Effect of Prone Positioning on Morbidity and Mortality of Obese Adults With ARDS

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Abstract

Background: Obesity is a worldwide epidemic that is expected to grow exponentially in the future. Obese patients are at risk of developing serious complications including acute respiratory distress syndrome (ARDS). Prone positioning (PP) has been shown to increase survival rates in patients with ARDS, but few studies have focused on the effect of PP on obese patients. This systematic review seeks to explore the research performed on the question: in obese adults with ARDS, can prone positioning increase the likelihood of morbidity or mortality when compared to supine positioning?

Methods: A comprehensive search of available medical literature was performed using MEDLINE-Ovid, CINAHL, and Web of Science using the following search terms: acute respiratory distress syndrome, prone position, and obesity. Quality of all relevant articles were assessed using the Grading of Recommendations, Assessment, Development, and Evaluation criteria (GRADE).

Results: Two articles met the inclusion criteria and provided original data regarding the clinical question. These articles included two retrospective observational studies. An observational case-control clinical study with 66 patients demonstrated that length of mechanical ventilation, intensive care unit (ICU) stay, and nosocomial infections did not differ significantly between obese and non-obese patients in PP, but mortality was significantly lower in obese patients. A retrospective observational study found that there was no significant difference in overall ICU mortality. However, it was found that obese patients developed renal and hepatic failure more often.

Conclusion: Prone positioning has been shown to reduce the rate of mortality in patients with ARDS. Current studies show that PP can also reduce mortality in obese patients, however studies conflict on their results regarding morbidity. Therefore more quality studies must be performed to determine the safety of PP in obese patients.

Keywords: prone positioning, obesity, ARDS, respiratory distress syndrome, adult

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Effect of Prone Positioning on Morbidity and Mortality of Obese Adults With ARDS

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Biography
Maia Lavarias was born in Honolulu, HI, and grew up in Woodinville, WA. She received a Bachelor of Science degree in biology at York College of Pennsylvania in York, PA. Before entering Physician Assistant school, she was a certified nursing assistant and research assistant for a study of obstructive sleep apnea’s effect on glucose metabolism. After graduation, Maia will be completing a year-long residency in critical care medicine at Johns Hopkins Hospital.
Abstract

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Table I: GRADE Profile: Prone positioning in obese adults with ARDS

List of Abbreviations

ARDS.................................................Acute Respiratory Distress Syndrome
BMI......................................................Body Mass Index
FIO2........................................................fraction of inspired oxygen
GRADE..........................Grading of Recommendation, Assessment, Development and Evaluation Criteria
ICU.............................................................Intensive Care Unit
PaO2..................................................partial pressure of oxygen in the blood
PaO2/FiO2..........................ratio of arterial oxygen partial pressure to fractional inspired oxygen
PP.............................................................Prone Position
PROSEVA............................................Proning Severe ARDS Patients Study
SAD............................................................Sagittal Abdominal Diameter
Effect of Prone Positioning on Morbidity and Mortality of Obese Adults With ARDS

BACKGROUND

Obesity is a worldwide epidemic affecting both advantaged and disadvantaged communities. The World Health Organization has noted a doubling of obesity in the past 30 years.\textsuperscript{1} Obesity not only predisposes patients to a variety of chronic illnesses, it has also been found to lengthen the stay in the intensive care unit (ICU), and it increases the likelihood of complications during admission, including acute respiratory distress syndrome (ARDS).\textsuperscript{2,3}

ARDS is a condition of the lungs where the alveolar sacs fill with fluid, causing decreased oxygenation of the blood leading to hypoxia of end organs. This syndrome can be caused by infection, trauma, or other conditions.\textsuperscript{4} In the ICU, the risk of ARDS increases in a weight-dependent manner.\textsuperscript{5}

Management of ARDS can be difficult. Over the past 30 years, patients with ARDS have been put in prone position (PP) to improve oxygenation.\textsuperscript{6} The Proning Severe ARDS Patients Study (PROSEVA study) is a randomized control trial that found patients with severe ARDS had a significantly higher survival rate when put in the prone position as opposed to the supine position.\textsuperscript{7} A study by Gattioni et al\textsuperscript{8} also found that PP improved arterial oxygenation with a limited number of complications. At this time, it is unknown exactly how prone positioning improves oxygenation in ventilated patients. Several theories have been explored, including: PP increases end expiratory lung volumes,\textsuperscript{9} it increases thoracoabdominal compliance,\textsuperscript{10} altered gravitational forces during PP cause an increase in ventilation/perfusion ratio of previously atelectatic areas,\textsuperscript{11} and PP allows areas of lung previously compressed by the heart in the supine position to ventilate.\textsuperscript{12}
With the increased prevalence of obesity in the United States and around the world, more and more patients admitted to the ICU will be obese or even morbidly obese. Pelosi et al\textsuperscript{13} found that placing obese patients in PP during surgical anesthesia can improve pulmonary function, provided that the abdomen has free movement. However, this study did not look at PP therapy for prolonged periods of time, or in patients with lung pathology like ARDS. It is important to know whether the current practices for non-obese patients affect our obese patients in the same way, or if they could potentially cause harm. In obese adults with ARDS, can prone positioning increase the likelihood of morbidity or mortality when compared to supine positioning?

METHODS

A comprehensive medical literature search was performed using MEDLINE-Ovid, CINAHL, and Web of Science with the following search terms: acute respiratory distress syndrome, prone position, and obesity. All articles were reviewed to determine that they contained original data regarding the use of prone positioning in obese patients with ARDS. The search was then narrowed to include only articles written in English and only those with adult participants. The bibliographies of the articles were further searched for relevant sources. Quality of all relevant articles were assessed using the Grading of Recommendations, Assessment, Development, and Evaluation criteria (GRADE).\textsuperscript{14}

RESULTS

An initial result of the medical literature search yielded 7 original articles. These articles were then screened to determine their relevance to the clinical question, and narrowed to include only papers written in English and those involving adults. Two articles met the inclusion criteria. These articles included two retrospective observational studies.\textsuperscript{15,16} See Table I.
Feasibility and Effectiveness of Prone Position in Morbidly Obese Patients with ARDS (De Jong, et al)

This observational case-control clinical study\(^{15}\) investigated whether prone positioning was a safe and useful treatment in obese patients with ARDS. The endpoints for this study were rate of complication, effect on gas exchange, nosocomial infection rates, and mortality. From January 2005 to December 2009 this study was conducted in a surgical and transplantation unit. Morbidly obese patients were defined as having a BMI of \(\geq 35\) kg/m\(^2\), and were selected if they received invasive mechanical ventilation and were diagnosed with ARDS. ARDS was defined by the definition created by the American-European Consensus Conference on ARDS\(^{17}\): a PaO\(_2\)/FIO\(_2\) ratio of \(< 200\) mmHg, at least 5 cm H\(_2\)O of positive end-expiratory pressure, radiographic evidence of bilateral pulmonary infiltrates, and no evidence of increased pulmonary venous pressure.\(^{15}\)

Exclusion criteria included evidence of cerebral edema or intracranial hypertension, fractures of the spine, or severe hemodynamic instability. These are all contraindication for PP itself, and therefore excluded the patient from the study. Obese patients with ARDS were matched with non-obese patients (BMI of \(< 30\) kg/m\(^2\)) with ARDS in a matching procedure defined in previous studies.\(^{18,19}\) They were matched according to age, sex, Simplified Acute Physiology Score II, admission time to ICU, and type of admission (medical or surgical). Baseline demographics and main causes of ARDS did not vary significantly between the two groups. Thirty-three obese patients and 33 non-obese patients were matched. PP was used within the first 48 hours of the ARDS course, and was used routinely in patients with a PaO\(_2\)/FIO\(_2\) ratio of \(> 150\) mmHg or by the discretion of the attending physician. PP sessions lasted from 6-18 hours/day and length was determined by the prescribing physician. PP was continued until
patients were ventilated with an FIO2 <60%. Patients were considered “responders” if the PaO2/FIO2 ratio increased by at least 20% when placed in PP, and were considered “strong responders” if the ratio increased by 40%. During PP, no significant difference was observed between the two groups regarding enteral feeding, NG tube use, vasoactive drug use, and myorelaxant use.\textsuperscript{15}

The authors found that the median length of PP sessions did not differ significantly between obese and non-obese patients (P=0.28). The study tracked complication rates including accidental extubation, pressure ulcers, loss of vascular or urinary catheter access, facial edema, bleeding, hemodynamic instability, vomiting, and cardiac arrest. There was no significant difference in number of complications between groups (10 patients from each group, P=1.00). Both groups of patients benefitted from increased oxygenation while in PP. PaO2/FIO2 ratio was significantly increased between supine and PP in both groups (P<.0001). In PP, obese patients had a significantly higher PaO2/FIO2 ratio than non-obese patients (P=.03), while there was no statistical difference between the two groups while in supine position. This suggests that while both groups benefitted from increased oxygenation while in PP, obese patients had more of a benefit while in PP. Seventy-seven percent of the obese patients were considered strong responders (20 of 26) to PP therapy, while 50% of the non-obese patients were strong responders (13 of 26) making this a significant difference (P=.044). The authors found that mortality outcome was not significantly different between the groups until 90 days, and that mortality at 90 days was significantly lower in the obese group than the non-obese group (P=.03, hazard ratio, 0.36; 95% CI, 0.14-0.93).\textsuperscript{15} See Table I.

The authors found that a limitation to this study was that it was a mono-center, unblinded, nonrandomized, observational case-controlled study, which weakens its conclusions.
Since the study is retrospective, it has to draw its data from the medical record, which may not always be complete. Also, the PP therapy time was not standardized and ranged from 1-19 hours, although the median time of therapy did not differ significantly. There was also no control group of patients who are not put in PP to compare to those put on PP.\(^{15}\)

The authors concluded that obese patients with ARDS can be treated safely, and effectively with PP and that the outcomes are favorable. They note that their unit has been using PP regularly since 1997 which could account for the low complication rates. They also use a reverse Trendelenburg position to reduce facial swelling. They also discussed a possible physiological explanation for the improved oxygenation in PP: PP recruits previously collapsed regions of lung tissue without increasing airway pressure or hyperventilation, causing a lung-protective effect.\(^{15}\)

**Influence of Abdominal Obesity on Multiorgan Dysfunction and Mortality in Acute Respiratory Distress Syndrome Patients Treated With Prone Positioning (Weig, et al)**

This retrospective observational study\(^{16}\) investigated whether increased abdominal obesity along with prone positioning was associated with higher morbidity and mortality in patients with ARDS. They also looked to determine which means of measuring obesity (sagittal abdominal diameter (SAD), intraperitoneal fat measurement, or body mass index (BMI)) correlated best with risk of complication. The study looked at 82 patients with severe ARDS, admitted to the ICU. The patients were split into two groups as described in a previous study.\(^{20}\) Group 1, called the XL group, had abdominal obesity with SAD of \(> \text{or} = 26\text{cm}\) (n=41). Group 2, called the ML group, was the control group with SAD of \(< 26\text{cm}\) (n=41). SAD was measured using abdominal CT images at the level of L5/L4. These images were also used to measure intraperitoneal fat volumes, and BMI was calculated using height and weight from recent
primary care visits, or information from family. Homogeneity was found regarding age, sex, and severity of disease upon admission to the ICU, in both groups. Exclusion criteria included death or discharge from the ICU before day 7 (n=12), because these patients did not provide enough information to add to the study. The endpoints studied included death, discharge from ICU, and development of renal or hepatic failure. All PP sessions lasted 12 hours, but deploying PP was based on clinical judgement and radiologic findings.\textsuperscript{16}

The authors found that the overall ICU survival for both groups was 65.9%; however, there was a significantly higher rate of renal failure (P<.0001) and hypoxic hepatitis (2% vs 2%, P=.015) in the XL group. Mortality rates also increased in the XL patients treated with prolonged cumulative PP, but not in ML patients. Similar results were found using SAD or intraperitoneal fat volume as a measure for obesity. No difference was found in the duration of mechanical ventilation or length of stay between the two groups.\textsuperscript{16} See Table I.

The authors concluded that patients with increased abdominal obesity (SAD of >26cm) may be at a higher risk of mortality with prolonged PP. They may also be at higher risk of complications, like renal and hepatic failure. It was also suggested that in order to successfully classify obese patients, it is necessary to utilize a more accurate tool, whether it be by bedside calipers or CT imaging. The authors also discussed that the major limitation to their study was size. They suggested that larger studies are needed in order to provide definitive evidence of the safety of PP use in obese patients.\textsuperscript{16}

**DISCUSSION**

Prone positioning is widely used in ICUs for hypoxic patients not responding well to mechanical ventilation in the supine position. A vast number of studies\textsuperscript{6-10,12,21} have been performed regarding the safety and efficacy of PP in the ICU, however few studies have focused
on the obese population. Due to the increasing prevalence of obesity worldwide, it is likely that many more critically ill patients will be obese, making it vitally important to determine the safety of PP therapy for this population. In past studies, PP has been found to be safe for obese patients during general anesthesia, provided that the abdomen is able to move freely. However, this study did not look at prolonged PP therapy. It also did not look at patients with lung pathology, like ARDS which is seen often in the ICU. This systematic review explored the research performed regarding the effect of prone positioning on morbidity and mortality in obese patients with ARDS.

After an extensive medical literature review, two studies were found to contain original data regarding prone positioning in obese patients with ARDS. De Jong et al and Weig et al both looked at the effect of PP on morbidity and mortality in obese patients with ARDS in the ICU. Both studies found that the rate of mortality did not differ between obese and non-obese patients, however the Weig et al study did state evidence that prolonged PP may increase mortality rates in obese patients. Moreover, the studies had very differing results when it came to complications. De Jong et al found that the rate of complication did not differ significantly between obese and non-obese patients and suggested that PP could be used safely in obese patients. Weig et al found that the rate of complication increased significantly in obese patients. Due to these results, they suggested clinicians be careful when prescribing PP therapy to obese patients.

There were many limitations to both of these studies. First of all, the size of both studies were small. De Jong et al had a patient population of 66, while Weig et al had a population of 82 people. This makes their evidence less substantial, and makes it difficult to suggest that any changes to clinical practice be made. There was also variability in results across both studies,
especially regarding morbidity. The study by Weig et al\textsuperscript{16} found that obese patients were substantially more at risk for renal and hepatic failure when put in the prone position. However, De Jong et al found that obese patients experienced the same amount of complications as non-obese patients. Again, these differing results make it very difficult, if not impossible, to draw a definitive conclusion about the safety of PP’s use in obese patients. Finally, the fact that both of these studies are observational, means they are both of low quality to start out. They both relied on medical record to procure information about PP time periods, complication rates, and lab results. This enters an opportunity for incomplete data in the study, because there is a chance that these records are not complete. These inconsistencies could introduce bias in the study results.

Patients with ARDS are at high risk of death from the illness, with estimates as high as 48\%.\textsuperscript{21} Both studies found that PP in obese patients had a similar decrease in rate of mortality as non-obese patients with ARDS. PP is a cost effective way to reduce this risk by improving oxygenation and therefore should be used for all patients with ARDS who are hypoxic while being mechanically ventilated. However, the results of these studies in regard to morbidity are conflicting. At this time, no definitive suggestion can be made for using PP with respect to morbidity. The most appropriate suggestion that can be made to prevent morbidity in obese patients with ARDS in the PP is to monitor organ function. Complications seen during these studies included renal and hepatic failure, pressure ulcers, cardiac arrest, and infection. If obese patients are put into PP due to failing oxygenation, it is suggested that daily labs be evaluated and skin checks performed to monitor for any complications. Until further research is completed, it is important for clinicians to be cautious of possible complications.

In order to provide more quality evidence, it is necessary to have larger, and more quality types of studies. However, due to the precarious nature of the health status of these patients, it is
unlikely that a randomized control study would be ethically just for studying prone positioning versus supine positioning in obese patients with ARDS. This is especially true considering studies have shown that PP in ARDS patients increases rate of survival\(^7\). Also, because of the general nature of the therapy, it would be impossible to blind the researchers or patient to their treatment group. Therefore, more extensive and larger observational studies would be suggested to determine whether PP in obese patients increases risk of morbidity.

**CONCLUSION**

Prone positioning has been used successfully for many years with non-obese patients. However, due to the increasing rates of obese patients throughout the world, it is vitally important that we know the effect of PP on this population. Current evidence regarding PP in obese patients with ARDS is sparse, and not of high quality. However the evidence that is presented seems to support improved mortality in obese patients when PP therapy is deployed, with some concerns regarding possible complications. More quality research must be done to better determine the safety of prone positioning on obese patients with larger study groups. Specifically, further research should be focused on morbidity from prolonged prone positioning due to the differing results shown in current studies.
References


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[^a]: Sample size too small to measure complications which occurred rarely
[^b]: Both studies measured different complications and reported different results