SCORING SYSTEMS FOR ASSESSING ORGAN DYSFUNCTION AND SURVIVAL

Jean-Louis Vincent, MD, PhD, Flavio Ferreira, MD, and Rui Moreno, MD, PhD

Scoring systems in the intensive care unit (ICU) can be useful to facilitate description of patient populations for ICU management and clinical trial enrollment, to enable comparison between ICUs or within the same ICU over time for quality control purposes, and perhaps, to guide and monitor individual patient treatment. To provide useful information, these systems must be extensively validated for use on different patient samples and in future populations. Scores must be accurate (good calibration and discrimination) and generalizable (good reproducibility and transportability across geographic, time, and methodologic boundaries).[32] Few scoring systems have been developed specifically for use in patients with sepsis although some have been customized for use in sepsis.[36, 43]

Two main types of scoring system have been developed for use in the ICU patient: those primarily focused on a single end-point, survival, and those focusing on describing morbidity as it evolves, organ dysfunction scores. This article briefly describes some of the most commonly used scoring systems that have been developed and discusses some practical issues related to their use.

GENERAL OUTCOME PREDICTION MODELS

Since the 1980s, many outcome prediction scores have been developed[38, 41]; the authors discuss in detail just three of the more com-

From the Department of Intensive Care, Erasme Hospital, Free University of Brussels, Belgium (JLV, FF); and Department of Intensive Care, Hospital St Antonio dos Capuchos, Alameda de St Antonio dos Capuchos, Portugal (RM)

monly used scores: acute physiology and chronic health evaluation (APACHE),[34, 37] simplified acute physiology score (SAPS),[41] and mortality probability models (MPM).[45, 46] All these models have been designed and validated for use on admission or within the first 24 hours after admission, relating the calculated score during the first 24 hours of admission to survival status on discharge from the hospital. They are not developed for repeated use at other time points during the patient's ICU stay, although it is probably acceptable to use either SAPS II or APACHE II on entry to a clinical trial even if this does not equate with the time of ICU admission. Some researchers have advocated the sequential application of these systems, possibly with correction for other factors, but such use is as yet experimental.[13, 64]

All these scores were developed using large patient databases but may be effective only in patients from cohorts similar to those in the original database; regional and international differences in patient demographics and selection for ICU admission may influence the behavior of such scoring systems[54, 55, 75] and necessitate adaptation to local populations.[1, 53, 63] The use of estimates of the risk of death to predict outcome in individual patients is, with the current status of the science, clearly inappropriate.[44]

Acute Physiology and Chronic Health Evaluation

First developed in 1981 by Knaus et al,[38] the APACHE score has become the most commonly used survival prediction model in ICUs worldwide. The APACHE II score, a revised and simplified version of the original prototype,[34] uses a point score based on initial values of 12 routine physiologic measures, age, and previous health status to provide a general measure of severity of disease. The values recorded are the worst values taken during the patient's first 24 hours in the ICU. The score is applied to one of 34 admission diagnoses to estimate a disease-specific probability of mortality (APACHE II predicted risk of death). The maximum possible APACHE II score is 71, and high scores have been well correlated with mortality. The APACHE II score has been widely used to stratify and compare various groups of critically ill patients, including patients with sepsis, by severity of illness on entry into clinical trials.[27, 28, 31, 34, 39, 70]

In 1991, the APACHE III was developed[37] and has been validated and further updated recently.[75] This is a more complex score, but may be useful for comparing the performance of ICUs.[3, 59, 68] APACHE III is not available in the public domain and a fee must be paid for using the predictive equations, limiting its use.

Simplified Acute Physiology Score

First validated in 1984, SAPS used 14 easily measured biologic and clinical variables to provide an indication of the risk of death of ICU

patients.[41] In 1993, SAPS II was developed and validated using data from 137 ICUs in 12 countries.[40] The 17 variables used in SAPS II were selected using logistic regression techniques, and comprise 12 physiologic variables, age, type of admission (scheduled surgical, unscheduled surgical, or medical), and 3 variables related to underlying disease (acquired immunodeficiency syndrome, metastatic cancer, and hematologic malignancy). Different points are assigned to each variable, for example, 0 to 3 for temperature, 0 to 26 for Glasgow coma score. For the physiologic variables, the worst values over the first 24 hours of ICU admission are taken into account. From the data set, an equation was developed to convert the SAPS II score to a probability of hospital mortality. The SAPS II score was validated on a heterogeneous group of ICU patients, and, as the authors point out, may not be as applicable in more specific patient groups.[40] In addition, the accuracy of the predictive power of SAPS II is lost over time, with mortality prediction remaining accurate only in patients who stay in the ICU for fewer than 5 days.[67] SAPS II has been used to classify and compare populations of critically ill patients in clinical trials.[15, 17]

Mortality Probability Models

MPM II was developed in 1993 as a revision of the earlier MPM system,[45] using logistic regression techniques on a large international database of ICU patients.[46] It consists of two scores: MPM_0, the admission model, which contains 15 variables, and MPM_{24}, the 24-hour model, which contains five of the admission variables and eight additional variables and is designed for patients who are in the ICU for more than 24 hours. Each variable, apart from age, is assigned as 0 or 1 depending on its absence or presence. Age is entered as the age in years. In this model, no score is computed, and a logistic regression equation directly provides the user with a probability of hospital mortality.

The performance of the MPM II models has been shown to be no better than SAPS II,[54] although some modifications to the equations can improve the predictive capability.[53]

Comparison and Discussion

Few studies have been published directly comparing the effectiveness of these scores at predicting mortality. Arregui et al[2] compared six systems including the APACHE II and MPM in patients with septic shock and found APACHE II to be a useful prognostic tool. Baumgartner et al[4] reported that the SAPS and APACHE II scores were less accurate in predicting the outcome of patients with septic shock than a simplified septic shock score, based on 14 clinical, biologic, and hemodynamic variables, suggesting again that we should be aware of the potential limitations of these scoring systems in specific patient groups. Recently,

Nouira et al[58] compared four systems (APACHE II, SAPS II, and the MPM_0 and MPM_{24}) in Tunisian ICUs, and found no differences in performance between them, although calibration performance of all the systems was unsatisfactory, a problem the authors suggested may be related to a different standard of care in the Tunisian ICUs compared with the American ICUs where these models were validated. Similarly, Moreno et al,[54] in comparing SAPS II and MPM_0 on a population of 10,027 ICU patients from 13 European ICUs, found that both scores overestimated the risk of death and suggested that this was because of differences between their patients and those in the original populations used to create the SAPS and MPM scores. Similar results had already been described in two national studies in Italy[1] and Portugal.[55] Comparing the APACHE II and the MPM II, Lemeshow et al[44] reported a good agreement in overall predicted mortality for 11,320 ICU patients, but when the predictions were analyzed at a patient per patient level, there were wide discrepancies between the two scores for some patients. This finding highlights the problems in using such scores to predict individual patient outcomes.

It has been demonstrated that the newer versions of these models have a better performance than their older counterparts.[1, 10, 58] In general, the SAPS II and APACHE II systems are equivalent; both have been extensively validated and are used widely, and selection is largely one of individual preference. In Europe, SAPS II, although not perfect, has been demonstrated to have a better predictive performance than APACHE II[55] and MPM II.[54]

ORGAN DYSFUNCTION DESCRIPTION SCORES

Organ failure scores are designed to describe organ dysfunction more than to predict survival. In the development of organ function scores, three important principles need to be remembered.[74] First, organ failure is not a simple all-or-nothing phenomenon; rather a spectrum or continuum of organ dysfunction exists from very mild altered function to total organ failure. Second, organ failure is not a static process, and the degree of dysfunction may vary with time during the course of disease so that scores need to be calculated repeatedly. Third, the variables chosen to evaluate each organ need to be objective, simple, and available but reliable, routinely measured in every institution, specific to the organ in question, and independent of patient variables, so that the score can be calculated easily for any patient in any ICU. Interobserver variability in scoring can be a problem with a more complex system,[62, 66] and the use of simple, unequivocal variables can avoid this potential problem. Ideally, scores should be independent of therapeutic variables as stressed by Marshall et al,[47] but, in fact, this is virtually impossible to achieve as all factors are more or less treatment-dependent. For example, Pa_{O_2}/Fi_{O_2} is dependent on ventilatory conditions and positive end-

expiratory pressure (PEEP), platelet count may be influenced by platelet transfusions, and urea levels are affected by hemofiltration, and so forth.

The process of organ function description is relatively new and there is no general agreement on which organs to assess and which parameters to use. Many different scoring systems have been developed for assessing organ dysfunction,[4, 5, 13, 18, 21, 23, 26, 35, 42, 47, 50, 71, 74] differing in the organ systems included in the score, the definitions used for organ dysfunction, and the grading scale used[6, 72] The majority of scores include six key organ systems, cardiovascular, respiratory, hematologic, central nervous, renal, and hepatic, with other systems, such as the gastrointestinal system, less commonly included. Early scoring systems assessed organ failure as either present or absent, but this approach is very dependent on where the limits for organ function are set, and newer scores consider organ failure as a spectrum of dysfunction. Most scores have been developed in the general ICU population, but some were aimed specifically at the patient with sepsis.[4, 18, 50, 71, 74]

Three of the more recently developed systems will be further discussed below, the main difference between them being in their definition of cardiovascular system dysfunction.

Multiple Organ Dysfunction Score

The multiple organ dysfunction (MODS) scoring system was developed by a literature review of clinical studies of multiple organ failure from 1969 to 1993.[47] Optimal descriptors of organ dysfunction were thus identified and validated against a clinical database. Six organ systems were chosen, and a score of 0–4 allotted for each organ according to function (0 being normal function through to 4 for most severe dysfunction) with a maximum score of 24. The worst score for each organ system in each 24-hour period is taken for calculation of the aggregate score. A high initial MODS correlated with ICU mortality and the delta MODS (calculated as the MODS over the whole ICU stay less the admission MODS) was even more predictive of outcome.[47] In a study of 368 critically ill patients, the MODS was found to better describe outcome groups than the APACHE II or the organ failure score, although the predicted risk of mortality was similar for all scoring systems.[30] The MODS has been used to assess organ dysfunction in clinical studies of various groups of critically ill patients, including those with severe sepsis.[22, 48, 61, 70]

Sequential Organ Failure Assessment

The sequential organ failure assessment (SOFA) score was developed in 1994 during a consensus conference organized by the European Society of Intensive Care and Emergency Medicine, in an attempt to provide a means of quantitatively and objectively describing the degree

of organ failure over time in individual, and groups of, septic patients.[74] Initially termed the sepsis-related organ failure assessment score, the score was then renamed the sequential organ failure assessment as it was realized that it could be applied equally to nonseptic patients. In devising the score, the participants of the conference decided to limit to six the number of systems studied: respiratory, coagulation, hepatic, cardiovascular, central nervous, and renal. A score of 0 is given for normal function through to 4 for most abnormal, and the worst values on each day are recorded. Individual organ function thus can be assessed and monitored over time, and an overall global score also can be calculated. A high total SOFA score (SOFA max) and a high delta SOFA (the total maximum SOFA minus the admission total SOFA) have been shown to be related to a worse outcome,[57, 73] and the total score has been shown to increase over time in nonsurvivors compared with survivors.[73] The SOFA score has been used for organ failure assessment in several clinical trials, including one in patients with septic shock.[7, 15, 20, 29]

Logistic Organ Dysfunction System

The logistic organ dysfunction system (LODS) score was developed in 1996 using multiple logistic regression applied to selected variables from a large database of ICU patients.[42] To calculate the score, each organ system receives points according to the worst value for any variable for that system on that day. If no organ dysfunction is present the score is 0, rising to a maximum of 5. As the relative severity of organ dysfunction differs between organ systems, the LODS score allows for the maximum 5 points to be awarded only to the neurologic, renal, and cardiovascular systems. For maximum dysfunction of the pulmonary and coagulation systems, a maximum of 3 points can be given for the most severe levels of dysfunction and for the liver, the most severe dysfunction only receives 1 point. Thus the total maximum score is 22. The LODS score is designed to be used as a once-only measure of organ dysfunction in the first 24 hours of ICU admission, rather than as a repeated assessment measure. The LODS system is quite complex and seldom used; nevertheless, it has been used to assess organ dysfunction in clinical studies.[69]

Comparison and Discussion

These are relatively new scoring systems. The main difference between them is the method chosen for the evaluation of cardiovascular dysfunction (Table 1). The MODS uses a composed variable (heart rate multiplied by the ratio of central venous pressure and mean arterial pressure); the SOFA uses the blood pressure and the level of adrenergic support; and the LODS uses the heart rate and systolic blood pressure. In calculating the scores, there are several practical issues that should be

Table 1. DIFFERENCES IN THE PARAMETERS CHOSEN TO ASSESS THE ORGAN SYSTEMS IN THREE ORGAN DYSFUNCTION SCORING SYSTEMS

Parameter	MODS[47]	SOFA[74]	LODS[42]
Respiratory	PaO_2/FiO_2 ratio	PaO_2/FiO_2 ratio and need for ventilatory support	PaO_2/FiO_2 ratio and ventilation/CPAP status
Coagulation	Platelet count	Platelet count	White blood cell and platelet counts
Hepatic	Bilirubin concentration	Bilirubin concentration	Bilirubin concentration and prothrombin time
Cardiovascular	Heart rate × ratio of central venous pressure and mean arterial pressure (HR × [CVP/MAP])	Blood pressure and adrenergic support	Heart rate and systolic blood pressure
Central Nervous System	Glasgow coma score	Glasgow coma score	Glasgow coma score
Renal	Creatinine concentration	Creatinine concentration or urine output	Urea and creatinine concentrations and urine output

discussed.[24, 72] First, exactly which value for any parameter should be considered? It is true that for many of the simpler variables, several measurements will be taken during any 24-hour period. Should the lowest, highest, or an average be taken as the representative value that day? There is a general consensus that, for the purposes of the score, the worst value in any 24-hour period should be considered. What should be done about missing values? Should the last known value be repeatedly considered as representative until a new value is obtained, or should the mean value between two successive values be taken? Both options make assumptions that may influence the reliability of the score. The first option assumes that we have no knowledge of the evolution of values with time and the second assumes that changes are usually fairly predictable and regular. The authors prefer this second option because values may be missing for several days and repeating the last known value may involve considerable errors in calculation. In addition, changes in most of the variables measured (platelet count, bilirubin, urea) are, in fact, usually fairly regular, moving up or down in a systematic manner.

MORBIDITY VERSUS MORTALITY

Much discussion has taken place in recent years over the use of mortality or morbidity as an outcome measure in intensive care.[60] Al-

though mortality prediction scores provide valuable information about the severity of illness of patient groups, they provide little information about individual patients.[11, 44, 64] For example, although a probability of mortality of 0.46 means that 46 of 100 patients will be expected to die, this figure does not, and cannot, tell which individual patients will form the 46 who die or the 54 who survive.[44] In addition, the use of mortality as an outcome measure may hide valuable information of improved morbidity. For example, two groups of patients in a clinical trial of treatment versus placebo may be shown to have the same overall mortality rate, and hence the treatment be declared to be ineffective. On closer observation, however, the treatment group could be found to have shorter ICU stays, reduced time on mechanical ventilation, reduced antibiotic requirements, and so forth, potentially valuable beneficial effects of the treatment, which were hidden by the emphasis on mortality.

Scores focusing predominantly on the development of organ dysfunction that allow for repeated assessment provide more information on individual patients and on disease development and response to treatment. For example, an APACHE II score of 20 does not say whether the patient has severe renal failure or acute respiratory failure with coma, whereas analysis of the component scores of an organ dysfunction score like SOFA will provide an accurate description of the patient's disease status. Although not developed to predict mortality, many morbidity prediction scores correlate well with outcome, but this does not mean they should replace prognostic systems; the two provide different information and should be used to complement each other (Table 2).

OTHER APPROACHES

Therapeutic Intervention Scoring System

The therapeutic intervention scoring system (TISS) was developed in 1974[14] and primarily evaluates needs in staffing and assesses utilization of ICU facilities, rather than stratifying severity of illness. The score increases with increasing interventions or nursing care, so a higher TISS

Table 2. COMPARISON OF MORTALITY PREDICTION VERSUS MORBIDITY PREDICTION SCORING SYSTEMS

	Mortality (APACHE II, SAPS II, etc)	Morbidity (MODS, SOFA, etc)
Aim	Predict mortality	Describe morbidity (organ failure)
Ease of use	Often complex calculations	Usually simple
Timing	Obtained on admission or within first 24 hours	Can be obtained repeatedly (daily)
Disease process	No information on individual organ function	Individualizes organ function

score usually implies a more severely ill ICU patient. The original score, which included 76 selected therapeutic activities was updated in 1983[33] and further simplified in 1996 to include just 28 items appropriately weighted so that the simplified TISS score compared favorably with the original TISS score even in independent populations.[51, 56] An easier alternative, the nine equivalents of nursing manpower use score (NEMS), has been published more recently and validated in large cohorts of ICU patients.[65] TISS (and its shorter versions) has been found to correlate well with ICU costs[16, 25] and may be a useful tool in the management of nursing staffing in the ICU,[51] but has little direct relevance in the assessment of illness severity or outcome.

Biologic Scores

As our understanding of the pathophysiologic mechanisms underlying sepsis has advanced, some authors have proposed that the inclusion of biologic markers of disease in scoring systems may be useful in certain categories of patients, such as those with sepsis.[8] One biologic scoring system developed by Casey et al[9] measured levels of lipopolysaccharide and the cytokines, tumor necrosis factor (TNF)-α, interleukin (IL)-1, and IL-6, and devised a total lipopolysaccharide-cytokine score, which correlated well with mortality in their population of 97 patients with sepsis syndrome. The accuracy of cytokine levels in the diagnosis of sepsis is controversial, and further study is needed to better define sepsis markers before such scores could be included in currently available disease severity scoring systems.

USES FOR SCORING SYSTEMS IN PATIENTS WITH SEPTIC SHOCK

There are several areas in which the use of the scoring systems discussed previously can be beneficial in patients with septic shock, as in other groups of critically ill patients[49] (Table 3). First, they can be invaluable in the classification and stratification of patients for enroll-

Table 3. POSSIBLE USES FOR MORTALITY PREDICTION (TYPE I) AND ORGAN DYSFUNCTION (TYPE II) SCORING SYSTEMS

Purpose	Type of Score
Therapeutic trials	I, II
Predict survival	I, (II)
Describe severity of disease in a general population	I, II
Evaluate ICU performance	I, II
Adjunct to clinical decision making (discharge policy)	(I), (II)

ment in clinical trials of new antisepsis treatments. Mortality prediction scores can be used to stratify groups of patients and assess outcome in terms of mortality, whereas organ dysfunction scores can help evaluate the effects of new treatments on morbidity, thus providing a change in emphasis of outcome measure from mortality to morbidity. Importantly, improved morbidity must be associated with a reduced, or trend to reduced, mortality. Second, they can be used to describe patient populations in epidemiologic studies for comparison of patients over time or from different institutions. Third, estimated probabilities of mortality and actual outcomes can be compared, creating a standardized mortality ratio (SMR). SMRs from a cross-section of different ICUs or from the same ICU over time could then be used to facilitate resource allocation. Before these scores can be used to compare ICU performance in different geographical areas or populations however, they need to be customized to the local population, and their use as a management instrument is limited.[52]

Importantly, while these scores are useful in the prediction of mortality of a group of patients, they have not been validated to provide a precise prediction of the outcome of individual patients. Clinical decisions concerning individual patient care should not be made exclusively on the basis of any scoring system, although such scores may provide valuable information to be used in addition to clinical assessment.[12, 19]

SUMMARY

Sepsis is an ongoing disease process carrying a high risk of organ failure and death. Scoring systems to determine disease severity and risk of mortality may be useful in patient management and clinical trial enrollment, although the role of either type of score in the determination of admission or discharge criteria or in decisions relating to the continuation or withholding of treatment remains controversial.

General scoring systems have been developed to quantify the severity of illness and the risk of mortality in ICU patients. Ideally, these should be customized before use in patients with septic shock, but in general noncustomized models are used, and this potential limitation should be acknowledged. Prognostic scores are remarkably reliable at predicting outcome in groups of patients and give an indication of severity of disease on admission, but they are unable to provide detail on how a patient is responding to treatment or on the disease progression. Organ function scores, however, can be assessed repeatedly and used to define a patient's progress. This approach can thus be used to evaluate individual patient care, to identify patients for enrollment in clinical trials or epidemiologic analyses, and to assess morbidity measures in clinical trials of new interventions. Organ dysfunction scores are just that, descriptors of organ dysfunction, and although high values correlate well with mortality, prognostication is not their prime aim; organ dysfunction scores and outcome prediction scores should rather

be viewed as complementary systems in the description of ICU populations.

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Address reprint requests to

Jean-Louis Vincent, MD, PhD
Department of Intensive Care
Erasme University Hospital
Route de Lennik 808
1070 Bruxelles
Belgium

Email: jlvincen@ulb.ac.be