Intensive Care Med (2005) 31:1693–1699
DOI 10.1007/s00134-005-2842-7

ORIGINAL

Damien du Cheyron
Bruno Bouchet
Jean-Jacques Parienti
Michel Ramakers
Pierre Charbonneau

The attributable mortality of acute renal failure in critically ill patients with liver cirrhosis

Received: 2 May 2005
Accepted: 23 September 2005
Published online: 22 October 2005

Electronic Supplementary Material
Electronic supplementary material to this paper can be obtained by using the Springer Link server located at http://dx.doi.org/10.1007/s00134-005-2842-7

D. du Cheyron (✉) · B. Bouchet · M. Ramakers · P. Charbonneau
Department of Medical Intensive Care, Caen University Hospital, Av côte de Nacre, 14033 Caen Cedex, France
e-mail: ducheyron-d@chu-caen.fr
Tel.: +33-2-31064716
Fax: +33-2-31064996

J.-J. Parienti
Department of Clinical Research, Caen University Hospital, Av côte de Nacre, 14033 Caen Cedex, France

Abstract *Objective:* To determine outcome and mortality risk related to acute renal failure (ARF) in critically ill patients with cirrhosis. *Design and setting:* A retrospective cohort analysis and two independent case-control analyses in a medical ICU. *Patients:* 41 and 32 patients who developed mild and severe ARF, respectively, matched (1:2 ratio) with cirrhotic patients without ARF during their ICU stay. *Measurements and results:* Cirrhotic patients with ARF had higher MELD, APACHE II, and SOFA scores at baseline that those without ARF. They had more respiratory failure and cardiovascular failure during ICU stay, longer stay in ICU, and a greater crude hospital mortality rate (65% vs. 32%). Multivariate survival analysis identified ARF (hazard ratio, HR, 4.1), alcohol abuse or dependency, and severe sepsis or septic shock as independent predictors of death. In case-control studies both mild and severe ARF were independently associated with mortality (HR, 2.6, and 4.2, respectively). Cirrhotic patients with mild ARF patients had a higher risk of death than those without ARF (relative risk, RR, 2.0). Severe ARF was associated with an increase matched risk of death (RR 2.6), higher mortality of 51%, and higher risk-adjusted mortality rate (2.1 vs. 0.9). *Conclusions:* ICU patients with liver cirrhosis still have a high crude mortality. In this specific population ARF is associated with an excess mortality, depending on the severity of renal dysfunction.

Keywords Cirrhosis · Acute renal failure · Intensive care unit · Outcome

Introduction

Patients on the waiting list for liver transplantation are the subgroup of cirrhotic patients in whom intensive care can be of most benefit. However, cirrhosis remains a common cause of death in intensive care patients, with a high mortality rate [1, 2, 3, 4, 5, 6, 7]. Thus the need for aggressive life support, such as mechanical ventilation, vasopressors, and renal replacement therapy (RRT), is frequently questioned. Several predictive factors of death have been reported in ICU subjects with cirrhosis: single organ dysfunction such as respiratory distress requiring mechanical ventilation [1], hemodynamic instability requiring vasopressors [1, 2], and disturbance of body water homeostasis such as dilutional hyponatremia associated with the existence of ascites [8]. It is now well established that patients die of acute renal failure (ARF) [9], and that those with nonoliguric ARF have a better prognosis than those with oliguric renal failure [10]. A rise in serum creatinine levels above 1.3 or 1.5 mg/dl has been reported as predictor of poor prognosis in patients with advanced liver cirrhosis [1, 11], but the clinical impact of ARF in ICU cirrhotic patients has never been specifically tested, and it remains uncertain whether the increase in mortality rate in patients with end-stage liver disease related to ARF depends on the severity of renal dysfunction. The need for RRT may be considered as a marker of the severity of the renal disorders as well as a critical step in

the management and prognosis of critically ill patients with cirrhosis [12].

The aim of this study was to compare outcomes of cirrhotic patients with and without ARF and to evaluate excess mortality rates associated with mild ARF (without RRT indications) and severe ARF (RRT requirement) in critically ill patients with cirrhosis.

Materials and methods

Patients

This was a retrospective population-based cohort study of cirrhotic patients with ARF carried out between January 1998 and December 2003. During the study period a total of 256 patients older than 18 years (258 admissions; 5.1% of ICU admissions) were admitted to the medical ICU of the 1,200-bed University Hospital of Caen with the diagnosis of cirrhosis and were prospectively recorded in a computer database. For patients who were admitted more than once (n=2), only the first admission was included. Sixty patients were considered for potential liver transplantation and were not included in the analysis. From the remaining, we excluded four patients for severe immunodepression, defined by the presence of advanced form of cancer (n=2), and those receiving chronic immunosuppressive therapy (chronic use of steroids $\geq$ 7.5 mg/day for more than 4 months, n=3; or immunosuppressive drugs, n=1). Patients (n=6) with records that lacked an adequate follow-up data (missing data for main cause of ARF, n=1; organ dysfunction during the stay in ICU, n=3; or RRT modality, n=2) were excluded as well. Thus there were 186 evaluable patients (mean age 54.9±13.0 years; mean Acute Physiology and Chronic Health Evaluation, APACHE, II score 18.0±9.1). The present study compared the 73 patients whose ICU stay was complicated with ARF with the 113 who did not develop ARF (Table 1). ARF was then categorized as mild (n=42) and severe (n=31) ARF. To adjust for differences in severity of illness, two independent case-control studies were performed (see the Electronic Supplementary Material). ICU mortality was 41%.

Data abstraction

The following clinical data were collected: age, gender, comorbidities, and primary diagnosis at admission to ICU such as sepsis, severe sepsis and septic shock, encephalopathy, acute respiratory distress syndrome (ARDS), and gastrointestinal bleeding. To assess the severity of the acute illness, we used the APACHE II [13] and the initial Sequential Organ Failure Assessment (SOFA) [14], determined within 24 h following ICU admission. The delay before discharge from ICU as well as ICU and hospital mortality rates were also recorded. Estimates of hospital mortality were calculated using the APACHE II system in the manner described by Knaus et al. [13].

Table 1 Baseline characteristics for the overall population of critically ill patients with cirrhosis (*ARF* acute renal failure, *MELD* Model for End-Stage Liver Disease, *COPD* chronic obstructive pulmonary disease, *ARDS* acute respiratory distress syndrome, *APACHE* Acute Physiology and Chronic Health Evaluation, *SOFA* Sequential Organ Failure Assessment, *ICU* intensive care unit, *O/E ratio* risk-adjusted hospital mortality rate)

	Cirrhosis with ARF (n=73)	Cirrhosis without ARF (n=113)	p
Age (years)	56.4±12.4	54.3±13.3	0.27
Gender: male	51 (70%)	78 (69%)	1.0
Cirrhosis main cause: alcohol	62 (85%)	72 (64%)	0.001
MELD score	14.3±3.1	9.2±2.5	<0.0001
Antecedents, comorbidities			
Tobacco	36 (49%)	68 (60%)	0.17
Diabetes	13 (18%)	17 (15%)	0.68
Cardiac disease	17 (23%)	24 (21%)	0.86
Hypertension	12 (16%)	20 (18%)	1.0
COPD	10 (14%)	21 (19%)	0.43
Primary diagnosis			0.1
Infection	28 (38%)	40 (35%)	
Sepsis	*7* (*25%*)	*28* (*70%*)	
Severe sepsis + septic shock	*21* (**75**%)	*12* (*30%*)	
Gastrointestinal bleed	23 (31%)	35 (31%)	
Encephalopathy	8 (11%)	14 (12%)	
ARDS	8 (11%)	19 (17%)	
Other	6 (8%)	6 (5%)	
APACHE II	20.1±9.9	16.4±8.1	0.009
SOFA score at ICU admission	9.8±4.3	8.0±3.3	0.002
Organ failure other than ARF[a]			
Respiratory failure	52 (71%)	62 (55%)	0.03
Neurological failure	13 (18%)	20 (18%)	1.0
Liver failure	36 (49%)	47 (42%)	0.36
Cardiovascular failure	47 (64%)	55 (49%)	0.04
Coagulation failure	41 (56%)	48 (42%)	0.07
Length of ventilation, median (days; range)	5 (0–90)	5 (0–46)	0.12
Length of stay in ICU, median (days; range)	10 (1–90)	7.5 (1–54)	0.03
Expected mortality (%)	35.6±25.1	26.6±21.2	0.009
ICU mortality	44 (60%)	33 (29%)	<0.0001
Hospital mortality	48 (65%)	36 (32%)	<0.0001
O/E ratio (95% CI)	1.8 (1.3–2.4)[b]	1.2 (0.8–1.7)	

[a] During the ICU stay as defined in [20].
[b] Observed mortality was significantly than that predicted by APACHE II.

Definitions

Cirrhosis was defined by a histologically confirmed and/or clinically diagnosed cirrhosis (portal hypertension with ascites, confirmed esophageal varices, clinical signs of hepatic failure, and a liver spleen scan consistent with liver disease). The main cause of cirrhosis was assessed by alcohol abuse or dependency as defined by the American Psychiatric Association [15], or other causes. The severity of liver disease was assessed by the Model for End-Stage Liver Disease (MELD) score [16] at ICU admission, calculated using a formula that relies on three variables: serum creatinine, total bilirubin, and international normalized ratio (INR). When INR was missing in the computer database, it was calculated by the formula: INR=(1/PT%+0.018)/0.028, which relates INR to prothrombin time [17].

ARF was defined according to the proposed classification of the Acute Dialysis Quality Initiative group, namely risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease [18]. We classified as mild ARF those patients with risk of renal dysfunction or injury to the kidney, and as severe ARF those with failure of kidney function. We classified ARF as hepatorenal syndrome as described

by Moreau et al. [12], acute tubular necrosis, and other causes. In patients requiring RRT, continuous RRT (CRRT) at a "standard dose" was the technique of choice for hemodynamically unstable patients; CRRT was switched to intermittent hemodialysis (IHD) as soon as possible (alternate day dialysis, except for a specific daily basis, depending on physician preference). In patients stable enough to tolerate either form of RRT, IHD was most frequently used.

Sepsis, severe sepsis, and septic shock were defined as recommended by the ACCP/SCCM [19]. During ICU stay, organ dysfunction was defined as a SOFA score of 3 or higher for each of the organ system considered [20]. For central nervous system the Coma Glasgow Scale was considered as normal in patients with sedoanalgesia.

Statistical analysis

Values are expressed as mean ±SD, median and range, or number and percentage as appropriate. For univariate analysis we used the χ^2 test for qualitative variables, Fisher's exact test for proportions, and Student's *t* test or the Mann-Whitney *U* test when appropriate for quantitative variables. Normal distribution of variables was assessed by the Kolmogorov-Smirnov test. Survival curves for cirrhotic patients with mild ARF, severe ARF, and their respective control groups were prepared according to the Kaplan-Meier method. For the analysis between patients with mild and severe ARF survival was compared from the peak of serum creatinine. For cases and controls survival curves were compared from admission to ICU. Survival status (hospital mortality) was checked at hospital discharge. Cox proportional-hazard regression models were performed on cohort and matched studies to determine the association between ARF and hospital mortality (additional details for the modeling procedure are given in the online supplement). Risk adjusted mortality rates (O/E ratio) and their confidence intervals were calculated [21]. For the matched analysis, the paired *t* test or the Wilcoxon signed rank test for continuous data were performed. The relative risk (RR) of death and its 95% confidence interval (CI) was calculated using a stratified Mantel-Haenszel RR where each stratum was a matched pair. We then estimated the excess mortality risks and their CIs for mild and severe ARF [22] (see additional details for the matched studies in the Electronic Supplementary Material). The analysis was performed using SAS version 8.2 (SAS Institute, Cary, N.C., USA) statistical software. The two-tailed significance level was set at $p<0.05$.

Results

Univariate analysis revealed that ARF patients were more alcoholic and severely ill, suffered from more organ dysfunction such as respiratory and cardiovascular failure during stay in ICU, and had a longer ICU stay. Infection was the main primary diagnosis in both groups, but incidence of severe sepsis and septic shock was higher in ARF patients. Multivariate analysis identified three factors as independent predictors of death: alcohol abuse or dependency, ARF, and severe sepsis or septic shock (Table 2). Finally, ARF patients had a higher hospital mortality rate than those without ARF. The risk adjusted mortality rate for cirrhotic ARF patients was 1.8 (95% CI 1.3–2.4). However, this O/E ratio did not differ significantly, despite a 50% increase, from that calculated in cirrhotic patients without ARF (1.8 vs. 1.2; overlapping CIs).

Table 2 Factors that affect hospital survival in critically ill patients with cirrhosis. Cox proportional-hazard regression analysis; backward deletion multivariate analysis. Patients who died had more respiratory failure ($p=0.01$) and cardiovascular failure ($p=0.009$) and longer ventilation ($p=0.15$). These variables were introduced in the model, then removed from the equation as described in the text

	Hazard ratio	95% CI	*p*
Alcohol abuse or dependency	4.8	1.3–19.5	0.009
Severe sepsis or septic shock	3.6	1.2–7.2	0.005
Acute renal failure	4.1	2.1-8.5	0.001
Age	1.5	0.7–2.3	0.10

The cohort study: mild ARF vs. severe ARF

Of the 42 patients with mild ARF, 23 (56%) presented criteria of risk of renal dysfunction and 18 (44%) injury to the kidney. The two groups were similar in age, gender, cirrhosis main cause, comorbidities, and MELD score. There was a significant difference between groups in APACHE II and SOFA scores at baseline, main cause of ARF, length of ventilation, and length of ICU stay. Patients with severe ARF developed more acute respiratory failure (Table 3). Multivariate survival analysis identified severe ARF and alcohol abuse or dependency as independent predictors of hospital mortality. Severe sepsis or septic shock reached a level of borderline significance (Table 4). Figure 1A shows survival curves for patients with mild and severe ARF. Hospital survival differed significantly between groups, with a greater crude mortality rate for severe ARF patients (84% vs. 51%, respectively). However, the risk-adjusted mortality rates did not differ significantly between both groups.

To further refine the estimate of mortality related to ARF, we performed two matched studies: the severe ARF case-control study and the mild ARF case-control study.

The severe ARF case-control study

Population characteristics of cases and controls are reported in T.S1. Controls were well-matched to patients with severe ARF in age, gender, cirrhosis main cause, primary diagnosis at admission, and SOFA. Patients with severe ARF had a higher MELD score, suffered more frequently from respiratory failure and cardiovascular failure during their stay in ICU, and had a longer ICU stay than controls, and their length of ventilator dependency tended to be longer. All patients with severe ARF were treated with RRT. Among these, 5 patients had only IHD, 18 had only hemofiltration, and 9 underwent both modalities of RRT. Multivariate analysis identified severe ARF (hazard ratio, HR, 4.2, 95% CI, 1.9–7.2; $p<0.0001$), and severe sepsis or septic shock (HR, 3.8, 95% CI, 1.3–12.6; $p=0.01$) as independent predictors of mortality.

Table 3 Baseline characteristics of the studied population of cirrhotic patients with mild ARF (risk of renal dysfunction, injury to the kidney) or severe ARF (failure of kidney function) (*ARF* acute renal failure, *MELD* Model for End-Stage Liver Disease, *COPD* chronic obstructive pulmonary disease, *ARDS* acute respiratory distress syndrome, *APACHE* Acute Physiology and Chronic Health Evaluation, *SOFA* Sequential Organ Failure Assessment, *ICU* intensive care unit, *O/E ratio* risk-adjusted hospital mortality rate)

	Mild ARF (*n*=41)	Severe ARF (*n*=32)	*p*
Age (years)	55.7±11.9	57.4±13.1	0.57
Gender: male	32 (78%)	19 (59%)	0.12
Cirrhosis main cause: alcohol	35 (85%)	27 (84%)	1
MELD score	13.9±3.4	15.0±2.6	0.14
Antecedents, comorbidities			
Tobacco	29 (71%)	17 (53%)	0.23
Diabetes	8 (20%)	5 (16%)	0.76
Cardiac disease	11 (26%)	6 (19%)	0.58
Hypertension	7 (17%)	5 (16%)	1
COPD	6 (15%)	4 (13%)	1
Time in ICU prior to ARF, median (days, range)	2 (0–25)	2 (0–32)	0.38
Primary diagnosis			0.28
Infection	12 (29%)	16 (50%)	
Sepsis	*5 (42)*	*2 (12%)*	
Severe sepsis + septic shock	*7 (58%)*	*14 (88%)*	
Gastrointestinal bleed	16 (39%)	7 (22%)	
Encephalopathy	6 (15%)	2 (6%)	
ARDS	4 (10%)	4 (12%)	
Other	3 (7%)	3 (10%)	
Peak of serum creatinine[a], median (mg/dl; range)	1.9 (1.5–3.9)	2.8 (1.4–5.7)	0.0003
Cause of acute renal failure			<0.0001
Hepatorenal syndrome	8 (20%)	9 (28%)	
Acute tubular necrosis	5 (12%)	18 (56%)	
Other	28 (68%)	5 (16%)	
Other organ failure[b]			
Respiratory failure	25 (61%)	27 (84%)	0.04
Neurological failure	6 (15%)	7 (22%)	0.54
Liver failure	18 (44%)	18 (56%)	0.35
Cardiovascular failure	25 (61)	22 (69)	0.62
Coagulation failure	21 (51%)	20 (62%)	0.35
APACHE II	17.9±8.3	21.6±10.8	0.01
SOFA score at ICU admission	8.2±3.9	10.0±4.3	0.03
Supportive therapy			
Length of ventilation, median (days; range)	3 (0–47)	10.5 (0–88)	0.02
Length of RRT dependency, median (days; range)	NA	4 (1–45)	NA
Length of stay in ICU, median (days; range))	8 (1–85)	13.5 (1–90)	0.04
Expected mortality (%)	30±21.5	40±27.8	0.04
ICU mortality	19 (46%)	25 (78%)	0.008
Hospital mortality	21 (51%)	27 (84%)	0.006
O/E ratio (95%CI)	1.7 (1.1–2.4)[c]	2.1 (1.5–2.7)[c]	

[a] During the ICU stay
[b] During the ICU stay as defined in [20]
[c] Observed mortality was significantly higher than that predicted by APACHE II

Table 4 Factors that affect hospital mortality in cirrhotic patients with ARF. Cox proportional-hazard regression analysis; backward deletion multivariate analysis. Patients who died had a higher age (p=0.09) and more respiratory failure (p=0.04) and cardiovascular failure (p=0.01). These variables were introduced in the model, then removed from the equation as described in the text

	Hazard ratio	95% CI	*p*
Alcohol abuse or dependency	6.3	1.1–38.3	0.03
Severe sepsis or septic shock	3.5	1.6–15.4	0.06
Severe acute renal failure	5.3	0.9–12.1	0.007

Severe ARF was associated with a higher risk of death than controls (matched Mantel-Haenszel adjusted RR, 2.6, 95% CI, 1.8–3.8), and with a matched excess risk of hospital death of 51% (95% CI, 27–75%). This is also demonstrated by the corresponding survival curves (p<0.0001; Fig. 1B). Finally, patients with severe ARF had a significant higher risk adjusted mortality rate (O/E ratio, 2.1, 95% CI, 1.5–2.7, vs. 0.9, 95% CI, 0.5–1.3; no overlap between CIs).

The mild ARF case-control study

Population characteristics of cases and controls are shown in T.S2. Controls were well-matched to patients with mild ARF in age, gender, cirrhosis main cause, primary diagnosis, SOFA, organ dysfunction, and length of stay in ICU but differed significantly in MELD score. The Cox model identified mild ARF (HR, 2.6, 95% CI, 1.2–5.7; p=0.009) as independent predictor of death. Alcohol reached a level of borderline significance (HR, 4.8; 95% CI, 0.9–18.5; p=0.06). Mild ARF was associated with a higher risk of death than controls (matched Mantel-Haenszel adjusted RR, 2.0; 95% CI, 1.2–3.2), and with a matched excess mortality of 25% (95% CI, 3–47). This is also illustrated in the corresponding survival curves (p=0.003) (Fig. 1C). However, the risk adjusted mortality rates did not differ significantly between cases and controls (overlap between CIs).

Discussion

In our study ARF was an independent risk factor of death (HR 4.1) in ICU patients with cirrhosis. To improve the robustness of this result and to evaluate the mortality risk related to ARF we used matched cohort method. Considering potential confounding factors, matching was based on primary diagnosis at admission and APACHE II classification. The APACHE II classification is considered a standard for the comparison of severity of illness in ICU patients. Thus this matching procedure resulted in an

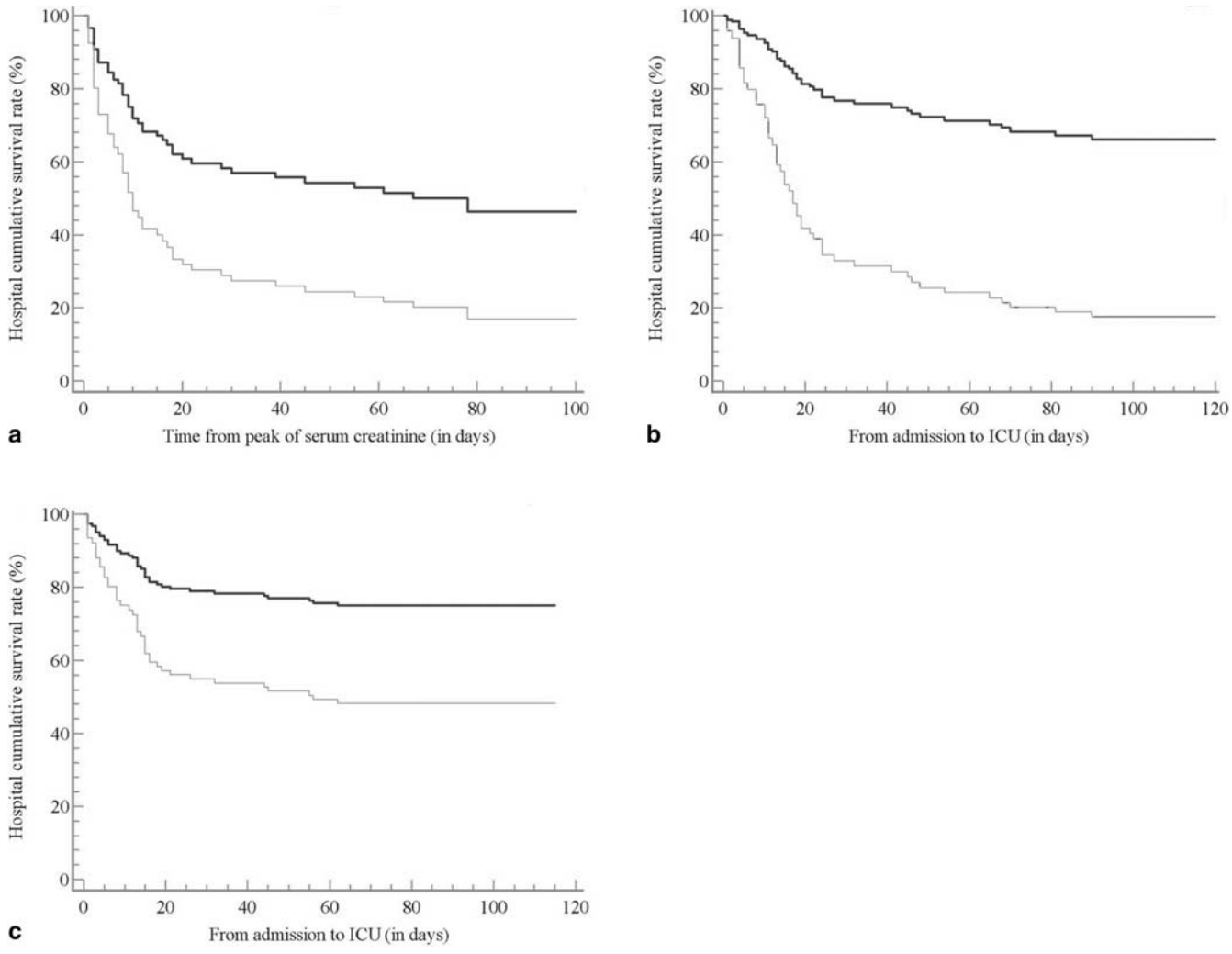

Fig. 1 A Survival curves in critically ill patients with cirrhosis and mild ARF (n=41) and cirrhotic patients with severe ARF (n=32; p=0.005 by log-rank test). **B** Survival curves for critically ill patients with cirrhosis and severe ARF (n=32) and control subjects (n=64; p<0.0001 by log-rank test). **C** Survival curves for critically ill patients with cirrhosis and mild ARF (n=41) and their control subjects (n=82; p=0.003 by log-rank test)

equal expected mortality rate for cases and controls. In the case-control studies, ARF, even modest degrees of ARF not resulting in dialysis treatment, was associated with an increase in mortality (RR, increase, 2.0 for mild ARF, and 2.6 for severe ARF), and mild ARF had a significant but more than twofold lower excess mortality risk than severe ARF (25% vs. 51%). However, using matched risk adjusted mortality rates, only severe ARF remained significantly associated with an excess risk of death in hospital. Together, these results support our hypothesis of an attributable excess mortality related to ARF and suggest that mild and severe ARF is a continuum in the severity of renal disease associated with progressive increase in mortality rates.

Despite advances in life support therapies in ICU over recent decades, cirrhosis and its complications related to end-stage liver dysfunction remain a potentially devastating disease that carries high mortality and morbidity rates [1, 2, 5, 23]. The purpose of the present study was to identify the impact of ARF on outcome of critically ill patients with cirrhosis. Among the main strengths were: the relatively large cohort studied with supporting care that reflects practice patterns for a specific severe population; the confirmation of the negative impact on outcome of chronic alcoholism, and of severe sepsis or septic shock in ICU cirrhotic patients. The study is the first to investigate outcomes between mild ARF and severe ARF patients with cirrhosis by comparing excess mortality and risk adjusted mortality rates obtained on case-control studies. Other studies have evaluated in ICU the impact on outcome of a rise in serum creatinine. ARF, from unmentioned causes, was found to be an independent predictor of

death after adjusting for other characteristics using regression analysis [1, 11, 24]. However, regression analysis can potentially yield distorted associations by selection of only a subset of variables that influence mortality risk, and by omission of key variables that would alter the findings if they were included. Our analysis of the excess mortality risk related to ARF used both comparison and regression methods. Consistency of the results between methods is an indication of their robustness to assumptions and hence provide more confidence of their validity.

The definition of ARF in the literature is quite controversial as its indication for any replacement therapy. Trials focusing on ARF have not been comparable because of widely differing definitions. Using the criteria of the Acute Dialysis Quality Initiative group across various causes of ARF made it possible to test the absolute excess risk of death related to ARF in ICU cirrhotic patients directly. However, a possible concern regarding the impact of ARF on outcome in cirrhotic patients is that the underlying disease process that results in ARF (e.g., sepsis vs. hepatorenal syndrome, HRS) may alter the clinical meaning of each degree of renal dysfunction [12]. It is well established that a progressive increase in ARF occurs with moderate and severe sepsis, and septic shock [25], and the effect of sepsis on renal function and outcome, significant in our series, has been confirmed in cirrhotic ICU patients [2, 26]. Furthermore, HRS, which is one of the most severe complications in advanced cirrhotic patients, is associated with a dramatical increase in mortality rate [12, 27]. Since the only possible preventive measure is to avoid the conditions known to be precipitating factors of HRS, the management of HRS is a major challenge for clinicians. In the absence of liver transplantation, which is theoretically the ideal treatment [28], CRRT is frequently used to control azotemia and maintain electrolyte balance. However, although patients with HRS without mechanical ventilation may benefit from RRT before liver transplantation, it has recently been reported that hemodialysis is futile in patients with mechanical ventilation [29]. Unfortunately, due to the small number of HRS in our study, we were unable specifically to test its negative impact on outcome or the effect of RRT in this subset of cirrhotic patients.

The present study has several limitations. First, the study was carried out in a single center, and the design is retrospective despite a prospective collection of data, compromising the ability to generalize the results. Second, the low number of cirrhotic patients with mild ARF did not allow us to determine an increase in the risk-adjusted mortality rate despite an excess risk of death related to mild ARF. Finally, due to the design study we were unable specifically to test the beneficial effect on outcome of new therapies in HRS, such as transjugular intrahepatic portosystemic shunt [30] and the molecular adsorbent recirculating system [31].

In summary, our data suggest the following conclusions: (a) cirrhosis continues to be a major cause of mortality in patients not eligible for liver transplantation admitted to the ICU; (b) chronic alcoholism and sepsis are at high risk of death; and (c) and in this specific population, ARF is an independent predictor of death with an excess mortality depending on the severity of renal dysfunction. Thus sustained efforts to prevent renal impairment and to avoid multiple systemic consequences of ARF [32] are quite justified in the future in cirrhotic patients.

References

1. Shellman RG, Fulkerson WJ, DeLong E, Piantadosi CA (1988) Prognosis of patients with cirrhosis and chronic liver disease admitted to the medical intensive care unit. Crit Care Med 16:671–678
2. Moreau R, Hadengue A, Soupison T, Kirstetter P, Mamzer MF, Vanjak D, Vauquelin P, Assous M, Sicot C (1992) Septic shock in patients with cirrhosis: hemodynamic and metabolic characteristics and intensive care unit outcome. Crit Care Med 20:746–750
3. Zimmerman JE, Wagner DP, Seneff MG, Becker RB, Sun X, Knaus WA (1996) Intensive care unit admissions with cirrhosis: risk-stratifying patient groups and predicting individual survival. Hepatology 23:1393–1401
4. Singh N, Gayowski T, Wagener MM, Marino IR (1998) Outcome of patients with cirrhosis requiring intensive care unit support: prospective assessment of predictors of mortality. J Gastroenterol 33:73–79
5. Kress JP, Rubin A, Pohlman AS, Hall JB (2000) Outcomes of critically ill patients denied consideration for liver transplantation. Am J Respir Crit Care Med 162:418–423
6. Wehler M, Kokoska J, Reulbach U, Hahn EG, Strauss R (2001) Short-term prognosis in critically ill patients with cirrhosis assessed by prognostic scoring systems. Hepatology 34:255–261
7. Aggarwal A, Ong JP, Younossi ZM, Nelson DR, Hoffman-Hogg L, Arroliga AC (2001) Predictors of mortality and resource utilization in cirrhotic patients admitted to the medical ICU. Chest 119:1489–1497
8. Gines P, Berl T, Bernardi M, Bichet DG, Hamon G, Jimenez W, Liard JF, Martin PY, Schrier RW (1998) Hyponatremia in cirrhosis: from pathogenesis to treatment. Hepatology 28:851–864
9. Metnitz PG, Krenn CG, Steltzer H, Lang T, Ploder J, Lenz K, Le Gall JR, Druml W (2002) Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. Crit Care Med 30:2051–2058
10. Thadhani R, Pascual M, Bonventre JV (1996) Acute renal failure. N Engl J Med 334:1448–1460
11. Chen YC, Tsai MH, Hsu CW, Ho YP, Lien JM, Chang MY, Fang JT, Huang CC, Chen PC (2003) Role of serum creatinine and prognostic scoring systems in assessing hospital mortality in critically ill cirrhotic patients with upper gastrointestinal bleeding. J Nephrol 16:558–565

12. Moreau R, Lebrec D (2003) Acute renal failure in patients with cirrhosis: perspectives in the age of MELD. Hepatology 37:233–243
13. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13:818–829
14. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, Reinhart CK, Suter PM, Thijs LG (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 22:707–710
15. O'Connor PG, Schottenfeld RS (1998) Patients with alcohol problems. N Engl J Med 338:592–602
16. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, D'Amico G, Dickson ER, Kim WR (2001) A model to predict survival in patients with end-stage liver disease. Hepatology 33:464–470
17. Lindahl TL, Egberg N, Hillarp A, Odegaard OR, Edlund B, Svensson J, Sandset PM, Ranby M (2004) INR calibration of Owren-type prothrombin time based on the relationship between PT% and INR utilizing normal plasma samples. Thromb Haemost 91:1223–1231
18. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P (2004) 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 8:R204–R212
19. 19 (1992) American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 20:864–874
20. Moreno R, Vincent JL, Matos R, Mendonca A, Cantraine F, Thijs L, Takala J, Sprung C, Antonelli M, Bruining H, Willatts S (1999) The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Working Group on Sepsis related Problems of the ESICM. Intensive Care Med 25:686–696
21. Hosmer DW, Lemeshow S (1995) Confidence interval estimates of an index of quality performance based on logistic regression models. Stat Med 14:2161–2172
22. Soufir L, Timsit JF, Mahe C, Carlet J, Regnier B, Chevret S (1999) Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: a matched, risk-adjusted, cohort study. Infect Control Hosp Epidemiol 20:396–401
23. Rabe C, Schmitz V, Paashaus M, Musch A, Zickermann H, Dumoulin FL, Sauerbruch T, Caselmann WH (2004) Does intubation really equal death in cirrhotic patients? Factors influencing outcome in patients with liver cirrhosis requiring mechanical ventilation. Intensive Care Med 30:1564–1571
24. Arabi Y, Ahmed QA, Haddad S, Aljumah A, Al-Shimemeri A (2004) Outcome predictors of cirrhosis patients admitted to the intensive care unit. Eur J Gastroenterol Hepatol 16:333–339
25. Schrier RW, Wang W (2004) Acute renal failure and sepsis. N Engl J Med 351:159–169
26. Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L, Castells L, Vargas V, Soriano G, Guevara M, Gines P, Rodes J (1999) Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. N Engl J Med 341:403–409
27. Gines P, Cardenas A, Arroyo V, Rodes J (2004) Management of cirrhosis and ascites. N Engl J Med 350:1646–1654
28. Runyon BA (2004) Management of adult patients with ascites due to cirrhosis. Hepatology 39:841–856
29. Witzke O, Baumann M, Patschan D, Patschan S, Mitchell A, Treichel U, Gerken G, Philipp T, Kribben A (2004) Which patients benefit from hemodialysis therapy in hepatorenal syndrome? J Gastroenterol Hepatol 19:1369–1373
30. Brensing KA, Textor J, Perz J, Schiedermaier P, Raab P, Strunk H, Klehr HU, Kramer HJ, Spengler U, Schild H, Sauerbruch T (2000) Long term outcome after transjugular intrahepatic portosystemic stent-shunt in non-transplant cirrhotics with hepatorenal syndrome: a phase II study. Gut 47:288–295
31. Mitzner SR, Stange J, Klammt S, Risler T, Erley CM, Bader BD, Berger ED, Lauchart W, Peszynski P, Freytag J, Hickstein H, Loock J, Lohr JM, Liebe S, Emmrich J, Korten G, Schmidt R (2000) Improvement of hepatorenal syndrome with extracorporeal albumin dialysis MARS: results of a prospective, randomized, controlled clinical trial. Liver Transpl 6:277–286
32. Druml W (2004) Acute renal failure is not a "cute" renal failure! Intensive Care Med 30:1886–1890