September 2011 Critical Care Journal Club

Levy MM, and colleagues. Association between Critical Care physician management and patient mortality in the intensive care unit. Annals of Internal Medicine 2008;148:801.

I picked this "oldy" because we have reviewed several large non-randomized observation studies over the past several months, and I thought reviewing this study might encourage more discussion regarding critical appraisal of such studies.

Levy's study was a cohort study that included data on 101, 832 patients from 123 ICUs. The aim was to quantitate the mortality benefit of care provided by a board certified intensivist. The Simplified Acute Physiology score (SAPS) II was used to quantitate severity of illness, and calculate standardized mortality ratios. Logistic regression and propensity scoring were used to adjust for the tendency to refer sicker patients to intensivist care.

The results reported in this study were confusing, because the data was fractionated into numerous subgroup analyses. However, it could be best summarized by observing that the standardized mortality ratio for patients who received intensivist-directed care in ICUs predominantly managed by intensivists was 1.09 (95% CI 1.05-1.13). Patients who did not receive intensivist-directed care, in institutions in which intensivists were involved <5% of the time, had a superior standardized mortality ratio of 0.91 (95% CI 0.88-0.94). Patient's receiving intensivist-directed care were sicker, but even after statistical adjustment for severity of illness, the OR for death was 1.40 ($p<0.001$) if an intensivist provided care.

An unbiased critical appraisal of this paper would have to consider the hypothesis that this result is valid – that intensivist involvement actually *increases* mortality. However, I am going to set that possibility aside, and proceed on the assumption that the training we receive as intensivists is of some mortality benefit to our patients. With this in mind, the question arises: How can an apparently well-designed cohort study, with data on over 100,000 patients, yield what appears likely to be a false result?

Several good explanations were put forth, and a general review of critical appraisal of cohort studies was referenced (Grimes DA et al. Cohort Studies. Lancet 2002;359:341). The main threats to the validity of cohort studies are bias and confounding. An example of bias in this study is that sicker patients were systematically referred to

intensivist care. Confounding is a similar concept in which there is no bias per se, but the natural association between variables leads to spurious associations. It's a little harder to conceptualize than bias, but suppose it was true that mortality was increased with each additional consultant that took care of a patient, independent from the patient's severity of illness. This could for instance be due to lack of coordination of patient care. In this case, consultation of an intensivist (along with all the other specialists) could be associated with increased mortality even though it had nothing to do with the care provided by the intensivists themselves.

All the sophisticated statistics used in this study were meant to try to reduce the effects of bias and confounding. The reason they don't always work, is that we have to be able to identify and measure *all* the determinants of mortality in order to optimally adjust for them. This just isn't possible. One look at SAPS II, Apache IV, or any of the other available severity adjustment tools should suggest to a critical thinker that much more must be involved in a patient's propensity to perish or survive than what is contained therein.

This essential flaw in observational studies is probably easiest to remember when the result doesn't make sense to us, as in this case. But equal caution should be exercised when the result makes sense – especially if we are biased in favor of the result *a priori*. Randomization is the key to handling bias and confounding, since even unrecognized sources will generally be effectively nullified by this approach. We don't have an RCT to guide every bedside decision, but I think that decisions to standardize care ought to be based on well-designed randomized controlled trials. This should help us avoid the situation in which we lock-step clinicians into providing useless or potentially harmful care.

Next, we looked at two current articles from Chest:

Marini JJ. Point: Is Pressure Assist-Control Preferred Over Volume Assist-Control Mode for Lung Protective Ventilation in Patients With ARDS? Yes. *Chest* August 2011 140:2 286-290.

and MacIntyre N. Counterpoint: Is Pressure Assist-Control Preferred Over Volume Assist-Control Mode for Lung Protective Ventilation in Patients With ARDS? No. *Chest* August 2011 140:2 290-292.

We felt from the onset that this debate likely was not going to yield a clear answer (and suspected that Drs. Marini and MacIntyre probably could easily have supported either side of the argument). There are

no randomized controlled trials that demonstrate the clinical benefit of any particular mode of ventilation over another.

There were several interesting aspects of the discussion we had over these articles. The essence of the debate revolved about whether strain (pressure) or stretch (volume) was more injurious to the lung. Proponents of the strain theory support pressure control – proponents of stretch theory, volume control. This debate has been going on for decades, and was clearly evident in the classic low-tidal-volume ARDSnet trial. The title of this trial suggested that the authors felt volume was the more important variable, yet plateau pressure was also strictly limited. I'm still not sure which of these closely related variables is more important, but it's worthwhile to know that some newer ventilator features minimize the clinical difference. For instance, the volume-controlled mode of controlled mechanical ventilation (CMV) on our Drager ventilators can provide the patient with variable flow rates and a flat pressure waveform. These allow volume controlled ventilation to mimic the advantages that Marini attributes to pressure controlled ventilation. Whichever mode you use, the lessons from ARDSnet should be remembered – limitation of tidal volume *and* plateau pressure should both be carefully observed.

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