feeding (11, 12). Furthermore, both of those randomized studies failed to demonstrate improved clinical outcomes from increased adequacy of enteral nutrition, suggesting that even if postpyloric feeding did increase energy delivery, it is unlikely to result in better outcomes. Combined with previous trials, this study demonstrates that routine use of postpyloric feeding, even in patients who have demonstrated some intolerance to gastric feeding, does not improve outcomes or facilitate delivery of more nutrition. As such, the routine use of postpyloric feeding tubes is unnecessary, and our effort in caring for these critically ill patients is better focused on other aspects of critical care.

Todd W. Rice, MD, MSc
Division of Allergy, Pulmonary, and Critical Care Medicine
Vanderbilt University School of Medicine
Center for Lung Research
Nashville, TN

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Generation of early warnings with smart monitors: The future is all about getting back to the basics!*

Observing the differences between what people have been taught, what they know they should do, and what they actually do is a fascinating study in human behavior. In addition to compelling clinical evidence, implementation of best practices in medicine is dependent upon social, political, cognitive, and interpersonal dynamics that we are only beginning to understand (1–4). We know that "failure to rescue" of patients on the regular wards whose course has changed for the worse is an important and potentially reversible source of morbidity and mortality (5–7). We also know that vital sign changes are an important predictor of subsequent cardiac arrest, intensive care unit (ICU) admission, mortality, and length of stay (8, 9). Yet rapid response systems—systems designed to care for this population—continue to receive some pushback and are underutilized even when they are implemented. Educational efforts, warning criteria, and hospital-wide policies that should facilitate greater use of the rapid response systems have fallen short of guaranteeing a call for all patients at risk (10–12). In fact, a "failure to call" rate of approximately 30% is rather common (11).

Bringing at-risk patients to the attention of the rapid response system depends upon a successful completion of several tasks, and each has revealed itself as a point of failure. Vital signs must be collected at an interval sufficient to detect a significant change; they must also be obtained correctly and recorded and reported in a predictable manner.

*See also p. 2349.

Key Words: failure to rescue; informatics; monitoring; mortality; rapid response systems; vital signs

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Additional computation of multiparameter warning scores may be needed, sometimes requiring tables and scales to obtain weighted values and their incorporation into subsequent calculations. Finally, nurse concern or specific warning criteria must be understood and respected to the extent that calls to the rapid response team (RRT) are made. Currently, there are no evidence-based standards for recording of vitals on the wards (13). Acquisition of complete vitals is sometimes incomplete. Despite being the vital sign with the greatest ability to predict critical events (receiver operator curve = 0.72 in one series [14]), documentation of respiratory rate in high-risk patients was found to be as low as 30% and 15% in two different reports (15, 16). Multiparameter warning scores, which have a somewhat higher predictive ability, are prone to interobserver calculation error (17). Finally, as noted before, about a third of patients meeting criteria for critical care evaluation will not receive such in a timely manner.

What can be done to improve this state of affairs? In this issue of *Critical Care Medicine*, Bellomo et al (18) report on a multicenter trial of an automated system for collecting and processing patient data and its impact on rapid response activity and outcomes. Specifically, study sites began using a multifunctional monitor and display as part of its vital sign collecting routine. The device displays the acquired data, prompts the user for manual entry of respiratory rate and level of consciousness, and degree of overall concern. Based on these inputs, the software generates a numerical and color-augmented score in its display as well as a written suggestion for action (i.e., "no action needed," "increase intensity of monitoring"). The software is sufficiently flexible to generate the relevant output for risk assessments based on single vital sign parameters or multiple and weighted parameters. Therefore, no new scoring system, policy, or computational algorithm was introduced, just the ability to match newly acquired patient data to the action dictated by existing hospital policy and practice.

Study sites included five centers from the United States and five from northern Europe and Australia. Compared with the three-month control period, use of the monitor in the subsequent 3 months surprisingly did not increase the number of RRT calls, but seemed to catch patients earlier in their descent. Consistent with this, significant findings included fewer vital sign abnormalities at the time of RRT call and decreased use of arterial lines, vasopressors, and mechanical ventilation in patients transferred to higher levels of care. Despite lower use of ICU-type interventions, interventions such as suctioning, medication changes, and use of diagnostic studies during RRT calls increased three-fold during the study period. The adjusted odds of an RRT patient dying during the intervention period was reduced, and all who survived RRT calls were discharged alive. Use of the monitor to obtain a set of vitals signs also took significantly less time than prior methods.

Approximately 80% of the patients in the study came from the five U.S. hospitals. There were substantial differences between U.S. and non-U.S. centers, the most striking being a substantial increase (2%–22%) in the use of respiratory criteria for RRT calls in non-U.S. hospitals. Transfers to higher acuity wards were significantly more frequent in the United States, with admission to non-ICU high acuity wards accounting for the majority of this effect.

The trial also included a comprehensive analysis of administrative data at all sites for the prevalence of predefined morbidities and adverse events. Length of stay was shorter in U.S. hospitals, as was the use of the mechanical ventilation in the ICU. In contrast, use of mechanical ventilation was significantly higher in the non-U.S. centers.

Prior studies that generated warnings through the electronic medical record have demonstrated decreased length of stay and increased attendance of the RRT to patients identified by improved triggering (17). A single-center study demonstrated an increase in recording of respiratory rate from approximately 30% to over 90% at 1 yr following the introduction of a multiparameter warning system to the general wards (19).

The study at hand strove to make the findings of these prior studies more generalizable via its multicenter design. The study is to be commended for attempting to find a signal across a wide and diverse landscape of participating hospitals by careful recording of diagnostic codes, type of admission, hospital length of stay, and condition on discharge. However, with great heterogeneity in structure and utilization and function of ICU resources amongst U.S. hospitals and non-U.S. hospitals and within these groups, the multicenter design may have left the trial underpowered to achieve its intended scientific impact.

Bellomo et al are on target in pointing out how the manual entry of respiratory rate serves as a forcing function for the collection of this data. It was proposed—but not directly demonstrated—that improved compliance with respiratory rate measurement was in part responsible for this effect. Likewise, the connection between the use of respiratory triggers and the changes in frequency of patients requiring mechanical ventilation in the non-U.S. ICUs could not be established. Given the potentially high predictive value of respiratory rate on critical events, it would have also been interesting to see how collection and reporting behavior (i.e., deviation from the value 20 in the latter) changed with the intervention. It is certainly reasonable to assume that the new analytic system eliminated some of the behavioral and interpersonal barriers to summoning the RRT, although it is not clear at which stage this occurred. Future work with this type of system may benefit from integration with larger data repositories to assess the relationship between values measured, potential RRT candidates, actual calls and outcomes, and over longer time periods.

A growing number of studies have demonstrated a reciprocal relationship between cardiac arrests and rapid response calls (20, 21). This study shows that set of deteriorating patients can be identified earlier in their descent. Perhaps for every hospitalized population, there is a fixed fraction of patients that will be improperly triaged, will not respond to their initial therapy, and will experience errors and complications. When these patients come to our attention and when corrective action starts may be the most controllable factor in preventing adverse outcomes.

This trial and its predecessors set new standards in data handling and reporting, and lay the groundwork for more definitive studies on improving patient rescue. With the current state of computers, there is no excuse for errors in the calculation and interpretation of warning scores. Physicians enjoy their autonomy and feel threatened by protocols and other decision aides; however, in well-ordered and predictable situations, these tools outperform human decisions. If it is hospital policy to summon the RRT based on warning values, why is this even negotiable? Additionally, pairing the thought with the right action is subject to both internal and external resistance; thus combining electronic decision supports with wireless alerts eliminates yet another point of vulnerability, and work in this area deserves our attention (17, 22). Finally, the article by Bellomo et al raises some important discussion regarding over-triage to

higher levels of care. In the U.S. centers, the increase in transfer rate may have assisted with reducing mortality and hospital length of stay. Many may feel that the critical care units should be reserved for the extremely sick; however, many are sent to the unit as a final resting place with no chance for meaningful survival. Careful studies on the relationship between severity of condition on ICU admission, length of stay, and ICU resource use and turnover in the context of earlier rescue will provide a clearer view on the true beneficiaries of intensive care.

Geoffrey K. Lighthall, MD
Stanford University
Palo Alto, CA

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Acute kidney injury with sepsis: Is nitric oxide a friend, foe, both, or neither?*

The high frequency of occurrence and adverse outcomes of sepsis-associated acute kidney injury demand a better understanding of the pathophysiology of this disorder (1, 2). The past three decades have witnessed intense efforts to delineate the regulatory role of nitric oxide (NO) in health and disease. Given that NO exerts a clear-cut role in controlling vascular tone and several cellular processes, substantial investigation has examined a possible role for NO in mediating renal responses to sepsis (1–7).

NO is a soluble gas with a half-life of a few seconds and readily diffuses across membranes. These properties allow NO to act as a within-cell (autocrine) and between-cell (paracrine) signal. Three isoforms of NO synthase (NOS) are responsible for NO formation. All these isoforms are constitutively expressed within the kidney resulting in the production of low concentrations of NO (6). Endothelial NOS produces NO in glomerular capillary cells, afferent and efferent arterioles, and intrarenal arteries. This vascular NO acts via soluble guanylate cyclase to promote cyclic guanosine monophosphate formation which exerts tonic vasodilation of the afferent and perhaps efferent arterioles. Neural NOS is constitutively expressed in the macula densa and inner medullary collecting duct cells, whereas inducible NOS (iNOS) is constitutively expressed in the outer medulla, especially in thick medullary ascending limb cells, and also in distal convoluted and proximal tubules, glomeruli, and interlobular and

*See also p. 2368.

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