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Anaesthesia: Lung Imaging and Gas Exchange Abnormalities

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ABSTRACT

A fall in functional residual capacity (FRC) by anaesthesia promotes airway closure. It impedes ventilation, primarily in dependent lung regions and causes atelectasis. The decrease or elimination of ventilation results in regions with low ventilation-perfusion ratios ($\dot{V}_A/\dot{Q}$) combined with those with intrapulmonary shunt. They occur early during induction of anaesthesia and may remain for a couple of days postoperatively. Both contribute to an oxygenation impairment but can be prevented by recruitment manoeuvres, followed by positive end-expiratory pressure (PEEP). Low $\dot{V}_A/\dot{Q}$ areas increase with age but shunt (caused by the atelectasis) has a peak at 45-50 years and then decreases with further rise in age. Shunt increases with increasing body mass index (BMI) whereas areas with low $\dot{V}_A/\dot{Q}$ do not. These findings suggest different approaches in ventilatory support during anaesthesia in the young to middle-aged and the elderly patient, and in the lean and over-weight patient. **(BRN Rev. 2019;5(2):135-149)**

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INTRODUCTION

More than 230 million anaesthesias are performed annually worldwide[1]. Most elective anaesthesias and surgeries are uneventful but in various multicentre studies postoperative pulmonary complications are substantial, opposite to general opinion. Thus, in a frequently cited study (Las Vegas study[2]) on postoperative lung complications the occurrence was as high as 28%. This means that around 65-70 million anaesthesias were not uneventful. Obviously, the complication rate will depend on the definition of complications, type of surgery and of patient category, but even with a complication rate of 5-10%[3,4], the number of perhaps more clinically important complications amount to somewhere between 10-30 million anaesthesias. Mortality is low in scheduled surgery but with increased odds and hazard ratios in frail patients[5]. Moreover, socioeconomic aspects of prolonged hospital stay and recovery at home may cost billions of euros. With this as a background, lung function impairment during anaesthesia and intra- or post-operative lung complications remain an important issue. This review will focus on oxygenation impairment during anaesthesia and the mechanisms behind this impairment. It will not discuss postoperative lung function that may deserve a review itself.

FUNCTIONAL RESIDUAL CAPACITY AND AIRWAY CLOSURE

The resting lung volume, or functional residual capacity (FRC), is reduced by 0.7-1.0 litres in the supine position compared to sitting or standing[6-8]. Anaesthesia reduces FRC further by another 0.4-0.5 litres[9]. The net result is that breathing during anaesthesia, supine and even more in head-down position, is close to residual volume. The fall in FRC occurs already during spontaneous breathing with no further change by muscle paralysis[10], which applies basically to all general anaesthetics except one, ketamine[11]. The latter preserves muscle tone[12,13] whereas the others, e.g. halogenated anaesthetics and barbiturates, cause decrease of the tonic activity of intercostal muscles and the diaphragm[14-16]. Muscle paralysis added to the ketamine anaesthesia will, however, lower the FRC. Spinal and epidural anaesthesia and other forms of local anaesthesia will in general not lower the FRC[17]. There is an age dependence with a slight increase in FRC with age due to loss of elastic tissue[18,19]. FRC also decreases with increasing body weight, expressed as body mass index (BMI)[7].

A decrease in FRC will promote airway closure that is a normal physiologic phenomenon[20]. Thus, a deep expiration in a healthy awake subject will reduce lung volume, and during expiration airways may begin to close; with the next inspiration airways will open up again. However, if breathing continues at a reduced FRC, as during anaesthesia, airways may be continuously closed in addition to those that close during expiration and open during inspiration. If continuous closure of airways lasts long enough, trapped gas behind the closed airway will be absorbed by the capillary blood flow and the alveoli will eventually collapse. The higher the inspired and alveolar oxygen concentration is, the faster are the absorption and collapse[21]. The airways that open and close during a breath reduce ventilation of the corresponding alveoli.

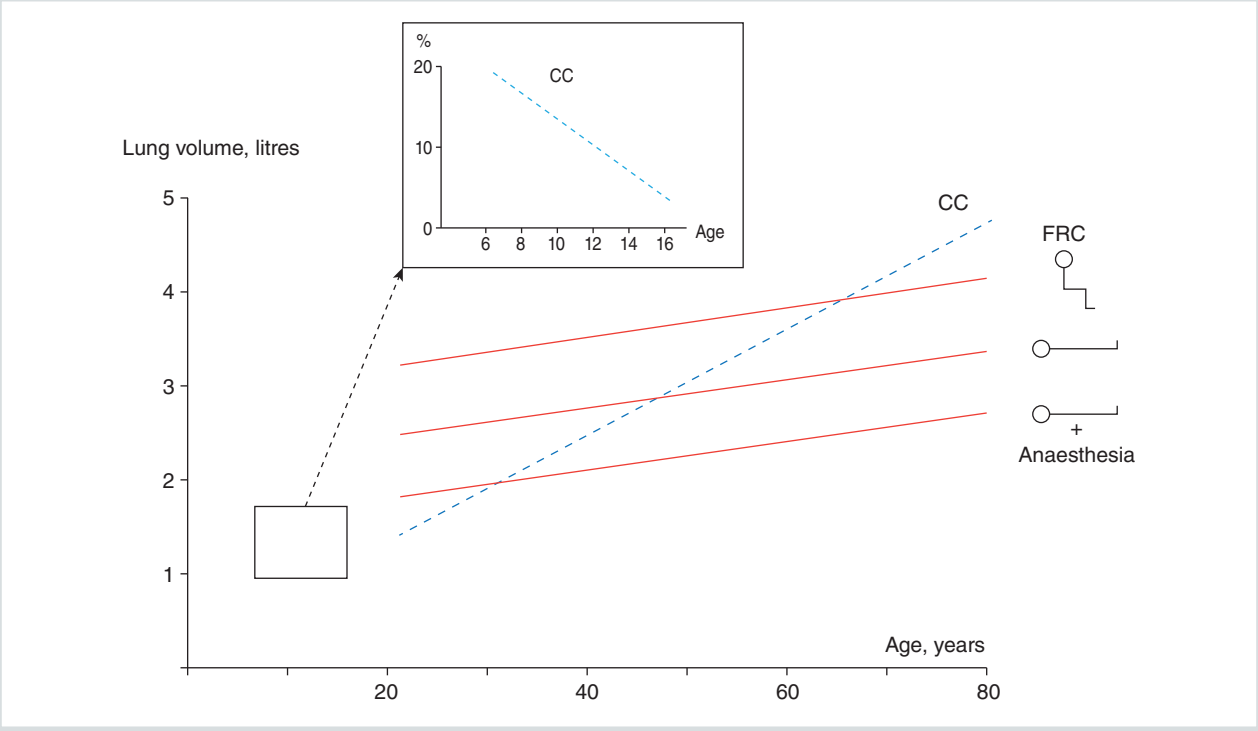

FIGURE 1. Functional residual capacity (FRC), versus age in the sitting position, supine and supine plus anaesthesia, as well as closing capacity (CC), i.e. the volume at which airways begin to close during an expiration. Note that FRC increases with age, assuming unaltered body configuration and the CC increases much faster. At an age of 20 years, airway closure does not occur even after very deep expiration (CC far below FRC). At an age of around 50 years CC begins to be higher than FRC in the supine position and at an age of 65-70 years CC may even exceed FRC in an upright position. During anaesthesia, due to the fall in FRC, almost all patients develop airway closure as indicated by a higher CC than FRC. Pooled data from various studies.
In the insert, a regression line for airway closure (expressed as CC) is shown for children from 6 to 16 years *(data taken from Mansell et al.[23])*. Airway closure is largest in the youngest children and can be as large in the 6 years old child as in the 50 years old subject.

The lung volume at which airways begin to close during expiration, closing capacity (CC), increases more rapidly than FRC with increase in age as illustrated in figure 1. As can be seen in the figure, young patients, around 20 years of age, do not develop airway closure even after a maximum expiration. But, with increasing age, CC soon exceeds FRC and airways may close during normal breathing in the supine position already in 50-year old subjects. Even worse, it occurs in an upright elderly subject of an age of 65 years or more[22]. The figure also shows results from airway closure measurements in young children[23]. Interestingly, the younger the child is, the larger is airway closure in proportion to the lung volume. Thus, a 6-year old child has as large amount of airway closure as a 50-year old subject. A growing lung in the young and loss of elastic lung tissue in the elderly may be factors that explain this age dependence.

ATELECTASIS

The suspicion of atelectasis during anaesthesia was brought forward already in 1963 in a classical paper by Bendixen et al[24]. However, atelectasis could not be demonstrated by conventional chest X-ray and was considered less likely. With the introduction of computed tomography (CT), a new and more detailed analysis of lung tissue was possible. In 1980, a paper was published on increased density of lung tissue in dependent lung regions close to the diaphragm in 29 anaesthetised paediatric patients[25]. The increased density was suggested to be caused by airway closure, impeding aeration. The reason for the study was that paediatric patients were often anaesthetised when undergoing a CT to optimize the quality of the image. It had been noticed that when CT was done to detect tumours and metastasis, densities had been seen in the lung which may have been interpreted as tumour. However, the authors were able to show that there were no densities when the patients were sedated before the anaesthesia and did not appear until they were anaesthetised. This can hardly be a sign of tumour. In our own studies in adult patients, no densities were seen when the patient was awake but they appeared when the patient was anaesthetised, whether breathing spontaneously or being paralysed and ventilated mechanically[26,27] (Fig. 2, left panel). Even when knowing the CT findings, chest X-ray did not show any signs despite retrospective analysis by radiologists. The most likely explanation is that the densities were located in dependent lung regions close to the spine and were to some extent indistinguishable from spine and ribs.

The densities were essentially airless with an attenuation number, expressed as Hounsfield Units (HU) around zero, where -1000 HU corresponds to ambient air, 0 HU to water and +1000 HU to bone. A question was whether the densities reflected atelectasis (airless lung tissue) or pooling of blood in distended vessels in dependent regions of the lung, and whether the densities were located in the lung or in the pleural space. Injection of radio contrast into the pleural space showed that the densities were inside the lung[28]. To distinguish between pure atelectasis and vascular congestion, animal studies had to be conducted. Sheep and pigs showed very small amount of densities[29]. In an effort to hopefully see larger densities, experiments were also conducted in Shetland ponies[30]. They were small enough to be positioned on the CT scan table and to be moved through the gantry of the CT scanner. These studies showed widespread densities and lung histology afterwards showed these regions to be completely collapsed, and thus atelectatic. Qualitatively, they were similar to those seen in other animals and in humans, although quantitatively larger, comprising most of the lung. It might be worth mentioning that an anaesthetised horse is difficult to oxygenate and may require 100% O_2 to keep partial pressure of oxygen (PaO_2) at a level of 10 kPa (75 mmHg)[31]. The atelectasis in the anesthetised human is on an average larger than seen in pigs and sheep but much smaller than in the horse. In the human it is largest close to the diaphragm, smaller at the hilar region and mostly absent in the apical regions (Fig. 2, right panel). Total atelectatic tissue volume is on an average 10-15% of the lung. Atelectasis is about the same size whether the patient is breathing spontaneously or is mechanically ventilated and paralysed[32]. The only general anaesthetic, so far studied, that does not produce atelectasis is

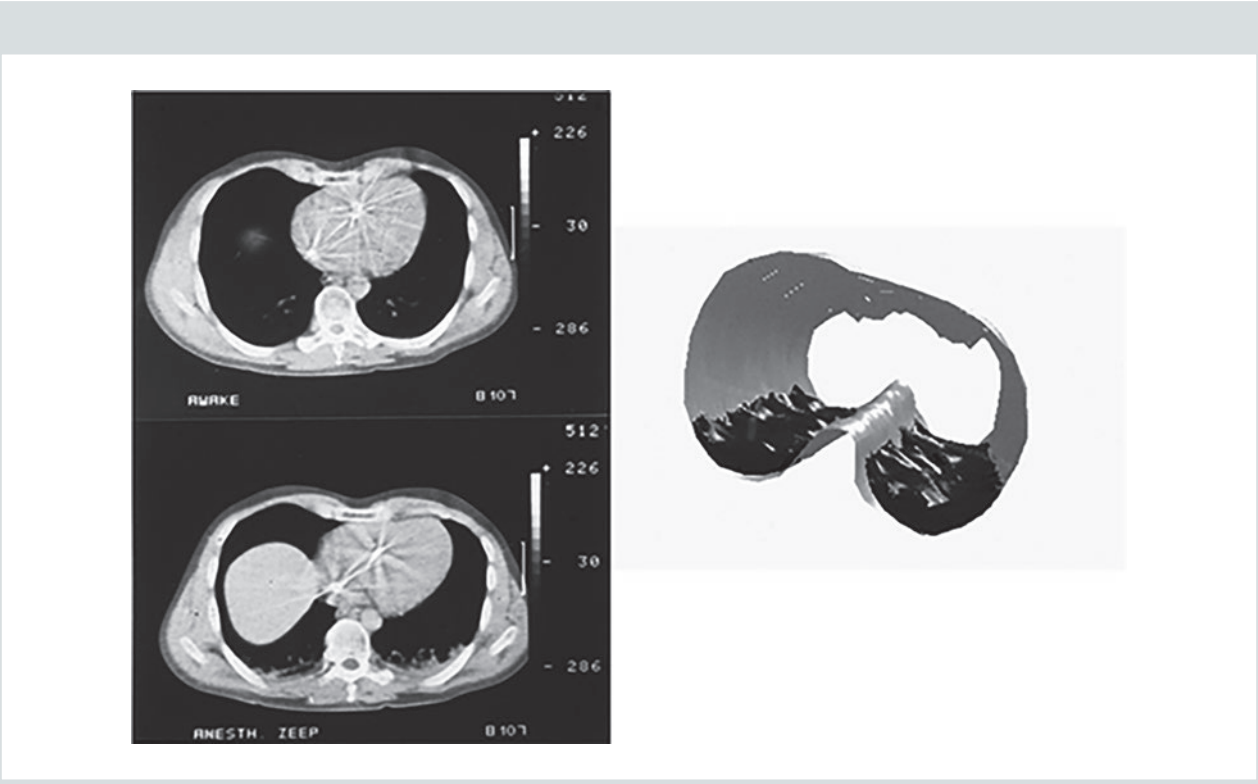

FIGURE 2. *Left panel:* transverse computed tomography (CT) of the chest, awake (upper image) and during anaesthesia and muscle paralysis (lower image). Note the aerated lung in the awake condition and the appearance of densities (atelectasis) in dependent regions during anaesthesia. The cut of the chest is at the same level under both conditions a few cm cranial to the top of the diaphragm awake. Note the much larger diaphragm area during anaesthesia, indicating cranial displacement of the diaphragm *(adapted and reproduced with permission from Gunnarsson et al.[37], © ERS 2018)*.
Right panel: three-dimensional reconstruction of the distribution of atelectasis in the thoracic space. Note the larger atelectatic volume (black area) near the diaphragm (left-most region) (grey area) and the decrease towards the apical lung regions (white area).

ketamine[11] and, as alluded to above, it does not lower FRC.

Influence of age. It was initially assumed that atelectasis would be larger the older the patient is, in view of the age-dependent increase in airway closure. However, anaesthetised children seemed to show as large atelectasis as adults when comparing different studies[25,33]. This prompted an analysis of a larger number of subjects by pooling data from different studies. All in all 80 patients, clinically free from heart and lung disease, between 19 and 69 years, were studied during similar anaesthesia and mechanical ventilation with zero end-expiratory pressure (ZEEP) and an inspired oxygen concentration of 30-40% before surgery[34]. Interestingly, atelectasis increased from 19 to 45-50 years but then decreased with further rise in age up to the oldest ones studied, 69 years (Fig. 3). There was no report on the size of the densities in the 29 paediatric patients referred to above[25]. However, in a few patients from 4 months to 6 years studied by our group, as much atelectasis was seen as in middle-aged patients after correction for lung volume (data not published).

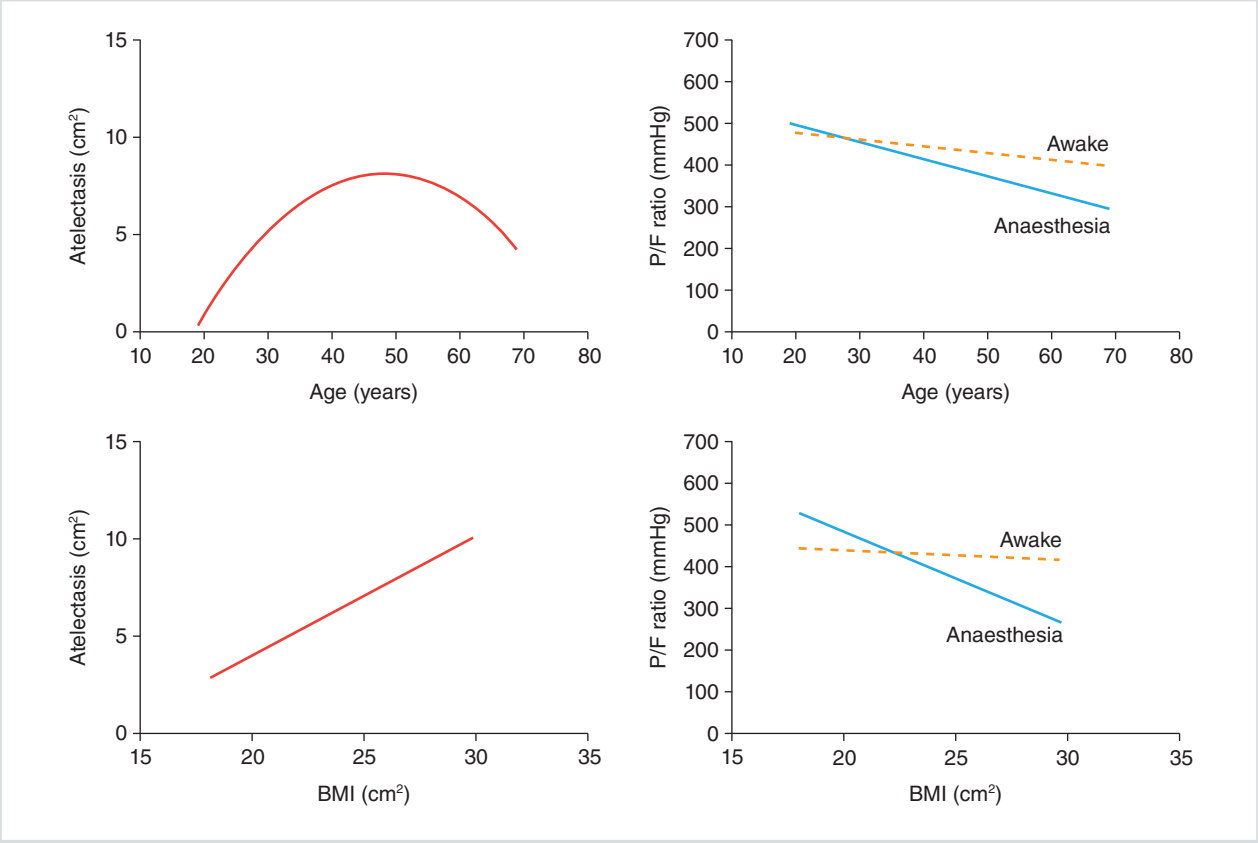

Figure 3. Schematic presentations of the size of atelectasis during anaesthesia and the ratio of arterial partial pressure of oxygen ($PaO_{2)}$ to fraction of inspired oxygen (F_IO_2) [P/F] awake and anaesthetised plotted against age (upper panels) and against body mass index (BMI) (lower panels). Note the binomial or quadratic function for atelectasis against age with a peak around 45-50 years. The P/F ratio decreases with age and more so during anaesthesia. Atelectasis increases linearly with increase in BMI. The awake P/F ratio shows no dependence on BMI up to 30 kg/m², but decreases with BMI during anaesthesia *(reproduced with permission from Hedenstierna G et al.[34])*.

Influence of body weight. Atelectasis increased in size with increase in BMI, in the 80 patients mentioned above (Fig. 3). They were all normal-weight or over-weight (BMI < 30 kg/m²)[34]. Anaesthetised obese patients with BMI > 30 kg/m² may have even larger atelectasis[35,36].

Influence of chronic obstructive pulmonary disease (COPD). In 10 patients with rather severe COPD with expiratory flow limitation in one second (FEV_1)/forced vital capacity (FVC): 47% predicted) and hyperinflation (FRC: 126% of predicted), no atelectasis, as assessed by CT, was seen awake. No patient developed atelectasis during anaesthesia[37] (see examples of lung-healthy and COPD patients in figure 4). The CTs also show hyperinflated lungs in the COPD patient, with no decrease in the transverse lung area and no cranial shift of the diaphragm by anaesthesia. The absence of a fall in lung dimensions by anaesthesia may be the explanation to why atelectasis did not occur.

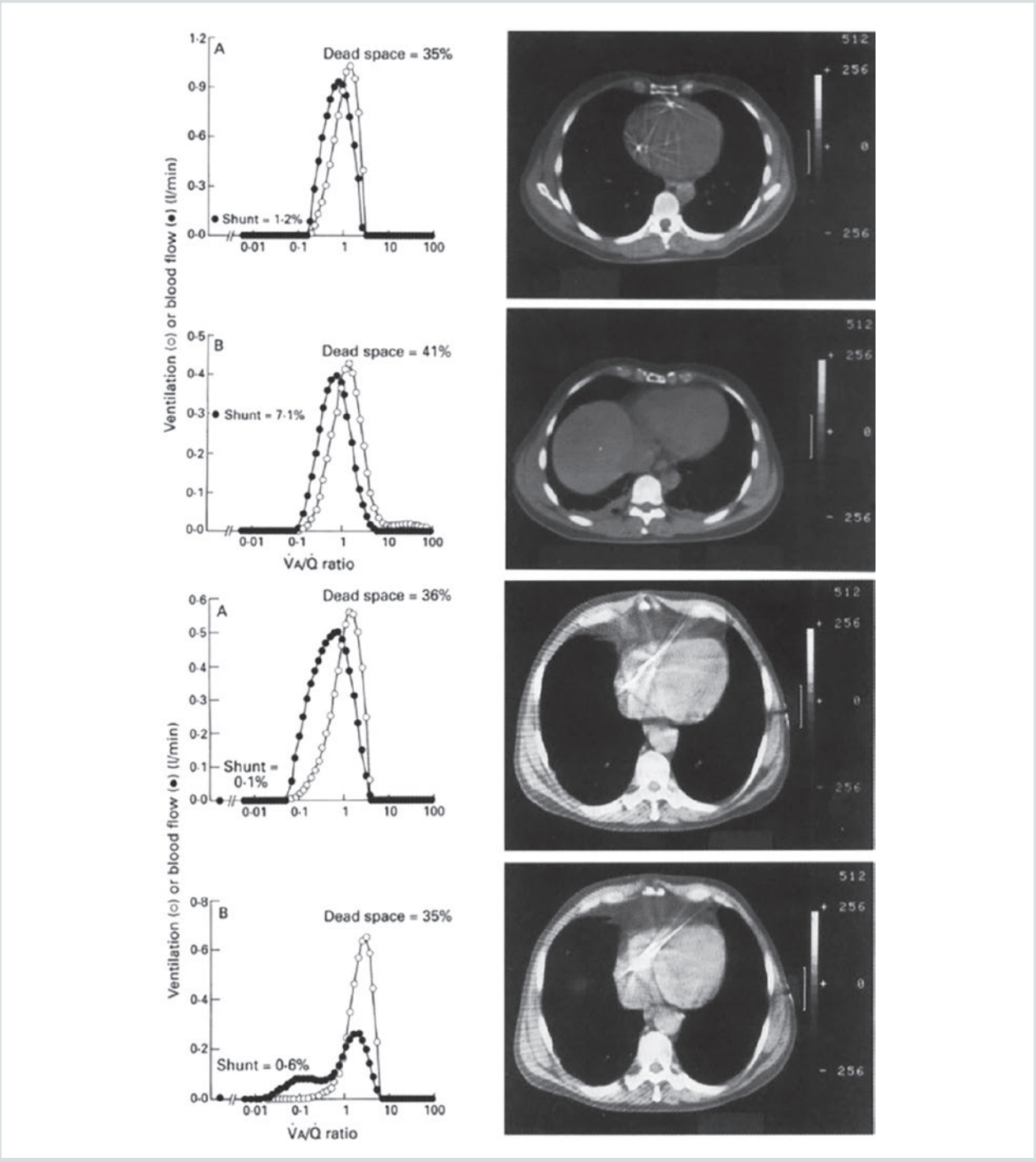

Figure 4. Ventilation-perfusion distributions, expressed as ventilation-perfusion ($\dot{V}_A/\dot{Q}$) ratios, and corresponding lung computed tomography (CT) awake and during anaesthesia in a lung-healthy subject (upper panels) and in a patient with advanced chronic obstructive pulmonary disease (COPD) (lower panels). Note the appearance of a shunt in the lung-healthy subject during anaesthesia and atelectasis in dependent regions of both lungs. Moreover, note the diaphragm that has moved cranially, indicating reduced functional residual capacity (FRC) (the CT cut was at the same level as the spine awake and during anaesthesia). In the COPD patient no shunt appeared with anaesthesia, but more regions with low $\dot{V}_A/\dot{Q}$ ratios. Note also the hyperinflated lung with no atelectasis awake or during anaesthesia.

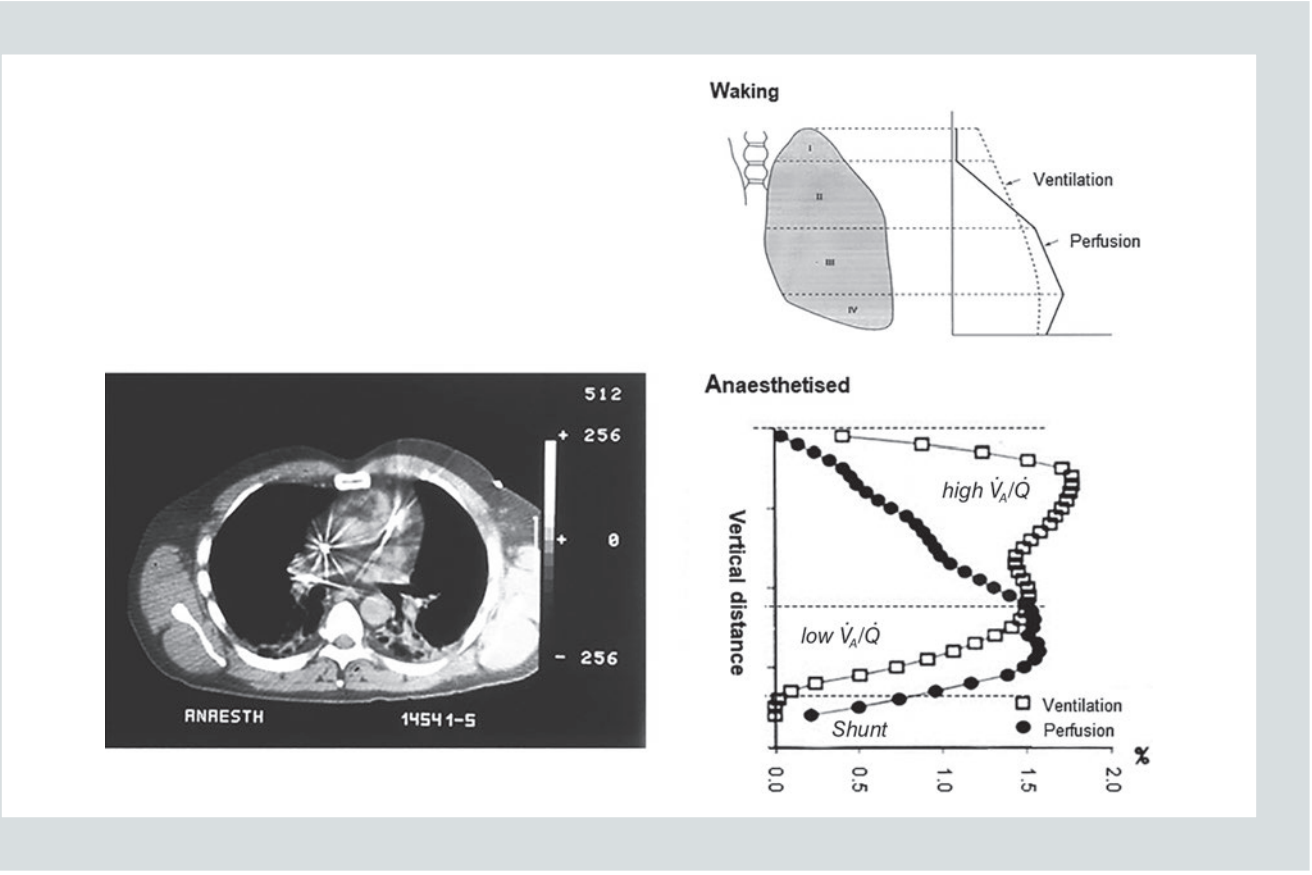

FIGURE 5. *Left:* Transverse computed tomography (CT) of the chest in an anaesthetised subject. Note the atelectasis in the bottom of both lungs. The radiating beams in the heart are artefacts from a Swan-Ganz catheter.
Lower right: Vertical distributions (anterior-posterior) of ventilation and perfusion in the same anaesthetised subject. Upper right: Schematic vertical distributions of ventilation and perfusion during awake conditions together with a lung illustrating the West's zones I, II, III and IV. Note the similarity in perfusion distribution, awake and during anaesthesia, but the marked change in ventilation distribution from more dependent regions to non-dependent regions during anaesthesia. Note also absence of ventilation corresponding to the location of atelectasis.

VENTILATION AND PERFUSION DISTRIBUTIONS

The distribution of ventilation and perfusion of the lung from top to bottom in the gravitational direction, i.e. from anterior to dorsal in the supine subject, is shown in figure 5. The technique assessed was single photon emission computed tomography (SPECT), using ^{113m}In-labelled particles dissolved in aerosol for assessing ventilation and ^{99m}Technecium (Tc) labelled macro aggregated albumin (MAA) injected in a central vein and deposited in the pulmonary circulation for the perfusion measurement. The SPECT technique has developed further since then and a recent approach can be found in reference 38. In addition, CT scans were taken awake and during anaesthesia[39]. For logistic reasons, no SPECT was done awake, only during anaesthesia. A lung CT from the same patient has been added to the ventilation-perfusion ($\dot{V}_A/\dot{Q}$) map, as well as a schematic distribution of ventilation and perfusion in awake subjects as shown in classical studies in the late 1960s[40-43] (Fig. 5). In the awake situation, both ventilation and

perfusion increase down the lung so that the $\dot{V}_A/\dot{Q}$ ratio is fairly close to 1.0 from anterior to posterior[44]. In the anaesthetised subject, perfusion shows a rather similar increase down the lung but with a decrease in the lowermost part, often referred to as a West's zone IV[43]. Ventilation on the other hand shows a dramatic difference from awake. In the lowermost, dependent part ventilation is absent, corresponding to what corresponds to atelectasis in the CT. This causes the development of intrapulmonary shunt since there is still some perfusion. At the level above the atelectasis, a decreased ventilation can be seen in comparison to the perfusion, most likely caused by cyclic airway closure. Finally, most of the ventilation is distributed to the upper half of the lung, well in excess of the perfusion. This causes a large region mimicking dead space, as it would have been interpreted with standard carbon dioxide (CO_2) wash-out technique. Thus, most of what is considered dead space with conventional technique is ventilation in excess of perfusion.

A non-gravitational inhomogeneity of perfusion distribution has also been demonstrated[45,46] and explained in a fractal model[47]. It will not be further discussed in this review, but it had been heavily debated before a certain consensus was reached on co-existence of both gravitational and non-gravitational influence on perfusion distribution[48-51].

SHUNT AND VENTILATION-PERFUSION MISMATCH

A more detailed analysis of causes of impaired oxygenation during anaesthesia has been done using the multiple inert gas elimination technique (MIGET)[52,53]. The MIGET is based on the infusion of "inert" gases with different solubilities in blood and, during steady-state conditions, blood sampling from a systemic artery and pulmonary artery, and collection of mixed expired gas for measurement of the inert gas concentrations. The infused gases were, from lowest to highest solubility, sulphur hexafluoride, ethane, cyclopropane, halothane (or enflurane), ether, and acetone. The technique allows separation of intrapulmonary shunt (defined as perfusion of regions with a $\dot{V}_A/\dot{Q}$ ratio lower than 0.005) and regions with poor ventilation in comparison with perfusion, so-called low $\dot{V}_A/\dot{Q}$ regions (regions with $0.005 \leq \dot{V}_A/\dot{Q} < 0.1$). These two are major determinants of impaired oxygenation. More details of the $\dot{V}_A/\dot{Q}$ matching can be extracted from MIGET but here the focus will be limited to these two factors. For further details regarding the technique, see reference 54. In a group of 45 patients of 23-69 years old, with no cardio-pulmonary disease, MIGET had been applied during waking conditions and then during inhalational anaesthesia and muscle paralysis. Awake, mean intrapulmonary shunt was no larger than 0.5% but it rose to 4.8% during anaesthesia[33]. An example is shown in figure 4, upper panels. In a study on anaesthetised younger patients[55], shunt was less than in another study on anaesthetised older patients[56].

Influence of age. Since an age dependence seemed to exist it was further analysed in a larger group of 80 patients[34]. They were all studied with MIGET and, as reported above, with CT of the lungs.

Intrapulmonary shunt was minor in the young patients, increased up to 45 years and

then decreased with further rise in age, up to 69 years, which was the oldest age studied with MIGET. Low $\dot{V}_A/\dot{Q}$ regions, on the other hand, increased continuously with age with a strong correlation with intrapulmonary shunt. Thus, in the 25-year old patient both shunt and areas with low $\dot{V}_A/\dot{Q}$ ratios were low (on an average 2.0 and 1.2% of cardiac output, respectively), in the 45-year old patient shunt had increased as had low $\dot{V}_A/\dot{Q}$ regions (5.8 and 4.6 %), whereas in the 65-year old patient shunt was reduced, but areas with low $\dot{V}_A/\dot{Q}$ ratios continued to increase (2.4 and 8.0). The amount of intrapulmonary shunt correlated with the extension of atelectasis. The low $\dot{V}_A/\dot{Q}$ regions can be considered to reflect cyclic airway closure and narrowing of airways, i.e. closing during expiration and opening up during inspiration. Continuous closure will result in shunt. A correlation has also been shown between CC and low $\dot{V}_A/\dot{Q}$ regions in a smaller setting of patients[57]. Moreover, an age dependence had been shown previously in awake subjects[22]. By adding into figure 1 a line that reflects the FRC during anaesthesia, the increasing importance of airway closure with age can be seen.

The question is why atelectasis with subsequent shunt is decreasing from an age of 45-50 years. A likely explanation is that when a patient of 45-50 years old is anaesthetised, he or she is already suffering from some airway closure awake (note that CC is above the FRC line already awake in the 50-year patient) and when the patient is pre-oxygenated, as is the standard procedure during induction of anaesthesia, those regions suffering from airway closure will receive less oxygen and maintain a certain amount of nitrogen. Nitrogen acts as a scaffold when FRC is reduced, preventing these regions to collapse or become atelectatic during anaesthesia. This may be the explanation to less atelectasis in patients above 50 years. However, these lung units remain as low $\dot{V}_A/\dot{Q}$ regions. The higher the inspired oxygen concentration is behind a closed or poorly ventilated lung region, the faster it will collapse because of the absorption of oxygen into the capillary blood[21]. This is why pre-oxygenation, routinely performed to increase patient safety during the induction, has a price, that of atelectasis formation. And the other way around, the more incomplete the pre-oxygenation is because of short duration, presence of airway closure (age) and the use of lower oxygen concentration, the less atelectasis is being produced[58].

Influence of body mass index. In the material of 80 patients we also found that intrapulmonary shunt increased linearly with increasing BMI. However, BMI had no influence on the development of areas with low $\dot{V}_A/\dot{Q}$ ratios[34]. Thus, the relative contributions by intrapulmonary shunt and low $\dot{V}_A/\dot{Q}$ regions in relation to age and to BMI were different, shunt being the major determinant of gas exchange impairment in the anaesthetised obese individuals whereas shunt and low $\dot{V}_A/\dot{Q}$ regions had varying effect in younger and older subjects. It should be noted however that there were no obese patients in this group of patients, only normal weight and over-weight ones. The potential influence of further increase in BMI to above 30 kg/m^2 shall not be neglected, as additional fall in FRC and more airway closure might be anticipated with potential effects on atelectasis formation and gas exchange. Morbidly obese patients who were studied with the MIGET before and one year after bariatric surgery showed improvement

in $\dot{V}_A/\dot{Q}$ ratio distributions after surgery[59]. The BMI fell from 45 to 31 kg/m^2 and arterial oxygenation improved, as shown earlier[60,61]. However, oxygen breathing resulted in much larger shunt before than after surgery, 9.8 versus 3.7%, and was suggested to be caused by absorption atelectasis behind closed airways. This is well in line with the increasing amount of atelectasis with increasing BMI during anaesthesia, as reported above[34].

Influence of chronic obstructive pulmonary disease. Patients with COPD and abnormal spirometric findings showed minor increase in shunt during anaesthesia before surgery[62,63], but influence of anaesthesia type and inspired oxygen concentration cannot be ruled out as confounding factors. However, the findings in patients with severe COPD, showing absence of atelectasis and shunt but appearance or increase of regions with low $\dot{V}_A/\dot{Q}$ ratios, give further support of COPD as an important and specific determinant of $\dot{V}_A/\dot{Q}$ mismatch[37] (see also Fig. 4).

Influence of positive end-expiratory pressure and cardiac output. A short note on the effect of a positive end-expiratory pressure (PEEP), is made here since it is a frequently used tool to improve gas exchange during anaesthesia and mechanical ventilation. Increase in lung volume by the application of a PEEP resulted in reduced atelectasis but not always in shunt in anaesthetised humans[26,32]. Moreover, any decrease in shunt was often accompanied by increase in low $\dot{V}_A/\dot{Q}$ regions, suggestive of reopening of previously closed lung units that were switched to regions that were still poorly ventilated in comparison with perfusion[64]. The effect of PEEP on the distribution of lung perfusion was studied in patients

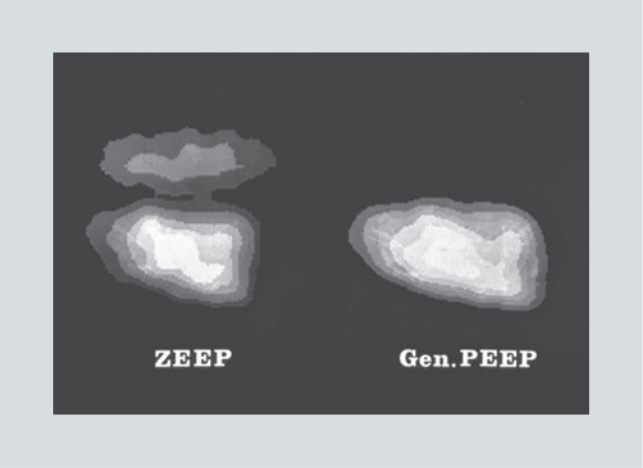

Figure 6. Distributions of lung perfusion in an anaesthetised subject in the lateral position. The images do not show the lung tissue per se but the perfusion. During zero end-expiratory pressure (ZEEP), modest amount of perfusion is distributed to the upper lung whereas with a general positive end-expiratory pressure (Gen. PEEP) of 8 cmH_2O almost no perfusion can be seen for the upper lung *(reproduced with permission from Hedenstierna et al.[37]).*

during anaesthesia in the lateral position to enhance the influence of gravity on the lung blood flow[65]. The perfusion distribution was assessed by SPECT after intravenous bolus injections of saline containing dissolved ^{133}xenon. During ventilation with ZEEP, 57% of perfusion was distributed to the dependent lung and 43% to the upper one (Fig. 5). After having applied a PEEP of 8 cmH_2O perfusion was now distributed by 81% to the dependent lung and only 19% to the non-dependent one. Thus, besides a fall in cardiac output in these patients from 4,5 to 3,8 l/min when comparing ZEEP and general PEEP, an additional rather dramatic redistribution of blood flow between the two lungs was seen (Fig. 6). Note that with PEEP, almost no perfusion can be seen in the upper lung in this particular patient (19% in the total group of subjects)[65]. This was the effect of a rather moderate PEEP and higher levels may limit upper lung perfusion even more. This emphasises that persisting

atelectasis in the dependent lung regions even when PEEP has been applied, can result in even lower PaO_2 than without PEEP[32].

Reduced cardiac output would, in addition to shunt and low $\dot{V}_A/\dot{Q}$ regions, impede arterial oxygenation. In a group of 50 patients during anaesthesia, comparisons were also made between arterial oxygenation and cardiac output in relation to the metabolic demand. This latter was calculated using the arterial-mixed venous oxygen content difference variable. If it was increased during anaesthesia, it would be a sign of reduced cardiac output. However, this was not seen[34]. Thus any decrease in cardiac output during anaesthesia may reflect a decreased need of oxygen supply rather than impeded blood flow. This is even likely, the metabolic rate often being reduced during anaesthesia[66].

ARTERIAL OXYGENATION

The combined effect of intrapulmonary shunt and low $\dot{V}_A/\dot{Q}$ areas will to a major extent determine the oxygenation of arterial blood. There are additional factors, e.g., cardiac output in proportion to the metabolic demand, as alluded to just above, and diffusion limitation over the alveolar-capillary interphase, the latter not seen in healthy lungs. Thus, PaO_2 is impaired in most patients during anaesthesia, and this has made it a rule to ventilate the patient with oxygen-enriched gas with an inspired oxygen fraction (F_IO_2) of 0.3–0.4 instead of the 0.21 of ambient air[24]. It is also known since earlier that PaO_2 is more reduced in elderly patients and in overweight patients during anaesthesia than in younger and leaner ones[67,68]. Despite different mechanisms of the decreased PaO_2 in young or elderly and lean or obese subjects, linear decreases are seen with both age and with BMI during anaesthesia. In figure 3 the arterial oxygenation is expressed as the P/F ratio (PaO_2/F_IO_2) to enable a rough comparison between measurements at different levels of F_IO_2. The P/F ratio decreased with age, breathing ambient air awake (F_IO_2, 0.21) and more so during anaesthesia and mechanical ventilation at increased oxygen concentration (F_IO_2, 0.3-0.4)[34]. As can be seen in figure 3, the P/F ratio was essentially the same awake and anaesthetised in the young patients, suggesting no worsening of gas exchange in this age group. With increasing age, the gap between waking and anaesthesia increased, indicating an age-dependent worsening of pulmonary gas exchange.

A similar comparison between the P/F ratio and BMI in the awake state showed that increasing BMI up to 30 kg/m^2 had little effect on PaO_2[34] but obese patients had a lowered PaO_2[59]. During anaesthesia, the P/F ratio fell with increase in BMI (Fig. 3)[34].

PREVENTION OF GAS EXCHANGE IMPAIRMENT

Knowing the mechanisms of oxygenation impairment, the question may arise how to counter this impairment. Application of a PEEP will reduce or eliminate atelectasis[26]. As alluded to above, PEEP may reduce cardiac output and will also force blood flow towards dependent lung regions where atelectasis may still exist although reduced in size. Hewlett et al.[69] warned already in 1976 for "the indiscriminate use of PEEP in routine anaesthesia". However, it remains as a standard tool

and is part of protective ventilation concepts. Thus, during the last 5-6 years, a number of multicentre studies have been published on "protective ventilation"[70-73]. The concept is based on what has been considered beneficial in patients with severe acute lung disease as in acute respiratory distress syndrome (ARDS) with the cornerstones of low tidal volume to decrease strain and stress[74,75], recruitment manoeuvres to open up collapsed lung regions and finally PEEP to keep the lung open[76], where it may be considered best practice[77]. Results have been varying with a number of possible explanations such as different sizes of tidal volumes, different recruitment manoeuvres and different PEEP level approaches. Also, whether the lung has been kept open from induction of anaesthesia until emergence has not been tested but only assumed. Another aspect is that the size of atelectasis varies markedly between patients, from zero to 20-30% of the lung area in a cut near the diaphragm[34], and the result of a recruitment manoeuvre and PEEP may vary between patients. Applying one and the same PEEP as a rule of thumb, as done in almost all "protective ventilation" studies, will be too little in some and too much in others. Individual titration of PEEP by electric impedance tomography to minimise atelectasis and optimise arterial oxygenation has been tested with positive results, but the titration procedure and use of additional equipment may be limiting factors[78,79].

Prevention of atelectasis by PEEP and also by recruitment manoeuvres may be of greater value in young and middle-aged patients where atelectasis is dominating. In elderly patients with less of atelectasis and more of airway closure PEEP may be of more limited value and if perfusion of the lung is more impeded in this age group, PEEP may even be deleterious. An interesting approach might be to impose expiratory flow limitation that may stabilise airways in similar with pursed lips breathing that is taught to patients with severe COPD. Flow limitation to produce slow expiratory flow has been tested during anaesthesia with improved respiratory mechanics and arterial oxygenation[80], but without focus on age dependence.

This review is limited to the anaesthesia and surgical period, but it should be worth to mention that anaesthesia-induced atelectasis may remain for several days post-operatively[81,82].

CONCLUSIONS

What can we learn from this review of different mechanisms of gas exchange impairment and potential inflammatory promoters in the perioperative period? It may be that atelectasis is not the major or the only cause of oxygenation impairment. Cyclic airway closure may be another important source. Atelectasis and airway closure occur within a few minutes after or even during induction of anaesthesia. Precautions by recruitment manoeuvres and application of PEEP have been suggested and used in different studies but the effect on keeping the lung open and preventing airway closure have not been studied, only assumed with regard to atelectasis formation.

Keeping the lung open during anaesthesia with a titrated PEEP is one step in a peri-operative lung protection concept. Titration to apply a PEEP high enough to prevent atelectasis and low enough to prevent circulatory

side effects is a desirable goal, if it can be met at all. There may be other approaches in keeping airways and alveoli open that should be tested, e.g., expiratory flow limitation. In view of the almost quarter billion anaesthesias performed annually in the world, there seems to be good reasons for more research in this field!

DISCLOSURES

The author has no conflict of interest to disclose.

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