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ORIGINAL ARTICLE

Prothrombin time predicts steroid response in severe alcohol-related hepatitis

Claudia Tarli[1] | Sergio Mannucci[1] | Michele Vecchione[2] | Mariangela Antonelli[1] | Luisa Sestito[1] | Francesco Antonio Mancarella[1] | Alberto Tosoni[1] | Tommaso Dionisi[1] | Valeria Maccauro[1] | Giovanna Di Sario[1] | Patrizia Burra[3] | Giacomo Germani[3] | Antonio Gasbarrini[4,5] | Giovanni Addolorato[1,5]

[1]Internal Medicine and Alcohol Related Disease Unit, Department of Medical and Surgical Sciences, Columbus-Gemelli Hospital, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

[2]Department of Social and Developmental Psychology Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy

[3]Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy

[4]Internal Medicine Unit, Department of Medical and Surgical Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

[5]CEMAD Digestive Disease Center, Department of Medical and Surgical Sciences, Hepatology and Gastroenterology Unit, Università Cattolica del Sacro Cuore, Rome, Italy

Correspondence
Giovanni Addolorato, Internal Medicine and Alcohol Related Diseases Unit, Department of Medical and Surgical Sciences, Columbus-Gemelli Hospital, Fondazione Policlinico Universitario A. Gemelli IRCCS; Università Cattolica del Sacro Cuore, Largo Agostino Gemelli 8, Rome 00168, Italy.
Email: giovanni.addolorato@unicatt.it

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Abstract

Background and Aims: Alcohol-related hepatitis (AH) is the most severe form of acute alcohol-related liver disease. Maddrey's discriminant function ≥32 defines the severe form of AH, which is associated with a high mortality. Steroid therapy represents the main medical treatment that may reduce short-term mortality. Lille score at day 7 assesses the therapeutic response to steroid therapy. At present, no parameters able to predict the response to steroid therapy have been highlighted. The aim of the present study was to evaluate if baseline prothrombin time (BPT) could predict the response to steroid in severe AH (sAH).

Methods: Patients consecutively admitted in two Italian Liver Units, from 2017 to 2022, suffering from sAH were included. Data were collected prospectively. In order to evaluate if BPT could predict steroid response, we assessed the correlation between BPT using the Lille score at day 7.

Results: A total of 52 patients received steroid treatment were enrolled in the study. The response to therapy was assessed by Lille score at day 7. Responders were 34 patients (65%), non-responders 18 patients (34%). BPT significantly predicted the steroid response ($p < .001$). The likelihood of not responding to the steroid therapy was significantly higher in patients with higher BPT (OR = 2.954).

Conclusions: BPT value predicted steroid response in patients with sAH. BPT could quickly identify non-responder patients to steroid therapy, reducing the risk of infections and it could allow the early evaluation for liver transplantation.

KEYWORDS
corticosteroid therapy, early liver transplantation, prothrombine time, severe alcohol-related hepatitis, steroid response

Abbreviations: AH, alcohol-related hepatitis; AUD, alcohol use disorder; BPT, baseline prothrombin time; CS, corticosteroids; eLT, early liver transplantation; mDF, Maddrey discriminant function; MELD, model for end-stage liver disease; sAH, severe alcohol-related hepatitis.

1 | INTRODUCTION

Alcohol-related hepatitis (AH) is an inflammatory syndrome characterized by the rapid onset of jaundice and liver impairment, that occurs in patients with a history of acute heavy and/or prolonged alcohol abuse.[1]

AH is the most severe form of acute alcohol-related liver disease. The onset of AH overlaps with liver cirrhosis in 50%–75% of patients,[2] so AH frequently represents an acute on chronic liver damage.[3] Clinical diagnosis of AH is often a challenge, because severe forms of AH can be indistinguishable from other causes of liver decompensation (e.g. drug-induced liver injury, gastrointestinal bleeding, infections, co-aetiologies in liver damage).[4] Laboratory, radiological and histological examinations are confirmatory tests of clinical diagnosis[1,5,6]; liver biopsy should be performed only in cases of diagnostic uncertainty, as it can be useful to confirm the diagnosis, rule out other diagnoses and for prognostic purposes.[7]

AH may be poorly symptomatic (mild forms) or it may present itself with a severe clinical picture (severe forms). Severe AH (sAH) is associated with a high short-term mortality,[1,8–10] particularly if it is not quickly recognized and treated. Some scoring systems are useful to assess the severity of AH. Among them, Maddrey's discriminant function (mDF) is used to define severe forms of AH, when the score is 32 or higher,[11] prompting immediate administration of therapy. The MELD (model for end-stage liver disease) score is also accurate to assess the severity of AH,[12,13] even though the optimal cut-off value for the decision to treat has yet to be proposed by experts.[14] Moreover, some recent evidence suggests that MELD score has the best performance to predict short-term mortality.[15,16]

Complete alcohol abstinence represents the cornerstone of treatment in patients with AH.[1,17–19] In addition, corticosteroid (CS) therapy represents the main medical treatment that may reduce short-term mortality in sAH.[20] The European[7] and US[21] guidelines recommend the administration of CS as a first-line treatment (methylprednisolone 32–40 mg per day IV), to be started as early as possible. Lille score at day 7 assesses the therapeutic response to CS therapy. The formula combines six variables (age, creatinine, albumin, BPT, serum bilirubin and serum bilirubin at day 7 of CS therapy) and is highly predictive of the risk of death at 6 months.[22] Patients with a Lille score above 0.45 are defined non-responders to CS therapy; these patients have a very low 6-month survival rate (around 20%–30%). Discontinuation of CS therapy is recommended in non-responders, because of the risk of severe infections.[22] Highly selected patients not responding to medical therapy should be considered for early liver transplantation (eLT), without mandated period of sobriety,[8,17,24] and they should be listed as soon as possible.

Recently, in an effort to assess quickly whether or not the patient is responding to CS therapy, Foncea et al.[25] examined the Lille score at day 4 of CS treatment instead of at day 7, with positive results. However, to date, no parameters able to predict the response to CS therapy at the start of the treatment have been found. The mDF is calculated as [4.6× (patient's prothrombin time − control prothrombin time, in seconds)] + serum bilirubin level, in milligrams per decilitre,[1] so it depends mainly on baseline prothrombin time (BPT). Aim of the present study was to evaluate if the BPT value before starting CS treatment could predict the response to CS therapy in patients with sAH. The role of serum bilirubin, albumin and creatinine values on the CS response outcome was also evaluated.

Key points

sAH is defined by a mDF ≥ 32 and should be treated with CS therapy, with an assessment of CS response at day 7 according to the Lille score. At present, no parameters able to predict the response to CS therapy have been highlighted. mDF depends mainly on prothrombin time (BPT). Aim of the present study was to evaluate if the BPT value could predict the response to CS in sAH. We assessed the correlation between BPT at baseline with Lille score at day 7. BPT significantly predicted the CS response ($p < .001$). BPT value could quickly identify non-responders to CS therapy, reducing the risk of infections related to unnecessary prolonged CS therapy and it could allow the early evaluation for liver transplantation.

2 | PATIENTS AND METHODS

This was a prospective, double-centre study involved patients with sAH consecutively admitted to the Internal Medicine and Alcohol-related Disease unit, at Agostino Gemelli University Hospital (Rome, Italy) and to the Multivisceral Transplant Unit at Padua University Hospital (Padua, Italy) from June 2017 to September 2022.

The inclusion criteria were age (between 18 to 70 years old) and a clinical diagnosis of first episode of sAH at the admission in inpatient Units, with mDF score of 32 or higher, and the absence of contraindication to CS therapy (non-controlled infections/sepsis, hepatic encephalopathy, recent acute gastrointestinal bleeding, severe kidney dysfunction). The diagnosis of AH was based on the criteria of the National Institute on Alcohol Abuse and Alcoholism (NIAAA)-funded Alcoholic Hepatitis Consortia.[26] In particular, we enrolled in the study patients with: heavy alcohol use for >6 months, with an average consumption of more than three drinks (~40 g alcohol) per day for women and 4 drinks (~50–60 g alcohol) per day for men and with <30 days of abstinence before the onset of jaundice; AST/ALT ratio >1.5 with an AST level >45 IU/L (1.5 times upper limit of normal) and <400 IU/L; serum bilirubin >3 mg/dL.

The exclusion criteria were acute or chronic viral hepatitis, non-alcoholic steatohepatitis, cocaine use, drug-induced liver injury, fulminant Wilson's disease, hepatocellular carcinoma, portal vein thrombosis, biliary obstruction, severe autoimmune liver disease, neoplasms and severe comorbidities.

Detailed history of alcohol use was collected in all patients, using the TLFB (time-line follow back) method. In particular, the number of standard drinks (one standard drink is equal to 12 g of absolute alcohol), number of heavy drinking days per week (men ≥five drinks per day; women ≥four drinks per day) and the duration of heavy alcohol use were investigated. At admission, it was recorded whether the sAH was the first episode of liver decompensation or not.

At admission, all patients underwent systematic screening of infection (chest x-ray, blood and urinary cultures, ascites culture when possible). Laboratory parameters, including BPT, serum bilirubin, albumin, creatinine and INR, were recorded.

Patients were assessed for the presence of pre-existing chronic liver disease and possible complications (ascites, jaundice, encephalopathy, gastrointestinal haemorrhage, spontaneous bacterial peritonitis, hepatorenal syndrome). All patients underwent abdominal ultrasound to exclude biliary obstruction, hepatocarcinoma, portal vein thrombosis. In case of uncertain ultrasound findings, a CT and/or MRI were also performed. Diagnosis of liver cirrhosis was performed by clinical parameters (sign/symptoms of advanced liver disease, laboratory findings, abdominal ultrasound).

Child-Pugh, MELD and mDF scores were calculated at admission. BPT reference of our laboratories was 10.6 s. Methylprednisolone (40 mg, i.v.) was administered at the admission and once daily to all patients. On day 7, the Lille score was assessed. If the Lille score was below 0.45 (responder patients), CS therapy was continued for additional 3 weeks. If the Lille score was above 0.45 (non-responder patients), CS therapy was stopped immediately. The correlation between BPT values before the start of CS treatment (baseline values) with the Lille score at day 7 was assessed. The possible correlation between serum bilirubin at baseline and between albumin at baseline and Lille score at day 7 was also evaluated.

Patients were provided with multiple feeds (35–40 kcal/kg energy) and supported by vitamin B1. Albumin was administered in patients with a serum albumin value below 28 g/L or as volume replacement therapy.

All infections that occurred at sAH diagnosis and during CS treatment were recorded. All non-responders to CS therapy were evaluated for eLT. Among them, selected patients were listed and underwent liver transplantation. The reason for not listing to eLT was recorded for all non-responder patients to CS therapy.

This study was approved by the Ethical Committee.

2.1 | Statistical analysis

Data were described for the whole sample and then split for responders and non-responders to CS, based on the cut-off value of 0.45 for the Lille score after 7 days of treatment. The chi-square test and analysis of variance were used to examine differences between groups on demographic variables, biological parameters, clinical data and outcomes. Subsequently, a binary logistic regression model was used to examine the role of BPT in predicting the probability of not responding to CS. Albumin and bilirubin at time 0 were also included in the analysis as controls. The regression coefficients we report are odd ratios (OR). They indicate the effect of a one-unit change in BPT, albumin and bilirubin on the odds that a patient was classified into the responder group (coded as 1) versus the non-responder group (coded as 0), holding the other predictors constant. Coefficients greater than 1 indicate a positive relationship between the independent variable and the odds of being classified as a non-responder. Coefficients smaller than 1 indicate a negative relationship. The likelihood ratio test has been used to test the statistical significance of individual regression coefficients. The Cox and Snell (1989) R-squared was used to assess the goodness of fit of the model. The discrimination ability of the model was assessed through its ability to correctly classify patients into the two groups (i.e. responders vs. non-responders to CS therapy).

3 | RESULTS

3.1 | Sample characteristics

Among 122 patients admitted in our inpatients for AH, 94 patients presented with a diagnosis of sAH with mDF score of 32 or higher. Among them, 52 patients (38.5% females) were treated with CS therapy (methylprednisolone 40 mg, i.v. once daily) and were consecutively enrolled in the study. Figure 1 reports the reasons for the exclusion from CS treatment.

All patients were suffering from alcohol use disorder (AUD) according to DSM-V criteria.[27]

All patients were active drinkers, reporting at least two heavy drinking days per week on average and an average overall consumption of 35 drinks per week or more for men and 28 drinks per week or more for women during the 2 weeks before enrolment. One outlier patient showed an extremely high BPT value of 57.7 s, with a z-statistic of 6.10 and was therefore excluded from further analysis. A total of 51 patients were considered for statistical analysis. Among them, 94% ($n=49$) had chronic liver disease (Child-Pugh classification, MELD and MELD-Na are reported in Table 2). The mDF score was 55.87 ± 20.11. BPT values ranged from 13.5 to 27 s, with a mean value of 18.65 ± 3.21. According to Lille score, at day 7 of CS treatment, 34 (66.7%) patients were classified as responders while 17 (33.3%) were classified as non-responders. Tables 1–3 (left panel) summarize the overall sample characteristics.

3.2 | Differences between responder and non-responder patients

Table 1 shows the differences between responder and non-responder patients to CS therapy in terms of demographic variables and clinical data. The two groups did not differ in gender composition, $\chi^2(1)=.671$, $p=.413$. Non-responder patients were significantly older than responders, $F(1,49)=10.680$, $p=.002$. No significant differences between responder and non-responders were found considering the following variables: first episode of liver decompensation, $\chi^2(1)=.425$,

$p=.514$, the amount of alcohol intake, $F(1,49)=.406$, $p=.527$ and duration of alcohol abuse, $F(1,49)=1.830$, $p=.183$.

Table 2 shows the differences in biological parameters between the two groups of patients. BPT value was significantly higher in non-responders (21.96±2.58) compared to responders (17.00±1.98), $F(1,49)=58.030$, $p<.001$. mDF, $F(1,49)=41.109$, $p<.001$, MELD, $F(1,49)=7.445$, $p=.009$ and MELDNa $F(1,49)=6.936$, $p=.011$ were significantly higher in the non-responder group. Moreover, although the difference did not reach the statistical significance ($p<.10$), patients in the non-responder group showed higher bilirubin levels (23.08±13.43) and lower albumin levels (24.53±5.29) than in the responder group (16.97±10.00 and 27.44±5.37, respectively). Within Lille score parameters, creatinine value at baseline did not show any correlation with response to CS therapy ($R=.042$, $p=.771$). In addition, Table 2 reports the Child-Pugh distribution in the two groups. A significant difference in the proportion of patients classified as A, B or C based on Child-Pugh scores was found, $\chi^2(2)=7.826$, $p=.020$; in particular, a higher number of responders to CS therapy were classified in class B compared to the non-responders, while the opposite pattern was observed for class C.

Table 3 reports differences in outcomes between the two groups. No significant difference was found in the number of patients who had infections during the hospitalization, although the difference was close to significance ($p=.09$). In particular, the occurrence of infections was higher in the responder group (50%) compared to the non-responder group (26.5%).

Further analysis has shown that the number of patients who had infections during the hospitalization did not significantly differ between patients with the first episode of liver decompensation or not, $\chi^2(1)=1.700$, $p=.192$. 2-year mortality was significantly higher ($p<.001$) in non-responder patients (70.6%) compared to responders (2.9%), $\chi^2(1)=27.307$, $p<.001$. Among non-responder patients, 2-year mortality was 0% (0/3) in patients who underwent eLT, compared to 85.7% (12/14) in patients who were denied eLT. Overall, five patients underwent liver transplant (two responders and three non-responders): all liver recipients are alive at the time this paper was submitted.

3.3 | Using prothrombin time as a predictor of the probability of not responding (vs. responding) to CS therapy

Entering the three factors (BPT, albumin and bilirubin) in the logistic regression analysis significantly improved the model that includes

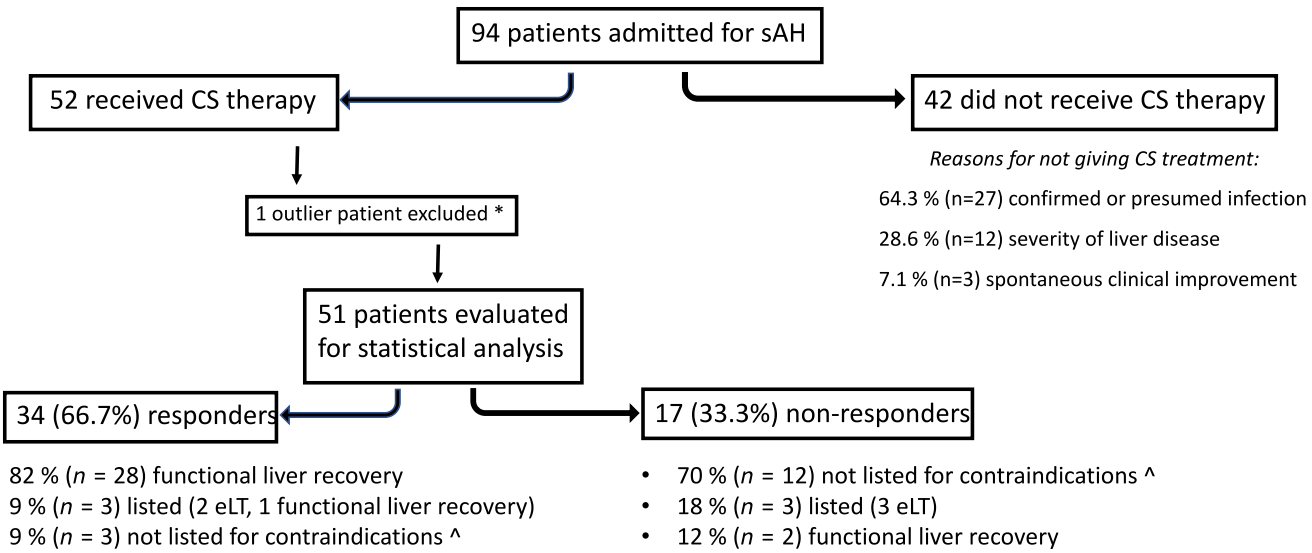

FIGURE 1 Flowchart of the study population. *Excluded for an extremely high PT value of 57.7 s, with a z-statistic of 6.10. ^Contraindications are non-controlled infections, non selected patients according to the SALT criteria.

TABLE 1 Sample characteristics (demographics and clinical data).

	Total sample, $n=51$	Responders (LM7 < 45) $n=34$	Non-responders (LM7 ≥ 45) $n=17$	p-value
Age (years at the time of admission)	46.14±9.20	43.41±8.79	51.59±7.60	.002
Gender (% female)	37.3%	41.2%	29.4%	.413
First episode of liver decompensation	70.6%	73.5%	64.7%	.514
Amount of alcohol intake (AU/day)	18.73±12.67	19.53±12.99	17.12±12.22	.527
Duration of alcohol abuse (years)	12.69±7.99	11.68±7.77	15.00±8.28	.183

Abbreviation: AU, Alcohol Unit (1 AU = 1 standard drink, 12 gr. absolute alcohol).

TABLE 2 Differences between responder and non-responder patients in biological parameters, Maddrey discriminant function, MELD and Child-Pugh classification.

	Total sample, $n=51$	Responders (LM7 < 45) $n=34$	Non-responders (LM7 ≥ 45) $n=17$	*p*-value
Serum bilirubin (mg/dL)	19.01 ± 11.49	16.97 ± 10.00	23.08 ± 13.43	.073
Serum albumin (mg/dL)	26.47 ± 5.47	27.44 ± 5.37	24.53 ± 5.29	.073
Prothrombin time (seconds)	18.65 ± 3.21	17.00 ± 1.98	21.96 ± 2.58	<.001
Maddrey discriminant function	55.87 ± 20.11	46.36 ± 10.07	74.89 ± 21.86	<.001
Meld	22.41 ± 6.94	20.65 ± 5.84	25.94 ± 7.77	.009
MeldNa	24.00 ± 6.80	22.32 ± 6.03	27.35 ± 7.18	.011
Child-Pugh classification (A, B, C)	A = 2% B = 21% C = 77%	A = 3% B = 32% C = 65%	A = 0% B = 0% C = 100%	.020

TABLE 3 Differences in listing, recovery, infections and mortality between responder and non-responder patients.

	Total sample, $n=51$	Responders (LM7 < 45) $n=34$	Non-responders (LM7 ≥ 45) $n=17$	*p*-value
Reasons for non-listing	Listing = 12% Recovery = 59% Contraindication = 29%	Listing = 9% Recovery = 82% Contraindication = 9%	Listing = 18% Recovery = 12% Contraindication = 70%	.001
Infections during hospitalization (% yes)	34.6%	26.5%	50.0%	.090
Early liver transplantation[a]	9.8%	3.9%	5.9%	NS
2-year mortality	25.5%	2.9%	70.6%	<.001
	Non-responders underwent eLT		Non-responders denied eLT	*p*-value
2-year mortality	0/3		12/14	NA[b]

Abbreviation: NA, not applicable.

[a]All liver recipients are alive.

[b]*p*-value cannot be calculated for the small sample size.

only the intercept, $\chi^2(3)=40.424$, $p<.001$. BPT significantly predicted response to CS. Specifically, the higher the BPT value, the higher the likelihood to be classified into the non-responder group vs. the responder one (OR = 2.954, 95% CI: 1.525, 5.722, $p<.001$). The baseline levels of albumin (OR = .847, 95% CI: .680, 1.055, $p=.139$) and bilirubin (OR = 1.027, 95% CI: .931, 1.133, $p=.592$) did not predict response to CS. The Cox-Snell R-squared of the model was .55. It allowed a correct classification of 91.2% of responders and 82.4% of non-responders, with an overall classification rate of 88.2%. Figure 2 represents the estimated probability of being in the non-responder group as a function of BPT. As shown, patients with a BPT score of 22 or higher had a probability of at least .90 to not benefit from CS therapy.

4 | DISCUSSION

Our results show that BPT value can predict response to CS in patients with sAH.

To the best of our knowledge, this is the first study identifying a possible clinical/laboratory parameter able to predict the possible response to CS therapy before its administration in patients with sAH.

In our sample, patients with a higher value of BPT responded less to CS therapy. PT is the main driver of the mDF score, according to his formula: 4.6 * (BPT − reference PT) + serum bilirubin. Therefore, the severity of AH evaluated by mDF takes into consideration more the BPT value, rather than serum bilirubin. This observation suggests that reduced hepatic synthesis is the main determinant of the severity of AH, more than the reduced hepatic biliary excretion. In this scenario, it is conceivable that severe impairment of hepatocyte synthesis may predict non-response to CS therapy in sAH and, consequently, the worst prognosis and higher short-term mortality. In line with this observation, MELD score also used to predict short-term mortality of sAH,[15] is more influenced by coagulation factors rather than by serum bilirubin, as seen in its formula: 9.57xln (creatinine(mg/dL)) + 3.78xln (bilirubin(mg/dL)) + 11.2xln (INR) + 6.43. In this regard, it is interesting to note that two recent studies showed that among patients with sAH, non-responders to CS therapy had significantly more severe disease when evaluated with MELD[23,24] and MELD-Na score.[24]

Parameters of hepatic synthesis also include albumin. In our sample, baseline albumin level was not significantly different between responders and non-responders to CS therapy, although it was lower in non-responder patients. Due to the acute onset of sAH, it is conceivable that short half-life parameters of liver synthesis (i.e.

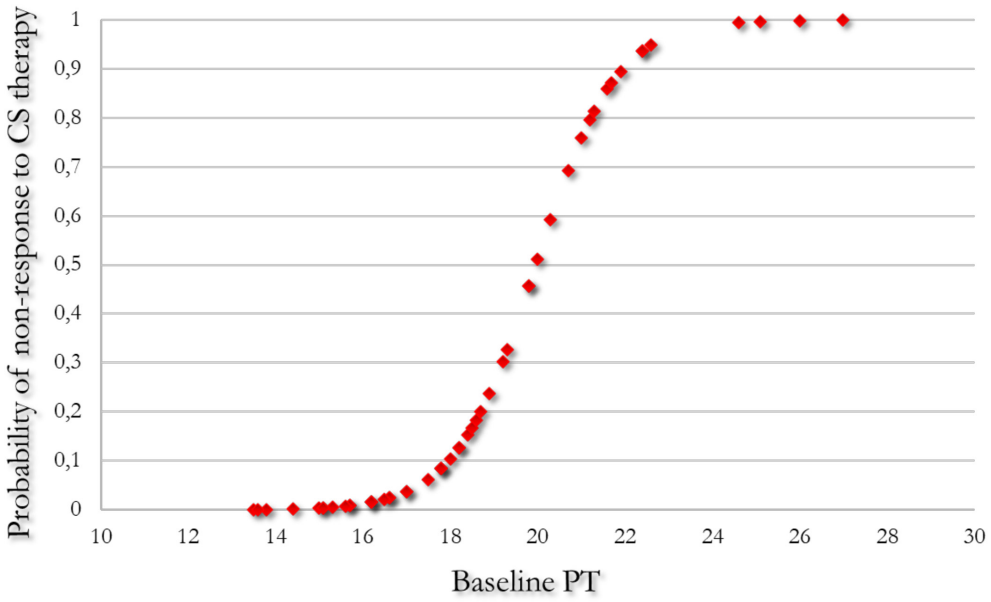

FIGURE 2 Estimated probability to belong in the non-responder group as a function of PT. The higher the PT value at baseline, the higher the likelihood to be classified into the non-responder group versus the responder one (OR = 2.954, 95% CI: 1.525, 5.722, $p < .001$). That is, patients with a PT score of 22 or higher have a probability of at least .90 to not benefit from CS therapy.

coagulation factors), compared to long half-life parameter (i.e. albumin), may be more effective in predicting the response to CS therapy. This observation is supported by data showing that in patients with hyperacute presentation of hepatitis, coagulation factors are involved more and before albumin.[28]

The availability of a parameter that could predict in advance the response to CS therapy in patients with sAH could be clinically relevant. This suggests that in the most severe group, steroids are more likely to cause harm than benefit. On the basis of our data, it could be conceivable that the decision to start steroid therapy should be established on a case-by-case analysis by clinician, not only based on the most used cut-off scores, but also on the severity of disease, balancing risk and benefit of steroid treatment. To assess as soon as possible response to CS in patients with sAH is, indeed, crucial, particularly considering that sAH is associated with a high risk of infection, which is one of the major causes of mortality in patients with Sah.[25] Approximately 20%–30% of sAH patients present with infections on admission and 25% of patients develops infections during the first month of CS treatment.[29] For this reason, at admission, systematic screening for bacterial, viral or fungal infections is mandatory in these patients and CS therapy should be administered only after a proper infection control.[29] The risk of infection in sAH patients treated with CS therapy is particularly evident in non-responders.[29] Louvet et al[29] showed that the probability to develop infections after CS initiation was significantly higher in non-responder patients with respect to responders (respectively 43% vs. 11%). Considering that non-responders are administered CS therapy for a shorter time than responders, it is likely that the risk of infection is related mainly to the severity of liver damage, in addition to the immunosuppressive effect of CS therapy. The early detection of non-responder patients could allow a better management of the risk of infections in patients with severe liver damage, avoiding unnecessary prolonged use of CS therapy and/or utilizing appropriate antibiotic therapy.

Furthermore, patients with a low probability to benefit from CS therapy need to be promptly evaluated for eLT,[30,31] at least in carefully selected cases.[8,32] The availability of a parameter effective to predict non-response to CS therapy could help begin the eLT evaluation as soon as possible.

Patients with sAH who do not respond to CS therapy showed an unequivocal improvement of survival when they received eLT.[8,24,32,33] eLT used to treat CS-non-responder sAH patients is an actively evolving area. A gradually increasing number of transplant centres are considering these patients in their transplant programs. As a result of a rigorous selection process, the pathfinder study by Mathurin and colleagues[8] evaluated only 7.7 percent of referred patients as appropriate candidates for eLT. Further, Lee et al.[33] listed 35.9% of patients with CS-non-responder sAH and 29.1% underwent eLT. More recently Louvet and colleagues[32] listed 68% of CS-non-responder sAH and 45% received eLT, and Germani and colleagues[24] listed 38% of CS-non-responder sAH and of these patients 30.7% received eLT.

In our study, the rate of approval for eLT by multidisciplinary transplantation committee was 27.7% among non-responders, and all of these patients underwent eLT. Also in our study 2-year survival was higher in eLT group (100%) compared to patient non-eligible for eLT (14.3%), confirming the positive influence of eLT on 2-year survival.

Despite the strong evidence on the benefits of eLT in non-responders to CS therapy,[7] there is still heterogeneity between countries and centres regarding whether or not to list patients with sAH.[34] The early detection of sAH not responding to CS therapy,

together with the identification of candidates at low risk of returning to alcohol drinking,[35] could limit the heterogeneity of the access to liver transplantation programs.

Nowadays, eLT as a rescue therapy for CS-non-responder sAH still raises several concerns,[34] particularly related to the risk of returning to alcohol drinking after liver transplantation, and the risk of failure to complete alcohol rehabilitation and counselling programs required for patients with less 6 months of alcohol abstinence before liver transplantation.[36] However, a recent study showed no difference in 2-year survival of patients who had eLT compared to patients who had standard liver transplantation selected after 6 months of abstinence, although eLT patients showed more frequently high alcohol intake and alcohol relapse.[32] The same study also showed that 2-year survival was higher in eLT group compared to patient non-eligible for eLT, confirming the benefit of eLT on survival outcomes.[32]

Our study has some limitations. First, the small sample size. Yet, sAH is a rare disease, accounting for approximately 4 of every 100 000 US hospital admissions.[33]

Second, all included sAH were not biopsy-proven. However, current clinical guidelines suggest performing a liver biopsy only when the clinical diagnosis of AH is uncertain[7] and all our patients showed enough clinical criteria to diagnose sAH. The histological examination was performed only in the explanted livers of transplanted patients, which confirmed the presence of an alcohol-related acute liver damage (acute inflammation with focal lobular neutrophil infiltration, hepatocellular necrosis, perivenular and perisinusoidal fibrosis, Mallory hyaline bodies in ballooned hepatocytes).

Third, in our sample a high percentage of patients (94%) had an acute on chronic liver damage, so the result could be influenced by the presence of chronic liver disease. This data is in line with scientific literature, since the onset of AH overlaps with liver cirrhosis in 50%–75% of patients.[2]

In conclusion, this work highlights that in patients with sAH, BPT value is able to predict the response to CS therapy before its administration. If further studies will confirm these data and the BPT futility cut-off value, BPT value could help clinicians to quickly identify non-responders to CS therapy, reducing the risk of infections related to unnecessary prolonged CS therapy and it could also allow early evaluation of non-responders for liver transplantation.

AUTHOR CONTRIBUTIONS

CT and GA designed the study. CT, SM, MA, LS, FAM, TD, VM, GDS, GG and PB collected data. CT, SM and GA drafted and wrote the study. MV provided his expertise in biomedical statistics. GA and AG provided their expertise throughout the course of the work. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to disclose.

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NCT05883891.

ORCID

Patrizia Burra https://orcid.org/0000-0002-8791-191X
Giacomo Germani https://orcid.org/0000-0002-4332-2072
Antonio Gasbarrini https://orcid.org/0000-0003-4863-6924
Giovanni Addolorato https://orcid.org/0000-0002-1522-9946

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