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ACUTE RESPIRATORY DISTRESS SYNDROME: A POINT OF VIEW

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Summary

Acute Respiratory Distress Syndrome (ARDS) is characterized by refractary hypoxemia due to a variable grade of alveolar collapse because of the gravitational gradient (sponge lung) and/or the alveolar occupation (alveolar floody). Current challenge is minimizing ventilator-induced lung injury (VILI) while providing a reasonable gas exchange.

Gas exchange and hemodynamics impact of mechanical ventilation (MV) depend on proportion of collapsed lung versus occupied alveoli which coexist in the same alveolar environment. When alveolar floody dominates, the lung has minimal recruitability and hemodynamic impact of insufflation is usually significant. When alveolar collapse is the most important phenomena we will have best recruitability and the hemodynamic impact of MV will be less.

Some authors have shown good results with the use of maximum lung recruitment maneuvers to recruit lungs, even when alveolar occupation is predominant. However, it is a mistake to consider all injured lung tissue as potentially recruitable. High level of PEEP and recruitment maneuvers despite substantially improve oxygenation have shown no reduction in mortality.

Reduce lung stress and strain using an appropriate ventilatory setting is achieved with very low tidal volumes (4 ml/kg PBW) and moderate/high level of PEEP, according to best respiratory system compliance. Currently, a study concluded that the driving pressure should be less than 16 cmH2O, because higher levels increase risk of death. These characteristics enforce to use an individual ventilatory approach.

Recently, it has been reported that VILI develops proportionally to external energy applied by the ventilator to the respiratory system; this concept is named mechanical power (MP). It considers the different variables related with the ventilator settings as cause of VILI: tidal volume (VT), driving pressure, respiratory

rate, inspiratory flow, resistance and PEEP (equation of motion). Furthermore, we have extrapulmonary variables such as: perfusion, pH, gas tension and temperature which can also influence.

1. Introduction

Acute Respiratory Distress Syndrome (ARDS) is a lung condition that is characterized by hypoxemia refractory to therapy with oxygen and secondary to the presence of a varying degree of alveolar collapse, dependent on the severity and / or the presence of alveolar occupation. Both disorders (collapse and occupation) can coexist within the same alveolar neighborhood, thus selected ventilatory strategies may benefit some alveolar units but not others, thus creating a heterogeneity that makes it difficult to clinically address this entity.

The concepts that govern the administration of mechanical ventilation (MV) have undergone substantial changes over the last forty years, both from the point of view of the ventilatory goals (plateau pressure, tidal volume, driving pressure, etc.) and those related to gas exchange (permissive hypercapnia). In the 70s, MV was set at 12-15 mL / kg tidal volumes (VT) and positive end-expiratory pressures (PEEP) between 5 and 10 cm H_2O. This setting pattern resulted in the development of hypocapnia[1], as well as the appearance of barotrauma (pneumothorax, pneumomediastinum, pneumoperitoneum), especially in patients with ARDS. These complications were associated with mortality rates as high as 90%[2].

Only in the early eighties did the concept of *lung rest* arise, with the aim of preventing the mechanical stress posed by the use of positive pressure in the airway. This concept was so relevant that some dared to use extracorporeal CO_2 removal, taking on the risks of this technique, in order to use MV at very low frequencies (2-4 rpm) [3].

Later studies made it possible to understand that various mechanical factors (volume and pressure) can both produce and accentuate the damage lung tissue present during ARDS. The tension (stress) brought on the alveolar walls (epithelium) and capillaries (endothelium) subject to abnormal alveolar excursion leads to shear forces that cause damage during each inflation[4]. Beyond that, we now know that there are molecular changes triggered by the activation of mechanoreceptors that increase the production of inflammatory mediators at a local and systemic level[5,6]. This review will focus on the morphological, mechanical and therapeutic aspects of this syndrome.

1.1. Ventilator Induced Lung Injury (VILI)

There is consistent evidence that the use of an inappropriate MV strategy can cause lung injury and amplify the damage that motivated MV. This process, known as ventilator induced lung injury (VILI), is related to the size of the systemic inflammatory response and the development of Multiple Organ Dysfunction Syndrome (MODS).

After the description of ARDS by Ashbaugh[7], Falke[8] proposes the use of PEEP as a therapeutic strategy for these patients. Subsequently, Tierney[9] associated ARDS with the development of MODS. It is now recognized that VILI is mainly related to two phenomena: the first takes place at the end of expiration and is linked to the use of a PEEP level which is insufficient for preventing cyclic alveolar collapse and reopening; and the second is associated with the use of elevated pressure or VT which can induce alveolar overdistension. Consequently, the main factor responsible for the development of VILI is the mechanical stress applied to a heterogeneous lung with low aeration capacity, where the main target structures are the lung's fibrous skeleton, including the microvasculature, terminal airways and delicate juxta-alveolar tissues[10].

1.2. Lung's Fibrous Skeleton Behavior

Epithelial (type I and II pneumocytes) and endothelial cells are anchored via integrins in the lung's fibrous skeleton, which is made up of extensible fibers (elastin) and inextensible fibers (collagen). Cell shape and arrangement depend on the changes the lung's fibrous skeleton may undergo, and the cell distortion limit is determined by the collagen fibers. The lung's fibrous skeleton responds with an increase in internal stress of equal magnitude and opposite direction to the pressure applied by the ventilator. However, the true factor responsible for

distension is the transpulmonary pressure (TPP), which corresponds to the difference between alveolar pressure (plateau) and pleural pressure (Ppl) [11]. Figure 1

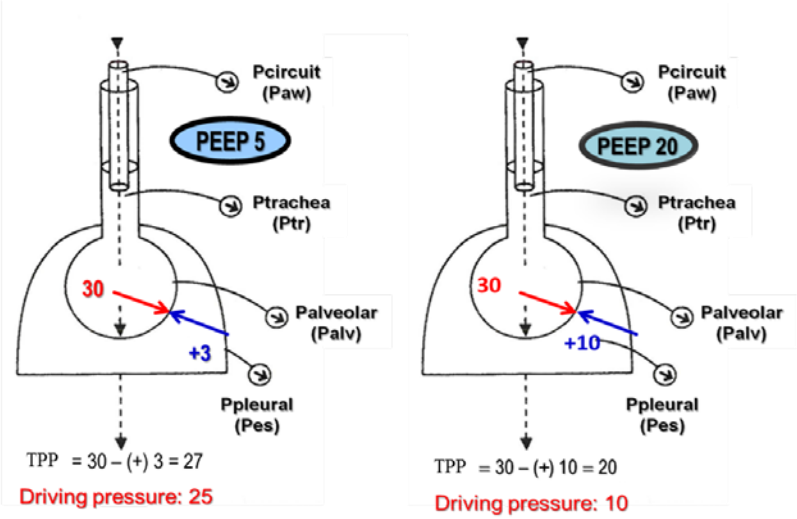

Figure 1: Transpulmonary Pressure (TPP): To the left, at 5 cm H_2O of PEEP. To the right, at 20 cm H_2O of PEEP. Sarge T, Minerva Anestesiologica 2009; 75: 293-299

The mechanical force applied over collagen fibers could determine what we know as stress or mechanical tension (end inspiratory lung stress); this holds true for both the lung as a whole as well as for each particular region. The biological consequence of mechanical stress is called *strain* and its magnitude can be represented by the ratio between the VT administered and the end-expiratory lung volume at rest (EELV), in other words VT divided by the size of the baby lung (measured using CT and no PEEP)[11].

Another concept that we must know to understand the mechanical damage is the specific lung compliance, since it is associated with the concepts of tension and strain and has to do with the pressure at which the baby lung doubles in size, ie, when the division between the VT and the baby lung is equal to 1. Under these conditions, the specific lung compliance is equal to the TPP[12].

In the normal lung the EELV doubles on reaching 80% of the total lung capacity and this level is considered to be the upper limit of the physiological strain of the lung's fibrous skeleton. Gattinoni[12] showed that the specific lung compliance in ARDS is similar to that of a normal lung (a small and non-stiff lung), corresponding to a TPP of approximately 12.5 cm H_2O, an amount that could be considered as a safe threshold during MV administration.
Recently, it has been reported that VILI develops proportionally to the external energy applied by the ventilator to the respiratory system; this concept is named mechanical power (MP). It considers the different variables related with the ventilatory settings as cause of VILI: VT, driving pressure, respiratory rate, inspiratory flow, resistance and PEEP (equation of motion). The energy applied for each insufflation can be obtained from the areas of the dynamic volume- pressure curve. This is measured as liter per cm H_2O, and expressed in joules. The MP is obtained by multiplying the energy of each insufflation by the respiratory frequency[13].

Tidal Volume, driving pressure and inspiratory flow changes, produce exponential increase in the MP, for example, when the VT is duplicated produces a fourfold increase in MP. Instead, an increase of PEEP, produce a linear increase in MP. The above is because PEEP does not contribute to the cyclic energy load associated with the ventilation, in other words, PEEP represents the baseline tension of the lung. Furthermore, we have extra pulmonary variables such as: perfusion, pH, gas tension and temperature[14].

2. Anatomical-Functional Lung Tissue Distribution

In ARDS the extent of lung damage that MV can induce is directly related to the heterogeneous distribution of anatomical and functional lung tissue and close coupling with the thoraco- diaphragmatic cupola. VT distribution is dependent on the vertical gradient exerted by the force of gravity on the pleural surface and lung parenchyma. This distribution makes it possible to divide the lung tissue into an upper or non-dependent region, and a lower or dependent lung region. Based on the aforementioned, the pleural pressure surrounding the lower surface of the lung is greater than at the upper region[15].

Hence, during MV the pleural pressure goes against the alveolar pressure. This becomes particularly noticeable when dealing with an increase in intra-abdominal pressure. As the pleural pressure is lower in the upper region of the lung, the TPP is greater at that level. In other words, the alveoli located at the upper end are under higher distension pressure and hence have a greater radius than those located in the dependent regions. Therefore, when faced with the same level of alveolar pressure, its ability to increase the alveolar radius during inflation is reduced, leaving it more susceptible to over distension[11].

This phenomenon could be avoided by limiting the VT, however, this isolated clinical approach does not guarantee control over alveolar reopening and closing with each respiratory cycle. If we maintain a constant VT and increase PEEP to avoid such phenomenon, we can face two situations: 1) that the end-expiratory volume does not increase with PEEP (low or no potencial of recruitment) or 2) increase EELV (high potential of recruitment). In the first case, the increase in PEEP will overdistend the available alveolar population and VT can overcome critical TPP of the sick lung, leading to stress and strain (VT> baby lung), and in the second, the same VT can be distributed among a higher number of alveolar units with the consequent reduction of TPP and hence an increase in lung compliance, thereby limiting strain (VT <baby lung). This mechanism is credited with the improvement observed in the prone position, since in this position the lung adjusts within the chest in such a way that alveolar distension becomes more uniform, and the compressive forces that in supine would lead to collapse in the thoracic region are reduced[16].

A logistic regression analysis[16] of the ARDS network study data reveals that before randomization of patients, the VT was titrated based on thoraco-pulmonary compliance. Surprisingly, the effects of VT change on mortality were significantly associated with that value, even after adjusting for population age, APACHE II and PaO_2 / FiO_2. To put it in other words, patients whose pre-randomization thoraco-pulmonary compliance was low and were assigned to the VT 12 ml/kg arm had a higher mortality than those assigned to VT of 6 ml/kg. In contrast, patients with high pre-randomization thoraco-pulmonary compliance assigned to 12 ml/kg had a lower mortality than those assigned to the low VT arm.

Recently, Amato[17] performed uni- and multivariate risk analyses to estimate the isolated effect of driving pressure changes on mortality in 9 randomized trials with 3562 patients. The results revealed that the relative risk of death associated to increases in driving

pressure in a standard deviation was 1.41 (95% CI 1.31 to 1.51; $p \leq 0.001$). Figures 2 and 3

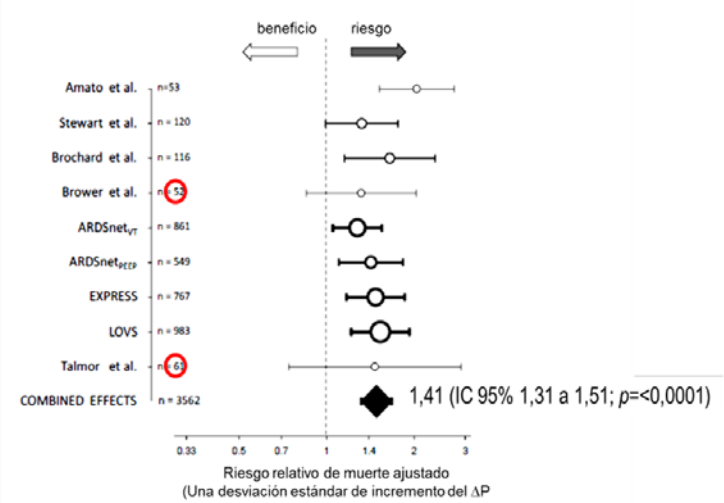

Figure 2. Relative Risk of Death associated with ▲P in each study. The circles show the studies bearing few patients. Amato MBP, et al. NEJM 2015; 372 (8): 747-755.

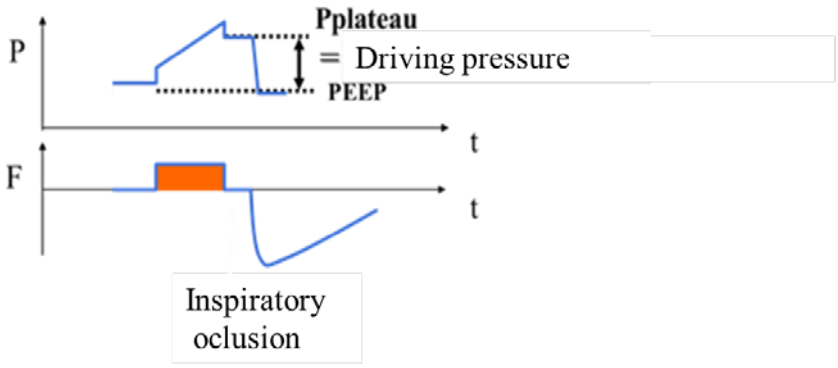

Figure 3. driving pressure = plateau pressure - PEEP

This reassessment of the results obtained in recent years strongly suggests that the benefits achieved using protective ventilation based solely on the administration of low VT should be regarded with caution since not all patients benefit from this ventilatory strategy. Today, everyone is aware of the presence of expiratory alveolar instability in ARDS; therefore, there should also be measures aimed at avoiding cyclic alveolar collapse and reopening. We must also consider that each of these patients has a lung condition with a unique distribution of lesions, so it is illogical to assume that another patient will present with the same structural and functional pattern, i.e., in these patients, MV setting should be performed on a case by case basis; we must not fall into the standard ventilation routine, far less with the most severe patients.

3. ARDS Morphological Distribution (Chest CT)

Some authors have proposed that morphological differences present in the chest computed tomography (CT) of patients with ARDS are related to the gasometric response observed vis-à- vis the application of PEEP. In their study, a group of patients –called diffuse ARDS– shows a massive loss of aeration which is evenly distributed throughout the lung parenchyma (diffuse and bilateral attenuation on CT); in others, the loss of aeration affects only the lower lobes, with preservation of the upper lobes (lobar ARDS); and a third group, presenting massive loss of lower lobe aeration, and only partial involvement of the upper lobes (patch-type lesions) [18,19]. Figures 4 and 5

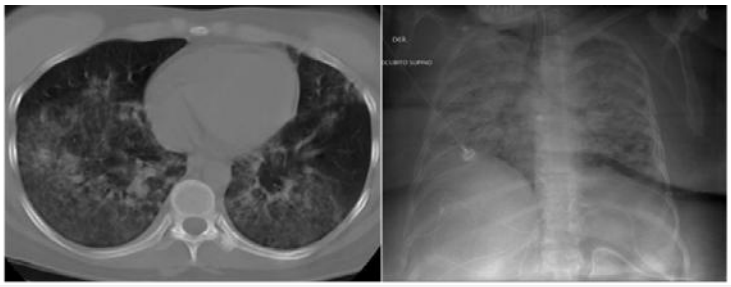

Figure 4. Diffuse ARDS (sponge lung). Rouby JJ, Eur Respir J 2003; 22: Suppl. 42, 27s-36s

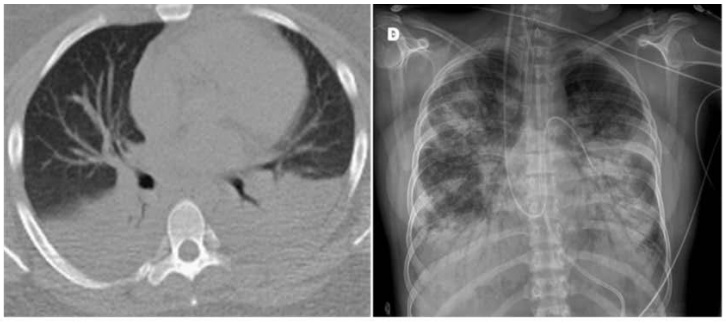

Figure 5. Focal ARDS (floody, or alveolar occupation) Rouby JJ, Eur Respir J 2003; 22: Suppl. 42, 27s-36s

They suggest that while in the diffuse ARDS group, the use of PEEP greater than 10 cm H_2O induces marked recruitment with no evidence of overdistension in the upper lobes, in lobar ARDS this level of PEEP was unable to induce alveolar recruitment, and was associated with overdistension of previously aerated areas[20]. This is particularly clear when the reduction of the EELV of the lower lobes depends on the presence of "compression atelectasis", a condition in which lung opening pressures exceed 30 cm H_2O.

This behavior differs from that observed by other authors who –using a maximum recruitment strategy– managed to recruit dependent areas, and by decreasingly adjusting the PEEP, they were able to prevent expiratory lung collapse, thereby improving gas exchange without overdistending susceptible areas (upper lobes)[21]. Moreover, 54% of patients required a higher plateau pressure of 40 cm H_2O to meet the proposed oxygenation criteria; a finding which would be expected considering the wide distribution of the critical opening pressures, which are higher than the pressures necessary to maintain the recruitment achieved during inspiration[22,23].

There is evidence that the use of suboptimal levels of PEEP –in the absence of prior alveolar recruitment strategies– can alter the alveolar excursion and facilitate the cyclic alveolar collapse/opening. Both of these phenomena result in an inappropriate distribution of tidal volume inflation, a mechanism involved in the injury induced by mechanical ventilation [24-26].

Consequently, it is very likely that the lung morphology revealed by CT using 10 cm H_2O PEEP at end-expiration is unable to correctly predict the gasometric and morphological response in patients with lobar ARDS. It is therefore proposed that the application of higher PEEP levels – after performing an alveolar recruitment maneuver and decremental PEEP titration – could maintain the aeration reached in the lower lobes without overdistending the upper ones[21].

4. Strategies for adjusting ventilation

4.1 Use of low V_T and PEEP based on fraction of inspired oxygen:

The ventilator strategy proposed by the study conducted by ARDS Network advocates minimizing lung strain while maintaining minimum accepted gas exchange[28]. These targets can be achieved by using 6 ml / kg V_T PBW with preset fraction of inspired oxygen (FiO_2) and PEEP, based on a table that combines levels of PEEP with FiO_2, aiming at a lower PEEP in order to maintain a plateau inspiratory pressure <30 cmH_2O and arterial oxygenation between 88 and 95%. This approach leds to a 22% reduction in mortality[28]. However, this strategy has been considered dichotomous, as it shares the prevention of relaxation attributed to low V_T and limits the alveolar excursion during inspiration and potentially the opening of collapsed units, which leads to progressive lung derecruitment[29,30]. The recruitment/derecruitment phenomenon may occur around 30,000 times per day and the resulting injury appears to be equal or even greater than that caused by overdistension [25,31]. However, there is evidence that lung recruitment has a toll on non-dependent areas (See *Overdistension: the hidden face of the recruitment*)[18].

4.2. Inspiratory pressure-volume curve

To adjust the PEEP individually, MV is programmed based on the characteristics of the thoraco- pulmonary mechanics obtained through an inspiratory pressure-volume (P-V curve) curve. In ARDS, this curve is generally sigmoidal (polynomial) and describes 3 segments: a lower one, a low compliance zone corresponding to collapsed alveoli having a similar TOP (threshold opening pressure); an intermediate zone, where compliance is kept constant during inflation (linear segment), and finally the upper, low compliance zone, which is linked to the phenomenon of overdistension. The intersection between the intermediate segment with the lower and upper segments determines the lower inflection point (LIP) and

the upper inflection point (UIP), respectively[31]. Although this technique was widely used to set the MV, setting the PEEP above the LIP has been abandoned, since it is now known that recruitment does not occur only at TOP, but throughout inspiration. Moreover, determining the inflection points holds large intra and inter-observer variability[32]. The application of PEEP and RM (recruitment maneuvers) can increase EELV through 2 opposing mechanisms: the first, by increasing the proportion of aerated alveoli at the end of expiration (recruitment), or due to inflation of previously opened lung regions (overdistension)[33]. Figure 6

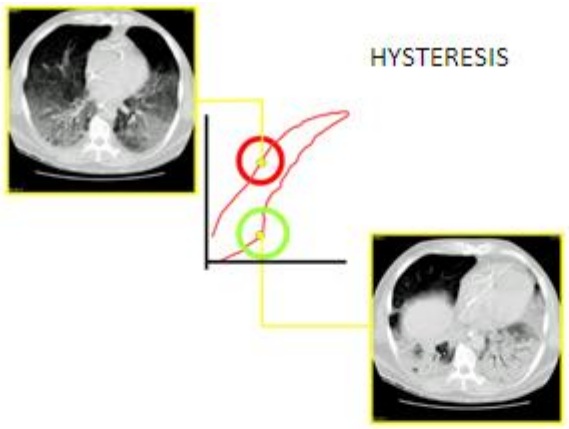

Figure 6. Inspiratory and expiratory limb from the P/V curve. LIP, circle green. Maximum expiratory curvature point, circle red (ideal PEEP). Albaiceta GM, et al. Am J Respir Crit CareMed 2004; 170: 1066-72.

The group commanded by Amato provided consistent evidence that the recruitment attained with the use of LIP is insufficient. The authors compared oxygenation and the presence of non-aerated lung tissue on chest CT using two strategies: the first, led by LIP plus 2 cm H_2O, and the second, with a PEEP adjusted by a decremental PEEP titration protocol (PEEP DT), after applying RM [34]. At that point, it was elucidated that the necessary pressures for overcoming collapse in adults with ARDS are much higher than those predicted by pressure overlap theory, which would indicate the presence of other factors involved, such as: increased surface tension, anisotropic inflation, increased intra-abdominal pressure or other causes still unknown[35].

5. Recruitment Maneuvers

The approach to lung recruitment that has garnered the most interest is the use of RM along with a sustained application of high pressure in the airway. Both were initially carried out by means of high frequency oscillation. Kolton[36] and McCulloch[37] demonstrated that a mean sustained airway pressure could restore arterial oxygenation in animals with ALI (acute lung injury) and maintain this benefit over time. Many authors assumed that such RM could be made only with high frequency ventilation. However, there are several reports that show that this strategy can be successfully achieved on conventional MV. Since the nineteen-eighties to date, various successful reports with this strategy in both animals and humans have been described. Vazquez de Anda[38] and Rimensberger[38] demonstrated in animal models that the RM during conventional mechanical ventilation were as effective as those made with high frequency ventilation. In patients with ARDS, Gattinoni et al[40] required a peak airway pressure of 46 cm H_2O to recruit part of the collapsed lung. Meanwhile, Amato[41] applied 35 to 40 cm H_2O CPAP for 30 to 40 seconds before starting a protective ventilatory strategy, and provided that mechanical ventilation was interrupted. Figure 7

- ✓ **Pressure based maneuvers**
  - 35-45 cm H_2O applied for 30 to 40 seconds
  - High V_T 'sighs' at regular intervals
  - PEEP increase for a few breaths
  - maximum recruitment
- ✓ **Ventilatory Modes**
  - APRV and HFOV
- ✓ **Chest wall modification**
  - Allowing spontaneous breathing
  - Abdominal decompression, effusion drainage
  - Abdominal and chest wall muscle relaxation
  - Negative abdominal pressure
- ✓ **Switching position (to prone)**
  - regional recruitment (dorsal TPP increase)
  - Regional PEEP-like, optimizing ventilation/perfusion ratio

Figure 7: Lung recruitment strategies. Marini JJ. Curr Opin Crit Care 2014;20:636-8

Lapinsky et al[42] showed that patients tolerate multiple RM without significant hemodynamic complications or barotrauma. The highest documented pressure in humans was applied by Medoff et al·[43] who reported the use of a peak pressure of 60 cm H_2O on a 32 year old woman with severe ARDS, secondary to sepsis. The recruitment was performed in pressure control mode with 40 cm H_2O of PEEP, distension pressure of 20 cm H_2O, 1:1 inspiration-expiration ratio, and RR of 10 bpm, maintained for 2 minutes. Prior to this maneuver, RM were attempted at peak pressures of 50 and 55 cm H_2O, yet these were unsuccessful. No hemodynamic involvement was recorded. There is clinical data has confirmed that there is a strong statistical association between high levels of PEEP and a reduction in mortality[41], as well as between the presence of non-aerated lung tissue –detected on chest CT scan– and an increase in mortality[44]. Higher than usual PEEP values were used as part of a protective mechanical ventilation strategy in a clinical trial[41]. Recently, a randomized clinical trial compared the open lung strategy (OLA: open lung approach) with the ARDS net strategy, but it did not exhibit significant differences in mortality. In the OLA group, improvement was observed regarding oxygenation and driving pressure, and there were no undesirable effects on mortality, MV-free days or barotrauma[45].

RM have emerged as a prerequisite to the use of protective MV strategies in ARDS; however, there is no consensus as of yet on what the best technique is, or when it should be applied. Although the use of plateau airway pressures of 30 to 35 cm H_2O has shown to be deleterious[46,47], the application of elevated airway pressures for a short period of time, as a lung recruitment method, constitutes an interesting alternative[47-49]. The rationale for this strategy is analogous to the concept of pulse therapy, i.e., the use of a risky and extreme treatment for a reduced time interval in order to attain long-term benefits.

The key issue is to strike a balance between the risk of the RM (which should be minimal), and overcoming lung collapse (which should be maximal). The long-term benefits are related to lung hysteresis, i.e. airspaces can be kept open at airway pressures lower than those necessary during the recruitment phase [50,51].

5.1. Decremental-PEEP Titration (DT-PEEP):

DT-PEEP after having made RM has been proposed with a view to decreasing the proportion of non-aerated lung tissue and limiting the cyclic recruitment / derecruitment phenomenon[21,35,52]. This technique is based on the presence of alveolar populations with different TOP and the difference between the pressures necessary to open the lung and those required to keeping it open (hysteresis). It is not easy to determine the optimum PEEP step, since the occurrence of collapse during DT-PEEP should begin with localized changes in lung compliance, mainly in the dependent region, which corresponds to the loss of functional units compressed by gravity. These changes should precede the deterioration of the overall lung compliance, and eventually lead to deterioration of gas exchange, due to reflex hypoxic vasoconstriction[53].

The dependent region compliance decreases significantly when the PEEP level falls below 21cm H_2O, a threshold associated with decreased aeration in this area. The optimal level of PEEP encountered using gas exchange and dynamic compliance was 20 and 16 cm H_2O, respectively. While overdistension relief due to reduction in PEEP, the compliance of the non-dependent region gradually improves, which counterbalances the dependent region compliance deterioration. Consequently, the overall lung compliance reaches its peak with a PEEP average lower than the actual collapse threshold (Figure 8). There is evidence that with quantitative analysis of images acquired through electrical impedance tomography (EIT), it is possible to detect the regional collapse before changes in overall lung compliance and gasometry appear [53, 54].

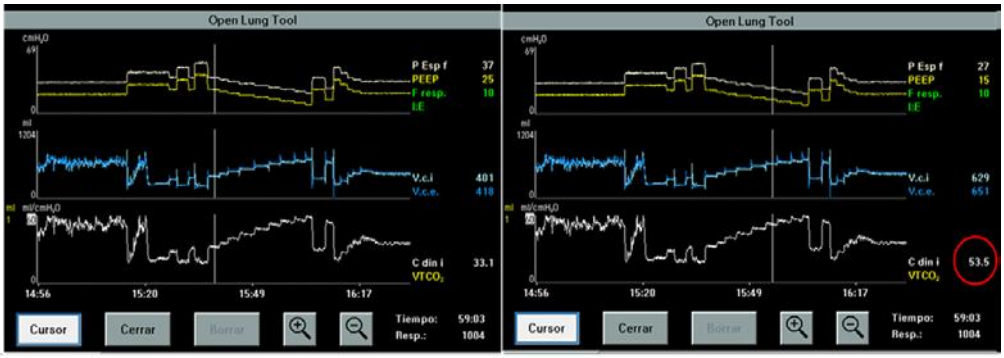

Figure 8: upper graph: PEEP stages; middle graph: expired tidal volume (in blue); lower graph: dynamic compliance right side: 33.1 with 25 cm H_2O PEEP; left side: 53.5 with 15 cm H_2O of PEEP

5.2. Expiratory pressure-volume curve

The expiratory limb of the P-V (pressure-volume) curve describes the process of lung emptying, which begins once the lung inflation has reached total lung capacity. In order to study this portion, the super-syringe technique, along with step-by-step continuous positive pressure decreasing maneuvers in the airway have been used. This is to obtain the plateau pressure (zero or minimum flow) on each volume step during exhalation [55,56]. PEEP is an expiratory maneuver; thus the optimum level should be correlated with derecruitment. Albaiceta demonstrated that loss of aeration and derecruitment were significant only in the case in which the pressures were lower than the point of maximum curvature on the expiratory limb of P-V curve (figure 6, red circle). Furthermore, at this point, the greatest amount of normally aerated tissue, measured by chest CT, compared with images obtained at the height of the lower inflection point on the inspiratory limb of the P-V curve (LIP) was observed. A noteworthy aspect was that the hyperinflated tissue did not increase significantly[56].

5.3. Anatomical versus functional recruitment

There is currently some debate regarding the 2 types of recruitment, namely ‘anatomical’ and ‘functional’. The first has to do with the reduction of the mass of collapsed lung tissue measured by chest CT (Figure 9), and the second applies to the reduction in intrapulmonary shunt, estimated from the mixed arterial and venous oxygen content. It has been indicated that the displacement of the perfusion can act as a causing mechanism for the dissociation between aeration gain induced by PEEP and the contribution the re-expanded region should have in the overall intrapulmonary shunt fraction. In case of partial recruitment, displacement of perfusion towards the dependent (collapsed regions) induced by PEEP can prevail over the beneficial effect expected upon improving aeration at the regional shunt. On the other hand, when using a maximum lung recruitment maneuver followed by an optimum PEEP level, the extensive re- expansion of collapsed lung tissue would mitigate this dissociation. The differences between 'anatomical' and 'functional' recruitment may depend on the strategy selected for titrating PEEP [58-60]. Moreover, the effects of lung recruitment maneuvers may be overshadowed by their potential impact on cardiac output and oxygen transport; i.e. a correct interpretation of the benefit of the RM would require simultaneous assessment of hemodynamic status and intrapulmonary shunt. The hemodynamic effect of carrying out P/V curves and lung recruitment maneuvers has been inconsistent[61,62]. Notwithstanding the above, currently it has been advocated to stabilize hemodynamics using volume administration and vasoactive drugs before applying any recruitment maneuver (hemodynamic

conditioning phase)[63].

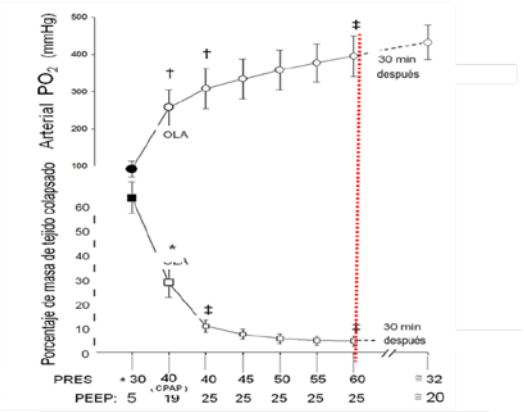

Figure 9: Percentage of collapsed tissue mass versus PaO_2 (mirror image)

6. Conclusion

In recent years we have learned that in ARDS, the lung is small and heterogeneous, and that MV can cause direct physical damage (stress), lung's Fibrous Skeleton elongation (strain), as well as local and remote inflammatory reactions. The clinical benefit of ventilating elegantly –based on overall and regional reduction in lung tissue stress/strain– has already been confirmed. However, when we are ventilating it is not possible to control all variables, such as trans-pulmonary pressure (TPP), alveolar pressure, alveolar time constants, blood flow, etc. To overcome these drawbacks, we have some clinical equivalents of these variables, such as the plateau pressure, the driving pressure and thoraco-pulmonary compliance.

The driving pressure serves as an indication of the functional size of the lung, and can be estimated by dividing VT by the static compliance of the respiratory system. These tools make it possible to fine-tune the ventilator settings based on different clinical conditions and moments. With the available evidence, we can say that the use of VT at 6 mL / kg of ideal weight is insufficient when it comes to preventing VILI, as EELV varies from patient to patient. It would therefore be advisable to associate VT with the driving pressure and to adjust DT-PEEP by using the best static compliance. Measuring variables such as TPP and EELV should be included in the daily routine.

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