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Perioperative Pulmonary Atelectasis - Part II: Clinical Implications

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Abstract

The development of pulmonary atelectasis is common in the surgical patient. Pulmonary atelectasis can cause various degrees of gas exchange and respiratory mechanics impairment during and after surgery. In its most serious presentations, lung collapse could contribute to postoperative respiratory insufficiency, pneumonia, and worse overall clinical outcomes. A specific risk assessment is critical to allow clinicians to optimally choose the anesthetic technique, prepare appropriate monitoring, adapt the perioperative plan and ensure patient's safety. Bedside diagnosis and management have benefited from recent imaging advancements, such as lung ultrasound and electrical impedance tomography, and monitoring such as esophageal manometry. Therapeutic management include a broad range of interventions aimed at promoting lung recruitment. During general anesthesia, these strategies have consistently demonstrated their effectiveness in improving intraoperative oxygenation and respiratory compliance. Yet, these same intraoperative strategies may fail to affect additional postoperative pulmonary outcomes. Specific attention to the postoperative period may be key for such outcome impact of lung expansion. Interventions such as non-invasive positive pressure ventilatory support are likely beneficial in patients at high-risk for pulmonary atelectasis (*e.g.,* obese) or those with clinical presentations consistent with lung collapse (*e.g.,* postoperative hypoxemia after abdominal and cardio-thoracic surgeries). Preoperative interventions may open new opportunities to minimize perioperative lung collapse and prevent pulmonary complications. Knowledge of pathophysiological mechanisms of atelectasis and their consequences in the healthy and diseased lung should provide the basis for current practice and help to stratify and match the intensity of selected interventions to clinical conditions.

Summary statement:

Up-to-date evidence on clinical risk factors, and advanced diagnostic approaches of pulmonary atelectasis are reviewed. Novel perspectives on perioperative therapeutic management based on lung imaging studies and recent clinical trials are provided to clinicians.

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Introduction

Pulmonary atelectasis contributes to perioperative lung dysfunction[1–3] and potential injury.[4–6] This emphasizes the relevance of an active clinical management based on the identification of risk factors, and implementation of specific diagnostic and therapeutic approaches to optimize lung function and minimize lung injury. Here, we review the clinical implications of perioperative pulmonary atelectasis in both a pathophysiological and evidence-based perspective.

Clinical Risk Factors for Perioperative Atelectasis

Risk factors for atelectasis can be categorized as patient, anesthesia and surgery related. Many risk factors have been identified, either directly with imaging techniques or indirectly through their association with global measurements of gas exchange and respiratory mechanics dysfunction. Along this review, we will give special attention to direct evidence from lung imaging. Anesthesiologists should identify such factors to anticipate the risk for perioperative respiratory dysfunction and adapt their management to both patient and surgery (Table 1).

Patient-related risk factors

Obesity—The increased weight of abdominal and thoracic adipose tissue exacerbates the compressive forces transmitted by the chest wall to the lung and exaggerates the cephalad displacement of the diaphragm.[7] These produce a rightward shift of the respiratory system pressure-volume curve,[8] higher pleural pressure,[9] lower respiratory system compliance[8,10] and lower functional residual capacity (FRC) before[11] and after induction of general anesthesia.[12] The combined effect of compression of the dorso-caudal lung and the gas absorption in lung units exposed to small airway closure result in greater risk of perioperative pulmonary atelectasis in obese than non-obese patients.[13,14] Post-intubation atelectasis at PEEP = 0 cmH_2O assessed by computed tomography linearly relates with body mass index (BMI; weight/square of the height) in the 18–30 range.[15] Also, during general anesthesia, transpulmonary pressure, *i.e.*, the pressure directly acting to expand the lungs,[16] decreases with BMI up to 40 corroborating the increased susceptibility to lung collapse with obesity. Indeed, mean PEEP estimates to produce positive end-expiratory transpulmonary pressure during general anesthesia in the overweight and obese were 9.1cmH_2O for BMI=25–29.9; 11.2cmH_2O for BMI=30–34.9; 12.8cmH_2O for BMI=35–39.9, and 16.8cmH_2O for BMI≥40.[9] Also, after tracheal extubation and during the first 24 postoperative hours morbidly obese patients present larger atelectasis than non-obese patients.[17]

Age—The susceptibility for airway closure, as judged by the difference between FRC and closing capacity, is minimal at young adulthood (20 years-old) and larger at younger and older ages.[18] Risk for intraoperative atelectasis would be expected to follow a similar pattern as airway closure promotes low $\dot{V}_A/\dot{Q}$ regions and absorption atelectasis. An association between atelectasis area measured with computed tomography immediately after induction of anesthesia and age has been demonstrated. Atelectasis area increases with age from

young adulthood to a peak at about 50 years-old, and decreases after 50 years-old.[15] Such reduction of atelectasis with age>~50 is presumably due to small airway closure delaying denitrogenation and alveolar collapse during preoxygenation.[15] In children, anesthesia-induced atelectasis is relevant particularly before 3 years-old.[19] The immature chest wall muscles and incompletely developed supporting structures in the lung parenchyma reduce outward tethering forces, while elastic recoil of the lung is fully preserved,[20] resulting in lower FRC and higher levels of required opening pressures.[18,21]

Diaphragmatic dysfunction—Perioperative diaphragmatic dysfunction as observed after upper abdominal and cardiothoracic surgery substantially increases the risk of atelectasis. For instance, preoperative diaphragmatic thickening fraction measured with ultrasound independently predicts postoperative pulmonary atelectasis, pneumonia or prolonged mechanical ventilation after cardiac surgery.[22] Similarly, diaphragmatic excursion less than 10 mm on ultrasound at 24h postoperatively is associated with higher incidence of atelectasis after thoracic surgery.[23]

Intra-abdominal hypertension—Intra-abdominal hypertension (ileus, ascites, tumor, hematoma) increases pleural pressure, reduces transpulmonary pressures, and can precipitate large pulmonary atelectasis in supine position particularly after loss of diaphragmatic tone.[24] Pregnancy (3rd trimester) can similarly increase the risk for intraoperative atelectasis.[25]

Pulmonary conditions—Pulmonary inflammation and/or pulmonary edema: substantially increase the risk of perioperative pulmonary atelectasis due to several mechanisms such as surfactant impairment, increased lung weight, and use of high FIO_2.[26]

Smoking: active smoking has been associated with perioperative respiratory morbidity and postoperative pulmonary complications (*e.g.*, obstructive atelectasis, pneumonia, and chest X-ray findings of atelectasis or consolidation),[27–29] even if not consistently related to anesthesia-induced intraoperative atelectasis.[3,30] Increased airway secretions in smokers leading to bronchial or bronchiolar obstruction, in addition to bronchospasm, could contribute to lung collapse.[31]

Chronic obstructive pulmonary disease (COPD): COPD is a risk factor for perioperative pulmonary complications. Specifically regarding lung collapse, COPD has been associated with resistance to atelectasis, *e.g.,* from oxygen absorption in awake[32] and surgical[33,34] patients despite small airway closure and substantial $\dot{V}_A/\dot{Q}$ mismatch.[32,34,35] Such resistance to lung collapse is likely due to the effect of hyperinflation and loss of lung elastic recoil. Perioperatively, the magnitude of atelectasis is determined by the net effect of factors contributing to and preventing lung collapse.

Chronic pulmonary hyperperfusion: encountered in congenital heart disease (*e.g.,* ventricular septal defect) protects from atelectasis as compared to hypoperfused lung (*e.g.,* tetralogy of Fallot) due to the stabilizing tethering effect of filled pulmonary capillaries on alveolar walls.[36]

Anesthesia-related risk factors

General anesthesia drugs—Sedative-hypnotics: Both intravenous[37] and inhalational anesthetics[38,39] have been associated with intraoperative pulmonary atelectasis. Inhalational anesthesia and total intra-venous anesthesia lead to similar incidence of pulmonary complications after non-cardiac surgery.[40] In cardiothoracic surgery, there is no evidence for superiority of any general anesthesia technique in the production of postoperative pulmonary complications as volatile agents have been found either superior,[40,41] equivalent[42] or inferior[43] to intravenous agents. Nitrous oxide presents higher lipid solubility than nitrogen promoting alveolar gas absorption[44] and increasing the risk of postoperative atelectasis.[45] Ketamine by itself maintains chest wall muscle tone, thus, preventing lung collapse.[46]

Opioids: As respiratory depressants, opioids decrease the central neural drive to the respiratory muscles and the sensitivity to carbon dioxide leading to respiratory depression and cough inhibition. Accordingly, intraoperative systemic opioids have been dose-dependently associated with postoperative atelectasis.[47]

Neuromuscular blocking agents and antagonists: neuromuscular blockade can compound with general anesthetics to facilitate the compressive effect of the abdomen onto the lungs, change chest wall cross-section, and ensuing atelectasis.[3] Postoperatively, residual neuromuscular blockade contributes to respiratory muscle dysfunction, atelectasis and hypoxemia[48,49] thus reinforcing the relevance of neuromuscular blockade reversal.[50] This should be accurately done as neostigmine administered at high doses (>60μg/kg) or not based on neuromuscular monitoring resulted in postoperative pulmonary atelectasis presumably from neostigmine–induced neuromuscular blockade.[51]

Regional anesthesia—Use of regional anesthesia as the main anesthetic technique in spontaneously breathing patient can preserve physiological diaphragmatic function and reduce intraoperative atelectasis.[3,52]

While regional techniques are associated with less atelectasis than general anesthesia,[53,54] they may still produce respiratory muscles dysfunctions and facilitate lung collapse.

Neuraxial anesthesia has been associated with a significant paresis of abdominal and accessory respiratory muscles (*e.g.*, intercostals) and deterioration of the exhalation force, breathing pattern, or ability to cough.[55] Reduction of lung volumes has been accordingly associated with neuraxial anesthesia, and depend mainly on the level and extension of the blockade (*i.e.*, impairment increases from lumbar to cervical). For example, thoracic epidural anesthesia with T1-T5 sensory block decreases vital and inspiratory capacity.[56,57] Spinal anesthesia similarly reduces vital capacity but contributes to a higher reduction of the expiratory reserve volume (- 48% with sensory block at T2) than thoracic epidural anesthesia.[58,59] Of note, reductions in intraoperative lung volumes during spinal anesthesia are greater in the overweight[53] or the obese[60] patient. Due to higher level of motor block and potential compromise of the diaphragmatic innervation, cervical epidural anesthesia may further deteriorate lung expansion as shown by a significant reduction in diaphragmatic excursion, maximal inspiratory pressure and tidal volume.[61] While such respiratory muscles dysfunction associated with both epidural and spinal anesthesia may compound to lung

collapse in at risk conditions,[25] this risk does not appear to be clinically relevant in patients without preexisting lung disease and might not surpass the benefits of avoiding general anesthesia in patients at high respiratory risk.[25,62]

Peripheral nerve blocks can also facilitate lung collapse. The risk of ipsilateral atelectasis due to phrenic nerve palsy and hemidiaphragmatic paresis may limit the use of interscalene block or other injections of local anesthetic in the cervical region (*e.g.*, supraclavicular, cervical plexus blocks) in patients presenting respiratory conditions.[63,64] Importantly, this risk is substantially reduced by the use of ultrasound-guided techniques and lowered volume of local anesthetic.[64,65]

Blood transfusion—Perioperative blood transfusion has been associated with postoperative pulmonary complications including atelectasis on systematic chest computed tomography after orthopedic surgery.[66,67]

Surgery-related risk factors

Body position—Operating table angle: The supine position is associated with a 27% decrease in FRC when compared to the sitting position (90°)[68] as it facilitates the cephalad shift of the diaphragm induced by the compression of intraabdominal organs. The Trendelenburg position further increases compression of the dorso-caudal lung as shown by additional reduction in FRC (~12%) in anesthetized children.[69] During robotic surgery, steep Trendelenburg reduces end-expiratory transpulmonary pressure[9] independently from patients' BMI and application of pneumoperitoneum.[9] The reduction in regional ventilation[70] and ~12% increase in silent spaces (lung areas with little or no ventilation suggestive of atelectasis) in the dorsal dependent lung has been confirmed by electrical impedance tomography.[71] In contrast, 40° reverse Trendelenburg position relieves lung compression by the abdomen with a marked benefit in obese patients, *e.g.*, homogenization of regional ventilation during bariatric laparoscopic surgery.[72]

Prone positioning: Normally, prone position reduces FRC from the sitting posture in awake, spontaneously breathing healthy humans.[73] In the anesthetized surgical patient, prone position with free abdominal movements (upper chest and pelvic supports) can markedly increase FRC by 53% when compared to supine posture,[74] even more in obese patients.[75] Frequently, anterior chest and abdominal wall movements are restricted in the prone position and lung expansion is predominantly determined by movement of the dorsal chest wall and diaphragm. The prone position reduces the mass of dependent lung exposed to the effect of gravity, favorably modifies the matching of lung and chest wall shapes, and reduces lung compression by cardiac and abdominal structures. These result in spatial homogenization of lung aeration and less deterioration of lung inflation and regional strain along time[76] due to both gravitational (dorsal>ventral expansion) and non-gravitational (caudal>cranial expansion) mechanisms.[77] Favorable effects on ventilation, ventilation-perfusion ratios[78–80] and oxygenation are also observed[81] while perfusion distribution is not significantly affected.[82]

Lateral decubitus: The dependent lung is exposed to compression from the weights of the non-dependent lung, mediastinum and abdominal organs.[83,84] Thus, atelectasis is

almost exclusively located in the dependent lung as detected by computed tomography in anesthetized patients.[83,85] Yet, the global FRC is larger in the lateral than in the supine position both before[86] and after[87] induction of general anesthesia due to the contribution of the non-dependent lung. This represents a larger non-dependent lung volume exposed to lower compression forces and larger transpulmonary pressures than that present in supine conditions.[88] Despite differences in lung size, the effect of lateral decubitus appears similar if the patient is lying on the left or right side.[68,88]

Lithotomy: lithotomy position has little differential effect on respiratory mechanics and the amount of poorly aerated lung tissue when compared with the supine position.[54,89]

Pneumoperitoneum—Pneumoperitoneum compresses the juxta-diaphragmatic lung regions by increasing intra-abdominal pressure, thus, promoting the cephalad displacement of the diaphragm.[90] Peritoneal insufflation independently reduces end-expiratory lung volume (~35% in the non-obese and ~15% reduction in the obese),[91] respiratory system compliance[92] and end-expiratory transpulmonary pressure.[9] These physiological changes are consistently associated with substantially higher atelectasis volume in the dependent lung (mean increase of 66% by computed tomography).[90,93] This effect was independent of the body position,[9,92] and has been confirmed, in humans, with relatively low intraabdominal pressure (11mmHg).[90] Combination of pneumoperitoneum and steep Trendelenburg position, as frequently implemented during robotic surgery, is associated with a high risk of severe atelectasis and may require a specific approach to lung recruitment.[70,94,95]

Cardiac surgery—Lung inflammation and ischemia-reperfusion injury from cardiopulmonary bypass are associated with substantial pulmonary compromise characterized by alveolocapillary membrane injury,[96] surfactant impairment[97] and mucociliary dysfunction.[98] Alterations of the chest wall function including the effect of sternotomy,[99,100] diaphragmatic dysfunction,[101] and pleural violation compound with those effects with impairment of lung expansion in the intra- and postoperative periods. Accordingly, atelectasis represents a frequent cause of hypoxemia both during and after surgery.[102–104] The predominance of retro-cardiac lung collapse in the postoperative period suggests an important contribution to atelectasis from compression by the weight of the heart (Fig.1).[105]

One-lung ventilation—Atelectasis produced by lung isolation is remarkable for its extension to a lung volume and its continuous character (*i.e.,* no tidal recruitment). Depending on the preoperative respiratory status and the effectiveness of hypoxic pulmonary vasoconstriction, one-lung ventilation may be associated with critical impairment of intraoperative gas exchange and cardiopulmonary function.[106] Lung isolation also exposes the collapsed lung to inflammatory,[107,108] ischemic[109] and reexpansion[110] insults, besides direct surgical trauma. The ventilated dependent lung is also at risk in this setting not only due to the potential systemic inflammatory response but also to mechanical ventilation injury and compressive atelectasis during lateral decubitus.[111,112] This effect can be exacerbated in the obese or if insufficient PEEP is associated with low tidal volume.[113] Such intraoperative insults to the collapsed and the ventilated lungs likely contribute to the

large number of pulmonary complications, including postoperative atelectasis, observed in the thoracic surgery population.[114–116]

Surgery duration—General anesthesia is responsible for nearly instantaneous diaphragmatic cephalad displacement in supine and semi-sitting patients.[71,103,117] Pulmonary atelectasis appears in the early minutes following loss of consciousness,[118,119] particularly when preoxygenation with FIO_2=1.0 is applied,[120] and additional gas absorption persists along the first 90 minutes.[121] Experiments in sheep revealed that lung collapse in healthy lungs with aeration heterogeneity comparable to that of humans occurs throughout 16-hours following initiation of general anesthesia with low-tidal volume ventilation without PEEP.[6] Such progressive collapse could contribute to the detrimental effect of anesthesia duration on postoperative pulmonary complications.[122] A combined effect of time and site of surgery is likely, as no time dependence of atelectasis volume was found in normal lung patients undergoing intracranial surgery[123] while gas exchange and FRC progressively deteriorate along cardiac or abdominal surgeries.[124,125]

Minimally invasive procedures—Abdominal minimally invasive procedures are frequently associated with the use of pneumoperitoneum and Trendelenburg position, thus, increasing the risk of intraoperative pulmonary atelectasis.[9] However, avoiding open thoracic or abdominal surgery may substantially reduce postoperative pain, improve postoperative lung volumes[126] and lower the rate of postoperative pulmonary complications and atelectasis.[127,128]

Diagnostic approach to pulmonary atelectasis

While frequently inferred from physiological measurements (respiratory mechanics and gas exchange), accurate diagnosis of atelectasis, as a primarily morphological process, should be based on direct quantification of the collapsed pulmonary parenchyma, *e.g.*, using imaging techniques.[129]

Direct morphological assessment

Chest radiography—Lung deaeration is associated with increased x-ray attenuation. Accordingly, opacification related to a lung segment or lobe is a typical finding of atelectasis. Yet, dorso-caudal or retrocardiac opacities can be missed in frontal chest radiography.[130] Mediastinal or hemidiaphragmatic shift together with compensatory overinflation of the expanded lung are additional classical findings.

Computed tomography—Similar to chest radiography, computed tomography is also based on X-ray attenuation yet with the important addition of 3-dimensional high-resolution quantitative assessment. Computed tomography is the gold standard for diagnosis and quantification of alveolar collapse,[131] and attenuation values of −100 to +100 Hounsfield units correspond to the operational definition of non-aerated lung.[132] Displacement of interlobar fissures; shift of the mediastinum, heart and pulmonary hilum towards the collapsed area; ipsilateral diaphragmatic elevation; intercostal space narrowing; and overinflation of the remainder aerated lung are typical findings of lobar atelectasis (Fig.1). Computed tomography is also useful to determine the cause of atelectasis by identification

of bronchial obstruction, or compressive pleural effusion.[133] The differential diagnosis between pneumonia, alveolar flooding and atelectasis may be difficult as lung attenuation can also result from fluid accumulation. Differentiation approaches have been investigated although not entirely established, *e.g.*, a threshold of contrast (iodixanol) enhancement ≥ 85 Hounsfield units to discriminate atelectasis and pneumonia demonstrated a sensitivity for atelectasis of 90% and specificity of 92%.[134]

Magnetic resonance imaging—Magnetic resonance imaging is a non-ionizing technique to diagnose and quantify lung atelectasis (Fig. 2).[135,136] T1- and T2-weighted images have been used in clinical conditions,[136] and the method validated against computed tomography in a preclinical study.[137] As T2-weighted magnetic resonance imaging allows for the identification of water-based tissue, it could significantly help to differentiate obstructive (hyperintensity due to accumulated secretions and total air resorption) from non-obstructive atelectasis (low signal intensity due to less free fluid and residual air).[136]

Pulmonary ultrasound—Lung ultrasound has been recently extensively validated for bedside assessment of lung collapse both in the operating room and in the intensive care unit.[138] As air is a strong ultrasound beam reflector, lung deaeration substantially increases the echogenicity of lung parenchyma. Accordingly, pulmonary atelectasis, similarly to other causes of lung consolidation, is visualized as a “tissue-like” or “hepatized” ultrasonographic structure (Fig.3A).[139] Lung ultrasound is highly accurate to diagnose pulmonary atelectasis both in children[140] and adults,[141] and performs better than auscultation or bedside radiography to differentiate important causes of increased density (*e.g.*, pulmonary consolidation *versus* pleural effusion).[142] Similar to computed tomography, the differential diagnosis of pulmonary consolidation with ultrasound (atelectasis *versus* pneumonia) remains challenging. The visualization of dynamic air bronchogram, revealed by a ventilation-synchronized, linear or pinpoint hyperechoic signal inside a lung consolidation, allows for high positive predictive value (86–97%) but moderate sensitivity (61%) in the diagnosis of pneumonia.[143,144] Assessment of atelectasis with ultrasound has been proposed for intraoperative individualization of alveolar recruitment[145–147] and postoperative prediction of pulmonary complications.[148] Transesophageal ultrasound may be used if transthoracic acoustic windows are unavailable.[149] Color doppler interrogation of a lung consolidation can help to evaluate local blood flow and the efficacy of hypoxic pulmonary vasoconstriction (Fig.3B).[150]

Indirect physiological assessment

Electrical Impedance Tomography—Electrical impedance tomography allows for continuous real time and bedside assessment of lung ventilation and aeration,[151] and has been proposed as a tool to monitor and individualize intraoperative lung recruitment.[152,153] Loss of aeration associated with atelectasis decreases the electrical impedance of lung tissue as air has high electrical impedance. Current devices provide assessment of a cross-sectional thoracic slice ~10–15 cm thick at the level of the transducer belt and allows for regional comparisons (*e.g.,* ventral *versus* dorsal or right versus left lung).[71,103] While signals are represented as a 2-dimensional lung-shaped image (Fig. 4), the image does not derive from a direct morphological assessment, but are mapped according to a presumed

chest geometry.[129] Changes in end-expiratory lung impedance produced by PEEP strongly correlate with changes of end-expiratory lung volumes measured with the nitrogen washout technique.[154] Measurements of the impedance variation produced by tidal ventilation have been used to describe the regional distribution of lung ventilation and estimate regional lung expansion as poorly-ventilated regions present less tidal impedance variation than normally ventilated regions.[71,103] An important technical limitation is that pulmonary consolidations and pleural effusion could produce a similar signal preventing differential diagnoses.

Respiratory system compliance and driving pressure—Pulmonary atelectasis may reduce respiratory system compliance, thus, increasing driving pressure.[155,156] Considering their presumed impact on patients' prognosis,[16,155–157] and easy assessment, monitoring of driving pressure during surgery may be particularly valuable. Indeed, large registry-based studies have consistently identified driving pressure ≥ 15 cmH_2O as a potential threshold to predict postoperative pulmonary complications and prompt interventions.[157,158] Yet, such observations are not specific to atelectasis as lung overdistension could lead to similar changes in compliance and driving pressures. Moreover, respiratory system mechanical properties are determined both by lungs and chest-wall. Accordingly, the use of absolute thresholds for respiratory system compliance or driving pressure is limited in patients presenting unphysiological or varying chest-wall mechanics (*e.g.*, obesity, pneumoperitoneum, abdominal surgery).[159] In those cases, monitoring intraoperative trends[16] to detect a deterioration (*e.g.*, >20% increase at constant tidal volume), use of PEEP titration, or additional monitoring for partitioning of lung and chest wall mechanical properties might be helpful (Fig.6).

Transpulmonary pressure—Transpulmonary pressure is conceptualized as the pressure across the lungs, *i.e.*, the difference between airway opening pressure and pleural pressure. While airway pressure is usually available, pleural pressure is not. Esophageal pressure measurement has been used to estimate pleural pressure.[160] The obtained measurement has been shown to correspond to the pleural pressure surrounding the region where the pressure is assessed (*i.e.*, dorso-caudal lung according to esophageal balloon location).[161] Exposure to negative transpulmonary pressure, notably at the end of expiration, increases the risk of lung collapse as shown by supine pigs and human cadavers imaging studies.[161,162] Negative end-expiratory transpulmonary pressures have also been consistently associated with hypoxemia and lung collapse during acute lung injury[163] and in surgical patients.[95,159] Hence, the continuous monitoring of esophageal pressure, targeting positive transpulmonary pressure,[16] has been proposed as a strategy to individualize airway pressure and maintain lung expansion during mechanical ventilation (Fig.5).[9,164]

Blood oxygenation—Pulmonary atelectasis correlates with the presence of shunt or regions of low $\dot{V}_A/\dot{Q}$ and contributes to intraoperative hypoxemia.[52,120,165] The magnitude of the hypoxemia will be determined by the degree of ventilation/perfusion mismatch including the volume of atelectatic lung and the adequacy of regional hypoxic pulmonary vasoconstriction. Pulse oxymetry is a simple and usually reliable continuous monitor of oxygenation allowing for the early detection of possible perioperative atelectasis.[166] Because absolute SpO_2 can be normalized by increasing FIO_2, use of the SpO_2/FIO_2 ratio

may help to diagnose impaired blood oxygenation. In injured lung patients, the range of SpO_2/FIO_2=235–315 is associated with PaO_2/FIO_2=200–300 mmHg.[167]

Therapeutic management of perioperative atelectasis

Several perioperative interventions have been explored to promote lung recruitment, and, ultimately, prevent pulmonary atelectasis. Yet, while studies tested interventions directed to reduce atelectasis, they rarely used its quantitative assessment as their primary endpoint, but, instead, used composite pulmonary outcomes including postoperative pulmonary atelectasis as a component.[168,169] The relevance of interventions directed to minimize atelectasis has been recently emphasized by an international expert panel classifying as highest quality of evidence that "formation of perioperative clinically significant atelectasis" could "be an important risk factor for the development of postoperative pulmonary complications".[168] In this section, we will discuss reported therapeutic approaches considering the clinical period (pre, intra or postoperative) and the underlying pulmonary condition (normal *vs.* inflamed lung).

Preoperative period

Prehabilitation combining patient education, preoperative physiotherapy, smoking cessation and nutritional optimization has been proposed to prevent postoperative pulmonary complications including pulmonary atelectasis.[170–175] In high-respiratory risk patients undergoing coronary artery bypass graft surgery (n=279), preoperative intensive inspiratory muscle training prevents post-operative pulmonary complications including atelectasis.[176] In patients undergoing upper-abdominal surgery, a randomized clinical trial found that a single preoperative physiotherapy session (30 minutes) significantly reduced postoperative pulmonary complications (including atelectasis on chest x-ray).[177] However, the relatively high rate of postoperative pulmonary complications in controls and the influence of regional practices should encourage the replication of these results in larger cohorts. Finally, meta-analysis findings suggested a beneficial effect of preoperative inspiratory muscle training before cardiac or major abdominal surgery for prevention of postoperative atelectasis and pneumonia. Yet, results could be overestimated due to lack of adequate blinding and study size.[178]

Intraoperative period

Tidal volume—Supraphysiological tidal volumes (10–15 ml/kg of predicted body weight) have been until recently the decades-long cornerstone of intraoperative atelectasis treatment.[1,179] Indeed, lower tidal volumes imply the potential for poorly-ventilated lung regions exposed, in the absence of PEEP, to progressive deaeration. Yet, while effective to prevent atelectasis, large tidal volumes have been associated with higher risk of postoperative pulmonary complications in metaanalyses,[180,181] registry-based studies,[182] and clinical trials in abdominal[183] and thoracic[184] surgery. The protective range of tidal volumes in surgical patients may be broader than more strict lower ranges utilized in critical care. A recent clinical trial found that tidal volumes of 6 *versus* 10 ml/kg of predicted body weight with PEEP=5 cmH_2O resulted in similar outcomes after major surgery (Table 2),[185] in line with a previous large registry-based study.[157] The presence of PEEP=5 cmH_2O in

these cases may be essential for equivalent outcomes, as absence of PEEP in association with low tidal volumes may be deleterious.[5] Such finding underscores a limitation of previous studies addressing tidal volumes using bundle interventions of tidal volume and PEEP settings,[183,184] which prevent the individual assessment of tidal volume and PEEP to outcomes. Overall, current evidence supports a tidal volume range of 6–10 ml/kg of predicted body weight for two-lung ventilation of surgical patients with non-inflamed lungs.

Of note, current data suggest that the protective effect may not derive from lower tidal volumes by themselves but from their role in limiting lung strain (change in lung volume divided by the initial lung volume), clinically estimated from driving pressures. Indeed, registry-based studies in surgical patients undergoing non-cardiothoracic[157] and cardiac surgery[158] and studies in ARDS[186] have indicated that improved outcomes are related primarily to driving pressures not to tidal volumes. While these two variables are related, driving pressure is more specifically associated with lung strain, a possible explanation to those findings. That would lead the clinician to consider ventilatory interventions when driving pressures increase, rather than merely focus on tidal volumes.[16]

Recruitment maneuvers—Recruitment maneuvers correspond to the transient application of high airway pressures that translate into high transpulmonary pressures aiming at reopening collapsed lung regions. Different types of maneuvers have been used including sustained inflation for 30 sec at airway pressure=30cmH_2O,[102,183,187] transient increase in tidal volume and PEEP for 3 breaths to reach plateau pressure of 30–35cmH_2O in normals[188] or 40–50 cmH_2O in the obese.[189] Recruitment maneuvers are efficacious in reducing pulmonary atelectasis volume[165] and improving intraoperative respiratory mechanics[190] and oxygenation.[91,187,191] However, this effect may be transient when high FIO_2 is used during the maneuvers[192] or when these are not associated with appropriate PEEP management.[14] For instance, recruitment maneuvers only lead to physiological and radiographic improvement in obese patients or during pneumoperitoneum when associated with increased PEEP.[14,91,193] In clinical trials, periodic recruitment maneuvers failed to improve postoperative pulmonary outcomes even if combined to high PEEP after abdominal or cardiac surgery (Table 2).[102,188,194,195] Accordingly, current recommendations limit the use of recruitment maneuvers to patients presenting a respiratory dysfunction suggestive of atelectasis according to an individual risk-benefit assessment and always combined with PEEP (Fig.6). Recruitment maneuvers should be performed with the ventilator instead of manually, with the lowest pressure, during the shortest effective time and with a continuous hemodynamic monitoring.[168]

Positive end-expiratory pressure—The application of PEEP aims to prevent or treat atelectasis by maintaining positive transpulmonary pressure when alveolar pressure reaches its lowest end-expiratory level. During general anesthesia, PEEP improves gas exchange and respiratory mechanics,[179] and reduces the volume of collapsed lung both in adults[3,196] and children.[197] This occurs either with mere application of PEEP to normal lungs,[3] or when PEEP follows lung recruitment maneuvers in high-risk settings for atelectasis (*e.g.*, obesity,).[14,91,193]

Besides those beneficial physiological effects, PEEP can also prevent the mechanical and biological lung injuries associated with atelectasis[26] and, consequently, improve postoperative pulmonary outcomes. Such protection has been implied by the observation of better postoperative pulmonary outcomes with moderate PEEP (=5–8cmH_2O) than with lower-no or high PEEP in large registry-based studies in non-cardiothoracic surgery,[157,198] and worse outcomes when PEEP ~0 is associated with low tidal volumes.[5] In multicenter randomized controlled trials, moderate PEEP bundled with low V_T leading to better outcomes than when no PEEP was combined with high tidal volumes further supported its value (Table 2).[183,184]

Application of PEEP higher than those moderate levels (*i.e.*, 8–12cmH_2O) has not brought additional improvement of postoperative pulmonary outcomes, although it reduces intraoperative atelectasis. Indeed, large randomized controlled trials using high PEEP (=12 cmH_2O) strategies consistently enhanced intraoperative oxygenation and respiratory mechanics, while they failed to improve postoperative pulmonary and extrapulmonary outcomes (Table 2).[188,189,194] Importantly, high PEEP may expose patients to excessive alveolar pressures as suggested by the finding of biomarkers of alveolar overdistension[103,199] and the higher incidence of arterial hypotension, bradycardia and need for vasopressors in patients exposed to it.[188,189,200] Consequently, recent expert recommendations propose the avoidance of PEEP=0 cmH_2O while limiting intraoperative PEEP to fixed low levels (=2–5 cmH_2O) as the standard intraoperative approach.[168] High PEEP strategies would be restricted to clinical scenarios strongly suggestive of significant atelectasis (*e.g.*, oxygenation or respiratory mechanics compromise)[156,201] or consistent with high risk for lung collapse (*e.g.*, BMI >50; obesity *plus* pneumoperitoneum or Trendelenburg; abdominal hypertension, Fig.6).[9,70,189,202]

The considerable variability in individual PEEP requirements for optimal lung mechanics, oxygenation, or aeration depending on patients characteristics (*e.g.*, BMI[9,14]) or surgical factors (*e.g.*, abdominal surgery,[90,164,203] robotic assisted laparoscopic surgeries,[9] stage of surgery,[159] one-lung ventilation[155]) has been increasingly documented. Such variability implies the need for PEEP individualization, which can be done using respiratory mechanics including estimates of transpulmonary pressure using esophageal balloons,[9,159,194,204] pulse oximetry,[205] and bedside lung imaging (US or EIT).[94,152,153,202] Studies to date, mostly physiological, indicate that these personalized interventions resulted in better transpulmonary pressures, driving pressures,[159] intraoperative lung expansion[94,202] and postoperative lung aeration[152] than fixed PEEP strategies. Demonstration of the outcome benefits of individualized PEEP approaches will require further investigation.

Inspired fraction of oxygen—Partial or complete alveolar denitrogenation with oxygen promotes oxygen absorption atelectasis.[117,192] Accordingly, atelectasis area quantified by computed tomography was 20x higher with preoxygenation with FIO_2=1.0 for intubation than with FIO_2=0.3 in nonobese patients.[120] Of note, desaturation time (*i.e.*, time to reach a SpO_2<90%) is still 1.8 minutes longer after preoxygenation with FIO_2=1.0 than with FIO_2=0.8.[206] In the obese, adding continuous positive airway pressure during preoxygenation, mitigates the collapsing effect of FIO_2=1.0 as it improves end-expiratory lung volume and oxygenation during and after intubation.[207] Besides the intubation period,

a dose-dependent association between median intraoperative FIO_2 and major postoperative pulmonary complications and 30-day mortality has been reported after non-cardiothoracic surgery in a large registry-based study, suggesting a protective effect of restrictive approaches.[208] Yet, in large randomized clinical trials, intraoperative $FIO_2 \geq 0.8$ *vs.* 0.3 did not significantly impact postoperative atelectasis (assessed by chest X-ray or computed tomography)[209], pulmonary complications[210] or supplemental oxygen requirements,[211] after abdominal surgery in mostly non-obese patients. Accordingly, intraoperative FIO_2 should target normoxic and not hyperoxic conditions. High FIO_2 should be particularly directed to treatment or prevention of hypoxemia (*e.g.*, pre-intubation and pre-extubation), and avoidance of FIO_2=1.0 might be most beneficial intraoperatively to patients at high risk for atelectasis.[212]

Spontaneous ventilation—Maintaining diaphragmatic tone during general anesthesia preserves negative pleural pressure and diaphragmatic shape favoring alveolar ventilation distribution[213] and aeration of the dorso-caudal lung in small clinical studies.[3,214] Adding high-flow oxygen in non-intubated spontaneously breathing anesthetized children further improved lung aeration.[135]

Lung recruitment during perioperative lung inflammation—Either in complex surgical cases or in the surgical ICU, anesthesiologists frequently manage critically ill patients with respiratory dysfunction due to or associated with significant acute inflammatory lung injury, *e.g.*, systemic inflammatory response, sepsis, post-cardiopulmonary bypass, transplant surgery, extrapulmonary surgical complications, lung trauma, transfusion-related acute lung injury, and lung ischemia. In such conditions, implementation of strategies for lung protection is particularly important as increased susceptibility to lung injury including mechanical lung injury is likely present, as supported by the concept of two-hit injury,[215,216] and determines an increased risk for further respiratory dysfunction, multi-organ failure and death.[186] The frequently present alveolar instability and higher opening pressures (45–60 cmH_2O)[217,218] than normal lungs (30–40 cmH_2O)[111] set these patients at increased risk for atelectasis. For these reasons, PEEP ≥ 5 cmH_2O should be used in virtually all patients presenting acute lung inflammation. PEEP higher than that required for oxygenation (*e.g..,* higher PEEP tables from ARDSNet)[219] is likely reserved to patients fulfilling criteria for moderate and severe ARDS (PaO_2/FIO_2≤200mmHg with bilateral lung infiltrates, acute onset, and not explained by cardiac failure or fluid overload).[220,221] Individualized PEEP settings have been increasingly advanced also in this group of patients aiming at optimal respiratory mechanics (*e.g.*, respiratory system compliance,[222] driving pressure,[186] transpulmonary pressure,[163] oxygenation,[219] or imaging measures of lung expansion).[223] Such approaches have shown physiological benefit to respiratory system mechanics and blood oxygenation,[163] while mortality benefits await confirmation. Attention to complications associated with high PEEP, *e.g,* hemodynamic instability and pneumothorax, is key for safety during severe lung injury as major morbidity has been associated with aggressive use of ‘open-lung’ strategies.[222] Systematic use of low tidal volumes (6–8 ml/kg of predicted body weight) and associated attention to driving pressure should compose the ventilatory management.[186]

Of note, critically ill patients presenting *uninjured lungs* did not benefit from the systematic use of low tidal volume (6ml/kg *vs.* 10ml/kg of predicted body weight)[224] and PEEP higher than 5cmH_2O.[225] Accordingly, the ventilatory management of lung recruitment in critically ill patients with normal lung function is consistent with the approach described above for the surgical patient.

Large airways hygiene—In intubated patients, muco-ciliary clearance impairment, bronchial hypersecretion, ineffective coughing and lack of gas humification could compound to produce airway obstruction as with mucus plugs, thus, precipitating obstructive atelectasis. Tracheal suctioning should be performed on an as-needed basis to avoid lung derecruitment and hypoxemia.[226] In case of lobar and segmental obstructive atelectasis, fiberoptic bronchoscopy allows for confirmation of diagnosis and etiological treatment with bronchial toilet under fiberoptic guidance and restoration of lung aeration.[227] Routine nebulization of N-acetylcysteine and salbutamol (every 6h) is not advantageous as no reduction of ventilator-free days was observed in intubated ICU patients ventilated for more than 24h as compared to on-demand treatment.[228]

Non ventilatory preventive strategies—Non-ventilatory intraoperative interventions contribute to prevention of postoperative atelectasis. Opioids are associated with ventilatory depression and a large registry-based study on a wide range of adult non-cardiac surgeries under general anesthesia showed that indeed lower dose of intraoperative fentanyl (~60–120 mcg for a 70 kg patient) was associated with lower rate of pulmonary complications including atelectasis than higher doses (~4 mcg/kg) and interestingly also than no fentanyl.[47] Lower doses of neuro-muscular blocking agents in a similar population also related to less major postoperative pulmonary complications. These are also reduced by accurate reversal of neuromuscular blocking agents with associated appropriate monitoring of neuromuscular function.[48,229] No advantage of the combination rocuronium-sugammadex as compared to neostigmine to reduce postoperative pulmonary complications has been definitely demonstrated.[230,231] Optimized fluid administration through perioperative monitoring of stroke volume (*e.g.*, esophageal doppler) and goal-directed hemodynamic therapy during major surgery prevent fluid overload and reduce postoperative pulmonary complications in randomized clinical trials.[169,232,233] Large observational studies in cardiac[234] and non-cardiac[235] surgery further suggest that optimized patient-blood management to limit blood products transfusion may help in preventing postoperative pulmonary complications.

Emergence from anesthesia and extubation—Emergence from anesthesia and extubation may hasten alveolar derecruitment.[94,103,147,153,236] Specifically, high pre-extubation FIO_2 has been associated with absorption atelectasis.[237,238] Yet, the clinical impact on postoperative outcomes is unknown and safety issues related to shortening desaturation time with $FIO_2<1.0$, such as for difficult extubations, should be considered.[239,240]

In mostly non-obese patients undergoing emergence from anesthesia with $FIO_2 =1.0$ at the end of non-cardiothoracic surgery, neither weaning PEEP to 0cmH_2O[236] nor performing recruitment maneuvers and adding PEEP=10cmH_2O[241] before extubation significantly affected postoperative atelectasis formation or gas exchange.

In contrast, in selected patients presenting hypoxemia (PaO_2/ FIO_2<250 mmHg) at the end of cardiac surgery, an intensive alveolar recruitment strategy (PEEP=13–30 cmH_2O) performed before extubation improved lung aeration and significantly reduced the incidence of postoperative pulmonary complications and hospital length of stay.[201] Limiting tracheal suction and applying positive airway pressure during cuff deflation before extubation to prevent postoperative atelectasis appears safe and has been suggested to prevent early postoperative atelectasis. However, the systematic use of this approach requires further validation.[242] Importantly, extubation should be performed in patients who have recovered from neuromuscular blockade (train-of-four greater than 0.9).[50,243]

Postoperative period

Intraoperative lung recruitment may not consistently translate into higher postoperative lung aeration.[103,147,152,153] Accordingly, strategies aiming to maintain lung recruitment in the post-anesthesia care unit, ICU or surgical ward may independently improve postoperative outcomes and be at least as valuable as intraoperative lung expansion interventions. Multimodal bundle strategies[244,245] aiming at reducing postoperative alveolar collapse have been advanced, but clinical trials are still highly required for high level evidence.[169,172,246]

Non-invasive ventilatory support—Non-invasive positive pressure ventilation after extubation may prevent pulmonary atelectasis and compensate for the postoperative reduction of FRC.[246,247] Continuous positive airway pressure (CPAP) and non-invasive ventilation increase the pressure at airway opening and improve gas exchange.[248,249] While mechanisms underlying the benefits of non-invasive positive pressure support have not been entirely defined, improvement in lung aeration through alveolar recruitment is likely the most relevant followed by the potential reduction in work of breathing, and improved cardiac function with reduction of pulmonary edema.[247] Recently, high-flow nasal cannula has been used to non-invasively increase pressure at the airway opening. In adults, at flow rates ~60L/min, with closed mouth, mean airway pressure is ~5cmH_2O,[250] which is satisfactory in many cases but may be inadequate in settings requiring higher airway pressures (*e.g.,* obesity). In children up to 6 years of age, a flow rate of 2L/kg/min had a significant effect on lung expansion.[135] Clinical studies have explored non-invasive ventilatory support to *treat* postoperative respiratory failure or to *prevent* postoperative pulmonary atelectasis and complications:

Curative use: In selected patients already presenting postoperative hypoxemia, the curative use of non-invasive ventilatory support substantially improved postoperative outcomes as compared to conventional oxygen therapy and should be considered as a standard of care. Recent European guidelines[251] propose the immediate use of non-invasive ventilation or CPAP rather than conventional oxygen therapy for hypoxemic patients after abdominal, cardiac or thoracic surgery to reduce atelectasis and prevent further respiratory failure.[251]

In hypoxemic patients after major abdominal surgery (*e.g.,* room air $SpO_2 \leq 96\%$ for 5 minutes[194]), postoperative CPAP (5 to 10 cmH_2O) was effective in preventing postoperative pulmonary complications[194] and reintubation;[252] and non-invasive ventilation (inspiratory pressure support=5–15 cmH_2O; PEEP=5–10 cmH_2O) reduced 90-day mortality as compared

to standard oxygen therapy.[253] Non-invasive ventilation prevented postoperative reintubation in patients presenting acute respiratory failure after cardiothoracic surgery, also reducing ICU length-of-stay;[254–256] and after solid organ transplantation, also reducing ICU mortality.[257] In patients presenting hypoxemia after cardiothoracic surgery (~32% with obesity), high-flow nasal oxygen therapy (flow=50L/min; FIO_2=50%) was non-inferior to non-invasive ventilation to prevent reintubation.[258]

Preventive use: High risk patients, *e.g.*, the obese, may particularly benefit from extended postoperative non-invasive ventilatory support.[259] After bariatric surgery, preventive CPAP or non-invasive ventilation improved blood oxygenation[260] and post-extubation lung volumes[261] while early application of high-flow nasal cannula decreased postoperative hypoxemia and prevented postoperative pulmonary atelectasis.[262] Similarly, in mostly non-obese patients who had undergone elective cardiac surgery, preventive nasal CPAP (10 cmH_2O, ≥6 hours) reduced the rate of postoperative complications and reintubation but had no significant effect on ICU or hospital length of stay.[263] Despite these results, recent randomized clinical trials assessing the preventive use of postoperative non-invasive ventilatory support did not demonstrate efficacy of: CPAP or high-flow nasal cannula after abdominal surgery in mostly non-obese patients at intermediate-to-high pulmonary risk,[194,264] non-invasive ventilation after thoracic surgery in chronic obstructive pulmonary disease patients[265] or high flow nasal cannula after cardiac surgery in overweight to obese patients.[266,267] These results emphasize the need for better treatment stratification (*e.g.*, super-obese, significant intraoperative atelectasis) and identification of the optimal interface, time of initiation and dose of preventive ventilatory support.

Early mobilization—Early mobilization, as part of enhanced recovery after surgery,[268] has been suggested to improve postoperative FRC.[269] In clinical trials, early mobilization relieve lung atelectasis after video-assisted thoracoscopic surgery[270] and coronary artery bypass graft surgery[271] but the effect on pulmonary complications was not significant after colo-rectal surgery.[272,273]

Respiratory Physiotherapy targeting Lung Expansion—Deep-breathing exercises and incentive inspiratory have been associated with improved FRC and atelectasis reduction after abdominal[274,275] and cardiothoracic surgeries.[276,277] A reminder system may improve outcomes and the adherence to postoperative physiotherapy.[276] Nonetheless, while presumably beneficial, the wide-spread use of incentive spirometry has been questioned, and appropriate matching of indications, techniques and doses need to be established due to low quality of evidence.[278–280]

Analgesia—When compared to systemic opioid-based analgesia, postoperative epidural analgesia is associated with a preventive effect on pulmonary atelectasis.[281,282] The potential mechanisms are the improvement of cough by greater expiratory muscle strength,[283] deep breathing with higher diaphragmatic inspiratory velocities[284] and earlier mobilization by enhanced analgesia,[285] while avoiding the respiratory depression produced by systemic opioids. After thoracotomy, paravertebral block is an alternative to epidural analgesia to prevent pneumonia and need for ventilatory support.[286]

Oxygen Therapy—In spite of scarce evidence during routine oxygenotherapy,[287] humidification of inspired gas may improve bronchial drainage and prevent mucus plug responsible for airway obstruction.[288] Room air trials should be regularly performed in patients receiving oxygen in order to reevaluate the indication for oxygen therapy, and, importantly, identify patients at risk for pulmonary complications as these could benefit from additional non-invasive respiratory support.[166,194]

Mucolytics—Prophylactic intravenous ambroxol may prevent postoperative atelectasis in at-risk patients, but the quality of evidence is low.[289] N-acetyl cysteine failed to prevent postoperative atelectasis after elective upper laparotomy.[290]

Relief of extrinsic compression—Along with lung expansion techniques, relieving severe extrinsic compression due to pleural effusion (*e.g.,* thoracocentesis) or abdominal hypertension (*e.g.,* paracentesis, medical treatment of ileus, laparostomy) as well as significant pneumothorax may be necessary to improve lung aeration. Gastric decompression should be strictly selective (*e.g.,* severe postoperative gastric distension). Routine use of nasogastric tube significantly increased the incidence of postoperative atelectasis and pneumonia in a meta-analysis of clinical trials.[291]

Interventions described in this section compose most of the current clinical tools to approach perioperative atelectasis. As can be derived from the presentation, the evidence on interventions specifically addressing atelectasis is dispersed in sources varying from clinical trials, in combination with other pulmonary outcomes, to individual studies or meta-analyses addressing subsets of patients, single interventions, and particular outcomes. Formal systematic analyses are needed to advance quantitative and specific understanding in the field.

Conclusion:

Pulmonary atelectasis is a prominent perioperative clinical entity. Hypoxemia and lowered respiratory system compliance are classical presentations of atelectasis in the operating room but specific and quantitative diagnosis always requires lung imaging. While patient and surgery related risk factors are well known, the direct impact of intraoperative pulmonary atelectasis on postoperative outcomes is still unclear. Mechanical ventilation strategies aiming to maximize alveolar recruitment in all-comers during surgery did reduce undesirable gas exchange and respiratory mechanics dysfunction, and are, consequently, effective in improving physiological dysfunction. Yet, they did not affect mid- or long-term postoperative pulmonary or composite outcomes. To date, generalizability of those results remains controversial as shown by the limited clinical guidelines. Future directions for anesthesiologists and investigators should primarily address the stratification of patients' risk for severe pulmonary atelectasis, the use of titrated physiology-based strategies and the extension of lung recruitment from the pre- to the postoperative period.

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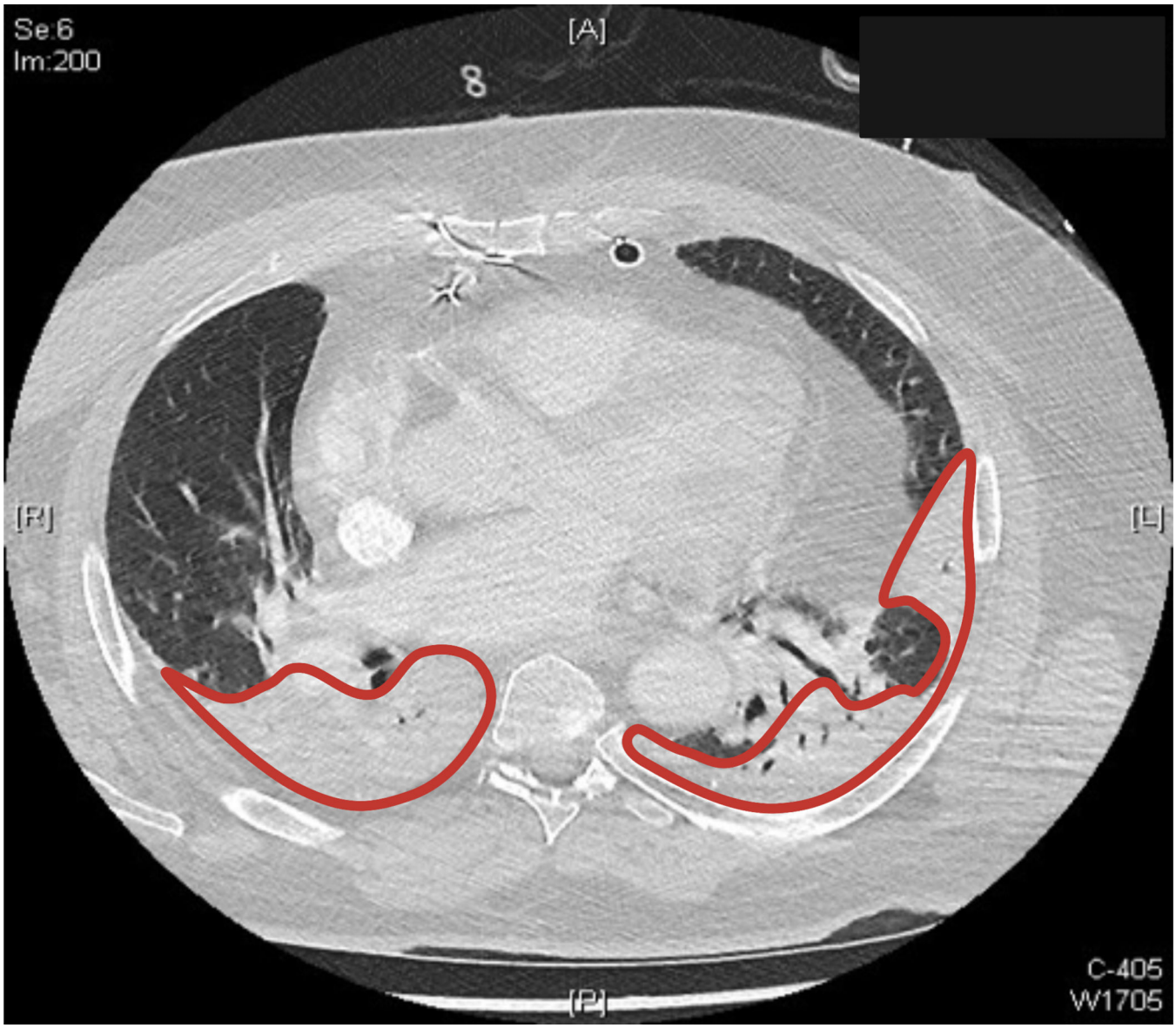

Figure 1:

Lung Computed Tomography: bilateral opacities of the dependent retrocardiac lung regions (red lines) revealing the typical aspect of severe perioperative pulmonary atelectasis in an obese patient requiring re-intubation for postoperative respiratory failure 2 days after coronary artery bypass graft surgery.

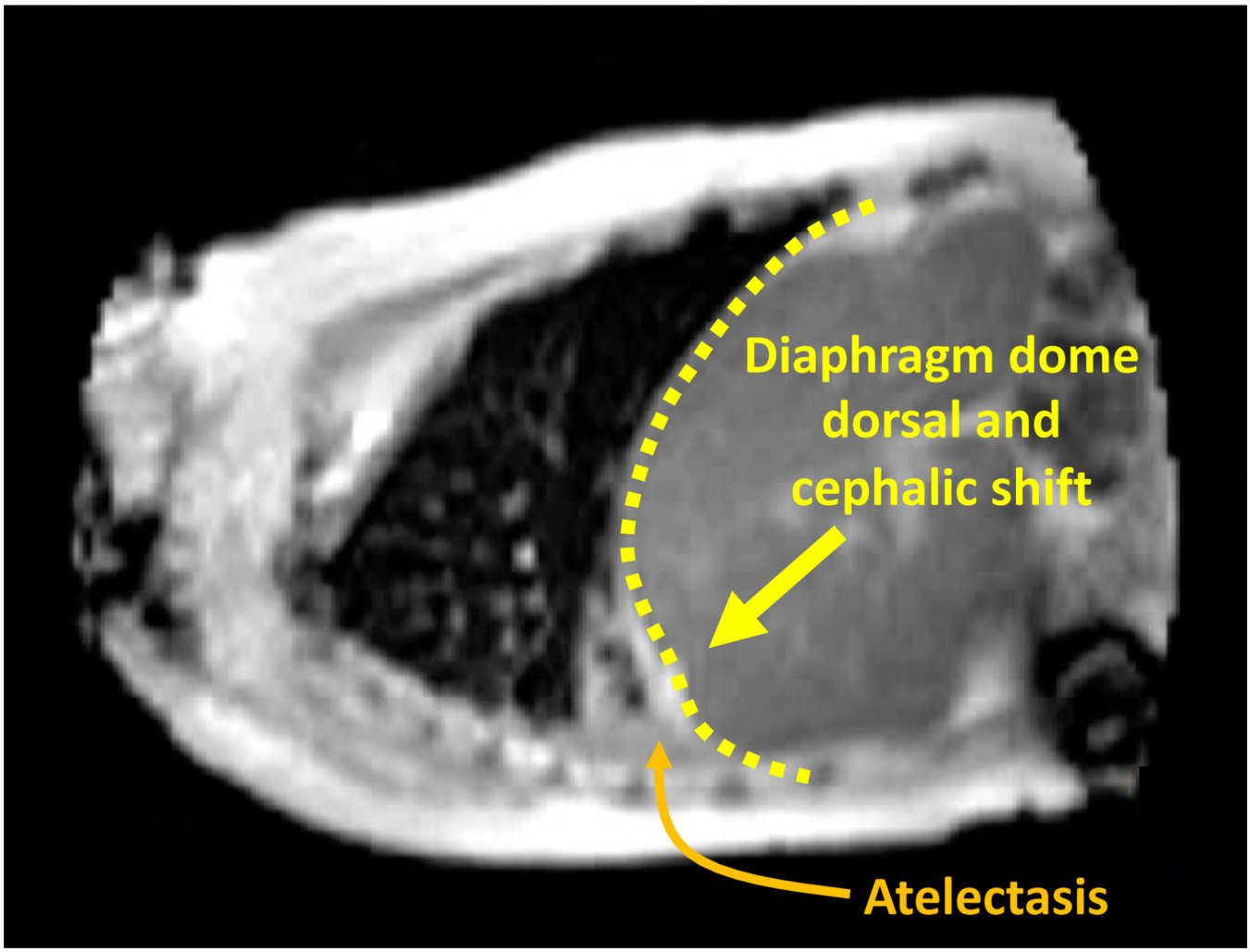

Figure 2:
Sagittal cross-section magnetic resonance images showing the effect of general anesthesia and paralysis in the supine position: dorsal cephalad shift of the diaphragm dome and atelectasis of the dorso-caudal lung.

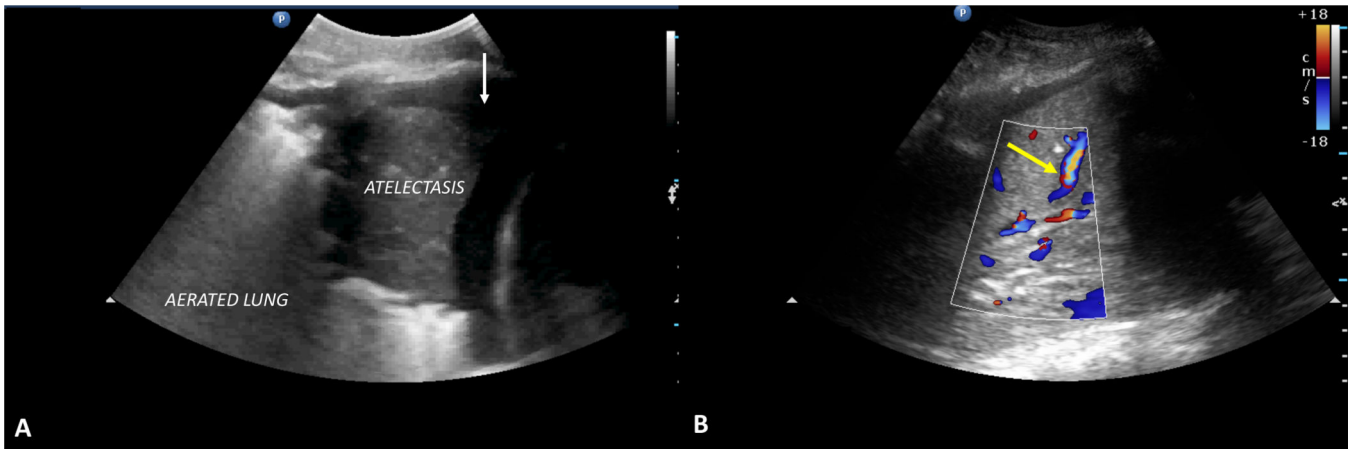

Figure 3:

Detection of pulmonary atelectasis by ultrasound. (A) Pulmonary atelectasis revealed using lung ultrasound by a pulmonary consolidation surrounded by a pleural effusion (white arrow). (B) Color doppler imaging showing the persisting pulmonary blood flow within consolidated lung (yellow arrow) due to incomplete hypoxic pulmonary vasoconstriction, which may result in a shunt effect.

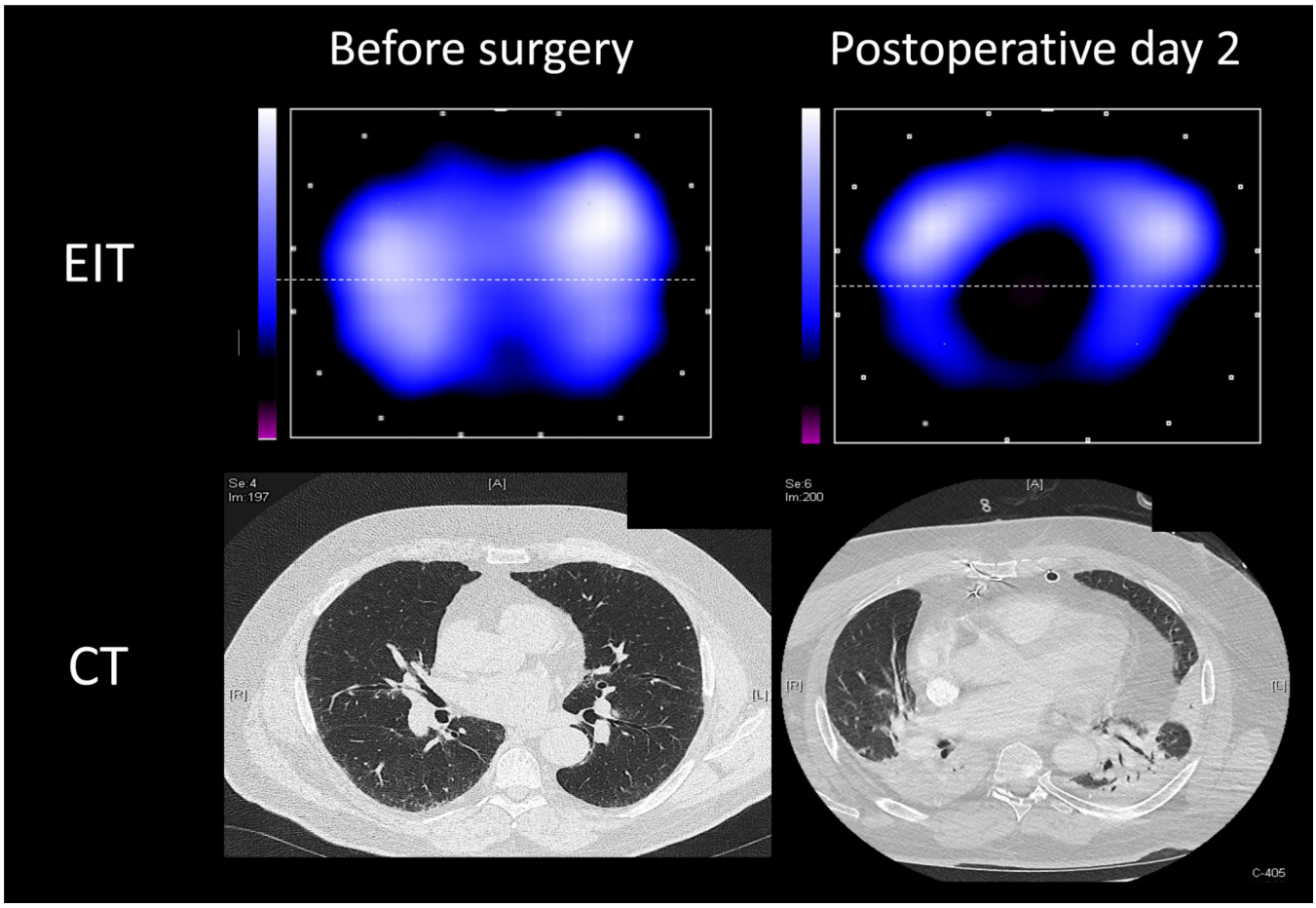

Figure 4:

Pre and postoperative regional distribution of the tidal impedance variation, assessed with lung electrical impedance tomography, in a patient presenting postoperative respiratory failure 2 days after coronary artery bypass graft surgery. Note that pulmonary atelectasis observed on computed tomography is associated with a reduced impedance variation signal in the dorsal hemithorax.

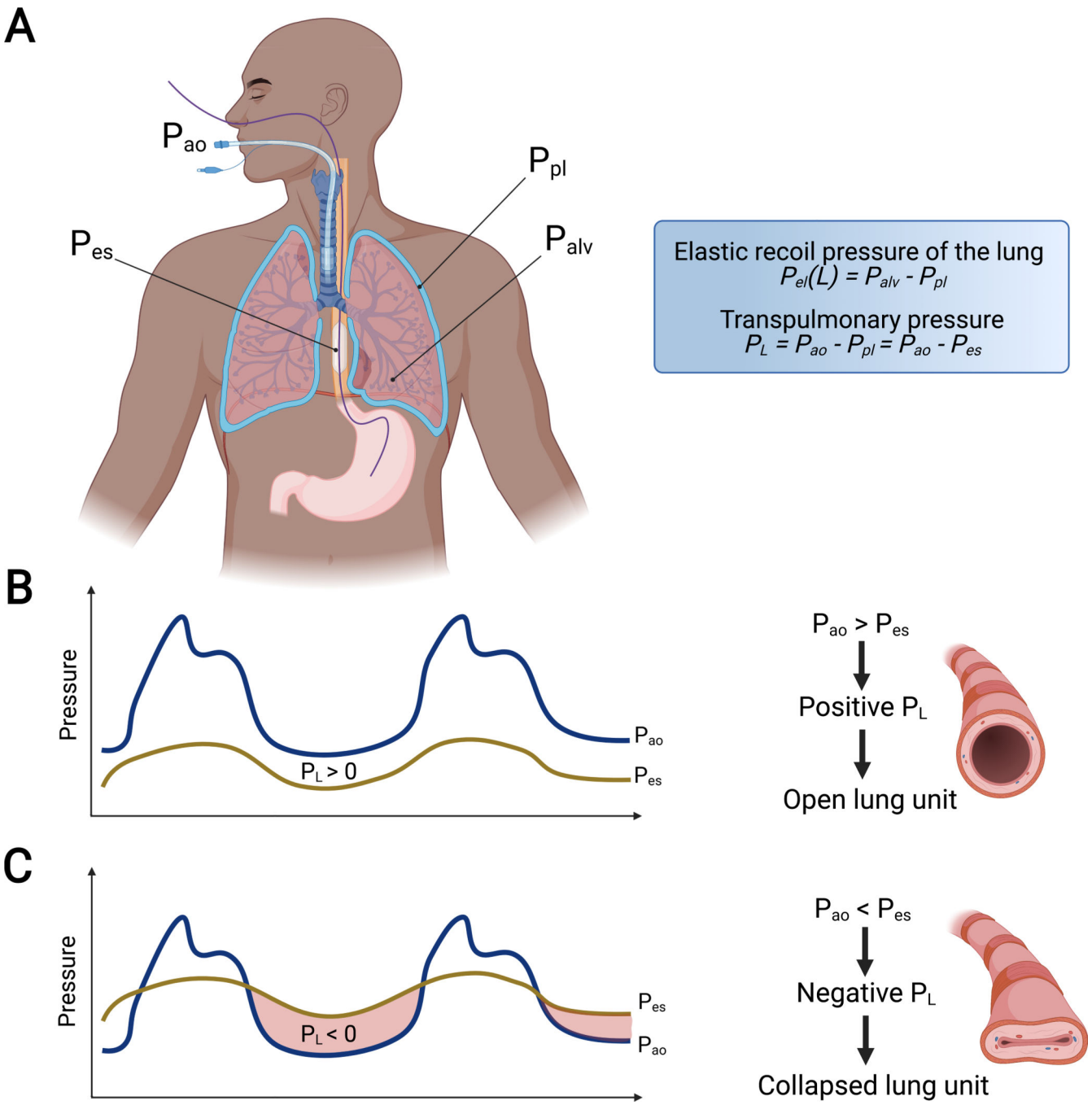

Figure 5:

Principles of esophageal manometry and the use of transpulmonary pressure. (A) position of the esophageal pressure balloon at the lower third of the esophagus, and relationship amongst the different pressures measured in the respiratory system. Transpulmonary pressure (P_L) is an approximate of the elastic recoil pressure of the lung or $P_{el}(L)$. (B) Selection of PEEP consistent with a positive P_L during the expiration period is expected to maintain alveoli recruited throughout the breathing cycle. (C) By contrast, negative P_L

allows for the collapse of lung units. P_{alv}=alveolar pressure; P_{ao}=pressure at airway opening; P_{es}=esophageal pressure; P_{pl}=pleural pressure.

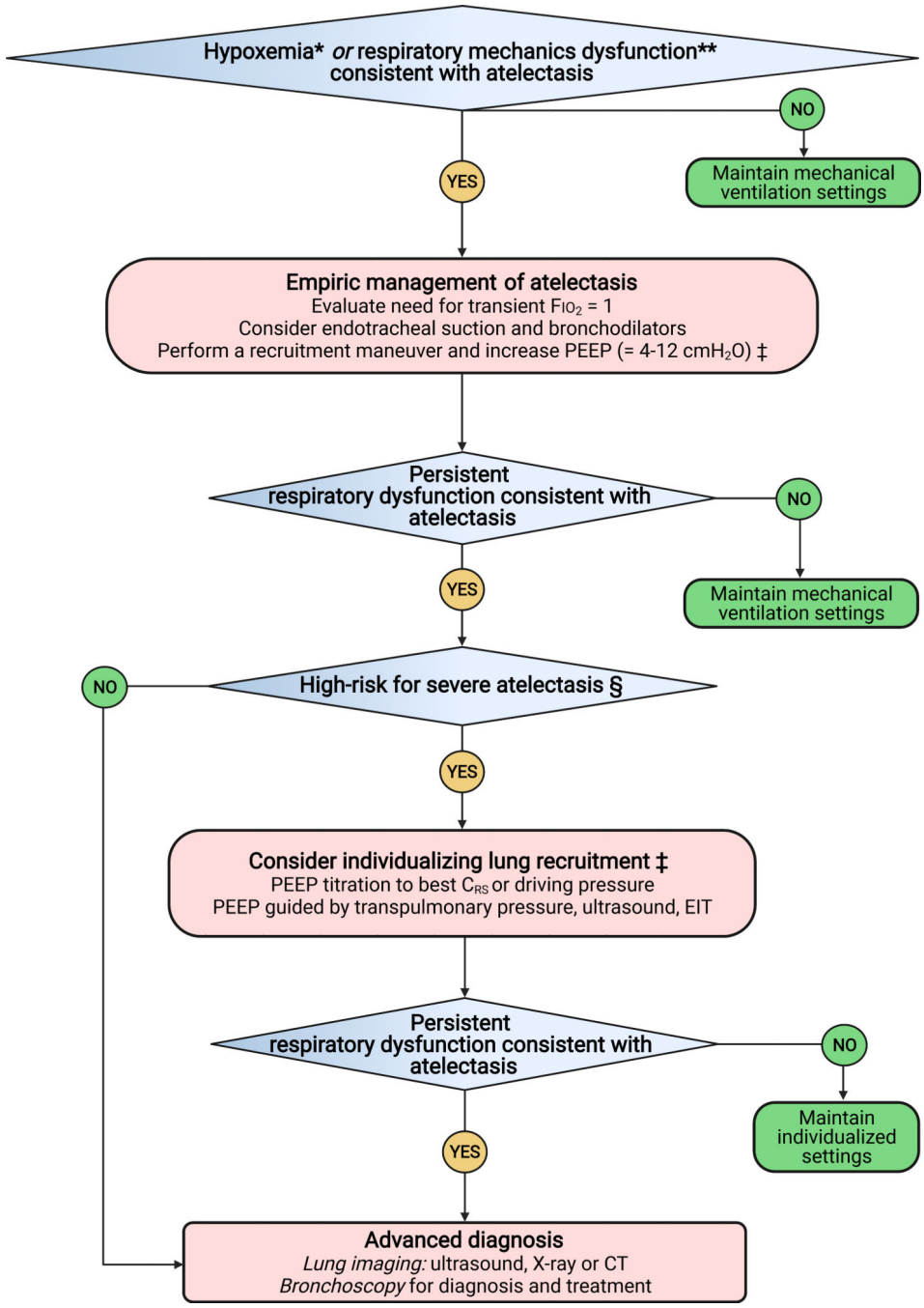

Figure 6:

Algorithm for intraoperative management of pulmonary atelectasis. A standard ventilatory strategy targeting surgical patients is implemented after anesthesia induction (PEEP 2–5 cmH_2O, no recruitment maneuvers, V_T 6–10 ml/kg of predicted body weight). In patients presenting intraoperative respiratory compromise consistent with pulmonary atelectasis, fixed higher PEEP is set following a recruitment maneuver. Attention is given to basic maneuvers to eliminate additional causes, e.g., secretions and bronchoconstriction, and maintain safety (transient increase in FIO_2). If the respiratory dysfunction persists despite

empiric alveolar expansion, an individualized strategy can be considered in high-risk conditions for atelectasis: PEEP titration targeting optimization of usually available (*e.g.*, compliance, driving pressure) or advanced respiratory measurements (transpulmonary pressure, ultrasound, electrical impedance tomography). If individualization of lung recruitment fails to improve lung function or in patients without specific risk for intraoperative atelectasis, a specific diagnostic approach should be implemented without delay using lung imaging or bronchoscopy. * hypoxemia may be defined by SpO_2 drop by more than 5% or FIO_2 increase by more than 30% to maintain oxygenation with PEEP=5cmH_2O (presuming other causes such as airway, ventilator, or hemodynamic issues have been excluded); ** significant respiratory mechanics change may be defined by a C_{RS} drop by more than 20%, or a driving pressure ≥15cmH_2O with PEEP=5cmH_2O and V_T=6ml/kg PBW; ‡ attend to hemodynamic stability during recruitment maneuvers; § BMI ⩾ 35 kg/m^2, pneumoperitoneum, Trendelenburg position, upper abdominal surgery with diaphragmatic surgical retractors, diaphragmatic injury, intraoperative lung injury or pulmonary edema. C_{RS}=compliance of the respiratory system; EIT= electrical impedance tomography.

Table 1:

Clinical risk factors for perioperative pulmonary atelectasis

Category	Risk factors
Patient-related	Body mass index > 25 kg/m^2 Age-dependent small airway closure Acute lung inflammation Non-inflammatory pulmonary edema Diaphragmatic and respiratory muscles dysfunction (amyotrophy, neurological or neuro-muscular disease) Abdominal hypertension (ileus, ascites, compartment syndrome, pregnancy) Bronchial congestion (*e.g.*, active tobacco consumption, chronic bronchitis) Chronic aspiration
Anesthesia-related	Diaphragmatic dysfunction (anesthesia depth, neuromuscular blockade, phrenic nerve block) High FIO_2 Nitrous oxide Lower tidal volume (without PEEP) Inappropriate neuromuscular blockade reversal Postoperative respiratory depression due to opioids or sedatives Fluid overload Transfusion related acute lung injury
Surgery-related	Body position (Trendelenburg, supine, lateral decubitus) Pneumoperitoneum One-lung ventilation Cardio-pulmonary bypass Surgery duration (cardio-thoracic, upper abdominal and laparoscopy) Open abdominal and thoracic surgery (postoperative pain)

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Table 2:

Randomized clinical trials on alveolar expansion strategies during general anesthesia.

Clinical Trial	Inclusion criteria		Groups								Outcomes	
			Intervention: Alveolar expansion				Control					
			Intraoperative				*Intraoperative*					
	Patients	*Surgery*	PEEP (cmH_2O)	RM	V_T (*ml/kg PBW*)	*Postoperative*	PEEP (cmH_2O)	RM	V_T (*ml/kg PBW*)	*Postoperative*	*Primary*	*Secondary*
IMPROVE[181] Multicenter (*n*=400)	BMI<35kg/m^2 Risk class>2*	Abdominal ≥ 2 hours	6–8	Yes	6–8	none	0	No	10–12	none	↓Pulmonary *or* Systemic Complications	↓ Postoperative atelectasis ↓Ventilatory support ↓Hospital LOS
PROVHILO[186] Multicenter (*n*=900)	BMI<40kg/m^2 Intermediate-high risk§	Open abdominal	12	Yes	8	none	≤2	No	8	none	No effect - Pulmonary Complications	Postoperative atelectasis: *NS* ↑Hypotension ↑Vasoactive drugs
iPROVE[192] Multicenter (*n*=1012)	BMI≤35kg/m^2 Intermediate-high risk§	Abdominal ≥ 2 hours	*I:* Titrated (C_{dyn}): 10±3	Yes	8	3h of CPAP (if SpO_2≤96% on room air)	5	No	8	Supplemental oxygen (Venturi mask)	No effect - Pulmonary *or* Systemic Complications	Group *I:* ↓Pulmonary atelectasis and complications; ↓ ICU LOS
			II: Titrated (C_{dyn}): 10±3	Yes	8	3h of CPAP						
			III: 5	No	8	3h of CPAP						
PROBESE[187] Multicenter (*n*=2013)	BMI≥35kg/m^2 Intermediate -high risk§	90% abdominal ≥ 2 hours	12	Yes	7	none	4	No	7	none	No effect - Pulmonary Complications	Postoperative atelectasis: *NS* ↑Hypotension ↑Bradycardia ↑Vasoactive drugs ↓Intraoperative hypoxemia
Karalapillai *et al.*[183] Single center (*n*=1236)	> 40 yo Invasive arterial pressure	56% abdominal ≥ 2 hours	5	No	10	none	5	No	6	none	No effect - Pulmonary Complications	Postoperative atelectasis: *NS* ↓Acidosis ↓Hypercapnia Similar PaO2/ FIO_2
PROVECS[101] Multicenter (*n*=494)	BMI<35kg/m^2	On-pump cardiac	8	Yes	6–8	*Before extubation:* RM 30cmH_2O PEEP 8cmH_2O	2	No	6–8	*Before extubation:* PEEP 2cmH_2O	No effect - Pulmonary Complications	Postoperative atelectasis: *NS* ↓Intraoperative hypoxemia

Clinical Trial	Inclusion criteria		Groups								Outcomes	
			Intervention: Alveolar expansion				Control					
	Patients	*Surgery*	*Intraoperative*			*Postoperative*	*Intraoperative*			*Postoperative*	*Primary*	*Secondary*
			PEEP (cmH_2O)	RM	V_T (*ml/kg PBW*)		PEEP (cmH_2O)	RM	V_T (*ml/kg PBW*)			
						After extubation: none				*After extubation:* none		
Leme *et al.* [199] Single center (*n*=320)	BMI<40kg/m^2 PaO2/FIO_2 <250 mmHg at ICU arrival	On- or Off-pump cardiac	-	-	-	*Before extubation:* RM 45cmH_2O PEEP 13cmH_2O	-	-	-	*Before extubation:* RM 20cmH_2O PEEP 8 cmH_2O	↓Pulmonary complications including atelectasis	↓ICU LOS ↓hospital LOS
						After extubation: CPAP if SpO_2<90% on O_2				*After extubation:* CPAP if SpO_2<90% on O_2		
PPV[182] Multicenter (*n*=346; *premature interruption*)	Lung cancer	Thoracic (one-lung ventilation)	*Two-lung:* 5–8	Yes	5	none	*Two-lung:* 0	Yes	10	none	↓Pulmonary complications including atelectasis	↓Systemic complications ↓Ventilatory support ↓Hospital LOS
			One-lung: 5–8		5		*One-lung:* 0	Yes	10			
Park *et al.* [154] Single center (*n*=312)	Lung or esophageal cancer	Thoracic (one-lung ventilation)	*Two-lung:* 5	Yes	6–8	Daily deep breathing exercises and incentive spirometry	*Two-lung:* 5	Yes	6–8	Daily deep breathing exercises and incentive spirometry	↓Pulmonary complications including atelectasis	No effect - ICU or hospital LOS
			One-lung: Titrated (DP): 3 [2,5]		6		*One-lung: 5*	Yes	*6*			

All listed trials were randomized, adequately powered to assess postoperative pulmonary outcomes, and included pulmonary atelectasis based on lung imaging at least as a component of the primary endpoint. *(BMI=Body mass index, C_{dyn}=Dynamic compliance of the respiratory system; CPAP= Continuous positive airway pressure; DP= Driving pressure of the respiratory system; LOS= Length of stay; NS= Nonsignificant; PBW= Predicted body weight; RM= Recruitment maneuver).*

* *Pulmonary risk quantified by Arozullah et al*[113];

§ *by ARISCAT*[283] *. Values shown as Mean (SD) or Median [IQR]*