Commentary

Pro/con clinical debate: The use of prone positioning in the management of patients with acute respiratory distress syndrome

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Abstract

Critical care medicine is a relatively new specialty and as such there is not a great deal of accumulated data to allow clinicians to practice 'evidence-based medicine' in all situations they encounter. When evidence does exist, intensivists may choose not to follow it based on 'gut feelings' or their own interpretation of how the data apply to their patient. It is perhaps not surprising that these latter events occur given that intensivists are often literally fighting for their patient's lives. Prone positioning evokes a large emotional response from many intensivists. Despite accumulating data there appears to be two camps of clinicians: those who strongly believe in the therapy, and those who want more data. The emotion and rationale for the mindset of the two camps is evident in this issue of *Critical Care Forum*. With compelling arguments on both sides of the fence, it is apparent that this debate is far from over. The authors of this pro/con debate, which is based on a clinical scenario, first describe their position and then respond to their opponent's position.

Keywords: prone position, ventilation, ventilation–perfusion ratio

The scenario

A 29-year-old obese man is involved in a motor vehicle accident and has a pulmonary contusion that results in severe acute respiratory distress syndrome (ARDS). He is mechanically ventilated with volume cycle ventilation (tidal volume, 6 ml/kg ideal body weight), a positive end-expiratory pressure of 18 cmH_2O, and a fractional inspired oxygen concentration of 0.8. His injuries are minimal and do not prevent him from being moved. Given your concerns about his oxygenation, you wonder whether there might be a benefit to prone positioning.

Pro: prone positioning is useful in the management of ARDS patients

John J Marini

Critically ill patients are frequently immobilized in the supine position for days to weeks with periodic 15–30° lateral positioning. Supine positioning allows access to vital structures, facilitates catheter placement, allows the patient to face caregivers and family, and avoids potential pressure-related complications, such as ocular injury, jugular vein compression, and skin ulceration at points of increased pressure (for instance, the nose, chin, or knees). Maintaining a supine position may also be mandated by the underlying condition (such as anterior burns or massive ventral trauma). In nature, however, an unrelieved supine orientation is never encountered for extended periods; postural variation is innate. Moreover, if one horizontal orientation is to be preferred, there are five reasons for choosing the prone position in preference to the supine position.

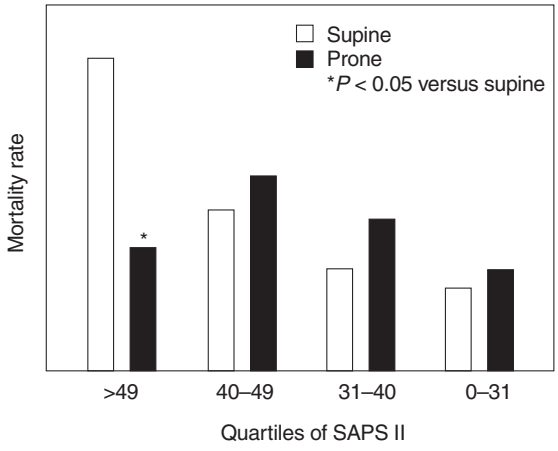
ARDS = acute respiratory distress syndrome.

Firstly, sinus and airway anatomy affords more efficient secretion drainage when prone. Secondly, the lung fits into the prone thorax with less distortion. This improved fit results from the repositioned diaphragm and heart; the heart compresses the dorsal lung when supine and rests on the sternum when prone [1].

Thirdly, the supine position predisposes to airway closure in the dorsal regions that receive the majority of blood flow [2]. Regional ventilation-to-perfusion relationships are more uniform in the prone position, especially in patients with ARDS. Increased ventilation-to-perfusion uniformity improves gas exchange to a clinically meaningful extent in most patients with ARDS when they are turned to the prone position [3,4]. Obese patients and those with congestive heart failure also benefit from prone positioning [5]. Because the distribution of ventilation improves, reduced chest wall compliance in the prone position may improve rather than impair oxygenation [6].

Fourthly, improved and/or more sustained response to recruiting maneuvers occurs in the prone position [7]. Finally, animal models have shown that, for the same pattern of ventilatory pressures, the prone position protects better against ventilator-induced lung injury [8].

Figure 1



Proning may benefit the most seriously ill subset of patients with acute respiratory distress syndrome. Those in the quartile with the highest Simplified Acute Physiology Score II (SAPS II) have a marked mortality benefit with 'proning'.

Clinical experience

Prone positioning has improved arterial oxygenation in all studies in patients with ARDS that have examined the question, especially in the early phase of illness [3]. Disappointingly, however, in the only randomized, controlled study of proning yet published, 6 hours of prone positioning did not influence mortality in the diverse patients entered from a large number of Italian centers [9]. Apart from questions that beset the majority of multicenter trials in patients with ARDS, such as definitional precision, co-intervention control, and execution variability across and within centers, this result hardly constitutes a basis for discarding the practice for many study-specific reasons.

Firstly, the brief duration of 'proning' (both in terms of number of hours per day and number of days) may not have been adequate. Secondly, the study was terminated prematurely before even one-half of the targeted number of subjects for whom the study was powered were enrolled. This was because the enrollment rate dwindled as the study proceeded, primarily because many investigators perceived that withholding the option to prone was unethical, based on their early experience.

Thirdly, a *post hoc* analysis of the data indicated a marked mortality benefit with proning in the subset of patients most seriously ill (see Fig. 1), and in those ventilated with the high tidal volumes (≥12 ml/kg) associated with higher mortality in the ARDS Network tidal volume trial [10]. Finally, as in all previous reports, proning was hemodynamically well tolerated and the incidence of serious iatrogenic complications, such as unintended extubation or skin ulceration, were no more common in the group whose position was varied than in the group that remained continuously supine.

Con: prone positioning is not useful in the management of ARDS patients

Gordon Rubenfeld

Imagine the following scenario. A novel treatment for a critical illness syndrome is reported in a case series [11,12]. Animal models support a physiologic rationale for the treatment, and small clinical trials look promising [8,13]. Finally, a large, randomized clinical trial is performed but the treatment has no effect on mortality [9]. Advocates regroup and claim that the wrong patients and doses were used, that there were baseline imbalances, and that the sample size was too small. Critics exult that it is time to stop using this treatment. This familiar story has recently been retold about prone ventilation for the management of ARDS patients [9].

A review of the clinical trial shows that, like inhaled nitric oxide, prone ventilation improves oxygenation without affecting mortality. Prone ventilation was neither free of cost nor completely safe; it required an additional 90 person-minutes of time per day to position the patient and was associated with an increase in pressure ulcers, sedation needs, muscle relaxants,

and ventilator discoordination. Of course, advocates of prone ventilation found solace in the arguments people resort to after negative clinical trials: 'proning' may still reduce mortality, but only in patients with the most severe ARDS; and negative trials do not *prove* that a treatment is useless.

Rather than enter the usual fray, let me suggest another route to understanding this debate [14]. At the heart of a discussion about the use of prone ventilation (or of nitric oxide) is an understanding of how clinicians make decisions when the probability of benefit is uncertain [15]. In making decisions, clinicians balance the risks, benefits, and costs of treatment by weighting potential outcomes by how important they are. Unfortunately, we tend to weigh these outcomes differently and quite personally. A clinician with a single bad experience with prone ventilation will overestimate its risks; a clinician who believes a patient with a severe case of ARDS was saved by prone ventilation will overestimate its benefits. Clinicians who are physiologically oriented (or who do physiologic research) will be persuaded by physiologic research; those who are outcomes oriented (or who do outcomes research) will only be persuaded by survival data. Finally, intensivists are strongly motivated by the 'rule of rescue'. Intensivists feel obliged to offer some therapy, any therapy, to a patient in imminent danger of dying [16].

As is often the case in critical care, a therapy that looks great from a basic science standpoint does not appear to save lives. The available evidence on prone ventilation neither conclusively proves nor disproves its benefit, but makes the probability of benefit small in the majority of ARDS patients. When the evidence of harm and cost is weak and the evidence of benefit is even weaker, decisions will be driven by factors other than the data. These factors include personal values about cost-effectiveness, rescue, and interpretation of the dictum 'first, do no harm'.

I think it is reasonable to conclude that there is no case of ARDS when an intensivist should feel obliged to provide prone ventilation. Intensive care unit nurses and respiratory therapists should not feel that they are preventing an effective therapy when they voice concerns about the safety of proning a particular patient. Finally, clinicians that disagree about the use of prone ventilation should appreciate they are probably disagreeing more on their own values than on the evidence.

Pro's response to Con's arguments

John J Marini

If the conclusions from randomized clinical trials (RCT) are to help guide practice, patients entered into them must share defining characteristics that investigators and physicians alike can reliably identify. Sadly, Dr Rubenfeld has shown us convincingly that this is not true for ARDS, even among 'experts' [17]. Moreover, 'negative' trial results spawned by design flaws, definitional or procedural aberrations may obscure benefit.

Severely affected patients with 'ARDS' were helped often enough by proning that Gattinoni found both a twofold mortality difference in this subset (despite the brief proning duration) and a growing reluctance among investigators to forgo the proning option (L Gattinoni, personal communication). Given this striking difference, it is debatable whether an RCT specifically targeting these difficult cases can be undertaken ethically.

Physiological understanding, experimental data, and prior clinical experience are key elements of the knowledge base that are highly relevant to bedside decision-making. Although not effective in all patients, those most seriously ill without contraindications clearly deserve an individualized 'N-of-1' proning trial.

Con's response to Pro's arguments

Gordon Rubenfeld

Dr Marini invokes the standard responses of an advocate of a therapy when the clinical trial results are different than the results he had expected. It is impossible to conclusively prove the negative hypothesis that a therapy is ineffective under all conceivable clinical conditions, doses, and patient subgroups.

The confidence interval around the treatment effect in the present study allows up to a 50% reduction in the risk of death, and there is certainly a possibility that a larger study would yield positive results. Neither of these are very persuasive arguments for using a therapy.

The real question for clinicians is: do physiologic improvement and animal studies justify using a treatment? My answer is still the same; no-one should feel that that they are withholding effective life-saving therapy from a patient with ARDS by deciding *not* to put the patient in the prone position. Clinicians who choose ventilation in the prone position are applying experimental therapy and must weigh its known potential for harm with the lack of data on its benefit to patient survival.

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