

Review article: scoring systems for assessing prognosis in critically ill adult cirrhotics

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SUMMARY

Background

Cirrhotic patients admitted to intensive care units (ICU) still have poor outcomes. Some current ICU prognostic models [Acute Physiology and Chronic Health Evaluation (APACHE), Organ System Failure (OSF) and Sequential Organ Failure Assessment (SOFA)] were used to stratify cirrhotics into risk categories, but few cirrhotics were included in the original model development. Liver-specific scores [Child-Turcotte-Pugh (CTP) and model for end-stage liver disease (MELD)] could be useful in this setting.

Aim

To evaluate whether ICU prognostic models perform better compared with liver-disease specific ones in cirrhotics admitted to ICU.

Methods

We performed a structured literature review identifying clinical studies focusing on prognosis and risk factors for mortality in adult cirrhotics admitted to ICU.

Results

We found 21 studies (five solely dealing with gastrointestinal bleeding) published during the last 20 years (54–420 patients in each). APACHE II and III, SOFA and OSF had better discrimination for correctly predicting death compared with the CTP score. The MELD score was evaluated only in one study and had good predictive accuracy [receiver operator characteristic (ROC) curve: 0.81]. Organ dysfunction models (OSF, SOFA) were superior compared with APACHE II and III (ROC curve: range 0.83–0.94 vs. 0.66–0.88 respectively). Cardiovascular, liver and renal system dysfunction were more frequently independently associated with mortality.

Conclusions

General-ICU models had better performance in cirrhotic populations compared with CTP score; OSF and SOFA had the best predictive ability. Further prospective and validation studies are needed.

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INTRODUCTION

Several predictive scoring systems have been developed and validated in general intensive care unit (ICU) populations, to evaluate the severity of illness and prognosis.^{1, 2} Although some prognostic models have also been validated in cirrhotics admitted to ICU, none was derived from a large cohort of cirrhotics. In addition, few studies developed new models from such cohorts; these had similar or better performance, compared with established scoring systems.^{3, 4}

Patients with different disease states and/or indications for ICU admission have widely different outcomes.⁵ Thus, patients with decompensated cirrhosis admitted to ICU with acute illness, have a poorer prognosis compared with non-cirrhotics without underlying chronic disease;^{6, 7} and cirrhotics admitted with septic shock have a worse outcome, compared with those admitted only for airway protection after gastrointestinal bleeding (GIB).⁶

Recently, there has been renewed interest in critically ill cirrhotics because of increasing use of sophisticated (but more expensive) technology and medical care: e.g. terlipressin in hepatorenal syndrome and GIB, transjugular intrahepatic portosystemic shunt placement in uncontrolled GIB, molecular adsorbent re-circulating system and bioartificial livers in liver failure. In addition, liver transplantation can offer long-term survival. These new therapeutic possibilities require reliable prognostic factors to construct useful therapeutic algorithms for critically ill cirrhotics. Conversely, it is useful to have some basis to assess when ICU therapy may be futile. ICU costs account for 20–30% of hospital costs in developed countries,^{8–10} but high technology medicine, which is expensive, may not necessarily improve patient outcome and quality of life.¹¹

Prognostic models are been used for comparison and quality assessment between different ICUs and within the same ICU over time, for audit and clinical research,^{12, 13} and for evaluating therapeutic effectiveness and guiding discussions between clinicians and families.^{13–16}

Scoring systems and ability to predict ICU outcome

Most prognostic models evaluate survival on discharge from ICU or hospital, using data collected at admission or within the first 24 h in ICU. There are two types:

general models derived from general ICU populations¹⁷ and disease-specific models.

There are two main categories of general prognostic models: first, those evaluating the severity of illness: Acute Physiology and Chronic Health Evaluation (APACHE) II and III (Table A1), Simplified Acute Physiology Score (SAPS) II and Mortality Prediction Model (MPM) II, which are most used, and secondly, models quantifying organ dysfunction and failure: Logistic Organ Dysfunction System, Multiple Organ Dysfunction Score, Organ System Failure (OSF) (Table A2) and Sequential Organ Failure Assessment (SOFA) (Table A3).²

The model performance is usually evaluated statistically by measuring both calibration and discriminative ability.¹⁸ The former is usually described by the goodness-of-fit statistic (Lemeshow-Hosmer chi-squared statistic), which compares the predicted mortality with the actual mortality,¹⁹ (chi-squared statistic with a *P*-value between 0.2 and 0.8 is considered good). The latter is usually estimated by the area under the receiver operator characteristic (ROC) curve (*AUC*), which is a plot of true positive rate (sensitivity) vs. false-positive rate (1 – specificity) and describes the ability of the model to separate patients who die from those with the same score who live.¹⁹ The *AUC* ranges from 0 to 1, with 0.5 corresponding to what is expected by chance alone and 1.0 to perfect discrimination. In general, an *AUC* > 0.7 indicates a useful test, but never can be 1.0.¹⁹ However, although most general scoring systems demonstrate good discrimination (*AUC* > 0.7–0.8), they do not have acceptable calibration ability (i.e. significant discrepancy between predicted and observed outcome).²⁰ In addition, their accuracy is reduced in patients differing from the original cohort, and/or with different indications for ICU admission and/or developing different complications during ICU stay.⁵ Another drawback is that patients with medium risk and not those with the highest or lowest scores are responsible for the large resource utilization in ICU.^{13, 21}

Scoring systems in cirrhotic patients admitted to ICU

Patients with cirrhosis have a poor prognosis, especially when they develop complications.^{22, 23} The Child and Turcotte classification (1964)²⁴ and Pugh's modification (1973)²⁵ [Child-Turcotte-Pugh (CTP) score] both assess the severity of liver disease but were originally

developed to assess the risk in undergoing surgical porto-caval shunting and oesophageal transection, respectively, using bilirubin, prothrombin time, albumin, severity of ascites and hepatic encephalopathy.²⁵ The model for end-stage liver disease (MELD) is a new liver-specific prognostic model, currently used to predict short-term survival in cirrhotics and to prioritize recipients for transplantation in the US.²⁶ Neither disease-specific model was designed for predicting outcome in cirrhotics admitted to ICU, who often have non-hepatic organ dysfunction and die of multiple organ failure.²⁷

The aim of this review was to assess the prognostic factors related to cirrhotic patients admitted to ICU and to evaluate whether general ICU prognostic models or liver disease-specific ones were best in this population.

METHODS

We performed a search for studies in the Cochrane Library, MEDLINE and EMBASE using both the English and non-English literature between 1986 and 2005, using the following key words: 'intensive care unit' and 'cirrhosis'. We only selected studies which evaluated the prognosis and risk factors for mortality in cirrhotics admitted to ICU, using general-ICU and/or liver-specific prognostic models. Published abstracts from gastroenterology/hepatology and intensive care conferences during the previous 5 years were also reviewed. Reference lists from studies selected by electronic searching were hand-searched to identify further relevant articles. The following variables were extracted from selected studies and checked independently by E. Cholongitas and A. K. Burroughs: age, length of ICU-stay, cause of cirrhosis, cause of admission to ICU, risk factors for mortality derived from multivariate analysis and the performance of scoring systems to predict ICU and/or in hospital mortality. Separately, we analysed studies related to cirrhotics admitted to ICU with different causes of GIB.

RESULTS

Studies with cirrhotics admitted to ICU

We identified 16 studies^{3, 4, 22, 27-39} (Table 1). Eight studies were published from three centres: four from Taiwan,^{28, 35, 37, 38} with overlapping study periods, and two each from Cleveland^{33, 34} and Vienna,^{3, 27} with

the same study period. In four studies,^{3, 27, 29, 38} the APACHE score was calculated on admission to ICU and not calculated as the worst value for each variable obtained during the first 24 h of admission, as recommended. In nine studies,^{4, 28, 30, 31, 35-39} re-admissions were excluded and only the first admission was evaluated. In only three studies, the impact of individual organ dysfunction was evaluated.^{28, 35, 36} In only four studies, an intrinsic prognostic model was generated.^{3, 4, 22, 35} Studies which did not specifically evaluate cirrhotics admitted to ICU²³ or did not evaluate prognostic models⁴⁰ were excluded.

The cohort size ranged from 54 to 420 patients; median age was 54.7 years (range 48-58.9). The most common cause for ICU admission was GIB in 10 studies^{22, 28, 30, 32-38} (25.6-66%), but six (four Taiwanese and two American) were from the same ICU. The second most common cause for ICU admission was encephalopathy/hepatic coma, followed by GIB and renal failure in four studies (range 22-52%), two from the same ICU.^{3, 27} Alcoholic cirrhosis was the most frequent aetiology (up to 75%) in eight studies,^{3, 4, 27, 30, 33, 34, 36, 39} and viral hepatitis in six studies.^{28, 29, 31, 35, 37, 38} Most patients were classified as Child-Turcotte-Pugh (CTP) C at admission to ICU (range 53-82%).

The mortality rate was high in all studies: after a median of 7 days in ICU, an average between 36% and 59% had died. The average in-hospital mortality was higher, ranging from 44% to 73.6%. Approximately one-third of patients had aspiration pneumonia on admission or developed it during their ICU stay (the latter only evaluated in two studies)^{29, 30} (Table 1).

Multivariate logistic regression analysis was performed in 11 studies^{3, 4, 22, 28-31, 33-35, 39} identifying independently associated factors with mortality: cardiovascular system dysfunction, i.e. low-mean arterial pressure or utilization of adrenergic support in four studies^{28, 33-35} [odds ratio (OR): 0.95-7.5], and in a single study,⁴ the number of failing organs, based on SOFA score. Renal insufficiency, defined as an abnormal serum creatinine, or urea, or reduced creatinine clearance, was associated independently with mortality in seven studies^{3, 4, 22, 29, 31, 33, 39} (OR: 1.06-5.3). OSF was an independent factor associated with mortality in two other studies from the same centre in which the renal insufficiency, as a component of OSF, had the highest adjusted OR (7.5 and 8.3, $P < 0.05$), after hepatic and cardiovascular failure.^{28, 35} Finally, severity of hepatic disease, defined as high bilirubin (or presence

Table 1. Review of published studies evaluating the outcome of cirrhotic patients admitted to intensive care unit

Study	Number of patients	Age (years)	Liver disease (%)	Cause of admission (%)	Scores (mean)	Mortality (%)	Days (ICU)	Multivariate analysis (odds or hazard ratio)	Prognostic models (ROC curve)	Aspiration pneumonia (%)
Zauner <i>et al.</i> ³	196	51	ALD (69)	Hepatic coma: 22 RF: 22 GIB: 17	APA III: 74	52	8.4	Bilirubin Cholesterol Cr clearance Lactate	ICCO: 0.83 APA III: 0.76	
Cholongitas <i>et al.</i> ⁴	312	49.6	ALD (62.3)	LF: 35.8 GIB: 22 RF: 12.6	CTP: 11.2 APA II: 19.4 MELD: 25.3 SOFA: 10.8	65.3	4	FiO ₂ : 22.8 Lactate: 1.32 Urea: 1.06 Bilirubin: 1.04 Failing organs	CTP: 0.72 APA II: 0.78 MELD: 0.81 SOFA: 0.83	
Shellman <i>et al.</i> ²²	100	51.2		GIB: 66 Sepsis: 7 Cardiac: 7	CT class (A: 22%, B: 25%, C: 53%)	54 (ICU) 64 (HOS)	5.4	CT class MV Cr >1.3		
Zauner <i>et al.</i> ²⁷	198	51	ALD (68)	Hepatic coma: 24.7 RF: 21.7 GIB: 17	APA III: 73.5 APA II: 20.9 Mayo: 10.5	52			APA III: 0.75 APA II: 0.69 Mayo: 0.72	
Tsai <i>et al.</i> ²⁸	160	56	CHB (37.5)	GIB: 39 Sepsis: 24 RF: 6.9	CTP: 11.5 OSF: 2.9 SOFA: 10.7	65 (HOS)	7	OSF: 0.16 Bilirubin: 0.9 MAP: 1.05	OSF: 0.90 SOFA: 0.89 CTP: 0.71	
Singh <i>et al.</i> ²⁹	54	48	Viral (35)	ENCE: 52 GIB: 20	CTP: 12 APA II: 16.5	43 (ICU)	9	Pulmonary infiltrate Cr >1.5 mg/dL		31
Rabe <i>et al.</i> ³⁰	76	55	ALD (59)	GIB: 57 ENCE: 25	CTP: 11 APA II: 16.7	59 (ICU)		CTP: 1.69 Infection: 19.8	APA II: 0.66 CTP: 0.87	38
Arabi <i>et al.</i> ³¹	129	54.9	Viral (78)		APA II: 27.2 SAPS II: 54.2 MPM II : 67	56.6 (ICU) 73.6 (HOS)	4.1	GCS: 7.17 RF: 5.3		
Zimmerman <i>et al.</i> ³²	117	53.3		GIB: 25.6	APA III: 97	63 (HOS)			M1 = APA III/MV/pressors M2 = APA III/pressors/ renal failure	M1: 0.903 M2: 0.907
Aggrawal <i>et al.</i> ³³	420	55.2	ALD (39.9)	GIB: 36.4 ENCE: 10.9 HRS: 7.6	CTP: 9.6 APA III: 90.1	36.6 (ICU) 49 (HOS)		APA III: 2.2 Pressors: 2.5 Jaundice: 1.7		
Gildea <i>et al.</i> ³⁴	420	55.2	ALD (39)	GIB: 36 ENCE: 11.8	CTP: 10 APA III: 84	44 (HOS)				
Tsai <i>et al.</i> ³⁵	111	58	CHB (48)	GIB: 41 Sepsis: 23 RF: 6	CTP: 11 OSF: 2.9	64.9 (HOS)	6.4	OSF: 5.15 MAP: 0.95 CTP: 1.49	CTP: 0.748 OSF: 0.90	

Table 1. Continued

Study	Number of patients	Age (years)	Liver disease (%)	Cause of admission (%)	Scores (mean)	Mortality (%)	Days (ICU)	Multivariate analysis (odds or hazard ratio)	Prognostic models (ROC curve)	Aspiration pneumonia (%)
Wehler <i>et al.</i> ³⁶	143	53	ALD (75)	GIB: 42 Sepsis: 26 RF: 13	CTP: 10 APA II: 20.6 SOFA: 8.6	36 (ICU) 46 (HOS)		CTP: 0.74 APA II: 0.79 SOFA: 0.94		
Chen <i>et al.</i> ³⁷	67	58.9	CHB (51)	GIB: 33 Sepsis: 28 RF: 8	CTP: 11.4 APA III: 118.5 APA II: 28.1 SOFA: 12.5	86.6	9.4	APA III: 0.87 APA II: 0.79 SOFA: 0.86 CTP: 0.77		
Ho <i>et al.</i> ³⁸	135	58	CHB (49)	GIB: 35 Sepsis: 24	CTP: 11.5 APA II: 24.3	67 (HOS)	-	APA II: 0.83 CTP: 0.75		
du Cheyron <i>et al.</i> ³⁹	186	54.9	ALD (72)	Infection: 36.5 GIB: 31	APA II: 18	41 (ICU) 45 (HOS)	8.7	ALD: 4.8 Sepsis: 3.6 RF: 4.1 Age: 1.5	-	

ROC, receiver operator characteristic; CHB, chronic hepatitis B; GIB, gastrointestinal bleeding; ALD, alcoholic liver disease; GCS, Glasgow scale; ENCE, hepatic encephalopathy; APA, Acute Physiology and Chronic Health Evaluation; CT, Child-Turcotte; CTP, Child-Turcotte-Pugh score; SAPS II, Simplified Acute Physiology Score II; MELD, model for end-stage liver disease; MPM II, Mortality Prediction Model II; MV, mechanical ventilation; Cr, creatinine; HRS, hepatorenal syndrome; RF, renal failure; ICU, intensive care unit; HOS, hospital; MAP, mean arterial pressure; LF, liver failure; ICCO, intensive care cirrhosis outcome; SOFA, Sequential Organ Failure Assessment; OSF, Organ System Failure [0.37 + (0.073 × bilirubin) - (0.0084 × cholesterol) - (0.0155 × creatinine clearance) + (0.1351 × lactate)].

of jaundice), severe encephalopathy, high Child-Pugh/Child-Turcotte score, or liver failure (as component of SOFA or OSF) was independently associated with mortality in all but two studies^{29, 33} (OR: 0.9–7.17).

Performance of general vs. liver-specific models

General models (APACHE II and III, SOFA, OSF) were compared with liver-specific (CTP, Mayo risk, MELD) prognostic models. The median values at admission were CTP: 11 (range 9.6–12), MELD: 24 (one study), APACHE II: 19.4 (16.5–28.9) and APACHE III: 90 (73.5–118.5), SOFA: 10.7 (8.6–12.5) and OSF: 2.9 (both studies had the same value)^{28, 35}. Differences between ROC curves of different scoring systems were compared statistically in five studies,^{28, 30, 35, 36, 38} and in all but one study³⁰ general scores had better discrimination compared with the CTP score. The *AUC* for OSF and SOFA was almost always more than 0.80 (very good accuracy) and better compared with APACHE II and III. In only one study³³ did APACHE III combined with the use of adrenergic support and the presence of acute renal failure, have excellent prognostic accuracy (*AUC* = 0.907). In the single study evaluating MELD score,⁴ MELD had almost the same discrimination as SOFA (*AUC*: 0.81 vs. 0.83), and was better than APACHE II and CTP scores. The performance of the prognostic models based on the goodness-of-fit statistic was evaluated only in four studies,^{28, 35, 37, 38} all from the same centre. Again, general-ICU models were better, than liver-specific ones, and SOFA or OSF had similar or better calibration ability, compared with APACHE II or III. Only one study validated its prognostic model in a separate cohort.³

Studies with cirrhotics admitted solely with GIB to ICU

We found five studies evaluating 840 cirrhotics (median age 50.2 years) admitted to ICU with GIB^{41–45} (Table 2), mostly from bleeding oesophageal varices followed by gastric ulcer bleeding. Most patients underwent endoscopic therapy and/or Blakemore-Sengstaken balloon tamponade. The median values of CTP and APACHE II were 9 (8.8–11.2) and 16.7 (16.5–17) respectively. SOFA and APACHE III were evaluated in only one study⁴¹ (Table 2).

Multivariate analysis was performed in three studies.^{41, 44, 45} Cardiovascular system dysfunction (defined

as low-mean arterial pressure or presence of hypovolemic shock on admission) was always independently prognostically significant. In addition, CTP score and the need for endoscopic therapy were independently associated with mortality but in only two studies. The performance of prognostic models was evaluated in two studies^{41, 43}: SOFA and APACHE III had better discrimination ability (*AUC*: 0.9 and 0.88 respectively) compared with APACHE II (*AUC* = 0.78) and CP (*AUC*: 0.7 and 0.76) scores. The performance of the prognostic models based on the goodness-of-fit statistic was evaluated only in one study⁴¹: general ICU models were superior compared with liver-specific ones; SOFA had better calibration ability than APACHE III (*P*-values: SOFA = 0.82, APACHE III = 0.30, CTP = 0.11).

DISCUSSION

Reviewing the literature, we found 21 cohort studies regarding cirrhotic patients admitted to ICU. Although there was heterogeneity as regards indications for admission, and several studies partly evaluated the same cohort of patients, some important points stand out.

First, and perhaps surprisingly, general prognostic models (APACHE II and III, SOFA, OSF) perform better (higher *AUC*) than liver-specific (CTP and Mayo risk) scores, despite the fact that cirrhotics only formed a very small part of the large heterogeneous ICU populations from which these models were derived, and that the selected studies describe different ICU settings. This finding probably reflects the fact that most cirrhotics are admitted to ICU suffering with multiple organ system dysfunction, in which the liver 'failure' may add little to the increased risk of dying. However, liver-specific parameters (serum albumin and bilirubin) are contained in APACHE III, and organ dysfunction models have a hepatic system assessment.

Secondly, organ dysfunction models had the best performance, compared with severity of illness systems. In particular, OSF and SOFA always had very good discrimination (*AUC* > 0.80) and similar or better calibration, compared with APACHE II or III. The SOFA score is simpler (can be calculated at the bedside in 1–2 min) than OSF. However, the superiority of SOFA and/or OSF was based on only five studies,^{4, 28, 35–37} with three^{28, 35, 37} from the same centre. The latter were the only ones in which calibration was

Table 2. Review of published studies evaluating outcome of cirrhotic patients admitted to intensive care unit with gastrointestinal bleeding

Study	Number of patients	Age (years)	Liver disease (%)	Purpose of study	Scores (mean)	Mortality (%)	Days (ICU)	Multivariate analysis (odds ratio)	Prognostic models (ROC curve)	Procedures (%)
Chen <i>et al.</i> ⁴¹	76	57	CHB (38) ALD (37)	Compare SOFA-APA III - risk factors for mortality	CP: 11.2 SOFA: 10.3 APA III: 100	68.4 (HOS)	6.6	CTP: 1.94 Cr: 1.54 MAP: 0.93	APA III: 0.88 SOFA: 0.9 CTP: 0.7	
Combiere <i>et al.</i> ⁴²	84			Cost effectiveness of terlipressin		27.5 (terlipressin)	6.4			Endo: 71.5 Blakemore: 36 TIPS: 12
Afessa and Kubilis ⁴³	111	48.7		Assessment of predictive models	CP: 9 APA II: 17	27 (HOS)	8		APA II: 0.78 CTP: 0.76	Endo: 77 Blakemore: 13 TIPS: 10
Carbonell <i>et al.</i> ⁴⁴	468			Survival for bleeding over the past two decades	CP: 8.8			CTP, age, hypovolemic shock, endoscopy, antibiotic prophylaxis		Endo: 39.7 Blakemore: 16 TIPS/surgery: 5
Lee <i>et al.</i> ⁴⁵	101	50.2	ALD: 66.3	Predictors of mortality and ARDS	APA II: 16.5	47.5 (HOS)	4.4	Ethanolamine: 1.2 transfusion: 6.1 GCS: 1.3 INR: 1.9 Shock: 3.7		Endo: 79.8 Blakemore: 51.6 Vasopressin: 37.9

ROC, receiver operator characteristic; ICU, intensive care unit; CHB, chronic hepatitis B; ALD, alcoholic liver disease; GCS, Glasgow scale; APA, Acute Physiology and Chronic Health Evaluation; CTP, Child-Turcotte-Pugh score; Cr, creatinine; HOS, hospital; MAP, mean arterial pressure; ARDS, acute respiratory syndrome; SOFA, Sequential Organ Failure Assessment; TIPS, transjugular intrahepatic portosystemic shunt; INR, international normalized ratio.

evaluated. Calibration of models is very important to guide clinical decision about an individual patient.²¹ Thus, more studies are needed to assess the model performance. The predictive abilities of APACHE II and CTP were comparable. Both were less accurate compared with organ dysfunction models (SOFA, OSF), but it is unclear if these differences are significant.

The MELD score has very good short-term (3-month) prediction for end-stage cirrhotics.^{26, 46} In the single study to date, it had similar accuracy to SOFA (*AUC*: 0.81 vs. 0.83) and was better than APACHE II and CTP,⁴ but it requires computer computation. Further evaluation is needed. Although MELD contains only objective variables reducing intra and inter-observer variability,²⁰ there is variable measurement of these.^{47, 48} Other models contain subjective variables: e.g. neurological status in intubated patients (SOFA and APACHE) and encephalopathy/ascites (CTP). A caveat in interpreting ROC curves in our review, as well as in any study, is that criteria for non-escalation or withdrawal of therapy are not stated and may already be present at ICU admission. This would lead to falsely high areas under the curves. However, within each study, a comparison of scoring systems would not have this bias.

Age was not an independent factor for mortality except in one study,³⁹ but it is a component of the APACHE scores. However, it appears that the age range of cirrhotics as reported is quite narrow with a minority of patients above 65 years of age – a prognostic factor reported in the SUPPORT study,²³ which, however, included hospitalized cirrhotics not necessarily admitted to ICU. In addition, respiratory failure was not a significant prognostic factor. This is likely to be due to not distinguishing between hypoxaemia requiring ventilatory support and elective intubation, particularly in cirrhotics with bleeding or encephalopathy. The SOFA scoring system gives a score of 3 or more whenever there is intubation regardless of indication. In our study,⁴ we discounted elective intubation as being equivalent to respiratory failure and found that FiO_2 as a surrogate marker was independently prognostic. Hypoxaemic respiratory and/or mechanical ventilation were prognostically significant in the SUPPORT study.²³ Lastly, hepatopulmonary syndrome which has a poor prognosis⁴⁹ was not specifically identified in any study.

However, cardiovascular, renal and hepatic dysfunction were associated with increased mortality. These findings should help to improve prognostication of

cirrhotics admitted to ICU⁴⁵ whose main cause of death is multisystem organ failure.^{22, 27} Deterioration in liver function was an independent prognostic factor predisposing to development of multisystem organ dysfunction/failure.^{7, 27} Renal dysfunction is associated with increased mortality in ICU,⁵⁰ especially in cirrhotics.^{39, 51} The superiority of MELD, which uses serum creatinine, compared with other liver disease-specific models, may relate to the impact of renal dysfunction on mortality.

Established prognostic models have low calibration (goodness-of-fit),⁵² and their specificity can never be 100%.¹⁷ They are usually estimated after the first 24 h of ICU admission. Thus, current models have weak prediction for individual patients and may not be suitable to decide on the appropriateness of admission to ICU, as clinical status may improve over the first 24 h with therapy or deteriorate due to complications.¹⁷ Other limitations are that they are not designed to predict prognosis for long stays or after ICU discharge and do not evaluate end points other than mortality, such as cost-effectiveness or recovery of physical activity or quality of life.^{19, 21, 52, 53}

The predictor variables used in models have been selected by consensus (e.g. APACHE I and II) or by statistical weighting from '*a priori*' chosen factors (e.g. MPM II, SAPS and APACHE III). Thus, non-selected variables could be as important, or more so, for outcome prediction.^{18, 21} For example, serum lactate is a component of prognostic models in fulminant hepatic failure⁵⁴ and concentrations are increased in cirrhotics.⁵⁵ In addition, serum lactate reflects cardiovascular, liver and renal dysfunction (all three having independent association with mortality in cirrhotics admitted to ICU). Serum lactate was selected as an independent predictor in two studies.^{3, 4} Inclusion of lactate as well as other markers (e.g. osmolal gap, ketone body ratio) may increase the discrimination and calibration of current prognostic scores.⁵⁶

In the future, evaluation of new specific models should preferably be based on a large number of cirrhotics admitted to ICU,⁵⁷ validating and comparing them with established scores, including an evaluation of added complications, such as adult respiratory distress syndrome and multisystem organ failure.^{21, 58} This may help in deciding when treatment is futile.

In conclusion, our review concerning cirrhotics admitted to ICU shows that general ICU prognostic models perform better than the liver-specific CTP

score. The performance of the MELD score needs further evaluation. In a recent abstract publication comprising 363 patients, the ROC analysis showed MELD and CTP scores to be inferior to SOFA and APACHE II, but with overlapping 95% confidence intervals.⁵⁹ The best models are those assessing failure of body sys-

tems, the most important being cardiovascular, renal and liver. New markers, in particular serum lactate, should be assessed. Future evaluation of prognostic factors before ICU admission may help to guide decisions about intensive care admission, or withdrawal or non-escalation of therapy.

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APPENDIX

Table A1. Acute physiology and chronic health evaluation (APACHE) II score

A - Physiology score (APS)									
Parameter	+4	+3	+2	+1	0	+1	+2	+3	+4
Rectal temperature (°C)	≥41	39-40.9	110-129	38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean arterial pressure (mmHg)	≥160	130-159	110-129	70-109	70-109	50-69	55-69	40-54	≤49
Heart rate/min	≥180	140-179	110-139	70-109	70-109	55-69	55-69	40-54	≤39
Ventilation rate/min*	≥50	35-49	110-139	25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg)	≥500	350-499	200-349	<200	>70	61-70	-	55-60	<55
FiO ₂ ≥ 0.5 A-aDO ₂	≥7.7	7.6-7.69	155-159	7.5-7.59	7.33-7.49	7.25-7.32	7.25-7.32	7.15-7.24	<7.15
Arterial pH	≥180	160-179	155-159	150-154	130-149	120-129	120-129	111-119	≤110
Serum sodium (mmol/L)	≥7	6-6.9	1.5-1.9	5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		≤2.5
Serum potassium (mmol/L)	≥3.5	2-3.4	50-59.9	46-49.9	30-45.9	20-29.9	20-29.9		<20
Serum creatinine (mg/dL)†	≥60		20-39.9	15-19.9	3-14.9	1-2.9	1-2.9		<1
Haematocrit (%)	≥40		32-40.9	32-40.9	22-31.9	18-21.9	18-21.9		<15
White blood cells (t/mm ³)	≥52	41-51.9							
HCO ₃ -venous (mmol/L)‡	Score = 15 - actual Glasgow Coma Scale								
Glasgow Coma Scale	C - Chronic Health points								
B - age points									

Age	Points	If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows
≤44	0	
45-54	2	(a) Non-operative or emergency postoperative patients 5 points (b) Elective postoperative patients 2 points
55-64	3	
65-74	5	
≥75	6	

* Non-ventilated or ventilated.

† Score points doubled for acute renal failure.

‡ Missing blood gas analysis.

Table A2. Criteria for calculation of the organ system failure (OSF) score	
Organ system	Criteria
Neurological	Glasgow Coma Scale ≤ 6 (in absence of sedation at any one-point in day)
Cardiovascular	Mean arterial pressure ≤ 50 mmHg
and/or	Heart rate ≤ 50 beats/min
and/or	Need for volume loading and/or vasoactive drugs to maintain systolic blood pressure above 100 mmHg
and/or	Occurrence of ventricular tachycardia/fibrillation
and/or	Cardiac arrest
and/or	Acute myocardial infarction
Pulmonary	Respiratory rate ≤ 5 /min or ≥ 50 /min
and/or	Mechanical ventilation for ≥ 3 days
and/or	Fraction of inspired oxygen (FiO_2) > 0.4 and/or positive end-expiratory pressure > 5 cm H_2O
Gastrointestinal	Stress ulcer necessitating transfusion of more than 2 U of blood per 24 h
and/or	Haemorrhagic pancreatitis
and/or	Acalculous cholecystitis
and/or	Necrotizing enterocolitis
and/or	Bowel perforation
Hepatic	Clinical jaundice or total bilirubin level ≥ 3 mg/dL in the absence of haemolysis
and/or	Serum glutamic-pyruvic transaminase $>$ twice normal
and/or	Hepatic encephalopathy
Renal	Serum creatinine level > 3.2 mg/dL
and/or	A two-fold creatinine rise in chronic renal failure, after correcting prerenal causes and mechanical obstruction
and/or	Acute need of renal replacement therapy (chronic renal failure was defined as serum creatinine > 2.3 mg/dL)
Haematological	Haematocrit $< 20\%$
and/or	Leucocyte count $\leq 0.3 \times 10^9/L$
and/or	Thrombocyte count $\leq 50 \times 10^9/L$
and/or	Disseminated intravascular coagulation

Table A3. Sequential organ failure assessment (SOFA) score					
Variables/score	0	1	2	3	4
Respiratory (PaO_2/FiO_2 , mmHg)	> 400	≤ 400	≤ 300	≤ 200	≤ 100
Coagulation ($PLT \times 10^3/\mu L$)	> 150	≤ 150	≤ 100	≤ 50	≤ 20
Liver (bilirubin, mg/dL)	< 1.2	1.2–1.9	2–5.9	6–11.9	> 12
Cardiovascular (Hg/kg/min)	–	MAP < 70	Dop ≤ 5	Dop > 5 (Epi ≤ 0.1)	(Epi > 0.1)
CNS (GCS)	15	13–14	10–12	6–9	< 6
Renal (creatinine, mg/dL)	< 1.2	1.2–1.9	2–3.4	3.5–4.9	> 5

MAP, mean arterial pressure; Dop, dopamine; Epi, epinephrine; CNS, central nervous system GCS, Glasgow Coma Scale; PLT, platelets.