

## Commentary

# Recently published papers: The message is clear – start early?

Mike Spivey<sup>1</sup> and Jonathan Ball<sup>2</sup>

<sup>1</sup>Registrar, ICU, Liverpool Hospital, Sydney, Australia

<sup>2</sup>Senior Registrar, ICU, Liverpool Hospital, Sydney, Australia

Correspondence: Jonathan Ball, [jball@sghms.ac.uk](mailto:jball@sghms.ac.uk)

Published online: 6 September 2004

This article is online at <http://ccforum.com/content/8/5/303>

© 2004 BioMed Central Ltd

*Critical Care* 2004, **8**:303-305 (DOI 10.1186/cc2957)

### Abstract

Recent papers discussed include a positive trial of early tracheostomy, two negative studies of targeted noninvasive ventilation, the long awaited results of the high versus low positive end-expiratory pressure Acute Respiratory Distress Syndrome Clinical Trial Network trial and a simple but illuminating study into prognostic markers and end-points of resuscitation.

**Keywords** ARDS, lactate, noninvasive ventilation, percutaneous tracheostomy

“When one admits that nothing is certain one must, I think, also admit that some things are more nearly certain than others”

Bertrand Russell

From “*Am I An Atheist Or An Agnostic?*”, 1947  
English author, mathematician and philosopher  
(1872–1970)

Intuitively, early definite therapy should produce outcome advantages. However, providing evidence to support this has been limited. Several recent studies, discussed below, add credence to this idea.

### Early tracheostomy saves lives

The detrimental consequences of long-term oral (and nasal) intubation in critically ill patients are well established. The clinicians' dilemma has always been one of deciding which patients will benefit from tracheostomy and, crucially, when to perform it. August saw the publication of a well designed trial by Rumbak and colleagues [1] that addressed this issue in severely ill patients. They randomly assigned 120 patients who had required intubation for respiratory failure either to early percutaneous tracheostomy (within 48 hours) or to delayed tracheostomy (at 14–16 days). Inclusion criteria were strictly defined; in particular, patients had to have an Acute Physiology and Chronic Health Evaluation (APACHE)

II score above 25 and be projected to require ventilatory support for longer than 14 days.

The results were dramatic. The authors demonstrated a significant reduction in mortality (31.7% versus 61.7%), incidence of ventilator-associated pneumonia (5% versus 25%), days spent on ventilatory support (8 versus 17) and days sedated (3 versus 14) in the early tracheostomy group. There was also a reduction in days spent in the intensive care unit (ICU; 5 versus 16), but this was heavily influenced by the ability to discharge patients to a weaning unit. The Kaplan–Meier survival curve is striking, with the mortality benefit emerging between days 17 and 22. The authors hypothesized that the benefits of early tracheostomy are the direct result of the reduction in ventilator-associated pneumonia, which in turn resulted from cessation of sedation at day 3, a reduction in time spent on ventilatory support and the ability to change tracheostomy inner cannulae on a daily basis, thereby preventing the accumulation of infected secretions in the tube. The authors conceded that the mortality in the delayed tracheostomy group was significantly higher than that predicted by the APACHE II scores (61.7% versus 50%) and caution against extrapolating these results to a general ICU population. However, it would appear that this study provides compelling evidence to consider early tracheostomy in those patients who seem likely to require prolonged ventilatory support.

## Noninvasive ventilation fails to improve outcome

Noninvasive ventilation (NIV) has become an established intervention, with advocates/enthusiasts employing this technique in a wide spectrum of patients with respiratory failure. In the 1990s there was flurry of positive trials of NIV versus intubation and intermittent positive pressure ventilation (IPPV), especially as a primary intervention in acute on chronic, hypercapnic respiratory failure. Since then, however, there have been a series of negative trials as investigators have extended the indications. Further negative evidence has emerged from two recent studies.

In the first, Esteban and colleagues [2] undertook a randomized, multicentre trial of NIV versus standard medical therapy in patients who were electively extubated following at least 48 hours of mechanical ventilation and who then subsequently developed respiratory failure within the next 48 hours. Of 980 patients enrolled, 221 patients developed respiratory failure and were then randomized to either NIV or standard medical therapy. The primary outcome measures were ICU mortality and need for reintubation. The trial was stopped at an interim analysis because of a statistically significant increase in mortality in the NIV group (25% versus 14%). The increased mortality came predominantly from the subgroup of patients who required reintubation (38% versus 11%). There was no difference in the rates of reintubation, but the interval between the development of respiratory failure and reintubation was significantly longer in the NIV group (12 versus 2.5 hours). The trial was well designed and, although ICU mortality is arguably a poor outcome measure, this trial suggests that NIV delays rather than prevents reintubation and that reintubation is associated with a worse outcome. Yet again, early definitive intervention appears to offer patients the best chance of survival.

In the second trial, Squadrone and colleagues [3] compared a trial of NIV in 64 chronic obstructive pulmonary disease patients with acute severe hypercapnic respiratory failure ( $\text{pH} < 7.25$  and arterial carbon dioxide tension  $> 70$  torr) with historical case control individuals who received IPPV. The authors introduced their study by quoting recent survey findings that, despite grade A evidence, NIV is under-utilized in chronic obstructive pulmonary disease patients with acute exacerbations. They conceded that there are limitations in their study design but argued that their observations provide a useful insight into the outcomes of such patients. Surprisingly, the pre-ICU hospital stay averaged 5–6 days in both groups. NIV failed in 62.5% of patients who went on to receive IPPV after an average interval of 7.5 hours. The delay in intubation, in contrast to the study by Esteban and coworkers, did not appear to have an adverse effect on outcome. As one would expect, those patients who avoided intubation had a better outcome. The authors concluded that a trial of NIV should be undertaken in such patients, albeit a high proportion will fail, because they detected a trend toward better outcomes in the NIV cohort.

As with other novel ICU interventions, initial enthusiasm for NIV appears to have resulted in overestimation of its efficacy. It often fails, and such failure is associated with a worse prognosis. However, when successful it offers significant advantages. Predicting failure is near impossible and the effects of delaying definitive intervention, at best, remain unclear. Although widely speculative, it is tempting to ask what effect early tracheostomy would have in the population who fail NIV and appear likely to require more than 7–10 days of ventilatory support.

## No to more PEEP

Once again the Acute Respiratory Distress Syndrome Clinical Trial Network has produced some more data to help in the quest for an optimal ventilatory strategy in the treatment of acute respiratory distress syndrome. Brower and coworkers [4] looked at the outcome effects of employing high versus low positive end-expiratory pressure (PEEP) levels in addition to a low tidal volume (6 ml/kg) strategy. The trial was abandoned after the second interim analysis because of no demonstrable benefit from higher PEEP levels. The trial had recruited 549 patients who were randomly assigned to receive predetermined combinations of PEEP and fractional inspired oxygen. The higher level group received a mean PEEP of  $13.2 \pm 3.5$  cmH<sub>2</sub>O and the lower level group  $8.3 \pm 3.2$  cmH<sub>2</sub>O. The primary outcome measure was in-hospital 60-day mortality. Not only was there no difference in 60-day mortality, but also there was no difference in ventilator-free days, ICU-free days, or organ failure-free days.

## Lactate clearance

From the emergency department in Detroit, home of early goal-directed therapy [5], comes another simple and elegant study of the art of resuscitation. Nguyen and colleagues [6] conducted an observational study to investigate the utility of estimating percentage lactate clearance in the first 6 hours of sepsis treatment. Statistical analysis led the authors to suggest that a 10% 6-hour lactate clearance is a useful prognostic indicator. Although otherwise well matched by a whole host of physiological measures, patients who failed to clear more than 10% of their lactate had significantly worse outcomes. Although not surprising, the authors suggested that such a measure may prove useful as an end-point of resuscitation.

## Other talking points

In a statistically challenging paper, a multinational group of intensivists investigated the link between diuretic use and mortality in acute renal failure [7]. The conclusion appears to be that there is no effect on mortality when diuretics are used in the management of acute renal failure and that a trial to determine efficacy is warranted.

The transmission of Creutzfeldt–Jakob disease in blood products and via surgical instruments has been a major

concern, especially in the UK. Three articles and an accompanying editorial in the *Lancet* discuss the latest research in the field and outline the benefits of a scientifically guided, pragmatic approach to these issues [8].

Finally, we were surprised to read an editorial in *JAMA* in which the author argued the case for open access visiting in ICUs [9]. Open access has been the policy on all units in both the UK and Australia in which we have worked, and we were unaware that the issue was even considered contentious. With that report coming from the USA, the cultural divide in critical care is all the more surprising. To all those practising in units with restricted visiting, we would encourage you to read and discuss this editorial.

## Conclusion

Let the friends and family in, consider lactate clearance and early tracheostomy but use NIV with care.

## Competing interests

The authors declare that they have no competing interests.

## References

1. Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB: **A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients.** *Crit Care Med* 2004, **32**:1689-1694.
2. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguia C, Gonzalez M, Epstein SK, Hill NS, Nava S, Soares MA, *et al.*: **Non-invasive positive-pressure ventilation for respiratory failure after extubation.** *N Engl J Med* 2004, **350**:2452-2460.
3. Squadrone E, Frigerio P, Fogliati C, Gregoretto C, Conti G, Antonelli M, Costa R, Baiardi P, Navalesi P: **Noninvasive vs invasive ventilation in COPD patients with severe acute respiratory failure deemed to require ventilatory assistance.** *Intensive Care Med* 2004, **30**:1303-1310.
4. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, Schoenfeld D, Thompson BT: **Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome.** *N Engl J Med* 2004, **351**:327-336.
5. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M, the Early Goal-Directed Therapy Collaborative Group: **Early goal-directed therapy in the treatment of severe sepsis and septic shock.** *N Engl J Med* 2001, **345**:1368-1377.
6. Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, Tomlanovich MC: **Early lactate clearance is associated with improved outcome in severe sepsis and septic shock.** *Crit Care Med* 2004, **32**:1637-1642.
7. Uchino S, Doig GS, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Nacendo E, Gibney N, *et al.*: **Diuretics and mortality in acute renal failure.** *Crit Care Med* 2004, **32**:1669-1677.
8. Wilson K, Ricketts MN: **Transfusion transmission of vCJD: a crisis avoided?** *Lancet* 2004, **364**:477-479.
9. Berwick DM, Kotagal M: **Restricted visiting hours in ICUs: time to change.** *JAMA* 2004, **292**:736-737.