Commentary

Variation in sepsis care: a wake-up call

Mary E Hartman[1] and Derek C Angus[2]

[1]Research Fellow, CRISMA (Clinical Research, Investigation and Systems Modeling of Acute Illness) Laboratory, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
[2]Vice Chair for Research, Department of Critical Care Medicine, and Director, CRISMA (Clinical Research, Investigation and Systems Modeling of Acute Illness) Laboratory, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Correspondence: Mary E Hartman, hartme@ccm.upmc.edu

Published online: 1 May 2003 *Critical Care* 2003, **7**:211-213 (DOI 10.1186/cc2191)
This article is online at http://ccforum.com/content/7/3/211

Abstract

There is important variation in the care of critically ill patients. While some of this variability is appropriate, and represents individually titrated care, residual variation indicates over- and under-use of precious resources and is clearly concerning. Recent advances in critical care medicine provide "road maps" to standardize care and use evidence-based medicine to improve patient outcomes. Knowledge about which therapies to use, and under what circumstances to use them, could form a basis for measuring the consistency and quality of our care processes. These simple process measures can be easily incorporated into daily rounds and serve to inform on the quality of our care.

Keywords critical care, evidence-based medicine, outcome, process assessment, variation

In this issue Yu and coworkers [1] present data on variation in treatment patterns for severe sepsis using a large cohort of patients at eight academic medical centers in the USA. This cohort was described previously by the same authors in a landmark paper exploring the epidemiology of severe sepsis [2]. Their new findings are that treatment patterns varied widely across the eight hospitals, despite the fact that the hospitals were all teaching centers and all in the same country. Although those investigators explored associations between the use of several elements of care and subsequent hospital mortality, the only significant correlation was that of delayed antibiotic use with higher mortality – a finding reported by others [3,4]. This study gives us cause to ponder a few issues. First, should we be surprised by this variation? Second, should we be surprised that the variation was generally not associated with differences in outcome? Third, do we think this observation still holds? Finally, how can we use this information going forward?

Variation in the provision of care is well described [5–8]. Variation due to differences in patient case-mix can be appropriate and represents individually titrated care. Variation not explained by differences in case-mix is more concerning, and suggests that some patients are receiving more care than necessary whereas others receive less. Yu and coworkers report significant 'residual' variation not obviously explained by differences in case-mix. One might argue over the rigor with which one can satisfactorily control for case-mix differences, but we generally concur with the authors' findings. Whether this variation matters depends on the effect on outcomes.

There are two broad sets of outcomes – economic and patient-centered. Generally, more intense care is more expensive. Although there are instances when 'more care sooner' may offset downstream costs, as suggested recently with early-goal directed therapy [9], greater use of interventions usually drives health care costs up. This is an unwanted outcome unless patient-centered outcomes improve as a consequence. That Yu and coworkers did not show differences in patient-centered outcomes can be explained in several ways. First, the interventions do not affect outcome. Certainly, there is mounting evidence that some of the studied interventions, such as application of the pulmonary artery catheter, have very small effects at best [10,11]. However, this explanation is insufficient because it is likely that some of the interventions, given their potent physiologic effects, have some influence on outcome. Second, any beneficial effects are offset by unwanted side effects. For example, better titration of care secondary to information gained by pulmonary artery catheter use may be offset by complications of catheter use, such as pulmonary

embolism [11] or bloodstream infection [12,13]. Third, although interventions have potential benefits, failure to administer them at the right time to the right patients obscures any benefit. For example, aggressive resuscitation in the early phase of severe illness improves patient outcomes, as with early goal-directed therapy [9], but can cause harm if used later in the course of illness [14]. Fourth, the simultaneous study of multiple interventions, used variably in an uncontrolled manner, precludes isolation of treatment effects, given the constraints of sample size and analytic techniques in this particular study. Thus, it appears there is variation that is unexplained by differences in case-mix and associated with increased costs, yet there is no obvious gain in patient-centered outcome.

Might this observation still hold today? The study was conducted in 1994. In 1994, we knew how to control infection but other elements of care were highly empiric. At that time there was no knowledge of the 'appropriate' rate of use of many modalities. Today, we have much better evidence to direct care of critically ill patients [9,15–20]. For example, sepsis care involves control of infection, organ support, and manipulation of the sepsis cascade. Control of infection is achieved through prompt administration of antibiotics and surgical drainage when appropriate. Organ support is more complicated, but better understood when broken down into its component parts. Let us consider the case of 'respiratory organ' support. Treatment for respiratory failure includes a trial of noninvasive positive pressure ventilation before intubation [21]. Once intubated, patients should have spontaneous breathing trials [22], daily awakening [19], continuous or frequent subglottic suctioning [23], H_2 blockade [24], and semirecumbent positioning [18]. If the patient develops acute respiratory distress syndrome, then the tidal volume should be lowered to 6 ml/kg [16]. Similarly, cardiovascular support includes early-goal directed therapy [9], metabolic support includes tight insulin control [20], and renal support includes avoidance of low-dose dopamine [25]. Finally, we can now manipulate the sepsis cascade with drotrecogin alpha (activated) [15] and steroids [26].

The problem is that it is unclear whether we are adopting this evidence into practice. Several recent studies have demonstrated that publication of trial results have no impact on physician practice, even within the institutions that one would think are most likely to incorporate new evidence, for example teaching hospitals and hospitals that participate in trials [27–30]. In addition, of course, there is a plethora of information from other fields about the slow diffusion of evidence to the bedside. For example, despite strong clinical evidence of the benefits of thrombolytic therapy for myocardial infarction, it was only slowly accepted into routine cardiology practice [31]. Thus, the findings of Yu and coworkers may well still hold today, despite a far clearer roadmap for optimal sepsis care.

So, what can we do going forward? By measuring rates of modality use, Yu and colleagues are describing processes. At the time of the study, we did not know which processes were best for many elements of care. That has changed. Now that we know what use is 'appropriate', we could measure compliance with these processes to inform on the quality of care. Analogous to measuring β-blocker use after myocardial infarction, we could operationalize simple measures to reflect the consistency and quality of our organ support and sepsis management. For example, each day a given patient is on a ventilator, the following checklist could be reviewed: has the patient had a spontaneous breathing trial today?; has sedation been interrupted to allow full wakening?; and is the head of the bed elevated? A rate of 'appropriate ventilator management' is thus easily calculated by dividing the number of 'yes' days by the total number of ventilator days.

There are a number of advantages of process measures such as these [32]. One of the most relevant is their simplicity. In contrast, outcome measures, such as standardized mortality ratios, require far greater resources and are fraught with controversy. In part because of their simplicity, the Joint Commission on Accreditation of Healthcare Organizations (an independent, not-for-profit organization that sets the standards by which health care quality is measured in the USA) will begin to implement process measure based evaluations of hospitals as soon as 2004 (Pronovost P, personal communication, April 2003). However, process measures need not be confined to the 'judges' of our care. We can even adapt these as simple checklists for our rounds ourselves! Asking the resident each morning, 'has the patient had a spontaneous breathing trial in the past 24 hours?' and so on, is a big step forward in increasing process measurement and decreasing variability.

In conclusion, Yu and coworkers have held a mirror to our practice. They point out the variability that, given the literature from other fields, we might even have predicted. The challenge is not to accept this information passively. With emerging evidence of the 'right' way to provide critical care, we can hope that a mirror to our future care will show us less variability and greater quality of care.

Competing interests

None declared.

Acknowledgements

MEH is supported by NIH/NICHD (NIH 5-T32 HD40686). DCA is supported by AHRQ/NHLBI (R01 HS/HL11620-02), NHLBI (R01 HL69991-01), NIGMS (R01 GM61992-01) and the Robert Wood Johnson Foundation.

References

1. Yu DT, Black E, Sands KE, Schwartz JS, Hibberd PL, Graman PS, Lanken PN, Kahn KL, Snydman DR, Parsonnet J, Moore R, Platt R, Bates DW, for the Academic Medical Center Consortium Sepsis Project Working Group: **Severe sepsis: variation in resource and therapeutic modality use among academic centers.** *Crit Care* 2003, **7**:R24-R34.

2. Sands KE, Bates DW, Lanken PN, Graman PS, Hibberd PL, Kahn KL, Parsonnet J, Panzer R, Orav EJ, Snydman DR: **Epidemiology of sepsis syndrome in 8 academic medical centers. Academic Medical Center Consortium Sepsis Project Working Group.** *JAMA* 1997, **278**:234-240.
3. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH: **Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia.** *Chest* 2002, **122**:262-268.
4. Kollef MH, Sherman G, Ward S, Fraser VJ: **Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients.** *Chest* 1999, **115**:462-474.
5. Tilford JM, Simpson PM, Yeh TS, Lensing S, Aitken ME, Green JW, Harr J, Fiser DH: **Variation in therapy and outcome for pediatric head trauma patients.** *Crit Care Med* 2001, **29**:1056-1061.
6. Bulger EM, Nathens AB, Rivara FP, Moore M, MacKenzie EJ, Jurkovich GJ: **Management of severe head injury: institutional variations in care and effect on outcome.** *Crit Care Med* 2002, **30**:1870-1876.
7. Jordan P, Hadcock W, Beaulieu C, Kamada S, Vomacka J, Garrett D, Frye L: **Decreasing process variation in the care of carotid endarterectomy patients.** *Top Health Inf Manage* 2001, **22**:24-34.
8. Lowers J, Gore MJ: **Reducing variation in care.** *Qual Lett Healthc Lead* 1999, **11**:2-7.
9. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; 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.
10. Connors AF Jr, Speroff T, Dawson NV, Thomas C, Harrell FE Jr, Wagner D, Desbiens N, Goldman L, Wu AW, Califf RM, Fulkerson WJ Jr, Vidaillet H, Broste S, Bellamy P, Lynn J, Knaus WA: **The effectiveness of right heart catheterization in the initial care of critically ill patients.** *JAMA* 1996, **276**:889-897.
11. Sandham JD, Hull RD, Brant RF, Knox L, Pineo GF, Doig CJ, Laporta DP, Viner S, Passerini L, Devitt H, Kirby A, Jacka M; Canadian Critical Care Clinical Trials Group: **A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients.** *N Engl J Med* 2003, **348**:5-14.
12. Kac G, Durain E, Amrein C, Herisson E, Fiemeyer A, Buu-Hoi A: **Colonization and infection of pulmonary artery catheter in cardiac surgery patients: epidemiology and multivariate analysis of risk factors.** *Crit Care Med* 2001, **29**:971-975.
13. Mermel LA, Maki DG: **Infectious complications of Swan-Ganz pulmonary artery catheters. Pathogenesis, epidemiology, prevention, and management.** *Am J Respir Crit Care Med* 1994, **149**:1020-1036.
14. Hayes MA, Timmins AC, Yau EHS, Palazzo M, Hinds CJ, Watson D: **Elevation of systemic oxygen delivery in the treatment of critically ill patients.** *N Engl J Med* 1994, **330**:1717-1722.
15. Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, Steingrub JS, Garber GE, Helterbrand JD, Ely EW, Fisher CJ Jr; Recombinant human protein C Worldwide Evaluation in Severe Sepsis (PROWESS) study group: **Efficacy and safety of recombinant human activated protein C for severe sepsis.** *N Engl J Med*, **344**:699-709.
16. The ARDS Network Authors for the ARDS 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.
17. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E: **A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group.** *N Engl J Med* 1999, **340**:409-417.
18. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M: **Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial.** *Lancet* 1999, **354**:1851-1858.
19. Kress JP, Pohlman AS, O'Connor MF, Hall JB: **Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation.** *N Engl J Med* 2000, **342**:1471-1477.
20. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: **Intensive insulin therapy in the critically ill patients.** *N Engl J Med* 2001, **345**:1359-1367.
21. Martin TJ, Hovis JD, Costantino JP, Bierman MI, Donahoe MP, Rogers RM, Kreit JW, Sciurba FC, Stiller RA, Sanders MH: **A randomized, prospective evaluation of noninvasive ventilation for acute respiratory failure.** *Am J Respir Crit Care Med* 2000, **161**: 807-813.
22. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, Johnson MM, Browder RW, Bowton DL, Haponik EF: **Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously.** *N Engl J Med* 1996, **335**: 1864-1869.
23. Valles J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, Fernandez R, Baigorri F, Mestre J: **Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia.** *Ann Intern Med* 1995, **122**:179-186.
24. Cook DJ, Reeve BK, Guyatt GH, Heyland DK, Griffith LE, Buckingham L, Tryba M: **Stress ulcer prophylaxis in critically ill patients. Resolving discordant meta-analyses.** *JAMA* 1996, **275**:308-314.
25. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group: **Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial.** *Lancet* 2000, **356**:2139-2143.
26. Bernard GR, Luce JM, Sprung CL, Rinaldo JE, Tate RM, Sibbald WJ, Kariman K, Higgins S, Bradley R, Metz CA, *et al.*: **High-dose corticosteroids in patients with the adult respiratory distress syndrome.** *N Engl J Med* 1987, **317**:1565-1570.
27. Weinert CR, Gross CR, Marinelli WA: **Impact of randomized trial results on acute lung injury ventilator therapy in teaching hospitals.** *Am J Respir Crit Care Med* 2003:in press.
28. Rubenfeld GD, Caldwell E, Hudson L: **Publications of study results does not increase use of lung protective ventilation in patients with acute lung injury [abstract].** *Am J Respir Crit Care Med* 2003, **163**:A295.
29. Majumdar SR, Chang WC, Armstrong PW: **Do the investigative sites that take part in a positive clinical trial translate that evidence into practice?** *Am J Med* 2002, **113**:140-145.
30. Lamas GA, Pfeffer MA, Hamm P, Wertheimer J, Rouleau JL, Braunwald E: **Do the results of randomized clinical trials of cardiovascular drugs influence medical practice? The SAVE Investigators.** *N Engl J Med* 1992, **327**:241-247.
31. Ketley D, Woods KL: **Impact of clinical trials on clinical practice: example of thrombolysis for acute myocardial infarction.** *Lancet* 1993, **342**:891-894.
32. Rotondi AJ, Sirio CA, Angus DC, Pinsky MR: **A new conceptual framework for ICU performance appraisal and improvement.** *J Crit Care* 2002, **17**:16-28.