Treatment algorithms and protocolized care

Alan H. Morris, MD

Purpose of review

Excess information in complex ICU environments exceeds human decision-making limits and likely contributes to unnecessary variation in clinical care, increasing the likelihood of clinical errors. I reviewed recent critical care clinical trials searching for information about the impact of protocol use on clinically pertinent outcomes.

Recent findings

Several recently published clinical trials illustrate the importance of distinguishing efficacy and effectiveness trials. One of these trials illustrates the danger of conducting effectiveness trials before the efficacy of an intervention is established. The trials also illustrate the importance of distinguishing guidelines and inadequately explicit protocols from adequately explicit protocols. Only adequately explicit protocols contain enough detail to lead different clinicians to the same decision when faced with the same clinical scenario.

Summary

Differences between guidelines and protocols are important. Guidelines lack detail and provide general guidance that requires clinicians to fill in many gaps. Computerized or paper-based protocols are detailed and, when used for complex clinical ICU problems, can generate patient-specific, evidence-based therapy instructions that can be carried out by different clinicians with almost no interclinician variability. Individualization of patient therapy can be preserved by these protocols when they are driven by individual patient data. Explicit decision-support tools (*eg*, guidelines and protocols) have favorable effects on clinician and patient outcomes and can reduce the variation in clinical practice. Guidelines and protocols that aid ICU decision makers should be more widely distributed.

Keywords

clinical trials, decision support, guidelines, protocols, research

Curr Opin Crit Care 9:236–240 © 2003 Lippincott Williams & Wilkins.

Pulmonary and Critical Care Divisions, Departments of Medicine, LDS Hospital and University of Utah School of Medicine, Salt Lake City, Utah, USA.

Supported by National Institutes of Health grants RO1-HL-36787 and NO1-HR-46062, Agency for Health Care Policy and Research grant HS 06594, the Deseret Foundation, the LDS Hospital, and Intermountain Health Care, Inc.

Correspondence to Alan H. Morris, MD, Pulmonary Division, LDS Hospital, Salt Lake City, UT 84143,USA; e-mail: ldamorri@ihc.com

Current Opinion in Critical Care 2003, 9:236–240

ISSN 1070–5295 © 2003 Lippincott Williams & Wilkins

Background

Guidelines versus protocols

Decision-support tools are intended to aid clinicians and to enable them to deliver evidence-based care consistently. Crucial to this effort is the application of decision support at the point of care (point of decision making). Several terms, including guidelines and protocols, are used to describe decision-support tools. The medical subject headings in Ovid® define guideline as "a systematic statement of policy rules or principles" and protocols as "precise and detailed plans for the study of a medical or biomedical problem and/or for a regimen of therapy." Guidelines are general statements or overviews of concepts that, like textbooks, provide little instruction about specific clinical decisions. In contrast, protocols (also called algorithms) are detailed and provide specific instructions for individual clinical decisions. Failure to make this distinction between guidelines and protocols is common [1] and fosters confusion. The claims that "protocols are meant as guides … as the general default management decision unless … clinician can justify a departure" [1] or "protocols should not represent strict rules but rather dynamic guidelines" [2] suggest a terminology use that is likely to mislead many readers and to foster confusion.

At their best, protocols capture the important rules of clinical judgment. Protocols are an extension of the common clinical care use of guidelines [3], such as critical paths and routine sets of orders, all of which are general efforts to standardize some aspect of clinical care [4]. Although a continuum exists from the general guideline to the detailed protocol, I divide the papers discussed into two categories: guidelines and protocols. Adequately explicit protocols, but not guidelines, have the attribute of eliciting the same decision from different clinicians. Protocols and guidelines complement and can enhance, but do not replace, the clinician decision maker. I restrict my discussion of decision-support tools to the use of guidelines and protocols in which clinicians always examine the decision-support tool output and make an explicit decision to accept or reject the general guideline recommendation or the specific protocol instruction. A recent review of guidelines and protocols in ICU care included many important publications but did not articulate the distinction between guidelines and protocols and, in particular, did not address the detail necessary to eliminate inappropriate interclinician variability [2]. Consequently, I discuss more recent publications with an emphasis on the difference between guidelines and protocols.

Protocol considerations

Although the favorable impact on clinically pertinent outcomes of guidelines and protocols is clearly established [2,5,6], much concern about threats to the physician's role exists and many emphasize the need to preserve physician judgment [1,7]. Some of this concern is justified because of external validity issues [8•]. The clinician must always establish the appropriateness of the protocol (*ie*, decide whether his or her patient belongs to the group for which the protocol rules were developed and in which the protocol was evaluated). For example, neurosurgical patients behave differently from medical ICU patients regarding predictors of successful endotracheal extubation. They are not appropriate candidates for a successful weaning protocol established for medical ICU patients [9]. The clinician always has the opportunity to judge whether the patient has changed and no longer belongs to the group for which the protocol was intended. This external validity–directed clinician judgment is appropriate. However, the common rejection of a validated protocol instruction because of a clinician's opinion (an opinion often not founded on evidence) is frequently inappropriate and can threaten the internal validity of clinical trials [8•]. This error is fostered by the well-recognized overconfidence of physicians in the correctness of their beliefs and opinions [10].

The tension between a detailed protocol, sometimes described as "rigid," and physician judgment, widely believed to be inherently flexible, is commonly used as a framework for discussion. This is, in my opinion, misdirected. A protocol that produces patient-specific instructions is not rigid but well tailored to individual patient needs. A better framework for discussion is provided by the tension between the need to capture the best reasoning for clinical decision making in the specific protocol rules and the need to preserve individualized (patient-specific) therapy.

An adequately explicit clinical method is one that contains adequate detail to generate specific instructions (patient-specific orders) without requiring judgments by the clinician. It produces the same instruction and elicits the same decision (for the same data) from multiple clinicians. Importantly, it preserves individualized (patient-specific) therapy [11,12] if the protocols are driven by patient data. In contrast to poor clinician compliance with guidelines [4,13–16], adequately explicit, detailed protocols that use complex rule sets have been associated with 90 to 95% clinician compliance in multicenter clinical trial settings [17–19].

Recent advances in guideline and protocol use in the intensive care unit

Guidelines

Spontaneous breathing

Spontaneous breathing during airway pressure release ventilation in traumatized patients at risk for acute respiratory distress syndrome appears to confer benefit in terms of less sedation, more favorable cardiac and pulmonary function, and shorter mechanical ventilation and ICU times [20]. The investigators applied rules to control a number of cointerventions in a nonblinded, randomized, controlled clinical trial of airway pressure release ventilation versus pressure-limited, time-cycled ventilation in 30 multiple trauma patients with injury severity scores greater than 40. They used lactated Ringer solution intravenously to maintain pulmonary artery balloon occlusion pressure between 14 and 18 mm Hg, 5% albumin to maintain serum albumin levels at more than 2 g/dL, packed erythrocytes to maintain hemoglobin at more than 10 g/dL, dobutamine when cardiac index decreased to less than 3 L/min/m^2, norepinephrine if systemic vascular resistance decreased to less than 600 dyn/s/cm^{-5} to keep systolic blood pressure at 70 to 80 mm Hg, and dopamine at 3 μg/kg/min if oliguria was present. No further details were provided, so these rules constitute guidelines with detail but do not qualify as protocols according to the medical subject heading definitions (see Background). Nevertheless, these rules reflect important consideration of nonexperimental cointerventions that could influence study outcomes, independent of the effect of the interventions (airway pressure release ventilation and time-cycled ventilation) being studied. They enhance credibility. Unfortunately, the mechanical effects of ventilatory support cannot be separated from other associated differences between the study groups, including the lesser sedation (and absence of paralysis) delivered to the airway pressure release ventilation group of patients. This diminishes credibility. The investigators reported not only more favorable cardiac and lung function, including increased lung compliance, but, importantly, also observed a significant decrease in the incidence of acute lung injury and acute respiratory distress syndrome (73% *vs* 100%) in the air way pressure release ventilation group. This is a most intriguing finding but in a small group of only 30 patients.

Spontaneous breathing was also evaluated in a prospective, randomized, nonblinded clinical trial and compared with pressure support ventilation in patients with chronic obstructive pulmonary disease requiring more than 15 days of mechanical ventilation in long-term weaning units [21]. After failing a "T-piece" trial of spontaneous breathing, 52 patients were randomly allocated to weaning protocols in a nonblinded trial with spontaneous breathing or with pressure support ventilation. The outcomes of the two concurrent study protocol groups were indistinguishable. Interestingly, the outcomes of both of the concurrent randomized study groups were more favorable than the outcome of historical control patients supported without protocols in the same long-term weaning units. The investigators concluded that a well-defined protocol, independent of the weaning mode, was associated with greater success than was uncontrolled

clinical practice. This conclusion was supported by others reviewing three studies of nonphysician healthcare provider–administered protocols [1]. Although historical control groups are notoriously unreliable, this improvement after protocol use may be due, at least in part, to nonspecific effects, such as the Hawthorne effect. It does, however, point to an important contribution of guidelines and protocols. The thought and effort required to develop and implement clinical protocols bring focus to the clinical care team, and the articulation of the rules for clinical decision making naturally clarifies clinical perceptions.

Pulmonary artery catheter use

An impressive multicenter study conducted by the Canadian Critical Care Clinical Trials Group revealed no difference in outcome of high-risk surgical patients managed with pulmonary artery catheters [22]. Patients at least 60 years old with class III or IV anesthesia risk were randomly assigned in a nonblinded, randomized, controlled clinical trial to a pulmonary artery catheter group or to a standard care (unregulated clinical practice with or without a central venous catheter) group. Crossover of patients was precluded. A predefined guideline was used. Treatment in the pulmonary artery catheter (intervention) group was directed at prospectively prioritized physiologic goals, without a detailed protocol for their achievement. The goals, in order of priority, were an oxygen delivery index of 550 to 600 mL/min/m^2, a cardiac index of 3.5 to 4.5 L/min/m^2, a pulmonary artery balloon occlusion pressure of 18 mm Hg, a heart rate less than 120 beats per minute, and a hematocrit greater than 27. This study is of interest because of what the investigators did and what they did not do. They managed to enlist the collaboration of a large number of surgical and other colleagues who agreed to abandon pulmonary artery catheters in those patients randomized to the standard care group. They adhered to this agreement with rare exceptions. This, in itself, is an admirable achievement. The results of this large trial support many previous publication results that have brought the common use of the pulmonary catheter in critical care patients into question. Use of the pulmonary artery catheter, it seems from these results, should be markedly curtailed. My interpretation of these results is tempered by the absence of a detailed protocol and the absence of a description of the care delivered to the control group. The investigators indicate in their background discussion that previous studies had methodologic problems, including noncompliance by physicians. Ironically, it is not possible to determine the compliance of the physicians in their report. They published only the highest values of physiologic variables. It is difficult to interpret the highest value of cardiac index, just as it would be difficult to interpret the highest value of arterial oxygen saturation. One satisfactory value would hardly produce an adequate basis for evaluating the adequacy of care. One should not assume a linear link between the highest value and clinically important outcomes. This admirable and important study, then, lacks both an adequately explicit protocol and a well-defined control group and does not allow assessment of physician compliance. The results are the best currently available for the evaluation of effectiveness of the pulmonary artery catheter. They support the conclusion that no clinically important advantage accompanies their use in elderly at-risk surgical patients. However, the results do not provide a definitive evaluation of its efficacy [8•]. Efficacy is often sought first in clinical investigations [8•]. Effectiveness studies must presume efficacy of the study intervention. Consequently, efficacy trials should, whenever possible, precede effectiveness trials. I am, therefore, not sure how to embrace these results for clinical decision making, despite the impressive accomplishment of this investigative group.

Management of blood glucose

van den Berghe *et al.* [23•] reported a significant decrease in mortality rate in primarily postoperative cardiothoracic surgery patients when their insulin treatment was directed at a lower blood sugar target than usual. This randomized, nonblinded, single-center, controlled clinical trial of 1548 surgical ICU patients used a bedside protocol executed by clinical nurses under the supervision of a study physician not responsible for the clinical care of the enrolled patients. One potential cointervention, nutrition, was instituted "according to a standardized schedule," but other factors were not described. The conventional insulin therapy group received insulin when blood sugar exceeded 215 mg/dL with titration to a target blood sugar of 180 to 200 mg/dL. The intensive insulin therapy group received insulin when blood sugar exceeded 110 mg/dL with titration to a blood sugar of 80 to 110 mg/dL. Almost all intensive insulin group patients (99%) received insulin versus only 39% of conventional insulin patients. Eight percent of conventional insulin patients died versus 4.6% of intensive insulin patients ($P < 0.04$). This striking improvement has stimulated much rethinking about blood glucose management, and many hospitals have or are adopting treatment plans with lower blood sugar targets. It is another example of a benefit after the application of a systematic care program with a predefined guideline. The internal validity [8•] of this trial is reduced by the nonblinded approach and by the absence of specific protocols for the interventions and for the many nonexperimental cointerventions that might influence the outcomes differentially. Among important questions left unanswered is the issue of generalizability (external validity). Whether the improved clinical outcome will be duplicated with general medical ICU patients remains to be explored.

Protocols

Emergency department management of septic shock

Rivers *et al.* [24••] provided impressive evidence of the beneficial effect of early goal-directed therapy for pa-

tients with septic shock when emergency department care was carried out according to a predefined protocol. Although the intravenous fluid administered to both groups was the same at 72 hours, the distribution of fluid administered in the first 6 hours compared with 7 to 72 hours differed significantly, with more fluid and packed erythrocytes administered to the early goal-directed protocol group during the first 6 hours. Their results led to the conclusion that timing of therapy is an important determinant of clinical outcome. The level of protocol detail was high, and the experimental method was more explicit than most. The experimental design was very strong, with clever blinding of the involved clinicians. Study clinicians assessed patients for inclusion and exclusion before they were aware of treatment assignment. The emergency department clinicians who cared for the patients during the initial 6 hours or more in the emergency department provided the treatment assignment. Patients were randomly allocated to standard care according to a published guideline [25] or to the explicit protocol for early goal-directed care. Thereafter, all patients were transferred to a critical care unit and treated by a critical care team that remained blinded to the emergency department treatment allocation. This maintenance of blinding for the remainder of care ensured uniform allocation of the many facets of care that could have differentially biased the outcomes of the two experimental groups. This enhanced internal validity [8•]. The enrollment of 91% of eligible patients enhanced external validity [8•]. This rigorous design makes the conclusions of Rivers *et al.* [24••] highly credible. The in-hospital mortality rate was 38% in the early goal-directed protocol group and 59% in the standard care group ($P = 0.009$). Remarkably, many of the changes in intermediate outcomes (*eg*, mean blood pressure, heart rate, arterial pH, hematocrit, central venous pressure) were small and would not likely catch a clinician's eye. The small changes in many of the intermediate outcome variables were associated with a large difference in survival. This is a reminder of the complexity of biologic systems and of their nonlinear character. Small, sometimes seemingly insignificant, changes can lead to large outcome differences. It is also a reminder of the limitation of mean values because small changes in mean values may belie the important changes in the distributions of these values in samples being compared [26].

Hyperbaric oxygen therapy for carbon monoxide poisoning

Weaver *et al.* [27••] established the value of hyperbaric oxygen therapy in a randomized, double-blinded trial with detailed explicit protocols for carbon monoxide–poisoned patients. This was the first randomized, double-blinded, single-center trial reported in hyperbaric medicine, an impressive accomplishment in itself. The trial results are important for several reasons. First, the preservation of cognitive function at 6 weeks is an important clinical outcome. Second, the preservation of cognitive function was maintained for 12 months, indicating a good chance of long-term outcome improvement. Third, Weaver *et al.* [27••] demonstrated that detailed, adequately explicit protocols could be applied in hyperbaric medicine. Their method could be reproduced by other interested clinicians. Hyperbaric medicine is a field in which many researchers would likely have declared such a scientifically rigorous clinical trial unachievable. The implications of these observations for critical care medicine are significant. If a rigorous clinical trial can be carried out in critically ill patients in a small monoplace hyperbaric chamber, it is probable that many difficult critical care issues are also amenable to rigorous evaluation.

Conclusions

These two groups of publications illustrate the value of systematic approaches to clinical care achieved through application of guidelines and protocols. Guidelines and protocols can reduce unnecessary variation in clinical practice and have produced favorable changes in patient outcomes. The differences between guidelines and protocols lead to different levels of experimental rigor and of credibility of study results. Adequately detailed protocols enhance randomized, controlled clinical trial rigor and increase the credibility of their results while preserving individualization of patient therapy. Guidelines and protocols that aid ICU decision makers should be more widely distributed.

Acknowledgments

The author thanks the medical, nursing, and respiratory therapy staffs of the Intermountain Respiratory Intensive Care Unit and of the Shock-Trauma/Intermountain Respiratory ICU and the Respiratory Care Department of the LDS Hospital for collaboration during the past 25 years. He recognizes the contributions of Drs. James Orme, Jr.; Terry Clemmer; Lindell Weaver; Frank Thomas; Tom East; Jane Wallace; George Thomsen; James Pearl; Nat Dean; Brad Rasmusson; Dean Sorenson; and Homer Warner, Sr. for collaboration in protocol development and implementation. Finally, he expresses his gratitude to Drs. Roberta Goldring, Robert Rogers, and Waldemar Johanson, who, through their vision and insight, enabled the decision-support effort that has engaged him and his colleagues for the past 18 years.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • Of special interest
- •• Of outstanding interest

1 MacIntyre NR, Cook DJ, Ely EW, et al.: Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. Chest 2001, 120(suppl):375S–396S.

2 Holcomb BW, Wheeler AP, Ely EW: New ways to reduce unnecessary variation and improve outcomes in the intensive care unit. Curr Opin Crit Care 2001, 7:304–311.

3 James B, Eddy D: CPI and practice guidelines. In Clinical Practice Improvement: A New Technology for Developing Cost-Effective Quality Health Care. Edited by Horn S, Hopkins D. New York: Faulker & Gray; 1994:127–140.

4 Redman B: Clinical practice guidelines as tools of public policy: conflicts of purpose, issues of autonomy, and justice. J Clin Ethics 1996, 5:303–309.

5 Hunt D, Haynes R, Hanna S, et al.: Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. JAMA 1998, 280:1339–1346.

6 Licker M, Khatchatourian G, Schweizer A, et al.: The impact of a cardioprotective protocol on the incidence of cardiac complications after aortic abdominal surgery. Anesth Analg 2002, 95:1525–1533.

7 Park G, Coursin D, Ely E, et al.: Commentary. Balancing sedation and analgesia in the critically ill. Crit Care Clin 2001, 17:1015–1027.

8 • Hebert PC, Cook DJ, Wells G, et al.: The design of randomized clinical trials in critically ill patients. Chest 2002, 121:1290–1300.
A clearly written review of the internal and external validity and of the efficacy and effectiveness of clinical trials. These concepts provide an important aid for interpreting clinical trial results in critical care.

9 Namen AM, Ely Wesley E, Tatter SB, et al.: Predictors of successful extubation in neurosurgical patients. Am J Respir Crit Care Med 2001, 163:658–664.

10 Friedman C, Gatti G, Elstein A, et al.: Are clinicians correct when they believe they are correct? Implications for medical decision support. Medinfo 2001, 10:454–458.

11 Morris A: Algorithm-based decision making. In Principles and Practice of Intensive Care Monitoring. Edited by Tobin MJ. New York: McGraw-Hill; 1998:1355–1381.

12 Morris A: Developing and implementing computerized protocols for standardization of clinical decisions. Ann Intern Med 2000, 132:373–383.

13 Safran C, Rind D, Davis R, et al.: Effects of a knowledge-based electronic patient record on adherence to practice guidelines. MD Comput 1996, 13:55–63.

14 Lobach D, Hammon W: Computerized decision support based on a clinical practice guideline improves compliance with care standards. Am J Med 1997, 102:89–98.

15 Nelson E, Splaine M, Batalden P, et al.: Building measurement and data collection into medical practice. Ann Intern Med 1998, 128:460–466.

16 McClave S, Sexton L, Spain D, et al.: Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. Crit Care Med 1999, 27:1252–1256.

17 East TD, Heermann LK, Bradshaw RL, et al.: Efficacy of computerized decision support for mechanical ventilation: results of a prospective multi-center randomized trial. Proc AMIA Symp 1999:251–255.

18 Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000, 342:1301–1308.

19 McKinley BA, Moore FA, Sailors RM, et al.: Computerized decision support for mechanical ventilation of trauma induced ARDS: results of a randomized clinical trial. J Trauma 2001, 50:415–425.

20 Putensen C, Zech S, Wrigge H, et al.: Long-term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. Am J Respir Crit Care Med 2001, 164:43–49.

21 Vitacca M, Vianello A, Colombo D, et al.: Comparison of two methods for weaning patients with chronic obstructive pulmonary disease requiring mechanical ventilation for more than 15 days. Am J Respir Crit Care Med 2001; 164:225–230.

22 • Sandham JD, Hull RD, Brant RF, et al.: A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med 2003, 348:5–14.
This impressive effectiveness clinical trial is an interesting illustration of the limitations of guideline use, undefined control groups, and nonblinded effectiveness trials conducted before efficacy has been established.

23 • van den Berghe G, Wouters P, Weekers F, et al.: Intensive insulin therapy in the critically ill patients. N Engl J Med 2001, 345:1359–1367.
This efficacy clinical trial is an interesting illustration of the limitations of guideline use and nonblinded trials.

24 •• Rivers E, Nguyen B, Havstad S, et al.: Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001, 345:1368–1377.
A rigorous clinical trial with good maintenance of blinding and use of detailed protocols. The results are credible and of importance. They identify the large impact of timing of interventions and set the stage for more attention to this variable in future clinical trials and clinical care.

25 Practice parameters for hemodynamic support of sepsis in adult patients in sepsis. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Crit Care Med 1999, 27:639–660.

26 Riou B, Landais P, Vivien B, et al.: Distribution of the probability of survival is a strategic issue for randomized trials in critically ill patients. Anesthesiology 2001, 95:56–63.

27 •• Weaver LK, Hopkins RO, Chan KJ, et al.: Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002, 347:1057–1067.
A double-blinded, randomized trial under challenging circumstances was completed successfully. The results provide credible evidence of efficacy of hyperbaric oxygen therapy in reducing cognitive deficits after carbon monoxide poisoning. This is the first double-blinded, randomized, single-center trial in hyperbaric medicine. It raises the bar for future studies in this and other critical care fields.