Research

Influence of support on intra-abdominal pressure, hepatic kinetics of indocyanine green and extravascular lung water during prone positioning in patients with ARDS: a randomized crossover study

Pierre Michelet, Antoine Roch, Marc Gainnier, Jean-Marie Sainty, Jean-Pierre Auffray and Laurent Papazian

Service de Réanimation Chirurgicale, Hôpitaux Sud, Marseille, France

Corresponding author: Pierre Michelet, pierre.michelet@mail.ap-hm.fr

Abstract

Introduction Prone positioning (PP) on an air-cushioned mattress is associated with a limited increase in intra-abdominal pressure (IAP) and an absence of organ dysfunction. The respective influence of posture by itself and the type of mattress on these limited modifications during the PP procedure remains unclear. The aim of this study was to evaluate whether the type of support modifies IAP, extravascular lung water (EVLW) and the plasma disappearance rate of indocyanine green (PDR_{ICG}) during PP.

Methods A prospective, randomized, crossover study of 20 patients with acute respiratory distress syndrome (ARDS) was conducted in a medical intensive care unit in a teaching hospital. Measurements were made at baseline and repeated after 1 and 6 hours of two randomized periods of 6 hours of PP with one of two support types: conventional foam mattress or air-cushioned mattress.

Results After logarithmic transformation of the data, an analysis of variance (ANOVA) showed that IAP and PDR_{ICG} were significantly influenced by the type of support during PP with an increase in IAP ($P < 0.05$ by ANOVA) and a decrease in PDR_{ICG} on the foam mattress ($P < 0.05$ by ANOVA). Conversely, the measurements of EVLW did not show significant modification between the two supports whatever the posture. The ratio of the arterial oxygen tension to the fraction of inspired oxygen significantly increased in PP ($P < 0.0001$ by ANOVA) without any influence of the support.

Conclusion In comparison with a conventional foam mattress, the use of an air-cushioned mattress limited the increase in IAP and prevented the decrease in PDR_{ICG} related to PP in patients with ARDS. Conversely, the type of support did not influence EVLW or oxygenation.

Introduction

Prone positioning (PP) improves arterial oxygenation in 50 to 75% of patients presenting with acute respiratory distress syndrome (ARDS) [1]. Although this postural treatment is currently considered simple and safe [1], the restriction of abdominal movements during PP is associated with an increase in intra-abdominal pressure (IAP) [2-5] with potential adverse effects on hemodynamic status and splanchnic perfusion [6-8]. Several studies have evaluated the clinical implications of this side effect of PP [4,5,9]. They reported significant but limited increases in IAP without impairment of cardiopulmonary, renal or hepatosplanchnic functions during short periods of PP. However, all patients included in these studies were placed on air-cushioned beds, which might have reduced the restriction of abdominal movement during PP [4,5,9] compared with a conventional foam mattress. Indeed, the air-cushioned mattress reduced interface pressure to a greater extent than the foam mattress [10,11]. Moreover, the addition of pillows under the thorax and the pelvis did not produce a decrease in IAP during the PP procedure with a foam mattress [12]. Because no direct comparison has been made between different supports, the respective influences of the type of

support and the posture itself on IAP and its related potential adverse effects remain unclear. Therefore, in the perspective of standardization, the question of the interest of a special device before the institution of PP should be clarified [1].

The aim of the present study was to investigate whether the evolution of IAP, liver function assessed by the plasma disappearance rate of indocyanine green (PDR_{ICG}) [5] and extravascular lung water is related to the type of support during PP. We therefore prospectively compared, in a population of medical-ARDS patients, the effects of an air-cushioned mattress and a conventional foam mattress during PP.

Methods
Patients
Twenty consecutive patients with ARDS were included and turned prone in the medical intensive care unit of Sainte Marguerite University Hospital in Marseille, France. Patients were prospectively included in this study after obtaining written informed consent from the next of kin. The study design was approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale of Marseille. ARDS was defined in accordance with the recommendations of the American–European Consensus Conference [13]. Patients with unstable cardiovascular function, cerebral injury or unstable spinal fractures, patients subjected to major abdominal surgery and patients with a history of neuromuscular disease were excluded.

Sedation, catheters and ventilation
All patients were sedated and paralyzed by the continuous infusion of sufentanil, midazolam and cisatracurium throughout the study period and were ventilated with conventional volume-controlled mechanical ventilation (7200 series or 840, Mallinckrodt Puritan Bennett, Carlsbad, CA, USA).

Respiratory and hemodynamic status was stable for 12 hours before inclusion. When patient received vasoactive drugs, the rate of infusion was kept stable throughout the study. On inclusion into the study, the mean tidal volume was 6.9 ± 1.9 ml/kg, the mean respiratory rate was 20 ± 4 cycles/min (the respiratory rate was adjusted to maintain a constant minute ventilation throughout the study period) and the positive end-expiratory pressure was 11.3 ± 2.0 cmH$_2$O. The selection of the appropriate PEEP level was performed by increasing PEEP in steps of 2 cmH$_2$O. A blood gas analysis was performed after a 30 min period of stabilization of blood oxygen saturation. Finally, the lower level of PEEP giving the greater improvement of oxygenation was chosen. The levels of PEEP, the tidal volume and a fraction of inspired oxygen (FiO$_2$) of 0.8 were maintained constant throughout the study period.

A pulmonary artery catheter (Baxter Healthcare Corporation, Irvine, CA, USA) was placed in all patients. It was inserted percutaneously through the right jugular or left subclavian vein and positioned with the distal port in the pulmonary artery and the proximal port in the right atrium. For measurements of the PDR_{ICG} and extravascular lung water (EVLW), a 5F catheter was placed into the left femoral artery, together with a thermistor-tipped fiber-optic catheter (Pulsiocath, 4F, FT, PV-2024-L; Pulsion Medical System, Munich, Germany) which was advanced into the descending aorta.

Support surfaces
The control surface was a three-piece molded foam mattress (APLOT®; Asklé, Nîmes, France). The specialist air mattress was a dynamic alternating cells design, with automatic adjustment for patient weight (ProNimbus®; Huntleigh Healthcare, Luton, UK).

Measurements
Hemodynamic parameters
Routine invasive hemodynamic monitoring included arterial and pulmonary artery thermodilution catheters. Systemic and pulmonary arterial pressures, pulmonary artery occlusion pressure and right atrial pressure were measured at end-expiration. The midaxillary line was taken as the zero reference point in the supine and prone positions. Cardiac index, venous admixture and pulmonary vascular resistance were calculated from conventional formulas.

Blood gas analysis
Systemic and pulmonary arterial blood samples were withdrawn simultaneously within 3 min after the measurement of cardiac output. Arterial pH, arterial oxygen tension (PaO$_2$) and arterial CO$_2$ tension were measured with a blood gas analyzer (278-blood gas system; Ciba Corning, Medfield, MA, USA). Arterial and mixed venous oxygen saturation (SaO$_2$ and SvO$_2$, respectively) were measured with a calibrated hemoximeter (270-CO-oxymeter; Ciba Corning).

Respiratory parameters
The respiratory parameters measured were compliance of the respiratory system, exhaled tidal volume, peak inspiratory pressure, mean inspiratory pressure, and respiratory rate. Quasi-static compliance of the total respiratory system was obtained by dividing the tidal volume by the difference between plateau pressure and the total PEEP according to the method described by Gattinoni and colleagues [14].

Thoracic volumes, EVLW and hepatosplanchnic perfusion measurements
The transpulmonary indicator dilution technique was used to determine the intrathoracic blood volume, the EVLW and the PDR_{ICG} [15]. PDR_{ICG} is derived from the half-life of indocyanine green and reflects the percentage of the initial plasma dye level eliminated by the liver [16]. A thermistor-tipped fiber-optic catheter placed in the descending aorta detected the dye and temperature dilution curves. The EVLW and the PDR_{ICG} were automatically calculated by a computer (Pulsion

Cold Z-021; Pulsion Medical System) from the average of three measurements [16].

Measurement of IAP
IAP was measured with a transurethral bladder catheter [17]. Normal saline (100 ml) was infused through the urinary catheter into the bladder. The catheter was then clamped and the IAP was recorded by a pressure transducer as mean pressure at end-expiration. Zero was set at the level of the pubis in both positions.

Protocol
Baseline measurements were performed in the supine position after 1 hour of steady-state conventional mechanical ventilation. Then the following two periods of PP were randomized: 6 hours of PP on the moulded foam mattress, and 6 hours of PP on the air-cushioned mattress. A period of 18 h in the supine position separated the two periods in the prone position. Each patient was his or her own control. Measurements were achieved in the supine position, after 1 and 6 hours of PP.

Change in position was performed manually by three nurses and two staff members. In the prone position, the arms were laid parallel to the body. Care was taken to avoid eye damage and any non-physiological movements of the limbs during posture changes. Whatever type of support was used, no pillow was used to support regions such as the chest or pelvis.

Measurements were performed before, after 1 hour and after 6 hours of each period of PP.

Statistical analysis
Statistical calculation was performed with the Sigma Stat 3.0 package (SPSS Inc., Chicago, IL, USA). Distribution was checked. Data were expressed as mean $\pm$ SD if the distribution was normal and as medians and interquartile range if the distribution was not normal. Significant differences were analyzed by general factorial analysis of variance (ANOVA) with a prior logarithmic transformation when required (non-parametric distribution). For intra-group changes, Tukey's test for multiple comparisons was applied to compare the variations between supports and different times of the study. For serum transaminases and creatinine, a Mann–Whitney U-test was used to compare the values before and after the protocol. When a correlation was calculated, Pearson's coefficient of correlation was used. When distribution was not normal, Spearman's rank correlation was used.

$P < 0.05$ was considered significant.

Results
Characteristics of the population are listed in Table 1. On admission, the mean Simplified Acute Physiologic Score II (SAPS II) score was 52 $\pm$ 12 and the severity of ARDS was assessed by a lung injury score of more than 2.5 in all patients

(3.1 $\pm$ 0.3). The mortality rate for the 20 patients (15 men, 5 women; age 53 $\pm$ 12) was 25%. Among the patients enrolled in the study, six patients received norepinephrine (noradrenaline) (dose 0.3 $\pm$ 0.2 µg/kg per min) and one patient received epinephrine (adrenaline) (0.4 µg/kg per min) on inclusion. No modification of the infusion rate of norepinephrine and epinephrine and no fluid expansion were undertaken during the study period.

Effects of prone position and support on IAP, hepatosplanchnic function and EVLW
A logarithmic transformation of the data led to normally distributed values of IAP and PDR_{ICG}. We therefore performed a two-way ANOVA that showed an increase in IAP after 1 and 6 hours of PP on a foam mattress in comparison with baseline values ($P < 0.01$ by Tukey's test; Fig. 1) whereas it remained unchanged when patients were positioned on a specialist air mattress. IAP was higher on a foam mattress after 6 hours of PP in comparison with a specialist air mattress ($P < 0.05$ by Tukey's test; Fig. 1). PDR_{ICG} decreased after 1 and 6 hours of PP on a foam mattress in comparison with baseline values ($P < 0.05$ by Tukey's test, Table 2 and Fig. 2) whereas it remained unchanged when patients were positioned on a specialist air mattress.

There was no correlation between changes in IAP and PDR_{ICG}. Furthermore, the analysis of hepatic and renal variables did not show any statistical variation after the PP procedure period (Table 3).

There was no modification in EVLW and intrathoracic blood volume related to posture or support changes (Table 2).

Effects of prone position and support on gas exchange (Table 2)
PP induced an increase in the PaO_2/FiO_2 ratio ($P < 0.001$ by ANOVA) regardless of the type of support. There was no correlation between evolution in PaO_2 and changes in IAP. PP reduced the true pulmonary shunt ($P < 0.05$ by ANOVA) without any influence of the kind of support.

Effects of prone position and support on hemodynamic and respiratory parameters (Table 2)
ANOVA showed that CVP, mean pulmonary arterial pressure and pulmonary artery occlusion pressure increased significantly in PP ($P < 0.001$) without any influence of the kind of support. Although PP induced a significant reduction in the static compliance of the total respiratory system ($P = 0.007$ by ANOVA), these modifications were not influenced by the kind of support. Other hemodynamic or respiratory parameters were not affected by prone position or type of support.

Discussion
The results of this study indicate that the use of an air-cushioned mattress for the PP procedure limited the increase of

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Table 1

Characteristics of the population

| Patient no.	Age (years)	Sex	BMI	LIS	SAPS II	ARDS duration (days)	Causes of ARDS	Outcome
1	51	M	42	3.0	39	4	Bacterial pneumonia	Alive
2	39	M	27	3.0	60	1	Aspiration pneumonia	Alive
3	65	M	33	3.3	46	1	Cytomegalovirus pneumonia	Alive
4	64	M	28	2.7	71	2	Bacterial pneumonia	Alive
5	50	F	23	2.7	49	7	Septic shock	Died
6	44	M	24	3.3	45	1	Bacterial pneumonia	Alive
7	71	M	26	3.6	51	7	Bacterial pneumonia	Died
8	37	M	34	3.2	30	3	Lung contusion	Alive
9	45	M	25	3.3	62	1	Bacterial pneumonia	Died
10	37	M	25	3.2	74	6	Community-acquired pneumonia	Alive
11	52	F	37	2.7	52	4	Aspiration pneumonia	Alive
12	49	M	25	2.7	40	2	Bacterial pneumonia	Alive
13	70	M	28	3.2	57	4	Bacterial pneumonia	Alive
14	48	F	31	3.5	72	1	Aspiration pneumonia	Alive
15	60	F	27	3.2	58	2	Septic shock	Alive
16	48	M	29	3.7	44	7	Bacterial pneumonia	Alive
17	73	M	38	3.3	62	4	Aspiration pneumonia	Died
18	56	M	25	2.7	56	3	Community-acquired pneumonia	Alive
19	34	F	28	2.5	32	3	Bacterial pneumonia	Alive
20	65	M	23	3.3	48	2	Aspiration pneumonia	Died

ARDS duration, duration of acute respiratory distress syndrome before inclusion BMI, body mass index; LIS, lung severity score; SAPS II, Simplified Acute Physiologic Score II

IAP and prevented a decrease in PDR_{ICG} related to PP. Nevertheless, these modifications were not associated with differences between supports for EVLW, oxygenation or cardiovascular parameters.

Even if the routine use of PP did not improve the survival of patients with ARDS in a recent multicenter randomized trial [18], it could be considered useful in the more hypoxemic patients. The improvement in oxygenation produced by PP is often related to an increase in aerated lung tissue with a decrease in venous admixture and a decrease in thoraco-abdominal compliance [19]. On the basis of these considerations, one can presume that the more the thoraco-abdominal wall is restricted during PP, the greater the gain in arterial oxygenation that should be obtained [4]. Nevertheless, in different settings, turning patients prone has been reported to induce an increase in IAP with potential side effects on cardiopulmonary, renal and hepatosplanchnic function [7,8]. The impaired hepatosplanchnic perfusion could lead to the development of

multiple system organ failure [7,20,21], increasing the mortality rate of patients with ARDS [22,23].

Several studies were therefore designed to investigate the effects of PP on IAP modifications and clinical consequences [4,5,9]. The cumulative results of these studies indicate that, despite a small increase in IAP, PP improves arterial oxygenation without affecting cardiopulmonary, renal or hepatosplanchnic function. Nevertheless, the constant use of air-cushioned beds during PP in these studies could have contributed to limiting the effects of PP on IAP [5]. Indeed, this specialist air mattress presents a dynamic alternating-cells design with automatic adjustment for patient weight and a redistribution in pressure from the heavy parts (abdomen) to other areas. This support has been extensively reported as providing the lowest interface pressure in comparison with other supports, including foam mattresses [10,11]. Conversely, the use of a foam rubber mattress has recently been associated with an increase in IAP during PP without further
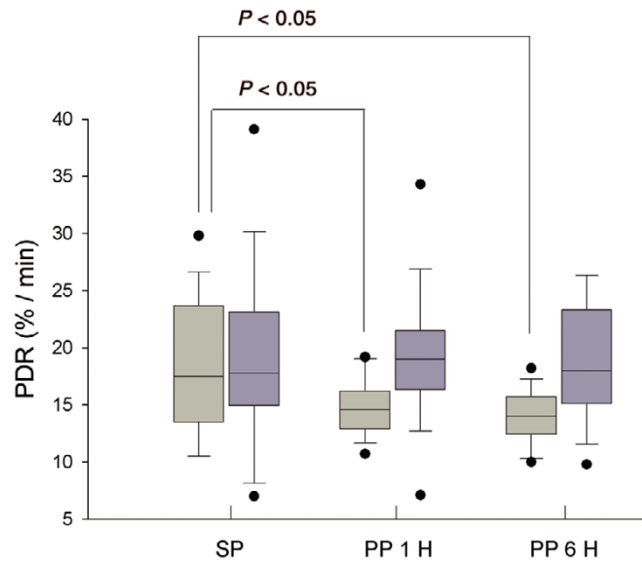
Figure 1
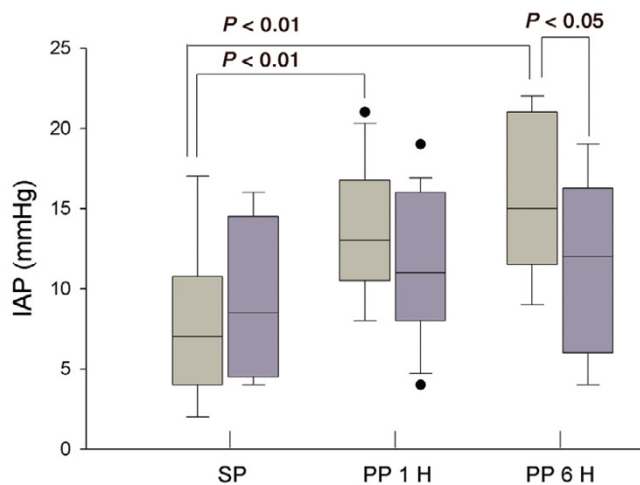
Effects of both supports on intra-abdominal pressure (IAP). The different durations of study are reported along the X-axis: SP, PP 1 H and PP 6 H represent baseline in supine position, prone position at 1 hour and prone position at 6 hours, respectively. Pale gray boxes, foam mattress; dark gray boxes, air-cushion mattress. Each box plot represents the median, the 25th and 75th centiles, and the largest and smallest values that are not outliers. Outliers are represented as filled circles. $P < 0.01$ and $P < 0.05$ by Tukey's post-hoc test.

Figure 2

Effects of both supports on the plasma disappearance rate (PDR) of indocyanine green. The different durations of study are reported along the x-axis: SP, PP 1 H and PP 6 H represent baseline in supine position, prone position at 1 hour and prone position at 6 hours, respectively. Pale gray box, foam mattress; dark gray box, air-cushion mattress. Each box plot represents the median, the 25th and 75th centiles, and the largest and smallest values that are not outliers. Outliers are represented as filled circles. $P < 0.05$ by Tukey's post-hoc test

reduction when pillows were added under the thorax and the pelvis [12].

Similarly, in our study, the use of foam rubber mattresses during PP induced a significant increase in IAP with a concomitant reduction in PDR_{ICG}, whereas air-cushion mattresses did not do so. Although these findings seem to indicate a superiority of the air-cushion support in terms of abdomen release, the clinical consequences of such modifications should be interpreted with regard to their duration. Indeed, despite an increase in IAP reaching 15 mmHg after 6 hours of PP on a foam mattress, the differences in liver function evaluated by PDR_{ICG} were limited during the PP procedure and did not induce significant modifications in hepatic biological variables during the period after PP. Conversely, although previous results have shown that a higher level must be reached to induce clinical modifications [24,25], a recent multicenter epidemiological study has reported the detrimental influence of a prolonged increase in IAP even for such moderate levels as 12 mmHg [26].

Another consequence of an increase in IAP during PP could be the modification of EVLW. Indeed, a decrease in EVLW has been proposed as an alternative mechanism that might account for the benefit related to PP [27]. Furthermore, an increase in IAP has recently been reported to worsen pulmonary edema in a lung injury induced by oleic acid [28]. Despite a PP-related increase in IAP with the foam mattress, our results did not demonstrate a significant modification in

EVLW. The basal levels and the limited differences in IAP between the two supports probably explained the lack of influence of support on pulmonary edema assessed by EVLW in our study. An alternative, although not mutually exclusive, explanation for the observed evolution in EVLW could result from the underestimation of edema by this technique, because several areas of the lung are underperfused during ARDS [29].

Because the first objective of PP is still the improvement of ARDS-related hypoxemia, the potential influence of the support on oxygenation evolution represents another subject of concern [19,30,31]. Our results confirm previous data on PP-related oxygenation improvement but do not report any difference between the supports. The fact that the type of support does not appreciably influence the effects of PP on gas exchange has been deduced from previously published studies. Although Pelosi and colleagues reported an improvement in PaO_2 that was correlated with a decrease in thoraco-abdominal compliance [19], these results were interpreted as being principally related to the modification of the chest-wall component of the thoraco-abdominal compliance during PP, without significant intervention of the abdominal part. Furthermore, Colmenero-Ruiz and colleagues, in an experimental study, showed that abdomen release in PP does not induce significant modification in oxygenation [31].

Table 2

Respiratory and hemodynamic parameters

Parameter	Foam mattress			Specialist mattress			ANOVA		
	Baseline	PP, 1 h	PP, 6 h	Baseline	PP, 1 h	PP, 6 h	Time	Group	Interaction
PaO_2/FiO_2	142 ± 63	178 ± 73	217 ± 69*	143 ± 44	206 ± 127*	243 ± 80*	$P < 0.001$	NS	NS
PaO_2 (mmHg)	45 ± 9	44 ± 9	44 ± 1 0	45 ± 6	46 ± 10	44 ± 11	NS	NS	NS
Q_{VA}/Q_T (%)	37 ± 8	37 ± 9	35 ± 9*	37 ± 8	36 ± 10	34 ± 10*	$P < 0.05$	NS	NS
Paw (cmH_2O)	18 ± 3.5	18.2 ± 3	18 ± 3	19 ± 4	19 ± 4	18.4 ± 4	NS	NS	NS
Cst (ml/cmH_2O)	38.4 ± 10	35.4 ± 8*	37.1 ± 9	38.6 ± 11	35.8 ± 8*	37 ± 8	$P = 0.007$	NS	NS
MPAP (mmHg)	27 ± 4	32 ± 7	30 ± 6	27 ± 4	31 ± 7	32 ± 7	NS	NS	NS
PAOP (mmHg)	12.2 ± 3.0	16.7 ± 4.0*	15.7 ± 4.0*	12.5 ± 5.0	15.8 ± 4.0*	15.9 ± 4.0*	$P = 0.02$	NS	NS
CVP (mmHg)	9.6 ± 4.1	13.7 ± 4	13.1 ± 5	9.4 ± 6	13 ± 5.0	13.5 ± 5.0	$P = 0.02$	NS	NS
CI (l/min per m²)	4.3 ± 1.1	4.3 ± 1.2	4 ± 0.9	4.5 ± 0.9	4.1 ± 1.3	4.1 ± 0.9	NS	NS	NS
EVLWI (ml/kg per m²)	11.2 ± 6.0	11.1 ± 6.2	10 ± 6.5	11.5 ± 7.3	9.5 ± 6.2	10.6 ± 6.0	NS	NS	NS
ITBV (ml)	1140 ± 475	1100 ± 535	942 ± 330	1165 ± 435	972 ± 205	985 ± 225	NS	NS	NS

Values are expressed as mean ± SD.
ANOVA, analysis of variance; CI, cardiac index; Cst, respiratory static compliance; CVP, central venous pressure; EVLWI, indexed extravascular lung water; FiO2, fraction of inspired oxygen; ITBV, intrathoracic blood volume; MPAP, mean pulmonary arterial pressure; PaCO2, arterial CO2 tension; PaO2, arterial oxygen tension; PAOP, pulmonary artery occlusion pressure; Paw, plateau airway pressure; PP, prone positioning; QVA/QT, venous admixture. *P < 0.05 compared with baseline by Tukey's post-hoc test.

Table 3

Hepatic and renal variables

Variable	On inclusion	End of protocol
Bilirubin (μmol/l)	14 ± 9	21 ± 17
ASAT (IU/l)	30 [20–40]	27 [18–52]
ALAT (IU/l)	22 [15–34]	24 [17–49]
Creatinine (μmol/l)	72 [58–100]	75 [58–91]
Prothrombin (%)	63 ± 9	61 ± 8

ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase. For bilirubin and prothrombin, data are expressed as mean ± SD. For transaminases and creatinine, data are expressed as median [interquartile range].

However, it should be noted that all patients included in the present study presented a medical etiology for their ARDS with an IAP in the supine position that was expected to be lower than in a surgical patient population. Consequently, our results must be interpreted with regard to our selected population because the effects of different support during PP could be different in patients with increased IAP (especially in surgical patients). Indeed, Gattinoni and colleagues [32] reported an IAP ranging from 6 mmHg in patients with ARDS of pulmonary cause to 16 mmHg in patients presenting with ARDS of extrapulmonary cause. The basal level of IAP and the magnitude of changes during PP for surgical patients could induce more relevant results than in our study and imply the need for further investigation in this population.

Our results suggest that the limited modifications in cardiovascular, renal or hepatosplanchnic function observed during PP are probably not related to the type of support but most probably to the relative harmlessness of this postural technique because patients do not present abdominal hypertension before prone positioning.

Conclusion
Consequently, the use of an air-cushion mattress for PP seems to be unnecessary in a standardized protocol in medical patients. However, the use of an air-cushion mattress is still of particular interest in reducing the incidence of pressure ulcers when prolonged periods of PP are needed and in facilitating the PP procedure for tracheostomized patients. Nevertheless, because the duration of PP period was limited to 6 hours in our protocol, a specific comparison between the two supports regarding skin lesions was not made in the present study and will require further evaluation.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

PM, AR and LP were the principal investigators and led the conceptual design of the design and the manuscript preparation. MG made contributions to the acquisition of data and to the analysis and interpretation of data. JMS, JPA and LP performed a first manuscript revision and gave final approval of the version to be submitted. All authors read and approved the final manuscript.

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