Beneficial Hemodynamic Effects of Prone Positioning in Patients with Acute Respiratory Distress Syndrome

Mathieu Jozwiak1,2, Jean-Louis Teboul1,2, Nadia Anguel1,2, Romain Persichini1,2, Serena Silva1,2, Denis Chemla2,3, Christian Richard1,2, and Xavier Monnet1,2

1Service de Réanimation Médicale and 2Service de Physiologie, AP-HP, Hôpitaux Universitaires Paris-Sud, Hôpital de Bicêtre, Le Kremlin-Bicêtre, France; and 3Hôpitaux Universitaires Paris-Sud, Faculté de Médecine Paris-Sud, Le Kremlin-Bicêtre, France

Rationale: The effects of prone positioning during acute respiratory distress syndrome on all the components of cardiac function have not been investigated under protective ventilation and maximal alveolar recruitment.

Objectives: To investigate the hemodynamic effects of prone positioning.

Methods: We included 18 patients with acute respiratory distress syndrome ventilated with protective ventilation and an end-expiratory positive pressure titrated to a plateau pressure of 28–30 cm H2O. Before and within 20 minutes of starting prone positioning, hemodynamic, respiratory, intraabdominal pressure, and echocardiographic data were collected. Before prone positioning, preload reserve was assessed by a passive leg raising test.

Measurements and Main Results: In all patients, prone positioning increased the ratio of arterial oxygen partial pressure over inspired oxygen fraction, the intraabdominal pressure, and the right and left cardiac preload. The pulmonary vascular resistance decreased along with the ratio of the right/left ventricular end-diastolic areas suggesting a decrease of the right ventricular afterload. In the nine patients with preload reserve, prone positioning significantly increased cardiac index (3.0 [2.3–3.5] to 3.6 [3.2–4.4] L/min/m²). In the remaining patients, cardiac index did not change despite a significant decrease in the pulmonary vascular resistance.

Conclusions: In patients with acute respiratory distress syndrome under protective ventilation and maximal alveolar recruitment, prone positioning increased the cardiac preload only in patients with preload reserve, emphasizing the important role of preload in the hemodynamic effects of prone positioning.

Keywords: acute respiratory distress syndrome; prone positioning; passive leg raising; pulmonary vascular resistance; intraabdominal pressure

Prone positioning (PP) reduces mortality in the most severe forms of acute respiratory distress syndrome (ARDS) (1–4). In particular, the PROSEVA study recently reported that early application of prolonged PP sessions in patients with severe ARDS significantly decreased 28- and 90-day mortality (5).

PP is now recognized as a potential therapeutic option in the most severe forms of ARDS (6, 7).

In theory, PP might exert different cardiovascular effects that have different effects on cardiac output (Figure 1). By increasing oxygenation and recruiting lung regions, PP might reduce the right ventricular (RV) afterload (8). By increasing the intraabdominal pressure (IAP), it might increase the venous return and the cardiac preload (9–12). This effect might depend on the level of IAP, because a high IAP might collapse the inferior vena cava (11, 12). If cardiac preload increases, the resultant effect on cardiac output might depend on the degree of preload reserve. Finally, by increasing the IAP, PP might increase the left ventricular (LV) afterload. Overall, the resultant effect on cardiac output may vary, depending on the respective weight of these mechanisms. This is what we investigated in the present study.

Some of the results of this study have been previously reported in the form of abstracts (13, 14).

METHODS

The study was conducted in a 15-bed intensive care unit and approved by the Institutional Review Board of our institution.

Patients

We included patients with ARDS (15), monitored by a pulmonary artery catheter and for whom the attending physician decided to perform PP. Exclusion criteria were contraindication to transesophageal echocardiography or PP and known chronic RV failure.

Ventilatory Settings and Respiratory Measurements

Patients were placed in the 45-degree semirecumbent position and ventilated in the volume assist–controlled mode (Evita 4; Dräger Medical, Lübeck, Germany) with protective ventilation (7). The positive end-
entire study time. Nitric oxide was not added in any other patient. Patients receiving nitric oxide, the dose was kept constant during the study. Compliance of the respiratory system was calculated as tidal volume / (plateau pressure – total PEEP). In patients receiving nitric oxide, the dose was kept constant during the entire study time. Nitric oxide was not added in any other patient.

Hemodynamic Measurements

Patients were monitored by a pulmonary artery catheter (Edwards Lifesciences, Irvine, CA) and a PICCO2 device (Pulsion Medical Systems, Munich, Germany). The pressure transducers were pasted on the patient’s thorax at the midaxillary line and were kept in this position. The pulmonary vascular resistance (PVR) was calculated as (mean pulmonary artery pressure – pulmonary artery occlusion pressure)/cardiac index. The ratio of venoarterial carbon dioxide gradient over pulmonary artery pressure – pulmonary artery occlusion pressure) / plateau pressure = (plateau pressure – total PEEP). In patients receiving nitric oxide, the dose was kept constant during the entire study time. Nitric oxide was not added in any other patient.

Echocardiographic Measurements

With transthoracic echocardiography (Envisor Philips B0; Philips Healthcare, Andover, CA) we assessed the anteroposterior and septolateral diameters of the left ventricle, the LV eccentricity index, the LV ejection fraction, and the presence of a paradoxical motion of the interventricular septum in the short-axis cross-sectional view and the end-diastolic area of the right and left ventricles in a long-axis four-chamber view.

IAP Measurements

IAP was estimated from the bladder pressure by injecting 25 ml of saline in the bladder after clamping the urinary drainage bag (AA6118 Fysyl; Coloplast, Humlebaek, Denmark) (20). The abdominal pressure transducer was fixed to the patient on the lateral side of the pelvis, 2 cm below the anterior superior iliac spine.

Statistical Analysis

Variables were summarized as median and interquartile range. Variables before and during PLR and before and after PP were compared by a Wilcoxon test. The presence of preload reserve was defined by a PLR-increase in cardiac index greater than or equal to 10% (21). Patients in whom PP increased cardiac index greater than or equal to 15% were compared with the other ones by a Mann-Whitney U test. Variables before and during PLR and before and after PP were compared by a Mann-Whitney U test as appropriate. P less than 0.05 was considered statistically significant. Statistical analysis was performed by using MedCalc 11.6.0 software (MedCalc Software, Mariakerke, Belgium).

RESULTS

Study Population

Eighteen patients were included in the study. Their characteristics are summarized in Table 1. Sixteen percent of patients received inhaled nitric oxide.

Changes in Respiratory Data

PP showed a trend toward increased compliance of the respiratory system (Table 2). The ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen significantly increased. The arterial carbon dioxide partial pressure showed a trend toward decrease during PP (Table 2).

TABLE 1. PATIENTS’ CHARACTERISTICS AT BASELINE

| Sex, F/M | 8/10 |
| Age, yr | 72 (48–76) |
| Cause of ARDS (pulmonary/extrapulmonary) | 14/4 |
| Septic shock | 15 |
| SAPS II | 46 (41–57) |
| PaO2/FIO2, mm Hg | 134 (113–154) |
| PaCO2, mm Hg | 83 (77–91) |
| Paco2, mm Hg | 34 (30–40) |
| Lactate, mmol/L | 1.8 (1.4–2.5) |
| Patients receiving norepinephrine | 15 |
| Dose of norepinephrine, μg/kg/min | 0.53 (0.13–0.72) |

Definition of abbreviations: ARDS = acute respiratory distress syndrome; SAPS = simplified acute physiology score.

N = 18; data are expressed as median (interquartile range) or number.
Changes in Cardiac Index and Oxygen Delivery Induced by PP

In nine patients, PP increased cardiac index by more than 15% (Table 2, Figure 2). In these patients, oxygen delivery and oxygen consumption significantly increased. PP did not modify lactate and significantly decreased the ratio of venoarterial carbon dioxide tension gradient over the arteriovenous oxygen content difference. The PLR test performed before PP increased cardiac index by more than 10% (Table 2).

In the remaining nine patients, cardiac index did not change significantly during PP (Table 2, Figure 2). Oxygen delivery, oxygen consumption, lactate, and the ratio of venoarterial carbon dioxide tension gradient over the arteriovenous oxygen content difference ratio were not modified. In this group of patients, the PLR test performed before PP did not increase cardiac index by more than 10% (Table 2).

The LV ejection fraction was significantly higher in patients in whom PP increased cardiac index than in the other patients (Table 2).

Changes in Cardiac Preload and Afterload

PP significantly increased the right atrial pressure and the pulmonary artery occlusion pressure in the overall population regardless of its effects on cardiac index. PVR significantly decreased, as did the difference between the mean pulmonary arterial pressure and the pulmonary artery occlusion pressure (Table 2, Figure 2). The mean arterial pressure increased in patients in whom PP did not increase cardiac index and tended to increase in the other group (Table 2). The product of the LV end-systolic area times the arterial systolic pressure increased in both groups (Table 2).

Changes in the RV Dimensions

In the overall population at baseline, the ratio of the RV/LV end-diastolic areas was above 0.6. We did not observe any acute cor pulmonale at baseline. PP did not induce any new case of acute cor pulmonale. PP significantly reduced the ratio of the RV/LV end-diastolic areas and the eccentricity index (Table 2).

Changes in IAP

At baseline in patients in whom PP increased cardiac index, IAP was between 12 and 15 mm Hg (20) in four patients, between 16 and 20 mm Hg in four patients, between 20 and 25 mm Hg in one patient, and greater than 25 mm Hg in any patient. In the remaining patients, IAP was between 12 and 15 mm Hg in seven patients and between 16 and 20 mm Hg in two patients. In both groups of patients, IAP significantly increased during PP (Table 2).
**DISCUSSION**

In patients with ARDS ventilated with protective ventilation and maximal alveolar recruitment, we observed that PP reduced RV afterload and increased cardiac preload. PP increased cardiac index in half of the patients. Significant preload reserve was documented in this group of patients. In the remaining patients, cardiac index did not change with PP and no preload reserve was documented.

Some studies have found that PP had no or minimal hemodynamic effect (23–31) but they have been conducted under different ventilator settings (23, 24, 26, 29–31) and investigated hemodynamics a long time after proning (23, 31). Other studies have shown that PP increased cardiac output (32, 33) but the responsible mechanisms were not fully investigated, in particular because RV afterload was not assessed. Finally, in patients with acute core pulmonale, Vieillard-Baron and coworkers (8) have shown that PP improved RV function and increased cardiac output. Their study was not conducted with protective ventilation and maximal alveolar recruitment (8). Moreover, it described hemodynamic effects 18 hours after PP. Thus, the acute hemodynamic effects induced by PP remained to be documented.

---

**Figure 2.** Changes in hemodynamic variables before and during prone positioning in patients with nonsignificant and significant changes in cardiac index induced by prone positioning. In box and whiskers, the median line corresponds to median, the lower and upper limits of the box to the extremes of the interquartile range, and the error bars to the extremes of the 5th–95th percentiles. The gray lines correspond to individual data. n = 18. *P less than 0.05 versus before prone positioning.
The present study confirms that, in the whole population, PP reduced the RV afterload, as assessed by the decrease in the PVR along with a reduction of difference between mean pulmonary arterial and pulmonary artery occlusion pressures and the ratio of RV/LV end-diastolic areas. It is noteworthy that the true PVR, which is underestimated by the calculated PVR in case of extended zone 2 conditions (Starling resistor effect), might be reduced by the recruitment of pulmonary microvasculature with PP. Indeed, the increase in central blood volume recruits some collapsed pulmonary microvessels (34) and transfers some lung regions from West zone 2 to zone 3 (35). Another explanation for the decrease in PVR and RV afterload might be the potential lung recruitment induced by PP, which possibly increased the lung volume in a way leading to a reduction of PVR (36), as suggested by the improvement of the respiratory system compliance and the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen (see Table ESM in the online supplement). Finally, we cannot exclude that the improvement in arterial oxygenation was associated with a reduction of the hypoxic pulmonary vasoconstriction in the most hypoxic patients (Figure 1) (37).

PP increased right and left cardiac preload in the whole population. First, this might be caused by the lowering of the trunk from the semirecumbent position, which transfers splanchnic venous blood toward the heart (38). Second, the increase in cardiac preload during PP could also be related to the compression of the splanchic compartment because of increased IAP (12). The increase in right cardiac preload suggests that this increase in IAP did not collapse the inferior vena cava (i.e., vena cava was in a zone 3 condition) (11, 12). This might be caused by the fact that the IAP was lower than the intramural pressure of the inferior vena cava. Importantly, it is unlikely that the increase in right atrial pressure and pulmonary artery occlusion pressure was simply caused by the transmission of the increased IAP to the thorax (39). Indeed, PEEP was adjusted to keep constant the plateau pressure, maintaining the intrathoracic pressure constant. In this regard, the fact that we did not assess that transmission is a limitation of the study. In the same line, we could not find any clear explanation for the higher right atrial pressure at baseline in patients with preload reserve than in patients without preload reserve. The fact that auto-PEEP and IAP were similar between groups is against the hypothesis that this difference was caused by a higher transmission of IAP or intrathoracic pressure.

Our results also suggest that PP increased the LV afterload in the whole population. This was suggested by the increase in mean arterial pressure (i.e., the main component of hydraulic load) (40) and in the product of the LV end-systolic area times the arterial systolic pressure. We cannot exclude that part of this effect resulted from the transmission of the increase in IAP to the abdominal arterial vasculature (10). This might have increased the intramural pressure of the easily compressible, small abdominal vessels, with essentially unchanged aortic intramural pressure, because the aorta is not easily compressible.

Eventually following PP, cardiac output significantly increased only in the patients with preload reserve. In these patients, both the increase in right cardiac preload and the reduction of RV afterload contributed to an increase in LV preload. Because of preload reserve, this led to an increase in cardiac output (Figure 1).

By contrast, in patients without preload reserve, PP did not change cardiac output. There might be two explanations. First, the reduction in RV afterload resulted in an increase in LV preload (Figure 1). Because of the absence of preload reserve, this did not induce an increase in cardiac output. Interestingly, LV ejection fraction was lower in these patients with no preload reserve than in the other group, consistent with physiology. Second, it is also plausible that the decrease in RV afterload had a small effect on cardiac index because RV dysfunction was not severe in our patients (no cor pulmonale and exclusion of patients with chronic RV failure).

It is noteworthy that LV ejection fraction did not change with PP in both groups. This suggests that the influence of changes in LV afterload on cardiac output was not major.

Our study has some limitations. First, we could not directly assess alveolar recruitment by the quasistatic respiratory system compliance. Second, we did not investigate patients with a very high IAP, in whom PP could collapse the inferior vena cava and decrease cardiac output. Third, our results cannot be extrapolated to PP performed by using thoracic and pelvic supports and with conventional foam mattress, because these factors may affect the effects of PP on the abdominal pressure (41, 42). Fourth, we could not assess preload responsiveness in the prone position. In particular, it was not possible to use pulse pressure and stroke volume respiratory variations for this purpose, because the low tidal volume and/or low lung compliance associated with ARDS preclude to use it for assessing preload dependence (43, 44). Fifth, we did not measure the pleural pressure and we could not assess the transmission of the IAP and the intrathoracic pressure to cardiac pressures. Thus, we could not assess whether the transmural pressures varied to the same extent than the intramural pressures with PP. Finally, the abdominal and cardiac pressures were not measured with the same reference level. However, in a series of 30 other patients, we observed that the difference in height between the two reference levels was 3 cm on average. This corresponds to a hydrostatic pressure gradient of 2.2 mm Hg. Applying this correction to our right atrial pressure values would not significantly change our results, in particular the significant increase in right atrial pressure with PP.

In conclusion, in patients with ARDS with protective ventilation, PP increased cardiac preload and reduced RV afterload. This resulted in an increase in cardiac output only in the patients with preload reserve.

Author disclosures are available with the text of this article at www.atjournal.org.

Acknowledgment: The authors thank Dr. Umar Ahmad for English editing.

References


