Predicting Short-term Mortality and Long-term Survival of Hospitalized U.S. Patients with Alcoholic Hepatitis

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Abstract

Background—No study has evaluated current scoring systems for their accuracy in predicting short- and long-term outcome of alcoholic hepatitis in a U.S. population.

Methods—We reviewed electronic records for patients with ALD admitted to Parkland Memorial Hospital between January 2002 and August 2005. Data and outcomes for 148 of 1761 admissions meeting pre-defined criteria were collected. The discriminant function (DF) was revised (INRdf) to account for changes in prothrombin time reagents that could potentially affect identification of risk using the prior DF threshold of > 32. Admission and theoretical peak scores using the Model for End-stage Liver Disease (MELD) were calculated. Analysis models compared 5 different scoring systems.

Results—INRdf was closely correlated with the old DF ($r^2 = 0.95$). Multivariate analysis of data showed that survival at 28 days was significantly associated with admission values for white blood cell count (p = 0.006), a scoring system using a combination of age, bilirubin, coagulation status and creatinine (p < 0.001) as well as an elevated ammonia result within 2 days of admission (p = 0.006). When peak values for MELD were included, they were the most significant predictor of short-term mortality (p < 0.001) followed by INRdf (p = 0.006

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Conclusion—On admission, 2 scoring systems that identify a subset of patients with severe alcoholic liver disease are able to predict > 50% mortality at 4 weeks as well as > 80% mortality at 6 months without specific treatment.

Keywords

discriminant function; Model of End-stage Liver Disease; prothrombin time; internal sensitivity index; alcoholic hepatitis scores

Introduction

Management of severe alcoholic hepatitis is not uniform in the U.S. despite decades of clinical research [1–3]. The value of corticosteroids for a sub-group of patients was often debated [4–6]. In 2008, the Cochrane Hepato-Biliary Group systematic review, with meta-analyses and trial sequential analyses, concluded that the current evidence base did not support the use of corticosteroids and that additional data were needed[7] while society guidelines advocated corticosteroids for more severe disease[8].

Factors that may influence short- (28 day) or intermediate-term (90 day or 6 month) survival in alcoholic hepatitis now include geographic location and availability of orthotopic liver transplantation. Limitations placed on transplantation arise from either lack of eligibility for liver transplantation, without 6 months of documented complete abstinence, or lack of financial resources or both. Identifying those likely to benefit from corticosteroids or alternative novel therapies in the short-term may be important for understanding not only intermediate- but also long-term (> 12 months) survival with or without rescue transplantation.

The criteria for defining steroid-responsive severe disease were originally established by Maddrey and colleagues[9]. The equation that discriminated those patients with the potential to benefit from corticosteroid therapy is often termed the Maddrey discriminant function (DF). The equation was a simple calculation based on the total bilirubin and the prothrombin time[9] which was then modified by Carithers *et al* so that prothrombin time (PT) measurements in different institutions could be compared and pooled in clinical trials[10].

Since the empiric generation of the Maddrey DF in the 1970s, measurements of total bilirubin have not changed. In contrast, measurement of the PT has undergone a series of improvements, designed to allow comparison of results between different laboratories [11–13]. New scoring systems to assess the severity of alcoholic hepatitis, with measures other than PT to assess coagulopathy, were developed in Scotland[14] and Spain[15] and compared with DF and the Model for End-stage Liver Disease (MELD) score in European[16–18] and Mexican[19] patients. We postulated that changes in PT reagents altered the DF threshold in a quantifiable manner. The current retrospective cross-sectional study was undertaken to examine this hypothesis and to identify factors that predicted survival in U.S. patients using 5 different scoring systems.

Materials and Methods

A UT Southwestern institutional review board approved, retrospective electronic chart review was performed of all patients with a diagnosis of alcoholic hepatitis between the dates of January 2002 and August 2005 at Parkland Memorial Hospital (PMH) an affiliated hospital of the University of Texas Southwestern Medical Center in Dallas, Texas. Subjects were identified by electronic health record query of all patients discharged with International Classification of Diseases, 9th revision codes 571.1 (acute alcoholic hepatitis), 571.2 (alcoholic cirrhosis) and 571.3 (alcoholic liver disease). A state institutional review board approved access to death certificate data from the Texas State Department of Health Statistics.

Patient selection criteria

Inclusion criteria were based on laboratory features consistent with jaundice from an acute decompensation in ALD (bilirubin > 5 mg/dL unaccounted for by another etiology or transfusion, AST increased and < 500 U/L with AST > ALT). Results from a clinical data repository were extracted; radiology, pathology and discharge summaries were reviewed for relevant information. Exclusion criteria were concomitant liver disease, persistent hyperbilirubinemia for > 2 months prior to admission, abstinence confirmed on multiple encounters, an alternative diagnosis or a previous index admission. Results of paracentesis in the first 2 days of the admission were used as a surrogate marker of clinical ascites and any elevated ammonia level in the first 2 days was used as a marker of deteriorated overall liver function. This time period allowed patients to improve or deteriorate when initially hospitalized, a strategy comparable to the observation period before using corticosteroids in management.

PT measurements

Conversion of PT measured in seconds, to International Normalized Ratio (INR), is dependent on the patient's PT, the reference PT and the international sensitivity index (ISI) of the manufacturer's reagents. The equation is INR = (patient PT / geometric mean of reference interval PT)^{ISI}. The geometric mean reference interval changed from 10.69 (July to October 1997) to 11.13 (November 1997 to November 1998) and then to 11.71 (since December 1998). The ISI changed in December 1998 from 1.5 to 1.0. We calculated the effect of these changes in reagent sensitivity (ISI) and reference interval on the PT. The old and new values were related using the following equation, old PT = 4.087 + 0.5297(new PT). These effects were validated by analyzing > 1000 patient samples simultaneously using new versus old technology following implementation in 1998. We used this relationship to derive a new DF that used the INR (INRdf) with INRdf > 50 being the equivalent to DF > 32 prior to 1997 (see supplementary Figure A and supplementary Table A). The old DF was highly correlated to INRdf ($r^2 = 0.95$), the correlation between admission MELD and either DF or INRdf was less strong ($r^2 = 0.71$ and 0.79 respectively, supplementary Figure B).

Data collection and analysis

Demographics and laboratory test results were collected for all patients and entered into a computerized database. The Maddrey DF as modified for multi-site studies[10], an INR-

based discriminant function (INRdf), MELD score with United Network for Organ Sharing modification[20], Glasgow alcoholic hepatitis score (GAHS)[14] and the age + serum bilirubin + INR + serum creatinine (ABIC) score[15] were calculated at admission. Peak bilirubin, PT, INR and creatinine levels were recorded and a theoretical peak MELD score was calculated from these data. Equations used for calculations of DF, INRdf, MELD and ABIC scores and GAHS are as shown (supplementary Table A).

Statistical analysis

Comparisons of demographics, laboratory values and mortality were performed among INRdf groups. Continuous variables were compared using Student's t-test, Wilcoxon rank-sum (Mann-Whitney) tests or Spearman's rank correlation; categorical variables were compared with chi-square tests or Fisher's exact tests. Patient survival rates were estimated using the Kaplan-Meier method. Log-rank tests were conducted to examine if there were significant differences in survival among groups. Univariate Cox proportional hazards model was used to examine the association between risk factors and survival. Risk factors with p value less than 0.05 from univariate Cox regression were entered as candidate risk factors for stepwise Cox proportional hazards model, which was used to identify significant factors associated with survival. Variables were automatically excluded from multivariate analysis for collinearity. Statistical analysis was performed using Stata 12.1 (College Station, TX, USA) and SAS 9.3 (SAS Institute, Cary, NC, USA).

Results

We reviewed the electronic charts of all patients with the diagnosis of acute alcoholic hepatitis, alcoholic cirrhosis or alcoholic liver disease not otherwise specified (ICD-9 571.1, 571.2 or 571.3) admitted to PMH between January 2002 and August 2005 (Figure 1). A total of 148 patients met the criteria for an index admission. Admissions for these 148 patients accounted for 9% (154/1,761) of the total hospitalizations with a diagnosis of alcoholic liver disease. Maximum bilirubin < 5 mg/dL was the commonest reason for exclusion followed by AST not matching entry criteria. AST was normal in 329 admissions (bilirubin also normal in 50, no recent alcohol in 21), ALT exceeded AST (n = 63) and AST > 500 IU/L (n = 57) were the findings. Based on the calculation of INRdf on admission, patients were classified into two mutually exclusive groups (Figure 1, Table I).

Demographic and initial clinical characteristics

As shown in Table I, patients with INRdf < 50 (n = 115, 78%) had less severe alcoholic hepatitis with MELD scores of 22 ± 5 (mean ± SD) and DF < 32 in 59%. Patients with INRdf > 50 had more severe disease with initial MELD scores 32 ± 6 (n = 33, 22%); all of these patients had a DF > 32 and MELD > 21. The two groups were similar with respect to gender and ethnicity (Table I); INRdf > 50 patients were younger, this was not statistically significant (p = 0.054).

The calculated DF, ABIC and MELD scores and GAHS were significantly different between the groups, reflecting the contribution of bilirubin and INR to the calculations (Table I). There was a wide range of creatinine values on admission (INRdf < 50 = 0.4 – 3.7 mg/dL;

INRdf > 50 = 0.6 – 6.0 mg/dL), explaining the lower correlation of INRdf with MELD than with the modified Maddrey DF (supplementary Figure B and Table B). An elevated ammonia within the first 2 days of admission was statistically more common in the patients with more severe disease (p = 0.016).

Hospitalization follow-up

The majority of patients developed worsening liver function during the index admission; bilirubin increased in 50%, PT in 51% and INR in 41% (supplementary Table B). The significant differences between the INRdf groups on admission persisted when peak values were compared. Renal function deteriorated in a subset of patients in both groups during the index hospitalization; overall creatinine increased in 56% of subjects, with higher frequency in those with more severe alcoholic hepatitis (supplementary Table B). Theoretical peak MELD scores (calculated from the highest values for each parameter) increased after admission in the majority of patients (58%). INRdf groups were statistically different when comparing peak MELD values and the distribution into MELD subgroups (< 21 and > 31).

Mortality

Death certificate data for all-cause mortality were obtained from the Texas State Department of Health Statistics. At each time point, (28 days, 90 days, 6 months, 5 years and overall) there were fewer survivors in the more severely affected groups (supplementary Table C, Figures 2 and 3); categories determined by INRdf, ABIC and MELD on admission gave similar results (40% – 44% alive at 28 days) with more subjects identified using INRdf (15/26 untreated with corticosteroids were deceased). Using DF > 32 for stratification was relatively less informative (66% alive at 28 days); the category included more subjects. The early end-points allow comparison with prior studies using 28 day or 90 day mortality to assess management strategies. When patients who received corticosteroids (n = 8) or corticosteroids and pentoxifylline (n = 1) were excluded, overall mortality was unchanged, reflecting the small number of subjects receiving specific treatments (supplementary Table C).

As expected, a peak MELD > 31 was highly predictive of mortality with 60% (28/47) succumbing by 28 days and 79% by 90 days. Regardless of its acuteness, those subjects with a creatinine that rose at least 0.3 mg/dL during the hospitalization (n = 48, with median peak creatinine 3.4 mg/dL, range 0.9 – 13.5 mg/dL), had a mortality that was high; 50% were known dead at 28 days and 69% at 90 days. In contrast, mortality was relatively low in those subjects with a creatinine that rose < 0.3 mg/dL during the hospitalization (n = 100, with median peak creatinine 0.9 mg/dL, range 0.45 – 4.35 mg/dL); 7% were known dead at 28 days and 19% at 90 days (5 and 7 unknown at 28 and 90 days respectively). None of the cohort was eligible for orthotopic liver transplantation, due to either financial or psychosocial barriers.

Survival analysis

The 28 day Kaplan-Meier survival curves of the different admission stratification groups were clearly separated; admission INRdf (p < 0.0001, chi = 36.20) and ABIC (p < 0.0001, chi = 23.47) were of higher statistical significance than admission MELD (log-rank p =

0.0012 for MELD < 21 and 0.0006 for MELD < 31). DF was the same as MELD > 31 (p = 0.0006) while the GAHS provided better differentiation (p = 0.0001, chi = 15.37). Theoretical peak MELD clearly demonstrated the high mortality in this group (MELD > 31, p < 0.0001, chi = 52.43) with less than half surviving 28 days, in sharp contrast to > 95% survival at 28 days when peak MELD was   31.

In the combined cohort of patients with DF > 32, only 9 patients received corticosteroids (2 with INRdf < 50, 7 with INRdf > 50). All but one was alive at 28 days, 5 had died by 90 days. The remaining 4 subjects (all with INRdf > 50) survived for at least a year after admission (for 13, 31, 70 and 71 months). Excluding the few subjects treated with steroids did not change the findings in the overall analysis.

Long term survival was different depending on severity of the alcoholic liver disease at the index admission as measured by INRdf, DF, ABIC, GAHS or MELD; peak MELD stratification was also informative (Figure 3). The dismal prognosis for all these patients is emphasized by the short median survival in those with a known 5 year outcome, even in the least affected groups (supplementary Table D). Only subjects with a peak MELD < 21 had a substantially longer median survival (65 months, see supplementary Table D). The co-existence of chronic hepatitis C and alcoholic liver disease further shortened survival (supplementary Table D). One abstinent subject with chronic hepatitis C underwent transplantation more than 12 months after admission for icteric liver disease.

Predictive factors

Cox proportional hazards model was used to identify factors predicting survival to 28 days from admission (Table II). In univariate analysis of continuous variables present on admission, higher bilirubin, creatinine, INR and PT levels, WBC counts and scoring systems other than GAHS were significantly associated with decreased survival. Categorical variables present on admission or within 2 days of admission (DF group, INRdf group, ABIC group, MELD group and elevated ammonia) were also significant predictors of decreased survival. When later data from the index admission were analyzed, peak MELD score and peak MELD group predicted decreased survival as did the difference in creatinine between admission and its peak value (Table II).

Stepwise Cox regression analysis identified independent predictors of 28 day survival (Table III). Of the "present on admission" variables, ABIC category and hyperammonemia within 2 days of admission were significant. INR was excluded for co-linearity. When peak MELD group was included in the analysis, it was the most significant independent predictor of outcome (p < 0.0001); however, 2 admission variables, total bilirubin and INRdf category, remained significant. Other variables including ABIC category and hyperammonemia were eliminated in the stepwise process when peak MELD was included. When 90 day survival was examined, hyperammonemia was no longer significant in multivariate analysis whereas DF on admission was significant. When MELD calculated with peak values during admission was included, the 3 significant factors were the same as at 28 days (supplementary table E).

Discussion

The data reported here clearly identify a subgroup of patients with alcoholic hepatitis and a significantly worse short-, intermediate- and long-term prognosis. Thus, patients with INRdf > 50, ABIC > 9 or MELD > 31 on admission had the highest 28 day, 90 day and 6 months mortality. These newer scoring systems identified a small fraction with a high early mortality (56 – 60% at 28 days). In comparison, large randomized placebo-controlled trials of corticosteroids using DF > 32 as a marker of poor outcome at 28 days averaged 34% mortality without corticosteroids[21] and mortality was 46% in the control subjects of the randomized trial of pentoxifylline where in-hospital deaths occurred in 24/52 control patients after 33 ± 27 days (mean $\pm$ SD)[22]. Of note, these studies enrolled patients in the last decades of the 20th century before the changes in PT and INR measurements. INRdf is a simple calculation that increases the number of subjects identified as high risk (sensitivity) while retaining specificity (58% mortality at 28 days) while accounting for changes in analytical reagents.

The observation that an elevated ammonia level within 2 days of admission was independently predictive of death within 28 days suggests that it is a poor prognostic sign in patients admitted with icteric alcoholic liver disease. We used a value obtained from the electronic medical record, which may indicate that altered mentation resulted in ordering the ammonia level. Thus, a normal ammonia level can exclude hyperammonemic encephalopathy and an elevated one is consistent with a contribution of abnormal hepatic nitrogen metabolism to mental status. For ease of use, the INRdf may be preferable to ABIC since it relies only on addition of two numbers one of which is not manipulated before summing. In addition, INRdf was equivalent or superior to ABIC in most comparisons, identifying more patients with a poor prognosis at the time of admission.

Although the number of subjects with INRdf > 50 was relatively small (33 patients, 26 not receiving steroids), the findings demonstrate that these patients have a different prognosis than those with less severe disease. When we compared our primary data for patients not receiving corticosteroids with earlier randomized controlled trials [21], the ranges were similar for age, bilirubin, creatinine, albumin and AST. The PT was longer, DF higher and survival lower in the current subjects with INRdf > 50 or ABIC > 9 (supplementary Table F). In contrast, those identified by DF > 32 or GAHS > 9 had mortality rates that were equivalent to the past but more prolonged PT values than in the earlier studies.

While familiar with the limitations inherent in a retrospective, single institution study, we propose that the strengths of this report are substantial. They include the completeness of data collection, long-term follow-up of the vast majority of those with DF > 32 and the possibility of future external validation with electronic health record data. Clinical data at PHHS, apart from discharge summaries and pathology and radiology reports, were not electronic in this period and not extracted; consequently the cohort is potentially different from other studies of acute alcoholic hepatitis. In prospective studies, the acuteness of the presentation and the concurrence of symptoms and signs such as anorexia, nausea, right upper quadrant pain, tender hepatomegaly and jaundice are used to enroll patients. None is specific when assessed alone and diagnosis relies on interpretation of clinical data. We used

a bilirubin of 5 mg/dL during the admission as a surrogate for jaundice; only 2 patients with DF > 32 were admitted with a bilirubin < 5 mg/dL (3.1 and 3.2 mg/dL) and neither had INRdf > 50. Of note, admission bilirubin was < 2.5 mg/dL in only 1 patient with DF < 32 (2.4 mg/dL) indicating that almost all the subjects were likely to be judged as jaundiced on admission.

Future efforts must focus on improving the immediate outcomes of this cohort of patients as well as the entire group. We have demonstrated that hospitalization with an acute decompensation of underlying chronic ALD that includes a bilirubin 5 mg/dL prior to discharge is a sentinel event. These are the patients for whom early liver transplantation is the one management that may prolong survival and only if that option is not eliminated by psychosocial or financial barriers. Prospective interventional trials of innovative management strategies are needed urgently, particularly for patients without a transplant option, since long-term survival is possible particularly with abstinence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations

ABIC score	Age, Bilirubin, INR, Creatinine score
DF	discriminant function
GAHS	Glasgow alcoholic hepatitis score
INRdf	modified DF using INR
INR	international normalized ratio
ISI	internal sensitivity index
MELD	Model of End-Stage Liver Disease
HCV	chronic hepatitis C
PT	prothrombin time
WBC	white blood cell

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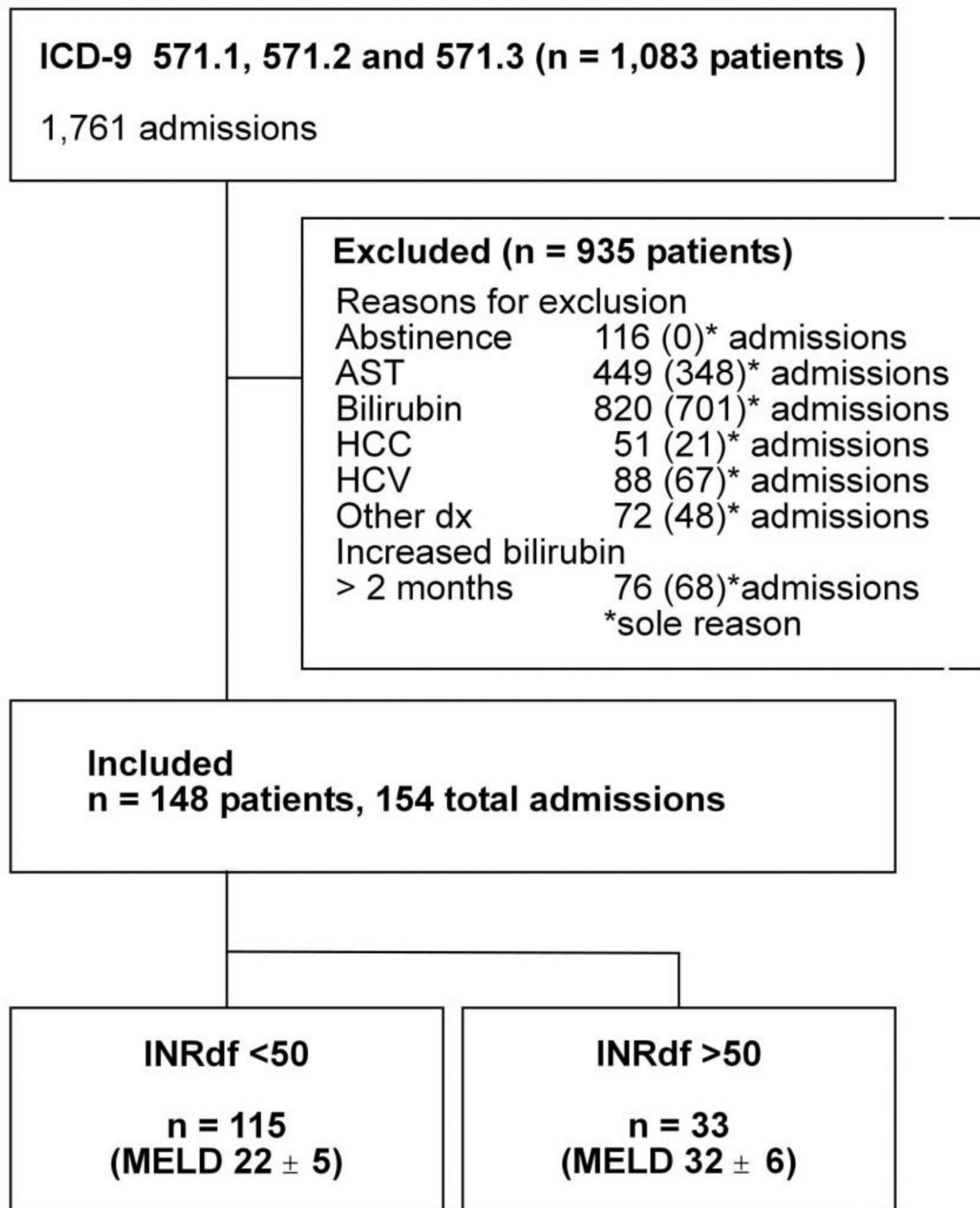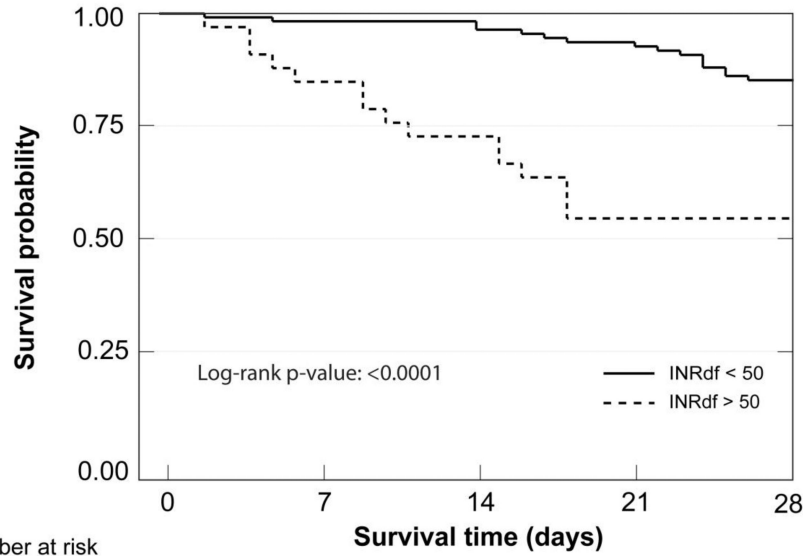
Figure 1.

Overall flow chart

Legend: Diagnoses resulting in exclusion, other than chronic hepatitis C and hepatocellular carcinoma, included acute and chronic hepatitis B, acute cholecystitis, acute kidney injury in an incarcerated patient, cholangiocarcinoma, chronic kidney disease with cirrhosis, cocaine ischemic liver injury, common bile duct transection, congestive heart failure, empyema of gall bladder, gas gangrene, hematoma, hemophagocytic histoplasmosis, incarcerated para-umbilical hernia, metastatic liver disease, motor vehicle accident, non-alcoholic fatty liver
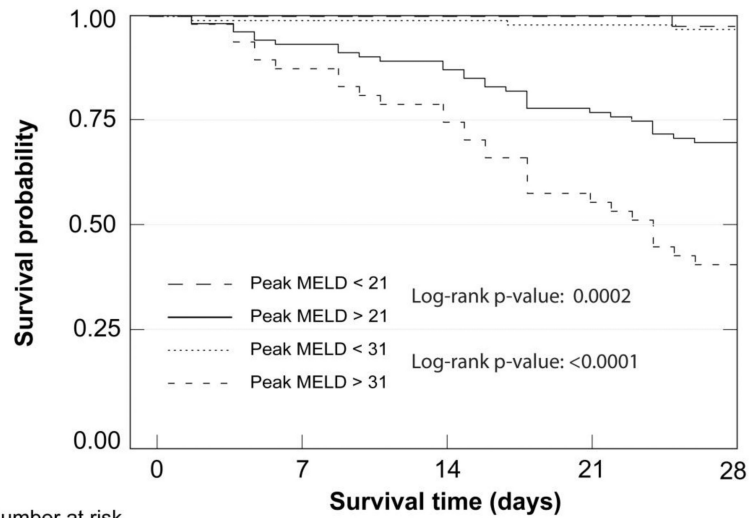
disease, pancreatitis, post-operative decompensation, primary biliary cirrhosis, renal cell carcinoma, secondary peritonitis, sepsis, Stevens-Johnson syndrome, subarachnoid hemorrhage, subdural hematoma and suspected drug-induced liver injury.
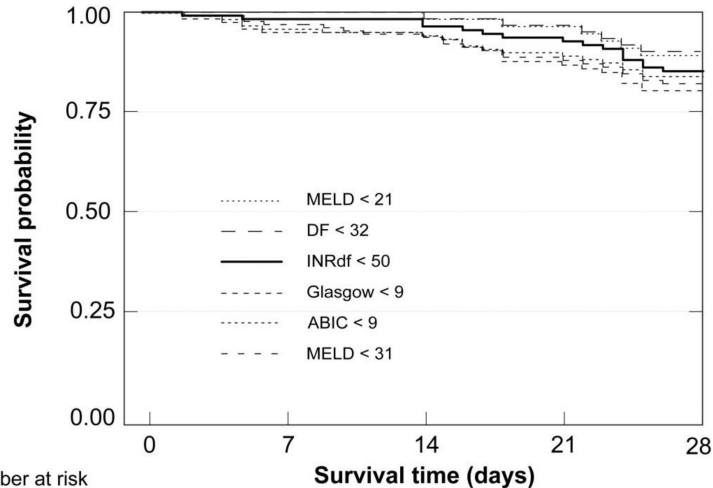
A. *Comparison of Admission INRdf Groups*

B. *Comparison of Peak MELD groups*

C. *Comparison of subjects with less severe disease on admission using different scoring systems*

Number at risk

MELD < 21	64	63	58	55	51
DF < 32	68	67	62	59	53
INRdf < 50	115	112	106	100	91
Glasgow < 9	121	114	108	91	90
ABIC < 9	124	119	112	106	98
MELD < 31	129	124	115	107	99

D. *Comparison of subjects with more severe disease on admission using different scoring systems*
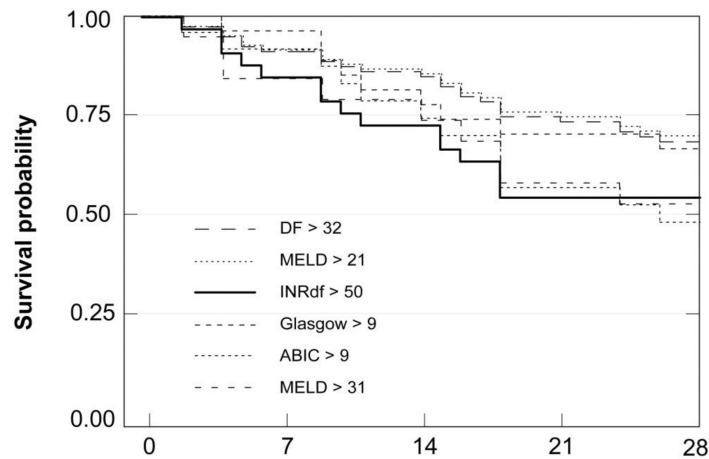
Number at risk

DF > 32	80	73	68	59	54
MELD > 21	84	77	72	63	58
INRdf > 50	33	28	24	18	18
Glasgow > 9	27	26	22	19	18
ABIC > 9	24	21	18	13	11
MELD > 31	19	16	15	11	10

Figure 2.
Kaplan-Meier 28 Day Survival Analyses

A. *Comparison of Admission INRdf Groups*
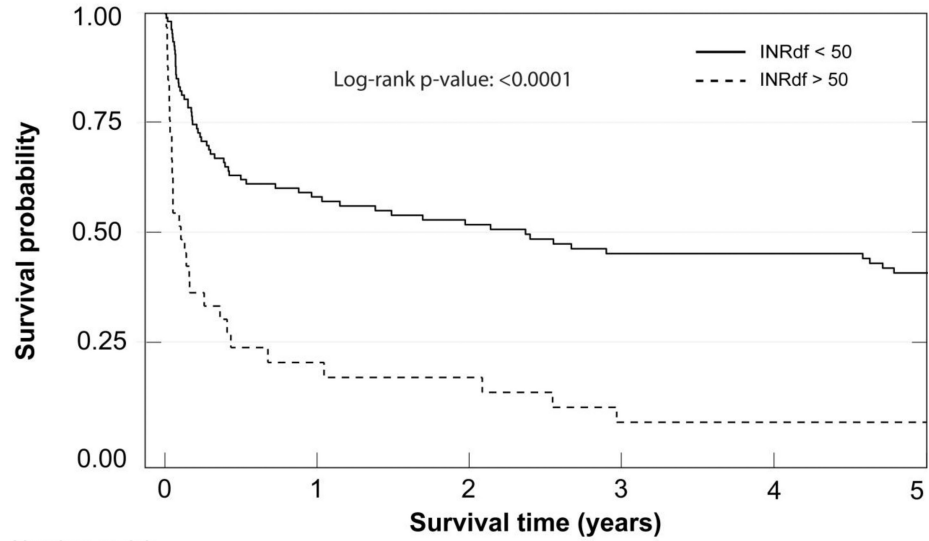
Number at risk

INRdf < 50	115	58	48	41	41	36
INRdf > 50	33	6	5	2	2	2

B. *Comparison of Peak MELD groups*
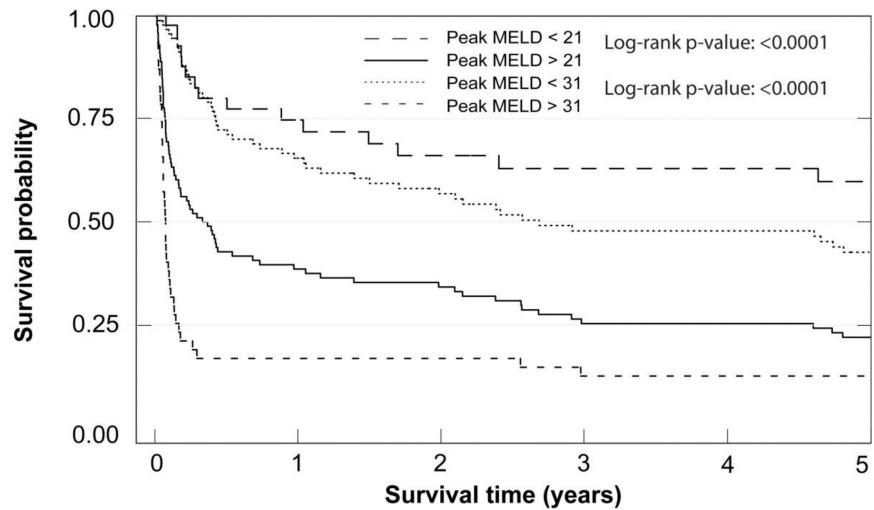
Number at risk

MELD < 21	47	28	22	20	20	18
MELD < 31	101	56	45	37	37	32
MELD > 21	101	36	31	23	23	20
MELD > 31	47	8	8	6	6	6

C. *Comparison of subjects with less severe disease on admission using different scoring systems*
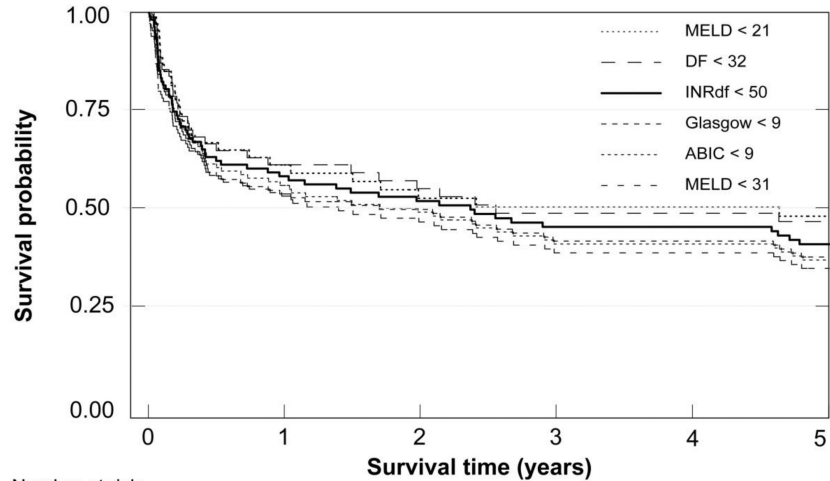
Number at risk						
MELD < 21	64	31	24	22	22	20
DF < 32	68	33	27	23	23	21
INRdf < 50	115	58	48	41	41	36
Glasgow < 9	121	57	50	41	41	36
ABIC < 9	124	60	49	40	40	35
MELD < 31	129	59	48	39	39	34

D. *Comparison of subjects with less severe disease on admission using different scoring systems*
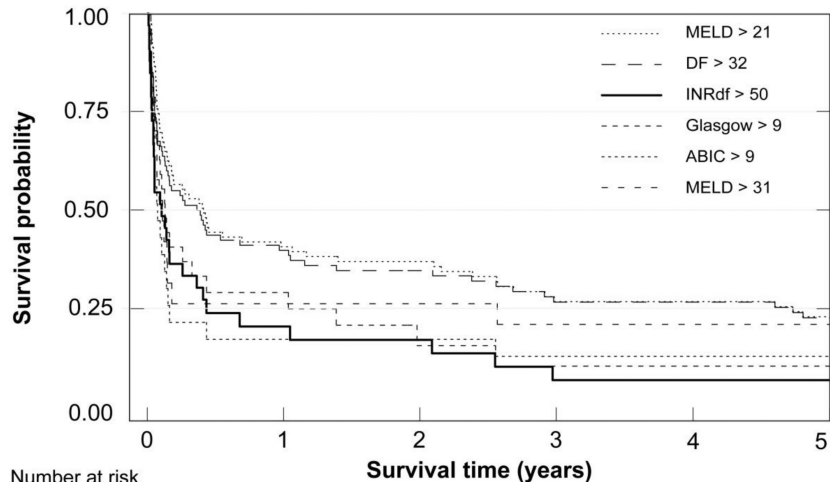
Number at risk						
MELD > 21	84	33	29	21	21	18
DF > 32	80	31	26	20	20	17
INRdf > 50	33	6	5	2	2	2
Glasgow > 9	27	7	3	2	2	2
ABIC > 9	24	4	4	3	3	3
MELD > 31	19	5	5	4	4	4

Figure 3.
Kaplan-Meier 5 year Survival Analyses

Table I

Demographic and Clinical Characteristics on Admission

	Total n = 148	INRdf < 50 n = 115 (78%)	INRdf > 50 n = 33 (22%)	p-value* †
Male	118 (80%)	91 (79%)	27 (82%)	0.74*
Age mean ± SD	45 ± 9	46 ± 9	43 ± 7	0.054
median, (range)	45 (24 – 69)	46 (24 – 69)	44 (30 – 56)	
Race & ethnicity				
African-American	14 (9%)	12 (10%)	2 (6%)	0.41†
Caucasian	67 (45%)	55 (48%)	12 (36%)	
Hispanic	63 (43%)	45 (39%)	18 (55%)	
Native American	4 (3%)	3 (3%)	1 (3%)	
DF mean ± SD	44 ± 34	29 ± 14	94 ± 36	< 0.001
median, (range)	34 (0 – 193)	28 (0 – 65)	85 (55 – 193)	
DF > 32	80 (54%)	47 (41%)	33 (100%)	< 0.001*
MELD mean ± SD	24 ± 6	22 ± 5	32 ± 6	< 0.0001
median, (range)	22 (12 – 45)	21 (12 – 35)	30 (25 – 45)	
MELD < 21	64 (43%)	64 (56%)	0	< 0.001†
MELD > 31	19 (13%)	6 (5%)	13 (39%)	<0.001†
GAHS mean ± SD	8 ± 1	8 ± 1	9 ± 1	< 0.0001
median, (range)	8 (5 – 11)	8 (5 – 11)	10 (7 – 11)	
GAHS > 9	27 (18%)	10 (9%)	17 (52%)	< 0.001*
ABIC mean ± SD	7.5 ± 1.4	7.1 ± 1.2	8.9 ± 1.2	< 0.0001
median, (range)	7.4 (4.3 – 12)	7.0 (4.3 – 10.6)	8.6 (7.3 – 12)	
ABIC > 9	24 (16%)	8 (7%)	16 (48%)	< 0.001*
ABIC < 6.71	43 (41%)	43 (54%)	0	<0.001†
Paracentesis**	54 (37%)	43 (37%)	11 (33%)	0.67*
Hyperammonemia**	90 (61%)	64 (56%)	26 (79%)	0.016*

*
Calculated from Chi-square test,

†
Fisher's exact test, otherwise two-sample t-test.

**
70/148 (47%) subjects had paracentesis during the admission, 54/70 occurring within 2 days; 101/148 (68%) patients had a blood ammonia level within 2 days of admission.

Table II

Univariate Analysis of Predictors of 28 Day Survival[*]

Variable	Parameter Estimate (± standard error)	HR (95% CI)	p value	Area Under Curve[†]
Bilirubin	0.03 (± 0.02)	1.03 (1.00 – 1.07)	0.044	
Creatinine	0.37 (± 0.15)	1.45 (1.08 – 1.95)	0.014	
INR	0.64 (± 0.15)	1.90 (1.42 – 2.56)	< 0.001	
PT	0.070 (± 0.016)	1.07 (1.04 – 1.11)	< 0.001	
WBC	0.063 (± 0.018)	1.07 (1.03 – 1.10)	< 0.001	
Hyperammonemia[‡]	1.65 (± 0.54)	5.18 (1.81 – 14.82)	0.002	
DF score	0.015 (± 0.00)	1.02 (1.01 – 1.02)	< 0.001	0.74
DF 32 category	1.37 (± 0.45)	3.92 (1.61 – 9.56)	0.003	
INRdf score	0.026 (± 0.006)	1.03 (1.01 – 1.04)	< 0.001	0.74
INRdf 50 category	1.44 (± 0.36)	4.23 (2.09 – 8.66)	< 0.001	
MELD score	0.09 (± 0.02)	1.10 (1.05 – 1.15)	< 0.001	0.74
MELD 21 category	1.24 (± 0.45)	3.45 (1.42 – 8.42)	0.006	
MELD 31 category	1.22 (± 0.40)	3.40 (1.56 – 7.40)	0.002	
ABIC score	0.34 (± 0.12)	1.40 (1.11 – 1.77)	0.005	0.68
ABIC category	0.95 (± 0.29)	2.58 (1.46 – 4.56)	0.001	
Peak MELD score	0.13 (± 0.019)	1.13 (1.10 – 1.18)	< 0.001	0.91
Peak MELD 21 category	2.75 (± 1.02)	15.66 (2.14 – 114.85)	0.007	
Peak MELD 31 category	3.31 (± 0.61)	27.27 (8.27 – 89.96)	< 0.001	
Creatinine increase	0.25 (± 0.044)	1.29 (1.18 – 1.40)	< 0.001	

[*] Univariate analysis used Cox Proportional Hazards model. No significant effect (p > 0.05) of age, AST, ALT, alkaline phosphatase, GGT, albumin, total protein, BUN, sodium, hematocrit, platelets; GAHS (Area Under [Receiver Operating] Curve = 0.62) and GAHS category; paracentesis during first 2 days of admission.

[†] Area under receiver operating curve (ROC);

[‡] Within 2 days of admission.

Table IIIA

Stepwise Cox Regression Analysis of Predictors of 28 Day Survival[*]

Variable	Parameter Estimate (± standard error)	HR (95% CI)	p value
Admission parameters			
ABIC 9 category	1.37 (± 0.37)	3.94 (1.90 – 8.17)	< 0.001
Hyperammonemia[†]	1.42 (± 0.56)	3.92 (1.60 – 13.41)	0.012
Admission & peak parameters			
Peak MELD 31 category	3.74 (± 0.67)	42.03 (11.30 – 156.40)	< 0.001
INRdf category	1.13 (± 0.50)	3.10 (1.57 – 8.33)	0.024
Admission bilirubin	−0.065(± 0.023)	0.94 (0.90 – 0.98)	0.005

[*] Included all parameters with p < 0.05 on univariate analysis except INR (collinearity)

[†] Within 2 days of admission