Research Square

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Substance use navigation is associated with improved 90-day survival after hospitalization for alcohol-associated hepatitis

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Abstract

Background: Alcohol abstinence is the most effective intervention to improve survival in alcohol-associated hepatitis (AH). In 2020 we implemented an inpatient Substance Use Navigation (SUN) program to link hospitalized AH patients to community-based addiction care. The study aim was to evaluate the effect of SUN on post-hospitalization outcomes in AH.

Methods: This retrospective cohort study included patients with no prior hospitalization for AH in the prior 6 months who survived an index AH admission from February 2020 to April 2024. Patients were stratified into SUN consulted (SUN^+), and SUN non-consulted (SUN^-) groups. Kaplan-Meier analysis and Cox models were used to assess relationships between SUN utilization, 90-day post-hospital survival, and 30-day readmission rates. Logistic regression was used to identify clinical factors associated with SUN utilization.

Results: Of 284 patients surviving AH hospitalization, 123 (43.3%) underwent SUN consultation. Logistic regression demonstrated that age, ascites, and ICU admission were associated with reduced SUN consultation, while increased BMI and white race were associated with increased SUN consultation. Age, MELD 3.0, and national area deprivation index (ADI), were associated with reduced 90-day survival, while SUN consultation was associated with improved 90-day survival in multivariate Cox models. Adjusted mean survival was longer in SUN^+ patients (86.6 vs. 68.9[JV1] days, $p < 0.001$). Thirty-day readmission was not affected by SUN consultation.

Conclusion: SUN consultation was associated with improved 90-day post-hospital survival in patients admitted with AH, independent of liver disease severity. These findings support early SUN utilization in this population.

[JV1]Replaced this with the value that was in the results section.

Introduction

Alcohol-associated liver disease encompasses a spectrum of pathology ranging from steatosis to cirrhosis in the setting of chronic alcohol use. It can acutely manifest as alcohol associated hepatitis (AH) - a severe form of acute on chronic liver failure that occurs in advanced stages of the disease. AH carries a high short-term mortality rate of up to 20 –50% at 90 days[1]. Even prior to the COVID pandemic, hospitalizations for AH accounted for almost 1% of all admissions in the United States[2]. With increased rates of alcohol use disorder in the last decade, hospitalizations for AH have risen over 2-fold in the last 5 years[3,4]. Pharmacotherapy for AH remains limited to corticosteroids, which provide only modest decrease in 28-day mortality with no impact on long-term survival[5]. Given the rising incidence and severity of AH, coupled with lack of effective pharmacotherapy, there is an urgent, unmet need for novel therapeutic approaches to the disease.

Previous studies have focused on the role of hospitalization as a controlled environment for medical stabilization, infection management, and nutritional support in AH[6-8]. However, hospital admission also provides a critical opportunity to address alcohol use disorder (AUD) in this population, as sustained abstinence from alcohol remains the cornerstone of AH management[9]. Rates of alcohol relapse and hospital readmission for alcohol-associated hepatitis remain high[10,11]. This is likely due to a complex interplay of factors including the neuropsychological effects of alcohol, environmental and social stressors, as well as gaps in healthcare delivery[9,12]Professional society guidelines recommend integrated substance use disorder care in the management of all patients with AUD, including those hospitalized with AH[13,14].Despite this, fewer than 20% of AH patients receive any form of addiction treatment during hospitalization, with less than 1% receiving pharmacological therapy[13]. Barriers to receiving appropriate treatment of AUD include provider discomfort with addiction pharmacotherapy and limited institutional infrastructure, as addiction medicine services are often limited to liver transplant programs[6,9]. Addressing this gap in inpatient addiction care represents a critical area for quality improvement in AH.

In February 2020, our institution implemented an inpatient Substance Use Navigation (SUN) program aimed at improving long-term abstinence from alcohol through structured, multidisciplinary interventions. SUN represents a promising approach to increasing in-hospital initiation of evidence-based treatment and reducing 30-day unplanned readmissions among patients with substance use disorder (SUD). Substance use navigators are certified alcohol and drug counselors who provide motivational interviewing, brief intervention, medication assisted therapy (MAT) initiation referrals, and care coordination to community-based programs during hospitalization and post-discharge. While integrated care models have demonstrated improved outcomes for alcohol-associated liver disease, most existing studies focus on outpatient settings[9,13].This study evaluates the impact of an inpatient SUN program on clinical outcomes in patients hospitalized with acute AH.

Methods

Study Design and Population

This was a retrospective cohort study of patients admitted with AH at University of California Davis Medical Center between February 2020 and April 2024. The electronic medical record was reviewed to identify patients aged 18-80 years for inclusion if they met diagnostic criteria for probable or definite AH as defined by National Institute on Alcohol Abuse and Alcoholism (NIAAA)[14] which include: (1) onset of jaundice within the previous 8 weeks, (2) ongoing alcohol consumption, (3) serum bilirubin >3 mg/dL, and (4) AST to ALT ratio >1.5 with both enzymes <400 IU/L or (5) liver biopsy confirmed diagnosis of AH. Exclusion criteria included abstinence from alcohol for more than 6 weeks prior to admission, histologic or serologic evidence of another liver disease other than AH, and prior solid organ or hematopoietic transplant. To capture new episodes of AH, we also excluded patients with prior hospitalization with AH in the prior 6 months, and patients who died during index hospitalization were not included. All patients

were reviewed by two transplant hepatologists (VR and LA) each with over 15 years of experience in the care of patients with AH. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul. This study was approved by the institutional review board (IRB) at the University of California Davis Medical Center (Project No. 203914-1) with an approved waiver for informed consent due to the retrospective nature of the investigation.

Clinical and Demographic Evaluation

Age, biological sex, ethnicity, and primary language were recorded, and patient survival up to 90 days after hospitalization were determined from clinical chart review and the Social Security Death Index. National Area Deprivation Index (ADI) scores were obtained using the University of Wisconsin Neighborhood Atlas based on patient addresses[15], and insurance status was recorded; unhoused patients (N=13) were assigned an ADI score of 99 (highest risk). Laboratory data were obtained on the first day of hospital admission and included serum albumin, creatinine, sodium, international normalized ratio (INR), platelet counts, and white blood cell count (WBC) with differential. MELD and MELD 3.0 scores were calculated as previously described[16,17]. Patients were then stratified into a SUN consulted cohort (SUN^{+}) and SUN non-consulted (SUN-) cohorts. The primary outcomes were 1) rate of SUN consult utilization, 2) 90-day post-hospital survival and 3) 30-day readmission rate. Ninety-day post-discharge survival was selected as a primary outcome as it has been shown as a preferred measure that captures high early mortality risk[14]. Thirty-day all cause readmission rate was chosen as an outcome measure as it serves as a surrogate for early clinical instability and the effectiveness of inpatient management and discharge planning[18].Secondary aims included discharge medication-assisted therapy (MAT) prescription rates for alcohol use disorder and predictors of SUN consultation.

Statistical analysis

Statistical analysis was performed with Stata version 16 (StataCorp, College Station, TX) and GraphPad Prism Version 9 (GraphPad, San Diego, CA). Clinical and demographic variables were reported as medians with interquartile ranges (IQR, 25^{th} – 75^{th} quartiles), absolute frequencies, and percentages. For continuous variables, comparisons between groups were performed using nonparametric Mann-Whitney U or Kruskal-Wallis tests with post-hoc Dunn test for multiple comparisons. Fisher exact tests were used to compare categorical variables between groups. For the primary outcome of 90-day transplant-free survival, patients alive without transplant were right-censored at 90 days. Time to event data was assessed using Kaplan-Meier analysis, and survival curves were compared with log-rank tests. Prognostic factors for transplant-free survival were analyzed using Cox proportional hazards models. To assess predictors of SUN consultation, logistic regression models were performed. For both Cox analysis and logistic regression, covariates on univariate analysis with $p < 0.1$ were then included in multivariate models. A p-value <0.05 was considered statistically significant for all analyses.

Results

Baseline Characteristics

A patient inclusion flow diagram is shown in **Figure 1**. Three hundred and eighty patients were hospitalized with severe AH during the study period; 74 (19.5%) were excluded due to recent hospitalizations for AH within the prior 6 months, and 22 (5.8%) died during hospitalization. Two hundred and eighty-four patients were included in the final analysis, and baseline characteristics are summarized in **Table 1**.Among all participants, 39.8% were female, 48.2% were white race, and 91.5% spoke English as a primary language. The median age was 44 years (IQR 36 – 54 years), and median BMI was 28.0 kg/m^2. Median MELD was 22 (IQR 18-27), median MELD 3.0 was 26 (IQR 21 – 32), and 166 patients (58.4%) had severe AH as defined by MELD > 20. Median length of stay was 6 days (IQR 3 – 10 days), and 77 patients (27.1%) were admitted to intensive care units (ICU). One hundred and fifty-seven patients had ascites (55.2%), 81 patients had hepatic encephalopathy (28.5%), 75 had variceal bleeding (26.4%), and 77 (N=27.1%) developed acute kidney injury during hospitalization. Inpatient hepatology consultation was obtained on 187 patients (65.8%).

Utilization of Substance Use Navigation and Medication-Assisted Therapy

In the study cohort 123 patients (43.3%, SUN$^+$) underwent SUN consultation, while 161 did not (56.7%, SUN$^-$). The primary reasons for no SUN consultation included lack of consult order (N=93, 57.8%), patient discharge prior to completion of ordered consult (N=55, 34.2%), and documented patient refusal (N=13, 8.0%) (**Fig. 2A)**. Interventions provided included motivational interviewing (N=105, 85.4%), referral to outpatient treatment (N=56, 45.5%) and providing literature on AUD community-based meetings (N=29, 23.4%, **Fig. 2B**).

Patients with SUN consultation were younger, [39 (IQR 33 – 51) years vs. 46 (39 – 55) years, p=0.001], but there were no significant differences in race, gender, primary language, ADI, BMI, health insurance status, or rates of hepatology consultation between groups. SUN$^+$ patients had lower rates of ICU admission [N=17 (13.8%) vs. 60 (37.3%), p<0.001] and shorter hospital length of stay [5 (3 – 9) days vs. 7 (4 – 11) days, p=0.014] than SUN$^-$ patients (**Table 1**). MELD [23 (19 – 29) vs 22 (16 – 25), p=0.002] and MELD 3.0 [28 (23 – 34) vs 25 (18 – 30), p=0.001] were higher in the SUN- cohort (**Table 1**), but rates of severe AH (defined as MELD > 20) did not differ between groups [67 (54.5%) in SUN+ vs 99 (61.5%) in SUN-, p=0.105], Patients without SUN consultation had more ascites, AKI, hepatic encephalopathy, and infections compared to SUN+ patients.

We utilized logistic regression to assess factors associated with no SUN consultation (**Table 2**). On univariate analysis, older age, increased hospital length of stay, any ICU disposition, higher MELD 3.0 and presence of ascites, AKI, hepatic encephalopathy, or infection were associated with lower likelihood of SUN consultation, while white race and higher BMI were associated with increased SUN consultation. On multivariate analysis, however, only age, ICU disposition and ascites were associated with lower rate of SUN consultation, while white race and BMI were associated with increased SUN utilization.

We then evaluated medication-assisted therapy (MAT) for AUD in our patient cohort. Only 58 patients (20.4%) received MAT prescription at hospital discharge (**Fig. 2C**). Among AUD medications, naltrexone was most commonly prescribed (N=29, 50.0% of prescriptions), followed by acamprosate (N=25, 43.1%), baclofen (N=17, 29.3%), and disulfiram (N=5, 8.6%). Recipients of MAT prescriptions were more likely to be white (62.1% vs. 44.7%, *p*=0.013), speak English as the primary language (100.0% vs. 89.3%, *p*=0.003), and experience lower risk area deprivation [ADI 24 (IQR 10 – 43) vs 35 (21 – 49), *p*=0.004] compared to patients without MAT therapy (**Table 3**). Importantly, insurance status differed between groups, and the cohort receiving MAT had higher rates of no insurance and Medicaid insurance. There were no differences in rates of decompensating events including ascites, hepatic encephalopathy, AKI, and variceal bleeding, but MELD 3.0 was lower in AUD recipients. SUN consultation did not affect rates of MAT prescription, as 48.3% of MAT recipients and 42.0% of patients without MAT underwent SUN consultation (*p*=0.239).

SUN consultation improves 90-day post-hospitalization survival in AH despite no improvement with 30-day readmission rate

Patients were followed for up to 90 days after hospital discharge, and subjects still living without liver transplantation were censored at 90 days. Over the study period, there were 60 events (21.1% of patients) including 58 deaths and 2 liver transplants, and mean transplant-free survival was 76.6 (95% CI 73.3 – 79.8) days.

We utilized Cox proportional hazards regression to determine factors associated with increased mortality in the study population (**Table 4**). On univariate analysis, age, ADI, English as a primary language, hospital length of stay, MELD 3.0 ICU admission, ascites, hepatic encephalopathy, acute kidney injury, infection, and gastrointestinal bleeding were associated with increased 90-day mortality, while SUN consultation was associated with improved survival. On multivariate analysis, age, ADI, and MELD 3.0 were associated with reduced 90-day transplant-free survival, while SUN consultation was associated with reduced 90-day mortality compared to no consultation [adjusted HR 0.256 (95% CI 0.105 – 0.623), *p*=0.003]. MAT for AUD was not associated with improved 30-day rehospitalization or 90-day survival. Raw mortality rate was lower in the SUN^+ cohort (7.3% vs. 31.7%, *p*<0.001, **Fig. 3A)**. In both unadjusted and adjusted Kaplan-Meier analyses SUN consultation was associated with improved survival [adjusted 90-day transplant free survival 86.6 (95% CI 84.0 – 89.1) vs 68.9 (63.9 – 74.0) days, *p*<0.001, **Fig. 3B**].

There were no significant differences in 30-day all-cause hospital readmission rates across the two cohorts (Table 1). Readmission occurred in 14.6% of patients in the SUN consulted group and 17.4% in the SUN non-consulted group These findings suggest that while SUN consultation was associated with improved short-term survival, it did not appear to influence early readmission risk within 30 days of discharge.

Discussion

In this retrospective study, we assessed the role of an inpatient substance use navigation (SUN) program in patients hospitalized with AH. Two important findings were observed. First, SUN utilization and MAT prescription rates were low, as only 43.3% of patients underwent consultation and 20.4% received MAT. Second, although SUN consultation was not associated with 30-day readmission rates, we observed improved 90-day transplant free survival independent of traditional markers of liver disease severity. Furthermore, the survival benefit attributable to SUN consultation was independent of ICU admission.

Though sustained alcohol abstinence remains the cornerstone of long-term management of AH, access to evidence-based treatment for alcohol use disorder (AUD) remains limited. Previous studies have demonstrated that early participation in alcohol rehabilitation within 30 days of hospitalization for severe AH is associated with reduced alcohol relapse rates, 30-day readmission rates, and long-term mortality[19]. Furthermore, among survivors of an index AH hospitalization, behavioral therapy within 6 months of hospitalization was also found to improve long-term survival in AH[20]. However, participation in behavioral therapy after hospitalization for AH remains low, as only 16-20% of patients receive any form of AUD treatment within 6 months of hospitalization[20]. Together, these findings highlight an unmet need to bridge patients with AH from hospitalization to community-based care for AUD.

The use of substance use navigators is another novel approach to connect AH patients with outpatient AUD treatment[21-23]. Substance use navigators are trained in harm reduction, motivational interviewing, and alcohol and drug counseling; many navigators have experienced substance use disorders firsthand. Navigators collaborate with clinicians to encourage MAT, administer brief counseling interventions to patients, initiate referrals to outpatient addiction medicine care, and provide information for community-based SUD treatment groups. We recently demonstrated that among 781 patients hospitalized with either a primary or secondary diagnosis of an SUD, substance use navigation was associated with a 2.29-fold increased likelihood of MAT prescription and 64% reduction in 30-day readmission rates[24], highlighting the utility of SUN consultation for connecting hospitalized patients with SUD to post-hospital community-based treatment.

During the study period, 284 patients survived to discharge from an index episode of AH, but only 123 (43.3%) received SUN consultations, and the leading reason for no consultation was lack of clinical orders. Similarly, among the entire study cohort, only 58 (20.4%) received prescriptions for AUD pharmacotherapy, and these figures are in line with low rates of AUD treatment reported in both AH and outpatients with chronic liver disease.[25,26] The absence of clinical orders from primary services may be related to gaps in knowledge regarding behavioral and medication approaches to AUD specifically in AH, as prior studies have demonstrated that over 70% of hepatology providers have never prescribed AUD medications, with lack of comfort and concerns regarding side effects of therapy as the most commonly cited reasons for avoidance[27]. In addition, future studies are warranted to assess strategies to overcome barriers to SUN utilization, including the use of disease-specific care bundles and enhanced provider education.

In the current study, SUN consultation was independently associated with increased 90-day survival even after controlling for age, ADI, and MELD 3.0. This observation is consistent with prior studies demonstrating that alcohol abstinence is the primary determinant of long-term survival after an index hospitalization for AH, and the survival benefit of abstinence was similarly independent of MELD[10,11]. However, patients with more advanced disease, including those with severe AH and requiring ICU-level care, were significantly less likely to be evaluated by SUN. Several factors may have contributed to this finding such as the prioritization of acute medical stabilization, perceived futility of addiction counseling in critically ill patients, and structural limitations in high-acuity settings[28]. Additionally, the visual appearance of advanced disease, such as ascites, cachexia, or encephalopathy, may inadvertently contribute to provider bias and assumptions that these patients are too far along in their disease course to benefit from substance use intervention. In contrast to SUN consultation, ADI was associated with reduced 90-day post-hospital survival, and this may reflect socioeconomic barriers to both liver disease and AUD care.

Despite the observed survival benefit, 30-day readmission rates did not differ significantly across cohorts. This may be due to SUN's role in linking patients to outpatient rehabilitation services, while medical care of liver disease may more strongly influence short-term outcomes. Similarly, MAT for AUD did not improve 30-day rehospitalization or 90-day survival. As only prescriptions for MAT were measured in the current study, and previous studies have demonstrated that MAT is effective for preventing hepatic decompensation and improving survival in alcohol-related liver disease[29,30], this finding may reflect reduced adherence to pharmacotherapy for AUD. Future studies are needed to determine whether SUN consultation enhances long-term adherence to AUD medications and participation in outpatient addiction therapy.

We observed racial and language-based differences in rates of SUN consultation and MAT, as white race was associated with increased rates of SUN utilization and MAT prescription, while non-English speakers and those with increased socioeconomic deprivation (as measured by neighborhood ADI) were less likely to receive prescriptions for AUD medications at discharge. This finding is consistent with prior studies demonstrating ethnic and other socioeconomic disparities in psychotherapy, medication treatment for AUD, healthcare utilization, and overall survival in AH[31,32]. These observations highlight the need for systematic approaches to increase equitable access to AUD treatment in AH.

This study has several important strengths. It evaluates a real world, inpatient addiction intervention in a large and well-defined cohort of patients with AH. We explicitly identified patients without prior recent hospitalizations for AH, and we included only survivors of index hospitalization for AH, to minimize medical and psychosocial variables that could confound associations between SUN consultation and clinical outcomes. Finally, the study population was ethnically diverse, which allows for greater generalizability of study results to other clinical cohorts.

However, our study has several limitations. Due to its retrospective nature, it is inherently subject to potential confounding and selection bias. Though we adjusted for key markers of liver disease severity,

residual confounding may still be present from unmeasured factors such as patient motivation, social support, or undocumented informal counseling by other providers – all of which could influence both rates of SUN consultation and survival outcomes. Despite this, we found that only 8% of patients declined SUN consultation, suggesting that patients were mostly open to AUD treatment. Next, we relied on electronic medical record documentation to confirm SUN engagement, which may not capture nuances in the quality or depth of addiction counseling provided. Finally, we did not have access to rates of abstinence, adherence to medications for AUD, or participation in community-based addiction therapy after hospital discharge, and therefore we could not assess the effect of SUN consultation or MAT prescription on alcohol abstinence after hospitalization.

In conclusion, our findings demonstrate that inpatient SUN consultation is associated with improved short-term survival, independent of liver disease severity and highlights an opportunity for the potential of integrated addiction care to influence outcomes in the AH population. These results also highlight the importance of addressing AUD as part of routine inpatient care for acute AH. The SUN program represents a scalable model that addresses a critical gap in the inpatient care of patients with alcohol-associated liver disease. As institutions seek to improve outcomes in this high-risk population, implementing multidisciplinary approaches to AUD treatment consistently regardless of disease severity should be a key priority. Future prospective studies with longitudinal follow-up are warranted to confirm the durability of these findings and to optimize models for inpatient addiction care for AH across diverse clinical settings.

Abbreviations

ADI, area of deprivation index AH, alcohol-associated hepatitis; AKI, acute kidney injury; AUD, alcohol use disorder; ICU, intensive care unit; LOS, length of stay; MAT, medication assisted therapy; MELD, model for end-stage liver disease; SUD, substance use disorder; SUN, substance use navigation.

Declarations

Author contributions: VR: design, conception and supervision of the whole study, data collection, analysis and interpretation, writing initial draft and critical review of final manuscript; JBV: data collection, interpretation, writing initial draft and critical review of final manuscript; LI: data collection, interpretation, revision of initial draft and critical review of final manuscript; RLP: data collection, interpretation, revision of initial draft and critical review of final manuscript; JH: data collection, critical review of final manuscript; AM: assistance with study design, data interpretation, and critical review of final manuscript; GM: data collection, analysis and interpretation, critical review of final manuscript; DC: data collection, analysis and interpretation, critical review of final manuscript; CR: data interpretation, critical review of final manuscript; LA: data collection, data interpretation, critical review of manuscript

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Tables

Tables 1 to 4 are available in the supplementary files section

Figures

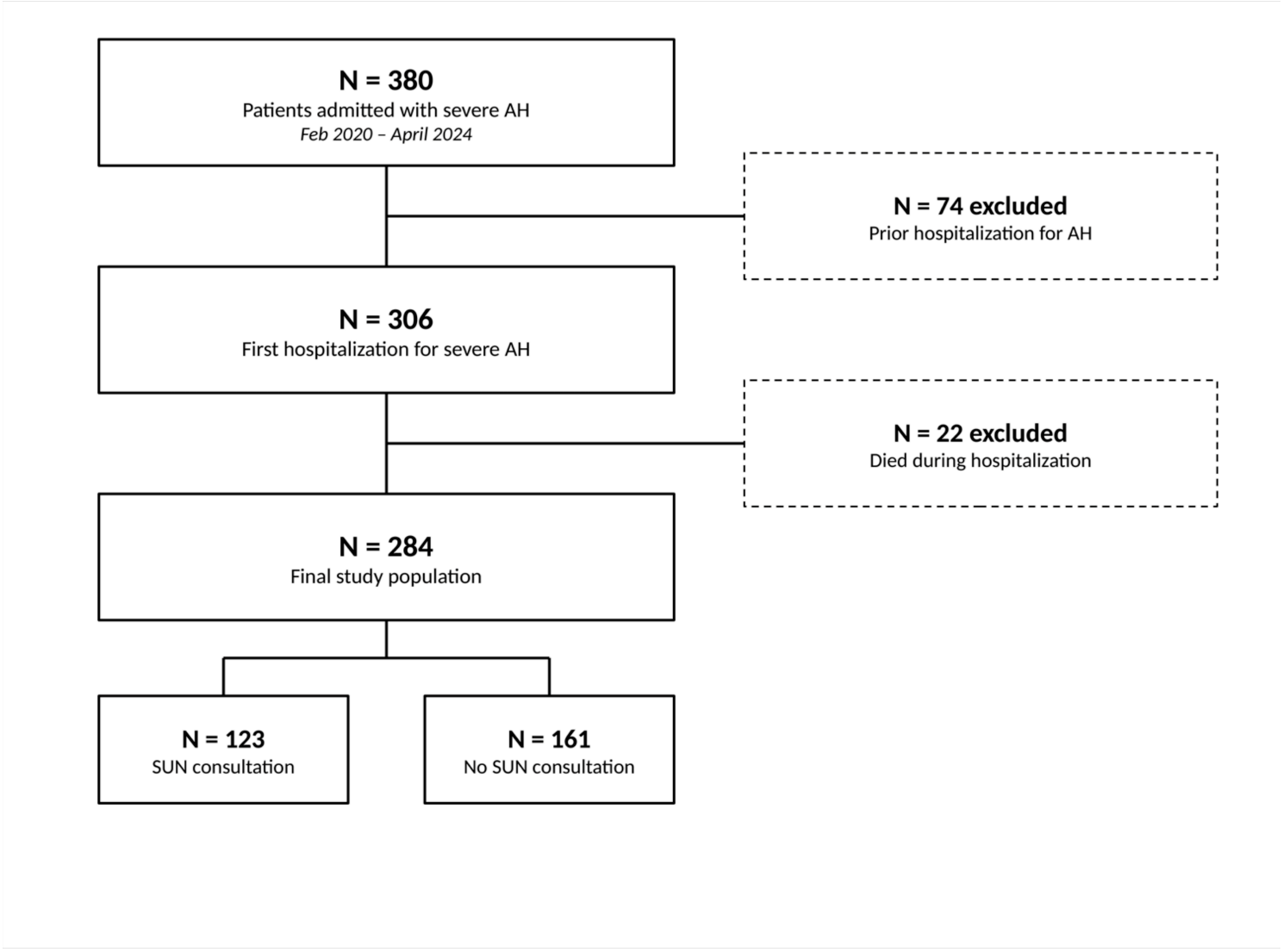


Figure 1

Patient enrollment flow diagram. A total of 380 patients admitted for severe acute alcohol-associated hepatitis (AH) between February 2020 and April 2024 were identified. Of these, 74 were excluded due to a prior hospitalization for AH, yielding 306 patients with an index hospitalization for severe AH. An additional 22 patients who died during the index hospitalization were subsequently excluded, resulting in a final study population of 284 patients. Patients were stratified by whether they received substance use navigator (SUN) during hospitalization: 123 patients received SUN consultation and 161 did not.

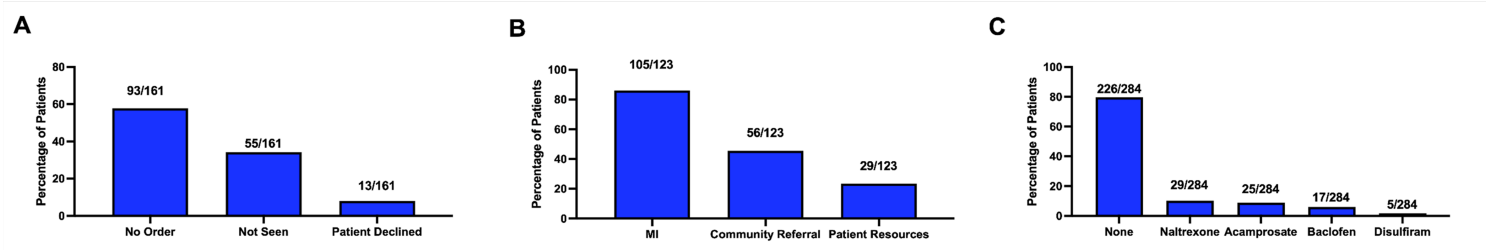


Figure 2

Substance use navigation (SUN) utilization patterns. **(A)** Reasons for lack of SUN consultation during the study period. **(B)** Alcohol use disorder (AUD) treatment modalities delivered to patients by SUN counselors. **(C)**Medication prescriptions for AUD at hospital discharge. AUD, alcohol use disorder, MI, motivational interviewing, SUN, substance use navigation.

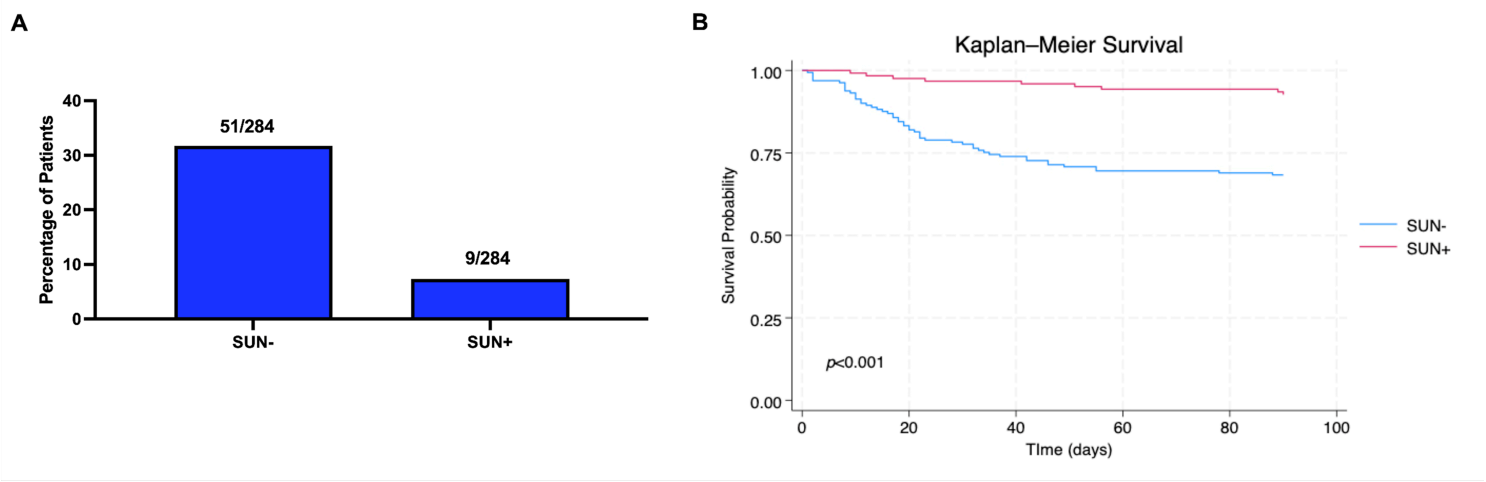


Figure 3

Association between SUN consultation and 90-day mortality in (**A**) raw proportions and (**B**) adjusted Kaplan-Meier analysis.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TablesSUNsubsetpaper1.docx