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EXPERIMENTAL

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Abdomen release in prone position does not improve oxygenation in an experimental model of acute lung injury

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Abstract *Objective*: To analyze the effect of abdomen release in the prone position on oxygenation in an experimental model of acute lung injury.
Design: Experimental randomized controlled study.
Setting: Experimental laboratory of a tertiary university hospital.
Participants: Mixed-breed adolescent pigs weighing between 25–31 kg.
Interventions: Thirty minutes after pulmonary edema was produced with oleic acid, the animals were turned prone and randomized into two groups: group I or control ($n = 9$), lying directly on the operating table; and group II ($n = 11$) with abdomen release, with positioning rolls under the upper part of the chest wall and the pelvis to allow free movement of the abdomen.
Measurements and results: The gas exchange, respiratory mechanics, hemodynamics, intra-abdominal pressure (IAP) and the extravascular lung water (EVLW), determined by double indicator dilution method (DI), were recorded at baseline (time 0) and at 30, 60, 90, 120 and 150 min. The PaO_2/FIO_2 increased in both groups at 30 min after the pigs were placed in the prone position (time 60) and then decreased progressively until the end of the experimental period, with no statistical differences between the groups at any time (73.1 ± 14.5 vs 79.5 ± 14.9 at 150 min). Abdomen release was not associated with changes in the respiratory mechanics, EVLW or intra-abdominal pressure.
Conclusions: Abdomen release in prone position does not improve oxygenation in an experimental model of acute lung injury.

Key words Acute lung injury · Extravascular lung water · Mechanical ventilation · Oleic acid · Pulmonary edema · Prone position

Introduction

Treatment for acute respiratory distress syndrome (ARDS) has been limited to life support measures such as mechanical ventilation with positive end-expiratory pressure (PEEP) [1]. However, correction of the hypoxemia is not always achieved and toxic concentrations of oxygen are sometimes required. A series of therapeutic alternatives have been proposed [2], including ventilation in the prone position.

The postural approach using the prone position has produced an improvement in the oxygenation of subjects with acute lung injury both experimentally [3, 4] and clinically [5, 6, 7, 8]. The mechanisms implicated in this effect have been studied in experimental animals [9], although only in short series and generally not in controlled studies. Published clinical experience is sparse, with only around 300 patients studied in total [10]. Nevertheless, the clinical studies raised issues that have yet to be addressed [1], including the absence of re-

sponse in a proportion of patients (20–40 %), the factors that predict response and the optimal length of treatment, since the prone position produces serious adverse effects, such as pressure ulcers, much faster than does the supine position.

A further issue to be addressed is the best way for the prone positioning to be carried out. Almost all of the clinical studies on the prone position as a treatment of severe hypoxemia in ARDS have introduced some element under the anterosuperior chest and/or pelvis so that the abdomen can move freely. Moreover, in the last few years, a series of devices have been proposed to assist postural change and to allow the abdomen to expand during inspiration, on the assumption that this enhances the treatment. This assumption has never been tested formally and is probably based on the observation that the prone position slightly increases pulmonary volumes, specifically the residual functional capacity (RFC), related to the reduction in intra-abdominal pressure that is produced when the abdomen is released.

Finally, we must also consider the persistence of the improved oxygenation versus basal values after the supine position has been restored. It would be important to know, as suggested recently [12], whether the prone position can limit the lung injury induced by mechanical ventilation. This can be measured with various methods, including the determination of the extravascular lung water (EVLW).

The aim of the present experimental study was to document the short-term effects of abdomen release in prone position on oxygenation in an experimental model of acute lung injury. The secondary objective was to investigate whether any benefit is related to alterations in respiratory mechanics (including intra-abdominal pressure) or EVLW.

Material and methods

Study design

This was a randomized controlled experimental study comparing two methods of prone positioning according to whether the abdomen is released or not. Adolescent mixed-breed pigs weighing 25–31 kg were used. The allocation sequence was generated using a random number table. The intervention could obviously not be blinded. It was calculated that a sample of 18 animals would give the study an 80 % power with an overall type I error of 0.05 to detect a difference of 16.5 mmHg (a shunt of 30 % permits an 0.1 reduction in FIO_2 [13]) assuming a PaO_2 of 76.5 ± 12.1 mmHg, based on previous studies with the same experimental model [14]. The study was approved by the ethics committee of our hospital. The handling of the animals was in accordance with Spanish laws governing the protection of research animals (Real Decreto 223/1988).

Anesthesia and catheterizations

Premedication was with intramuscular injection of ketamine (10 mg/kg) and azoperone (5 mg/kg). Anesthesia was induced by the intravenous injection of atropine (1 mg), fentanyl (0.15 mg), midazolam (15 mg) and ketamine (150 mg), and was followed by tracheostomy and intubation with a cuffed tube (5 mm internal diameter). Mechanical ventilation was provided with a Bear 1 ventilator (Bournes Medical Systems, USA). The ventilation regime was controlled with a tidal volume of 12 ml/kg, a respiratory rate of 14 per min (approximate minute volume of 170 ml/kg), a FIO_2 of 100 % and an inspiratory/expiratory (I:E) ratio of 1:1.5. Anesthesia was maintained with a perfusion of ketamine (20 mg·kg·h) and atracurium (1 mg·kg·h), supplemented by boluses of fentanyl when necessary. During the experiment, the animals received 10 ml·kg·h (250–350 ml/h) of 0.9 % saline solution.

A catheter (Certofix©, Braun, Menselungen, Germany) was introduced via the jugular vein for the infusion of anesthesia and fluids and measurement of central venous pressure, and a Swan-Ganz catheter (Baxter Edwards Laboratories, Irvine, USA) was placed in the same site for monitoring pulmonary artery and capillary wedge pressures (PAP, PCWP) and for the extraction of mixed venous blood. A catheter (Certofix©, Braun, Menselungen, Germany) was placed in the carotid artery for the continuous monitoring of arterial pressure and for the intermittent extraction of samples for gas analysis. A fiberoptic catheter (Pulsiocath©, Pulsion Medizintechnik, München, Germany) was introduced via the femoral artery to the aortic root for cardiac output (CO) measurement and determination of EVLW by the double indicator method (EVLW-DI). A Foley catheter was surgically inserted into the bladder of half of the animals of each group in order to measure the intra-abdominal pressure.

At the end of the experimental period, the animals were killed by the administration of potassium chloride.

Measurements

Gas exchange and respiratory mechanics

Arterial and mixed venous blood gas samples were analyzed immediately after sampling at 37 °C with an ABL-520 (Radiometer, Copenhagen, Denmark) blood gas analyzer. The PaO_2, $PaCO_2$ and pH were recorded and the intrapulmonary venous admixture (Qva/Qt) was calculated according to the standard formula. The pressure and flow transducers of the ventilator were used to measure the respiratory mechanics. In order to achieve static conditions, an inspiratory pause of more than 4 s was transiently applied and the static compliance (Cst,rs) and resistance (Rst,rs) of the respiratory system were calculated according to the standard formulas. We did not measure auto-PEEP because this phenomenon is unlikely to be present in this model, as evidenced in other identical experimental models.

Hemodynamics

The following parameters were recorded or derived: mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (Pw) and cardiac output (CO) through thermodilution. Vascular pressures were referenced to the mid-chest and measured at end-expiration.

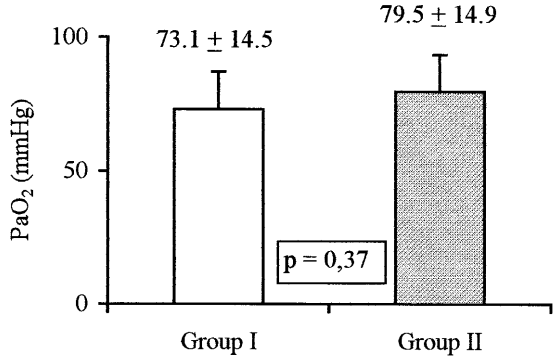

Fig. 1 Results of oxygenation at 150 minutes

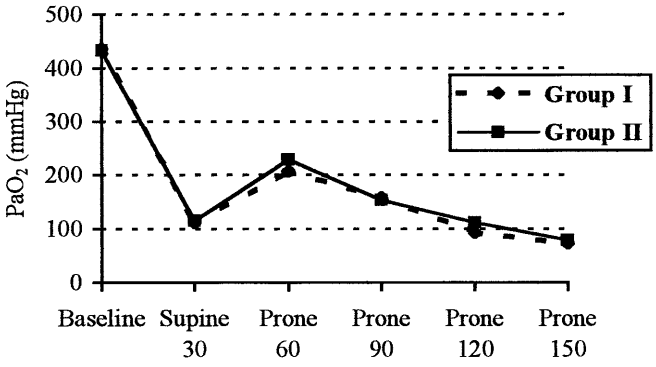

Fig. 2 Evolution of oxygenation assessed by $PaO_2/FIO2$

Extravascular lung water

The EVLW was determined by the double indicator method (indocyanine green and cold): 10 ml of 5 % glucose solution containing 1 mg/ml of indocyanine green at a temperature of between 0 °C and 100 °C was injected into the right atrium via the catheter in the internal jugular. Densimetric and thermal data were gathered by the fiberoptic catheter in the aortic root and analyzed on a Pulsion Cold Z-021 computer (Pulsion Medizintechnik, Munchen, Germany). The EVLW was calculated from the CO and mean transit times (MTt) of both indicators according to the formula:

EVLW = CO × (extravascular MTt-intravascular MTt).

The same computer was used for the measurement of CO and intrathoracic volumes (pulmonary blood, intrathoracic blood and global end-diastolic) by thermodilution, using the standard formulas. All of these values were calculated from the average of three measurements with a variation between them of less than 10 %.

Intra-abdominal pressure

The bladder catheter was filled with fluid and clamped distally to the sampling port. A 20-gauge needle was inserted through the catheter sampling membrane and the bladder catheter pressures were measured with reference to atmospheric pressure at the pubic level. This measure was performed in five animals from each group.

Protocol and experimental groups

After a baseline determination (time 0), 10 ml of saline solution containing 0.1 ml/kg of oleic acid was infused into the right atrium via the internal jugular catheter for a period of 10 min. After 30 min, the pigs were randomized into two groups and all parameters were measured at 30, 60, 90,120 and 150 min after the production of the pulmonary edema. The FIO_2 was increased in all groups to 100 % to avoid hypoxemia, since no positive end-expiratory pressure (ZEEP) was added. The groups were as follows:Group I (n = 9): The pigs lay directly on the operating table in the prone position with the abdomen unsupported. One animal in this group died from severe hypoxemia 120 min after the production of the lung edema. This animal was not included in the statistical study.- Group II (n = 11): The pigs lay in the prone position with rolls positioned under the upper part of the chest wall and the pelvis in order to allow free movement of the abdomen.

Statistical analysis

The data is expressed as means ± standard deviation. ANOVA for repeated measures was used between the measurement stages and, if significant, comparisons with baseline were made. For testing significance level for oxygenation, a non-parametric independent t-test was used between groups (at 150 min) and a paired t-test between the supine and prone positions. A p less than 0.05 was considered statistically significant.

Results

Evolution of arterial oxygenation

There was no difference in arterial oxygenation between the groups at 150 min, as depicted in Fig. 1. The PaO_2/FIO_2 ratios for the two groups over the experimental period (times 0, 30, 60, 90, 120 and 150 min) are represented in Fig. 2. Shortly after the induction of pulmonary edema by oleic acid infusion, there was a sharp decline in oxygenation that was partially reverted by prone positioning. Nevertheless, the oxygenation progressively deteriorated until the end of the experiment, with no statistical difference between the groups at any time.

Evolution of pulmonary edema by double indicator dilution method

Table 1 lists the results for the two groups over the experimental period (times 0, 30, 60, 90, 120 and 150 min) and shows the absence of differences between the groups. The EVLW-DI increased after the infusion of oleic acid in both groups ($p < 0.05$) and increased slightly at the next measurement (time 60 min) after the

Table 1 Evolution of extravascular lung water (EVLW)[a] in milliliters/kilogram

	Baseline 0 min	Supine 30 min	Prone 60 min	Prone 90 min	Prone 120 min	Prone 150 min
Group I	5.4 ± 3.0[b]	10.1 ± 5.3	12.3 ± 5.7	12.6 ± 3.8	12.3 ± 3.2	14.1 ± 3.7
Group II	5.0 ± 1.9[b]	10.6 ± 4.0	13.2 ± 4.9	13.7 ± 4.0	14.3 ± 3.9	15.0 ± 4.1

[a] Values are expressed as means ± standard deviation
[b] $p < 0.05$ compared to all other times

Table 2 Hemodynamic parameters[a] (*HR* heart rate, *MAP* mean arterial pressure, *MPAP* mean pulmonary artery pressure, *Pw* wedge pressure, *CO* cardiac output, *PBV* pulmonary blood volume, *ITBV* intrathoracic blood volume, *GEDV* global end-diastolic volume)

	Baseline 0 min	Supine 30 min	Prone 60 min	Prone 90 min	Prone 120 min	Prone 150 min
HR (beats/min)						
Group I	104.0 ± 23.6	105.6 ± 26.3	99.2 ± 20.9	104.8 ± 31.2	102.3 ± 34.8	103.1 ± 34.8
Group II	113.1 ± 18.4	90.6 ± 45.9	114.0 ± 33.2	118.0 ± 26.4	114.6 ± 27.9	119.5 ± 36.1
MAP (mmHg)						
Group I	80.7 ± 14.7	74.3 ± 15.4	69.4 ± 14.0	71.5 ± 14.2	66.5 ± 10.8	65.1 ± 11.2
Group II	76.1 ± 14.0	69.6 ± 12.0	66.0 ± 14.4	65.8 ± 12.9	67.2 ± 15.3	67.3 ± 15.8
MPAP (mmHg)						
Group I	11.7 ± 5.0[b]	29.4 ± 5.6	30.1 ± 6.4	32.2 ± 9.0	32.2 ± 6.9	32.6 ± 7.3
Group II	16.0 ± 4.8[b]	30.8 ± 6.9	29.8 ± 7.6	29.9 ± 7.4	32.0 ± 10.2	33.7 ± 9.9
Pw (mmHg)						
Group I	5.0 ± 2.0	3.8 ± 2.0	4.7 ± 2.7	6.0 ± 3.7	6.0 ± 3.7	6.6 ± 3.5
Group II	4.4 ± 3.7	5.9 ± 4.5	7.9 ± 6.2	8.3 ± 5.6	8.3 ± 5.6	10.0 ± 7.5
CO (l/min)						
Group I	4.5 ± 1.1	4.2 ± 1.2	4.0 ± 1.2	4.1 ± 1.5	4.1 ± 1.4	4.1 ± 1.5
Group II	4.2 ± 0.9	4.5 ± 1.4	3.5 ± 0.8	3.4 ± 1.3	3.6 ± 1.3	3.5 ± 1.3
PBV (ml)						
Group I	228.0 ± 61.8	204.7 ± 54.3	191.5 ± 57.9	208.6 ± 135.5	174.7 ± 56.7	232.4 ± 137.1
Group II	232.4 ± 92.1	168.2 ± 65.0	193.7 ± 126.9	180.5 ± 79.3	173.4 ± 102.5	177.2 ± 132.7
ITBV (ml)						
Group I	719.2 ± 154.0	697.5 ± 137.7	735.5 ± 191.2	707.2 ± 192.9	684.4 ± 76.6	764.5 ± 260.8
Group II	712.9 ± 155.2	656.4 ± 168.1	638.0 ± 208.4	601.0 ± 163.8	595.5 ± 156.9	600.4 ± 178.2
GEDV (ml)						
Group I	480.0 ± 134.4	493.6 ± 114.8	507.4 ± 123.1	498.1 ± 95.1	499.2 ± 85.9	532.0 ± 159
Group II	480.2 ± 121.9	488.1 ± 141.5	432.7 ± 123.9	439.2 ± 100.2	439.0 ± 98.5	424.0 ± 74

[a] Values are expressed as mean ± standard deviation
[b] $p < 0.05$ compared to all other times

prone positioning. From then on, there was a small but steady non-significant increment until the end of the experimental period.

Responses of other hemodynamic and respiratory parameters

The production of pulmonary edema induced an increase in venous admixture ($p < 0.001$) and a continuous respiratory acidemia, with a concomitant increase in $PaCO_2$ and reduction in arterial pH. Likewise, it provoked a pulmonary hypertensive reaction ($p < 0.05$) that remained unmodified during the whole experimental period. The Cst,rs decreased immediately after the infusion of oleic acid, with a modest non-significant reduction thereafter despite the prone positioning.

The abdomen release maneuver was associated with a modest non-significant decrease in CO and parameters related to preload (intrathoracic blood and global end-diastolic volumes). Although not statistically significant, the Cst,rs was smaller in the group with abdomen release, associated with a greater efficiency of CO_2 removal. There was no difference in intra-abdominal pressures between the groups. These results are detailed in Tables 2 and 3.

Table 3 Respiratory mechanics and gas exchange parameters[a] (*IAP*: intra-abdominal pressure, *Cst,rs* total respiratory system static compliance, *Rst,rs* total respiratory system static resistance, *Qva/Qt* venous admixture, PaO_2 arterial partial pressure of oxygen, $PaCO_2$ arterial partial pressure of carbon dioxide, *pHa* arterial pH)

	Baseline 0 min	Supine 30 min	Prone 60 min	Prone 90 min	Prone 120 min	Prone 150 min
IAP (mmHg)						
Group I	3.7 ± 2.8	4.0 ± 3.8	5.7 ± 5.7	6.2 ± 2.6	6.2 ± 2.2	6.5 ± 5.3
Group II	3.4 ± 2.0	3.8 ± 2.3	4.2 ± 3.3	6.6 ± 1.9	5.8 ± 3.0	7.2 ± 3.0
Cst,rs (ml/cmH_2O)						
Group I	88.7 ± 18.8[b]	50.6 ± 18.7	44.6 ± 12.2	35.5 ± 16.5	31.6 ± 14.4	33.5 ± 16.6
Group II	86.6 ± 20.8[b]	50.8 ± 18.9	45.0 ± 17.9	42.4 ± 16.4	41.3 ± 20.3	37.3 ± 19.4
Rst,rs (cmH_2O/l/s)						
Group I	23.6 ± 1.8[b]	39.8 ± 6.0	44.2 ± 8.7	50.2 ± 10.0	53.6 ± 10.9	53.8 ± 11.6
Group II	23.2 ± 2.8[b]	38.4 ± 4.7	44.6 ± 7.8	46.4 ± 8.2	49.4 ± 10.3	53.5 ± 11.8
Qva/Qt (%)						
Group I	7.4 ± 1.6[b]	34.0 ± 5.4	32.8 ± 11.3	37.8 ± 10.9	39.0 ± 18.6	47.6 ± 12.6
Group II	6.9 ± 2.1[b]	33.1 ± 7.2	35.2 ± 17.7	32.7 ± 14.4	33.3 ± 17.1	44.7 ± 22.7
PaO_2 (mmHg)						
Group I	436.0 ± 59.6[b]	112.5 ± 54.3	208.2 ± 83.6[d]	158.8 ± 52.5	93.4 ± 23.4	73.1 ± 14.5
Group II	432.9 ± 48.4[b]	115.6 ± 41.0	229.6 ± 74.0[d]	155.5 ± 74.0	112.5 ± 61.5	79.5 ± 14.9
$PaCO_2$ (mmHg)						
Group I	33.8 ± 6.4[c]	43.3 ± 9.4	47.1 ± 10.9	50.8 ± 14.5	53.7 ± 14.7	56.7 ± 15.2
Group II	31.0 ± 5.7[c]	43.3 ± 9.8	43.5 ± 09.5	44.7 ± 09.6	45.7 ± 10.4	48.3 ± 11.6
PHa						
Group I	7.46 ± 0.07[b]	7.34 ± 0.08	7.30 ± 0.09	7.27 ± 0.10	7.24 ± 0.11	7.21 ± 0.12
Group II	7.53 ± 0.06[b]	7.32 ± 0.09	7.30 ± 0.11	7.30 ± 0.10	7.31 ± 0.12	7.27 ± 0.12

[a] Values are expressed as mean ± standard deviation. Data on IAP refer to five animals in each group
[b] $p < 0.05$ compared to all other times
[c] $p < 0.05$ compared with prone 150 min
[d] $p < 0.05$ compared with supine 30 min

Discussion

The main result of this study is that the prone position with abdomen release does not improve short-term arterial oxygenation compared to the prone position without it, at least not to a degree that would allow a significant reduction in the concentrations of oxygen administered to a patient if extrapolated to the clinical setting. The difference between the groups was 6.4 mmHg, well below the pre-established level of 16.5 mmHg. More than 100 (166) animals would have been required to prove that abdomen release increases PaO_2 by this amount. As we considered such an increase to have no clinical relevance, we concluded the experiments when we reached the initial calculated sample size (at least nine per group). The results of the study contradicted our initial hypothesis and we cannot support the statement by Froese and Bryan [15] that "the only way to ventilate dorsal lung regions is to modify the effect of abdominal mass by manipulating posture. In this respect, the optimal position would be prone with the abdomen unsupported". We found no significant changes in the respiratory mechanics, intra-abdominal pressure or EVLW as a result of the abdomen release and its supposed effect on oxygenation.

The mechanisms by which prone positioning improves oxygenation remain controversial. Although the present study was not designed to elucidate all of them, we can postulate a general theory based on some of its results and on other published reports. As previously mentioned, the improvement was initially attributed to changes in the RFC or its equivalent, the end-expiratory lung volume (EELV). This was demonstrated in spontaneously breathing healthy subjects [16] and in patients that underwent mechanical ventilation under general anesthesia [17], although with the caveat that there was no clear correlation between RFC changes and oxygenation improvement, so that other mechanisms must also be involved. None of the studies on acute lung injury that have addressed this issue [18] could demonstrate that the RFC changes (generally small) were significant or related to gas exchange amelioration. Mure et al. [19] postulated that the effects on lung volume depend on interactions between the rib cage, the diaphragm and the abdomen. They produced abdominal distension with balloon inflation, which increased the FRC in the supine but not the prone position, because in supine the abdominal wall could freely displace outwards and allow the rib cage to move, whereas in prone the pressure increase preferentially produced a rise of the dia-

phragm. In our study, it is very likely that the abdomen release allowed a greater caudal movement of the diaphragm but that the increase in EELV that it produced was partly counteracted by the reduction in rib cage diameter caused by the weight of the abdomen.

Research then focused on the changes that the prone position induces in ventilation-perfusion (V/Q) relationships. It was hypothesized that the main effects on the flow of pulmonary blood would be gravitational, as occurs in the standing position [20]. However, it has been well demonstrated that pulmonary blood flow is primarily determined by anatomic factors and is preferentially distributed to the dorsal lung regions regardless of the body position [21, 22]. The blood flow distribution was not measured in the present study but parameters related to intrathoracic fluid volumes were recorded. The abdomen release maneuver produced a reduction in CO and in intrathoracic and global end-diastolic volumes that may be related to a certain degree of abdominal blood sequestration. This must have influenced the modest shunt reduction that the abdomen-release animals showed and would therefore be a further factor to consider in the final effect on arterial oxygenation.

Nevertheless, the changes induced by the prone position are fundamentally a result of a redistribution of the ventilation, which has been related to various factors. First, the change in the pleural pressure of the dependent lung regions, which becomes more negative, so that the inflation gradient and thus the ventilation increases. The reasons for this phenomenon are not well-defined, but may include the effects of the prone position on the direction of the weight of the heart and on the position and motion of the diaphragm [23]. Second, as Pelosi et al. demonstrated, the change from supine to prone causes a significant reduction in the compliance of the thoraco-abdominal cage, accounted for by the greater rigidity of the rib cage component of the chest wall. In prone, the dorsal zone is free to move with insufflations; because it is more rigid, it redistributes the tidal ventilation towards the dependent ventral regions, resulting in a more even regional distribution. We did not measure the different components of thoracopulmonary compliance. However, there were no differences in severity of lung injury, confirmed by the similar EVLW levels (representing lung compliance), and we can speculate that the lesser thoracopulmonary compliance in the group without abdomen release, although not significant, may be due to a greater restriction of diaphragmatic mobility.

Finally, we consider the influence of abdominal pressure on the prone position. There have been one clinical and two experimental studies on gas exchange changes induced by the prone position in the presence of abdominal distension. The first, a study on obese patients under general anesthetic [24], only investigated the difference between the supine and prone positions. The experimental studies induced abdominal distension through intravascular volume overload [25] or abdominal balloon inflation [18], although in healthy animals. Both concluded that the increase in oxygenation produced by a change from supine to prone is greater in the presence of abdominal distension, apparently contradicting our results. The different methods of producing the abdominal distension would account for the discrepancy, since those used by the other studies would ensure an intra-abdominal pressure difference between the groups, unlike in our case. Moreover, when the comparison was between animals with normal or distended abdomen in the same position (prone), the findings were in line with ours, with no changes in the gas exchange. Finally, our study is the first on animals with lung injury and the first to use a model that is not restricted to particular situations, such as obesity, paralytic ileum or pregnancy, and is relevant to all patients that are placed in prone.

Effect of the prone position on lung injury

The amount of EVLW is an indirect measure of lung injury and was not modified by abdomen release in our study. Although we had no concurrent control group in the supine position, we can compare the findings with a historic control group from an earlier study by our group [14] that used the same experimental model and identical ventilation parameters. There were no differences in EVLW evolution between the historic group (in supine) and either of the present groups (in prone). In fact, despite the improvement in oxygenation after the change from supine to prone, the oxygenation progressively deteriorated until the end of the experimental period, when it reached similar levels to those in the historic control group in supine. Our findings are at variance with those of other clinical and experimental studies. The former claimed that indirect evidence of improvement in the lung injury was shown by the persistence of the oxygenation amelioration or by the reduction in lung infiltrates in the chest scan when the patients returned to the supine position after a variable time in prone position [26]. Only one experimental study by Broccard et al. [12] addressed this issue, comparing the extension and distribution of lung injury between two groups of six dogs randomly assigned to the supine or prone positions; the respiratory distress was induced with a very similar amount of oleic acid to that in our study, and the ventilation regimen used high tidal values and a PEEP of 10 cmH_2O or more. They found no differences between the two groups in the extension of the lung injury, as determined by the gravimetric method (wet/dry weight ratio), although its distribution, analyzed by histologic examination, revealed greater

lung damage in the supine versus the prone position, primarily in dependent zones.

Our findings are consistent with theirs in that the prone position did not modify the extension of lung injury, although we used a different quantification method, a non-destructive technique that has been validated using the gravimetric method as reference. We cannot confirm their finding that the distribution may be modified by the prone position, because we did not perform a histologic analysis of the lungs. At any rate, we believe that the distribution change may be related not only to the postural treatment but also to the simultaneous use of PEEP, which has been shown to modify the distribution of the blood perfusion, making it more homogeneous in the prone versus the supine position [27, 28].

Study limitations and clinical relevance

Our study can help in the definition of postural treatment guidelines for patients with ARDS, always bearing in mind the limitations of extrapolating experimental results to the human clinical setting. We must consider the anatomic and physiologic differences between animal species as well as the ventilation modality utilized in prone positioning. The lower weight of the pig and of its abdominal viscera and the different geometry and compliance of the pig thorax may modify the interactions between the anatomic structures involved (rib cage, diaphragm and abdomen), probably with a greater influence of the abdomen release, although this has yet to be demonstrated. Furthermore, the duration in the prone position was only 150 min in the present study, whereas in the clinical setting the prone position is normally maintained for hours and can be applied several times. However, the oxygenation response was obtained within the first few minutes in both of our groups, suggesting that longer periods in the prone position would not have modified our results. Finally, our ventilation approach was very different from normal clinical practice in patients with acute lung injury because we did not apply PEEP. This decision was taken to avoid any interference with the effect of possible variations in abdominal pressure on the mobility of the diaphragm, since PEEP acts as a pneumatic force from the thoracic side. The use of PEEP probably attenuates the impact of the abdomen on the redistribution of lung ventilation in the prone position. There is no definitive method to measure lung injury. We used the quantification of EVLW by the double indicator method. This is a perfusion-dependent method, so that the results are not valid for comparing injuries of different etiologies, with different degrees of vascular involvement. However, this was not the case with the present controlled study, where the same type of oleic acid injury was induced in all the animals of both groups.

Our results suggest that additional devices [29] are not required to enhance prone positioning treatment, although they may be of value to the caregivers in carrying out the maneuver, or to the patients for their greater safety. Regarding the possible protective role of prone positioning against acute lung injury and, thus, its effects on the mortality of the patients, the discrepancies in the findings of the scant experimental studies published to date and the expectations generated by this form of treatment in a disease with such a poor prognosis mean that controlled clinical studies are required to address these issues.

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