Intensive Care Med (2010) 36:559–561
DOI 10.1007/s00134-009-1749-0

EDITORIAL

John J. Marini

Prone positioning for ARDS: defining the target

Received: 17 November 2009
Accepted: 18 November 2009
Published online: 4 February 2010

This editorial refers to the article available at:
doi:10.1007/s00134-009-1748-1.

J. J. Marini (✉)
University of Minnesota, Minneapolis/St. Paul, USA
e-mail: john.j.marini@healthpartners.com

Although variation of position is innate to healthy subjects, practitioners usually orient critically ill patients in a supine, semirecumbent posture for days to weeks, with only periodic, side-to-side repositioning through a relatively shallow 30–60° arc. Experimental data [1] and clinical observations [2–4] demonstrate physiologic benefit from prone positioning during acute lung injury (ALI), but recent large clinical trials have been unable to confirm survival benefit in diverse populations of patients labeled as having ALI/acute respiratory distress syndrome (ARDS) [5–7]. However, posttrial subgroup analyses hint that certain patient subgroups may indeed benefit from prone orientation. Severely ill patients, those experiencing improved CO_2 exchange, and those ventilated with large tidal volumes appear more likely to benefit than other members of the general cohort [5]. A superb meta-analysis of pooled data appears in this issue, focusing on those relative few with the worst oxygen exchange [8]. This analysis shows convincingly that, while proning cannot be recommended for all patients with acute lung injury, it does hold therapeutic value for some.

With the ascendance of evidence-based approaches to medical practice, clinicians have come to depend on randomized clinical trials (RCTs) to confirm or refute the value of therapeutic options used in medical practice. Although RCTs are of unquestioned benefit when realistic outcome variables and mechanistically sound trial design are applied to an appropriate population, numerous failed trials conducted in critical care settings demonstrate how vulnerable RCTs are to imprecise definitions, loose selection criteria, incomplete physiological understanding, and restricted availability of suitable subjects. In the wake of an RCT that fails to demonstrate outcome benefit, an intervention of life-saving value for a well-selected few may be shelved due to the lack of definitional precision and sufficient numbers.

Prone positioning (PP) provides an illuminating example. There is little question that PP can be expected to redistribute trans-lung forces, reduce the supine gradient of trans-lung pressure [2], recruit and stabilize dorsal lung units, relieve cardiac compression of lung tissue [4], and favor mouthward migration of retained airway secretions [3]. Such actions—on average—reliably improve oxygenation and airway drainage, particularly in the earlier stages of the injury process. However, currently we know neither the optimal daily duration of prone positioning nor when to initiate PP, nor once applied how many days to persist with it.

While many nursing units are now proficient in effecting PP when indicated [9], experience has shown that proning holds the potential for harm as well as good. Stringent precautions must be observed to prevent pressure ulcers and inadvertent misadventures with displaced or kinked tubes and catheters. Such problems are likely to parallel the duration of prone positioning. In theory, mobile and gravity-driven biofluids (infected secretions, inflammatory edema) migrating along the airway have the potential to propagate initially focal injury or infection from dorsal to more ventral zones [10].

Clues from the first large Italian trial of PP suggested that, with mortality reduction as the objective, only

restricted subsets of patients—those with the most severe disease and those who are recruitable—are good candidates [5, 11]. At first glance, the just published prospective follow-up RCT of PP conducted in ARDS patients with moderate to severe hypoxemia both disappoints in not showing overall benefit and affirms that potential benefits are most likely to accrue in those most severely affected [12]. The signal, while clearly present, is not overwhelmingly strong and would have required enrolment of many more patients for the trend to reach statistical significance. To achieve sufficiently large sample size in such a low-incidence disease state would have required additional years of data collection. Exactly *why* the signal from the severity-targeted study was not stronger is debatable, but one attractive possibility is that ventilator-induced lung injury (VILI) is strongly influenced by tidal volume and plateau pressure, which were more closely regulated in the prospective follow-up study. This lung-protective measure would dampen VILI risk and mask any benefit from proning maneuvers.

The novel contribution of the report by Sud et al. [8], which included studies regardless of proning duration and timing, is that the meta-analysis pools the collective published experience with patients with uncommonly severe disease and thereby helps define the subpopulation likely to benefit from an inconsistently life-saving intervention. Even severe hypoxemia, however, may itself be too inclusive a category to identify those most amenable to PP. The key to survival benefit may not be improved oxygen exchange—which occurs in most proned subjects and can be achieved by redistributing perfusion without increasing the number of functional lung units or relieving stress and strain. As suggested by Gattinoni's earlier analysis [11], recruitment may be the characteristic that determines PP's value, and "recruitable" patients are only a subset of those with severe hypoxemia. Quantitating recruitment at the bedside remains elusive in today's medical practice, but techniques that are just now coming on line, such as electrical impedance tomography (EIT) and gas dilution functional residual capacity (FRC), raise hopes for better precision and logistical feasibility.

Failed RCTs do not invalidate PP as a tool for ARDS management. The work by Sud et al. [8] clearly demonstrates that PP can be life-saving if the patients are well selected and the timing of the intervention is appropriate. How then to best utilize this tool, and in whom? In the absence of unassailable RCT guidance, there are no absolute mandates or prohibitions; the decision to implement PP remains a matter of individual judgment, tempered by empiricism. My own approach is as follows: Unless otherwise contraindicated, an empirical trial of proning should be attempted in those receiving ventilatory support whose severely impaired oxygenation fails to respond to usual measures, including sedation, recruiting maneuvers, and high positive end-expiratory pressure (PEEP). Because misadventures may arise during PP, proning should be limited to those with severe ARDS (as indicated by PaO_2/FiO_2 <100 mmHg) who show convincingly positive recruiting responses within a few hours of being turned. Even when successful, PP is continued no longer than 3–4 days, or until dramatic improvement in the underlying process is documented. Though PaO_2 may adequately classify disease severity, $PaCO_2$ better tracks gas exchange efficiency and perhaps better reflects the recruitment that appears to be central to PP benefit [11]. Recruiting maneuvers are employed after PP, both for their potential to reopen refractory units as well as to set the appropriate level of PEEP. In my view, proning clearly is not to be used in every patient with acute lung injury, but remains a valuable, even life-saving, option for those most likely to succumb to this devastating problem.

References

1. Broccard AF, Shapiro RS, Schmitz LL, Ravenscraft SA, Marini JJ (1997) Influence of prone position on the extent and distribution of lung injury in a high tidal volume oleic acid model of acute respiratory distress syndrome. Crit Care Med 25:16–27
2. Pelosi P, Brazzi L, Gattinoni L (2002) Prone position in acute respiratory distress syndrome. Eur Respir J 20:1017–1028
3. Gillart T, Bazin JE, Guelon D, Constantin JM, Mansoor O, Conio N, Schoeffler P (2000) Effect of bronchial drainage on the improvement in gas exchange observed in ventral decubitus in ARDS. Ann Fr Anesth Reanim 19:156–163
4. Albert RK, Hubmayr RD (2000) The prone position eliminates compression of the lungs by the heart. Am J Respir Crit Care Med 161:1660–1665
5. Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, Malacrida R, Di Giulio P, Fumagalli R, Pelosi P, Brazzi L, Latini R, Prone-Supine Study Group (2001) Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 345:568–573
6. Guerin C, Gaillard S, Lemasson S, Ayzac L, Girard R, Beuret P, Palmier B, Le QV, Sirodot M, Rosselli S, Cadiergue V, Sainty JM, Barbe P, Combourieu E, Debatty D, Rouffineau J, Ezingeard E, Millet O, Guelon D, Rodriguez L, Martin O, Renault A, Sibille JP, Kaidomar M (2004) Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. JAMA 292:2379–2387

7. Mancebo J, Fernández R, Blanch L, Rialp G, Gordo F, Ferrer M, Rodríguez F, Garro P, Ricart P, Vallverdú I, Gich I, Castaño J, Saura P, Domínguez G, Bonet A, Albert RK (2006) A multicenter trial of prolonged prone ventilation in severe acute respiratory distress syndrome. Am J Respir Crit Care Med 173:1233–1239
8. Sud S, Friedrich JO, Taccone P, Polli F, Adhikari NK, Latini R, Pesenti A, Guerin C, Mancebo J, Curley MA, Fernandez R, Chan M-C, Beuret P, Voggenreiter G, Sud M, Tognoni G, Gattinoni L (2010) Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: Systematic review and meta-analysis. Intensive Care Med. doi: 10.1007/s00134-009-1748-1
9. Messerole E, Peine P, Wittkopp S, Marini JJ, Albert RK (2002) The pragmatics of prone positioning. Am J Respir Crit Care Med 165:1359–1363
10. Marini JJ, Gattinoni L (2008) Propagation prevention: a complementary mechanism for lung protective ventilation in ARDS. Crit Care Med 36:3252–3258
11. Gattinoni L, Vagginelli F, Carlesso E, Taccone P, Conte V, Chiumello D, Valenza F, Caironi P, Pesenti A, Prone-Supine Study Group (2003) Decrease in $PaCO_2$ with prone position is predictive of improved outcome in acute respiratory distress syndrome. Crit Care Med 31:2727–2733
12. Taccone P, Pesenti A, Latini R, Polli F, Vagginelli F, Mietto C, Caspani L, Raimondi F, Bordone G, Iapichino G, Mancebo J, Guérin C, Ayzac L, Blanch L, Fumagalli R, Tognoni G, Gattinoni L, Prone-Supine II Study Group (2009) Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. JAMA 302:1977–1984