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Douma, C.E.; Redekop, W.K.; van der Meulen, J.H.P.; van Olden, R.W.; Haeck, J.; Struijk, D.G.; Krediet, R.T.

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Predicting Mortality in Intensive Care Patients with Acute Renal Failure Treated with Dialysis

CAROLINE E. DOUMA,* W. KEN REDEKOP,† JAN H.P. VAN DER MEULEN,† RUDOLF W. VAN OLDEN,* JAN HAECK,‡ DIRK G. STRUIJK,§ and RAYMOND T. KREDIET*

**Renal Unit, Department of Medicine, Academic Medical Center, Amsterdam, The Netherlands; †Department of Clinical Epidemiology and Biostatistics, Academic Medical Center, Amsterdam, The Netherlands; ‡Department of Intensive Care, Academic Medical Center, Amsterdam, The Netherlands; and §The Foundation of Home Dialysis Midden-West Nederland, Utrecht, The Netherlands.*

Abstract. Existing prognostic methods were compared in their ability to predict mortality in intensive care unit (ICU) patients on dialysis for acute renal failure (ARF). The clinical goal of this study was to determine whether these models could identify a group of patients where dialysis would provide no benefit because of a near 100% certainty of death even with dialysis treatment. This retrospective cohort study included 238 adult patients who received a first dialysis treatment for ARF in the ICU. This study examined the performance of seven general ICU mortality prediction models and four mortality prediction models developed for patients with ARF. These models were assessed for their ability to discriminate mortality from survival and for their ability to calibrate the observed mortality rate with the expected mortality rate. The observed inhospital mortality was 76% for our patient group. Areas under the receiver operating characteristic curve ranged from 0.50 to 0.78. With the Acute Physiology and Chronic Health Evaluation (APACHE) III and the Liano models, the observed mortality in the highest quintiles of risk were 97% and 98%. In conclusion, although none of the models examined in this study showed excellent discrimination between those patients who died in hospital and those who did not, some models (APACHE III, Liano) were able to identify a group of patients with a near 100% chance of mortality. This indicates that these models may have some use in supporting the decision not to initiate dialysis in a subgroup of patients. (J Am Soc Nephrol 8: 111–117, 1997)

The mortality of patients on an intensive care unit (ICU) with acute renal failure (ARF) is still very high and has not improved over the last few years despite technical improvements (1,2). Particularly when dialysis is needed, many of these patients will die even with this treatment, and it is doubtful whether its initiation is always beneficial. Given the fact that ARF requiring dialysis is "clinically devastating and extremely costly" (3), the question emerges as to whether it is possible to predict, before dialysis is initiated, the likelihood of mortality.

Numerous mortality prediction models have been developed in the past few years. Several general models have been developed for predicting the risk of patient mortality in multidisciplinary ICU (4–9). Other prediction models have been developed specifically for use with ARF patients (10–13), sometimes based on only those patients receiving dialysis (12,13).

The primary aim of this study was to compare the above-mentioned prognostic methods in terms of their ability to predict mortality in ICU patients needing dialysis treatment because of ARF. This study examined both general ICU mortality prediction models, as well as prediction models designed for use with ARF patients only. The clinical goal of this study was to determine whether these models could identify a group of patients where dialysis would provide no benefit because of a near-100% certainty of death, despite dialysis treatment.

Materials and Methods

Patients

Patient records from the general ICU of the Academic Medical Center (AMC), Amsterdam, The Netherlands, between January 1985 and December 1993 were examined retrospectively. Included in this study were patients aged 18 years or older who received a first dialysis treatment for ARF in the ICU. Chronic dialysis patients ($N = 62$) were not included in this study, as well as 20 patients already dialyzed for ARF in our hospital or in another hospital before transfer to the ICU. Thirty-six patients were excluded because they stayed in the ICU for <8 h before dialysis was initiated, yielding insufficient data to score. Of the remaining patients, 14 had to be excluded because of missing records. These exclusions resulted in a total of 238 patients available for analysis. All patients were dialyzed by intermittent or continuous hemodialysis or continuous peritoneal dialysis. Cellulosic or polysulphon membranes were used for hemodialysis. The data necessary to calculate the different prognostic methods were collected for each patient by the same investigator (C.E.D). The worst values of the prognostic model variables in the 24 h before the first dialysis treatment were used in this study.

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Correspondence to Dr. Caroline E. Douma, Academic Medical Center, University of Amsterdam, Department of Medicine, Renal Unit, F4-215, PO Box 22700, 1100 DE Amsterdam, The Netherlands.

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Prediction Models

General models. The Acute Physiology and Chronic Health Evaluation (APACHE) II system (14) (APACHE is a trademark of APACHE Medical Systems, Inc., McLean, VA) is a modification of the original system developed by Knaus *et al.* (4). This scoring system consists of an Acute Physiology Score (APS) based on 12 physiological measures, age, and the presence of severe chronic health problems. Together with the principal reason for ICU admission, it is possible to use the APACHE II to calculate a predicted risk of death for each patient. The APACHE III prognostic system is the most recent modification of the APACHE system (5). Changes include refinements in the scoring of physiologic parameters and consideration of the patient's location prior to ICU admission. As with the APACHE II method, a predicted risk of mortality can be calculated. In both the APACHE II and APACHE III models, patients with coronary artery bypass grafts (CABG) are excluded.

The Simplified Acute Physiology Score (SAPS) consists of a selection of measurements of the original APACHE system without an adjustment for chronic health problems (6). Le Gall *et al.* selected routinely available measurements to avoid the possibility of a systematic bias in using the APACHE score, which may arise because missing values are interpreted as normal in the APACHE method (6). Viviand *et al.* (7) attempted to improve the predictive values of the SAPS by adding or removing model components. From the 14 original SAPS measurements, five variables were selected for the SAPS-R (R = reduced) model using multiple logistic regression analysis. The SAPS-E (E = extended) model was derived from the SAPS variables plus eight more measurements. Stepwise regression analysis of these 22 variables resulted in a model with seven components. The Sickness Scoring (SS) model (8) is a modification of the APACHE II containing additional physiological measures but not including the reason for ICU admission.

Lemeshow *et al.* (15) used multiple logistic regression and stepwise linear discriminant analysis on a large number of variables for mortality prediction of general ICU patients at the time of ICU admission and 24 and 48 h after admission to create a Mortality Prediction Model (MPM). Teres *et al.* modified this model and replaced the number of organ systems in failure with information about the use of cardiopulmonary resuscitation before ICU admission (9).

Acute renal failure models. Rasmussen *et al.* (10) studied 148 patients referred to the renal unit because of ARF. Fifty percent of these patients required dialysis. Predictors of mortality were selected by review of the literature; a stepwise discriminant analysis resulted in the selection of 10 variables. Liano *et al.* (11) developed both a linear regression model and a logistic regression model based on a study of 228 patients with acute tubular necrosis, 50 percent of whom required dialysis. Because the performance of the linear regression model has been reported to be the better of the two, the latter was used in the present study. Lohr *et al.* (12) collected clinical data of 126 patients treated with dialysis for ARF. Eleven variables were significantly related to mortality. After elimination or combination of clinically similar variables, a clinical survival index consisting of five variables was developed. Schaefer *et al.* (13) analyzed data from 134 patients with ARF requiring dialysis in a medical ICU. Stepwise discriminant analysis of the data collected immediately before dialysis resulted in a model with six variables.

Statistical Analysis

The above-mentioned models were used to calculate a score or, when possible, a mortality risk for each patient. The models were then assigned for discrimination and calibration, concepts that Lemeshow and Le Gall (16) describe extensively.

Discrimination. Discrimination, the ability of a model to distinguish between patients who survive and patients who die, can be assessed using receiver operating characteristic (ROC) curve analysis. ROC curves show the relationship between sensitivity (correct identification of those who die) and 1.0 minus the specificity (or the incorrect identification of those who survive). If all possible pairs of patients where one patient survived and the other died were identified, the area under the ROC curve (17) can be interpreted as the proportion of the pairs where the model can correctly identify the patient who died (by assigning a higher score to that patient). If the area under the ROC curve is 0.5, the model has no discriminatory power, and if the area is 1.0, the model discriminates perfectly.

Calibration. Calibration refers to the degree of correspondence between the estimated probabilities of mortality produced by a model and the actual mortality experience of patients (16). Patients were grouped into five equally sized quintiles of predicted mortality risk for each method. In each quintile of risk, the predicted mortality was compared with the observed mortality. Whereas deciles of risk are recommended for use in these instances (18), the scores from some of the models resulted in so many ties that separation into 10 groups was not feasible.

Relative contribution of the variables. We also examined for each prediction model the relative contribution of the various clinical components to the model's prediction in our patient group. For this reason, we first grouped the variables into clinical components, including metabolic, cardiovascular, respiratory, renal, neurologic, hematological/malignancy, infection, gastrointestinal, cardiopulmonary resuscitation, chronic diseases, personal characteristics, and reason for ICU admission. Second, we calculated for each patient the model's scores using all variables in the model (the model's overall score), as well as the model's scores using only the variables that belong to one of the clinical components (the model's component scores). Third, we fit a linear regression equation with the overall scores as dependent and the component scores as independent variables. Finally, the relative weights of a clinical component in the model were calculated by dividing the standardized β coefficient of that clinical component by the sum of the standardized β coefficients of all clinical components. For example, the standardized β coefficients of the Schaefer model were 0.64 for the metabolic component of the model (blood glucose), 0.98 for the cardiovascular component (mean pressure and heart failure), 0.32 for the respiratory component (mechanical ventilation), 0.20 for the infection component (septic shock), and 0.14 for the chronic disease component (liver cirrhosis). Consequently, the relative weight of the metabolic component in the model could be calculated to be 28% (0.64 divided by 0.64 + 0.98 + 0.32 + 0.20 + 0.14). In this way, it was possible to compare the relative contribution of the different clinical components in our study population within one method and between methods.

Results

The observed inhospital mortality for the 238 patients included in this study was 76%. Descriptive information on these patients is shown in Table 1. Most of the patients were treated by cardiopulmonary surgical (35%), internal (32%), or general surgical specialists (19%). The etiology of the ARF was acute tubular necrosis in >90% of the patients. ROC curves for the various methods are shown in Figure 1. Areas under the ROC curves for the general ICU models were (in increasing order): 0.50 (SAPS-R), 0.58 (SAPS-E), 0.62 (SS), 0.62 (APACHE II), 0.66 (SAPS), 0.71 (MPM), and 0.74 (APACHE III). Areas under the ROC curve for the ARF-specific models were (in increasing order): 0.63 (Rasmussen), 0.65 (Lohr), 0.69

Table 1. Patient characteristics (N = 238)

	Patients (no.)	Proportion (%)
Males	161	68
Age, (y, mean ± SD)	61 ± 15y	
Specialty of the Treating Physician		
Cardiopulmonary surgery	83	35
Internal medicine	75	32
General surgery	45	19
Cardiology	14	6
Vascular surgery	15	6
Neurosurgery	4	2
Gynecology	1	0
Neurology	1	0
Etiology		
Glomerular	4	2
Acute interstitial nephritis	2	1
ATN, postischemic	73	31
ATN, nephrotoxic	5	2
ATN, pigment	5	2
ATN, multicausal	120	50
ATN, unknown origin	17	7
Other reasons	8	3
Unknown	4	2
Status at Discharge		
Home	32	14
Transfer to another hospital	24	10
Death	182	76

(Schaefer), and 0.78 (Liano). Given the clinical goal of identifying patients for whom dialysis would be futile because of a near-100% chance of mortality despite dialysis, we determined whether any of the models could achieve a near-100% specificity in combination with a sensitivity appreciably greater than 0%. In ROC terms, this meant focusing on the slope of the curve in the bottom left corner of the square. Note the relatively good performance of the APACHE III and Liano models in this corner of the graph.

Figure 2 presents the observed and predicted mortalities in five quintiles of risk for the APACHE III, MPM, Liano, and Schaefer models, the best performing prognostic models according to ROC analysis. Both of the general prognostic methods underestimated the risk of mortality. The performance of the Liano model was better than that of Schaefer *et al.*. Whereas the observed mortality risks followed the Liano model risk estimates closely, the Schaefer method overestimated the risk of mortality. Table 2 summarizes the inhospital mortality results of the highest quintile. Patients in the highest quintiles of risk based on the APACHE III model (predicted mortality risk of 59% or higher) and the Liano model (predicted mortality risk of 84% or higher) had a near-100% chance of mortality. Table 2 also includes the number of parameters in the different categories, as well as the relative weights of the clinical categories for the APACHE III, MPM, Liano, and Schaefer models. An examination of the prognostic variables of the models categorized according to the different clinical components revealed some interesting differences (Table 2). The relative weight of renal failure was only 4% of the total weight in the APACHE III model but 21% in the Liano model and not included in the Shaefer model. The Schaefer model was developed using only patients with ARF who received dialysis treatment. Another striking difference between the Liano and Schaefer models was the high relative weight of metabolic and cardiovascular variables in the Schaefer model (71% in total). In the APACHE III model, the relative weight accorded to the reason for ICU admission was very high (48%).

The long-term outcome of patients who were in the highest quintiles of predicted mortality risk and alive at discharge from the hospital was also poor (Table 3).

Discussion

The performance of 11 mortality prediction models was examined in this study for the prediction of inhospital mortality in patients with ARF receiving acute dialysis in the ICU of an academic hospital. Both general and ARF-specific models were selected for examination. The general ICU prediction models were included because they have been developed and evaluated in large patient groups. Obviously, ARF-specific models were used because they were specifically developed for predicting mortality in patients with ARF. Not all existing models were tested in this study. Some of these models required prospective data collection and, therefore, were not appropriate for this study—*e.g.*, the model developed by Lien *et al.* (19). Others were published after the start of this study, such as MPM II (20) and SAPS II (21).

The 76% inhospital mortality observed in our study is comparable with the results of some studies of patients with ARF receiving dialysis (3,12) but higher than the results that other studies report—57% (13) and 44% (22). One explanation for the lower mortality noted by Schaefer *et al.* (13) is their use of only ICU mortality instead of inhospital mortality.

The results from the ROC analysis showed that no model performed exceptionally well in its ability to identify patients who die in hospital. None of the models tested in this study showed an area under the ROC curve of >0.78. In contrast to the area under the ROC curve observed in our population of 0.62 for APACHE II, others have reported larger areas when the model was applied to patients with ARF receiving dialysis, including Parker *et al.*—0.79 (22)—and Chertow *et al.*—0.74 (3).

The clinical goal of this study was to determine whether it would be possible to use these models to identify a group of patients with a near-100% chance of mortality despite dialysis. One method to ascertain the models' ability to identify such patients is to examine the lower left corner of the ROC curve, which represents sensitivity while maintaining a near-100% specificity. With the APACHE III model, 33 of the 143 patients (23%) who died had a score of >71%, the highest predicted risk of a surviving patient. This is rather close to observations by Dobkin *et al.* (23), who observed that 39% of the patients who died and no patients who survived had scores

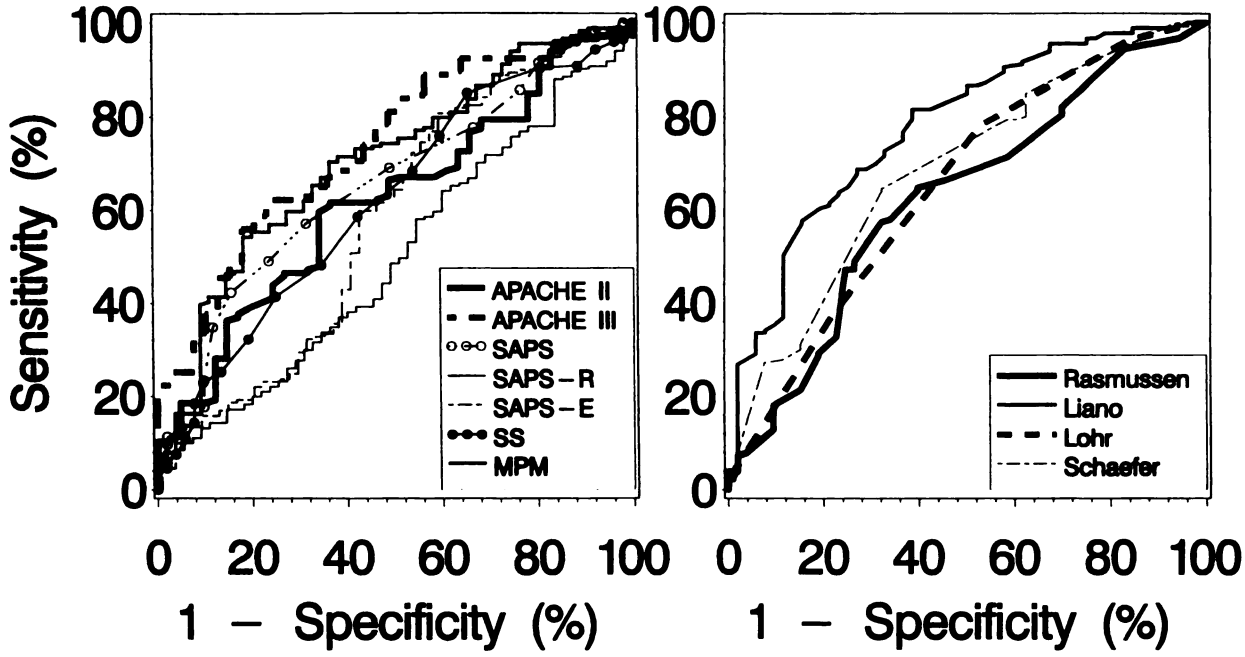

Figure 1. ROC curve analysis for seven general mortality prediction models (left panel) and four models specifically developed for patients with acute renal failure (right panel).

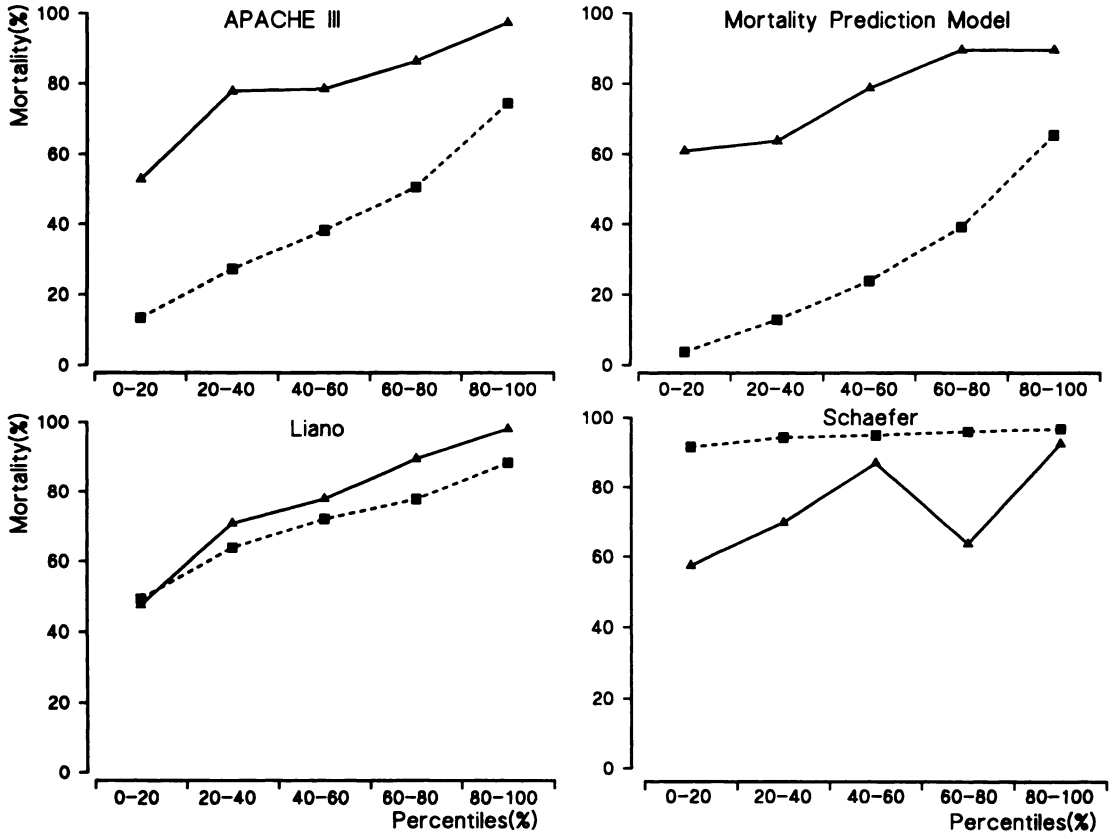

Figure 2. The observed (—) and predicted (- - -) mortality in each quintile of risk for two general prognostic models (APACHE III, Mortality Prediction Model) and two ARF-specific models (Liano, Schaefer).

of a >70% cutoff point for the APACHE II score. However, Schaefer *et al.* (13) questioned the usefulness of the 70% cutoff point according to the APACHE II model. They reported that certain-death patients could not be identified using the APACHE II model based on risk cutoff points of 50% and 70%.

Table 2. Number of patients available for different models (*N*), number of parameters, (no.) of clinical components of different models, relative weight (%) of these variables in each model, area under the ROC curve, mortality in the highest quintile with confidence intervals, and lower limit of the highest quintile of the predicted mortality risk[a]

	APACHE III (N = 182)[b]Pb	MPM (N = 234)	Liano (N = 231)	Schaefer (N = 233)
Parameter				
Metabolic	5 (8)		1 (11)	1 (28)
Cardiovascular	2 (6)	1 (16)	1 (16)	2 (43)
Respiratory	2 (5)		1 (19)	1 (14)
Renal	3 (4)		2 (21)	
Neurological	1 (4)	1 (10)	2 (9)	
Hematology/malignancy	1 (0)	1 (14)		
Infection	2 (3)	1 (14)		1 (9)
Cardiopulmonary recuscitation		1 (9)		
Chronic diseases	7 (8)			1 (6)
Personal characteristics	1 (12)	1 (15)	2 (25)	
Reason for ICU admission	3 (48)	1 (22)		
Area under ROC curve (SE)	0.74 (0.04)	0.71 (0.04)	0.78 (0.03)	0.69 (0.04)
Observed mortality in highest quintile, 95% confidence interval, % (no.)	97 (86–100)	89 (77–97)	98 (89–100)	93 (82–98)
Lower limit of highest quintile of predicted risk (%)	59	49	84	97

[a] APACHE, Acute Physiology and Chronic Health Evaluation; MPM, Mortality Prediction Model; ICU, intensive care unit; ROC, receiver operating characteristics; SE, standard error; CABG, coronary artery bypass graft.
[b]For APACHE III, CABG patients were excluded.

Another, and clinically more relevant, approach to identify patients with a near-100% chance of mortality involves examination of the group of patients in the highest quintile of risk. In this study, we found that the patients in the highest quintiles using the APACHE III and Liano models experienced a near-100% mortality (97% and 98%, respectively).

Comparisons of the observed and predicted risks in the five quintiles of risk generally showed a gross underestimation of risk by all general ICU models. In contrast, the ARF-specific models assigned risks more consistent with the high risk of mortality in this group, and Schaefer's model even overestimated this risk. These differences in calibration may be explained by the fact that the average risk of mortality among patients with ARF receiving dialysis is much higher than the average overall mortality risk in the ICU and that the differences between ICU patients with ARF and general ICU patients are not completely represented by the predictors of the general ICU models. Another explanation for the lack of calibration may be the fact that the information used to assign risks of mortality were collected within the 24 h before dialysis treatment, whereas some of the models included in this study were designed particularly for use in the first 24 h after admission to the ICU. Because the probability of mortality increases as the duration of stay in the ICU increases, Lemeshow *et al.* (24) noted that the MPM model must be recalibrated by adding a constant term to the model. It is likely that the discriminative performances of the general ICU models would probably have been poorer had the first 24 h after ICU admission been used in scoring the patients. Others have noted, for example, that APACHE scores from the previous 24-h period show a better predictive value than those based on the first 24-h period after ICU admission (25).

One possible explanation for the better performance of the APACHE III model compared with some of the other models was that the patients receiving CABG surgery were not assigned APACHE III risks and, thus, were not included in its assessment. To determine whether their exclusion from the assessments of model performance had influenced the results, we reassessed the other models after removing these patients from the analyses. No major changes in performance were observed after their exclusion. Another remarkable difference is the relative weight of the reason for ICU admission. In the APACHE III score, this variable provides almost 50% of the total score, but most other models do not even include this variable.

In examining the identification of futile dialysis treatment, greater consideration of the choice of outcome measure is

Table 3. Long-term outcome of patients in highest quintiles[a]

	APACHE III	MPM	Liano	Schaefer
Hospital Survivors (no.)	1	5	1	4
Alive 1 y after Discharge (alive without dialysis)	0	1 (0)	1 (1)	2 (2)

[a] APACHE, Acute Physiology and Chronic Health Evaluation; MPM, Mortality Prediction Model.

worthwhile. Inhospital mortality has been the outcome used most widely. However, attention should also be directed toward the long-term survival and quality of life expected after discharge from the ICU. For example, the single surviving patient in the highest quintile based on the APACHE III predicted risk died within 1 yr of discharge from the hospital. In terms of long-term prognosis of renal function, some studies have demonstrated that some patients show a deterioration in renal function in the years following ARF (26,27). Bonomini *et al.* (28) reported that only 45% of their surviving patients had a normal renal function after 5 yr. Chertow *et al.* (3) noted that after discharge, many patients required placement in long-term care facilities for all or nearly all surviving months.

In conclusion, the predictive abilities of the mortality prediction models examined in this study varied widely when applied to patients with ARF receiving dialysis. All models showed poor-to-moderate discriminatory ability, but some could identify a subgroup of patients with a near-100% inhospital mortality despite dialysis, which suggests that clinicians can use the risk estimates based on the APACHE III and Liano models as a method of decision support when considering the value of dialysis for an individual patient with ARF. In this way, it can be considered an "adjunct to their informed but subjective opinion" (16). Specifically, when the mortality risks estimated by the APACHE III and the model of Liano are in the highest quintiles of risk, the factors responsible for the high estimate should be examined. In this way, mortality risk estimates might, indeed, serve as a decision-support method rather than a decision rule, dictating whether or not to provide costly and unpleasant treatment. The results of this present study suggest the need for prospective evaluation of these predictive models in a large number of patients.

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