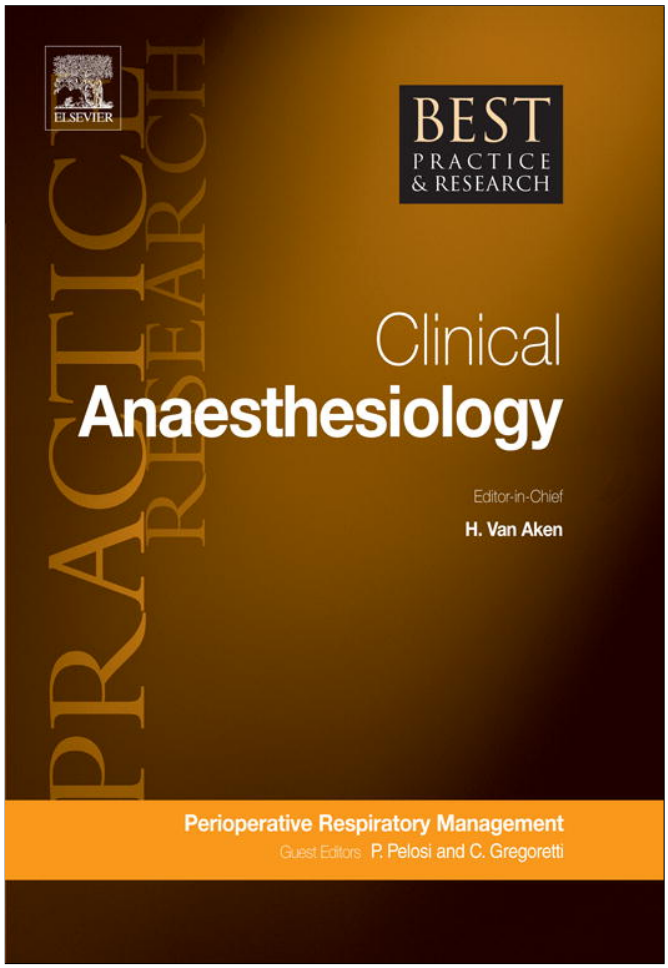

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Prevention and reversal of lung collapse during the intra-operative period

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General anaesthesia induces ventilation/perfusion mismatch by lung collapse. Such lung collapse predisposes patients to preoperative complications since it can persist for several hours or days after surgery.

Atelectasis can be partially prevented by using continuous positive airway pressure (CPAP) and/or by lowering FiO_2 during anaesthesia induction. However, these manoeuvres are dangerous for patients presenting with challenging airway or ventilator conditions.

Lung recruitment manoeuvres (RMs) are ventilatory strategies that aim to restore the aeration of normal lungs. They consist of a brief and controlled increment in airway pressure to open up collapsed areas of the lungs and sufficient positive end-expiratory pressure (PEEP) to keep them open afterward. The application of RMs during anaesthesia normalises lung function along the intra-operative period. There is physiological evidence that patients of all ages and any kind of surgery benefit from such an active intervention. The effect of RMs on patient outcome in the post-operative period is, however, not yet known.

General anaesthesia causes collapse in the most dependent parts of the lungs in almost all patients.[1,2] The lung collapses very rapidly during the induction of anaesthesia and this collapse persists for hours or even days after surgery.[3,4] The collapsed lung areas do not only impair gas exchange but might provoke other complications in the preoperative period.[5–7]

This article focuses on solutions for the ubiquitous problem of lung collapse on both, the preventive measures as well as therapeutic interventions.

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Physiological background of lung collapse and recruitment

The surface tension between the two mediums, gas and blood, which meet at the alveolar–capillary membrane lead to a natural instability of the lung tissue. Three main factors tend to stabilise the lung parenchyma and keep it free from collapse. The first of these is the lung's natural surfactant, which preserves the lung architecture by decreasing alveolar surface tension, especially at end-expiration. The second one is the mechanical support of the parenchyma by the elastic/collagen fibres of the lung interstice. The 'tethering' of these fibres decreases the radial stress within the acini at end-expiration.[8] The third factor is the outward directed transpulmonary pressure (Ptp) or the difference between airway (Paw) and pleural (Ppl) pressures during the entire respiratory cycle. Pulmonary diseases, general anaesthesia and mechanical ventilation have negative effects on all of these factors and therefore make the lungs prone to collapse.[2,9,10]

Lung collapse develops at the acinar level, the same location where respiratory gases are exchanged. There are three potential sites of collapse within the lung unit, which are responsible for the mismatch of ventilation and perfusion (V/Q) as can be observed during general anaesthesia:

- Alveolar collapse, the loss of aeration of a whole acinus also known as atelectasis. It is commonly caused by the mechanisms of resorption of oxygen, lack of sufficient distending pressures and also by a physical compression of the lung tissue within the dependent lung zones. Atelectasis also causes shunt.[1,2]
- Bronchiolar collapse or airway closure creates lung zones, the ventilation of which is low relative to their respective perfusion (low V/Q). Due to the lack of an adequate supply of fresh gas, these zones easily convert to completely collapsed and thus shunting zones by resorption.[11–14]
- Capillary collapse increases alveolar dead space, zones characterised by a high ratio of ventilation and perfusion (high V/Q). This kind of collapse can be seen in the more ventrally located areas of the lung where the combination of high airway pressures in conjunction with an absolute or relative intravascular hypovolaemia render the vasculature prone to collapse.[15] Zones of capillary collapse can also be found in dependent atelectatic parts of the lungs and can be the result of an intact hypoxic pulmonary vasoconstriction reflex.[16]

Lung collapse is a pressure-dependent phenomenon. Each acinus has a critical closing pressure, i.e., the minimum Ptp below which the acinus begins to collapse. While Paw is homogeneously distributed within all lung units, Ppl increases along the vertical gravitational vector because of the lung's weight. As a consequence, the decreased Ptp in the dependent zones promotes collapse. This means that patients in the supine position suffer from increasing closing pressures in the ventral to dorsal direction (Fig. 1). The lowest Ptp is reached at end-expiration and thus, at least initially, lung collapse is primarily an expiratory phenomenon.

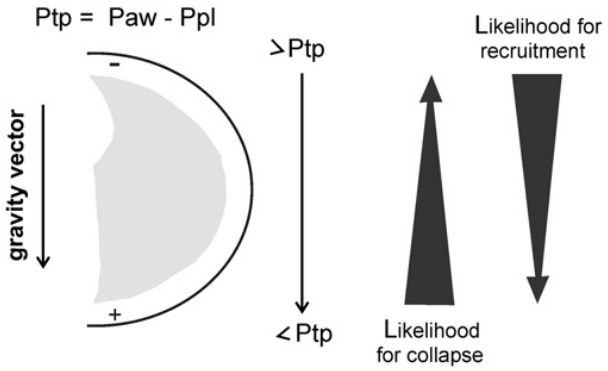

Fig. 1. Axial view of the right hemi-thorax. Trans-pulmonary pressure (Ptp) is the difference between airway pressure (Paw) and pleural pressure (Ppl). In mechanical ventilation, the Paw is positive and homogeneously distributed within lungs while the Ppl shows a vertical gradient of pressure following the gravity vector. This results in higher Ptp in the ventral zones and lower Ptp in more dependent areas of the lungs. Lung collapse predominates in the dependent lung because the closing pressures of alveoli located in this dependent zone become exceed the low Ptp. Moving upward towards the non-dependent areas of the lungs the tendency for collapse diminishes progressively. The opposite is true for the opening pressure and the potential for a successful recruitment.

Lung recruitment is defined as any manoeuvre aimed at recovering collapsed lung areas.[17] Numerous natural manoeuvres such as crying, coughing, sneezing, sighing, expectorating or postural changes have recruiting effects. Most of these physiological manoeuvres are executed subconsciously and frequently, which might explain why healthy patients undergoing general anaesthesia overcome the problem of lung collapse quite quickly after surgery.

However, when talking about recruitment manoeuvres (RMs) in mechanically ventilated patients we refer to intentional therapeutic strategies designed to treat lung collapse. These manoeuvres were primarily applied in patients with acute lung injury (ALI),[17] but their potential role in the treatment of anaesthesia-induced atelectasis in the operating room was first described by our group based on the pioneering physiological work of Rothen et al.[18,19]

Like lung collapse, lung recruitment too is a pressure-dependent phenomenon. Each lung unit has a critical opening pressure or a minimum Ptp value where this particular unit changes its state from collapsed to open. The typical potential for lung recruitment decreases from ventral to dorsal. This means that recruitment is continuous and follows the Ptp gradient, which begins in ventral areas and ends in the most dependent zones of the lung (Figure 1). During mechanical ventilation, the highest Ptp is reached at end-inspiration, thereby making lung recruitment an inspiratory phenomenon.

Prevention of lung collapse during induction, maintenance and emergence from anaesthesia

Anaesthesia induction

The literature discloses two main strategies for the prevention of lung collapse during anaesthesia induction. One of these is the use of continuous positive airway pressure (CPAP) before endotracheal intubation. It is argued that CPAP prevents the loss of functional residual capacity (FRC) typically seen during anaesthesia induction by maintaining sufficient positive pressure within the airways and alveoli at the end of expiration. The assumption is that compression atelectasis can be avoided if Ptp is maintained higher than the closing pressure. Rusca et al. proved this hypothesis in patients with normal weight. During induction of anaesthesia, 6 cmH_2O of CPAP significantly reduced atelectasis formation when compared to a group ventilated without CPAP.[20] The same result was observed in children, where 6 cmH_2O of CPAP maintained normal FRC and oxygenation regardless of the FiO_2 used.[21] Coussa et al. observed in morbidly obese patients that 10 cmH_2O of CPAP during the induction of anaesthesia decreased the amount of atelectasis as measured by computed tomography (CT) scan when compared with similar patients without CPAP ($1.7 \pm 1.3\%$ vs. $10.4 \pm 4.8\%$, respectively; $p < 0.001$).[22]

The other strategy is the use of lower than maximal FiO_2 during the induction of anaesthesia. It is argued that this way the resorption of oxygen in areas with low V/Q and thus the development of atelectasis can be markedly reduced. In such pulmonary zones, airway closure creates a 'pocket' of tissue without proper connection to the main airways leading to a poor supply of fresh gas. At the same time the highly diffusive oxygen molecules already residing within such 'pockets' can easily pass into pulmonary capillaries, which are well perfused.[23] The higher the FiO_2 in the inspired gases, the faster the process of atelectasis formation will become. Diluting O_2 by a less soluble gas like N_2 decreases both, the amount and the velocity of atelectasis formation, considerably.

Some studies confirmed the physiological validity of this approach.[24–26] The use of pure O_2 during anaesthesia induction increased the area of atelectasis, as seen on CTscans, by about 8 cm^2 compared to minimal atelectasis (0.2 cm^2) at FiO_2 of 30%[24] and no atelectasis if no preoxygenation is performed.[25] Akca et al. showed that preoxygenation with 80% was associated with 0.8% of atelectasis compared with 6.8% at 100% oxygen. Moreover, the efficiency of gas exchange and the degree of atelectasis were similar when using oxygen-enriched mixtures with either 80% or 30%.[26]

Neither of the two proposed methods for the prevention of lung collapse is 100% effective, although when combined their preventive effects might be additive or even synergistic because each one is acting on a different kind of atelectasis. While CPAP tries to prevent the occurrence of compression atelectasis, lower oxygen concentrations slow down the rate of transition from low V/Q to shunting atelectatic lung tissue.

Despite the potentially beneficial effects, both methods reduce the margin of safety for patients during anaesthesia induction. On the one hand, CPAP maintains a normal FRC and thus expands the

period of safe apnoea,[27] on the other it also increases the intragastric pressure and therefore predisposes the patient to regurgitation and vomiting during anaesthesia induction when vital reflexes are abolished. Besides, CPAP cannot be applied easily with standard anaesthesia machines especially in a non-breathing relaxed patient. Moreover, some degree of atelectatis will occur as soon as CPAP is discontinued during laryngoscopy and endotracheal intubation because the lungs collapse within fractions of a second.[28]

Lowering FiO_2 decreases the pool of oxygen within the lungs and thus the critical time available for intubation.[29] Difficulties during ventilation and/or intubation may lead to potentially life-threatening complications in any patient during anaesthesia induction, and are at times hard to predict. Therefore, the authors of this article can neither recommended lowering FiO_2 nor applying CPAP as a standard procedure during induction of anaesthesia because the associated risks by far exceed the partial benefits of these preventive measures. This advice becomes even more evident in lieu of a simple therapeutic intervention such as an alveolar recruitment manoeuvre, which can easily resolve the problem of lung collapse during anaesthesia and surgery once the patient's airway is secured.

Maintenance of anaesthesia

During maintenance of anaesthesia, positive end-expiratory pressure (PEEP) without an RM has contradictory effects on lung function and atelectasis prevention. Sometimes PEEP improves gas exchange and decreases the amount of lung collapse but sometimes it does not.[30–32] These contradictory effects of PEEP depend on the total level of PEEP applied but more importantly on the patient's opening and closing pressure of the lungs. The level of PEEP commonly used during anaesthesia ($\leq$10 cmH_2O) can open collapsed airways but usually fails to recruit completely atelectatic areas. Therefore, PEEP without a prior recruitment of atelectasis cannot overcome the problem of persistent shunt. At the same time ventilation in some hypoventilated zones may increase towards normal conditions, while PEEP causes an excess of ventilation in the already normally ventilated zones, thereby increasing the relative amount of areas with high V/Q or even dead space.[30]

Decreasing FiO_2 during the course of anaesthesia is common practice based on the rationale that lower FiO_2 is less cytotoxic and causes fewer resorption atelectasis.[23,24] FiO_2 of 100% during anaesthesia increased atelectasis in the presence of low V/Q areas.[13,14,33] Agarwal et al. showed that lowering FiO_2 to 40% improved arterial oxygenation when compared with a FiO_2 of 100% in healthy anaesthetised patients.[34] It seems that low FiO_2 not only reduces atelectasis formation but also does not inhibit the hypoxic pulmonary vasoconstriction in areas of the lungs with low V/Q. However, there are other scenarios where high FiO_2 might be necessary such as during one-lung ventilation, an ischaemic event, an intra-operative acute shock or colonic surgery.[35] Moreover, there are some proven extra benefits of high FiO_2 such as significantly better anti-bacterial properties of alveolar macrophages or, on the phenomenological side, a decrease in the incidence of wound infection, nausea and vomiting after surgery.[35–37] As the efficiency of gas exchange and the extent of atelectasis were similar between using 80% or 30% oxygen, an FiO_2 of 80% can be recommended in those clinical scenarios.[26]

Emergence of anaesthesia

The above-mentioned treatment concepts of CPAP and low FiO_2 clearly have a more important role during the emergence as compared to the induction of anaesthesia.

Once patients start breathing again during the emergence of anaesthesia, sufficiently high CPAP should maintain the lungs free from collapse before extubation. The beneficial effect of CPAP during assisted spontaneous ventilation is well known.[38] Such benefits can also be observed in the post-operative period. Joris et al.[39] showed that bi-level positive airway pressure (BiPAP) with an inspiratory pressure of 12 cmH_2O at 4 cmH_2O of PEEP applied after gastroplasty in morbidly obese patients reduces pulmonary dysfunction when compared with either lower BiPAP pressures or supplemental O_2 via a face mask. Squadrone et al. have demonstrated in high-risk postoperative patients that CPAP after extubation decreased the need for re-intubation as well as the incidence of pneumonia, wound infection and sepsis.[40] These data show the positive effects that CPAP has on the rate of known typical complications related to lung collapse.

Dilution of alveolar O_2 by N_2 after extubation protects the lungs from resorption atelectasis particularly in the hypoventilated areas. This is a crucial moment during the conduct of anaesthesia since the residual effect of anaesthetic drugs, hypothermia, pain and other deleterious consequences of the surgical procedure predispose the patient to hypoventilation and thus make the lungs prone to re-collapse. In support of this, Benoit et al. showed that increasing FiO_2 to 100% before extubation promoted post-operative atelectasis.[33] Loeckinger et al. demonstrated in an experimental model that lowering FiO_2 from 100% to 30% before extubation decreased significantly areas with low V/Q from $17 \pm 15\%$ to $7 \pm 5\%$ and Log $_{SD}Q$ the indicator of a mal-distribution of perfusion from 1.31 ± 0.30 to 0.77 ± 0.31.[41]

We can conclude that a combination of low FiO_2 and CPAP during the emergence of anaesthesia and after tracheal extubation decreases lung collapse and leads to better lung function in the early post-operative period.

Recruitment manoeuvres (RMs)

Bendixen et al. were the first to describe the physiological rationale of a lung RM during anaesthesia.[42] They reached Paw of 40 cmH_2O using the anaesthesia bag for 15 s and thus, normalised arterial oxygenation and compliance for a short lapse of time. Anaesthesiologists have intuitively performed such manoeuvres without a clear understanding of the pathophysiology of lung collapse. In the early 1990s, Lachmann proposed and studied the fundamentals of lung recruitment in acutely injured lungs,[17] which were subsequently adapted to deal with the specific problem of anaesthesia-induced atelectasis in 'healthy' lungs.[18,19] Since then, RMs have been performed using a ventilator instead of a manually operated ventilation bag. This made them reproducible, easy to teach and safer because Paw and VT were now adequately controlled.

The goals of any RMs are to open up the lungs and keep them open afterward.[17] They will be successful only if these two goals are covered irrespective of the way they are performed. As lung collapse and recruitment are both pressure-dependent phenomena, they are directly related to the Ptp reached within each one of the pulmonary acini. The lung's opening pressure needs to be overcome at end-inspiration as the Ptp is highest during this phase while at end-expiration this pressure may never become lower than the closing pressure (Figure 1). To put it in simple terms, pulmonary recruitment is achieved by the plateau pressure and re-collapse of the newly recruited areas is prevented by PEEP.

Two main types of recruitment manoeuvres have been described in the literature:

'CPAP' manoeuvres. During this kind of manoeuvre a CPAP of 40 cmH_2O is applied for 10–30 s and then returned back to baseline ventilation.[18] CPAP manoeuvres have been associated with haemodynamic instability because the pressure level applied constantly during the manoeuvre is high and its changes abrupt.[43] For the same reason, the shear stress between normally aerated and collapsed areas could potentially be also very large.[8] In the early days, CPAP manoeuvres were not combined with the systematic use of PEEP due to its contradictory effect on gas exchange during anaesthesia.[19,24,30] Thus, the physiological effects of such manoeuvres were short-lived and lung collapse re-appeared at a rate indirectly proportional to the level of FiO_2 used.[25] Later on, Neumann et al. showed that sufficient levels of PEEP applied after the CPAP manoeuvres maintained the lungs open over prolonged periods of time even if ventilated with pure oxygen.[44]

'Cycling' manoeuvres: These are ventilatory strategies that consist of fluctuating airway pressure during the respiratory cycle. The alveolar recruitment strategy (ARS),[19] one of the cycling manoeuvres, has some advantages over CPAP manoeuvres. First, before proceeding with the actual lung recruitment, haemodynamic stability is systematically tested for during a so-called haemodynamic preconditioning phase. The initial stepwise increases in PEEP give the patient's haemodynamics time to adapt to these higher intrathoracic pressures and help the anaesthesiologist diagnose and treat an unrecognised hypovolaemic state. Second, pulmonary tissue stress is, at least theoretically, lower than during CPAP manoeuvres because the stepwise increments in intrathoracic pressure and gas volume spread progressively within more and more 'recruited' tissue as the manoeuvre proceeds.[8] Just as PEEP has demonstrated its protective effect on the lung parenchyma by reducing tissue stress and avoiding tidal recruitment, cycling manoeuvres can be viewed as protective too but on a sliding scale of increasing

and decreasing levels of PEEP.[45] Third, the PEEP titration phase helps to detect the level of PEEP that undercuts the collapsing point of the lungs.[46–48] Only a level of PEEP higher than this closing pressure is capable of mechanically maintaining the lung open irrespective of the FiO_2.[19,49] Fourth, cycling manoeuvres reveal on a breath-by-breath basis real-time information about the lung's functional state if appropriate ventilatory variables are monitored.[19,48,50–52] Table 1 shows the main methods for monitoring the physiological effects of RMs.

Over the past few years we have adapted our original ARS procedure as our comprehension of the interaction between the lung and the mechanical ventilator expanded.[19,49–56] We always perform the manoeuvre in a pressure control mode of ventilation and it consists of the following phases (Fig. 2):

- Haemodynamic preconditioning

By applying a constant driving pressure that results in a tidal volume (VT) of ≤ 8 ml kg^{-1} ($\sim$10–15 cm H_2O in normal lungs) PEEP is increased in steps of 5 cmH_2O, from 5 to 20. Each PEEP level is maintained for at least five breaths, although a few minutes might be needed to diagnose any occult hypovolaemia at PEEPs between 10 and 15 cmH_2O. According to our experience, this is the critical pressure level at which an unsuspected hypovolaemia in a patient could present itself by an increasing degree of haemodynamic instability. The manoeuvre is interrupted if mean arterial pressure and heart rate (and cardiac output if available) changes by more than 15–20% from baseline or if mean arterial pressure decreases below 55 mmHg. If this is the case, PEEP is reduced to a known safe level. A thus detected occult hypovolaemia is treated by an intravenous infusion of crystalloids/colloids before the manoeuvre is re-instituted. The amount of volume expansion will depend on the degree of hypovolaemia and the type of surgery. For cases with light hypovolaemia 3–4 ml kg^{-1} of crystalloids/colloids should be enough.

- Recruitment

If a patient is haemodynamically stable or has been stabilised successfully during the previous phase, PEEP is increased to about 20 cmH_2O and the driving pressure to 20 cmH_2O in order to reach the lung's opening pressures. For normal lungs, this pressure is around 40 cmH_2O of plateau pressure but may be higher in morbidly obese or cardiac surgery patients.[18,19,52,55,57] This setting is maintained for 10 breaths.

- Decremental PEEP titration trial

A decremental PEEP trial following the recruitment phase identifies the PEEP level required to prevent de-recruitment or lung re-collapse.[17,46–48] During the PEEP titration phase, PEEP is decreased progressively in steps of 2 cmH_2O to determine the lung's closing pressure. Once this pressure has been determined using one or more of the methodologies cited in Table 1, another recruitment manoeuvre is applied to recover any lung tissue that might have collapsed during the PEEP titration process.[46] Baseline ventilation is then resumed, but at a PEEP 2 cmH_2O above the closing pressure.

The lack of real-time monitoring of lung recruitment and collapse at the bedside in the early days of ARS, obliged us to work with predefined values for opening and closing pressures. These target values were derived from physiological studies performed in anesthetised patients. Thus, the opening pressure of normal lungs was assumed to be around 40 cmH_2O[18,19,55] while the closing pressure was expected to be somewhere between 5 and 15 cmH_2O depending on the clinical circumstances.[19,52,54,56,57] In the absence of sensitive means for monitoring, this meant that PEEP was usually set to predefined values making a proper PEEP titration phase after lung recruitment dispensable. The PEEP to be set on the ventilator was somewhat arbitrarily chosen taking into account the factors mentioned in Tables 2 and 3.

Clinical and physiological results of intra-operative recruitment manoeuvres

To date, the safety and beneficial effects of RMs during anaesthesia have been shown for lung-healthy patients. In an experimental model with healthy lungs Magnusson et al. demonstrated the

Table 1
Monitoring of cycling recruitment manoeuvres.

Variable		Comments
Lung mechanics	FRC	The absolute or relative value (change) of FRC can be non-invasely assessed at the bedside. It detects the volume of gas gained or lost during recruitment or collapse, respectively. It cannot differentiate between recruitment (an increase in the number of functional lung units) and over-distension (of a fixed number of lung units).
	Crs	Static respiratory system compliance can be determined using different non-invasive techniques. They cannot be applied in real-time. Dynamic Crs on the other hand can be determined non-invasively and in real-time at the bedside. Low Crs can be observed in lung collapse and over-distension. The highest Crs defines the open-lung condition and is best determined during a decremental PEEP titration.
	Raw	Dynamic Raw can be measured non-invasively and on-line at the bedside. High Raw can be observed in lung collapse and over-distension. The lowest Raw is observed in the open-lung condition.
	Stress index	Non-invasive, on-line assessment of lung over-distension. It can be used to determine the optimal plateau pressure after the recruitment manoeuvre.
Gas exchange	SpO_2	Non-invasive and on-line assessment of haemoglobin saturation. Detects hypoxemic episodes as defined by values *L* 90%. At usual or high FiO_2 it is insensible to changes in the area of gas exchange and thus unsuitable to detect an open-lung condition and over-distension
	PaO_2	Values higher 450 mmHg (at $FiO_2$100%) marks an open-lung state. Its determination, however, needs arterial blood samples at given points in time. While low PaO_2 values are indicative of lung collapse they are non-specific. Furthermore, PaO_2 is insensitive to lung over-distension.
	Dead space	Detects states of open-lung and over-distension. Some dead space parameters can be determined non-invasively while others require arterial blood gases and are thus only minimally invasive. All of them require volumetric capnography for their calculation.
	CO_2flow	The optimal elimination of CO_2 is closely related to the lung's optimal state of expansion. The index, which combines both, CO_2 elimination and lung mechanics, can be obtained non-invasively and on a breath-by-breath basis. It allows an on-line assessment of lung function and the states of open-lung or over-distension.
Lung imaging	CT scan	Reference method to evaluate the state of expansion in different lung areas. A percentage of non-areated areas below 5% defines an open-lung state. CT is, however, much less accurate to define lung over-distension. While CT has contribute a lot to current understanding of lung function during anaesthesia, it exposes patients to X-ray and cannot be used at the bedside. Therefore it is not suitable for routine use.
	RMI	It is a radiation-free method for the evaluation of lung aeration in scientific investigations but cannot be used at the bedside.
	SPECT/PET	Sensitive and specific methods to evaluate the regional distribution of ventilation and lung perfusion at a given point in time. However, patients are exposed to radioactive substances or X-ray and the devices cannot be at the bedside.
	Lung Echography	Non-invasive, radiation-free and on-line imaging technology for the lung. It is useful to diagnose at the bedside specific pathological conditions of the respiratory system close to the lung's surface as pneumothorax, pleural effussion and parenchymal consolidation (including atelectasis). However, pathologies deep within the lungs can not be detected.
	EIT	Provides functional images of the lungs in a non-invasive and real-time manner based on local changes in the electrical properties of the lung tissue. It is a radiation-free and might prove useful to diagnose lung collapse, over-distension and pneumothorax at the bedside. Furthermore, it is sensitive to lung collapse and can thus be used to guide the PEEP titration process.
	VRI	Functional non-invasive and real-time images of the lungs based on the distribution of sounds within the lungs. Radiation-free. Potential utility for diagnosing the state of lung expansion. However, due to its orientation towards the gravitational vector it could not be sensitive to lung collapse.

FRC = functional residual capacity, Crs = respiratory system compliance, Raw = airway resistance during expiration, stress index (airway pressure = a * inspiratory time b + c), CO_{2flow} = the elimination of CO_2 per breath times Crs divided by Raw, CT = computerized tomography, MRI = magnetic resonance imaging, SPECT = single photon emission tomography, PET = positron emission tomography, EIT = electrical impedance tomography and VRI = vibration response imaging.

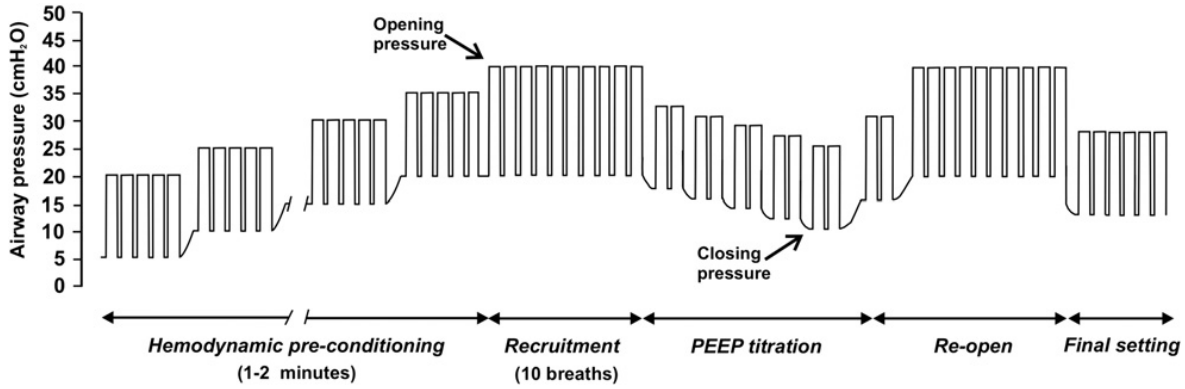

Fig. 2. Schematic representation of a systematic implementation of an alveolar recruitment strategy. Each tidal breath is represented by a rectangle. In a pressure controlled mode of ventilation the driving pressure is adjusted to obtain a tidal volume of ≤ 8 mL kg^{-1} and then PEEP is increased in steps of 5 cmH_2O, from 0 to 20 cmH_2O. At PEEP levels between 10 and 15 cmH_2O the maintained until the hemodynamics status is evaluated. This is the so-called "hemodynamic pre-conditioning phase". Provided that hemodynamics were already stable or have been stabilized successfully, the manoeuvre is continued. Once PEEP reaches 20 cmH_2O, the driving pressure is augmented to 20 cmH_2O to reach the opening pressure in healthy lungs (40 cmH_2O of plateau pressure). Those pressures are maintained for about ten respiratory cycles. The most likely closing pressure and thus the level of PEEP capable of keeping the lungs open can either be determined on the basis of theoretical considerations, a-prior knowledge and data from clinical studies or from own experience. If such information is neither available nor applicable for an individual patient, the closing pressure needs to be determined by a systematic decremental PEEP titration trial. Once the re-collapse of the lung has started, a second recruitment manoeuvre is applied to re-open the lungs before the final ventilatory settings at a PEEP 2 cmH_2O higher than the closing pressure are implemented to keep the lung in an open state until the end of surgery (adapted from ref. 19 and 46).

absence of injury of alveolar–capillary membrane in the presence of repetitive RMs.[58] Table 3 summarises the main clinical studies related to recruitment manoeuvres in anaesthetised patients.

Studies using lung imaging like CT, magnetic resonance imaging or electrical impedance tomography (EIT) confirmed that the beneficial effect of RM is related to the reversal of overt lung collapse.[1,2,18,49,59] These imaging technologies were able to differentiate atelectasis from other densities like pleural effusions or alveolar oedema. Recently, the lung collapse-recruitment physiology has been elegantly described observing the sub-pleural alveoli *in vivo* and in real time during mechanical ventilation. Halter et al. gave visual evidence for the potentially beneficial effect of RM and PEEP on collapsed alveoli using intra-vital microscopy.[60]

The negative consequences of lung collapse on gas exchange and lung mechanics and their reversal by RMs were also well described by Hedenstierna's group demonstrating a clear link between

Table 2
Surgical and patient factors promoting lung collapse.

Surgical factors:
• Thoracic and abdominal surgeries
• Body position (Trendelenburg)
• Change in chest compliance by surgical retractors
• Cardiopulmonary bypass
• One-lung ventilation
• Increased intra-abdominal pressure (pneumoperitoneum)
Patient factors:
• Age
• Increased body mass index
• Smoking
• Bronchopulmonary infections
• Pregnancy
• Abdominal distension
• Chest deformations
• Chronic obstructive pulmonary diseases

Table 3
Main clinical studies on lung recruitment manoeuvres during anaesthesia.

Author, year	*n*	Type of RM	Paw (cmH_2O)	PEEP (cmH_2O)	Main finding	Level of evidence
Bendixen, 1963[42]	18	CPAP	20,30,40	—	PaO_2 and compliance increased for a short period.	Level II-3
Rothen, 1993[18]	16	CPAP	10 to 40	—	CPAP 40 cmH_2O reverted atelectasis assessed by CT scan.	Level II-3
Tusman, 1999[19]	30	Cycling	40	5	ARS increased $PaO_2$and compliance along the study (120').	Level I
Rothen, 1999[77]	12	CPAP	40	—	7–8 seconds of CPAP reverted atelectasis assessed by CT scan.	Level II-3
Neumann, 1999[44]	13	CPAP	40	10	Lung recruitment and PEEP kept the lung open despite $FiO_2$100%.	Level II-2
Tusman, 2000[55]	24	Cycling	35,40,45	5	40 cmH_2O of Paw showed highest PaO_2 and compliance.	Level II-2
Tusman, 2002[56]	30	Cycling	40	5,10	10 PEEP was better than 5 PEEP after ARS in obese patients.	Level 11-1
Tusman, 2002[53]	10	Cycling	40	5	ARS increased oxygenation during one-lung ventilation.	Level II-3
Benoit, 2002[33]	30	CPAP	40	—	FiO_2 40 vs 100% after CPAP decreased postoperative atelectasis.	Level I
Tusman, 2003[49]	24	Cycling	40	5	ARS resolved atelectasis in children despite FiO_2 of 100%.	Level I
Claxon, 2003[71]	78	Cycling	40	5	Lung recruitment increased PaO_2 in cardiac patients.	Level I
Pang, 2003[78]	24	Cycling	40	5	Lung recruitment increased PaO_2 during laparoscopy.	Level I
R. Miranda, 2004[70]	24	Cycling	45	17	Lung recruitment increased PaO_2 after cardiac surgery.	Level I
Tusman, 2004[54]	12	Cycling	40	8	ARS improved PaO_2 and dead space during one-lung ventilation.	Level II-3
Tusman, 2004[50]	16	Cycling	40	5	ARS increased PaO_2 and decreased dead space.	Level II-3
Dyhr, 2004[57]	30	CPAP	45	12	12 PEEP after recruitment increased PaO_2 and lung volume.	Level I
Whalen, 2006[79]	20	Cycling	40	12	ARS improved oxygenation in morbidly obese during anesthesia.	Level I
Malbouisson, 2008[75]	10	CPAP	40	10	Lung recruitment reverted hypoxemia in cardiogenic shock.	Level II-3
Almarakbi, 2009[80]	60	CPAP	40	10	Repeated lung recruitments improved PaO_2 in morbidly obese.	Level I
Bohm, 2009[52]	11	Cycling	50	5,10,15	15 PEEP after ARS improved lung function in mordibly obese.	Level II-3

RM = recruitment manoeuvre, *n* = number of patients, Paw = airway pressures used to achieve recruitment effect and PEEP = positive end-expiratory pressure. The U.S. Preventive Services Task Force [Ann Intern Med 2007; 147: 117-122] was adapted to stratify evidence: Level I represent evidence obtained for a randomized controlled trial; Level II-1 represent evidence obtained from controlled trials without randomization; Level II-2 represent evidence obtained from cohort or case-control studies; Level II-3 represent evidence obtained from time-series with or without intervention and Level III evidence is derive from expert opinions based on clinical experience or from reports of expert committees.

atelectatic areas and shunt by using the multiple inert gas technique.[2,13,14] While airway collapse initially protects the lung from compression atelectasis it creates areas of low V/Q, which progress within minutes to areas of shunt by way of resorption atelectasis. This last effect is more evident in elderly than in young patients.[13,14]

As lung recruitment restores lung aeration by re-expanding collapsed areas, arterial PO_2 is also normalised. If the level of PEEP after RMs is lower than the lung's closing pressure or if no PEEP is applied at all, lung de-recruitment (or re-collapse) takes place quickly, thereby losing the beneficial effect of the previous RMs.[46] However, sufficient levels of PEEP applied after RMs will keep the lungs open maintaining arterial oxygenation efficient and constant even in the presence of high FiO_2.[19,44,49]

Less obvious but equally important is the fact that RMs also improve the CO_2 kinetics. Dead space is reduced and the amount of CO_2 eliminated per breath is increased after RMs have been applied. We have demonstrated the role of dead space as a promising monitoring variable for the lung recruitment-collapse phenomenon in a model of acute lung injury: dead space-derived indexes were closely related to both, the amount of non-aerated areas on CT scans and to shunt. Ventilatory efficiency progressively improved as atelectasis and shunt were resolved by lung recruitment.[61] The same effect was demonstrated in elderly, obese and thoracic surgery patients.[50,52,54]

The repercussions of the lung's collapse-recruitment process on lung mechanics are closely associated with those on gas exchange. The lung, as an elastic structure, has the lowest compliance at both, very low (residual volume) and very high lung volumes (total lung capacity). In normal lungs the highest compliance values are observed at normal FRC and are associated with an optimal PaO_2, a condition compatible with a state of an 'open lung'. Suarez Sipmann et al. described how respiratory system compliance behaves during a lung recruitment manoeuvre in a model of ALI.[48] The authors showed that dynamic compliance was closely related to arterial oxygenation and the state of aeration as assessed by CT images. The effect of RMs on compliance was also demonstrated in anesthetised patients.[19,50,52–56]

The above examples explain why a close monitoring of the lung's collapse-recruitment phenomenon by respiratory gas and mechanics analysis and non-invasive bedside imaging technologies such as EIT might be useful (Table 1).

Effect of RMs on haemodynamics

The physiological effects of positive pressure ventilation on the cardiovascular system are due to changes in pulmonary vessels, transmural pressures and ventricular inter-dependency. All these factors affect haemodynamics in a complex and sometimes opposing fashion. As a rule of thumb, it can be stated that high intrathoracic pressures do not affect myocardial contractility, they decrease RV and LV preload in parallel but affect the afterload of both ventricles in an opposite way; while RV afterload increases that of the LV decreases.[62,63] The main effect of high Paw on haemodynamics is exerted by a compression of the pulmonary capillaries at the alveolar level, which decreases venous return and cardiac output. Therefore, hypovolaemic patients will not tolerate high Paw, while those with an optimal preload do so.[59,64,65] Hypervolaemia, however, did not improve haemodynamic tolerance during RMs as compared to normovolaemia in a recent experimental study.[66]

Recently, more attention has been paid to the haemodynamic consequences of RMs during anaesthesia. On the one hand, some authors have described a haemodynamic compromise mainly during CPAP manoeuvres.[43,67–69] Nielsen et al. found more than 50% decreases in cardiac output, in left ventricle end-diastolic area by 45% and in mean arterial pressure by 20% during a CPAP manoeuvre after cardiopulmonary bypass.[43] The authors showed a time-dependent transient reversible haemodynamic effect of high Paw where the impairment started as soon as the 10-s CPAP–RM began, but continued thereafter for another 10 s. Other authors described a decrease in mesenteric perfusion during RM. [67–69] The haemodynamic compromise in these studies was short-lived and patients recovered quickly after the RMs.

On the other hand, there is evidence for a good haemodynamic tolerance of recruitment manoeuvres. Reis Miranda and co-workers showed that RM and high PEEP are well tolerated after cardiac surgery.[70] The same results were found by other groups.[57,71] For example, Dyhr et al. (2004) showed that haemodynamics remained stable for 60 min after an RM at 12 cmH_2O of PEEP even in cardiovascular patients.[57]

In another study, Reis Miranda et al. showed that RM and subsequently applied rather high levels of PEEPs of 14 cmH_2O in cardiac patients decrease dynamic RV impedance along the respiratory cycle as assessed by Echo-Doppler.[72] Contrarily, ventilation without recruitment and low PEEP (5 cmH_2O) increased RV outflow impedance during inspiration; a similar finding was described by Jardin et al..[73] These results could explain why Celebi et al. observed that cycling RMs were better tolerated than CPAP manoeuvres.[74] The intermittent increases in Paw during a cycling manoeuvre as opposed to

a continuously high Paw during CPAP affect RV impedance during expiration favourably and could be the reason why haemodynamic conditions are more stable.

While most studies deal with the negative repercussions of positive pressure ventilation and RMs on haemodynamics, it is worth noting that these same pressures can also improve the haemodynamic situation under some special circumstances. Mechanical ventilation in patients with heart failure may decrease O_2 consumption, increase O_2 delivery and improve cardiac function by a decrement in LV afterload.[62] Malbuisson et al. described an improvement in haemodynamics after RM in patients with cardiogenic shock presumably mediated by this mechanism.[75]

Our group observed in patients with poor left ventricular function (ejection fraction of $28 \pm 3\%$) a reduction in pulmonary vascular resistance (PVR) after RM and PEEP of 10 cmH_2O. Haemodynamics remained stable during and after a cycling RM and PVR decreased significantly when compared to values before recruitment (from 261 ± 21 to 173 ± 36 dynes s cm^{-5} m^{-2}).[76] It can be cautiously concluded that PVR was indeed reduced by RM and PEEP due to: (1) a fast release of the hypoxic pulmonary vasoconstriction reflex by treating its underlying cause, the lung collapse, and (2) a PEEP of 10 cmH_2O was enough to prevent re-collapse after the RM but was not too high to cause compression of the pulmonary capillaries in the normally ventilated areas.

Indications and contraindications

Less than 10% of all patients undergoing general anaesthesia do not develop atelectasis.[2] The absence of atelectasis in these patients can be explained by the lack of adverse patient and surgical factors that predispose to lung collapse (Table 2). Therefore, RMs are indicated in all intubated patient except for those with a low likelihood of developing atelectasis. These latter patients are mostly healthy, young and thin and undergo minor day-case surgeries which affect neither thorax nor abdomen.

RMs are contraindicated in:

- haemodynamically unstable patients until stability has been accomplished;
- patients without a proper anaesthetic level;
- bronchospasm;
- pneumothorax/bronchopleural fistula;
- elevated intracranial pressure; and
- when the alteration of gas exchange is caused by mechanisms other than lung collapse.

Conclusion

Clinical experience using lung RMs in the operating theatre shows that such manoeuvres normalise arterial oxygenation, improve lung mechanics and reduce dead space. RMs are particularly useful to quickly overcome states of moderate to severe hypoxaemia caused by the primary mechanism of lung collapse. Beyond the role of RMs in treating these acute hypoxaemic episodes, one of their main benefits is an increase in the patient's margin of safety due to an increasing arterial content of oxygen and oxygen delivery.

RMs should only be performed in normovolaemic patients. Therefore, a haemodynamic preconditioning phase prior to the actual recruitment intervention should be an integral part of any alveolar recruitment strategy. This preconditioning phase helps detect and treat any occult hypovolaemia, a common condition which is usually difficult to diagnose without advanced monitoring.

Improved lung mechanics and CO_2 elimination after an RM performed just prior to the start of surgery set the stage for a lung-protective ventilatory strategy with low tidal volumes and plateau pressure throughout the surgical procedure. This is of particular importance now that there is increasing evidence for lung injury due to atelectrauma also in healthy but partially atelectatic lungs. RMs in conjunction with adequate levels of PEEP avoid tidal recruitment and its deleterious effect.

Further clinical trials are needed to evaluate the effect of RMs on patient outcome.

Practice points

- Lung collapse during anaesthesia predominates in alveoli and terminal airway (acini), and this is why gas exchange deteriorates.
- Lung collapse occurs during expiration, while lung recruitment is an inspiratory phenomenon.
- While CPAP can theoretically prevent atelectasis formation during anaesthesia induction, in clinical practice, however, a truly continuous airway pressure cannot be maintained during manual mask ventilation and intubation thereby rendering this treatment inappropriate in daily practice.
- Low FiO_2 can also prevent atelectasis formation during induction of anaesthesia; however, lower oxygen concentrations go along with a lower margin of safety. Therefore, such practice cannot be recommended as difficulties in ventilating and intubating even normal patients can never be ruled out.
- During anaesthesia CPAP/PEEP and low FiO_2 are ineffective in treating established atelectasis. Lung collapse can only be overcome by RMs.
- However, in an open lung, CPAP/PEEP and low FiO_2 are recommended during the emergence of anaesthesia.
- The main goal of RMs is to open up collapsed areas by plateau pressures.
- The main role of PEEP is to keep the lungs open over time.
- RMs performed automatically by a ventilator will not only replace the anaesthesiologist's 'bagging hands' but make them reproducible, safe and easier to teach.
- Cycling RMs are more advantageous than CPAP manoeuvres of the same pressure because they are haemodynamically better tolerated and, in addition, provide more meaningful ventilatory data during real-time monitoring.
- The main physiological benefits of RMs are an increased efficiency of gas exchange; by overcoming tidal recruitment they presumably have a protective effect against lung injury.
- Patients must be normovolaemic and haemodynamically stable before RMs can be performed safely.
- Although clinical evidence for the safety, effectiveness and efficiency of RMs in the operating room has been collected over the last 10 years, their effect on patient outcome has not been determined, yet.

Research agenda

- RMs should be personalised in an attempt to best match an individual's opening and closing pressures. This means that the target plateau and PEEP pressures have to be determined from monitoring parameters that are both sensitive and specific for lung collapse.
- Real-time and non-invasive monitoring tools for lung collapse and recruitment effects should be developed for routine bedside use.
- Non-invasive haemodynamic monitoring and diagnosis means should be developed to detect occult intravascular hypovolaemia not only during RMs but also for anaesthesia use in general.
- Further research is warranted to evaluate the effect of RMs on the early and late postoperative period.
- Finally, multicentre randomised controlled trials testing the outcome of patients subjected to RMs must be conducted.

Conflict of interest statement

None.

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