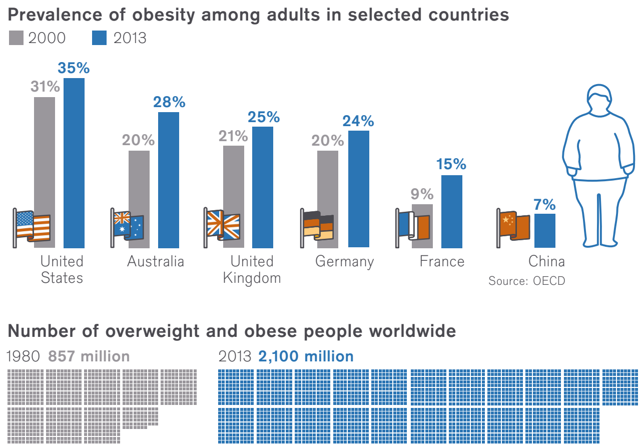
Perioperative Lung Protection

Intraoperative Ventilation of Obese Patients

Obesity leads to anatomical and physiological peculiarities that can cause threatening complications under general anaesthesia, and thus can worsen the results of an otherwise successful surgery. As an increasingly large proportion of obese people will need general anaesthesia at least once in their life, obesity is a major challenge for anaesthetists. In order to avoid complications, the management of general anaesthesia in obese patients requires different approaches for intraoperative ventilation compared to those customary for lean patients. In this whitepaper, we present the approaches required to minimise risks for obese patients during intraoperative ventilation, based on the anatomical and physiological effects of obesity on the respiratory system.

For literature-recommended approaches to pre-oxygenation and induction, please go to "Effective Pre-oxygenation and Induction in Obese Patients". (link).

According to the World Health Organization (WHO), in 2016, more than 1.9 billion adults were overweight, and of these, over 650 million were obese. In the same year, 41 million children under 5 years of age, and over 340 million 5- to 19-year-olds were overweight or obese. A recent report shows a prevalence of obesity of 32 % in males and 34 % in females in the US, while in the UK, 25 % of males and females are obese. In Germany, 21 % of the entire population is obese, and 37 % present as overweight, with numbers continuing to increase.



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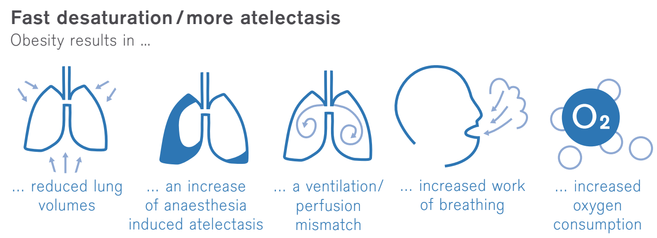
I. How the anatomy and physiology of obesity affects intraoperative ventilation.

The additional fat present in cases of obesity increases the thoracic and intra-abdominal pressure. The latter hinders diaphragm excursions, and leads to stiffening of the thoracic wall, a decrease in lung volume due to compression atelectasis, and a decrease in both chest wall and lung compliance. Furthermore, compression of the small airways increases resistance and promotes airway closure during expiration.[2,3,4,5,6] The resulting diaphragmatic elevation, which ultimately is a consequence of the compression and eventual collapse of lung tissue caused by pressure transmission from the abdomen on pleura and lungs,[7,8] increases further in a supine position and even more in the Trendelenburg position.[7,9] Compression atelectasis occurs when the local pleural pressure is higher than the airway pressure in the alveoli.The high abdominal pressure may also increase the pressure on the lower vena cava and thus shift blood from the abdomen to the thorax, which further increases pressure on the alveoli.[10,11,12]

Overall, atelectasis can be detected during general anaesthesia in up to 90 % of all patients.[13] Even if the patient is only moderately overweight,[14] the above-mentioned circumstances can reduce functional residual capacity (FRC) and, during mechanical ventilation[15], reduce end-expiratory lung volume (EELV). This may result in very low respiratory reserves, making it more challenging to manage the airway and apply lung-protective ventilation strategies in terms of low volumes and pressures. In turn, this can have consequences for the postoperative phase, such as persistence of atelectasis. In morbidly obese patients, the FRC can reduce by as much as 50 % after induction of general anaesthesia.[10,11,12,16]

For a detailed summary of the pathophysiological changes in obese patients, and literature-recommended approaches to pre-oxygenation and induction, please read Effective Pre-oxygenation and Induction in Obese Patients.



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II. Additional factors that can influence intraoperative ventilation and the postoperative phase in obese patients.

In addition to the above-mentioned complication, the following circumstances should be kept in mind, which might have a direct effect on intraoperative ventilation of obese patients due to the extra amount of fatty tissue on the thorax wall and inside and outside the abdomen.

Supine position in the OR

While obese patients already have around 20 % less lung volume than expected before induction of anaesthesia,[13] in a supine position their lung volume is further reduced by about 50 %.[17] The trans diaphragmatic pressure fluctuations also in-crease significantly, leading to lung tissue strain and increased work of breathing in the spontaneously breathing patient, e. g., during induction or in the post-op phase.[9] In a study, 7 out of 8 patients showed flow restriction due to collapse of the small airways in a supine position, compared to 2 out of 8 patients in upright position. Steier et al.[9] measured in their study an aver-age intrinsic PEEP (PEEPi) of 5.3 cm H_2O in obese patients in a supine position. Pankow et al.[10] were in agreement with this finding and showed that the PEEPi in obese patients increased from 1.4 cm H_2O to 4.1 cm H_2O when changing from an upright to a supine position. On average PEEPi, increases by 0.2 cm H_2O per unit of BMI,[10] when supine. "Even without anaesthesia, obese patients in a supine position can have significant ventilation restrictions," warns Prof. Dr. med. Hermann Wrigge from the Department of Anaesthesiology and Intensive Care at the University of Leipzig. He continues, "Patients should therefore remain upright as long as possible, and at least when on PACU or ICU and medically feasible, and if surgery allows, all patients with BMI > 40 kg/m^2 should be ventilated in an elevated upper body position". Another way of relieving the pressure on the diaphragm and optimising intraoperative ventilation is to maintain reverse Trendelenburg positioning from the induction of anaesthesia until immediately after extubation[18].

Increased work of breathing

Obesity is associated with increased work of breathing, mainly as a result of increased airway resistance and decreased respiratory system compliance.[10,19,20,21] This limits the expiratory flow, and leads to air entrapment due to early closing of airways and subsequent generation of intrinsic positive end-expiratory pressure (PEEPi)[11], and ventilation perfusion mismatch due to atelectasis. "This does not play a major role during controlled ventilation in a general anaesthesia because the ventilator does the work," Prof. Wrigge says. "The problem of increased respiratory work becomes relevant in the post-operative phase on PACU and ICU. If the extubated patient is missing half of the lung volume postoperatively due to atelectasis and has a high in-trinsic PEEP, this means increased work of breathing."

Obstructive sleep apnoea (OSA)

OSA is associated with a higher incidence of postoperative acute respiratory failure, cardiac events, and intensive care unit (ICU) stays. Studies estimate the prevalence of OSA to be between 2 and 24 % of the population,[22,23,24] with half of all patients with a BMI > 40 kg/m^2 suffering from OSA.[25] Because of endotracheal intubation, OSA does not directly influence intraoperative ventilation.[26] Even on the post anaesthesia care unit (PACU) or the intensive care unit (ICU), usually no characteristic apnoea occurs. This may be caused by an opioid-induced change in sleep pattern resulting in a decreased incidence of obstructive episodes. However, central apnoea episodes may increase under the influence of opioids. "OSA influences spontaneous breathing after waking up from general anaesthesia, mainly due to the effect of the opiates given during surgery. Apnoea occurs more frequently under the influence of opiates, thus anaesthetists should work opiate-preventative or with short acting opiates and be economical with opiates to mitigate the risk of respiratory problems," Prof. Wrigge warns. "Since CPAP reduces the frequency of apnoea, treatment with CPAP should start right after extubation and continue in the PACU and, at best, even in the regular ward."

In this context, it should be remembered that OSA episodes mainly happen during the rapid eye movement (REM) phases of sleep. Opioids may reduce REM and slow wave sleep, thus resulting in a decreased incidence of obstructive episodes in this phase.[26] "Obese patients often show a pathological sleep pattern without REM phases after waking up from general anaesthesia in the PACU or ICU," Prof. Wrigge explains. "Thus, OSA might not be observed in the PACU or on the ICU, and it might be incorrectly assumed that there is no OSA problem." However, obstructive events may recur with increased frequency and severity during an intense REM sleep rebound after the third postoperative night in the regular ward.[26] "This is frequently not taken into account when the patient is no longer under the direct control of the anaesthetist, e.g., on a regular ward. Ideally, CPAP therapy should therefore be continued after extubation not only because of the danger of increased postoperative atelectasis, but also because OSA returns when the REM phases begin again. This could also be a future domain for telemetric monitoring."

Remember?

Intrinsic PEEP (PEEPi) is caused by as air trapping. PEEPi occurs when the expiratory time is shorter than the time needed to fully deflate the lungs, preventing the lung and chest wall from reaching an elastic equilibrium point. Steier et al. found that the single independent predictor for the development of PEEPi is BMI. On average, in their study, PEEPi increased by 0.2 cm H_2O per unit of BMI when supine.[10]

Acute respiratory distress syndrome (ARDS) in obese patients

ARDS can be the result of postoperative pulmonary complications, which occur, if at all, a few days after surgery. "Although ARDS is an extremely rare complication in general, obese patients may be at increased risk due to their more pronounced atelectasis, poor breathing mechanics and often concomitant metabolic diseases," Prof. Wrigge explains. As recent studies and meta-analyses[27,28] suggest, even widespread non-protective intraoperative ventilatory practices can induce ARDS. Therefore, lung-protective ventilation regimens should be deployed in order to minimise the risk.

All patients with ARDS should be ventilated according to lung-protective principles. "This means a small V_T of 6 – 8 ml, a driving pressure of less than 13 – 15 cm H_2O, and an adequate PEEP between 10 – 26 cm H_2O," advises Prof. Wrigge. "But it should be kept in mind that a higher respiratory pressure increases the intrathoracic pressure and thus requires higher fluid demand or vasopressors to keep up the filling volume in the heart and maintain adequate perfusion pressure," explains Prof. Wrigge.

III. How adaptations in the approach to intraoperative ventilation can avoid complications[29]

Morbidly obese patients present with specific physiological and mechanical properties of the lung as mentioned above. These properties can affect the entire process of general anaesthesia, and may cause severe postoperative pulmonary complications. Thus, the known risks of general anaesthesia increase dramatically. "Almost all these complications can be deduced from a reduced lung volume," Prof. Wrigge explains. However, intraoperative lung-protective ventilation is associated with a reduced risk of these complications.[30] It consists mainly of the following adaptations:

Which obesity level corresponds to which BMI?[1]

BMI	Nutritional status
Below 18.5	Underweight
18.5 – 24.9	Normal weight
25.0 – 29.9	Pre-obesity
30.0 – 34.9	Obesity class I
35.0 – 39.9	Obesity class II
Above 40	Obesity class III

Tidal Volume (V_T) and Driving Pressure (DP).

"V_T should be limited to 6 – 8 ml/kg predicted body weight (PBW), not actual body weight, as lungs do not grow with body fat. This V_T can usually be achieved by driving pressures below 13 cm H_2O in obese patients with healthy lungs. That applies especially to morbidly obese patients," says Prof. Wrigge. With regard to calculating the correct V_T, due to false estimation of ideal body weight (IBW), small overweight women are most at risk of being ventilated with too high a V_T. "For a lung-protective intraoperative ventilation with low V_T and DP of 13 cm H_2O maximum, good lung compliance and thus an open lung is essential," Prof. Wrigge explains. "Lungs with atelectasis tend to be stiff because a lower lung volume has to take the V_T, which means that lung compliance is significantly lower. In order to be able to apply the above lung protective pressures during intraoperative ventilation, the atelectasis may need to be dissolved with a recruitment manoeuvre, so the lung compliance increases or even normalizes."

In this context, gas dosing with a focus on O_2 to avoid additional resorption atelectasis is controversial. "It is known that 80 % oxygen prevents resorption atelectasis. However, if a patient is pre-oxygenated with 80 % oxygen and ventilation problems occur along the process, the time to correct the problem is shorter if there is less oxygen in the alveoli," Prof. Wrigge explains. Thus, a lower F_IO_2 during induction of anaesthesia is not recommended.

Recruitment manoeuvre (RM).[31]

If high DP is needed to achieve adequate tidal volume in obese patients, it indicates poor compliance of the lungs, which is usually due to atelectasis. RM with subsequent setting of adequate PEEP would be necessary to improve compliance. Perioperative lung protective ventilation consists of low V_T, low driving pressures and also an initial RM.[32] In obese patients, this combination can reduce the risk of postoperative pulmonary complications.[33] An RM means that the lung is ventilated with intermittent higher plateau pressure. When properly performed, an RM can increase FRC by opening the atelectatic lung areas and thus prevent hypoxemia, improve oxygen saturation and airway compliance, as well as reduce respiratory work. “It is important to know that the recruitment of basal lung regions which are strongly affected by atelectasis can be difficult due to the much higher pressure required for this under mechanical ventilation,” warns Prof. Wrigge. “Excessive recruitment pressure, i.e. more than 60 cm H_2O, can lead to complications that are fatal in the end, especially in patients with ARDS. Obesity requires pressures of 50 – 55 cm H_2O for RM. However, this is basically harmless for lung healthy people, if hemodynamic consequences are treated with vasopressors.”

Stepwise Recruitment manoeuvre.

Various approaches to the recruitment of atelectatic lung areas exist. Performing an RM with the manual ventilation bag is widespread, although high pressure peaks can lead to severe hemodynamic and pulmonary side effects. “Recruitment with the bag means that uncontrolled high pressures are applied because the pressure exerted with the bag cannot be controlled easily; when switching over to mechanical ventilation, PEEP may also be briefly lost,” explains Prof. Wrigge. “The ventilator, on the other hand, offers full pressure control and no PEEP drop. Thus, the bag method is not recommended any longer.”

A stepwise RM is a ventilator-controlled procedure that may cause less hemodynamic, inflammatory, and barotraumatic complications.[34, 35, 36, 37, 38] To recruit the lung, and thus determine the optimal PEEP, the pressure is stepwise increased under control of the ventilation parameters and hemodynamics. The delta between inspiratory pressure and PEEP (driving pressure) is kept constant,[13] whereby the maximum pressure must be at least equal to the alveolar opening pressure. “If the PEEP is sufficiently high after the recruitment manoeuvre, you only have to recruit once,” Prof. Wrigge explains.

The stepwise manoeuvre can be individually adapted to the patient, if changes in compliance and hemodynamics are ob-served in the RM process. The manoeuvre can be discontinued when the oxygen saturation is sufficient, or if hemodynamics collapse. Finally, the optimum PEEP is read off at the decremental branch of the stepwise manoeuvre and can be set accord-ingly. A second recruitment is then carried out followed by the previously set PEEP. The main advantage of the stepwise RM is that it consists of an incremental and a decremental part. “In the incremental part, the opening pressure of the atelectasis is gently overcome by gradually increasing the pressure level,” explains Prof. Wrigge. “The body better adapts to the increasing pressure, which reduces the side effects of high ventilation pressures and prevents severe hemodynamic side effects. The decremental part of the manoeuvre is then used to measure the PEEP, which is then able to maintain the recruited status.[39] In this regard, studies document a lower release of inflammatory mediators with in-creased compliance and oxygenation.[40] In addition, new studies confirm the better toleration of a stepwise recruitment, with fewer alveolar lesions and less endothelial cell damage.[41]

A disadvantage of the stepwise RM is its longer duration and the number of operating steps. Australian anaesthetist Dr. Chris Thompson presented a very pragmatic recruitment process at the 2015 annual meeting of the Australian and New Zealand College of Anaesthetists (ANZCA). Essentially, the process consists of determining the patient-specific PEEP by comparing the V_T/PEEP curve in the incremental versus decremental phase of the stepwise recruitment manoeuvre, and determining the PEEP for the individual patient in the decrement phase where the compliance is best. (link to video).

For a detailed summary of recruitment manoeuvres see (link).

Adequate individual PEEP post-RM.[10,42,43]

Ideally, an RM should be followed by the adequate patient-specific PEEP determined by the stepwise M to prevent new atelectasis.[44,45,46,47,48,49] Some studies[50] suggest low V_T ventilation with a PEEP of 6 – 8 cm H_2O for this purpose. Other studies show that a PEEP of 10 – 18 cm H_2O is more effective in improving oxygenation and reducing atelectasis than a PEEP of 5 cm H_2O or a pure RM without PEEP.[12,17,51] Pelosi et al. showed that the application of a PEEP of 10 cm H_2O in morbidly obese patients led to improved oxygenation. “These results do not mean that the lung remains open with a PEEP of e. g. 6, 8, 10 or 18 cm H_2O,” explains Prof. Wrigge. “But clearly a PEEP, which keeps the lungs open after RM is crucial, because the small airways and alveoli collapse and atelectasis reoccur when PEEP is too low. According to recent studies, the PEEP should therefore be in the range of 10 – 26 cm H_2O, ideally as a result of a patient-specific stepwise RM.”

Although there is evidently no consensus on PEEP parameters in obese patients, there are indeed indications that a significantly higher PEEP is required post-RM to prevent repeated atelectasis.[34] It seems obvious that this is useful for reducing complications, but scientific evidence has yet to be provided. “The high PEEP levels required to keep an obese patient’s lungs open can result in severe hemodynamic side effects with increased catecholamine and fluid requirements,” Prof. Wrigge explains. “But it is still unclear whether an ‘open lung’ justifies these side effects. A study with about 2,000 obese patients investigating the effect of PEEP 4 versus 12 is underway.”[52]

IV. Executive summary.

Obese patients present with specific lung physiology and mechanical characteristics, and have an increased risk of postoperative pulmonary complications. Intraoperatively, lung-protective ventilation with a low V_T, and RMs with much higher PEEP levels than currently used are recommended. In this context, a stepwise RM has been shown to be advantageous for obese patients, provided that an individualised patient-specific PEEP is set.

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REFERENCE:

1 *World Health Organization, Regional Office Europe, http://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi; retrieved on 3 November 2017*

2 *Rossaint R., Werner Ch.: Die Anästhesiologie: Allgemeine und spezielle Anästhesiologie, Schmerztherapie und Intensivmedizin, 3. Auflage, Springer Verlag*

3 *Salome CM, Munoz PA, Berend N, et al. Effect of obesity on breathlessness and airway responsiveness to methacholine in non-asthmatic subjects. Int J Obes (Lond) 2008;32:502-9.*

4 *Eriksen J, Andersen J, Rasmussen JP, et al. Effects of ventilation with large tidal volumes or positive endexpiratory pressure on cardiorespiratory function in anesthetized obese patients. Acta Anaesthesiol Scand 1978;22:241-8.*

5 *Hackney JD, Crane mg, Collier CC, et al. Syndrome of extreme obesity and hypoventilation: studies of etiology. Ann Intern Med 1959;51:541-52*

6 *Pelosi P, Croci M, Ravagnan I, et al. The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. Anesth Analg 1998;87:654-60.*

7 *Hodgson LE, Murphy PB, Hart N. Respiratory management of the obese patient undergoing surgery. J Thorac Dis. 2015 May;7(5):943-52.*

8 *Ferretti A, Giampiccolo P, Cavalli A, et al. Expiratory flow limitation and orthopnea in massively obese subjects. Chest 2001;119:1401-8.*

9 *Steier J, Jolley CJ, Seymour J, et al. Neural respiratory drive in obesity. Thorax. 2009 Aug;64(8):719-25.*

10 *Pankow W, Podszus T, Gutheil T, et al. Expiratory flow limitation and intrinsic positive end-expiratory pressure in obesity. J Appl Physiol (1985) 1998;85:1236-43.*

11 *Smetana GW. Preoperative pulmonary evaluation. N Engl J Med 1999;340:937-44.*

12 *Reinius H, Jonsson L, Gustafsson S, et al. Prevention of atelectasis in morbidly obese patients during general anesthesia and paralysis: a computerized tomography study. Anesthesiology 2009;111:979-87.*

13 *Eichenberger A, Proietti S, Wicky S, et al. Morbid obesity and postoperative pulmonary atelectasis: an underestimated problem. Anesth Analg. 2002 Dec;95(6):1788-92.*

14 *Salome CM.: Physiology of obesity and effects on lung function; Physiology of obesity and effects on lung function; J Appl Physiol 108: 206–211, 2010.*

15 *Rubinstein I, Zamel N, DuBarry L, et al. Airflow limitation in morbidly obese, nonsmoking men. Ann Intern Med 1990;112:828-32.*

16 *Tanoubi I, Drolet P, Donati F. Optimizing preoxygenation in adults. Can J Anaesth. 2009 Jun;56(6):449-66.*

17 *Nestler, C., Wrigge H. et al.: Individualized positive end-expiratory pressure in obese patients during general anesthesia: a randiomized controlled clinical trial using electrical impedance tomography; Br J Anaesth. 2017 Oct 16. doi: 10.1093/bja/aex192. [Epub ahead of print]*

18 *Schumann, R.: Pulmonary Physiology of the Morbidly Obese and the Effects of Anesthesia. International Anesthesiology Clinics. 51 (3): 41-51, summer 2013 DOI: 10.1097/AIA. 0b013e3182981252.*

19 *Sharp JT, Henry JP, Sweany SK, et al. The total work of breathing in normal and obese men. J Clin Invest 1964;43:728-39.*

20 *Zerah F, Harf A, Perlemuter L, et al. Effects of obesity on respiratory resistance. Chest 1993;103:1470-6.*

21 *Kress JP, Pohlman AS, Alverdy J, et al. The impact of morbid obesity on oxygen cost of breathing (VO(2RESP)) at rest. Am J Respir Crit Care Med 1999;160:883-6.*

22 *Mandal S, Hart N. Respiratory complications of obesity. Clin Med 2012;12:75-8.*

23 *Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. NEngl J Med 1993;328:1230-5.*

24 *Young T, Peppard PE, Taheri S. Excess weight and sleepdisordered breathing. J Appl Physiol (1985) 2005;99:1592-9.*

25 *Resta O, Foschino-Barbaro MP, Legari G, et al. Sleeprelated breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. Int J Obes Relat Metab Disord 2001;25:669-75.*

26 *Lam KK et al.: Obstructive sleep apnea, pain, and opioids: is the riddle solved? Curr Opin Anaesthesiol. 2016 Feb; 29(1): 134–140. Published online 2015 Nov 28. doi:10.1097/ACO.0000000000000265 PMCID: PMC4927322*

27 *Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Esposito DC, Pasqualucci Mde O, et al. Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. JAMA. 2012;308(16):1651–9.*

28 *Hemmes SN, Serpa Neto A, Schultz MJ. Intraoperative ventilatory strategies to prevent postoperative pulmonary complications: a meta-analysis. Curr Opin Anaesthesiol. 2013;26(2):126–33.*

29 *Murphy C et al.: Airway management and oxygenation in obese patients; Can J Anesth/J Can Anesth (2013) 60:929–945.*

REFERENCE:

30 *Ladha K. et al.: Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study, BMJ 2015;351:h3646.*

31 *Futier E et al.: Noninvasive Ventilation and Alveolar Recruitment Maneuver Improve Respiratory Function during and after Intubation of Morbidly Obese Patients; Anesthesiology 2011; 114:1354 – 63.*

32 *Ball L, Pelosi P: Intraoperative mechanical ventilation in patients with non-injured lungs: time to talk about tailored protective ventilation?; Ann Transl Med. 2016 Jan;4(1):17.*

33 *Futier E, Marret E, Jaber S; Perioperative Positive Pressure Ventilation: An Integrated Approach to Improve Pulmonary Care, Anesthesiology. 2014 Aug;121(2):400-8.*

34 *Andreas Güldner & Marcelo Gama de Abreu: Intraoperative protective ventilation reduces postoperative pulmonary complications, Anästhesiol Intensivmed Notfallmed Schmerzther 2015; 50(9): 524-528.*

35 *Expert Interview with Prof. Dr. med. Hermann Wrigge, University Hospital Leipzig, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, 03.11.2016.*

36 *Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G.; Dynamics of re-expansion of atelectasis during general anaesthesia.; Br J Anaesth. 1999 Apr;82(4):551-6.*

37 *Tusman G, Groisman I, Fiolo FE, Scandurra A, Arca JM, Krumrick G, Bohm SH, Sipmann FS; Noninvasive monitoring of lung recruitment maneuvers in morbidly obese patients: the role of pulse oximetry and volu-metric capnography. Anesth Analg. 2014 Jan;118(1):137-44.*

38 *Pelosi P, Gama de Abreu M, Rocco PR; New and conventional strategies for lung recruitment in acute respiratory distress syndrome. Crit Care. 2010;14(2):210.*

39 *Suarez-Sipmann, Böhm SH, Tusman G, Pesch T, Thamm O, Reissmann H, Reske A, Magnusson A, Hedenstierna G.; Use of dynamic compliance for open lung positive end-expiratory pressure titration in an experi-mental study.; Crit Care Med. 2007 Jan;35(1):214-21.*

40 *Hodgson C et al. A randomised controlled trial of an open lung strategy with staircase recruitment, titrated PEEP and targeted low airway pressures in patients with acute respiratory distress syndrome, Crit Care. 2011; 15(3): R133. Published online 2011 Jun 2.*

41 *Santos RS, Moraes L, Samary CS, Santos CL, Ramos MB, Vasconcellos AP, Horta LF, Morales MM, Capelozzi VL, Garcia CS, Marini JJ, Gama de Abreu M, Pelosi P, Silva PL, Rocco PR; Fast Versus Slow Recruit-ment Maneuver at Different Degrees of Acute Lung Inflammation Induced by Experimental Sepsis, Anesth Analg. 2016 Apr;122(4):1089-100. doi: 10.1213/ANE.0000000000001173.*

42 *Futier E et al.: Positive end-expiratory pressure improves end-expiratory lung volume but not oxygenation after induction of anaesthesia; Eur J Anaesthesiol 2010;27:508–513.*

43 *Barbosa FT et al.: Positive end-expiratory pressure (PEEP) during anaesthesia for prevention of mortality and postoperative pulmonary complications (Review); 2014, The Cochrane Collaboration. Published by JohnWiley & Sons, Ltd.*

44 *Brismar B, Hedenstierna G, Lundquist H, et al. Pulmonary densities during anesthesia with muscular relaxation—a proposal of atelectasis. Anesthesiology 1985;62:422-8.*

45 *Neumann P, Rothen HU, Berglund JE, et al. Positive endexpiratory pressure prevents atelectasis during general anaesthesia even in the presence of a high inspired oxygen concentration. Acta Anaesthesiol Scand 1999;43:295-301.*

46 *Tokics L, Hedenstierna G, Strandberg A, et al. Lung collapse and gas exchange during general anesthesia: effects of spontaneous breathing, muscle paralysis, and positive end-expiratory pressure. Anesthesiology 1987;66:157-67.*

47 *Clarke JP, Schuitemaker MN, Sleigh JW. The effect of intraoperative ventilation strategies on perioperative atelectasis. Anaesth Intensive Care 1998;26:262-6.*

48 *Maracajá-Neto LF, Verçosa N, Roncally AC, et al. Beneficial effects of high positive end-expiratory pressure in lung respiratory mechanics during laparoscopic surgery. Acta Anaesthesiol Scand 2009;53:210-7.*

49 *Meininger D, Byhahn C, Mierdl S, et al. Positive endexpiratory pressure improves arterial oxygenation during prolonged pneumoperitoneum. Acta Anaesthesiol Scand 2005;49:778-83.*

50 *Futier E, Constantin JM, Paugam-Burtz C, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013;369:428-37.*

51 *Talab HF, Zabani IA, Abdelrahman HS, Bukhari WL, Mamoun I, Ashour MA, Sadeq BB, El Sayed SI; Intraoperative ventilatory strategies for prevention of pulmonary atelectasis in obese patients undergoing laparo-scopic bariatric surgery. Anesth Analg. 2009 Nov;109(5):1511-6.*

52 *Bluth T. et al.: Protective intraoperative ventilation with higher versus lower levels of positive end-expiratory pressure in obese patients (PROBESE): study protocol for a randomized controlled trial; Trials. 2017 Apr 28;18(1):202. doi: 10.1186/s13063-017-1929-0.*

