

Prone to Survive

To the Editor:

Gattinoni and colleagues have reported that prone ventilation does not improve survival (1, 2). In contrast to this, we have recently completed a small pilot study (a randomized, controlled trial) that showed improved survival among pediatric patients with prone ventilation (3). The odds ratio for survival in the prone group was 6.72 (confidence interval, 1.28–39.15). We use this communication to highlight crucial protocol differences between the studies, which may be responsible for this difference in outcome. We hope it provides impetus for further research into this relatively simple intervention.

The protocol of Gattinoni et al. stipulated that physicians must “not change the ventilator settings during the period of pronation, in order to standardize the changes in gas exchange induced by the maneuver” (3). Thus both prone and supine patients in their study were subjected to the same mean airway pressure (MAP) and tidal volumes, even after it was noted that the PaO<sub>2</sub>:FIO<sub>2</sub> ratio had improved (and they could be managed with lower MAP). On the other hand, in our study, the attending pediatrician was permitted to adjust ventilatory settings as needed. We found that prone patients had better oxygenation (PaO<sub>2</sub>:FIO<sub>2</sub> ratio) within an hour of ventilation than did supine patients, and they were being ventilated at lower pressures (MAP) at the end of 4 hrs (Table 1).

This use of lower MAP could be crucial for better survival. Slutsky has noted that ventilator-induced lung injury, not hypoxemia, may be the primary cause of death in many cases of acute respiratory distress syndrome (ARDS) (4). A study sponsored by the National Institute of Science found mortality in cases of ARDS could be decreased by 22% by reducing tidal volumes from 12 to 6 mL/kg (5). Prone ventilation, by improving oxygenation, allows ventilation at lower pressures. We believe the protocol of the study by Gattinoni et al. prevented participants from getting this benefit of ven-

Table 1. Table showing secondary outcome measures

Parameters	Time	Prone Mean (SEM)	Supine Mean (SEM)	p Value
Oxygenation index	Baseline	6.6 (1.3)	9.4 (1.2)	.12
	1 hr	2.9 (0.5)	7.5 (1.2)	.0004
	4 hrs	3.3 (0.6)	6.3 (1.2)	.015
	5 hrs	3.5 (0.7)	8.5 (2.3)	.02
	Baseline	255.4 (56.6)	139.6 (37.3)	.1
PaO <sub>2</sub> /FIO <sub>2</sub>	1 hr	453.9 (89.9)	247.6 (94.1)	.003
	4 hrs	452.9 (106.9)	319.9 (108.3)	.3
	5 hrs	386.7 (94.1)	203.5 (30.2)	.07
	Baseline	6.6 (0.4)	7.5 (0.4)	.13
Mean airway pressure	1 hr	6.8 (0.4)	7.7 (0.4)	.11
	4 hrs	6.5 (0.4)	8.3 (0.6)	.02
	5 hrs	6.6 (0.5)	8.6 (0.7)	.01
	Baseline	32.7 (3.3)	40.5 (3.2)	.1
Paco <sub>2</sub>	1 hr	29.3 (2.7)	34.6 (2.4)	.15
	4 hrs	34.8 (2.5)	35.9 (3.3)	.7
	5 hrs	29.5 (1.9)	43.4 (5.8)	.02

tilation at lower MAP. This may explain the enigma of why this multicenter study did not confirm benefits that were speculated on theoretical grounds before the study.

Gattinoni and colleagues note in their article (2) that *post hoc* analysis indicates the need for another trial, designed to clarify the role of prone position in patients with severe ARDS. When this is being done it may be crucial to allow the attending doctor to adjust ventilator settings (lower the pressures used, as soon as possible) to achieve the benefits of prone ventilation on survival. Bigger studies are needed to confirm our findings. Multicenter trials are extremely expensive to conduct, but we are vehemently in favor of such a trial, because the intervention itself is so simple to institute and the potential for saving lives is huge.

The authors have no financial interests to disclose.

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REFERENCES

- Gattinoni L, Vagginielli F, Carlesso E, et al: Decrease in Paco<sub>2</sub> with prone position is predictive of improved outcome in acute respiratory distress syndrome. *Crit Care Med* 2003; 31:2804–2805
- Gattinoni L, Tognoni G, Pesenti A, et al: Effect

of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001; 345:568–573

- Sawhney A, Kumar N, Sreenivas V, et al: Prone versus supine position in mechanically ventilated children: A pilot study. *Med Sci Monit* 2005; 11:CR235–CR240
- Slutsky AS: The acute respiratory distress syndrome, mechanical ventilation, and the prone position. *N Engl J Med* 2001; 345:610–612
- The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342:1301–1308

DOI: 10.1097/01.CCM.0000179028.29815.08

The authors reply:

I read with interest the letter of Sawhney and co-workers, and I congratulate them for their promising results, which appear to contrast with those of the previous study on prone position by my colleagues and myself (1, 2).

Before any discussion, however, I believe that is important to examine our results in their historical perspective. When we designed that study in 1997 the results of the ARDS Network trial (3) and the experimental works consistently showing the possible advantages of prone position in reducing ventilator-induced lung injury (4–7) were not available.

Indeed, at that time, we had two choices: either to change the ventilator setting from supine to prone to maintain the oxygenation constant (by decreasing

FIO<sub>2</sub>, positive end-expiratory pressure, etc.) or to maintain the ventilator setting to document the effects of prone position on the physiologic variables (PO<sub>2</sub> and PCO<sub>2</sub>) in a large population. We chose the latter approach, although, as very often happens, *a posteriori* the former approach would have been more appropriate.

Second, we chose 6 hrs of prone position according to the nurses' shifts (to have more manpower available). This is not a very scientific rationale, but at that time nobody (we and other experts in the field) had any idea of the best amount of time to keep patients in prone position.

Third, we limited the study to 10 days simply because 1 wk seemed too short and 2 wks too long. Once again, the scientific rationale was lacking, just because there was nothing on which to base it.

However, that study definitely proved that in most patients the oxygenation sharply increased, that PCO<sub>2</sub> changes are associated with outcome in prone position, and that, in the way we performed the study, mortality was not affected.

At present we are conducting a new study involving adult patients in which the ventilator setting is controlled in both arms (prone and supine), according to the lung-protective strategy. The

prone position is maintained for at least 20 hrs/day, and most units use a special device for prone positioning (RotoProne, KCI Medical Products, San Antonio, TX). No 10-day limit is set.

Indeed, we agree with the authors about the limit of our previous study, which represented, however, a modest step toward better comprehension of the effects of prone position and its complications. To date, more than 100 patients have been enrolled in the ongoing study, and the first interim analysis will be performed on 140 patients. We will see. As always, we must be prepared for both positive and negative results, but at least another step forward in our knowledge will be accomplished.

The author is a member of the International Advisory Board of KCI Medical Products, San Antonio, TX.

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## REFERENCES

1. Gattinoni L, Vagginelli F, Carlesso E, et al: Decrease in PaCO<sub>2</sub> with prone position is pre-

dictive of improved outcome in acute respiratory distress syndrome. *Crit Care Med* 2003; 31:2727–2733

2. Gattinoni L, Tognoni G, Pesenti A, et al: Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001; 345:568–573
3. The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342:1301–1308
4. Valenza F, Guglielmi M, Maffioletti M, et al: Prone position delays the progression of ventilator-induced lung injury in rats: Does lung strain distribution play a role? *Crit Care Med* 2005; 33:361–367
5. Du HL, Yamada Y, Orii R, et al: Beneficial effects of the prone position on the incidence of barotrauma in oleic acid-induced lung injury under continuous positive pressure ventilation. *Acta Anaesthesiol Scand* 1997; 41:701–707
6. Broccard A, Shapiro RS, Schmitz LL, et al: Prone positioning attenuates and redistributes ventilator-induced lung injury in dogs. *Crit Care Med* 2000; 28:295–303
7. Nishimura M, Honda O, Tomiyama N, et al: Body position does not influence the location of ventilator-induced lung injury. *Intensive Care Med* 2000; 26:1664–1669

DOI: 10.1097/01.CCM.0000179034.85196.2F