Intensive Care Med (2000) 26: 1037–1045

ORIGINAL

U. Janssens
C. Graf
J. Graf
P. W. Radke
B. Königs
K. Ch. Koch
W. Lepper
J. vom Dahl
P. Hanrath

Evaluation of the SOFA score: a single-center experience of a medical intensive care unit in 303 consecutive patients with predominantly cardiovascular disorders

Received: 6 August 1999
Final revision received: 3 January 2000
Accepted: 28 March 2000

U. Janssens (✉) · C. Graf · J. Graf · P. W. Radke · B. Königs · K. C. Koch · W. Lepper · J. vom Dahl · P. Hanrath
Medical Clinic I,
University Hospital of Aachen,
Pauwelsstrasse 30, 52057 Aachen,
Germany
e-mail: ujan@pcserver.mk1.rwth-aachen.de
Tel.: + 49-241-8089669
Fax: + 49-241-8888414

Abstract *Objective*: To evaluate the use of the Sequential Organ Failure Assessment (SOFA) score, the total maximum SOFA (TMS) score, and a derived variable, the ΔSOFA (TMS score minus total SOFA score on day 1) in medical, cardiovascular patients as a means for describing the incidence and severity of organ dysfunction and the prognostic value regarding outcome.
Design: Prospective, clinical study.
Setting: Medical intensive care unit in a university hospital.
Patients: A total of 303 consecutive patients were included (216 men, 87 women; mean age 62 ± 12.6 years; SAPS II 26.2 ± 12.7). They were evaluated 24 h after admission and thereafter every 24 h until ICU discharge or death between November 1997 and March 1998. Readmissions and patients with an ICU stay shorter than 12 h were excluded.
Main outcome measure: Survival status at hospital discharge, incidence of organ dysfunction/failure.
Interventions: Collection of clinical and demographic data and raw data for the computation of the SOFA score every 24 h until ICU discharge.
Measurements and main results: Length of ICU stay was 3.7 ± 4.7 days. ICU mortality was 8.3 % and hospital mortality 14.5 %. Nonsurvivors had a higher total SOFA score on day 1 (5.9 ± 3.7 vs. 1.9 ± 2.3, $p < 0.001$) and thereafter until day 8. High SOFA scores for any organ system and increasing number of organ failures (SOFA score ≥ 3) were associated with increased mortality. Cardiovascular and neurological systems (day 1) were related to outcome and cardiovascular and respiratory systems, and admission from another ICU to length of ICU stay. TMS score was higher in nonsurvivors (1.76 ± 2.55 vs. 0.58 ± 1.39, $p < 0.01$), and ΔSOFA/total SOFA on day 1 was independently related to outcome. The area under the receiver-operating characteristic curve was 0.86 for TMS, 0.82 for SOFA on day 1, and 0.77 for SAPS II.
Conclusions: The SOFA, TMS, and ΔSOFA scores provide the clinician with important information on degree and progression of organ dysfunction in medical, cardiovascular patients. On day 1 both SOFA score and TMS score had a better prognostic value than SAPS II score. The model is closely related to outcome and identifies patients who are at increased risk for prolonged ICU stay.

Key words Severity of illness index · Multiple organ failure · Critically ill · Morbidity · Organ failure · Outcome

Introduction

Although mortality continues to be a leading endpoint of clinical research, morbidity allows the impact of intensive care to be assessed on quality of life, length of ICU, and length of hospital stay, and costs and is considered to be the paramount outcome measure [1]. While mortality is a hard primary endpoint, morbidity offers other advantages in outcome research [1]; for example, individual organ functions may benefit from new interventions and therefore assessment of morbidity is important for cost-effectiveness analysis of new treatment modalities. Moreover, it may improve our understanding of the natural history of organ dysfunction and the interaction between the failure of one organ and that of others [2,3]. Instruments for the scoring of illness severity, such as Acute Physiology And Chronic Health Evaluation (APACHE) II and III [4,5], Simplified Acute Physiology Score (SAPS) II [6], are widely used in critically ill patients. More recently the Sequential Organ Failure Assessment (SOFA) score [3] has been developed and validated. Although the SOFA score was originally a tool for describing the severity of organ dysfunction, Vincent et al. have demonstrated in both retrospective [3] and prospective studies [1] that high SOFA score for any individual organ is associated with increased mortality.

Different patient groups may develop different patterns of organ dysfunction. Little is known about the distribution and time course of organ failure in cardiovascular patients. Therefore the primary objective of this prospective study was to evaluate the SOFA score in predominantly cardiovascular patients of a medical intensive care unit with respect to (a) the pattern of organ dysfunction and (b) the discrimination of survivors and nonsurvivors in this particular patient population. Secondary endpoints were (a) the additional information gained by the recently introduced total maximum SOFA score (TMS) and the ΔSOFA score [7], i.e., difference in TMS and admission SOFA score and (b) the association of SOFA score with length of ICU stay.

Materials and methods

Our medical ICU is a 12-bed unit serving a 1480-bed university hospital with a catchment area population of 1.2 million. Predominantly patients with cardiovascular and pulmonary diseases are admitted. All consecutive patients who stayed longer than 12 h in the ICU were included in the study between November 1997 and February 1998; readmissions and patients with an ICU stay shorter than 12 h were excluded. A total of 303 patients were investigated (216 men, 87 women; mean age 62 ± 12.6 years; SAPS II 26.2 ± 12.7; Table 1). The Institutional Review Board waived the need for informed consent since this was an epidemiological study.

SOFA score and SAPS II were determined 24 h after admission according to the published mode of data assessment [3,6]. Thereafter SOFA score was assessed daily. The worst values for each parameter int any 24 h period were recorded. All data were collected by a single experienced investigator (C. G.). The data were retrieved at the same time each day from the patient chart and entered into a palm top computer system directly at the bedside. The time to collect the raw data for the SOFA score and SAPS II score was assessed on 7 consecutive days and took an average of 182 ± 52 s per day and patient, based on 87 evaluated data sets. A random check carried out once a week by one of the authors (J. G.) was used to eliminate errors in the data collection and transferring processes. Any observed inconsistency was then corrected. If correction was impossible because of inconsistent or missing data in the patient chart the parameter was considered a missing value according to the original publication on each system. For further analysis spreadsheets containing all data were transferred into a desktop computer system. ICU/hospital length of stay and mortality was assessed at ICU and hospital discharge. Organ failure was defined by a SOFA score of 3 or higher. Maximum organ failure scores were calculated for all the six components of the system during the entire ICU stay. The aggregate score (TMS score) was calculated by summing the worst scores for each of the organ systems [7]. The ΔSOFA was computed by substracting the total SOFA score at admission from the total maximum SOFA score.

All statistical tests were two-tailed, and a significance level of $p = 0.05$ or less was used except when otherwise stated. Descriptive statistics included mean and SD values except when otherwise stated. All variables were tested for normal distribution by the Kolmogorov-Smirnov test. Student's t test was used for comparisons of means of continuous variables and normally distributed data. A nonparametric rank test (Mann-Whitney U test) was used in the case of nonnormally distributed data. Categorical data were tested using the χ^2 statistic, with Yates' correction when appropriate. The effect of the various organ systems (day 1), gender, age, type of admission, and diagnostic categories on the risk of hospital death was evaluated with Cox' proportional hazards nonstepwise regression analysis. The effect of maximum SOFA score for each organ system on outcome in the hospital was also tested with the same method. Finally, total SOFA score on day 1 and ΔSOFA were the independent variables in a logistic regression model with hospital outcome as the dependent variable [7]. The impact of each variable (day 1) on the length of ICU stay was analyzed with multiple stepwise regression analysis. The area under the receiver operating characteristic (AUROC) curve was utilized for discrimination, for example, ability of SAPS II and SOFA score on day 1, TMS score, and ΔSOFA to discriminate between patients who lived and patients who died, as proposed by Hanley and McNeil [8]. The comparison of the AUROC curve used the Z statistic with correction for correlation introduced by studying the same sample [9]. Data were analyzed using SPSS 8.0 (SPSS, Chicago, Ill., USA), and AUROC analysis was performed with MedCalc 4.16a (F. Schoonjans, Ghent, Belgium). A retrospective power calculation demonstrated sufficient power on days 1–3 (99%, 95%, and 80%, respectively). Due to the overall low mortality rate, the study was slightly underpowered from day 4 on.

Results

The overall ICU mortality rate was 8.3% and hospital mortality 14.5%. Nonsurvivors differed significantly from survivors with regard to sex and length of ICU stay. Diagnostic categories and type of admission demonstrated divergent mortality rates. Nonsurvivors had

Table 1 Demographic data of study population

	All (n = 303)	Survivors (S) (n = 259)	Non-Survivors (NS) (n = 44)	ICU mortality	Hospital mortality
Age (years) (mean ± SD)	62.4 ± 12.6	62.2 ± 12.7	64.1 ± 11.9	25 (8.3)	44 (14.5)
Gender male, n (%)	216 (71.3)	191 (73.7)	25 (56.8)	15 (6.9)	25 (11.6)
Age (years) (mean ± SD)	61.1 ± 11.7	61.1 ± 11.6	61.4 ± 12.9	n. a.	n. a.
Gender female, n (%)	87 (28.7)	68 (26.3)	19 (43.2)	10 (11.5)	19 (21.8)[b]
Age (years) (mean ± SD)	65.7 ± 14.1[a]	65.2 ± 15.1[a]	67.6 ± 9.8	n. a.	n. a.
ICU stay (day) (mean ± SD [min–max])	3.7 ± 4.7 [1–36]	3.3 ± 3.9 [1–36]	6.1 ± 7.3 [1–27]	n. a.	n. a.
Median (25 th/75 th percentile)	2 (1/4)	2 (1/3)	3 (1/7.5)[c]		
Hospital stay (day) (mean ± SD [min–max])	15.2 ± 13.2 [1–79]	15.4 ± 13.1 [1–79]	13.7 ± 14.0 [1–58]	n. a.	n. a.
Median (25 th/75 th percentile)	11 (6/20)	12 (7/19)	8 (3/22)		
SAPS II (mean ± SD)	26.2 ± 12.7	23.9 ± 9.1	40.2 ± 19.8[d]	n. a.	n. a.
SAPS II predicted risk of death (%) (mean ± SD)	11.6 ± 17.0	8.1 ± 10.0	32.1 ± 30.5[d]	n. a.	n. a.
Diagnostic categories, n (%)					
Acute myocardial infarction	76 (25.1)	71 (27.4)	5 (11.4)	2 (2.6)	5 (6.6)
Unstable angina	31 (10.2)	31 (12.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arrhythmia	31 (10.2)	31 (12.0)	0 (0.0)	0 (0.0)	0 (0.0)
Left heart failure	29 (9.6)	27 (10.5)	2 (4.5)	0 (0)	2 (6.9)
Cardiomyopathy	21 (9.6)	15 (5.8)	6 (13.6)	1 (4.8)	6 (28.6)
Cardiogenic shock	17 (5.6)	7 (2.7)	10 (22.7)	8 (47.1)	10 (58.8)
Cardiopulmonary resuscitation	17 (5.6)	4 (1.5)	13 (29.5)	10 (58.8)	13 (76.5)
Respiratory failure	13 (4.3)	12 (4.6)	1 (2.3)	0 (0.0)	1 (7.7)
Pulmonary embolism	9 (3.0)	6 (2.3)	3 (6.8)	3 (33.3)	3 (33.3)
Sepsis	8 (2.6)	7 (2.7)	1 (2.3)	1 (12.5)	1 (12.5)
Aortic dissection	3 (1.0)	1 (0.4)	2 (0.7)	0 (0.0)	2 (66.7)
Myocarditis	2 (0.7)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Others	46 (15.2)	45 (17.4)	1 (2.3)[e]	0 (0.0)	1 (2.3)
Source of admission					
Direct	88 (29.0)	70 (27.0)	18 (40.9)	15 (17.0)	18 (20.5)
Hospital ward	112 (37.0)	102 (39.4)	10 (22.7)	3 (2.7)	10 (8.9)
Other hospital	73 (24.1)	65 (25.1)	8 (18.2)	2 (2.7)	8 (11.0)
Other icu	19 (6.3)	12 (4.6)	7 (15.9)	5 (26.3)	7 (36.8)
Operating room	11 (3.6)	10 (3.9)	1 (2.3)[f]	0 (0.0)	1 (9.1)

n = number of patients; SD = standard deviation; los = length of stay; [a] $p < 0.05$ female older than male pts; [b] mortality rate female higher vs. male pts (chi-square test with continuity correction = 4.47, df = 1, $p = 0.034$); [c] $p < 0.05$ ICU stay longer in NS; [d] $p < 0.0001$ SAPS II and SAPS II predicted mortality rate higher in non-survivors; [e] mortality rate within diagnostic categories (chi-square test = 114, df = 12, $p < 0.0001$); [f] mortality rate within source of admission (chi-square test = 13.95, df = 4, $p = 0.007$)

a higher total SOFA score on day 1 (5.9 ± 3.7 vs. 1.9 ± 2.3, $p < 0.001$) and thereafter until day 8 (Fig. 1). The distribution of SOFA scores for each organ system is displayed in Fig. 2. There were almost no hepatic organ complications during the first few days. In addition to, the neurological and coagulation systems contribute negligibly to the overall score. Patients with cardiovascular ($n = 64$) and respiratory ($n = 53$) organ failure had the highest scores within 1.7 ± 1.9 days (1; 1–2) and 1.5 ± 0.9 (1; 1–2) days, respectively. Neurological ($n = 18$) organ failure took place after 4.5 ± 3.2 days (4; 1–7) and coagulation ($n = 9$) after 3.4 ± 2.2 days (3; 1–4). Increasing SOFA score for any organ was associated with raising mortality over time (Table 2). Cardiovascular organ failure occurred in 45 patients (14.8 %) [25 patients (12.5 %)] 24 h [48 h] after admission, renal failure in 31 (10.2 %) [13 (6.5 %)], respiratory failure in 28 (9.2 %) [13 (6.5 %)], severe neurological dysfunction in 5 (1.6 %) [2 (1.0 %)], and severe coagulation disorder in 5 (1.6 %) [3 (1.5 %)]. There was no liver failure at this time point. Moreover, mortality increased with growing number of organ failures (Fig. 3).

SOFA score for cardiovascular and respiratory system on day 1 and admission to the ICU from another ICU were associated with a longer ICU stay (Table 3). Neither renal, coagulatory, hepatic, or neurological organ systems nor the other types of admission were associated with length of ICU stay. Cox' proportional hazard analysis showed that risk of death increased by 1.45

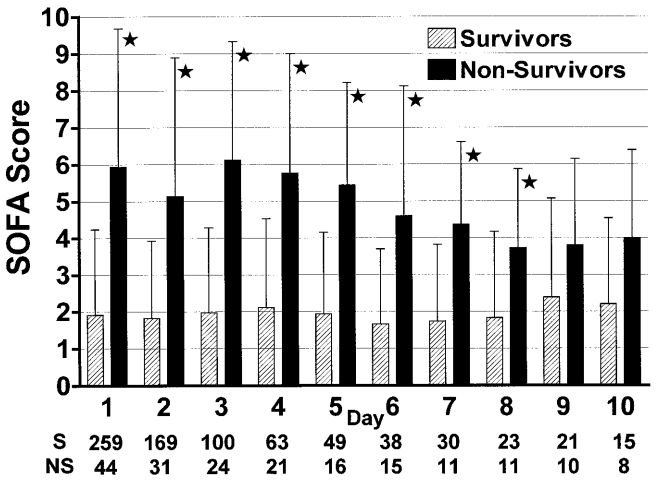

Fig. 1 SOFA score (mean ± SD) on days 1–10 in survivors (*S*) and nonsurvivors (*NS*). *Stars* $p < 0.05$, NS vs. S

(1.17–1.81, 95 % CI) with each point in the cardiovascular system on day 1 and by 1.35 (1.03–1.77, 95 % CI) with each point in the neurological system. The other organ systems were not associated with risk of death. Moreover, men had a significantly lower probability of death than women (risk ratio 0.48; 0.24–0.97, 95 % CI]). Within diagnostic categories, the following were linked with a significantly increased risk of death: cardiogenic shock (risk ratio 19.1; 2.4–151.1, 95 % CI), cardiopulmonary resuscitation (risk ratio 40.4; 5.3–309.8, 95 % CI), cardiomyopathy (risk ratio 10.2; 1.2–84.7, 95 % CI), and aortic dissection (risk ratio 31.6; 2.8–349.4, 95 % CI).

TMS and ΔSOFA scores for each organ system are shown in Table 4. Nonsurvivors had significantly higher scores than survivors. The TMS score developed 1.6 ± 1.5 days after admission. The time to reach the maximum score was 1.2 days (1.1–1.2, 95 % confidence interval) for the cardiovascular and 1.3 days (1.1–1.4, 95 % confidence interval) for the neurological system. Cox' nonstepwise regression hazard analysis demonstrated that maximum SOFA scores for the hepatic, cardiovascular, and respiratory systems were linked significantly to the risk of death (Table 5). Additionally, SOFA score on day 1 [risk ratio 1.310 (1.211–1.418, 95 % CI) and ΔSOFA [risk ratio 1.353 (1.196–1.532, 95 % CI)] were closely related to outcome.

Mortality discrimination by total SOFA score on day 1, TMS score, and SAPS II was reliable. The AUROC curve value for total SOFA score on day 1 was 0.82 ± 0.04, for TMS score 0.86 ± 0.03, and for SAPS II 0.77 ± 0.04 (Fig. 4) without significant differences between the two scores. Discrimination by ΔSOFA score was insufficient (AUROC curve value 0.62 ± 0.05) and diverged significantly from SOFA, TMS, and SAPS II ($p < 0.05$).

Table 2 Statistical analysis of mortality rate vs. SOFA score for each organ system on days 1–6

	χ^2	df	*p*
Respiratory			
Day 1	41	4	0.0001
Day 2	37	4	0.0001
Day 3	37	4	0.0001
Day 4	23	4	0.0001
Day 6	17	4	0.002
Coagulation			
Day 1	8.4	3	0.038
Day 5	14.1	4	0.007
Hepatic			
Day 2	17.4	3	0.001
Day 3	12.8	2	0.002
Cardiovascular			
Day 1	70	4	0.0001
Day 2	24	4	0.0001
Day 3	24	4	0.0001
Day 4	14.4	4	0.006
Day 5	11.7	4	0.02
Day 6	9.9	4	0.041
Neurological			
Day 1	38	3	0.0001
Day 2	17.5	4	0.002
Day 4	7.9	3	0.047
Day 5	13.5	4	0.009
Renal			
Day 1	16.6	4	0.002
Day 2	12.5	4	0.014
Day 3	16	4	0.003
Day 5	10.3	4	0.036
Day 6	9.6	4	0.047

Table 3 Multiple linear regression analysis with length of ICU stay as the response variable. SOFA score day 1 for the cardiovascular/respiratory system and the type of admission (from another ICU) are the explanatory variable

Variable	β	SE	95 % CI	p values
SOFA score day 1				
Cardiovascular	0.750	0.226	0.305 to 1.196	0.001
Respiratory	0.714	0.243	0.236 to 1.192	0.004
Admission from another ICU	3.322	1.095	1.167 to 5.477	0.003

β, coefficient; SE, standard error; 95 % CI, 95 % confidence interval

Discussion

The development of several scoring systems has provided the intensive care physician the ability to accurately and reliably measure severity of illness in the ICU. The majority of scoring systems focus on mortality as the main outcome measure. In view of limited resources and curtailed reimbursement, coupled with growing questions about the efficacy of ICU care, it has been

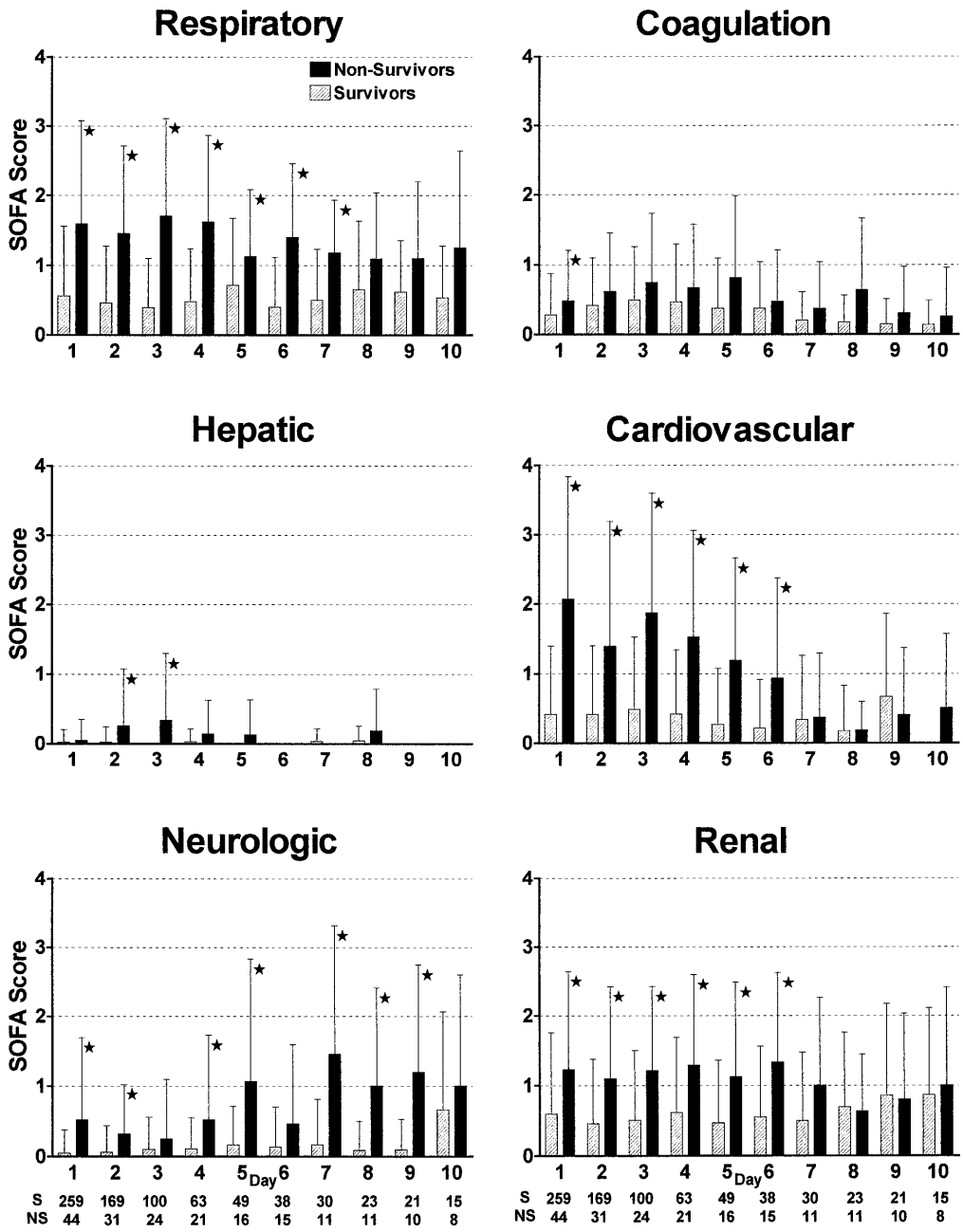

Fig. 2 SOFA (mean ± SD) score on days 1–6 for each organ system in survivors (*S*) and nonsurvivors (*NS*). *Stars* $p < 0.05$, NS vs. S

suggested that appraisal of morbidity should be the paramount target.

Multiple organ failure (MOF), or the multiple organ dysfunction syndrome [10], is a process rather than an event and develops as a consequence of progressive physiological dysfunction in organ systems. The emergence of MOF as a major threat to the survival of patients in the ICU has followed improvements in the ability to support organ function during and immediately after life-threatening illnesses that would previously have been associated with death in the short term [2]. Compared to those today, initial definitions of MOF were subjective, and single-organ failure was defined in various ways. The resulting lack of reproducibility of objective physiological measurements of single-organ dysfunction confounded determination of the incidence of MOF across studies [11]. Therefore several authors developed novel scoring systems to quantify the severity of MOF as an outcome measure in critical illness [3, 12,13].

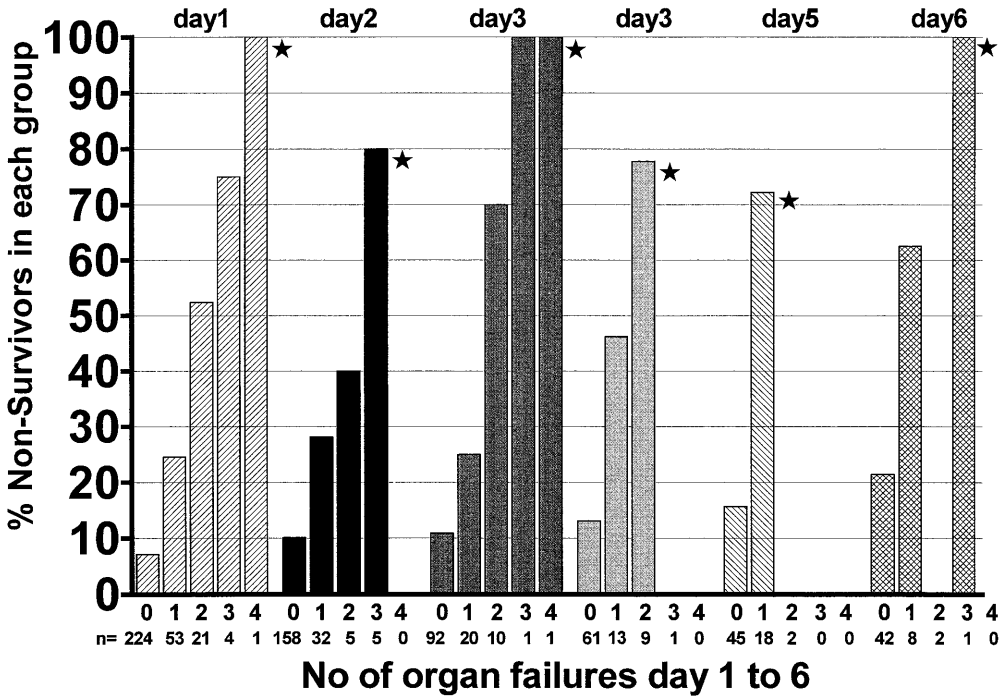

Fig. 3 Mortality rate (%) and number of failing organs on days 1–day 6. *Stars* χ^2 test for trend with continuity correction: day 1 $\chi^2 = 65$, df = 4, $p < 0.0001$; day 2 $\chi^2 = 25$, df = 3, $p < 0.0001$; day 3 $\chi^2 = 29$, df = 4, $p < 0.0001$; day 4 $\chi^2 = 21$, df = 3, $p < 0.0001$; day 5 $\chi^2 = 30$, df = 2, $p < 0.0001$; day 6 $\chi^2 = 8.9$, df = 3, $p = 0.03$)

The main finding of our prospective study is that the SOFA score characterizes the progress of MOF in cardiovascular patients of a medical intensive care unit.

SOFA score

Vincent et al. [3] introduced the SOFA score in 1996 on behalf of the working group on sepsis of the European society of intensive care medicine [3]. The relationship between the SOFA score on ICU admission and mortality was studied retrospectively in 1643 patients with sepsis. Patient prognosis was related to the initial score. Data of a prospective multicenter study with 1449 medical/surgical patients corroborated these findings [1]. Antonelli and coworkers [14] analyzed retrospectively all 181 trauma patients in this dataset and demonstrated that the SOFA score was reliable in this subgroup in identifying categories of patients at major risk of prolonged ICU stay or death [14]. The results of our study strongly support the SOFA score as an excellent tool for assessing the extent of organ dysfunction not only in patients with sepsis and those after surgery or trauma but also in medical cardiovascular patients. The total

Table 4 Maximum SOFA scores for the six organ systems total maximum SOFA score and delta SOFA for all patients, survivors and non-survivors (mean ± standard deviation)

	All (n = 303)	Survivors (n = 259)	Non-Survivors (n = 44)
Cardiovascular	0.83 ± 1.38	0.54 ± 1.09	2.50 ± 1.72*
Delta cardiovascular	0.17 ± 0.64	0.13 ± 0.55	0.43 ± 1.02*
Renal	0.97 ± 1.37	0.84 ± 1.31	1.79 ± 1.47*
Delta renal	0.29 ± 0.81	0.24 ± 0.74	0.57 ± 1.11*
Respiratory	0.94 ± 1.29	0.70 ± 1.08	2.36 ± 1.46*
Delta respiratory	0.24 ± 0.64	0.15 ± 0.44	0.77 ± 1.17*
Coagulation	0.52 ± 0.82	0.45 ± 0.76	0.88 ± 1.06*
Delta coagulation	0.22 ± 0.54	0.18 ± 0.49	0.41 ± 0.76*
Hepatic	0.09 ± 0.43	0.05 ± 0.26	0.38 ± 0.87*
Delta hepatic	0.07 ± 0.38	0.03 ± 0.20	0.34 ± 0.83*
Neurological	0.28 ± 0.87	0.18 ± 0.70	0.84 ± 1.41*
Delta neurological	0.19 ± 0.77	0.14 ± 0.63	0.52 ± 1.23*
TMS score	3.26 ± 3.27	2.49 ± 2.47	7.73 ± 3.78*
Delta TMS score	0.76 ± 1.66	0.58 ± 1.39	1.76 ± 2.55*

TMS, total maximum SOFA score; delta SOFA, TMS score minus SOFA score on day 1; * significant difference between survivors and non-survivors, $p < 0.01$ (Mann Whitney-U-test)

Table 5 Cox proportional hazards non stepwise regression analysis showing the effect of the maximum SOFA score during ICU stay for different organ systems on the risk of death

Variable	β	Standard error	Wald χ^2	p values	Risk ratio	95 % CI
Cardiovascular	0.440	0.118	13.968	0.0002	1.554	1.233 to 1.958
Renal	0.112	0.119	0.896	0.343	1.119	0.886 to 1.412
Respiratory	0.311	0.134	5.427	0.019	1.366	1.050 to 1.776
Coagulation	0.002	0.155	0.0002	0.988	1.002	0.740 to 1.357
Hepatic	0.561	0.202	7.682	0.006	1.753	1.178 to 2.607
Neurologic	0.223	0.131	2.886	0.893	0.800	0.618 to 1.034

β, coefficient; SE, standard error; Wald χ^2, Wald test statistic calculated from the data to be compared with the chi-square distribution with 1 degree of freedom; risk-ratios are presented for a 1-point change in the scores. 95 % CI, 95 % confidence interval

SOFA score discriminated well between survivors and nonsurvivors after admission and over time. Vincent et al. [1] showed that in patients with organ failure (SOFA score ≥ 3) the length of time taken to reach the highest SOFA score was longest for the hepatic system [1]. Neurological organ failure did not occur within 4.5 days of admission whereas cardiovascular and respiratory failure was observed early in the course, thus reflecting the composition of our patients. Liver failure (SOFA score ≥ 3) was observed only in a single patient although a significant portion of our patients had a severe left and right heart failure with consequent liver congestion. Therefore serum bilirubin may not be the ideal indicator of liver dysfunction.

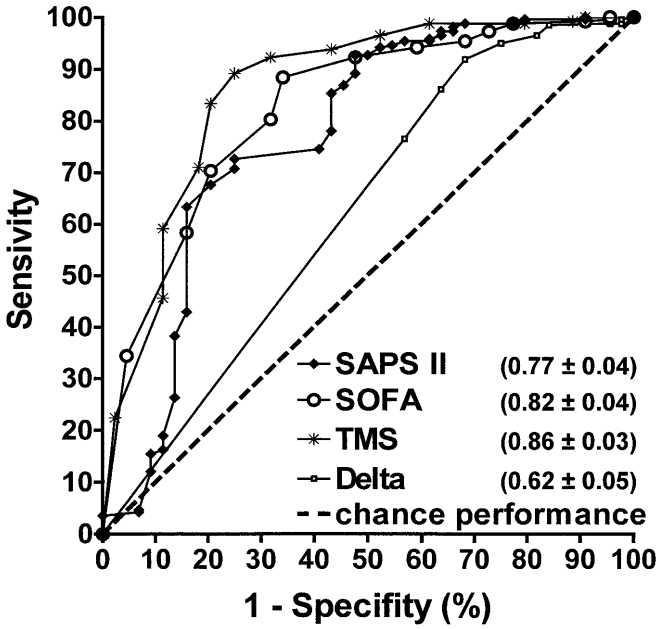

Fig. 4 Receiver operating characteristic curves for SAPS II, total SOFA score on day 1, TMS score, and ΔSOFA score (*Delta*) demonstrating the relationship between true positives (*Sensitivity*) and false positives (*1 minus Specificity*) for all models. *45° diagonal* (chance performance) represents the discriminative power of a score no better than chance. *Parentheses* AUROC curve values for each model ± standard error

Marshall et al. [12] evaluated the association of multiple biochemical measures of hepatic function in the development set for the multiple organ dysfunction score. For reasons of construct validity and simplicity they chose to use the serum bilirubin concentration as the hepatic component of the score although recognizing that this indicator lacks specificity for hepatic dysfunction and has limited ability to reflect the full spectrum of liver dysfunction in critical illness. In addition, acute liver dysfunction may be impossible to differentiate from preexisting chronic disease. Le Gall et al. [13] found that of the six systems described by the logistic organ dysfunction system, neurological, cardiovascular, and renal dysfunctions were the most severe and received the maximum of 5 points whereas the hepatic system received only 1 point. Fagon et al. [15] studied the presence or absence of organ dysfunctions and/or infection to predict the outcome of intensive care unit patients and found that the impact of hematological and hepatic organ system dysfunction was less severe.

We also did not encounter severe dysfunction of the coagulation system in our patients. Platelet counts may, as with bilirubin, not be the ideal predictor of coagulation dysfunction. Beyond that one might argue that our patients were not sufficiently ill to develop a significant dysfunction of the two organ systems. The Glasgow Coma Score as the indicator for neurological organ failure remains difficult, since it is nearly impossible to judge sedated patients. Nevertheless, the cardiovascular and neurological systems were associated with an increased risk of death. These findings are in agreement with those of Vincent et al. who implicated the cardiovascular, neurological, and the renal systems in the risk of death [2]. We found no clear relationship between number of organ failures and mortality; similar findings have been reported elsewhere [1, 12, 13, 16]. We were not able reliably to investigate the combined effect of numerous organ failures on death due to the small population. Vincent et al. [1] have shown that mortality rates are lower in patients with organ dysfunction associated with respiratory failure than with combined organ failure (mortality range 65–74 %). In contrast to these findings Zimmerman and colleagues [16] demon-

strated with differing combinations of organ system failure that hospital mortality varies from a low of 20% with combined hematological and cardiovascular failure to a high of 76% with combined cardiovascular and neurological failure.

Patients older than 65 years with a SOFA score of 5 or higher on admission had a significantly higher probability of death in the subgroup "trauma" (original SOFA dataset) as reported by Antonelli et al. [14]. Age was not related to death in our patients, but when we retrospectively applied the cutoff score of 5, Cox' analysis showed that these patients had a significantly increased mortality that was 5.5 times (3.1–10.1, 95% CI) that of patients with a lower score. Admission from another ICU and cardiovascular and respiratory dysfunctions were associated with length of ICU stay. Additionally, Antonelli et al. [14] found that a higher SOFA score, admission to the ICU from the same hospital, and the presence of infection were the three major variables associated with a longer ICU stay in trauma patients. Taken together, these data show that the SOFA score is closely related to length of ICU stay. Therefore it may contribute substantially to the measurement of resource utilization.

TMS score

Recently Moreno and coworkers [7] reported that the TMS score and ΔSOFA score can be used to quantify the degree of organ dysfunction/failure even at ICU admission and during the ICU stay [7]. Our findings are similar to those of this study but differ with regard to the relevance of single organ systems. Moreover, we did not assess SOFA score on admission but report the SOFA score on day 1, which implies the worst values within the last 24 h and may have affected the ΔSOFA but not the TMS score. Interestingly, the TMS scores of the cardiovascular, respiratory, and hepatic systems were associated with risk of death, in contrast to day 1 where only the cardiovascular and neurological systems contributed to increased mortality. The hepatic system did not contribute to outcome in the patients reported by Moreno et al. However, this group defined outcome as the dependent variable in regression analysis. When we retrospectively performed Cox' regression analysis with "ICU mortality" as the dependent variable, our results remained unchanged. A further difference to the data set of Moreno et al. is that both overall TMS score and maximum SOFA score for various organ systems were significantly lower in our patients. This observation is closely coupled to the divergent mortality rates in the two studies.

TMS score reflects more accurately the cumulative insult suffered by patients during ICU stay and may help to identify specific patterns of organ dysfunction/failure in different patient groups. Therefore these proposed systems may help to judge the efficacy of therapeutic interventions more precisely since they describe the development of overall or organ specific dysfunction/failure and the total insult suffered by the patient [7] and do not rely solely on mortality as the single end-point.

Discriminative power of the scores

Discriminatory power was excellent for the TMS and SOFA scores on day 1 and satisfactory for SAPS II, in contrast to ΔSOFA which did not discriminate well between survivors and nonsurvivors. ΔSOFA does not distinquish between patients with high admission score and high TMS and patients without organ dysfunction throughout the ICU stay. Nevertheless, increasing ΔSOFA seems to possess eminent predictive power, as evidenced by patient populations in the studies of Moreno et al. [7] and our own, where it was an independent prognostic factor for death.

In summary, SOFA score and its extensions, TMS score and ΔSOFA provide the clinician with feasible techniques for evaluating the degree of organ dysfunction on admission and for following-up the progress of organ dysfunction/failure during the ICU stay. The TMS and ΔSOFA scores may be helpful in judging the efficacy of therapeutic interventions. The SOFA score may be a valuable tool for evaluating organ dysfunction/failure in future trials directed at prevention and treatment of MOF. Nevertheless, initial validation of the score in the target population appears necessary.

References

1. Vincent JL, De Mendonca A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S (1998) Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med 26: 1793–1800
2. Sibbald WJ, Darrah WC (1993) Multiple organ system failure in sepsis. In Carlson RW, Geheb MA (eds) Principles and practice of medical intensive care. Saunders, Philadelphia, pp 340–352
3. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, Reinhart CK, Suter PM, Thijs LG (1996) The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 22: 707–710
4. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13: 818–829
5. Knaus WA, Wagner D, Draper EA, Zimmerman JE, Bergner M, Bastos PG, Sirio CA, Murphy DJ, Lotring T, Damiano A, Harrell FE (1991) The APACHE III prognostic system risk prediction of hospital mortality for critically ill hospitalized adults. Chest 100: 1619–1636
6. Le Gall JR, Lemeshow S, Saulnier F (1993) A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. JAMA 270: 2957–2963
7. Moreno R, Vincent JL, Matos R, Mendonça A, Cantraine F, Thijs LG, Takala J, Sprung CL, Antonelli M, Bruining H, Willatts S (1999) The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Intensive Care Med 25: 686–696
8. Hanley JA, McNeil BJ (1982) The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 143: 29–36
9. Hanley JA, McNeil BJ (1983) A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148: 839–843
10. Members of the ACCP/SCCM Consensus Conference Committee (1992) American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definition for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 20: 864–874
11. Matuschak GM (1998) Multiple organ system failure: clinical expression, pathogenesis and therapy. In Hall JB, Schmidt GA, Wood LD (eds) Principles of critical care. McGraw-Hill, New York, pp 221–248
12. Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ (1995) Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med 23: 1638–1652
13. Le Gall JR, Klar J, Lemeshow S, Saulnier F, Alberti C, Artigas A, Teres D (1996) The logistic organ dysfunction system. A new way to assess organ dysfunction in the intensive care unit. ICU Scoring Group. JAMA 276: 802–810
14. Antonelli M, Moreno R, Vincent JL, Sprung CL, Mendoca A, Passariello M, Riccioni L, Osborn J (1999) Application of SOFA score to trauma patients. Sequential organ failure assessment. Intensive Care Med 25: 389–394
15. Fagon JY, Chastre J, Novara A, Medioni P, Gibert C (1993) Characterization of intensive care unit patients using a model based on the presence or absence of organ dysfunctions and/or infection: the ODIN model. Intensive Care Med 19: 137–144
16. Zimmerman JE, Knaus WA, Wagner DP, Sun X, Hakim RB, Nystrom PO (1996) A comparison of risks and outcomes for patients with organ system failure: 1982–1990. Crit Care Med 24: 1633–1641