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ORIGINAL ARTICLE

Scoring Short-Term Mortality After Liver Transplantation

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Liver transplantation can prolong survival and improve the quality of life of patients with end-stage liver disease. This study retrospectively reviewed the medical records of 149 patients who had received liver transplants in a tertiary care university hospital from January 2000 to December 2007. Demographic, clinical, and laboratory variables were recorded. Each patient was assessed by 4 scoring systems before transplantation and on postoperative days 1, 3, 7, and 14. The overall 1-year survival rate was 77.9%. The Sequential Organ Failure Assessment (SOFA) score had better discriminatory power than the Child-Pugh points, Model for End-Stage Liver Disease score, and RIFLE (risk of renal dysfunction, injury to the kidney, failure of the kidney, loss of kidney function, and end-stage kidney disease) criteria. Moreover, the SOFA score on day 7 post–liver transplant had the best Youden index and highest overall correctness of prediction for 3-month (0.86, 93%) and 1-year mortality (0.62, 81%). Cumulative survival rates at the 1-year follow-up after liver transplantation differed significantly ($P < 0.001$) between patients who had SOFA scores ≤ 7 on post–liver transplant day 7 and those who had SOFA scores > 7 on post–liver transplant day 7. In conclusion, of the 4 evaluated scoring systems, only the SOFA scores calculated before liver transplantation were statistically significant predictors of 3-month and 1-year posttransplant mortality. SOFA on post–liver transplant day 7 had the best discriminative power for predicting 3-month and 1-year mortality after liver transplantation.

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End-stage liver disease refers to a progressive, diffuse fibrosing, nodular condition that disrupts the entire normal architecture of the liver. The major complications include jaundice, ascites, hepatic encephalopathy, dilutional hyponatremia, portal hypertension, variceal bleeding, hepatorenal syndrome, and hepatopulmonary syndrome. Patients admitted to intensive care units (ICUs) with end-stage liver disease have an extremely poor prognosis and a life expectancy of only months to years.[1-6] Besides the management of its complications, no specific treatment protocol has been developed for critically ill patients with end-stage liver disease. The success rate of liver transplantation has improved over the last decade, largely because of improved immunosuppression and surgical techniques and experience in managing liver allograft recipients. Thus, liver transplantation offers the only hope of prolonged survival and improved quality of life for

Abbreviations: ALT, alanine aminotransferase; ARF, acute renal failure; AST, aspartate aminotransferase; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; CNS, central nervous system; df, degrees of freedom; epi, epinephrine; FiO_2, fractional inspired oxygen; ICU, intensive care unit; INR, international normalized ratio; MAP, mean arterial pressure; MELD, Model for End-Stage Liver Disease; norepi, norepinephrine; NS, not significant; PaO_2, arterial oxygen tension; RIFLE, risk of renal dysfunction, injury to the kidney, failure of the kidney, loss of kidney function, and end-stage kidney disease; SE, standard error; SOFA, Sequential Organ Failure Assessment.

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these patients.[7] Unfortunately, although transplantation is effective, the possibility of transplantation depends on the availability of a liver donor. Therefore, predictors of mortality risk and models for the short-term prognosis of end-stage liver disease are needed to help clinicians and policymakers predict the outcomes of liver transplantation, and they would be beneficial in both clinical and research settings.

The Child-Pugh scoring system is widely used to stratify risks in patients with cirrhosis and to assess the efficiency of therapeutic procedures such as sclerotherapy, band ligation of varices, transjugular intrahepatic portosystemic shunt, and surgery.[8] The Model for End-Stage Liver Disease (MELD) score was initially developed to predict mortality in cirrhosis patients receiving a transjugular intrahepatic portosystemic shunt.[9] In February 2002, the United Network for Organ Sharing implemented MELD to prioritize organ allocation in patients with advanced liver disease awaiting liver transplantation. Subsequent analysis has shown that the MELD score objectively predicts short-term mortality in patients awaiting liver transplantation, and unlike the Child-Pugh scoring system, the MELD score is independent of "subjective" assessments such as hepatic encephalopathy or ascites. Many countries currently use this method for organ allocation in liver transplantation.[10-12]

The Sequential Organ Failure Assessment (SOFA) score[13] is a simple and objective score that allows for the calculation of both the number of organ dysfunctions and the severity of organ dysfunction in 6 organ systems (respiratory, coagulatory, liver, cardiovascular, renal, and neurological; see the appendix), and the score can measure individual or aggregate organ dysfunction that is currently used in the ICU to describe morbidity. Although it was originally designed for classifying organ failure rather than for predicting outcomes, various investigations have identified a clear relationship between organ dysfunction and mortality.[14,15]

The RIFLE (risk of renal dysfunction, injury to the kidney, failure of the kidney, loss of kidney function, and end-stage kidney disease) criteria are changes in the glomerular filtration rate and/or urine output. The criteria were first proposed by the Acute Dialysis Quality Initiative Group to standardize acute renal failure.[16] Several studies have used the classification to show the high mortality rate of acute renal disease.[17-20]

The evaluation of the MELD score for predicting survival after liver transplantation has produced conflicting results. Some authors have reported no correlation between the MELD score and short-term posttransplantation survival.[21,22] However, other reports have suggested that the pretransplant MELD score predicts posttransplantation survival.[23,24] On the other hand, the relationship between posttransplant scoring system changes and postoperative outcomes in these patients is unknown. Thus, the aim of our study was to evaluate and compare the accuracy of liver disease–specific scores (Child-Pugh points and MELD score), the SOFA score, and the RIFLE criteria for predicting 3-month and 1-year mortality in posttransplant patients.

PATIENTS AND METHODS

Patient Information and Data Collection

The local institutional review board waived the need for informed consent. This study was performed in a 2000-bed university hospital in Taiwan between January 2000 and December 2007. This study enrolled a total of 149 consecutive end-stage liver disease patients who had underwent liver transplantation. The following patients were excluded: pediatric patients ($\leq$18 years old) and patients who had undergone liver transplantation previously.

Retrospective data included the following: demographic data, laboratory variables, etiologies of liver disease, donor type, intraoperative blood loss, anesthesia time, length of ICU stay and hospitalization, and outcome. The Child-Pugh points, MELD score, SOFA score, and RIFLE criteria were used to assess illness severity on the first day of admission before transplantation and on posttransplantation days 1, 3, 7, and 14. The study outcomes were the 3-month and 1-year mortality rates after liver transplantation. Follow-up at 1 year after transplantation was performed via patient record review or by telephone interview.

Definitions

The severity of liver disease was graded by the Child-Pugh points and the MELD score. The MELD score was calculated with the following formula:[10]

$$\begin{aligned}\text{MELD score} = (&0.957\ \ln[\text{creatinine}] + 0.378\ \ln[\text{bilirubin}] \\ &+ 1.120\ \ln[\text{international normalized} \\ &\text{ratio of prothrombin}] + 0.643) \times 10\end{aligned}$$

Illness severity was assessed by the SOFA score. The worst physiological and biochemical values during the days were recorded. The RIFLE criteria were also used to group patients according to risk, injury, and failure.[16] No patient met the criteria for loss or end-stage renal disease. The following simple model for mortality was constructed: non–acute renal failure (0 points), RIFLE-R (1 point), RIFLE-I (2 points), and RIFLE-F (3 points).[18]

Statistical Analysis

Continuous variables were summarized with means and standard deviations unless otherwise stated. All variables were tested for normal distributions with the Kolmogorov-Smirnov test. Means of continuous variables and normally distributed data were compared by the Student *t* test; otherwise, the Mann-Whitney U test was employed. Categorical data were tested by the chi-square test. Cumulative survival curves as a function of time were constructed with the Kaplan-Meier approach and compared with the log rank test.

TABLE 1. Patient Demographic Data and Clinical Characteristics According to 1-Year Mortality

	All Patients (n = 149)	Survivors (n = 116)	Nonsurvivors (n = 33)	*P* Value
Age (years)	50 ± 9	50 ± 9	52 ± 8	NS (0.216)
Gender (male/female)	112/37	88/28	24/9	NS (0.889)
Body weight (kg)	66 ± 12	67 ± 12	61 ± 11	0.009
Hemoglobin on admission (g/dL)	10.3 ± 2.1	10.4± 2.2	9.6 ± 1.9	NS (0.055)
Leukocytes on admission ($\times 10^9$/L)	5.3 ± 4.0	5.1± 4.0	6.1 ± 4.2	NS (0.251)
Platelets on admission ($\times 10^9$/L)	68 ± 43	71 ± 46	56 ± 30	NS (0.069)
Prothrombin time INR on admission	1.9 ± 0.7	2.0 ± 0.8	1.8 ± 0.5	NS (0.291)
Serum sodium on admission (mmol/L)	138 ± 6	137 ± 6	138 ± 8	NS (0.786)
AST on admission (U/L)	88 ± 82	89 ± 86	86 ± 68	NS (0.872)
ALT on admission (U/L)	72 ± 155	77 ± 174	53 ± 41	NS (0.431)
Total bilirubin on admission (mg/dL)	9.7 ± 12.2	8.8 ± 10.5	13.0 ± 16.7	NS (0.081)
Serum creatinine on admission (mg/dL)	1.3 ± 1.1	1.1 ± 0.9	1.7 ± 1.5	0.002
Serum albumin on admission (g/L)	2.9 ± 0.6	2.8 ± 0.6	3.0 ± 0.5	NS (0.356)
MAP on admission (mm Hg)	84 ± 12	84 ± 13	86 ± 9	NS (0.348)
MELD score on admission	21 ± 9	20 ± 9	23 ± 10	NS (0.139)
Child-Pugh points on admission	12 ± 2	12 ± 2	12 ± 2	NS (0.683)
SOFA on admission	5 ± 2	5 ± 2	6 ± 3	0.012
RIFLE on admission: not ARF	143	114	29	0.022
R category	3	1	2	NS (0.124)
I category	1	1	0	NS (1.000)
F category	2	0	2	0.048
Anesthesia time (hours)	12 ± 2	12 ± 2	12 ± 1	NS (0.227)
Donor type (deceased/splint/living)	32/19/98	26/13/77	6/6/21	NS (0.542)
Volume of blood loss (mL)	3663 ± 4378	3381 ± 3874	4648 ± 5769	NS (0.143)
Length of ICU stay (days)	24 ± 26	20 ± 19	40 ± 37	<0.001
Length of hospital stay (days)	49 ± 34	45 ± 29	65 ± 44	0.002

Calibration was assessed with the Hosmer-Lemeshow goodness-of-fit test to compare the numbers of observed and predicted deaths in risk groups for the entire range of probabilities of death. Discrimination was explored with the area under the receiver operating characteristic curve (AUROC). Areas under 2 AUROC curves were compared by a nonparametric approach. The AUROC analysis was also performed to calculate the cutoff values, sensitivity, specificity, and overall correctness. Finally, we calculated cutoff points by obtaining the best Youden index (sensitivity + specificity − 1).[25] The SOFA scores, calculated in the preoperative period and on postoperative days 1, 3, and 7, were compared between 1-year survival and mortality groups by repeated-measures analysis of variance with the general linear model procedure. All statistical tests were 2-tailed; a value of $P < 0.05$ was considered statistically significant.

RESULTS

Subject Characteristics

The study population included 149 patients who underwent liver transplantation between January 2000 and December 2007. The mean patient age was 50 years; 112 patients were male (75%), and 37 were female (25%). The overall 3-month and 1-year survival rates were 85.9% (128/149) and 77.9% (116/149), respectively. Table 1 compares patient demographic data and clinical characteristics of 1-year survivors and nonsurvivors. Only the SOFA scores calculated before liver transplantation were statistically significant predictors of 1-year posttransplant mortality; the pretransplant Child-Pugh points, MELD score, and RIFLE criteria were not. Thirty-two patients (21.5%) received deceased-donor grafts; there was no significant difference in the age or gender of the 1-year survivors and nonsurvivors. Table 2 lists the causes of cirrhosis. Liver disease was largely attributed to hepatitis B viral infections.

Calibration, Discrimination, and Severity of the Illness Scoring Systems

Tables 3 and 4 show the goodness of fit, as measured by the Hosmer-Lemeshow chi-square statistic, for predicted mortality risk and the predictive accuracy of the Child-Pugh points, MELD score, SOFA score, and RIFLE criteria in predicting 3-month and 1-year mortality, respectively. Tables 3 and 4 also list the discrimination for the Child-Pugh points, MELD score, SOFA score, and RIFLE criteria for predicting 3-month and 1-year mortality, respectively. The discriminatory power of the SOFA score was excellent and superior to that of the Child-Pugh points, MELD score, and RIFLE criteria for predicting both 3-month and 1-year

mortality. The AUROC curves were highest for the SOFA score on post–liver transplant day 7 for predicting 3-month mortality (0.953 ± 0.026) and for predicting 1-year mortality (0.834 ± 0.048). Moreover, the posttransplant day 7 SOFA score was a significantly ($P < 0.05$) better predictor of 3-month and 1-year mortality than the pretransplant Child-Pugh points, RIFLE criteria, SOFA score, and MELD score.

Indices for Predicting Short-Term Prognosis

To assess the predictive value of selected cutoff points for predicting 3-month and 1-year mortality, the sensitivity, specificity, and overall correctness of prediction were determined. Tables 5 and 6 list the data calculated with the cutoff point providing the best Youden index. On post–liver transplant day 7, the Youden index and overall correctness for predicting 3-month and 1-year mortality were higher for the SOFA score than for the Child-Pugh points, MELD score, and RIFLE criteria.

Figure 1A illustrates that the cumulative survival rates in the study population significantly ($P < 0.001$) differed between patients with a SOFA score ≤ 7 and those with a SOFA score > 7 on post–liver transplant day 7. Figure 2A illustrates that by repeated-measures analysis of variance, the SOFA scores significantly increased between the periods (before transplantation and on postoperative days 1, 3, and 7) in the 1-year death group but not in the 1-year survival group.

TABLE 2. Causes of Cirrhosis

Causes of Cirrhosis	All Patients (n = 149)
Hepatitis B, n (%)	79 (53)
Hepatitis B + hepatitis C, n (%)	15 (10)
Hepatitis B + alcoholic, n (%)	17 (11)
Hepatitis C, n (%)	17 (11)
Hepatitis C + alcoholic, n (%)	4 (3)
Alcoholic, n (%)	6 (4)
Other causes, n (%)*	11 (8)

*Biliary cirrhosis, biliary sclerosis, autoimmune hepatitis, drugs, and unknown causes.

DISCUSSION

Previous studies have reported 1-year survival rates of 72% and 87% for end-stage liver disease patients who had undergone liver transplantation.[26-28] The overall 1-year survival rate in the current study was 77.9%. Only the SOFA scores calculated before liver transplantation were statistically significant predictors of 3-month and 1-year posttransplant mortality; the pretransplant Child-Pugh points, MELD score, and RIFLE criteria were not (Tables 1, 3, and 4). The SOFA score had better discriminatory power than the

TABLE 3. Calibration and Discrimination for the Scoring Methods Used in Predicting 3-Month Mortality

	Calibration			Discrimination		
	Goodness of Fit (χ^2)	df	*P*	AUROC ± SE	95% CI	*P*
Child-Pugh points						
On admission	3.387	5	0.641	0.514 ± 0.063*	0.391-0.637	0.836
Postoperative day 1	2.992	4	0.559	0.740 ± 0.062*	0.618-0.861	<0.001
Postoperative day 3	9.217	4	0.056	0.811 ± 0.057	0.698-0.923	<0.001
Postoperative day 7	7.144	3	0.067	0.846 ± 0.052	0.744-0.949	<0.001
Postoperative day 14	1.643	3	0.650	0.816 ± 0.059	0.700-0.933	<0.001
MELD						
On admission	7.946	8	0.439	0.624 ± 0.067*	0.492-0.756	0.070
Postoperative day 1	9.057	8	0.337	0.773 ± 0.058*	0.659-0.886	<0.001
Postoperative day 3	7.099	7	0.419	0.852 ± 0.039	0.775-0.928	<0.001
Postoperative day 7	12.567	8	0.128	0.909 ± 0.044	0.823-0.995	<0.001
Postoperative day 14	9.403	8	0.309	0.917 ± 0.042	0.836-0.999	<0.001
RIFLE						
On admission	—	—	—	0.561 ± 0.073*	0.418-0.703	0.375
Postoperative day 1	0.958	2	0.619	0.675 ± 0.068*	0.543-0.808	0.010
Postoperative day 3	0.691	1	0.406	0.671 ± 0.073*	0.582-0.814	0.012
Postoperative day 7	0.582	1	0.446	0.874 ± 0.053	0.769-0.978	<0.001
Postoperative day 14	0.587	2	0.746	0.883 ± 0.064	0.757-1.000	<0.001
SOFA						
On admission	1.153	5	0.949	0.637 ± 0.067*	0.506-0.769	0.044
Postoperative day 1	5.905	5	0.316	0.802 ± 0.060	0.684-0.919	<0.001
Postoperative day 3	1.437	6	0.946	0.865 ± 0.046	0.775-0.956	<0.001
Postoperative day 7	6.703	5	0.244	0.953 ± 0.026	0.902-1.000	<0.001
Postoperative day 14	8.505	7	0.290	0.945 ± 0.032	0.883-1.000	<0.001

*$P < 0.05$ versus SOFA on postoperative day 7.

TABLE 4. Calibration and Discrimination for the Scoring Methods Used in Predicting 1-Year Mortality

	Calibration			Discrimination		
	Goodness of Fit (χ^2)	df	*P*	AUROC ± SE	95% CI	*P*
On admission						
Child-Pugh points	4.412	5	0.492	0.516 ± 0.053*	0.413-0.620	0.773
MELD	10.687	8	0.220	0.584 ± 0.056*	0.475-0.693	0.141
RIFLE	—	—	—	0.552 ± 0.060*	0.435-0.669	0.362
SOFA	2.961	5	0.706	0.625 ± 0.054*	0.520-0.730	0.029
Postoperative day 1						
Child-Pugh points	3.948	4	0.413	0.669 ± 0.057	0.557-0.780	0.003
MELD	10.212	8	0.250	0.692 ± 0.056	0.582-0.801	0.001
RIFLE	1.892	2	0.388	0.671 ± 0.056	0.561-0.782	0.003
SOFA	3.425	5	0.635	0.696 ± 0.057	0.585-0.808	0.001
Postoperative day 3						
Child-Pugh points	11.447	4	0.022	0.727 ± 0.056	0.616-0.837	<0.001
MELD	7.388	7	0.390	0.758 ± 0.051	0.657-0.858	<0.001
RIFLE	0.364	1	0.546	0.649 ± 0.060	0.531-0.766	0.009
SOFA	6.410	6	0.379	0.774 ± 0.052	0.673-0.876	<0.001
Postoperative day 7						
Child-Pugh points	6.618	3	0.085	0.701 ± 0.060	0.584-0.819	<0.001
MELD	19.582	8	0.012	0.793 ± 0.053	0.690-0.896	<0.001
RIFLE	5.488	1	0.019	0.756 ± 0.057	0.644-0.867	<0.001
SOFA	6.590	5	0.253	0.834 ± 0.048	0.740-0.928	<0.001
Postoperative day 14						
Child-Pugh points	3.466	3	0.325	0.727 ± 0.054	0.621-0.832	<0.001
MELD	10.484	8	0.233	0.793 ± 0.054	0.687-0.898	<0.001
RIFLE	5.668	2	0.059	0.673 ± 0.069	0.537-0.809	0.007
SOFA	8.548	7	0.287	0.815 ± 0.052	0.714-0.916	<0.001

*$P < 0.05$ versus SOFA on postoperative day 7.

TABLE 5. Prediction of Subsequent 3-Month Mortality

Predictive Factor	Cutoff Point	Youden Index	Sensitivity (%)	Specificity (%)	Overall Correctness (%)
Child-Pugh points					
On admission	11	0.07	67	41	54
Postoperative day 1	12	0.39	71	67	69
Postoperative day 3	10	0.56	76	80	78
Postoperative day 7*	10	0.58	62	96	79
Postoperative day 14	8	0.51	77	74	76
MELD					
On admission	24	0.27	52	74	63
Postoperative day 1	26	0.46	71	74	73
Postoperative day 3	22	0.61	86	75	81
Postoperative day 7	30	0.71	71	99	85
Postoperative day 14*	23	0.72	85	88	87
SOFA					
On admission	7	0.19	33	85	59
Postoperative day 1	7	0.51	81	70	76
Postoperative day 3	7	0.61	76	84	80
Postoperative day 7*	7	0.86	95	91	93
Postoperative day 14	7	0.80	86	94	90
RIFLE					
On admission	R category	0.12	14	98	56
Postoperative day 1	F category	0.29	43	87	65
Postoperative day 3	I category	0.34	43	91	67
Postoperative day 7	R category	0.69	81	88	85
Postoperative day 14*	I category	0.70	78	93	86

*Value giving the best Youden index for each score.

TABLE 6. Prediction of Subsequent 1-Year Mortality

Predictive Factor	Cutoff Point	Youden Index	Sensitivity (%)	Specificity (%)	Overall Correctness (%)
On admission					
Child-Pugh points	10	0.07	79	28	54
MELD	24	0.17	42	74	58
SOFA*	4	0.21	82	40	61
RIFLE	R category	0.10	12	98	55
Postoperative day 1					
Child-Pugh points	12	0.29	61	68	65
MELD*	26	0.36	61	76	69
SOFA	7	0.33	64	70	67
RIFLE	F category	0.28	39	89	64
Postoperative day 3					
Child-Pugh points	10	0.42	61	81	71
MELD	22	0.46	70	77	74
SOFA*	7	0.51	64	87	76
RIFLE	I category	0.29	36	93	65
Postoperative day 7					
Child-Pugh points	10	0.35	39	96	68
MELD	20	0.53	82	71	77
SOFA*	7	0.62	70	92	81
RIFLE	R category	0.46	58	89	74
Postoperative day 14					
Child-Pugh points	8	0.36	60	76	68
MELD	22	0.50	64	86	75
SOFA*	7	0.53	58	96	77
RIFLE	F category	0.37	40	97	69

*Value giving the best Youden index for each period.

Child-Pugh points, MELD score, and RIFLE classification (Tables 3 and 4). Furthermore, the SOFA score also had the best Youden index and the highest overall correctness of prediction (Tables 5 and 6).

Both the MELD score and Child-Pugh points were used to stratify prospective liver allograft recipients. The accuracy of the MELD score for predicting short-term mortality in end-stage liver disease patients is well established.[10] However, in earlier investigations of the predictive value of MELD for posttransplantation outcome, the follow-up periods were only 1 to 2 years, and reported outcome results have been inconsistent. Thus, a clear consensus has not emerged.[21-24] In this study, AUROC curves have verified that the discriminatory power of the MELD score is superior to Child-Pugh points in predicting 3-month and 1-year mortality.

The mortality risk associated with acute renal failure, one of the most common complications of liver transplantation, has been established in several studies.[29,30] The criteria used to define acute renal failure are the absolute cutoff values for serum creatinine and oliguria. However, as some patients with chronic renal dysfunction may be receiving diuretics or may have systemic hemodynamic changes, such criteria require several stepwise cutoff values for serum creatinine and urine output to accompany increments. The RIFLE criteria provide a diagnostic definition for the stage at which kidney injury can be prevented (risk stratum) after the kidney has been damaged (injury) or after renal failure occurs (failure).[31] The RIFLE criteria have also been tested in clinical practice and are apparently consistent with outcomes observed in patients with acute kidney injury. As demonstrated in our previous and present studies, this at least partly explains why RIFLE criteria can precisely predict short-term mortality.[18,32]

Our previous studies described the good discriminative power and accuracy of the SOFA score in independently predicting in-hospital mortality in critically ill patients with cirrhosis.[33,34] A feature of end-stage liver disease is disturbed systemic circulation characterized by marked arterial vasodilation in splanchnic circulation, which reduces total peripheral vascular resistance and arterial pressure while causing a secondary increase in cardiac output.[1-6] These abnormalities are implicated in several major cirrhotic complications such as severe liver damage with jaundice, coagulopathy, hepatic encephalopathy, hepatorenal syndrome, hepatocardiac syndrome, and hepatopulmonary syndrome. The involvement of such abnormalities makes the SOFA score an excellent tool for assessing the extent of organ dysfunction and predicting mortality. The posttransplant day 7 SOFA score revealed the best Youden index and highest overall correctness of prediction for predicting both 3-month and 1-year mortality (Tables 5 and 6). After transplantation day 7, uncorrected multiple organ dysfunction

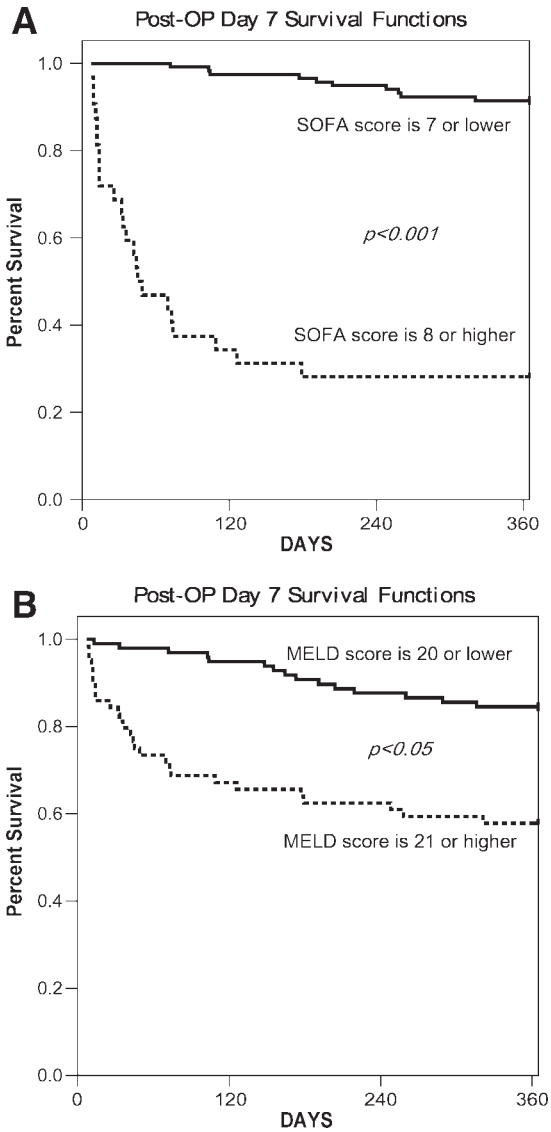

Figure 1. Cumulative survival rate for 149 liver transplant patients according to (A) the SOFA scores and (B) the MELD scores on day 7 after liver transplantation.

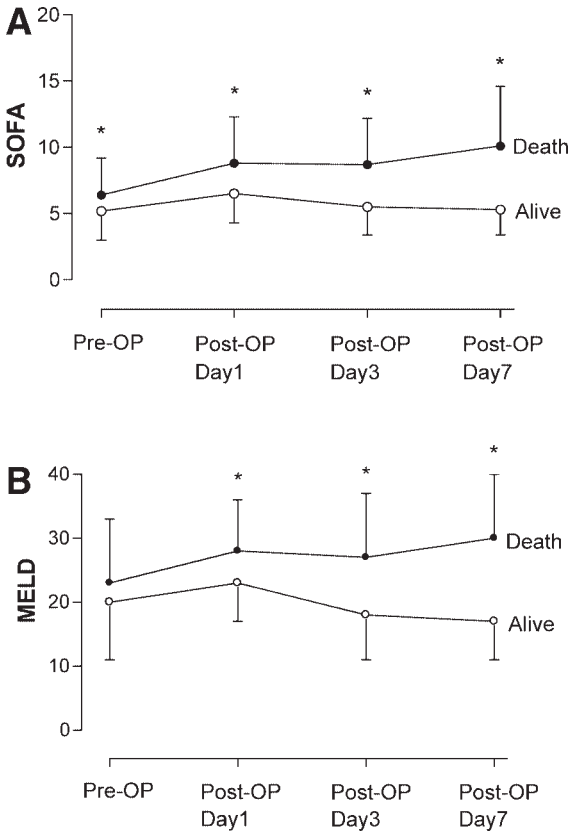

Figure 2. (A) Estimated SOFA scores and (B) estimated MELD scores (mean ± standard deviation) for the 1-year survival group (alive, n = 116) and the 1-year mortality group (death, n = 33) during the preoperative period and on postoperative days 1, 3, and 7 (*$P < 0.05$ for living and dead patients). Significant increases in the SOFA scores between the periods for the mortality group but not for the survival group were found by repeated-measures analysis of variance.

results in delayed recovery of liver function and poor short-term prognosis. A lack of extrahepatic parameters in Child-Pugh scores and a lack of extrarenal predictors in the RIFLE classification may account for their discriminative inferiority to the SOFA score (Tables 3 and 4).

Compared to traditional outcome prediction models performed at the time of ICU admission, the use of SOFA in serial assessments provides a more complete representation of illness dynamics such as therapeutic effects. Trends in the SOFA score over time could reflect a patient's response to therapeutic strategies and allow physicians to monitor daily progress by providing an objective evaluation of the treatment response.[35] As demonstrated in our study, a SOFA score increasing during the pretransplant period and on postoperative days 1, 3, and 7 is associated with a poor 1-year prognosis (Fig. 2).

Despite the encouraging results, potential limitations of our study should be mentioned. First, the subjects were drawn from only 1 medical center; consequently, the results cannot be directly extrapolated to other patient populations. Second, because of the retrospective nature of this study, some laboratory data were unavailable. Finally, the patient population had a high proportion of hepatitis B patients (hepatitis B alone: 53%; hepatitis B and C: 10%; hepatitis B and alcoholic: 11%); therefore, these findings may have limited applicability to typical North American and European patients who have hepatitis C or who are alcoholics.

In conclusion, this study demonstrates the excellent discriminatory power of the SOFA score and its superiority to the Child-Pugh points, MELD score, and RIFLE criteria in predicting both 3-month and 1-year mortality. This study also indicates that the SOFA score on post–liver transplant day 7 has the best Youden index of the 4 measures and the highest overall

correctness of prediction. Finally, a SOFA score > 7 on post–liver transplant day 7 should be considered an indicator of negative short-term outcome. The analytical results of this study suggest that pretransplant and postoperative SOFA scores accurately predict short-term prognosis in this subset of patients. Because of the excess mortality and relatively small sample size, the predictive role of SOFA needs further external validation.

REFERENCES

1. Schrier RW, Arroyo V, Bernardi M, Epstein M, Henriksen JH, Rodés J. Peripheral arterial vasodilation hypothesis: a proposal for the initiation of sodium and water retention in cirrhosis. Hepatology 1988;8:1151-1157.
2. Ginès P, Cardenas A, Arroyo V, Rodés J. Management of cirrhosis and ascites. N Engl J Med 2004;350: 1646-1654.
3. Iwakiri Y, Groszmann RJ. The hyperdynamic circulation of chronic liver diseases: from the patient to the molecule. Hepatology 2006;43:S121-S131.
4. Martin PY, Ginès P, Schrier RW. Nitric oxide as a mediator of hemodynamic abnormalities and sodium and water retention in cirrhosis. N Engl J Med 1998;339: 533-541.
5. Xu L, Carter EP, Ohara M, Martin PY, Rogachev B, Morris K, et al. Neuronal nitric oxide synthase and systemic vasodilation in rats with cirrhosis. Am J Physiol Renal Physiol 2000;279:F1110-F1115.
6. Chen YC, Ginès P, Yang J, Summer SN, Falk S, Russell NS, et al. Increased vascular heme oxygenase-1 expression contributes to arterial vasodilation in experimental cirrhosis in rats. Hepatology 2004;39:1075-1087.
7. Shellman RG, Fulkerson WJ, DeLong E, Piantadosi CA. Prognosis of patients with cirrhosis and chronic liver disease admitted to the medical intensive care unit. Crit Care Med 1998;16:671-678.
8. Chen YC, Tsai MH, Hsu CW, Ho YP, Lien JM, Chang MY, et al. Role of serum creatinine and prognostic scoring systems in assessing hospital mortality in critically ill cirrhotic patients with upper gastrointestinal bleeding. J Nephrol 2003;16:558-565.
9. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology 2000;31:864-871.
10. Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al. Model for End-Stage Liver Disease (MELD) and allocation of donor livers. Gastroenterology 2003;124:91-96.
11. Wiesner RH, McDiarmid SV, Kamath PS, Edwards EB, Malinchoc M, Kremers WK, et al. MELD and PELD: application of survival models to liver allocation. Liver Transpl 2001;7:567-580.
12. Freeman RB Jr, Wiesner RH, Harper A, McDiarmid SV, Lake J, Edwards E, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl 2002;8:851-858.
13. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, for the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. The SOFA score to describe organ dysfunction/failure. Intensive Care Med 1996; 22:707-710.
14. Moreno R, Vincent JL, Matos R, Mendonca A, Cantraine F, Thijs L, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Working Group on Sepsis Related Problems of the ESICM. Intensive Care Med 1999;25:686-696.
15. Tsai MH, Chen YC, Ho YP, Fang JT, Lien JM, Chiu CT, et al. Organ system failure scoring system can predict hospital mortality in critically ill cirrhotic patients. J Clin Gastroenterol 2003;37:251-257.
16. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, for the Acute Dialysis Quality Initiative Workgroup. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8:R204-R212.
17. Abosaif NY, Tolba YA, Heap M, Russell J, El Nahas AM. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity, and predictability. Am J Kidney Dis 2005;46: 1038-1048.
18. Lin CY, Chen YC, Tsai FC, Tian YC, Jenq CC, Fang JT, et al. RIFLE classification is predictive of short-term prognosis in critically ill patients with acute renal failure supported by extracorporeal membrane oxygenation. Nephrol Dial Transplant 2006;21:2867-2873.
19. Guitard J, Cointault O, Kamar N, Muscari F, Lavayssière L, Suc B, et al. Acute renal failure following liver transplantation with induction therapy. Clin Nephrol 2006; 65:103-112.
20. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care 2006; 10:R73-R83.
21. Hayashi PH, Forman L, Steinberg T, Bak T, Wachs M, Kugelmas M, et al. Model for End-Stage Liver Disease score does not predict patient or graft survival in living donor liver transplant recipients. Liver Transpl 2003;9: 737-740.
22. Desai NM, Mange KC, Crawford MD, Abt PL, Frank AM, Markmann JW, et al. Predicting outcome after liver transplantation: utility of the Model for End-Stage Liver Disease and a newly derived discrimination function. Transplantation 2004;77:99-106.
23. Onaca NN, Levy MF, Netto GJ, Thomas MJ, Sanchez EQ, Chinnakotla S, et al. Pretransplant MELD score as a predictor of outcome after liver transplantation for chronic hepatitis C. Am J Transplant 2003;3:626-630.
24. Jacob M, Copley LP, Lewsey JD, Gimson A, Toogood GJ, Rela M, et al. Pretransplant MELD score and post liver transplantation survival in the UK and Ireland. Liver Transpl 2004;10:903-907.
25. Youden WJ. Index for rating diagnosis tests. Cancer 1950;3:32-35.
26. Akyildiz M, Karasu Z, Arikan C, Kilic M, Zeytunlu M, Gunsar F, et al. Impact of pretransplant MELD score on posttransplant outcome in living donor liver transplantation. Transplant Proc 2004;36:1442-1444.
27. Lin NC, Hsia CY, Loong CC, Liu CS, Tsai HL, Lui WY, et al. Liver transplantation at a small-volume procedure center—preliminary result from Taipei Veterans General Hospital. J Chin Med Assoc 2008;71:186-190.
28. Smith CM, Beasley GG, Cheng Y, Ormond DB, Spain PG. Annual report of the US organ procurement and transplantation network OPTN/SR AR 1990-1999;2000; 191-237.
29. Gainza FJ, Valdivieso A, Quintanilla N, Errazti G, Gastaca M, Campo M, et al. Evaluation of acute renal failure in the liver transplantation perioperative period: incidence and impact. Transplant Proc 2002;34: 250-251.

30. Narayanan Menon KV, Nyberg SL, Harmsen WS, DeSouza NF, Rosen CB, Krom RA, Wiesner RH. MELD and other factors associated with survival after liver transplantation. Am J Transplant 2004;4:819-825.
31. Uchino S, Bellomo R, Goldsmith D, Bates S, Ronco C. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. Crit Care Med 2006;34:1913-1917.
32. O'Riordan A, Wong V, McQuillan R, McCormick PA, Hegarty JE, Waston AJ. Acute renal disease, as defined by the RIFLE criteria, post-liver transplantation. Am J Transplant 2007;7:168-176.
33. Jenq CC, Tsai MH, Tian YC, Lin CY, Yang C, Liu NJ, et al. RIFLE classification can predict short-term prognosis in critically ill cirrhotic patients. Intensive Care Med 2007;33:1921-1930.
34. Fang JT, Tsai MH, Tian YC, Jenq CC, Lin CY, Chen YC, et al. Outcome predictors and new score of critically ill cirrhotic patients with acute renal failure. Nephrol Dial Transplant 2008;23:1961-1969.
35. Goldhill DR, Sumner A. Outcome of intensive care patients in a group of British intensive care units. Crit Care Med 1998;26:1337-1345.