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Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study

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Abstract

Objective: To evaluate the use of the Sequential Organ Failure Assessment (SOFA) score in assessing the incidence and severity of organ dysfunction in critically ill patients.

Design: Prospective, multicenter study.

Setting: Forty intensive care units (ICUs) in 16 countries.

Patients: Patients admitted to the ICU in May 1995 (n = 1,449), excluding patients who underwent uncomplicated elective surgery with an ICU length of stay <48 hrs.

Interventions: None.

Measurements and Main Results: The main outcome measures included incidence of dysfunction/failure of different organs and the relationship of this dysfunction with outcome. In this cohort of patients, the median length of ICU stay was 5 days, and the ICU mortality rate was 22%. Multiple organ dysfunction and high SOFA scores for any individual organ were associated with increased mortality. The presence of infection on admission (28.7% of patients) was associated with higher SOFA scores for each organ. The evaluation of a subgroup of 544 patients who stayed in the ICU for at least 1 wk showed that survivors and nonsurvivors followed a different course. This subgroup had greater respiratory, cardiovascular, and neurologic scores than the other patients. In this subgroup, the total SOFA score increased in 44% of the nonsurvivors but in only 20% of the survivors ($p < .001$). Conversely, the total SOFA score decreased in 33% of the survivors compared with 21% of the nonsurvivors ($p < .001$).

Conclusions: The SOFA score is a simple, but effective method to describe organ dysfunction/failure in critically ill patients. Regular, repeated scoring enables patient condition and disease development to be monitored and better understood. The SOFA score may enable comparison between patients that would benefit clinical trials. (Crit Care Med 1998; 26:1793-1800)

Key Words: outcome; morbidity; organ failure; critically Ill; intensive care; respiratory failure; renal failure; hepatic failure; coagulation abnormalities; neurologic dysfunction; circulatory shock; circulatory failure

Clinical trials of new therapeutic interventions in sepsis have yielded frustrating results [1-5], but these trials were perhaps limited by their emphasis on mortality. While mortality remains a very important end-point of clinical trials, morbidity should also be taken into account for several reasons [6]. First, in a heterogeneous intensive care unit (ICU) population, it may be difficult to demonstrate that a new intervention has a significant impact on mortality, whereas individual organ function may benefit. Second, as organ failure may prolong the length of ICU stay and involves increased use of resources, assessment of morbidity is important for the cost-effective analysis of therapeutic interventions. Third, the ability to quantify a

complex clinical situation using simple scores may facilitate communication and appreciation of the processes involved. For example, the simple Glasgow Coma Scale [7], which is used to describe degrees of brain injury, has earned widespread acceptance as a valuable tool in patient assessment [8,9]. The same principle of simplicity should be applied to an organ failure scale. Fourth, improved assessment of morbidity may help in the identification of different patterns of organ dysfunction/failure, and thereby enhance our understanding of the disease process.

The assessment of organ dysfunction should be based on three important principles [10]. First, organ failure should not be seen as an all-or-none phenomenon, but rather as a continuum of alterations. The introduction of "acute lung injury" as a lesser degree of acute respiratory failure than full-blown acute respiratory distress syndrome [11] is in accordance with this concept. Existing systems too often describe organ failure as being either present or absent, ignoring the presence of degrees of severity between the two extremes. Second, the time course must be taken into account. Organ failure is a dynamic process and the degree of dysfunction may vary with time [12]. People who die early may not even have time to develop organ failure. Regular assessment of organ function is therefore required to enable the physician to follow the evolving disease process. Third, the description of organ dysfunction/failure should be based on simple variables, specific to the organ in question, and routinely available everywhere [13-15]. The ideal descriptors should be derived from simple, independent clinical laboratory data measuring physiologic dysfunction. Therapeutic interventions may differ between hospitals, and even between physicians within a hospital, and their use in such scores should therefore be limited. Employed parameters should be readily available in heterogeneous groups of critically ill patients. These factors will enable the score to be used widely, and facilitate comparisons between patient groups from different countries and continents.

With these principles in mind, a group of critical care physicians developed, by consensus, the so-called "Sepsis-Related Organ Failure Assessment" (SOFA) score [14] in December 1994. Since the score is not specific for sepsis, it was later called "Sequential Organ Failure Assessment." The SOFA score is composed of scores from six organ systems, graded from 0 to 4 according to the degree of dysfunction/failure (Table 1). While primarily designed to describe morbidity, a retro-spective analysis of the relationship between the SOFA score and mortality was obtained, using the European/North American Study of Severity System database [16]. This analysis indicated a good correlation of the score with survival, and also a good distribution of patients among the different score values.

	SOFA Score				
	0	1	2	3	4
Respiration					
Pao_2/Fio_2 (torr)	>400	≤400	≤300	≤200 With respiratory support	≤100 With respiratory support
Coagulation					
Platelets ($\times 10^3/mm^3$)	>150	≤150	≤100	≤50	≤20
Liver					
Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
(μmol/L)	<20	20–32	33–101	102–204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mm Hg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine >5 or epi ≤0.1 or norepi ≤0.1[a]	Dopamine >15 or epi >0.1 or norepi >0.1[a]
Central Nervous System					
Glasgow Coma Score	15	13–14	10–12	6–9	<6
Renal					
Creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
(μmol/L)	<110	110–170	171–299	300–440	>440
or urine output				or <500 mL/day	or <200 mL/day

epi, epinephrine; norepi, norepinephrine.
[a]Adrenergic agents administered for at least 1 hr (doses given are in μg/kg/min).
To convert torr to kPa, multiply the value by 0.1333.

Table 1. The Sequential Organ Failure Assessment (SOFA) score

The current study presents data from a prospective collection of 1,449 critically ill patients in 40 ICUs.

MATERIALS AND METHODS

The study was initiated within a working group of the European Society of Intensive Care Medicine. Each member of the consensus group was invited to participate in the data collection. Since this was an epidemiologic study, approval from Institutional Review Board was usually not required, but the decision to submit to the board was left to each investigator. All patients >12 yrs of age admitted to the ICU during May 1995, except those patients who stayed in the ICU for <48 hrs after uncomplicated surgery, were included in the study, a total of 1,449 patients from 40 centers (Table 2). Data were collected at the time of admission and throughout the ICU stay. The most abnormal value for each parameter in each 24-hr period was recorded. Mortality was assessed at ICU discharge. The presence or absence of infection was evaluated by the attending physician. For a single missing value (which occurred sometimes for bilirubin concentrations, more rarely for platelet count), a replacement was calculated using the mean value of the result preceding, and the result after, the missing one. When more than one consecutive result was missing, it was considered as a missing value in the analysis.

Country	No. of Centers	Patients
Australia	1	27
Austria	1	8
Belgium	3	272
Brazil	3	165
Canada	1	31
Finland	1	75
France	5	189
Germany	1	41
Greece	1	18
Israel	1	27
Italy	6	144
The Netherlands	4	74
Portugal	4	84
Spain	2	114
Switzerland	1	63
United Kingdom	5	117
Total	40	1,449

Table 2. Participating countries and numbers of patients

Data were analyzed in the Department of Computer Science of the Free University of Brussels (F.C.), using a SPSS/PC+program (Version 5.0, SPSS, Chicago, IL). Means of continuous data were compared by two-tailed Student's t-test in subgroups with normal data distribution. In subgroups with nonnormal frequency distribution (large positive skewness), nonparametric rank tests were used (Kruskal-Wallis test). Categorical data were evaluated, using the chi-square test. A Cox proportional hazards analysis was used to model time to death with the different organ systems as covariates. Results are expressed as mean +/- SD (or as median when the data distribution was not normal). A $p < .05$ was considered statistically significant.

RESULTS

The demographics of the study population are shown in Table 3. There was a mixture of medical and surgical patients. The patients' mean age was 55 yrs (range 12 to 95). Sixty-three percent of the patients were male. The median length of ICU stay was 5 days. The ICU mortality rate was 22%, with a hospital mortality rate of 26%. Figure 1 shows the distribution of survivors and nonsurvivors with time.

Number of patients	1,449
Age (yr)	55 ± 19[a]
Range	12–95
Gender (male/female)	909/524[b]
Source of Admission	
Emergency room	520 (36.0)
Hospital ward	370 (25.6)
Operating room	376 (26.0)
Other hospital	153 (10.6)
Others	30 (1.8)
Type of Admission	
Elective surgery	260 (18.0)
Emergency surgery	253 (17.5)
Trauma	181 (12.5)
Medical	641 (44.4)
Acute coronary	78 (5.4)
Others	36 (2.2)
ICU stay (day)	7.9 ± 7.8[a]
ICU mortality	313 (21.7)
Hospital mortality	377 (26.3)
DNR order	139 (9.6)
Withdrawal of support	114 (7.9)
Readmission in ICU	117 (8.1)

DNR, do not resuscitate; ICU, intensive care unit.

[a]Mean ± SD; [b]missing data (n = 16).

Numbers in parentheses indicate percentage.

Table 3. Demographics of study population

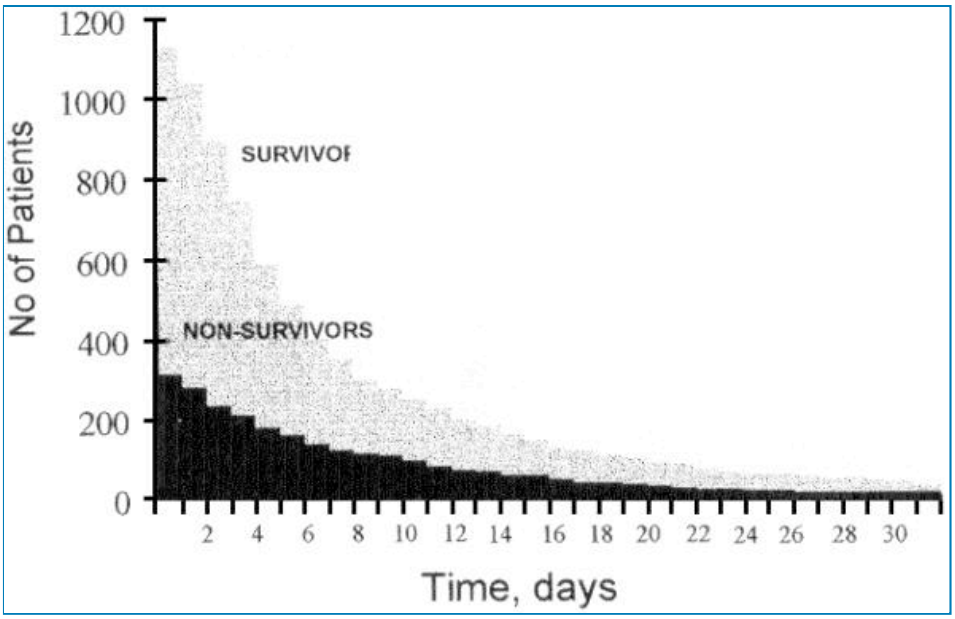

Figure 1. Intensive care unit survival. The Figure representsthe number of patients with time: survivors (light gray); nonsurvivors (dark gray).

The distribution of organ dysfunction at the time of admission is shown in Figure 2. On admission, the majority of patients had low SOFA scores for each organ system, but there were still significant numbers of patients in each group. There was an almost parallel time course between survivors and nonsurvivors for each organ score (Figure 3), and for the total SOFA score (Figure 4), with nonsurvivors consistently having greater scores. A Cox proportional hazards analysis implicated the cardiovascular, the neurologic, and the renal system (in that order of importance, each $p < .01$) in the risk of death.

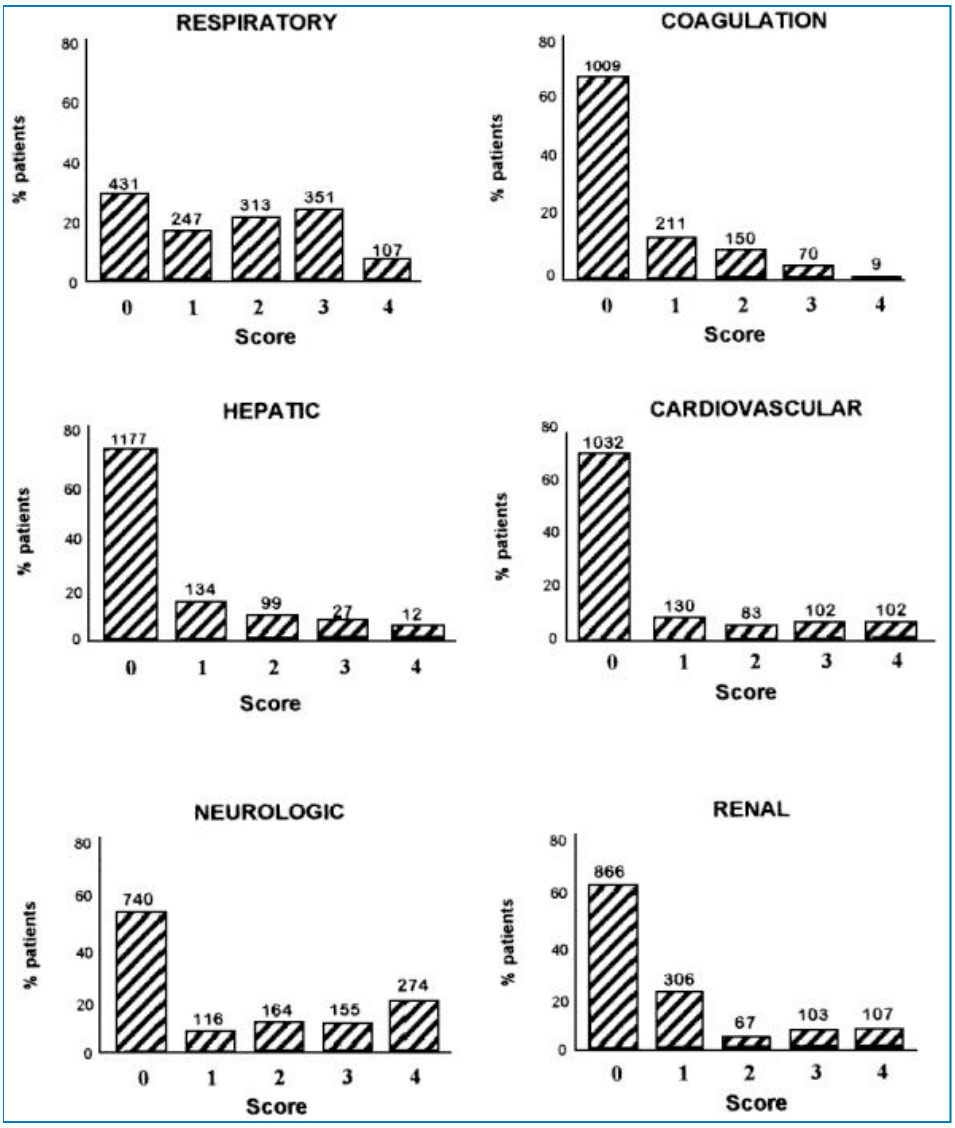

Figure 2. Number of patients associated with each Sequential Organ Failure Assessment score for each organ system at the time of intensive care unit admission.

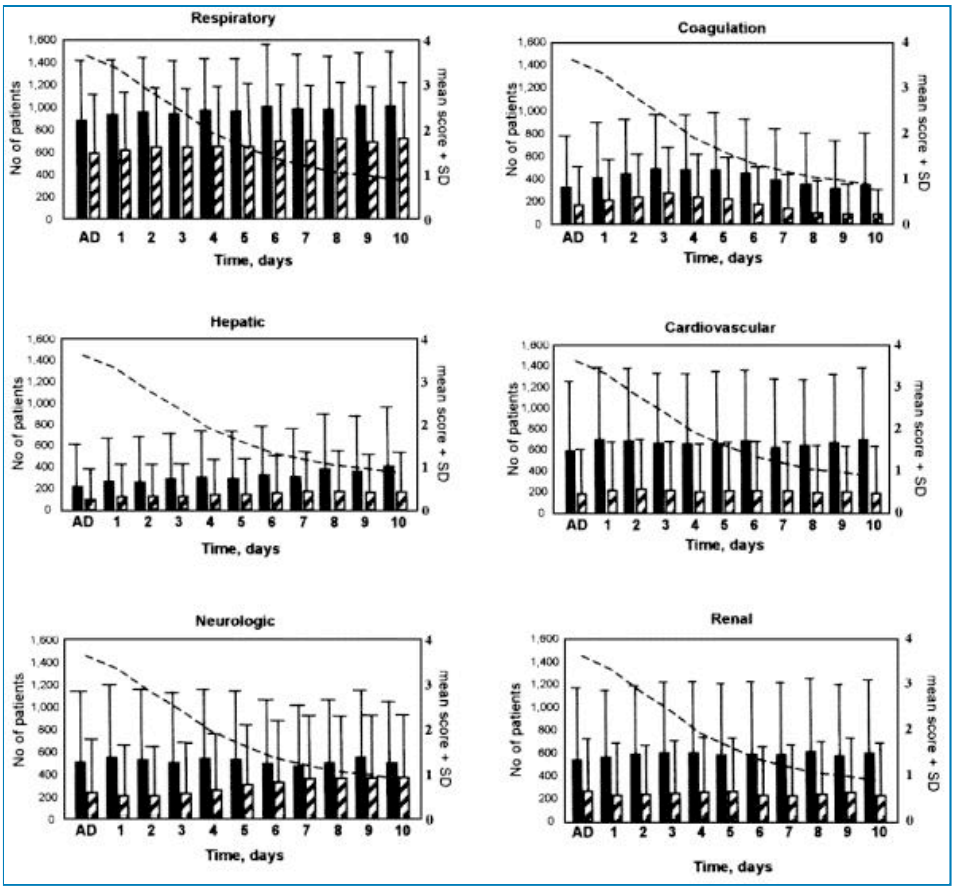

Figure 3. Mean Sequential Organ Failure Assessment scores for each organ system in nonsurvivors (solid bars) and survivors (striped bars). Dashed lines represent the total population over time. The difference between the mean scores for nonsurvivors and survivors was highly significant for all systems ($p < .01$). AD, admission day. Mean +/- SD values.

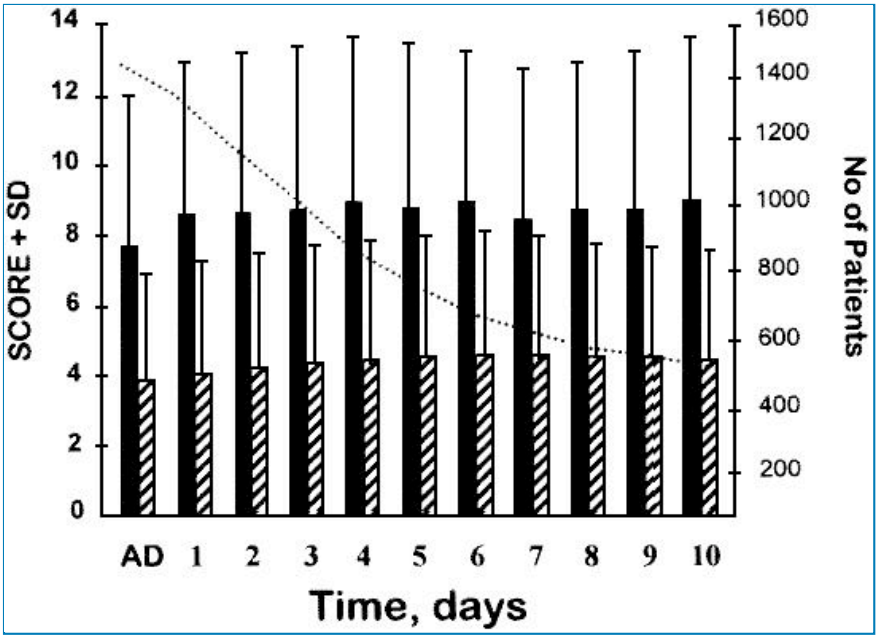

Figure 4. The mean Sequential Organ Failure Assessment score for 10 days of intensive care unit stay in survivors (striped bars, n = 1,131) and nonsurvivors (solid bars, n = 313). The dashed line shows a progressive decrease in the total number of patients with time. The difference between the mean scores from the two groups was significant ($p < .01$) (missing data, n = 5). AD, admission day. Mean +/- SD values.

A total of 544 patients stayed for at least 1 wk in the ICU. These patients had higher respiratory, cardiovascular, and neurologic scores at the time of admission than the other patients. In this subgroup of patients, 44% of the nonsurvivors increased their total SOFA score compared with only 20% of the survivors ($p < .001$). Conversely, 33% of the survivors decreased their total score compared with 21% of the nonsurvivors ($p < .001$).

For patients with organ failure, as defined by a SOFA score for any organ of >or=to3, the length of time taken to reach the highest SOFA score within one organ system was shortest for the respiratory system (2.1 +/- 3.8 days), and longest for the hepatic system (4.9 +/- 5.4 days). Mortality rates were lower in patients with organ dysfunction associated with respiratory failure vs. other combinations of organ failure. For all other combinations of organ failure, there was a narrow range of mortality rates (65% to 74%), with no discernible pattern (Figure 5).

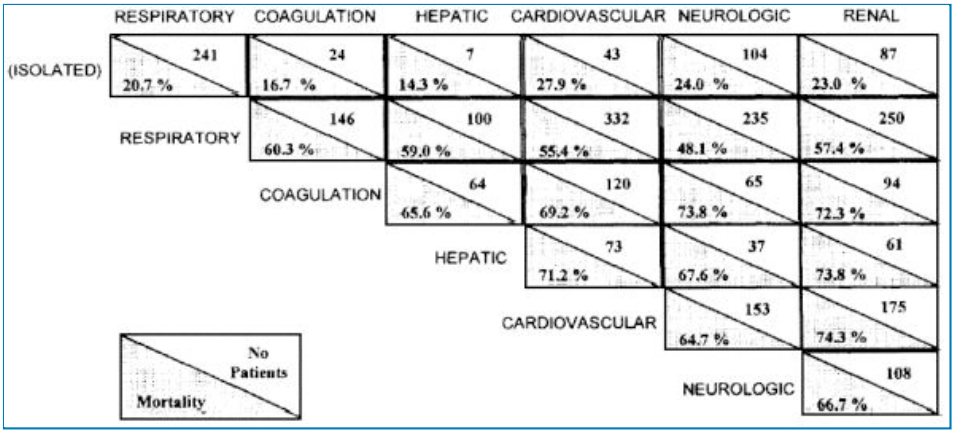

Figure 5. Relation between organ failure on admission (a Sequential Organ Failure Assessment score for any organ of >or=to3) and mortality.

Infection was identified by the physician in 28.7% of patients at the time of admission. Infected and noninfected patients followed a parallel time course. The infected patients had a more severe degree of organ dysfunction, with higher SOFA scores for each organ (data not shown). The mortality rate increased with the number of failing organs present at the time of admission (Figure 6A). The mortality rate was 9% for patients with no organ failure on admission, increasing to 82.6% for patients with four or more failing organs. The proportion of infected patients increased in groups with more failing organs (Figure 6B): 74% of patients with four failing organs were infected, compared with only 17% of patients with no organ failure.

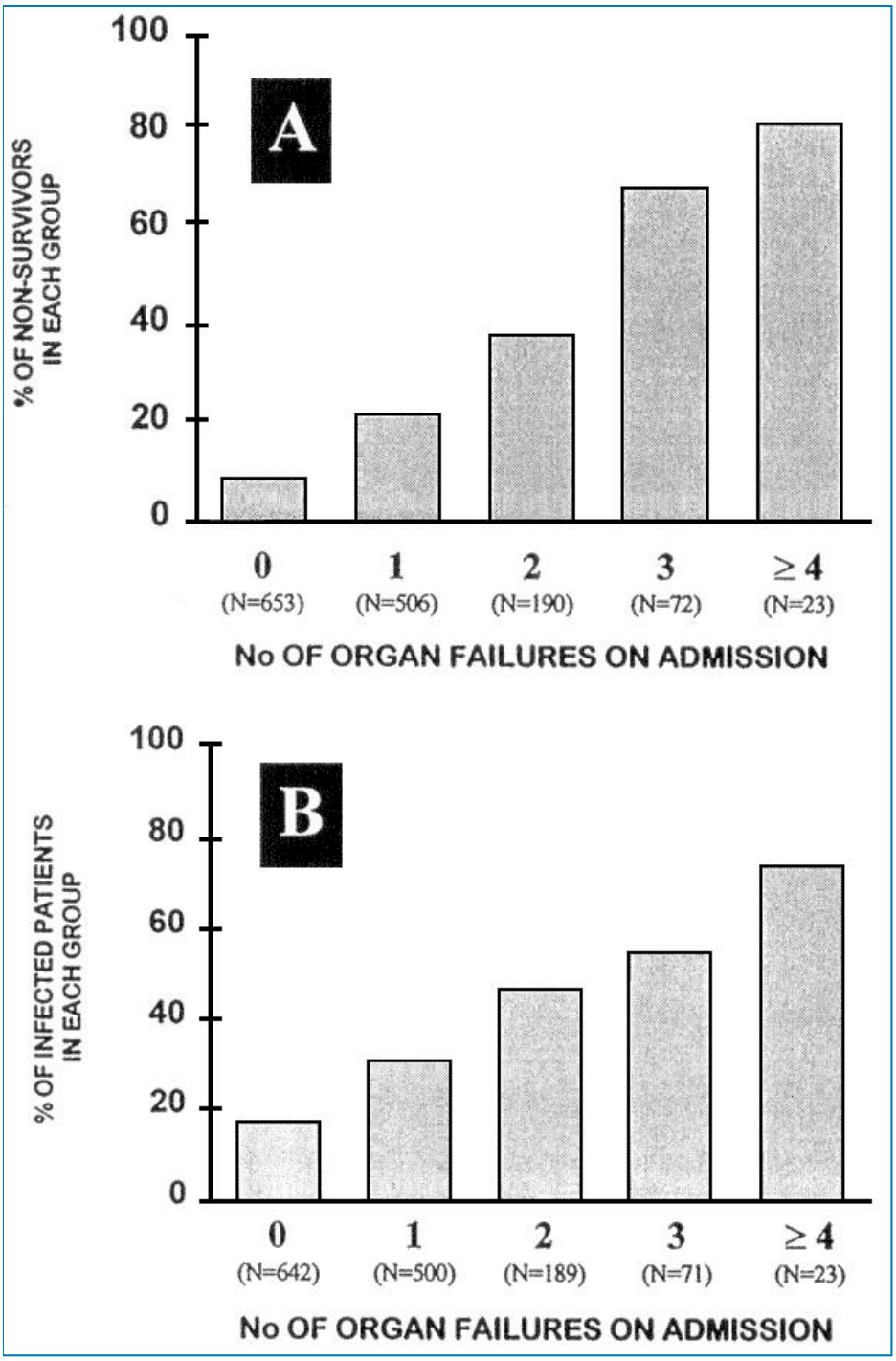

Figure 6. A) Number of failing organs on admission vs. mortality. The mortality rate was 9% in patients with no organ failure, 22% in patients with one failing organ, 38% in patients with two failing organs, 69% in patients with three failing organs, and 83% in patients with four or more failing organs (chi-square test for trend = 229, p < .00001). B) Number of failing organs on admission vs. presence of infection; 17% of patients with no organ failure were infected, 31% of patients with one failing organ were infected, 47% of patients with two failing organs were infected, 55% of patients with three failing organs were infected, and 74% of patients with four or more failing organs were infected (chi-square test for trend = 121, p < .00001).

As the maximum total SOFA score reached during the ICU stay increased, so the mortality rate increased (Figure 7). For a total score of >15, the mortality rate was 90% (sensitivity 31%, specificity 99%; correct classification 84%).

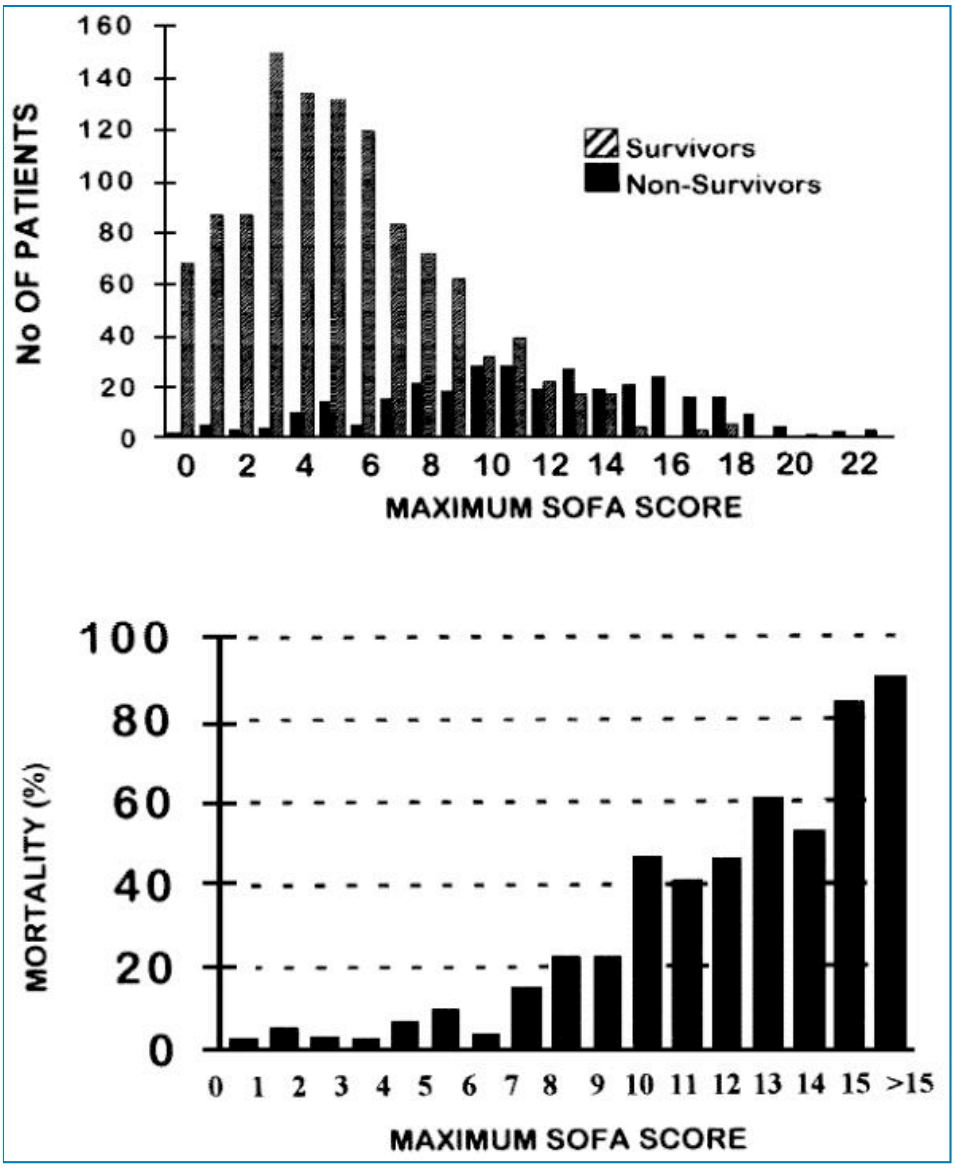

Figure 7. Maximum Sequential Organ Failure Assessment (SOFA) score and mortality. Maximum SOFA score is defined as the highest score achieved by each patient during his/her intensive care unit stay. Top: Distribution of survivors (hatched bars) and nonsurvivors (solid bars) by maximum SOFA score; bottom: mortality rate associated with maximum SOFA score. The mortality rate was >90% in patients whose maximum SOFA score was >15. A cut-off value of a maximum SOFA score of 15 had a sensitivity of 30.7%, a specificity of 98.9%, and a correct classification of 84.2%

DISCUSSION

Advances in our understanding of the pathways involved in the development of sepsis, shock, and multiple organ failure have led to the development of many potential therapies for these conditions. In assessing the efficacy and cost-effectiveness of these new therapies, it is increasingly recognized that the analysis of morbidity is important. Mortality alone is now considered insufficient for assessing ICU efficiency [17]. In postoperative patients, Ferraris and Ferraris [18] demonstrated that risk factors for morbidity are different from those for mortality, which further indicates the importance of being able to differentiate between these two outcome variables. On a more practical and economic level, the use of prognostic scores is of little value in calculating resource utilization. Patients with the highest scores tend to die quickly, and those with the lowest scores are discharged quickly. It is the patients with intermediary scores who tend to have a protracted, costly ICU course, and such scores do not identify which of these patients will survive and which will not. Most currently available scores [19,20] are aimed at predicting mortality, but more recent scoring systems, such as the SOFA score, have tried to focus on morbidity [10,13].

While the primary aim of the SOFA score is thus not to predict mortality, nevertheless, there is a relationship between organ failure and death, between morbidity and mortality. In a previous study [14], we evaluated the relationship between the SOFA score and outcome in a retrospective analysis. In this study, we extended those findings, comparing scores for ICU survivors and nonsurvivors in a prospective evaluation. Overall, we noted a somewhat higher mortality rate and length of ICU stay than has been observed in other studies [21,22], but this finding might have resulted because we excluded patients admitted after uncomplicated elective surgery.

The total SOFA score discriminated survivors from nonsurvivors very well, and was clearly related to outcome. However, the use of an aggregate score could be hazardous, as we cannot ascertain that each patient's total score carries the same weight. For instance, a total score of 4 could represent severe failure of one organ, but also moderate failure of two organs, or mild failure of four organs. It is difficult to determine which of these scores carries a better outlook. The SOFA score is primarily a means of describing organ dysfunction, of characterizing the degree of dysfunction of individual organ systems, not merely reporting a global number offering no information about individual organ status. Since the limits of each organ score were defined by a consensus rather than based on data analysis [14], it was important to determine the distribution of patients in the different organ groups for validation. Although only a minority of patients had severe thrombocytopenia or hyperbilirubinemia, enough patients were present in each category to allow a meaningful analysis.

From the data obtained, it was apparent that respiratory dysfunction was more common than dysfunction of the other organs. This finding may, in part, be inherent to the parameter used in the score to assess the respiratory system (e.g., the $PaO_{2/FIO2}$ ratio is a sensitive measure of respiratory function). The high sensitivity of this parameter may also account for the finding that patients with respiratory failure reached their highest SOFA score much more rapidly than patients with hepatic failure. The increase in bilirubin concentration takes time and liver failure may therefore be recognized more slowly than respiratory failure. When two organ systems were failing, as defined by a SOFA score of 3 or 4, the presence of respiratory failure as one of the two failing systems was associated with a lower mortality rate than any other combination. For combinations of other organs, there was a narrow range of mortality (65% to 74%), and no identifiable pattern of increased risk with any specific organ. This situation therefore excludes the possibility that one organ system overly influences the SOFA score, since, if this were the case, one would expect a higher mortality when failure of this particular organ was present.

Most prognostic scoring systems rely on a single analysis of patient data to calculate mortality risk. The importance of repeated scoring, allowing serial patient assessment and enabling measurement of resource utilization, has been noted by several groups [10,12,22,23]. Regular data collection will also assist in the evaluation of new therapies. A first-day severity score may, however, lose its predictive value in patients with longer ICU stays, as the course of ICU stay is unpredictable and can negatively influence the performance of such scores [24]. Predictive scores give no information about individual organ function, and newer scores have focused more on the objective assessment of organ dysfunction. Recently, one such score, based on a sophisticated statistical analysis, has been proposed by Le Gall et al [15]. However, the principle of the Logistic Organ Dysfunction System score is different from the SOFA score, even though both scores describe organ dysfunction. The Logistic Organ Dysfunction System score is more complex, combines the level of dysfunction of all organs in a global score, and is calculated only on the day of admission.

The main difference between the SOFA score and other recent scores [10,13] developed to describe organ dysfunction is in their definitions of cardiovascular dysfunction. Multiple Organ Dysfunction Score [10] uses a derived parameter, the pressure-adjusted heart rate, calculated as the product of the heart rate and the ratio of the central venous pressure to the mean arterial pressure. This derived parameter removes the simplicity of the score and the bedside availability. The Brussels score [13] uses hypotension and acidemia as their guide to cardiovascular dysfunction but acidemia may be due to other factors, including renal failure. Another difference between the scoring systems is that the SOFA score introduces the requirement for respiratory support in respiratory failure and oliguria as a possible criterium for renal failure.

Organ dysfunction is a dynamic process, and the simplicity of the SOFA score and the parameters used makes repeated measures an easy task. Calculating the score is straightforward, and the use of computerized systems with automatic data collection may make it even easier. To the clinician, the ability to follow patient progress and disease development is of value and, in this study, scores were calculated every day. Survivors and non-survivors followed an almost parallel SOFA score course, but the non-survivors had a more severe degree of organ dysfunction from the time of ICU admission. This analysis was potentially affected by the continuous turnover of patients on the ICU, with patients leaving the unit at various times, either because they died or were discharged. We therefore analyzed a subgroup of patients who remained in the ICU for at least 1 wk. In this subgroup also, a greater degree of organ dysfunction was noted in the nonsurvivors. A prolonged ICU stay could be predicted at the time of admission on the basis of the dysfunction of those organ systems that generally require more prolonged ICU support, that is, cardiovascular, respiratory, and neurologic systems.

Infected patients consistently showed a greater degree of organ dysfunction for all organ systems, which supports the widely acknowledged relationship between sepsis and multiple organ failure. We were not able to identify any particular pattern of organ dysfunction in the infected patients. We focused on the presence of infection, as this disease indicator is more clear-cut than sepsis. Also, since defining the exact time of the onset of infection during the ICU stay can be problematic, we just recorded the presence or absence of infection at the time of admission. Although we initially called the score "sepsis-related," the data show that the SOFA score is not specific to sepsis and can be applied equally to the nonseptic patient, so that we now prefer to refer to "sequential" organ failure assessment.

The SOFA score remains a gross evaluation, but this is the only way to keep it simple and widely available. Using more sophisticated parameters may restrict its use to centers where such tests are routinely used, or may result in missing data. In this study, except for some bilirubin concentrations, there were very few missing data. Despite the potential limitations imposed by its simplicity, the SOFA score can serve several purposes. First, it could be useful in clinical trials, as there is increasing awareness that mortality should not be the only outcome measure. Survival is influenced by so many factors that it may be difficult to show the significant impact of new therapeutic interventions on mortality, whereas these interventions may have a significant impact on individual organ function. The ability to separate the analysis of various organ systems, and describe individual organ dysfunction over time, could enable us to identify the benefits of new therapies that have remained hidden by previous outcome scoring systems. Second, the SOFA score may be used to characterize groups of patients for comparison in trials and for epidemiologic analysis. Third, the SOFA score may be used to describe the time course of organ dysfunction in individual patients. Such an analysis may help to identify patterns of organ dysfunction development

and promote a better understanding of the pathophysiology of such a clinically important problem. We believe this scoring system is a useful tool for clinical trials and also for the ICU physician in day-to-day patient assessment.

Appendix 1. Participating centers

Erasme University Hospital, Brussels, Belgium (J.L. Vincent); Universita La Sapienza, Rome, Italy (M. Antonelli); Hospital Santa Maria delle Grazie, Naples, Italy (E. de Blazio); Universitatsklinik fur Chirurgie, Vienna, Austria (M. Rogy); Klinik Friedrich-Schiller University, Jena, Germany (K. Rienhardt); Charing Cross Hospital, London, UK (M. Palazzo); Hospital Geral Santo Antonio, Porto, Portugal (A. Marinho); C.H.U. Vaudois, Lausanne, Switzerland (M. Glauser); University Catholique del Sacro Cuore, Rome, Italy (G. Sganga); University Hospital, Ghent, Belgium (F. Colardyn); University Hospital, Milan, Italy (A. Pesenti); H.G.U. Vall d'Hebron, Barcelona, Spain (A. Salgado); Hopital St Joseph, Paris, France (J. Carlet); University Hospital, Kuopio, Finland (J. Takala); Ospedale Maggiore di Milano, Milan, Italy (M. Langer); Hadassah Hebrew University Medical Center, Jerusalem, Israel (C. Sprung); Free University Hospital, Amsterdam, the Netherlands (L.G. Thijs); Cattinara Hospital, Trieste, Italy (A. Gullo, G. Berlot); UCIP Guimaraes, Guimaraes, Portugal (M. Lafuente); Academisch Ziekenhuis, Nijmegen, the Netherlands (J. Goris); Academic Hospital Dijkzigt, Rotterdam, the Netherlands (H. Bruining); Complexo Hospitalar Santa Casa, Porto Alegre, Brazil (G. Friedman); Hopital Boucicaut, Paris, France (J. Labrousse); Western General Hospital, Edinburgh, United Kingdom (I. Grant); Hospital de Santo Antonio dos Capuchos, Lisbon, Portugal (R. Moreno); Bristol Royal Infirmary, Bristol, United Kingdom (S. Willats); KAT General Hospital, Athens, Greece (H. Ioanidou); C.H.U. de Nantes, Nantes, France (D. Villers); Casa de Saude Santa Marcelina, Sao Paulo, Brazil (S. Blecher); Guy's Hospital, London, UK (R. Beale); UCIP Santo Antonio, Porto, Portugal (A. Carneiro); St Elizabeth Ziekenhuis, Tilburg, the Netherlands (L. Leenen); University Hospital, Manchester, UK (P. Nightingale); Royal Prince Alfred Hospital, Sydney, Australia (S. Smith); C.H.U. de Liege, Liege, Belgium (P. Damas); C.H.R.U. de Marseille, Marseille, France (C. Martin); Hospital Israelita Albert Einstein, Sao Paulo, Brazil (E. Knobel); The Toronto Hospital, Toronto, ON, Canada (J.C. Marshall); Hospital General de Castellon, Castellon, Spain (A. Abizanda); C.H.U. Cochin Port Royal, Paris, France (J.F. Dhainaut).

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