Efficacy and predictive factors of glucocorticoid therapy for patients with hepatitis B virus-related acute-on-chronic liver failure

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Abstract

Background and study aims: **Glucocorticoid (GC) treatment for liver failure is controversial. This study sought to evaluate the efficacy and predictive factors of glucocorticoid therapy for hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF).**

Patients and methods: **A total of 302 patients with HBV-ACLF were enrolled and categorized by treatment modality (GC vs. Control). Baseline characteristics, liver function, disease complications, and mortality were recorded. Univariate and multivariate analysis were used to identify predictive factors for HBV-ACLF-related mortality.**

Results: **GC therapy significantly improved the 30- and 60-day mortality of HBV-ACLF patients (4.64% vs. 11.92%, P=0.022 and 16.56% vs. 25.83%, P=0.049 for the Control and GC groups, respectively) and GC was an independent prognostic factor for 30-day mortality (OR = 0.177, 95% CI 0.051-0.616, P = 0.007). However, enhanced survival was not associated with improved liver function. There were no significant differences in the incidence of complications (i.e., ascites, bacterial infection, encephalopathy, hepatorenal syndrome, and gastrointestinal bleeding) between the GC and Control groups (P >0.05), except that fungal infection occurred with higher frequency in the GC group (P = 0.037). A significant improvement in the 30-day survival associated with GC therapy was observed among patients <40 years of age, a Model for End-stage Liver Disease (MELD) score of 25-35 or a CLIF-Consortium ACLF (CLIF-C ACLF) grade 0-1 (all P <0.05).**

Conclusions: **GC therapy improved the short-term (30- and 60-day) mortality of patients with HBV-ACLF. This treatment may be of particular benefit to patients who are <40 years of age, have a MELD score of 25-35, or have a CLIF-C ACLF grade of 0-1.** (Acta gastroenterol. belg., **2022,** 85, **593-600**).

Keywords: acute-on-chronic liver failure, hepatitis B virus, glucocorticoid, prognosis

Introduction

Acute-on-chronic liver failure (ACLF) is a complex syndrome characterized by acute deterioration of liver function and both hepatic and extrahepatic organ failure in the context of pre-existing chronic liver disease (1). Elevated hepatitis B virus (HBV) DNA levels are associated with the occurrence of liver-related events (2). In Asia, HBV-related acute-on-chronic liver failure (HBV-ACLF) accounts for about 70% of all ACLF cases. The 28-day mortality is high, ranging from 58 to 74% (3,4). HBV-ACLF pathogenesis is complex and is currently thought to involve a combination of immune damage, ischemia and hypoxia, and endotoxemia (5,6).

No new breakthrough medicines have been developed to treat HBV-ACLF so most patients receive comprehensive therapies such as an artificial liver support system (ALSS) or liver transplantation (LT). While LT is the most effective treatment, the expense of this procedure and a shortage of donor livers has restricted its use. ALSS is only effective for some patients and is not widely available due to limitations in plasma availability. Thus, there is a critical need for the development of more effective and available treatments for liver failure.

Glucocorticoid (GC) is the most used anti-inflammatory and immunosuppressant drug and has a theoretical basis for the treatment of liver failure. For liver failure caused by autoimmune hepatitis and alcoholic liver disease (7,8), there is some consensus on the application of GC. However, its use as a treatment for HBV-ACLF remains uncertain and there is still significant debate about the appropriate timing of GC application, type, dosage, and course of treatment (9,10). The current study sought to evaluate the efficacy of GC for HBV-ACLF treatment and to identify particular at-risk populations that may benefit from this therapy.

Methods

Patient selection

Patients with HBV-ACLF who were admitted to the Department of Infectious Diseases at the First Affiliated Hospital of Nanchang University from May 2014 to January 2022 were retrospectively investigated. Patients were included if they were i) seropositive for HBV surface antigen for at least 6 months and ii) met the diagnostic criteria for ACLF that are consistent with the Asian Pacific Association for the Study of the Liver (APASL): acute hepatic insult manifesting as severe jaundice (serum bilirubin ≥5mg/dl) and coagulopathy (international normalized ratio [INR] ≥1.5 or prothrombin activity [PTA] ≤40%) complicated within 4 weeks by encephalopathy and/or ascites in a patient with previously diagnosed or undiagnosed chronic liver disease (3). Patients were excluded from the study if they

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i) had other serious systemic diseases such as cancer, HIV, previous renal dysfunction, or heart failure, ii) had other causes of liver injury including drug-induced hepatitis, autoimmune hepatitis, or another viral hepatitis, or iii) were pregnant.

A total of 302 patients who met the inclusion and exclusion criteria were enrolled in the study. All patients received standard medical treatment including antiviral therapy with a nucleotide analog, hepatoprotective drugs, nutritional support, blood transfusion, and prevention and treatment of complications, and were given artificial liver support system (ALSS) therapy as needed. Of the enrolled patients, 151 patients received additional GC therapy, 5-10 mg/d dexamethasone or 40-80 mg/d methylprednisolone that was gradually tapered off within 1 week. GC treatment was prescribed at the discretion of three doctors with the ranking of associate chief physician or higher based on each patient's condition.

Data collection

Basic demographic and clinical information for each patient, including sex, age, presence of cirrhosis, and time from disease onset to admission was collected. Laboratory tests for white blood cells (WBC), hemoglobin, platelets, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBil), albumin (ALB), alpha-fetoprotein (AFP), prothrombin time (PT), prothrombin activity (PTA), international normalized ratio (INR), hepatitis B e-antigen (HBeAg), HBV-DNA, serum urea, creatinine (Cr), MELD score and CLIF-C ACLF grade, were performed at baseline and/or before discharge. Complications from ACLF were also documented, including ascites, bacterial infection, fungal infection, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), and gastrointestinal bleeding. Ascites was diagnosed by abdominal imaging, paracentesis, and clinical evidence of pre-existing decompensation. Bacterial infection was confirmed by a positive culture result (11). Common bacterial infections caused by ACLF include spontaneous bacterial peritonitis (SBP), pulmonary infection, biliary tract infection, and enteric infection. Spontaneous bacterial peritonitis was defined as a polymorphonuclear leukocyte count in the ascites that was >250 cells/mm3 (12). Fungal infections were diagnosed using the EORTC/MSG definition (13). Hepatic encephalopathy was diagnosed based on the presence of a neuropsychiatric syndrome caused by liver failure and hyperammonemia (14). Hepatorenal syndrome (HRS) was diagnosed using the International Club of Ascites for acute kidney injury criteria (15). Gastrointestinal bleeding was confirmed by hematemesis, hematochezia, or melena.

The MELD score (16) was calculated as follows: 3.78 × LN (TBil [mg/dL]) + 11.2 × LN (INR) + 9.57 × LN (Cr [mg/dL]) + 6.43 × cause (0 for cholestatic or alcoholic liver diseases and 1 for all others). ACLF grades 0, 1, 2, and 3 were defined using the CLIF-C ACLF classification (17).

Patients were followed up for 60 days after the onset of HBV-ACLF. The main outcome was 30-day mortality and prognostic factors for 30-day survival. Secondary outcomes included 60-day mortality, changes in laboratory indices during treatment, and the incidence of complications.

Statistical analysis

Categorical variables were expressed as a frequency (%) and analyzed using a chi-square or Fisher's exact test. Continuous variables were shown as the mean ± standard deviation or median (interquartile range) and were analyzed using the Student's t-test or non-parametric Mann-Whitney *U*-test, as appropriate. Kaplan-Meier curves were plotted and checked using log-rank tests. Significantly predictive factors of mortality identified by univariate analysis (P <0.05) were included in the multivariate Cox proportional hazards model. SPSS 23.0 software (IBM Corp., Armonk, NY, USA) was used for all data analyses. A two-tailed P value <0.05 was considered statistically significant.

Results

Patient demographic and clinical characteristics at baseline

A total of 302 HBV-ACLF patients were enrolled in the study, including 267 males and 35 females with an average age of 42.51 ± 10.61 years (range: 20-76 years). There were 151 patients (50%) in the GC group and 151 patients (50%) in the Control group (Figure 1). Laboratory data (except hemoglobin), CLIF-C ACLF grade, and complications at baseline were comparable between the GC and Control groups. At baseline, more than half the patients fulfilled the CLIF-C ACLF criteria (90/151 in the GC group vs. 95/151 in the Control group, P >0.05) (Table 1).

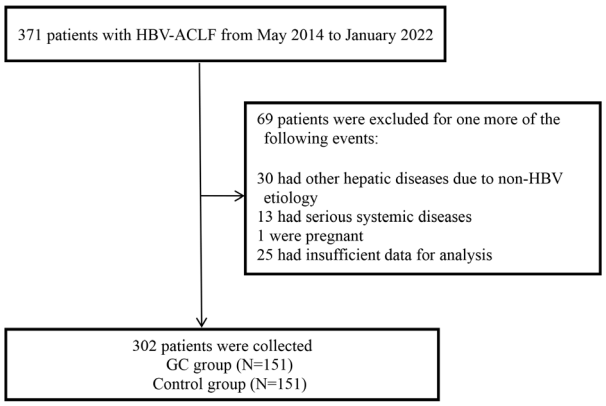

Figure 1. — Flow diagram of HBV-ACLF patient inclusion in the study. HBV-ACLF: hepatitis B virus-related acute-on-chronic liver failure; GC: glucocorticoid therapy.

Table 1. — **Patient demographic and clinical characteristics at baseline**

	GC (n=151)	Control (n=151)	*P* value
Age (years)	41 (34, 48)	43 (35, 51)	0.174
Sex (n, %)			0.857
Male	134 (88.74)	133 (88.08)	
Female	17 (11.26)	18 (11.92)	
CLIF-C ACLF grade (n, %)			0.059
No ACLF	61 (40.4)	56 (37.09)	
ACLF I	36 (23.84)	18 (11.92)	
ACLF II	50 (33.11)	69 (45.7)	
ACLF III	4 (2.65)	8 (5.3)	
Cirrhosis (n, %)	36 (23.84)	49 (32.45)	0.096
Time from onset to admission (days)	10 (7, 15)	10 (7, 15)	0.113
Laboratory data			
WBC ($\times 10^9$/L)	6.25 (4.89, 8.67)	6.42 (5.07, 7.96)	0.907
Hemoglobin (g/L)	140 (127, 149)	133 (120, 146)	0.006
Platelet ($\times 10^9$/L)	120 (82, 161)	123 (90, 154)	0.695
ALT (U/L)	856 (448, 1346)	700 (275, 1340)	0.074
AST (U/L)	451 (217, 1027)	486 (206, 917)	0.930
Albumin (g/L)	34 (31.5, 36.2)	33.3 (29.8, 36.1)	0.057
TBil (μmol/L)	272.7 (185.5, 362.1)	280.9 (203.5, 377.6)	0.400
Serum urea (mmol/L)	3.4 (2.6, 4.3)	3.1 (2.4, 4.2)	0.297
Cr (μmol/L)	65.2 (56.2, 75.4)	63.8 (56.3, 71.9)	0.315
AFP (ng/mL)	59.86 (18.14, 147)	75.53 (24.14, 175)	0.163
PT (s)	25.6 (20.1, 32.7)	24.2 (20.2, 27.5)	0.054
PTA (%)	29.9 (22.2, 39)	31.4 (25.5, 38.6)	0.103
INR	2.22 (1.76, 2.97)	2.15 (1.85, 2.49)	0.136
MELD score	26 (23, 30)	26 (24, 28)	0.189
HBeAg positive (n, %)	19 (46.34)	18 (48.65)	0.247
HBV DNA (lg IU/mL)	5.95 (4.66, 7.32)	5.75 (4.53, 7.24)	0.410
Complications (n, %)			
Ascites	76 (50.33)	91 (60.26)	0.083
Bacterial infection	38 (25.17)	52 (34.44)	0.078
Hepatic encephalopathy	23 (15.23)	30 (19.87)	0.290
Hepatorenal syndrome	11 (7.28)	19 (12.58)	0.124

GC: glucocorticoid therapy; CLIF-C ACLF: European Association for the Study of Chronic Liver Failure; WBC: white blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TBil: total bilirubin; Cr: creatinine; AFP: alpha-fetoprotein; PT: prothrombin time, PTA: prothrombin activity; INR: international normalized ratio; MELD: Model for End-stage Liver Disease; HBeAg: hepatitis B e-antigen; HBV: hepatitis B virus.

Outcomes of patients treated with or without GC

At the 30-day primary endpoint, the GC group had a lower mortality rate than the Control group (4.64% vs. 11.92%, respectively; $P=0.022$). At the 60-day follow-up, the mortality rate increased to 16.56% and 25.83%, respectively ($P=0.049$). No patients required a liver transplantation. The cumulative survival curves for patients treated with or without GC are shown in Figure 2. While liver function (ALT, AST, TBil) decreased significantly in the GC group (all $P<0.05$), no improvements and even some exacerbation in Cr levels, INR, or MELD scores were observed after GC treatment. ALT levels were lower in the Control group than in the GC group ($P<0.05$), but no differences were observed in other liver and coagulation function indices (all $P>0.05$) (Table 2). These results indicated that GC improved the short-term survival of patients, but increased survival was not associated with an improvement in liver and coagulation functions.

Bacterial infection, >50% of which was caused by spontaneous bacterial peritonitis (SBP) or lung infection, was the most frequent secondary complication. No significant differences were observed in the incidence of ascites, bacterial infection, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), or gastrointestinal

Table 2. — **Liver function of patients treated with or without glucocorticoids**

	GC (n=151)		*P* value	Control (n=151)		*P* value
	Before treatment	After treatment		Before treatment	After treatment	
ALT (U/L)	856(448, 1346)	67 (38, 135)	<0.001	700 (275, 1340)	48.7 (35, 88)*	<0.001
AST (U/L)	451 (217, 1027)	77 (50, 114)	<0.001	486 (206, 917)	73 (53, 117)	<0.001
TBil (μmol/L)	272.7 (185.5, 362.1)	200.3 (89.6, 400.5)	0.043	280.9 (203.5, 377.6)	210 (93, 440.2)	0.106
Cr (μmol/L)	65.2 (56.2, 75.4)	66.8 (55.1, 85.0)	0.002	63.8 (56.3, 71.9)	70.3 (57.1, 87.6)	<0.001
INR	2.22 (1.76, 2.97)	2.43 (1.32, 3.33)	0.980	2.15 (1.85, 2.49)	2.18 (1.43, 3.09)	0.382
MELD score	26 (23, 30)	27 (16, 32)	0.141	26 (24, 28)	25 (17, 32)	0.404

GC: glucocorticoid therapy; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TBil: total bilirubin; Cr: creatinine; INR: international normalized ratio; MELD: Model for End-stage Liver Disease. Compared with GC group after treatment: * P= 0.020 The average treatment duration was 23 (11, 43) days for GC group and 26 (17, 46) days for Control group

Table 3. — **Secondary complications in patients during treatment**

	GC (n=151)	Control (n=151)	*P* value
Ascites (n, %)	40 (26.49)	35(23.18)	0.505
Bacterial infection (n, %)	76 (50.33)	64 (42.38)	0.166
Spontaneous bacterial peritonitis	27 (17.88)	18 (11.92)	
Lung infection	35 (23.18)	27 (17.88)	
Biliary tract infection	10 (6.62)	13(8.61)	
Enteric infection	4 (2.65)	6 (3.97)	
Fungal infection (n, %)	25(16.56)	13(8.61)	0.037
Hepatic encephalopathy (n, %)	34 (22.52)	44 (29.14)	0.075
Hepatorenal syndrome (n, %)	10 (6.62)	19 (12.58)	0.079
Gastrointestinal bleeding (n, %)	9 (5.96)	10 (6.62)	0.813

GC: glucocorticoid therapy. The average treatment duration was 23 (11, 43) days for GC group and 26 (17, 46) days for Control group

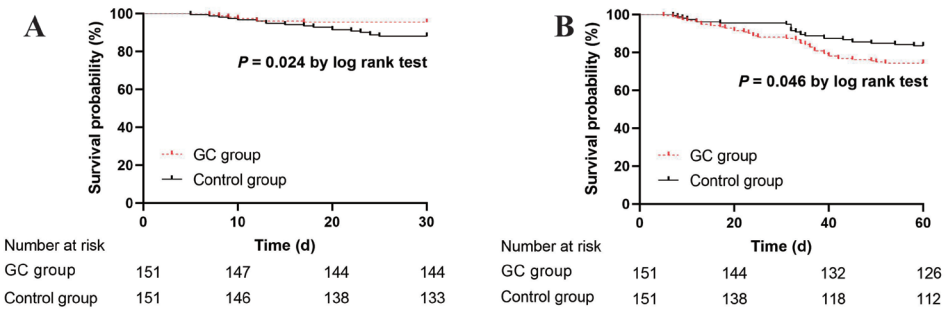

Figure 2. — Survival analysis of patients treated with or without glucocorticoids (A) within 30 days and (B) within 60 days. GC: glucocorticoid therapy.

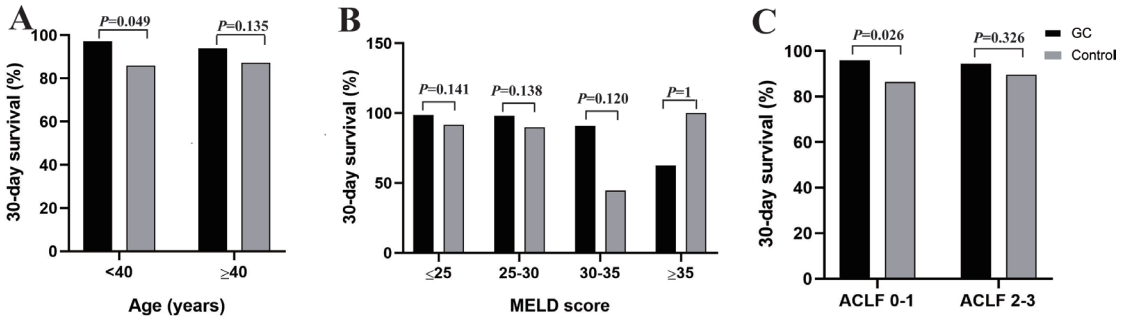

Figure 3. — Stratified analysis of independent prognostic factors. (A) 30-day survival by age group. (B) 30-day survival by MELD score range. (C) 30-day survival by CLIF-C ACLF grade. GC: glucocorticoid therapy; MELD: Model for End-stage Liver Disease; CLIF-C ACLF: European Association for the Study of Chronic Liver Failure.

Table 4. — **Univariate and multivariate cox analysis of factors associated with 30-day mortality**

Variables	Univariate		Multivariate	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age	1.059 (1.024, 1.096)	0.001	1.049 (1.005, 1.095)	0.027
Sex, male	1.456 (0.500, 4.243)	0.491		
Cirrhosis	1.453 (0.642, 3.288)	0.370		
Time from onset to admission (days)	0.996 (0.960, 1.033)	0.825		
WBC (× 10^9/L)	1.064 (0.958, 1.181)	0.248		
Hemoglobin (g/L)	0.984 (0.966, 1.002)	0.074		
Platelet (× 10^9/L)	0.999 (0.993, 1.005)	0.720		
ALT (U/L)	1 (0.999, 1.000)	0.786		
AST (U/L)	1 (1.000, 1.001)	0.468		
Albumin (g/L)	1.037 (0.940, 1.145)	0.468		
TBil (μmol/L)	1.003 (1.000, 1.005)	0.052		
Serum urea (mmol/L)	1.094 (0.960, 1.247)	0.176		
Cr (μmol/L)	1.009 (0.995, 1.024)	0.200		
AFP (ng/mL)	1 (0.998, 1.002)	0.897		
PT (s)	1.033 (1.011, 1.056)	0.003		
PTA (%)	0.942 (0.904, 0.981)	0.004		
INR	1.517 (1.193, 1.929)	0.001		
MELD score	1.157 (1.070, 1.251)	<0.001	2.086 (1.437, 3.028)	<0.001
CLIF-C ACLF grade 2-3 vs. grade 0-1	3.959 (1.486, 10.549)	0.006	7.656 (1.988, 29.490)	0.003
HBeAg positive	0.703 (0.321, 1.542)	0.380		
HBV DNA (lg IU/mL)	1.352 (1.031, 1.773)	0.029		
Ascites	0.712 (0.325, 1.560)	0.395		
Bacterial infection	2.144 (0.896, 5.134)	0.087		
Hepatic encephalopathy	3.409 (1.327, 6.332)	0.007		
Hepatorenal syndrome	4.073 (1.701, 9.755)	0.002		
Glucocorticoid therapy	0.304 (0.121, 0.760)	0.011	0.177 (0.051, 0.616)	0.007
Artificial liver support therapy	1.408 (0.483, 4.103)	0.530		

WBC: white blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TBil: total bilirubin; Cr: creatinine; AFP: alpha fetoprotein; PT: prothrombin time, PTA: prothrombin activity; INR: international normalized ratio; MELD: Model for End-stage Liver Disease; CLIF-C ACLF: European Association for the Study of Chronic Liver Failure; HBeAg: hepatitis B e-antigen; HBV: hepatitis B virus.

bleeding (GI bleeding) between the two groups (all P >0.05). The incidence of fungal infection was higher in the GC group than the control group (P = 0.037) (Table 3).

Predictive factors associated with the 30-day mortality of HBV-ACLF patients

Univariate and multivariate analyses were used to explore independent predictive factors of HBV-ACLF patient 30-day mortality rates. In the univariate analysis, age, PT, PTA, INR, MELD score, baseline CLIF-C ACLF grade, HBV DNA, GC therapy, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), and GI bleeding were significantly associated with 30-day mortality. Multivariate analysis revealed that age (HR 1.049, P = 0.027), MELD score (HR 2.086, P <0.001), baseline CLIF-C ACLF grade (grade 2-3 vs. grade 0-1, HR 7.656, P = 0.003) and GC therapy (HR 0.177, P = 0.007) were independent predictors of mortality (Table 4).

Screening for optimal GC treatment conditions

To further identify the optimal conditions for GC therapy, the independent prognostic indicators identified by the multivariate analysis, including age, MELD score, and baseline CLIF-C ACLF grade, were quantified and stratified. Patients who were <40 years of age had a significantly higher 30-day survival rate in the GC group than in the Control group [97.10% (67/69) vs. 85.96% (49/57); P = 0.049], while those ³40 years of age had a similar 30-day survival rate in the two groups [93.90% (77/82) vs. 87.23% (82/94); P = 0.135] (Fig 3A). The lower 30-day survival rate was associated with a higher MELD score. Patients in the GC group with a MELD score of 25-35 had a significantly higher 30-day survival rate than those in the Control group [96.05% (73/76) vs. 84.62% (66/78); P = 0.017] (Fig 3B). For patients with a CLIF-C ACLF grade 0-1, the 30-day survival rate was also significantly higher in the GC group than in the Control group [95.88% (93/97) vs. 86.49% (64/74); P =

0.026]. Meanwhile, for patients with CLIF-C ACLF grade 2-3, the 30-day survival was non-significantly higher in the GC group than in the Control group [94.44% (51/54) vs. 89.61% (69/77); $P = 0.326$] (Fig 3C).

Discussion

GC is the most widely used anti-inflammatory and immunosuppressive agent and has shown success in treating liver failure caused by hepatotoxic drugs or autoimmune hepatitis (18,19). However, the use of GC for patients with HBV-ACLF has transitioned from blind recommendation to blind rejection to conditional acceptance (20). Indeed, the efficacy of GC therapy for patients with ACLF remains controversial. Zhao et al. (21) showed that methylprednisolone therapy can improve the 28-day survival of ACLF patients by inhibiting myeloid dendritic cell function and Zhang et al. (22) found that dexamethasone therapy can improve the 3-month survival of patients with acute-on-chronic pre-liver failure. However, Chen et al. (23) showed that dexamethasone is unable to curb the clinical progression of HBV-related acute-on-chronic pre-liver failure and Chen et al. (24) demonstrated that dexamethasone does not improve the liver function or 3-month survival of HBV-ACLF patients. All these studies had a small sample size and most were retrospective. A multicenter randomized controlled trial (RCT) with a larger sample size was recently published indicating that methylprednisolone therapy is an effective and safe clinical strategy for HBV-ACLF patients, effectively increasing the 6-month cumulative survival rate (25).

Systemic inflammation is the primary reason for ACLF pathology. GC can inhibit the function of cytotoxic T lymphocytes (CTL) and intercellular adhesion molecule-1 (ICAM-1), thereby preventing or delaying excessive cellular immunity and alleviating liver cell injury (26,27). This treatment also suppresses the release of inflammatory mediators from intrahepatic and extrahepatic mononuclear phagocytes, preventing or delaying secondary hepatic microcirculation disorder (28-30). In addition, GCs can inhibit TNF-related apoptosis-inducing ligand (TRAIL) mediated apoptosis of hepatocytes by up-regulating P-glycoprotein (P-gp) expression (31-33).

The current study found that GC therapy significantly improved HBV-ACLF 30- and 60-day mortality rates but did not improve short-term liver function. GC treatment also failed to reduce the incidence of ascites, bacterial infection, HE, HRS, or GI bleeding, and promoted a rise in fungal infections. This may be because fungal infections are a primary cause of ACLF and associated mortality (34), keeping patients in a state of immunoparesis. Thus, while GC treatment is unable to improve liver and coagulation function, it may effective for particular patient populations.

This study explored the impact of baseline disease status on 30-day mortality. Multivariate Cox and survival analysis results showed that GC treatment improved the short-term mortality rate of HBV-ACLF patients, which is consistent with previous findings (22,25). Age was an independent factor influencing the survival rate, with GC treatment specifically benefiting patients <40 years of age. Other studies have also shown higher survival rates among HBV-ACLF patients in this age group (22,24). The MELD and CLIF-C ACLF are prognostic scoring systems that reflect HBV-ACLF disease severity (35). Prior studies have shown that high MELD and CLIF-C ACLF scores are risk factors for ACLF mortality (36-38), a finding confirmed by the present study.

To identify an optimal population for GC therapy, patients were assigned to subgroups based on their age, MELD score, and ACLF grade at baseline. Results showed a significant improvement in the 30-day survival associated with GC therapy among patients who were <40 years old or who had a MELD score of 25-35 or a CLIF-C ACLF grade of 0-1. It was speculated that steroids are most beneficial for patients with less severe disease (39,40).

Both the disease severity and the potential risk of disease progression should be fully considered when evaluating the effect of GC therapy. The current study identified factors that are associated with better responses to treatment. However, this study also had some important limitations. First, because this was a retrospective study, it was difficult to control for confounding factors. Second, medium- or long-term outcomes of GC therapy were not evaluated due to a lack of follow-up information. Finally, there was not enough clinical data to evaluate the timing of GC treatment. In addition, the optimal GC doses and treatment course will require verification using additional clinical data and multicenter studies. This will be necessary to develop a safe and effective therapeutic regimen for the clinical application of GC for HBV-ACLF.

In summary, GC therapy was effective at improving HBV-ACLF short-term (30- and 60-day) mortality rates but had no impact on short-term liver function. However, GC treatment failed to improve ascites, bacterial infection, HE, HRS, and GI bleeding, and was associated with higher rates of fungal infection. The patients who mounted the best response to GC were those with less severe liver failure and at higher risk of rapid disease progression, who were <40 years of age or who had a MELD score of 25-35 or a CLIF-C ACLF grade of 0-1. These findings could serve as a helpful reference for clinical practice.

Data Availability Statement

The research data involve private patient data so cannot be publicly available on ethical grounds. The data relating to this study are available from the corresponding author based on reasonable request.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

Author contributions

Pei Shi designed the study and drafted the original manuscript. Wentao Zhu created the methodology and cleaned/organized the data. An Liang, Jun Wan, and Jiwei Fu collected the clinical data. Xiaoping Wu made critical revisions to the original draft. All authors contributed to the article and approved the submitted version.

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Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki. The methods involving human participants were reviewed and approved by the Medical Research Committee of The First Affiliated Hospital of Nanchang University. The data are anonymous so the requirement for informed consent was waived.

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