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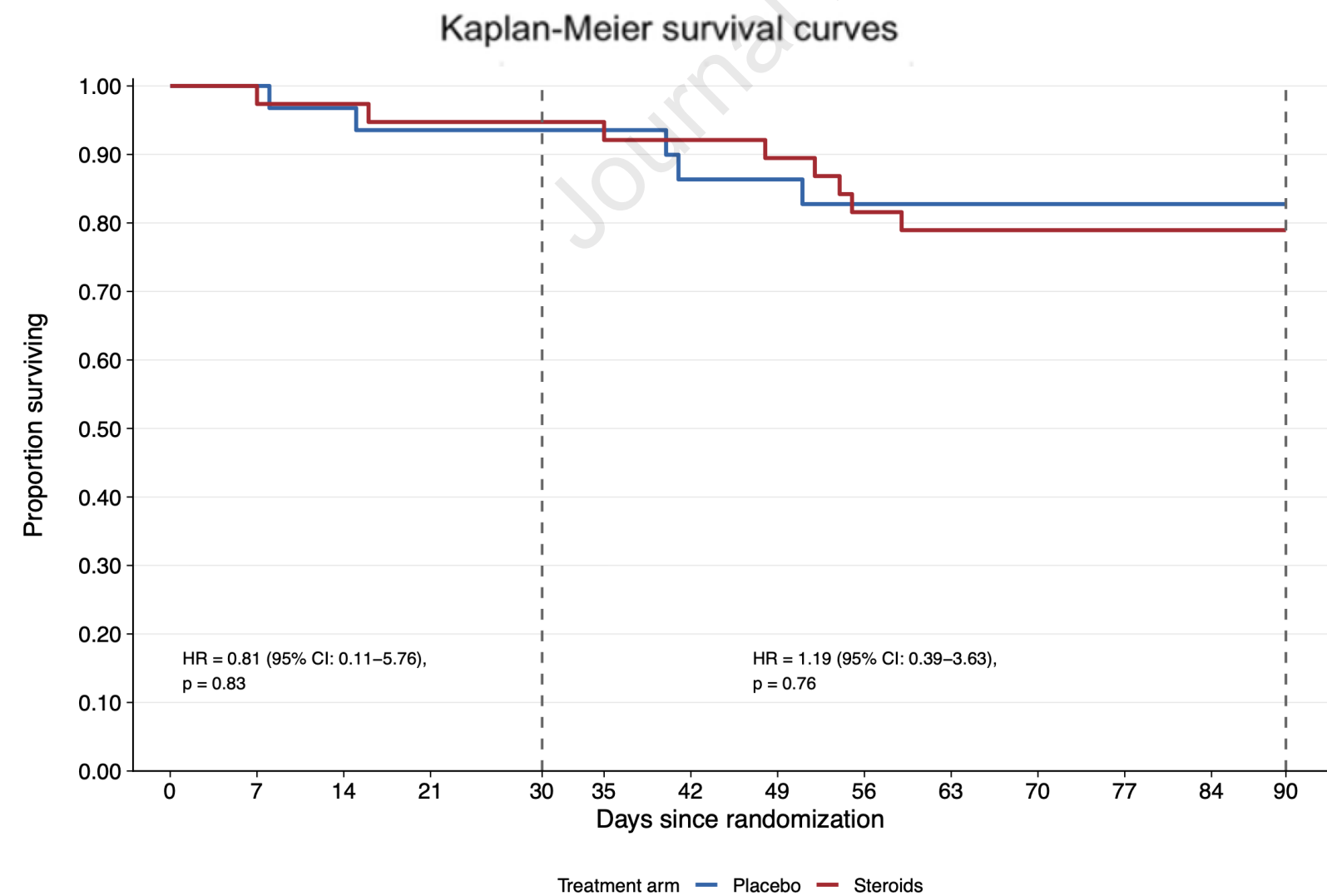
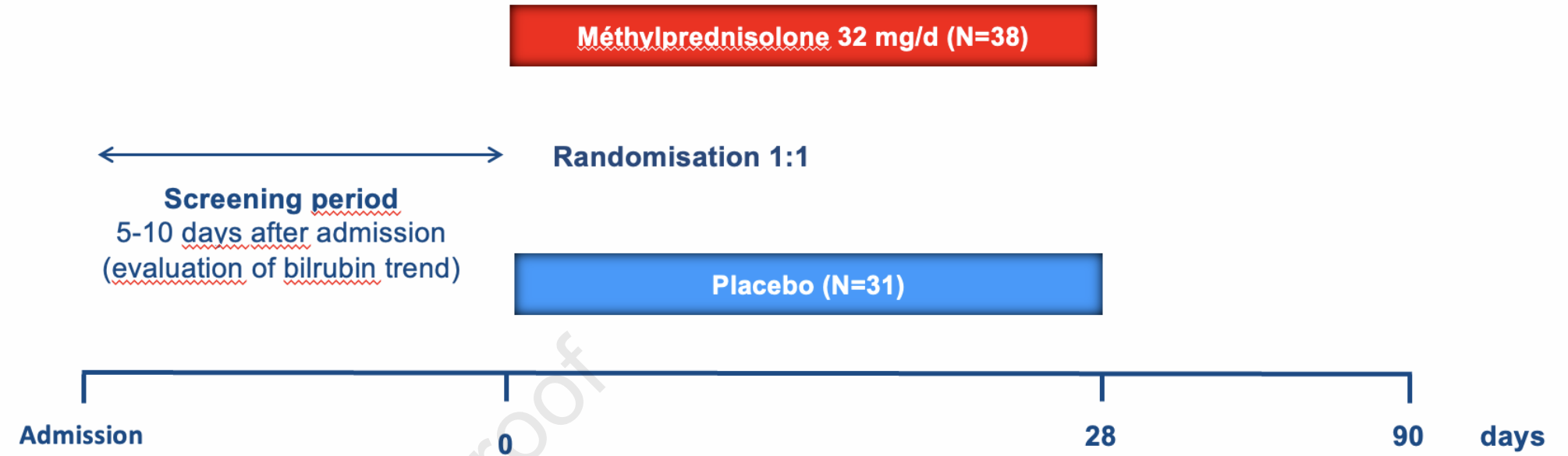
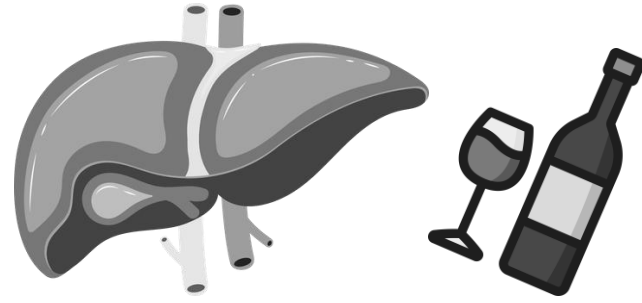
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69 analysed patients with
severe biopsy-proven AH and
spontaneous bilirubin decrease > 10%



Corticosteroids in severe alcohol-related hepatitis: a multicenter randomized clinical trial

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Abbreviations: CORTISAVE: Corticosteroids In Severe Alcoholic hepatitis patients with early spontaneous improvement, AH: Alcohol-related hepatitis, ALD: Alcohol-related liver disease , ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, mDF: Maddrey discriminant function, MELD: Model for End-Stage Liver Disease, ACLF: Acute-on-Chronic Liver Failure, EASL: European Association for the Study of the Liver, BMI: Body mass index, INR: International normalized ratio, SHR: Subdistribution hazard ratios, COVID: Coronavirus Disease

Highlights:

- Severe AH patients with early spontaneous bilirubin improvement have a relatively favorable prognosis (~80% 90-day survival)
- In this population, corticosteroid therapy was not associated with improved 90-day or 30-day survival
- The trial was underpowered due to slow recruitment and lower-than-anticipated mortality in the placebo arm
- Corticosteroids were associated with a numerically higher infection rate (47% vs 34%), though not significant
- A 5–10 day observation period may help to identify severe AH patients who do not require corticosteroid therapy

Abstract

Background & Aims

Severe alcohol-related hepatitis (AH) has high short-term mortality, and corticosteroid therapy is recommended in the absence of contraindications. However, its benefit in patients with early spontaneous bilirubin improvement remains unknown. We determined whether corticosteroid therapy improves survival compared with placebo in this specific population.

Methods

In this multicenter, randomized, placebo-controlled trial conducted in 10 Belgian hospitals (February 2018–May 2024), patients aged ≥ 18 years with biopsy-proven severe AH and spontaneous bilirubin decline $>10\%$ between admission and day 5–10 were randomized 1:1 to methylprednisolone 32 mg daily or placebo for 28 days. The primary outcome was 90-day survival; other outcomes included 30-day survival and cumulative incidence of infection at 90 days.

Results

Sixty-nine of the 140 planned patients were analyzed (38 corticosteroid, 31 placebo), representing 49% of the planned sample size. Baseline characteristics were well balanced. At 90 days, survival was 79% (95% CI, 67%–93%) versus 83% (95% CI, 70%–98%) (hazard ratio, 1.19; 95% CI, 0.39–3.63; $P=0.76$). Eight deaths occurred in the corticosteroid arm versus 5 in the placebo arm. At 30 days, survival was 95% versus 94% ($P=0.83$). Cumulative incidence of infection at 90 days was 47% versus 34% (subdistribution hazard ratio, 1.55; 95% CI, 0.72–3.34; $P=0.26$). Lille score was an independent predictor of 90-day mortality.

Conclusions

In patients with severe AH and early spontaneous bilirubin improvement, corticosteroid therapy was not associated with improved survival, but the underpowered trial cannot exclude a benefit. A short observation period after admission may help identify patients who can be managed without corticosteroids.

Impact and Implications

Corticosteroid therapy is recommended for patients with severe alcohol-related hepatitis (AH), but whether this benefit extends to the subgroup who show early spontaneous improvement in bilirubin after admission was previously unknown. In this multicenter, randomized, placebo-controlled trial, corticosteroid therapy was not associated with improved 90-day or 30-day survival in patients with severe, biopsy-proven AH and a spontaneous bilirubin decline greater than 10% within 5 to 10 days of admission, and was associated with a numerically higher, though not statistically significant, risk of infection. These findings are most relevant to hepatologists and other clinicians managing patients with severe AH, and to researchers designing future AH trials, as they identify a subgroup in whom

the benefit of corticosteroids is uncertain. They support a risk-stratified approach in which a brief observation period after admission—incorporating bilirubin trend, infection screening, and liver biopsy—may help identify patients with a relatively favorable prognosis who can be spared corticosteroid therapy and its associated risks. However, because the trial was stopped early after enrolling only 69 of the 140 planned patients, it was underpowered, and a modest survival benefit of corticosteroids cannot be excluded. These results should therefore not be interpreted as definitive evidence against corticosteroid use in this population and require confirmation in larger, adequately powered studies before informing clinical guidelines or being generalized beyond this specific patient subgroup.

Introduction

Alcohol-related hepatitis (AH) is an acute manifestation of alcohol-related liver disease characterized by recent-onset jaundice, chronic alcohol consumption, and typical laboratory findings (increased bilirubin level, AST > 50, ALT and AST < 400, AST/ALT ratio > 1.5) [1,2]. In its severe forms, defined either by a Maddrey discriminant function (mDF) ≥ 32 or a Model for End-Stage Liver Disease (MELD) score > 20, short-term mortality is high and estimated around 30% at 90 days [3,4]. Corticosteroid therapy is the only treatment demonstrating a survival benefit and is recommended by clinical guidelines in severe AH [5]. The STOPAH trial, the largest randomized trial in the field, showed reduced 30-day mortality with corticosteroids [6], and a meta-analysis of individual patient data on 2111 patients with severe AH reported 1-month survival of 84% with corticosteroids versus 76% without treatment [7]. However, corticosteroids do not improve survival beyond 1 month and may increase infection risk [6,8].

AH is heterogeneous in severity, and treatment benefit varies across the disease spectrum. At the most severe end of the disease spectrum, patients with multiple organ dysfunctions (ACLF grade 3) have a very low probability of responding to CS and a very high risk of short-term mortality [9]. In a large retrospective, international multi-center cohort study including 3380 patients with clinical and/or histological diagnosis of AH, corticosteroids improved survival in AH patients with MELD scores between 21 and 51, with the maximum effect observed with MELD scores between 25 and 39 [10]. Apart from their retrospective nature, these studies assessed disease severity at a single time point without considering early spontaneous evolution after admission.

Importantly, there is a clear lack of data and clinical guidance regarding corticosteroid use in the subset of patients with severe AH who demonstrate spontaneous improvement in total serum bilirubin level shortly after admission. Although previous cohort data suggest that severe AH patients with spontaneous bilirubin improvement early after admission had better 3-month survival than those without improvement, there was particular uncertainty on whether corticosteroids provide any additional benefit in this subgroup. Focusing on this population allowed us to address this knowledge gap, while patients without spontaneous improvement of bilirubin already have more robust data regarding corticosteroid efficacy.

The CORTISAVE study aimed to determine whether corticosteroid therapy improves survival compared with placebo in patients with severe AH and spontaneous bilirubin improvement after admission.

Patients and methods

Study design

This multicenter, double-blind, randomized, placebo-controlled trial was conducted in 10 Belgian hospitals between February 2018 and February 2024. The study was approved by the ethics committee of CUB Hôpital Erasme and by local institutional review boards at each participating center. The trial was registered on ClinicalTrials.gov (NCT03160651) and was supported by the Belgian Association for the Study of the Liver.

Participants

Eligible patients were aged 18 years or older, consumed more than 40 g of alcohol daily, had recent-onset jaundice within 3 months, had serum bilirubin level greater than 5 mg/dL, had biopsy-proven steatohepatitis, and had mDF equal or greater to 32 at admission. Spontaneous improvement was required, defined as serum bilirubin decrease greater than 10% between admission and day 5 to 10. Investigators had therefore a window of 5 to 10 days after admission to the hospitalization ward to assess eligibility for randomization, whereas the baseline bilirubin value was defined as the level measured at initial hospital admission. For some patients admitted via the emergency department, there could therefore be a delay between the initial bilirubin assessment and the admission to the hospitalization ward. As a result, in certain cases, the time required to observe a $\geq 10\%$ decrease in serum bilirubin could extend beyond 10 days after hospital admission, although it remained within the 5–10 days window following admission to the ward. Maximum time from admission to randomization was 14 days. Histological confirmation of AH required steatosis, hepatocyte ballooning, and polymorphonuclear neutrophil infiltrate [1].

Exclusion criteria included hepatitis B surface antigen positivity, human immunodeficiency virus antibodies, chronic hepatitis C infection (positive HCV RNA), severe concurrent disease compromising 90-day survival, uncontrolled infection (required control for ≥ 2 days), uncontrolled upper gastrointestinal bleeding (required control for ≥ 5 days), serum creatinine greater than 2.5 mg/dL, receipt of renal replacement therapy, terlipressin, or pentoxifylline.

Written informed consent was obtained from all participants; proxy consent from a relative was obtained for patients with significant encephalopathy.

Randomization

Patients were randomized 1:1 to receive methylprednisolone 32 mg once daily or matching placebo. Randomization sequences were generated centrally at CUB Hôpital Erasme by an independent statistician using variable block sizes of 2, 4, or 6 without stratification, and provided to each site. At the time of patient inclusion, the investigator asked for a randomization number, which was then communicated to the site pharmacist. The

pharmacist, who was the only unblinded member of the study team at each site, prepared the corresponding treatment according to the pre-established randomization list.

Randomization lists were accessible only to the pharmacists, ensuring that investigators and other study personnel remained blinded throughout the trial.

Procedures

After admission, patients with suspected severe AH (mDF > 32) underwent infection screening and liver biopsy according to local practices. Liver function was reassessed 5 to 10 days later. Patients with serum bilirubin decrease greater than 10% who met all eligibility criteria were randomized. Patients could be randomized before biopsy results were available but were excluded if steatohepatitis was not confirmed histologically.

At admission, serum bilirubin and mDF were measured. At randomization, the following were assessed: body mass index, encephalopathy and ascites grade, international normalized ratio, bilirubin, albumin, serum sodium, creatinine, aspartate aminotransferase, alanine aminotransferase, and MELD score. Follow-up visits at day 7, month 1, and month 3 included clinical examination and laboratory analyses. Treatment response was assessed using the Lille score at day 7 [11]. Early corticosteroid discontinuation based on Lille score was recommended but left to investigator discretion. Alcohol consumption was assessed by patient self-report at each visit.

Outcomes

The primary endpoint was 90-day survival following treatment initiation. Other exploratory endpoints included 30-day survival and the 90-day cumulative incidence of infection, with death considered as a competing risk.

Statistical analysis

The sample size calculation was based on an anticipated 90-day mortality of 35% in the placebo group and 15% in the methylprednisolone group, corresponding to an absolute risk reduction of 20%. Assuming a two-sided alpha level of 0.05, 80% power, and a 1:1 allocation ratio, and applying a continuity correction, a total of at least 140 patients (70 per group) was required to detect this difference. The population analyzed was a modified intention-to-treat (mITT) population, in which patients randomized before the biopsy result was available and for whom steatohepatitis lesions were not present were excluded. The decision to perform a mITT was chosen in order to improve the homogeneity of the study population by restricting the analysis to patients with histologically confirmed alcohol-related hepatitis.

Variables with normal distribution are presented as means $\pm$ standard deviations, while skewed variables are presented as medians with interquartile ranges (IQR). Categorical variables are expressed as counts and percentages. Baseline characteristics were compared between treatment groups using Student's t-test for normally distributed continuous variables, Wilcoxon rank-sum test for non-normally distributed continuous variables, and chi-squared test for categorical variables.

Survival was estimated using the Kaplan-Meier method, and survival curves were compared between treatment groups using Cox proportional hazards regression with Wald test. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated. Univariate Cox proportional hazards regression analyses were conducted to identify factors associated with 90-day mortality. In addition to treatment arm, covariates with a p-value < 0.10 in univariate analysis were included in the multivariable model. Composite prognostic scores (Lille, mDF, MELD) and their individual components were not included together in regression models to avoid collinearity [12].

The cumulative incidence of infection was estimated, treating death without prior infection as a competing event. Differences between treatment groups were assessed using the Fine-Gray subdistribution hazards model, and subdistribution hazard ratios (SHRs) with 95% confidence intervals (CIs) are reported. All statistical tests were two-tailed, and $p < 0.05$ was considered statistically significant. Analyses were performed using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and baseline characteristics

Between February 2018 and February 2024, 348 patients were assessed for suspected AH across 10 Belgian centers, with 276 patients ineligible primarily due to absence of spontaneous bilirubin improvement (196 patients, 71%). Other reasons were absence of biopsy-proven AH (44 patients), mDF < 32 at admission (8 patients), refusal to participate in a clinical trial (3 patients), or others (25 patients) (**Figure 1**). Seventy-two patients were randomized (40 in the corticosteroid arm, 32 in the placebo arm). Three patients were excluded after randomization due to absence of steatohepatitis on liver biopsy, leaving 69 patients in the modified intention-to-treat analysis (38 in corticosteroid arm, 31 in the placebo arm). The study was prematurely stopped due to a slow recruitment.

Baseline characteristics were well balanced between treatment arms (**Table 1**). The median percentage decrease in bilirubin levels between admission and randomization was 29% (IQR, 21%-36%) in the corticosteroid arm versus 24% (IQR, 17%-33%) in the placebo arm ($P=0.35$). Among the 69 analyzed patients, 6 had a mDF < 32 at randomization, 5 in the corticosteroid arm and 1 in the placebo arm. No patient had liver transplantation or was lost to follow-up.

during the study period.

Primary endpoint

At 90 days, the cumulative probability of survival was 79% (95% CI, 67%-93%) in the corticosteroid group compared with 83% (95% CI, 70%-98%) in the placebo group (hazard ratio [HR], 1.19; 95% CI, 0.39-3.63; $P=0.76$; **Figure 2**). Eight deaths occurred among 38 patients (21%) in the corticosteroid arm and 5 deaths among 31 patients (16%) in the placebo arm. Of the 56 patients who survived beyond day 90, 41 completed the full 90-day follow-up; 15 were censored before day 90 (corticosteroid arm: 6 patients, median 88 days [IQR 86–89 days]; placebo arm: 9 patients, median 77 days [IQR 28–87 days]). All censoring was due to study termination; no patient was lost to follow-up. In univariate Cox regression analysis, age (HR per year, 1.08; 95% CI, 1.01-1.15; $P=0.027$) and Lille score (HR per 0.1-unit increase, 1.33; 95% CI, 1.06-1.67; $P=0.015$) were significantly associated with 90-day mortality, while treatment assignment and other baseline variables were not (**Table 3**). In multivariable analysis adjusting for treatment assignment, Lille score was independently associated with 90-day mortality (HR per 0.1-unit increase, 1.37; 95% CI, 1.06-1.76; $P=0.021$).

Other exploratory endpoints

At 30 days, the cumulative probability of survival was 95% (95% CI, 88%-100%) in the corticosteroid group compared with 94% (95% CI, 85%-100%) in the placebo group (HR, 0.81; 95% CI, 0.11-5.76; $P=0.83$; **Figure 2**). Two deaths occurred in each treatment group.

The cumulative incidence of infection at 90 days, with death as a competing risk, was 47% (95% CI, 30%-63%) in the corticosteroid arm (17 patients with infection) compared with 34% (95% CI, 17%-51%) in the placebo arm (10 patients with infection) (subdistribution HR, 1.55; 95% CI, 0.72-3.34; $P=0.26$; **Figure 3**). The distribution of infection types is shown in **Table 2**.

Discussion

In this randomized, placebo-controlled trial of patients with biopsy-proven severe alcohol-related hepatitis and early spontaneous bilirubin improvement, corticosteroid therapy did not improve survival at 90 days compared with placebo. These findings suggest that patients with severe AH demonstrating spontaneous bilirubin decline greater than 10% within 5 to 10 days of admission do not benefit from corticosteroid therapy and may be exposed to unnecessary infection risk.

The heterogeneity of AH has important implications for treatment selection. While corticosteroids remain standard of care for severe AH, benefit is not uniform across the disease spectrum. Patients with mild disease ($mDF < 32$) or multiorgan failure derive minimal or no benefit [10,15], and a large cohort study found maximal benefit in patients with MELD scores between 25 and 39 [10]. The present study identifies another subgroup unlikely to benefit: patients with severe disease at admission and early spontaneous improvement. Prior cohort data suggested better outcomes in such patients, but because all received

corticosteroids, the specific contribution of therapy remained uncertain [13]. Our randomized trial demonstrates that spontaneous improvement identifies favorable prognosis independent of corticosteroid treatment.

These findings align with observational data showing better prognosis in patients with rapid bilirubin decline ("fast-fallers") without clear corticosteroid benefit [3], though that study was limited by selection bias. Importantly, treatment delay was not associated with worse outcomes in observational studies [3,14], supporting feasibility of a 5- to 10-day observation period.

The mechanism likely reflects disease biology [15]. Bilirubin decline within the first week suggests resolution of acute inflammation, the pathophysiologic target of corticosteroid therapy. Patients without spontaneous improvement have ongoing hepatocellular injury that may be corticosteroid-responsive. This interpretation is supported by the Lille score remaining the only independent predictor of 90-day mortality in our analysis, reinforcing that early treatment response, whether spontaneous or treatment-induced, is the critical outcome determinant [11,16].

A key limitation of our study was the smaller-than-planned sample size, with only 72 of the 140 required patients enrolled. Recruitment was particularly challenging due to the COVID-19 pandemic, decreased indication for liver biopsies in some centers, and strict entry criteria requiring histologically confirmed steatohepatitis and evidence of spontaneous bilirubin decline. Of 348 patients with suspected AH, 276 (79%) were not recruited. This highlights the difficulty of conducting randomized trials in AH and underscores the need for consideration of broader or more pragmatic entry criteria in future studies (like potentially relaxing biopsy requirements or incorporating broader inclusion criteria, such as the NIAAA criteria, and considering pragmatic, community-based approaches to enhance recruitment).

We performed a modified intention-to-treat (mITT) analysis, excluding three patients without histological evidence of steatohepatitis. This approach was decided to ensure a homogeneous study population and is unlikely to have introduced meaningful selection bias, since only 3 patients were excluded due to absence of confirmed histological steatohepatitis.

Mortality was numerically lower in the placebo group, but this difference was not statistically significant, and the trial was underpowered to detect a modest effect. The initial assumption of a 20% absolute reduction in mortality (anticipating 35% mortality in the placebo group versus 15% with corticosteroids) appears to have overestimated both the expected event rate and the plausible benefit of corticosteroids in this population. Patients with alcohol-related hepatitis who exhibit spontaneous improvement in bilirubin levels have a more favorable prognosis, which contributed to the lower-than-anticipated mortality and further limited the power to detect any treatment effect.

The clinical implications are significant. We propose a risk-stratified approach: upon admission with suspected severe AH, observe bilirubin trajectory for 5 to 10 days while completing infection screening and liver biopsy. Patients with bilirubin decline greater than 10% can be managed without corticosteroids, achieving survival rates comparable to non-severe disease [17]. Patients without spontaneous improvement should be considered for corticosteroid therapy. This approach optimizes patient selection while ensuring rigorous infection screening before treatment initiation—critical given that infection is common before corticosteroids and associated with worse outcomes [18].

Cumulative incidence of infection at 90 days was numerically higher in the corticosteroid group, with a more frequent pulmonary location, consistent with prior studies [6,8],

underscoring the importance of avoiding unnecessary corticosteroid exposure in populations without survival benefit.

Our study has important strengths. To our knowledge, this is the first randomized, placebo-controlled trial evaluating corticosteroids specifically in severe AH with early spontaneous improvement. All participants had biopsy-proven AH, eliminating diagnostic uncertainty. Although the study was terminated early due to recruitment challenges, the findings provide meaningful insights for clinical practice.

In conclusion, corticosteroid therapy was not associated with improved survival in patients with severe alcohol-related hepatitis who demonstrate spontaneous bilirubin decline greater than 10% within 5 to 10 days of admission; however, this finding should be interpreted with caution given that the trial was underpowered due to incomplete recruitment and lower-than-anticipated 90-day mortality in the placebo arm, precluding a definitive conclusion on the absence of corticosteroid benefit. Observation for 5 to 10 days after admission may help identify patients with favorable prognosis who could be spared corticosteroid therapy and its associated infection risk, though this requires confirmation in adequately powered studies.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the author(s) used ChatGPT in order to improve the English and phrasing in certain parts of the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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Tables

Table 1. Baseline characteristics of patients included in the modified intention-to-treat analysis

Characteristics	Total (N=69)	Corticosteroids (N=38)	Placebo (N=31)
Age (years)	69	52 ± 8	51 ±10
Male gender (%)	69	29 (76)	20 (65)
Diabetes (%)	65	2 (5.7)	3 (10)
Ascites ≥ grade II (%)	68	15 (41)	16 (52)
HE ≥ grade II (%)	66	2 (5.4)	4 (14)
Total bilirubin (mg/dL) at admission	69	9 (8,15)	14 (9,20)
mDF at admission	69	45 (38,59)	47 (40,58)
Delay admission-randomization (days)	69	8 (7,12)	9 (7,12)
AST at randomization (IU/L)	66	110 (92,145)	103 (91,132)
ALT at randomization (IU/L)	67	45 (31,74)	44 (33,53)
Creatinine at randomization (mg/dL)	69	0.78 (0.65,0.94)	0.71 (0.61,0.86)
INR at randomization	68	1.66 (1.41,1.80)	1.60 (1.40,1.98)
Total bilirubin at randomization (mg/dL)	69	7.4 (5.1,10.8)	9.3 (5.8,17.6)
Percentage of bilirubin decrease admission-randomization	69	29 (21,36)	24 (17,33)
mDF at randomization	69	41 (34,51)	41 (35,53)
MELD at randomization	69	21 (19,23)	21 (19,24)
Lille score	67	0.18 (0.07-0.30)	0.18 (0.07-0.49)

Data are presented as mean ± standard deviation for normally distributed variables, median (interquartile range, IQR) for non-normally distributed variables, and number (percentage) for categorical variables.

Table 2. Sites of infection between Corticosteroids and placebo-treated groups

Site of infection	Corticosteroids	Placebo
Spontaneous bacterial peritonitis	2	2
Pulmonary	6	2
Urinary tract infection	1	1
Bacteriema	3	3
Other infection	5	2

Table 3. Factors associated with 90-day mortality

Variable	Univariate analysis			Multivariable analysis*		
	HR	95%CI	p-value	HR	95%CI	p-value
Corticosteroids	1.19	0.39-3.63	0.76	1.64	0.45-6.01	0.45
Age (years)	1.08	1.01-1.15	0.027			
Gender, Male	0.63	0.20-1.92	0.41			
Percentage of bilirubin improvement	0.99	0.95-1.04	0.67			
MELD	1.08	0.96-1.21	0.19			
Infection	2.46	0.72-8.41	0.15			
Lille score (per 0.1)†	1.33	1.06-1.67	0.015	1.37	1.06-1.76	0.021

HR: Hazard ratio; CI: confidence interval. MELD, model for end-stage liver disease

*In addition to the treatment arm, covariates with a p-value < 0.10 in univariate analysis were included in the multivariable model.

†Composite prognostic scores and their individual components were not included together in regression models to avoid collinearity.

Figure legends

Figure 1. Patient disposition AH: Alcohol-related hepatitis, mDF: Maddrey discriminant function, mITT: modified intention-to-treat

Figure 2. Kaplan-Meier estimates of survival

Kaplan-Meier survival curves for patients with severe alcohol-related hepatitis and early spontaneous bilirubin improvement randomized to corticosteroids (n=38) or placebo (n=31). Hazard ratios (HR) with 95% confidence intervals and P values from Cox proportional hazards regression are shown at 30 days and 90 days. Numbers at risk (and number of events) are displayed below the x-axis. The analysis includes all patients in the modified intention-to-treat population (ineligible randomized patients excluded).

Figure 3. Cumulative incidence of infection at 90 days

Cumulative incidence curves for infection with death as a competing risk in patients randomized to corticosteroids (n=38) or placebo (n=31). The subdistribution hazard ratio (SHR) with 95% confidence interval and P value from Fine-Gray competing risks model is shown. Numbers at risk (and number of events) are displayed below the x-axis. SHR, subdistribution hazard ratio.

Figure 1. Patient disposition

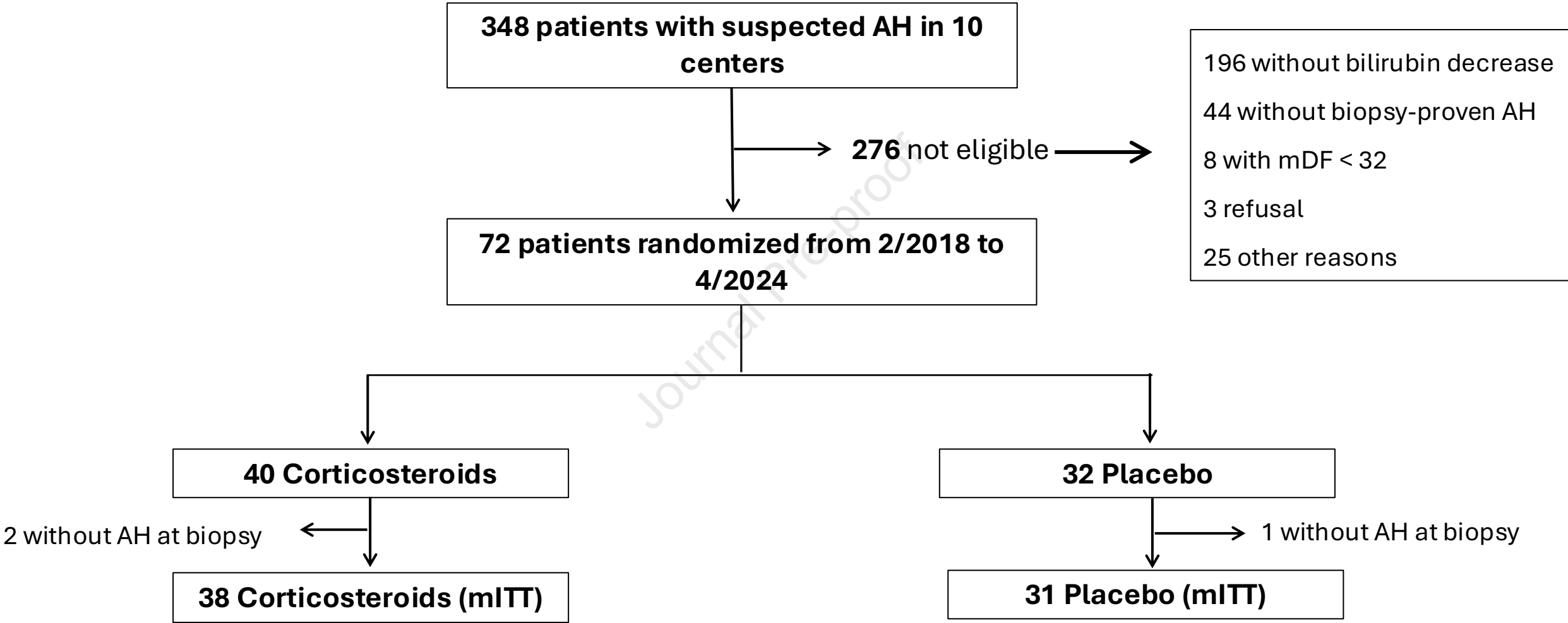
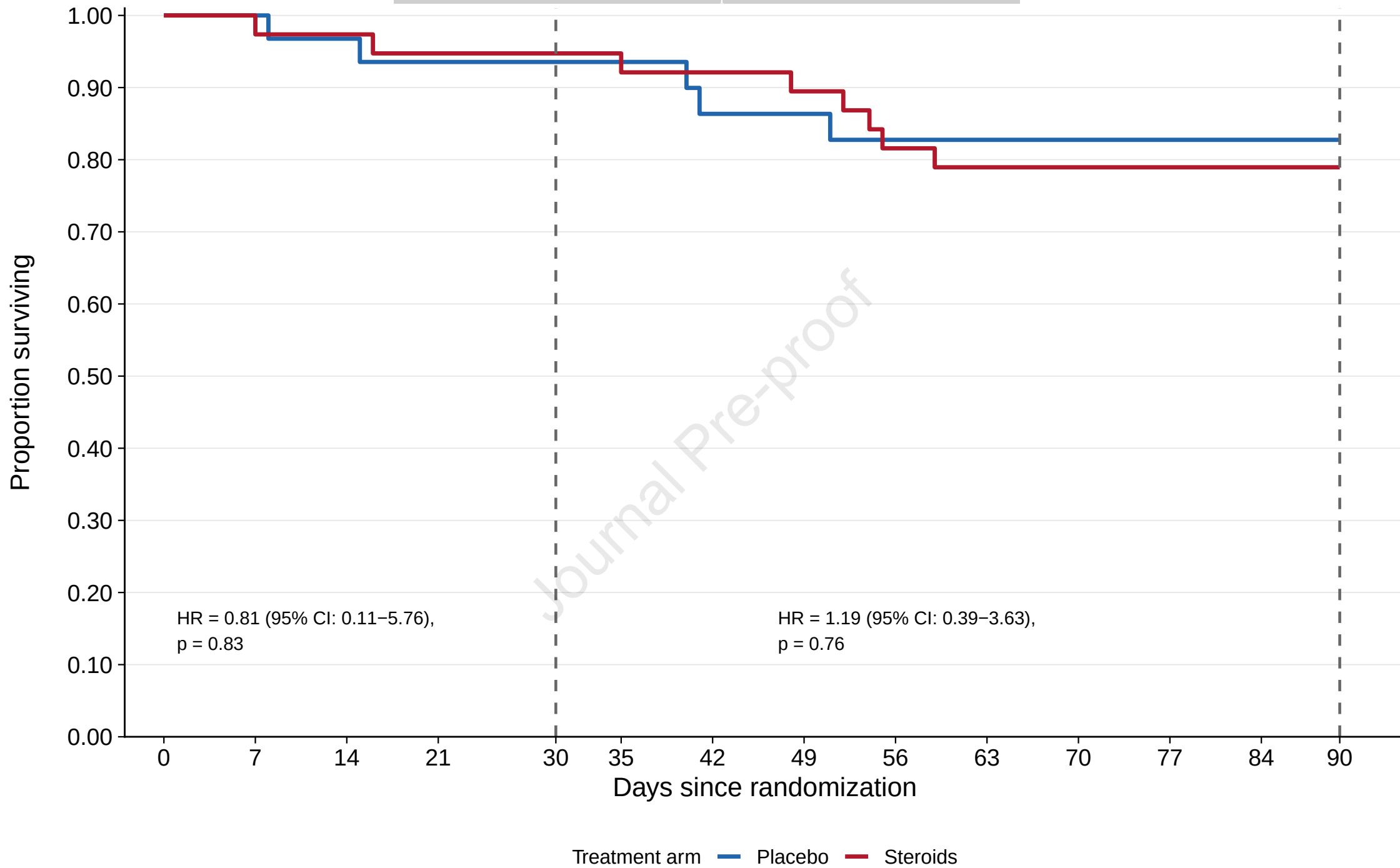


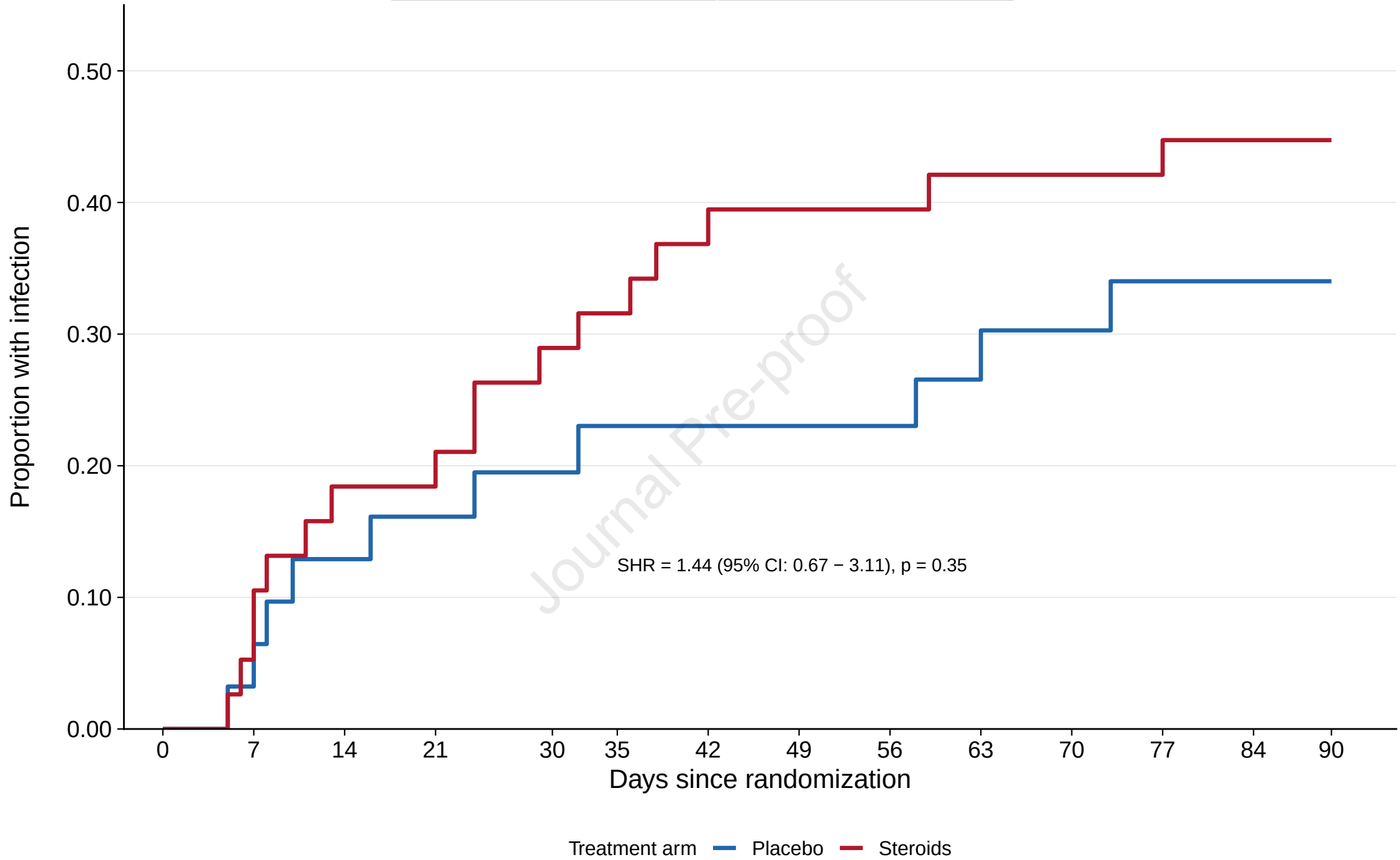
Figure 2. Kaplan–Meier estimates of survival



Placebo	31 (0)	31 (0)	30 (1)	28 (1)	26 (0)	26 (0)	24 (2)	24 (0)	23 (1)	22 (0)	22 (0)	22 (0)	21 (0)	17 (0)
Steroids	38 (0)	38 (1)	37 (0)	36 (1)	36 (0)	36 (1)	35 (0)	34 (1)	31 (3)	30 (1)	30 (0)	30 (0)	30 (0)	24 (0)

Figure 3. Cumulative incidence of infection at 90 days

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Placebo	31 (0)	30 (2)	26 (2)	23 (1)	21 (1)	20 (1)	20 (0)	20 (0)	19 (0)	17 (2)	16 (0)	15 (1)	14 (0)	11 (0)
Steroids	38 (0)	36 (4)	30 (3)	29 (1)	25 (3)	24 (1)	22 (3)	20 (0)	20 (0)	19 (1)	19 (0)	19 (1)	18 (0)	14 (0)

Highlights:

- Severe AH patients with early spontaneous bilirubin improvement have a relatively favorable prognosis (~80% 90-day survival)
- In this population, corticosteroid therapy was not associated with improved 90-day or 30-day survival
- The trial was underpowered due to slow recruitment and lower-than-anticipated mortality in the placebo arm
- Corticosteroids were associated with a numerically higher infection rate (47% vs 34%), though not significant
- A 5–10 day observation period may help to identify severe AH patients who do not require corticosteroid therapy