Real-Time Identification of Serious Infection in Geriatric Patients Using Clinical Information System Surveillance

William J. Meurer, MD,[*] Barbara L. Smith, BA,[*] Eve D. Losman, MD,[*] Diana Sherman, RN,[*] Joseph D. Yaksich, RN, ASN,[*] Jeremy D. Jared, BS,[†] Preeti N. Malani, MD, MSJ,[‡§] and John G. Younger, MD, MS[‖]*

OBJECTIVES: To develop and characterize an automated syndromic surveillance mechanism for early identification of older emergency department (ED) patients with possible life-threatening infection.

DESIGN: Prospective, consecutive-enrollment, single-site observational study.

SETTING: A large university medical center with an annual ED census of 75,273.

PARTICIPANTS: Patients aged 70 and older admitted to the ED and having two or more systemic inflammatory response syndrome (SIRS) criteria during their ED stay.

MEASUREMENTS: A search algorithm was developed to screen the census of the ED through its clinical information system. A study coordinator confirmed all patients electronically identified as having a probable infectious explanation for their visit.

RESULTS: Infection accounted for 28% of ED and 34% of final hospital diagnoses. Identification using the software tool alone carried a 1.63 relative risk of infection (95% confidence interval CI = 1.09–2.44) compared with other ED patients sufficiently ill to require admission. Follow-up confirmation by a study coordinator increased the risk to 3.06 (95% CI = 2.11–4.44). The sensitivity of the strategy overall was modest (14%), but patients identified were likely to have an infectious diagnosis (specificity = 98%). The most common SIRS criterion triggering the electronic notification was the combination of tachycardia and tachypnea.

CONCLUSION: A simple clinical informatics algorithm can detect infection in elderly patients in real time with high specificity. The utility of this tool for research and clinical care may be substantial. **J Am Geriatr Soc 57:40–45, 2009.**

Key words: sepsis; aged; sentinel surveillance; informatics

Emergency departments (EDs) are an important source of health care for elderly people. Data from the National Hospital Ambulatory Medical Care Survey from 2003 have described high utilization of EDs by older Americans, with infections being among the most frequent and most serious reasons for these visits and the need for subsequent hospitalization.[1] Unscheduled admission to the hospital is an important prognostic factor for elderly patients. Estimates suggest that, of elderly patients with chronic conditions who survive hospitalization, 33% will die within 6 months.[1] Although infection is common and frequently serious, its presentation in older patients is notoriously difficult to detect. Senile changes in the immune system and the inflammatory response serve to mute classic symptoms and signs of invasive bacterial processes.[2] For clinical care and for clinical research, a hospital environment wherein caregivers are personally unfamiliar with patients and where levels of activity are often near, at, or even above 100% facility capacity seriously compounds subtle presenting signs and symptoms in this population.

Improved strategies for early detection of serious infection in older emergency patients would be beneficial for several reasons. Earlier detection during ED evaluation presumably would shorten delays to comprehensive evaluation, antibiotics, and in some instances advanced monitoring and goal-directed therapy. Just as valuable would be a means of rapidly and reliably identifying such patients to recruit them for observational and interventional studies in the ED. EDs are increasingly challenging environments in which to comprehensively identify and recruit subjects for clinical research. Methods of identifying serious infection in

From the [*]Department of Emergency Medicine and Divisions of [‡]Geriatrics and [§]Infectious Disease, Department of Internal Medicine, Ann Arbor Veterans Affairs Healthcare System, Geriatric Research, Education and Clinical Center, Ann Arbor, Michigan; and [†]Department of Anesthesiology and [‖]Center for Computational Medicine and Biology, University of Michigan, Ann Arbor, Michigan.

Address correspondence to William J. Meurer, Department of Emergency Medicine, University of Michigan, Taubman Center B1354 SPC 533, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-5303. E-mail: wmeurer@umich.edu

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elderly people would be expected to improve clinical research in this population as well as improve care.

The current report describes and characterizes a novel strategy for identifying elderly ED patients likely to have serious infections. The method was built around a simple algorithm that continuously interrogated a clinical information system for abnormal vital signs and laboratory data in older patients. Flagged patients were electronically brought to the attention of a study coordinator (BLS) who completed patient evaluation at the bedside.

MATERIALS AND METHODS

This was a prospective, consecutive-enrollment, single-site observational study performed at the ED of a large university medical center with an annual census of 75,273.

Study Protocol

ED Informatics Structure

The clinical information system used in this study is shown in Figure 1. In brief, the system was built on SQL 2000 Enterprise (Microsoft Corporation, Redmond, WA). The user interface through which clinical information was entered manually was Centricity 7.5.x (General Electric Healthcare, Piscataway, NJ). Vital signs were also entered automatically using a monitor capture server interfaced to the department's bedside patient telemetry units. Laboratory data were transmitted automatically from the clinical laboratory's server.

Automated Surveillance Algorithm

The surveillance protocol was developed as a tool for an ongoing study of infection in elderly people. Inclusion criteria for that study included patient age of 70 and older, time from ED admission to identification as a subject in the study of no more than 6 hours, and two or more systemic inflammatory response syndrome (SIRS) criteria accumulated at any time during the ED stay (respiratory rate $\geq$20/min, temperature $\leq$36 or $\geq$38°C, heart rate $\geq$90 betas/min, and total white blood cell count $\leq$4,000 or $\geq$12,000/mm^3).[3]

These criteria were used to develop a rules engine that would execute a scheduled query of the ED's SQL server every 15 minutes from 9:00 a.m. to 4:00 p.m. every weekday. Whenever age and SIRS inclusion criteria were met, an alphanumeric page (electronic notification) containing a patient identifier, the patient's location within the ED, and which inclusion criteria had been met was sent to a study coordinator. The coordinator was responsible for the second element of patient identification, a confirmation with the physician in charge that a noninfectious explanation for the patient's condition was not present. Although this criterion appears circuitous, it was designed to avoid physicians' preconceptions as to what might or might not

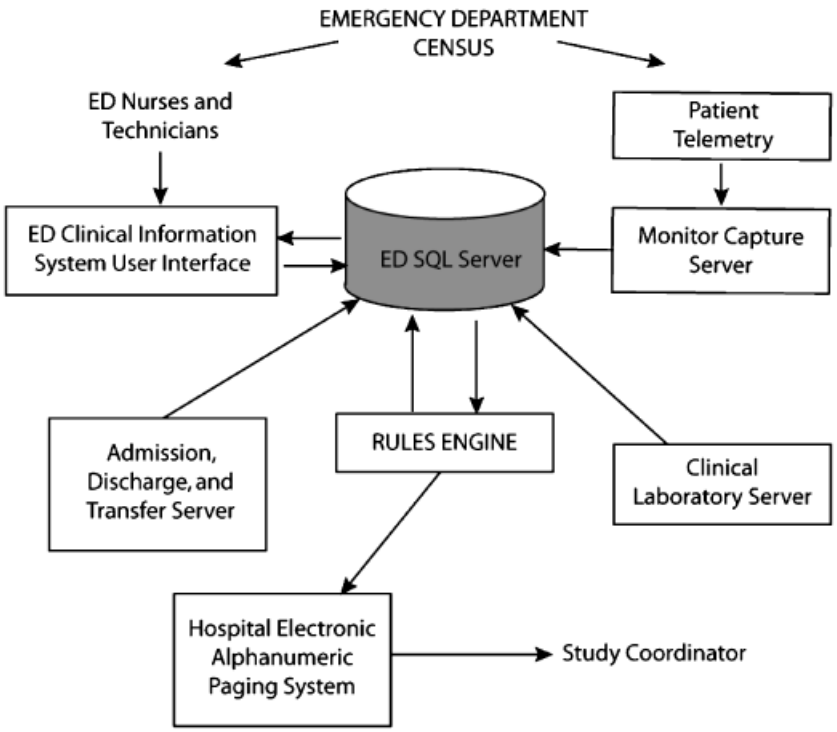

Figure 1. Informatics architecture used in the current study. The patient identification strategy was centered on the department's SQL server. An admission, discharge, and transfer (ADT) server drives the database of current patients. Once the ADT server placed a patient's identifiers into the SQL database, that patient was under surveillance for the duration of his or her stay. Systemic inflammatory response syndrome criteria could enter the system manually (through emergency department (ED) staff by way of the user interface), through automated capture of patient telemetry, or through information from the medical center's clinical laboratory server (for white blood cell count information). The rules engine executed its query every 15 minutes from 9:00 a.m. to 4:00 p.m. on weekdays. When candidates were identified, pertinent data were sent to the study coordinator through the medical center's alphanumeric paging system.

constitute a serious infection or even sepsis in the study population. From this point forward, this criterion will be stated as "suspected infection" for the sake of clarity.

Measurements

The strategy was characterized in two phases. From July 1 through August 15, 2007, the validity of the strategy as a classification tool was evaluated in all patients aged 70 and older presenting between 3:00 a.m. and 4:00 p.m. on weekdays. Because the enrollment criteria allowed a patient to be identified as long as 6 hours after presentation, the 9:00 a.m. start time could capture patients presenting as early as 3:00 a.m. Structured chart review of this population was conducted to confirm or exclude an ED diagnosis of infection and a final hospital discharge diagnosis of infection. Three trained chart abstracters whose interrater agreement was assessed using the Fleiss kappa score (0.81) conducted reviews. The performance of the surveillance algorithm and the combination of the algorithm followed by confirmation by the study coordinator were quantified using the sensitivity, specificity, and relative risk of an affirmative screen for identifying an ED diagnosis of infection, hospital discharge diagnosis of infection, and the need for intensive care unit admission. To determine short-term (90-day) mortality, electronic medical records of the study hospital and federal Social Security mortality data were examined. For the latter, records were not studied for at least 9 months after enrollment to maximize the probability of capturing all deaths within the cohort. Survival analysis of patients identified by the algorithm, compared with all other patients aged 70 and older presenting during the study window, was performed using standard proportional hazards analysis.

The strategy was also characterized according to the time required, from presentation, time of triage, and the time that a patient was placed in an ED bed, for inclusion criteria to be met. Presumably, whenever criteria were present, they would be detected at the time of the next executed query, which was never more than 15 minutes distant. Rather, the delay from presentation until detection is a reflection of the time required for sufficient signs of infection to accumulate in these patients.

The second phase of characterization occurred between July 1 and November 15, 2007, and was limited to patients in whom automated detection occurred; patients from the first phase who met two or more SIRS criteria were included. The goal of this phase was to examine the frequency and utility of the observed combinations of SIRS criteria. In these individuals, the association between the particular SIRS criteria met and the likelihood that a suspected infection was present was evaluated using log odds.

Statistical Analysis

All analysis was performed in R 2.6.0 (The Comprehensive R Archive Network, www.r-project.org). The *epibasix* package was used to calculate relative risk, sensitivity, and specificity, along with appropriate confidence intervals. The *irr* package was used to calculate the Fleiss kappa.

The local institutional review board approved all protocols.

RESULTS

Between July 1 and August 15, 2007, 583 patients aged 70 and older were evaluated during the daily study window, 248 of these were admitted and included for further analysis: of these, 69 (28%) had an ED diagnosis of infection of any kind, and 84 (34%) had a final hospital discharge diagnosis of infection. The clinical characteristics of all patients with an ED infection diagnosis (regardless of whether they were detected by the system) are shown in Table 1.

An electronic notification was generated in 61 (25%) of those admitted, and 13 (5%) of those admitted had a suspected infection. The combination of electronic notification and suspected infection was a strong indicator of overall degree of illness; only one patient meeting these criteria was not admitted to the hospital. This patient left against medical advice and subsequently returned and was admitted.

The surveillance system correctly identified all potentially eligible patients. The clinometric performance of the overall identification strategy is reported in Table 2. Patients triggering the SIRS rules engine were approximately 1.6 times as likely to have an infectious diagnosis as those who did not trigger this system. Patients initially identified by the surveillance system who also had suspected infection were three times as likely to have an ED diagnosis of infection as those not triggering the system ($P < .05$).

To determine the extent to which the detection algorithm identified patients who were truly seriously ill, a follow-up chart review was conducted on these 248 patients. All patients were first tracked through the study site's electronic medical record. Any patients for whom that search did not confirm survival or death at 90 days post-ED visit were submitted to the Social Security Death Index. Queries to this data set were not conducted for at least 9 months after the ED visit to maximize the likelihood of uncovering undetected deaths in the cohort. Kaplan-Meier curves for these data are shown in Figure 2. Of all patients aged 70 and older admitted to the hospital from the ED, 13.7% experienced mortality at 90 days. In contrast, patients identified first by the computerized algorithm and then by follow-up confirmation of a likely infectious diagnosis suffered 37.5%

Table 1. Characteristics of Patients with an Emergency Department Diagnosis of Infection (N = 69)

Characteristic	Value
Age, median (IQR)	81.5 (10)
Female, n (%)	33 (47.8)
Hospital length of stay, days, median (IQR)	4 (3)
Index hospitalization mortality, n (%)	5 (7.2)
90-day case fatality, n (%)	10 (14.5)
Infectious source, n (%)	
Urine	22 (31.9)
Lung	13 (18.8)
Skin	7 (10.1)
Gastrointestinal	6 (8.7)
Multiple sites	6 (8.7)
Other	3 (4.3)
Undetermined	12 (17.4)

IQR = interquartile range.

Table 2. Performance of Patient Identification System

Diagnosis	Infection* n (%)	Other Diagnosis† n (%)	Sensitivity (95% CI)	Specificity (95% CI)	Relative Risk (95% CI)
Emergency department diagnosis					
Electronic notification	25 (36)	36 (20)	0.362 (0.249–0.476)	0.782 (0.722–0.843)	1.63 (1.09–2.44)
Notification and confirmation‡	10 (14)	3 (2)	0.145 (0.062–0.228)	0.983 (0.964–1.000)	3.06 (2.11–4.44)
Final hospital diagnosis					
Electronic notification	26 (31)	35 (21)	0.333 (0.233–0.434)	0.780 (0.717–0.844)	1.43 (1.01–2.05)
Notification and confirmation‡	9 (11)	4 (2)	0.107 (0.041–0.173)	0.976 (0.952–0.999)	2.17 (1.44–3.26)

* Emergency department (ED) diagnosis, n = 69; final hospital diagnosis, n = 84.
† ED diagnosis, n = 179; final hospital diagnosis, n = 164.
‡ Confirmation denotes verbal affirmation with attending physician that a noninfectious explanation was absent.
CI = confidence interval.

mortality in the same time frame ($P < .01$ according to proportional hazards modeling).

The median time from ED arrival to notification was 109 minutes (interquartile range (IQR) = 59–177), from triage to notification was 93 minutes (IQR = 50–170), and from placement in room to notification was 89 minutes (IQR = 47–164). One reason for delay in notification was the time needed for collection, measurement, and reporting of peripheral white blood cell counts. In addition, patients frequently did not meet two SIRS criteria at triage. Rather, their disease course tended to evolve over the early hours of observation and treatment.

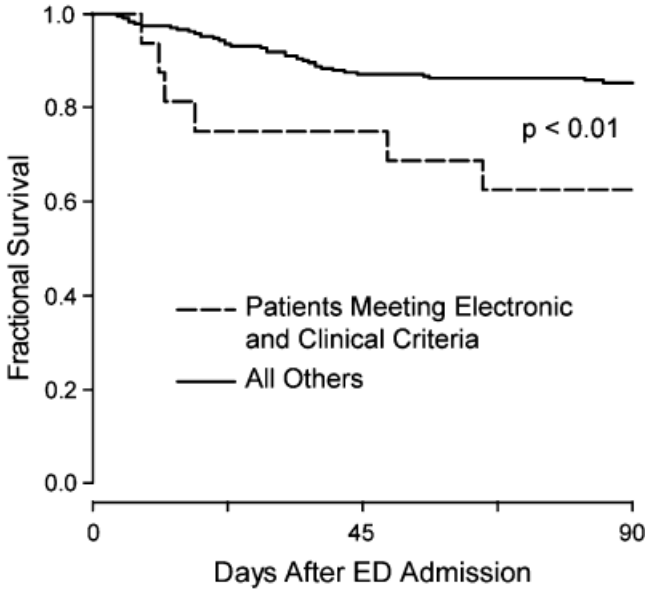

Figure 2. Ninety-day survival in patients in this study. Following identification in the emergency department (ED), patients' electronic medical records and federal databases were subsequently examined to determine short-term mortality. Patients meeting the combined criteria of aged 70 and older, two or more systemic inflammatory response syndrome criteria, and suspected infection at ED evaluation experienced 37.5% 90-day mortality, whereas all ED patients aged 70 and older not meeting the criteria for serious infection enrolled over the same period faced 13.7% mortality ($P < .01$).

Because the SIRS criterion respiratory rate has variously been noted as 20 or more per minute or more than 20 per minute, a sensitivity analysis of this distinction was conducted, which removed patients who met the SIRS criteria by virtue of a respiratory rate of 20 breaths per minute or less. The specificity of the electronic notification for ED infection diagnosis increased to 86.0% (95% CI = 81.0–91.1%), and the sensitivity decreased to 30.4% (95% CI = 19.6–41.3%).

The performance of the system from July 1 through November 15 was further considered in all patients for whom automated notification occurred. Specifically, in these patients, which patterns of SIRS criteria were mostly likely to be associated with patients going on to meet the second tier of the inclusion criteria related to suspected infection was of interest. For this analysis, 434 patients were included. The associations between each combination of possible criteria and a patient being considered likely to have a serious infection are shown in Figure 3. Although the combination of tachycardia and tachypnea had the weakest association with patients being considered candidates for study, this combination's frequency (48% of all cases) led it to be the pattern from which most patients of interest were identified.

DISCUSSION

The current study found that a two-stage patient identification protocol identified all potentially eligible patients for an investigation of serious infection in elderly ED patients. Infectious diagnoses were common in the sample; patients included had both apparently serious (SIRS) and nonserious infections (incidental urinary tract infection). As a result, the sensitivity for identifying all patients with infection was low. A validated, inclusive definition of serious infection in emergency and critical care is elusive; therefore, the low sensitivity observed was not surprising. Nevertheless, for older patients requiring admission, the automated strategy with a single follow-up question performed by a study coordinator produced a population three times as likely to have an ED infectious diagnosis as the general ED population.

High patient volume can affect timely and reliable study candidate identification. Furthermore, geriatric populations are frequently underrepresented in ED research.[4]

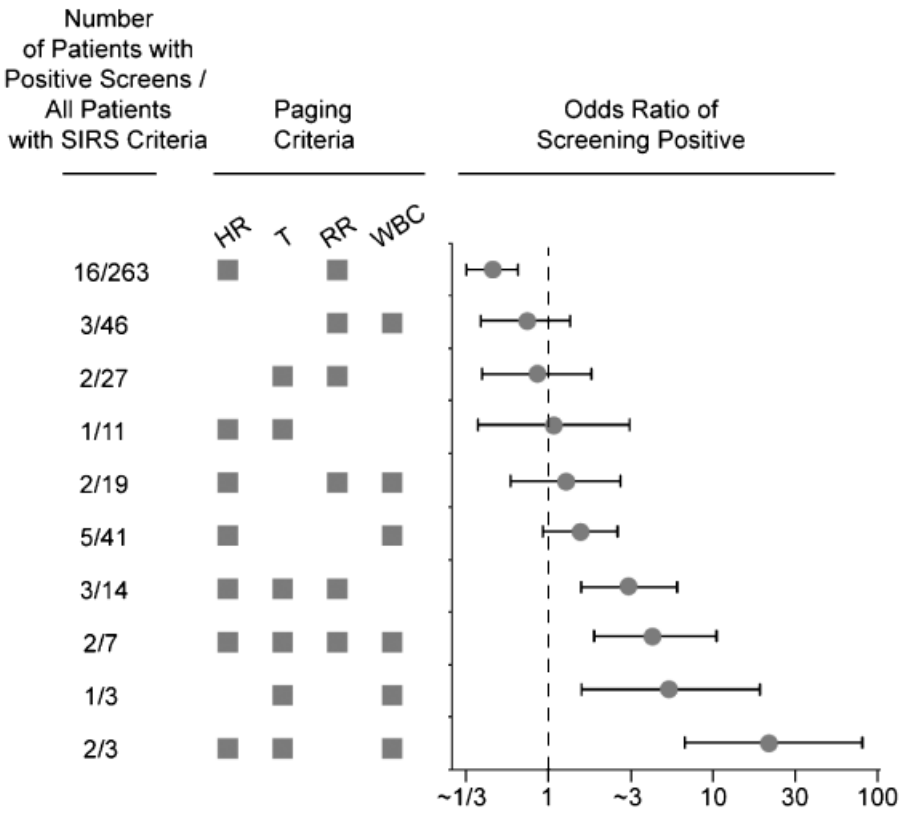

Figure 3. Relationship between all possible combinations of two or more systemic inflammatory response syndrome (SIRS) criteria and the odds of ultimately having a study coordinator confirm a likely infectious diagnosis. All patients who generated an automated notification in this study (July–November) are included. Although the combination of tachycardia and tachypnea had the weakest association with a patient being suspected of having an infectious diagnosis, the high frequency of this combination of criteria resulted in most patients being captured from that pattern. In contrast, patterns including both abnormal temperature (T) and abnormal white blood cell count (WBC) were more strongly associated with a suspected infectious diagnosis. HR = heart rate; RR = respiratory rate.

Busy frontline medical providers are less likely to take an additional step to contact a study coordinator when an eligible patient arrives. Therefore, an automated system to reliably identify candidates could eliminate this potential barrier to subject recruitment. This can have beneficial effects including but not limited to a reduction of selection bias due to ED volume, less demand on and distraction of clinical staff, simplified departmental monitoring by study coordinators, and shorter overall study duration because of faster enrollment. Each of these would be expected to reduce the cost and administrative burden of conducting ED clinical research.

Prior investigations have described the use of information systems for real-time screening of patients for research and clinical purposes. An automated system, which similarly used the hospital information system to identify syncope patients as part of the development of a clinical decision rule, has been described.[5] The current work expands upon this by using clinical parameters from the information system as opposed to the reported reason for visit. Additionally, the majority of patients in the current study "evolved" into meeting inclusion criteria; for potentially seriously infected patients, a one-time screening would have been insufficient. Others have explored the use of computerized clinical information data as an "early warning system" to identify inpatients who are in distress or are in a pre-arrest state.[6] The surveillance schema developed for the current study has potential utility in this respect as well. Extension of surveillance to identifying clinical parameters that predict a well-defined serious disease process before clinically apparent deterioration would be beneficial. The present work on identifying serious infections in older ED patients demonstrates the feasibility of such a system in the scope of existing hospital information databases. Adaptation of this process to a diagnostically more-concrete disease could potentially greatly improve the sensitivity of such a strategy.

This work has several important limitations. The characteristics of patients without an ED diagnosis of infection were not collected, and thus the cohort studied cannot be differentiated from the full population of older ED patients. An additional limitation is that this investigation was performed at a single academic medical center, with a relatively demographically homogenous catchment area.

Clinical informatics systems differ widely between institutions. It is therefore not possible to comment specifically on the ease with which this strategy might be deployed in other EDs, although in the SQL environment in which the algorithm was developed, the entire query was implemented in just a few lines of code and ran fast enough not to interfere meaningfully with other clinical information system data management tasks.

CONCLUSIONS

The current study prospectively evaluated a simple two-part syndromic surveillance strategy consisting of an automated clinical information system search algorithm followed by a single-question confirmation. This work describes the methodology for automated patient identification. The results indicate that such strategies are feasible as a tool for conducting clinical research and provide valuable proof of concept as a tool that could be useful in a variety of research and clinical applications. Further work is needed in optimizing the sensitivity and specificity of the method and in adapting it for applications in direct clinical care.

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REFERENCES

1. Wieland D, Lamb VL, Sutton SR et al. Hospitalization in the Program of All-Inclusive Care for the Elderly (PACE): Rates, concomitants, and predictors. J Am Geriatr Soc 2000;48:1373–1380.
2. Gavazzi G, Krause K-H. Ageing and infection. Lancet Infect Dis 2002;2:659–666.
3. Bone RC. Toward an epidemiology and natural history of SIRS (systemic inflammatory response syndrome). JAMA 1992;268:3452–3455.
4. Glickman SW, Anstrom KJ, Lin L et al. Challenges in enrollment of minority, pediatric, and geriatric patients in emergency and acute care clinical research. Ann Emerg Med 2008;51:775–780.e3.
5. Quinn J, Durski K. A real-time tracking, notification, and web-based enrollment system for emergency department research. Acad Emerg Med 2004;11:1245–1248.
6. Goldhill DR, McNarry AF, Mandersloot G et al. A physiologically-based early warning score for ward patients: The association between score and outcome. Anaesthesia 2005;60:547–553.