38. Finkel KJ, Searleman AC, Tymkew H, et al. Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Med*. 2009;10:753–8.
39. Chung F, Ward B, Ho J, Yuan H, Kayumov L, Shapiro C. Preoperative identification of sleep apnea risk in elective surgical patients, using the Berlin questionnaire. *J Clin Anesth*. 2007;19:130–4.
40. Gross JB, Bachenberg KL, Benumof JL, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology*. 2006;104:10817–1093, quiz 117–118.
41. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology*. 2008;108:812–21.
42. Adesanya AO, Lee W, Greilich NB, Joshi GP. Perioperative management of obstructive sleep apnea. *Chest*. 2010;138:1489–98.
43. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg*. 2003;97:1558–65.
44. O'Brien MM, Gonzales R, Shroyer AL, et al. Modest serum creatinine elevation affects adverse outcome after general surgery. *Kidney Int*. 2002;62:585–92.
45. Archer C, Levy AR, McGregor M. Value of routine preoperative chest x-rays: a meta-analysis. *Can J Anaesth*. 1993;40:1022–7.
46. Gualandro DM, Yu PC, Calderaro D, et al. II Guidelines for perioperative evaluation of the Brazilian Society of Cardiology. *Arq Bras Cardiol*. 2011;96:1–68.
47. Zibrak JD, O'Donnell CR, Marton K. Indications for pulmonary function testing. *Ann Intern Med*. 1990;112:763–71.
48. Meyer S, McLaughlin VV, Seyfarth HJ, et al. Outcome of non-cardiac, non-obstetric surgery in patients with pulmonary arterial hypertension: results from an international prospective survey. *Eur Respir J*. 2012, <http://dx.doi.org/10.1183/09031936.00089212>.
49. Damhuis RA, Schutte PR. Resection rates and postoperative mortality in 7,899 patients with lung cancer. *Eur Respir J*. 1996;9:7–10.
50. Wyser C, Stulz P, Soler M, et al. Prospective evaluation of an algorithm for the functional assessment of lung resection candidates. *Am J Respir Crit Care Med*. 1999;159:1450–6.
51. Beckles MA, Spiro SG, Colice GL, Rudd RM. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. *Chest*. 2003;123:1055–145.
52. Lau KK, Martin-Ucar AE, Nakas A, Waller DA. Lung cancer surgery in the breathless patient – the benefits of avoiding the gold standard. *Eur J Cardiothorac Surg*. 2010;38:6–13.
53. Linden PA, Bueno R, Colson YL, et al. Lung resection in patients with preoperative FEV1 <35% predicted. *Chest*. 2005;127:1984–90.
54. Martin-Ucar AE, Fared KR, Nakas A, Vaughan P, Edwards JG, Waller DA. Is the initial feasibility of lobectomy for stage I non-small cell lung cancer in severe heterogeneous emphysema justified by long-term survival? *Thorax*. 2007;62:577–80.
55. Donington J, Ferguson M, Mazzone P, et al. American College of Chest Physicians and Society of Thoracic Surgeons consensus statement for evaluation and management for high-risk patients with stage I non-small cell lung cancer. *Chest*. 2012;142:1620–35.
56. Bobbio A, Chetta A, Carbognani P, et al. Changes in pulmonary function test and cardio-pulmonary exercise capacity in COPD patients after lobar pulmonary resection. *Eur J Cardiothorac Surg*. 2005;28:754–8.
57. Brunelli A, Xiume F, Refai M, et al. Evaluation of expiratory volume, diffusion capacity, and exercise tolerance following

- major lung resection: a prospective follow-up analysis. *Chest*. 2007;131:141–7.
58. Kushibe K, Takahama M, Tojo T, Kawaguchi T, Kimura M, Taniguchi S. Assessment of pulmonary function after lobectomy for lung cancer – upper lobectomy might have the same effect as lung volume reduction surgery. *Eur J Cardiothorac Surg*. 2006;29:886–90.
  59. Luzzi L, Tenconi S, Voltolini L, et al. Long-term respiratory functional results after pneumonectomy. *Eur J Cardiothorac Surg*. 2008;34:64–8.
  60. Varela G, Brunelli A, Rocco G, Jimenez MF, Salati M, Gatani T. Evidence of lower alteration of expiratory volume in patients with airflow limitation in the immediate period after lobectomy. *Ann Thorac Surg*. 2007;84:417–22.
  61. Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143: e166S–90S.
  62. Brunelli A, Belardinelli R, Refai M, et al. Peak oxygen consumption during cardiopulmonary exercise test improves risk stratification in candidates to major lung resection. *Chest*. 2009;135:1260–7.
  63. Win T, Jackson A, Sharples L, et al. Cardiopulmonary exercise tests and lung cancer surgical outcome. *Chest*. 2005;127:1159–65.
  64. Holden DA, Rice TW, Stelmach K, Meeker DP. Exercise testing, 6-min walk, and stair climb in the evaluation of patients at high risk for pulmonary resection. *Chest*. 1992;102:1774–9.
  65. Brunelli A, Varela G, Salati M, et al. Recalibration of the revised cardiac risk index in lung resection candidates. *Ann Thorac Surg*. 2010;90:199–203.
  66. Ferguson MK, Celauro AD, Vigneswaran WT. Validation of a modified scoring system for cardiovascular risk associated with major lung resection. *Eur J Cardiothorac Surg*. 2012;41:598–602.
  67. Barnes PJ. Muscarinic receptor subtypes in airways. *Life Sci*. 1993;52:521–7.
  68. Groeben H, Silvanus MT, Beste M, Peters J. Combined lidocaine and salbutamol inhalation for airway anesthesia markedly protects against reflex bronchoconstriction. *Chest*. 2000;118:509–15.
  69. Groeben H, Schlicht M, Stieglitz S, Pavlakovic G, Peters J. Both local anesthetics and salbutamol pretreatment affect reflex bronchoconstriction in volunteers with asthma undergoing awake fiberoptic intubation. *Anesthesiology*. 2002;97:1445–50.
  70. Warner DO. Perioperative abstinence from cigarettes: physiologic and clinical consequences. *Anesthesiology*. 2006;104:356–67.
  71. Theadom A, Cropley M. Effects of preoperative smoking cessation on the incidence and risk of intraoperative and postoperative complications in adult smokers: a systematic review. *Tob Control*. 2006;15:352–8.
  72. Myers K, Hajek P, Hinds C, McRobbie H. Stopping smoking shortly before surgery and postoperative complications: a systematic review and meta-analysis. *Arch Intern Med*. 2011;171:983–9.
  73. Warner DO, Colligan RC, Hurt RD, Croghan IT, Schroeder DR. Cough following initiation of smoking abstinence. *Nicotine Tob Res*. 2007;9:1207–12.
  74. Yamashita S, Yamaguchi H, Sakaguchi M, et al. Effect of smoking on intraoperative sputum and postoperative pulmonary complication in minor surgical patients. *Respir Med*. 2004;98:760–6.
  75. Nakagawa M, Tanaka H, Tsukuma H, Kishi Y. Relationship between the duration of the preoperative smoke-free period and the incidence of postoperative pulmonary complications after pulmonary surgery. *Chest*. 2001;120:705–10.
  76. Billert H, Gaca M, Adamski D. Smoking cessation as regards anesthesia and surgery. *Przegl Lek*. 2008;65:687–91.
  77. Wong J, Abrishami A, Yang Y, et al. A perioperative smoking cessation intervention with varenicline: a double-blind, randomized placebo-controlled trial. *Anesthesiology*. 2012;117(4):755–64.
  78. Dronkers J, Veldman A, Hoberg E, van der Waal C, van Meeteren N. Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. *Clin Rehabil*. 2008;22:134–42.
  79. Sakai EM, Connolly LA, Klauck JA. Inhalation anesthesiology and volatile liquid anesthetics: focus on isoflurane, desflurane, and sevoflurane. *Pharmacotherapy*. 2005;25:1773–88.
  80. von Ungern-Sternberg BS, Frei FJ, Hammer J, Schibler A, Doerig R, Erb TO. Impact of depth of propofol anaesthesia on functional residual capacity and ventilation distribution in healthy preschool children. *Br J Anaesth*. 2007;98:503–8.
  81. Pattinson KT. Opioids and the control of respiration. *Br J Anaesth*. 2008;100:747–58.
  82. Ansermino JM, Magruder W, Dosani M. Spontaneous respiration during intravenous anesthesia in children. *Curr Opin Anaesthesiol*. 2009;22:383–7.
  83. Luginbuhl M, Vuilleumier P, Schumacher P, Stuber F. Anesthesia or sedation for gastroenterologic endoscopies. *Curr Opin Anaesthesiol*. 2009;22:524–31.
  84. Herbstreit F, Peters J, Eikermann M. Impaired upper airway integrity by residual neuromuscular blockade: increased airway collapsibility and blunted genioglossus muscle activity in response to negative pharyngeal pressure. *Anesthesiology*. 2009;110:1253–60.
  85. Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology*. 2008;109: 389–98.
  86. Berg H. Is residual neuromuscular block following pancuronium a risk factor for postoperative pulmonary complications? *Acta Anaesthesiol Scand Suppl*. 1997;110:156–8.
  87. Bissinger U, Schimek F, Lenz G. Postoperative residual paralysis and respiratory status: a comparative study of pancuronium and vecuronium. *Physiol Res*. 2000;49:455–62.
  88. Murphy GS, Szokol JW, Franklin M, Marymont JH, Avram MJ, Vender JS. Postanesthesia care unit recovery times and neuromuscular blocking drugs: a prospective study of orthopedic surgical patients randomized to receive pancuronium or rocuronium. *Anesth Analg*. 2004;98:193–200 [table of contents].
  89. Faller S, Strosing KM, Ryter SW, et al. The volatile anesthetic isoflurane prevents ventilator-induced lung injury via phosphoinositide 3-kinase/Akt signaling in mice. *Anesth Analg*. 2012;114:747–56.
  90. Schlapfer M, Leutert AC, Voigtsberger S, Lachmann RA, Booy C, Beck-Schimmer B. Sevoflurane reduces severity of acute lung injury possibly by impairing formation of alveolar oedema. *Clin Exp Immunol*. 2012;168:125–34.
  91. Belhomme D, Peynet J, Louzy M, Launay JM, Kitakaze M, Menasché P. Evidence for preconditioning by isoflurane in coronary artery bypass graft surgery. *Circulation*. 1999;100:11340–4.
  92. Roscoe AK, Christensen JD, Lynch 3rd C. Isoflurane, but not halothane, induces protection of human myocardium via adenosine A1 receptors and adenosine triphosphate-sensitive potassium channels. *Anesthesiology*. 2000;92:1692–701.
  93. Jiang MT, Nakae Y, Ljubkovic M, Kwok WM, Stowe DF, Bosnjak ZJ. Isoflurane activates human cardiac mitochondrial

- adenosine triphosphate-sensitive  $K^+$  channels reconstituted in lipid bilayers. *Anesth Analg.* 2007;105:926–32 [table of contents].
94. Fujinaga T, Nakamura T, Fukuse T, et al. Isoflurane inhalation after circulatory arrest protects against warm ischemia reperfusion injury of the lungs. *Transplantation.* 2006;82:1168–74.
  95. Li QF, Zhu YS, Jiang H, Xu H, Sun Y. Isoflurane preconditioning ameliorates endotoxin-induced acute lung injury and mortality in rats. *Anesth Analg.* 2009;109:1591–7.
  96. Mu J, Xie K, Hou L, et al. Subanesthetic dose of isoflurane protects against zymosan-induced generalized inflammation and its associated acute lung injury in mice. *Shock.* 2010;34:183–9.
  97. Vaneker M, Santosa JP, Heunks LM, et al. Isoflurane attenuates pulmonary interleukin-1beta and systemic tumor necrosis factor-alpha following mechanical ventilation in healthy mice. *Acta Anaesthesiol Scand.* 2009;53:742–8.
  98. Dikmen Y, Eminoglu E, Salihoglu Z, Demiroglu S. Pulmonary mechanics during isoflurane, sevoflurane and desflurane anaesthesia. *Anaesthesia.* 2003;58:745–8.
  99. Volta CA, Alvisi V, Petrini S, et al. The effect of volatile anesthetics on respiratory system resistance in patients with chronic obstructive pulmonary disease. *Anesth Analg.* 2005;100:348–53.
  100. Falcão LF, Perez MV, de Castro I, et al. Minimum effective volume of 0.5% bupivacaine with epinephrine in ultrasound-guided interscalene brachial plexus block. *Br J Anaesth.* 2013;110:450–5.
  101. Holte K, Jensen P, Kehlet H. Physiologic effects of intravenous fluid administration in healthy volunteers. *Anesth Analg.* 2003;96:1504–9 [table of contents].
  102. Grocott MP, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcomes in adults. *Anesth Analg.* 2005;100:1093–106.
  103. Nelson R, Edwards S, Tse B. Prophylactic nasogastric decompression after abdominal surgery. *Cochrane Database Syst Rev.* 2005;25(1):CD004929.
  104. Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine: a review of clinical applications. *Curr Opin Anaesthesiol.* 2008;21:457–61.