

ACCEPTED MANUSCRIPT

1 **Alcohol Rehabilitation Within 30 Days of Hospital Discharge is Associated With Reduced**
2 **Readmission, Relapse, and Death in Patients with Alcoholic Hepatitis**

3

4 Short title: Alcohol rehabilitation in alcoholic hepatitis

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9

10 **Abbreviations List:**

11 ABIC Age, serum Bilirubin, international normalized ratio, and serum Creatinine

12 AH Alcoholic hepatitis

13 BMI Body mass index

14 CTP Child-Turcotte-Pugh scores

15 mDF Maddrey discriminant

16 MELD Model for End-Stage Liver Disease

17 PT Prothrombin time

18 INR International normalized ratio

19

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2 Thoetchai (Bee) Peeraphatdit developed the concept, acquired and analyzed the data, drafting the
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4 concept and critically revised the paper; Brian Davis and Vivek Desai acquired and analyzed the data;
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6

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8 The authors who have taken part in this study declared that they do not have any conflict of interest with
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10

1 **Background & Aims:** Patients admitted to the hospital for alcoholic hepatitis (AH) are at increased risk of
2 readmission and death. We aimed to identify factors associated with readmission, alcohol relapse, and
3 mortality.

4 **Methods:** We performed a retrospective analysis of consecutive patients admitted with AH to a tertiary
5 care hospital from 1999 through 2016 (test cohort, n=135). We validated our findings in a prospective
6 analysis of patients in a multi-center AH research consortium from 2013 through 2017 (validation cohort,
7 n=159). Alcohol relapse was defined as any amount of alcohol consumption within 30 days after hospital
8 discharge. Early alcohol rehabilitation was defined as residential or outpatient addiction treatment or
9 mutual support group participation within 30 days after hospital discharge.

10 **Results:** Thirty-day readmission rates were 30% in both cohorts. Alcohol relapse rates were 37% in the
11 test and 34% in the validation cohort. Following hospital discharge, 27 patients (20%) in the test cohort
12 and 19 patients (16%) in the validation cohort attended early alcohol rehabilitation. There were 53 deaths
13 (39%) in a median follow-up time of 2.8 years and 42 deaths (26%) in a median follow-up time of 1.3
14 years, respectively. In the test cohort, early alcohol rehabilitation reduced odds for 30-day readmission
15 (adjusted odds ratios [AOR] 0.16; 95% CI, 0.04–0.65; P=.01), 30-day alcohol relapse (AOR, 0.11; 95%
16 CI, 0.02–0.53; P<.001), and death (adjusted hazard ratio [AHR], 0.20; 95% CI, 0.05–0.56; P=.001). In the
17 validation cohort early alcohol rehabilitation reduced odds for 30-day readmission (AOR, 0.30; 95% CI,
18 0.09–0.98; P=.04), 30-day alcohol relapse (AOR 0.09; 95% CI, 0.01–0.73; P=.02), and death (AHR, 0.20;
19 95% CI, 0.01–0.94; P=.04). A model combining alcohol rehabilitation and bilirubin identified patients with
20 readmission to the hospital within 30 days with an area under the receiver operating characteristic curve
21 of 0.73.

22 **Conclusions:** In an analysis from two cohorts of patients admitted with AH, early alcohol rehabilitation
23 can reduce risk of hospital readmission, alcohol relapse, and death and should be considered as a quality
24 indicator in AH hospitalization treatment.

25 **Keywords:** chemical dependency; addiction treatment; alcohol use disorder; alcohol abstinence

26

1 Introduction

2 Alcoholic hepatitis or alcohol-associated hepatitis (AH) is the most severe form of alcohol related liver
3 disease (ALD) and accounts for 0.71% of all admissions in the United States with in-hospital mortality rate
4 up to 46%.^{1,2} Patients surviving an admission for AH are at increased risk of readmission and subsequent
5 death. Previous studies have mainly evaluated short-term mortality outcomes,^{3,4} while other clinically
6 important outcomes i.e. alcohol relapse and hospital readmission after surviving an index AH admission
7 have not been well studied.

8 In patients surviving an AH admission, preventing alcohol relapse is crucial because long-term survival is
9 dependent on abstinence rather than severity of liver disease.⁵ Medical therapy with corticosteroids
10 improve short-term survival and no pharmacologic intervention has been shown to improve long-term
11 survival.⁴ Thus, it is important to prevent alcohol relapse after hospital discharge to ensure long-term
12 alcohol abstinence. Previous studies reported alcohol relapse rates in this population as high as 25% at
13 1-year⁵ and 60% at 5-years follow up.⁶ Multidisciplinary teams including addiction specialists are
14 recommended in treating patients with ALD.² However, this integrated approach is prevalent only in liver
15 transplant settings.⁷ A gap in knowledge is whether participation in alcohol rehabilitation programs after
16 hospital discharge can improve clinical outcomes in patients with AH.

17 In addition to early alcohol relapse, early hospital readmission is another important clinical outcome of AH
18 that has not been well studied. Hospital readmissions are associated with increased costs to the
19 healthcare system, patient mortality, and may be preventable.⁸ Therefore, 30-day readmission rate has
20 become a key quality indicator used by Center for Medicare and Medicaid Services (CMS) to assess
21 reimbursement penalties.⁹ For these reasons, it is pertinent to evaluate the rate of 30-day hospital
22 readmission in patients with AH.

23 The aims of the study were to determine the rates and predictors of 30-day readmission, 30-day alcohol
24 relapse, and mortality after surviving an index AH admission.

25

1 **Patients and Methods**

2 *Patient cohorts*

3 The test cohort (N=135) was derived retrospectively from consecutive patients admitted with AH at Mayo
4 Clinic (Rochester, MN) between 1999 and 2016. A validation cohort (n=159) was derived prospectively
5 from the ongoing NIAAA Translational Research and Evolving Alcoholic Hepatitis Treatment (TREAT)
6 consortium 001 study including patients admitted with AH at three tertiary care hospitals: Mayo Clinic
7 (Rochester, MN), Indiana University (Indianapolis, IN), and Virginia Commonwealth University (Richmond,
8 VA), between 2013 and 2017. The consortium design has been reported previously.^{10, 11} Overlapping
9 patients were removed from the test cohort (n=19). Exclusion criteria include 1) death during index
10 admission (n=15 and n=5 in test and validation cohort) and 2) Patients who died or were lost to follow
11 within 1 month after hospital discharge (n=29 and n=50 in test and validation cohort) and 3) Patients who
12 had previously undergone liver transplantation (n=3 in test cohort). The study was approved by the
13 institutional review boards (IRB) for all study sites. Some patients included in the validation cohort have
14 been included in other papers published previously by the TREAT consortium.¹⁰⁻¹⁴

15 *Clinical criteria for alcoholic hepatitis diagnosis*

16 As per NIAAA clinical criteria,¹⁵ the AH diagnosis was based on the average daily ethanol consumption of
17 more than 40 g/day for women and more than 60 g/day for men for a minimum of 6 months and within the
18 6 weeks before study enrollment; and on clinical evaluation and appropriate laboratory testing as defined
19 by a total bilirubin concentration greater than 3 mg/dL and an aspartate aminotransferase (AST)
20 concentration greater than 50 U/L, and AST to alanine aminotransferase (ALT) ratio of > 1.5. When the
21 diagnosis of AH remained in question, a liver biopsy was obtained for confirmation of AH. Patients with
22 suspected or proven cirrhosis were eligible for enrollment if they met inclusion criteria for AH. Individuals
23 with positive hepatitis B or hepatitis C virus markers were eligible for enrollment to include the full
24 spectrum of AH patients seen in clinical practice. However, cases with current or previous diagnosis of
25 autoimmune hepatitis, drug induced liver disease, hemochromatosis, or Wilson disease were excluded.

26 *Data collection at the time of admission*

1 Baseline data were collected on (1) demographic factors, body mass index (BMI) and average number of
2 alcohol drinks per day (1 standard drink equals 12-14 grams of pure alcohol) (2) hepatic decompensation
3 (ascites, variceal bleeding, hepatic encephalopathy); (3) laboratory values (4) AH severity scores:
4 Maddrey discriminant (mDF); Model for End-Stage Liver Disease (MELD); Age, serum bilirubin,
5 international normalized ratio (INR), and serum Creatinine (ABIC); and Child-Turcotte-Pugh (CTP)
6 scores^{16, 17} and (5) the use of alcohol relapse prevention medications during admission.

7 *Follow up*

8 In test cohort, subjects were followed until death or last follow up date or August 5, 2017. Alcohol relapse
9 was based on patient's report and/or detection of ethanol or its metabolites in urine or blood. In the
10 validation cohort, subjects were followed for 1 year after enrollment. Follow up included telephone call at
11 1 month, clinic visit at 6 months, and clinic visit at 1 year, in addition to regular clinical follow up. At each
12 follow up visit, trained interviewers asked subjects about attendance to alcohol rehabilitation, and hospital
13 readmission. The latter was confirmed by review of the medical records. At each follow up visit, subjects
14 self-reported alcohol consumption in the past 30 days using a validated timeline followback
15 questionnaire.¹⁸ Alcohol biomarkers (i.e. blood ethanol level or urine ethyl glucuronide) were not routinely
16 collected and were collected at the discretion of the medical providers.

17 *Outcomes of interest*

18 The 30-day hospital readmission was defined as any hospital admission within 30 days after discharge.
19 Alcohol relapse was defined as any alcohol consumption within 30 days after hospital discharge. Early
20 alcohol rehabilitation was defined as attending either residential or outpatient addiction treatment or
21 mutual support group (i.e. alcoholics anonymous) within 30 days after hospital discharge. Mortality status
22 was collected at the time of last follow up or August 5, 2017 for test cohort, and at last follow up or at one
23 year for the validation cohort.

24 *Statistical analysis*

1 The rates of 30-day hospital readmission, 30-day alcohol relapse, and death at last follow up were
2 evaluated. Multivariable Logistic regression analysis was performed to determine independent predictors
3 for 30-day hospital readmission and 30-day alcohol relapse. The prognostic model for 30-day hospital
4 readmission (AH readmission score) was developed using independent predictors from the test cohort
5 and validated in the validation cohort. The performance of the AH readmission score was evaluated using
6 the area under the receiver operating characteristics (AUC). Multivariable Cox regression analysis was
7 performed to determine independent predictors of mortality. Landmark analysis was performed, i.e. all
8 patients were alive at 30 days after hospital discharge, thus limiting the immortal time bias associated
9 with alcohol rehabilitation attendance. Variables with $P < .05$ in the univariate analysis were included in the
10 multivariable model to identify independent predictors for each outcome. All statistical analyses were
11 performed using JMP statistical software, version 9.0 (SAS Institute Inc, Cary, NC). All comparisons were
12 2-sided. $P < 0.05$ was considered statistically significant.

13

1 Results

2 Baseline characteristics

3 After excluding patients who were lost to follow up, there were 135 and 159 patients in the test and
4 validation cohorts respectively. Baseline clinical characteristics of both cohorts are shown in Table 1. In
5 the test cohort, mean age was 48.0 ± 10.2 years and mean MELD score was 20.5 ± 7.2 . In the validation
6 cohort, mean age was 50.0 ± 11.0 years old and mean MELD score was 21.8 ± 7.2 . Alcohol relapse
7 prevention medications (all were gabapentin) were prescribed to 10(7.4%), and 7(4.4%) patients in test
8 and validation cohorts respectively. Of 10 patients who received gabapentin in test cohort, five were for
9 alcohol use disorder and the others were for combination of alcohol use disorder and neuropathic pain.

10 Alcohol rehabilitation within 30 days after hospital discharge

11 In the test cohort, 96 out of 135(71.1%) patients were referred for evaluation by alcohol addiction
12 specialists (either board certified addiction psychiatrists or licensed alcohol and drug counselor) during
13 index admission, and complete evaluation was performed in 87 out of 135(64.4%) patients. The main
14 reason for incomplete evaluation was patient's refusal. This information was not available in the validation
15 cohort.

16 Alcohol rehabilitation data was available in all patients in the test cohort and in 74.8% (119 out of 159
17 patients) in the validation cohort. The analyses evaluating the effect of alcohol rehabilitation were
18 performed using only cases with available data. There were 27(20.0%) and 19(16.0%) patients attended
19 alcohol rehabilitation in test and validation cohort, respectively (Table 1). The types of alcohol
20 rehabilitation were residential rehabilitation ($n=12$, $n=11$), outpatient rehabilitation ($n=12$, $n=2$), and mutual
21 support group, i.e. alcoholics anonymous ($n=3$, $n=6$) in test and validation cohort respectively.

22 Next, we evaluate predictors of alcohol rehabilitation attendance. Patients who attended alcohol
23 rehabilitation were more likely to be evaluated by alcohol addiction specialists and have college degrees
24 (Supplemental Table 1). Interestingly, the liver severity scores were not different between the two groups.
25 For test cohort, evaluation by alcohol addiction specialists was a predictor of attending alcohol
26 rehabilitation (OR 2.91 [95%CI 1.02-8.27], $P=0.03$) in univariate analysis (Supplemental Table 2) but not

1 in multivariable analysis (Supplemental Table 3). For validation cohort, having college degree or above
2 (AOR 4.62 [95%CI 1.19-17.9], $P=0.03$) was an independent predictor of attending alcohol rehabilitation in
3 multivariable analysis (Supplemental Table 3).

4 **30-day readmission after hospital discharge**

5 The 30-day readmission rate was 30.4% ($n=41$) and 30.8% ($n=49$) in test and validation cohorts,
6 respectively (Figure 1). The 30-day readmission rate was lower in those who attended early alcohol
7 rehabilitation compared to those who did not attend alcohol rehabilitation in both test (11.0% vs. 35.2%,
8 $P=0.02$) and validation cohorts (21.1% vs. 45.0%, $P=0.07$) (Figure 1).

9 In test cohort, patients readmitted within 30 days were less likely to attend alcohol rehabilitation (7.3% vs.
10 25.5%, $P=0.02$) and were more likely to experience alcohol relapse within 1 month after hospital
11 discharge (56.1% vs 28.7%, $P=0.003$) (Table 1). Patients readmitted within 30 days had higher rates of
12 hepatic decompensation, higher total bilirubin level and higher CTP score compared to those without
13 readmission. Similarly, in validation cohort, patients readmitted within 30 days were less likely to attend
14 alcohol rehabilitation (8.2% vs. 21.4%, $P=0.04$) and were more likely to experience alcohol relapse
15 (57.5% vs 22.3%, $P=0.003$). Additionally, patients with readmission were more likely to have higher
16 MELD and CTP scores compared to those without readmission.

17 In test cohort, causes of readmission included hepatic decompensation (39%), recurrent AH (19%),
18 infection (15%), other medical conditions (19%) and alcohol intoxication or withdrawal (8%). In validation
19 cohort, causes of readmission included hepatic decompensation (51%), other medical conditions (29%),
20 infection (12%), alcohol intoxication or withdrawal (6%) and recurrent AH (2%).

21 For test cohort, early alcohol rehabilitation was a protective factor (AOR 0.16 [95%CI 0.04-0.65], $P=0.01$)
22 and increase in total bilirubin (AOR 1.04 [95%CI 1.09-0.96, $P=0.04$) was a risk factor for 30-day
23 readmission in multivariable analysis after adjusting for hepatic decompensation (Table 2). For validation
24 cohort, early alcohol rehabilitation was a protective factor against 30-day readmission (AOR 0.30 [95%CI
25 0.09-0.98], $P=0.04$) after adjusting for hepatic decompensation and total bilirubin level. Univariate
26 analysis is shown in Supplemental Table 4.

1 To generate an AH readmission score for 30-day readmission, independent predictors of readmission in
2 the test cohort were used. The AH readmission score = $-1.32 + 0.06 \times (\text{total bilirubin}) - 1.80 \times (\text{alcohol}$
3 $\text{rehabilitation attendance: yes}=1, \text{no}=0)$. The area under the receiver operating characteristic curve (AUC)
4 for the AH readmission score were 0.73 (95%CI 0.64-0.80) in test cohort and 0.64 (95%CI 0.54-0.72) in
5 validation cohort (Figure 2).

6 **Alcohol relapse within 30 days after hospital discharge**

7 The 30-day alcohol relapse data were available in all patients in test cohort and in 88.7% (141 out of 159)
8 in validation cohort. The 30-day alcohol relapse rate was 37.0% (n=50) and 34.0% (n=48) in test and
9 validation cohort, respectively (Figure 1). The 30-day alcohol relapse was lower in those who attended
10 early alcohol rehabilitation compared to those who did not attend alcohol rehabilitation in both test (7.4%
11 vs. 44.4%, $P < 0.001$) and validation cohorts (5.3% vs. 45.9%, $P < 0.001$) (Figure 1). Among those who
12 relapsed, only 2 out of 50 in test cohort and only 1 out of 48 in the validation cohort attended alcohol
13 rehabilitation after hospital discharge.

14 In univariate analysis (Supplemental Table 5), early alcohol rehabilitation was a protective factor for 30-
15 day alcohol relapse in both test and validation cohorts. Additionally, higher MELD score, CTP score, mDF
16 scores, INR and having college degree were protective factors for alcohol relapse. In multivariable
17 analysis (Table 2), participation in alcohol rehabilitation within 30-days after hospital discharge was the
18 only independent protective factor against 30-day alcohol relapse (AOR 0.11, [95%CI 0.02-0.53], $P < 0.001$
19 and AOR 0.09, [95%CI 0.01-0.73], $P = 0.02$) in test and validation cohort, respectively.

20 **Mortality**

21 There were 53 (39.3%) and 42 (26.4%) deaths during a median follow up time of 2.8 and 1.3 years in test
22 and validation cohorts, respectively. The mortality rate at one year was 14% in the test and 16% in the
23 validation cohort. As shown in Figure 3, patients who attended early alcohol rehabilitation had
24 significantly improved survival compared to patients who did not attend alcohol rehabilitation in both test
25 and validation cohorts.

1 Univariate analysis is shown in Supplemental Table 6. In multivariable analysis (Table 2), attendance to
2 early alcohol rehabilitation was an independent protective factor (adjusted hazard ratio [AHR] 0.20
3 [95%CI 0.05-0.56], $P=0.001$), while variceal bleeding was an independent predictor of mortality (AHR
4 11.1 [95%CI 2.52-34.4], $P=0.004$) after adjusting for age and sex. In validation cohort, attendance to
5 alcohol rehabilitation was an independent protective factor (AHR 0.20 [95%CI 0.01-0.94], $P=0.04$),
6 whereas age (AHR 1.04 [95%CI 1.01-1.08], $P=0.04$) and hepatic decompensation (AHR 2.11 [95%CI
7 1.01-4.99], $P=0.04$) were significant predictors of mortality, after adjusting for sex and ABIC score.
8

1 Discussion

2 Recent studies on AH reported that alcohol relapse is the most important predictor of long-term
3 mortality.^{5, 6} However, hospital readmission rates, alcohol relapse along with alcohol rehabilitation
4 attendance have not been well characterized in the AH population. We utilized a test (single-center
5 retrospective) and a validation (multi-center prospective) cohort of hospitalized AH patients to evaluate
6 30-day readmission, 30-day alcohol relapse, and long-term mortality. At 30-days after surviving AH
7 admission, readmission rate was 30%, alcohol relapse rate was 34-37%, and only 16-20% of patients
8 participated in alcohol rehabilitation. The current study showed that alcohol rehabilitation after hospital
9 discharge was associated with decreased 30-day readmission, decreased 30-day alcohol relapse and
10 importantly, decreased mortality. While alcohol rehabilitation is routinely recommended in this clinical
11 scenario, this is one of the first studies that documents the benefits of this intervention on clinically
12 significant patient endpoints including mortality.

13 In multivariable analysis, participating in alcohol rehabilitation was associated with 70-84% lower risk of
14 30-day readmission, 89-91% lower risk of 30-day alcohol relapse, and 80% lower risk of long-term
15 mortality. This is an important finding because alcohol relapse is the most important predictor for long-
16 term mortality and there is currently no proven pharmacological intervention to prevent alcohol relapse in
17 patients with AH.^{5, 6, 19, 20} Evidence suggests that psychosocial interventions including cognitive behavioral
18 therapy and motivational interviewing may be effective in supporting alcohol abstinence in patients with
19 alcoholic cirrhosis.²¹⁻²³ It is also important to emphasize that the most common type of alcohol
20 rehabilitation was at a residential (44% in test cohort and 53% in validation cohort) level of care. Future
21 studies are necessary to test whether the intensity of treatment along with timelines (within 30 days of
22 discharge) are important prerequisites of success.

23 After AH admission, only 16-20% of patients with AH attended alcohol rehabilitation. The results
24 challenge us to do better as a specialty in connecting patients who survive AH episodes to alcohol
25 rehabilitation and to build stronger bridges with our addiction specialist colleagues. Our study results
26 strongly suggest that alcohol rehabilitation should be arranged for AH patients during their index hospital
27 admission and early alcohol rehabilitation referral should be documented as a quality metric in the

1 management of all hospitalized AH patients. Patients evaluated by alcohol addiction specialists during
2 their hospitalization demonstrated higher attendance rates of alcohol rehabilitation compared to patients
3 who were not assessed (25.3% vs. 10.4%). Therefore, an addiction specialist should meet with the
4 patient during hospital admission. Unfortunately, less than 8% of patients received alcohol relapse
5 prevention medication, which were all gabapentin. It is important to note that the use of gabapentin was
6 an off-label use.²⁴ The integration of addiction medicine in hepatology practice is becoming even more
7 important with the development of effective treatments for hepatitis C viral(HCV) infection because
8 alcohol abstinence is necessary for optimal treatment of HCV.²⁰

9 Our results emphasize the high disease burden of AH. The 30-day readmission rate was 30%, which is
10 comparable to patients with decompensated cirrhosis (32%).²⁵ Recurrent AH and alcohol intoxication or
11 withdrawal were causes of readmission in 19% and 8% in the test cohort, respectively. A previous study
12 suggested that subsequent episodes of AH in alcohol relapsers are more severe compared to the index
13 episode with close to 60% mortality.²⁶ Only total bilirubin at the time of admission and participation in
14 alcohol rehabilitation after hospital discharge were independent predictors of readmission. Interestingly,
15 the liver severity scores, e.g. MELD score or CTP score, were not predictors for readmission. In contrast,
16 MELD score has been previously found to be an independent predictor of readmission in cirrhotic
17 patients.²⁷ Although we attempted to create a model to predict 30-day readmission using alcohol
18 rehabilitation attendance and total bilirubin, the AUC were only 0.73 and 0.63 in test and validation
19 cohorts, respectively. Unfortunately, the risk of readmission in this patient population is likely difficult to
20 predict due to many socioeconomic factors involved. Similar findings have been reported in patients with
21 decompensated cirrhosis.²⁸

22 The major strengths of our study were the utilization of two separate cohorts. Importantly, the validation
23 group was a multicenter prospective cohort with well-defined AH patients. The findings from both cohorts
24 were consistent. However, our study has few limitations worth mentioning. First, the diagnosis of AH was
25 made without a liver biopsy, as is common in real practice, which may occasionally lead to misdiagnosis.
26 However, using the NIAAA clinical criteria, less than 10% of patients would have a diagnosis other than
27 AH on liver biopsy.¹⁵ Second, alcohol relapse was based on self-report and the data may not be fully

1 accurate. However, the well validated timeline followback questionnaire was used and we considered
2 any alcohol consumption after discharge as relapse. Future studies should include blood or urine markers
3 to screen for alcohol relapse. Third, we were not able to evaluate the effect of central obesity, factor
4 shown to have negative effect on outcomes in patients with alcoholic hepatitis.²⁹ This is because waist
5 and hip circumference data were not available. However, BMI data was analyzed and did not affect the
6 outcomes in our cohort. Lastly, the reasons for patients not attending rehabilitation are difficult to
7 ascertain and the benefit of rehabilitation may be reflective of the high motivation of those patients to
8 discontinue alcohol rather than the rehabilitation process itself.

9 In conclusion, the 30-day readmission and 30-day alcohol relapse rates are 30% and 37% respectively
10 after an AH admission. Early alcohol rehabilitation is associated with reduction in hospital readmission,
11 alcohol relapse, and death and should be pursued in all AH patients during and/or immediately following
12 their hospitalization.

13

1 **Figure legends**

2

3 **Figure 1.** Rates of 30-day readmission and 30-day alcohol relapse

4

5 **Figure 2.** Area under the receiver operating characteristic curve of AH readmission score for predicting
6 30-day readmission in A) test and B) validation cohort.

7

8 **Figure 3.** Kaplan–Meier curves showing in patients attending vs. not attending alcohol rehabilitation in A)
9 test and B) validation cohort

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29

30

1 Table 1. Baseline characteristics of retrospective and prospective cohort

	Test cohort				Validation cohort			
	All patients (n=135)	Readmission in 30 days (n=41)	No readmission (n=94)	P*	All patients (n=159)	Readmission in 30 days (n=49)	No readmission (n=110)	P**
Age, years (mean±SD)	48.0±10.2	47.2±8.7	48.4±10.8	0.50	50.0±11.0	48.4±12.0	50.8±10.5	0.24
Male (n, %)	90 (66.7%)	29 (70.7%)	61 (64.9%)	0.51	92 (57.9%)	29 (59.2%)	63 (57.3%)	0.82
BMI, kg/m ² (mean±SD)	28.6±7.4	28.4±7.7	28.7±7.3	0.86	28.9±7.0	28.2±6.0	29.2±7.3	0.33
White (n, %)	130 (96.3%)	39 (95.1%)	91 (96.8%)	0.64	137 (86.2%)	41 (83.7%)	96 (87.3%)	0.54
Married or living with significant other (n, %)	42 (31.1%)	14 (33.3%)	28 (29.8%)	0.61	59 (40.1%)	21 (44.7%)	38 (38.0%)	0.44
College degree or above (n, %)	n/a	n/a	n/a		73 (49.7%)	25 (53.2%)	48 (48.0%)	0.56
Average number of drinks/day (median, IQR)	n/a	n/a	n/a		8 (5, 13)	7 (5, 11)	9 (5, 15)	0.12
Hepatic decompensation (n, %)	49 (36.3%)	22 (53.7%)	27 (28.7%)	0.006	106 (66.7%)	35 (71.4%)	71 (64.6%)	0.40
- Hepatic encephalopathy (n, %)	17 (12.6%)	7 (17.1%)	10 (10.6%)	0.30	40 (25.2%)	10 (20.4%)	30 (27.3%)	0.35
- Variceal bleeding (n, %)	3 (2.2%)	2 (4.9%)	1 (1.7%)	0.22	24 (15.1%)	8 (16.3%)	16 (14.6%)	0.77
- Ascites (n, %)	53 (39.3%)	20 (48.8%)	33 (35.1%)	0.13	90 (56.6%)	29 (59.2%)	61 (55.5%)	0.66
Use of alcohol relapse prevention medication	10 (7.4%)	5 (12.2%)	5 (5.3%)	0.17	7 (4.4%)	0 (0%)	7 (6.4%)	0.10
Labs								
Platelet, 10 ⁹ /L (median, IQR)	147 (86, 196)	159 (122, 205)	129 (78, 190)	0.02	127 (87, 184)	119 (74, 184)	130 (87, 187)	0.76
Albumin, g/dL (median, IQR)	3.0 (2.7, 3.4)	3.1 (2.5, 3.3)	3.0 (2.7, 3.5)	0.17	2.8 (2.4, 3.2)	2.8 (2.3, 3.2)	2.8 (2.4, 3.3)	0.51
Creatinine, mg/dL (median, IQR)	0.7 (0.6, 1.1)	0.6 (0.5, 1.0)	0.7 (0.6, 1.1)	0.10	0.7 (0.6, 1.1)	0.82 (0.63, 1.2)	0.7 (0.6, 1.0)	0.45
Total bilirubin, mg/dL (median, IQR)	8.7 (4.0, 19.6)	14.4 (6.3, 23.5)	6.9 (3.7, 14.3)	0.004	9.6 (3.9, 19.1)	13.3 (5.5, 19.1)	8.3 (3.5, 19.4)	0.25

INR (median, IQR)	1.4 (1.2, 1.7)	1.5 (1.3, 1.8)	1.3 (1.2, 1.7)	0.21	1.7 (1.4, 2.1)	1.8 (1.5, 2.1)	1.6 (1.3, 2.1)	0.19
PT, seconds (median, IQR)	15 (13, 19)	15 (13, 18)	15 (12, 19)	0.52	20 (16, 23)	20 (18, 23)	19 (15, 27)	0.07
Severity scores								
MELD score (mean±SD)	20.5±7.2	21.6±6.8	20.0±7.4	0.22	21.8±7.2	23.3±6.7	21.2±7.3	0.04
CTP score (mean±SD)	8.9±1.5	9.3±1.3	8.8±1.6	0.03	9.5±1.8	9.9±1.5	9.4±1.9	0.04
mDF score (median, IQR)	30 (16, 50)	37 (19, 56)	25 (14, 50)	0.11	37 (15, 61)	45 (26, 63)	34 (13, 57)	0.15
mDF score≥32 (n, %)	64 (49.2%)	25 (62.5%)	39 (43.3%)	0.044	89 (56.3%)	31 (64.6%)	58 (52.7%)	0.17
ABIC score (mean±SD)	7.4±1.5	7.6±1.4	7.3±1.6	0.39	7.8±1.3	7.7±1.3	7.8±1.3	0.82
Outcomes								
Hospital stay, days (median, IQR)	7 (4, 12)	7 (4, 12)	6 (4,12)	0.74	6 (3, 10)	6 (3, 10)	7 (3, 10)	0.75
Attendance to alcohol rehabilitation within 30 days after discharge (n, %)	27 (20%)	3 (7.3%)	24 (25.5%)	0.02	19 (16.0%) (n=119)	4 (8.2%) (n=49)	15 (21.4%) (n=70)	0.04
Alcohol relapse within 30 days after discharge (n, %)	50 (37%)	23 (56.1%)	27 (28.7%)	0.003	48 (34.0%) (n=141)	27 (57.5%) (n=47)	21 (22.3%) (n=94)	<0.001

1 *P-value comparing those who readmitted vs. who did not readmit in test cohort

2 **P-value comparing those who readmitted vs. who did not readmit in validation cohort

3 n/a = data not available in test cohort

4 Abbreviations: ABIC = Age, serum Bilirubin, international normalized ratio, and serum Creatinine,

5 BMI = body mass index, CTP= Child-Turcotte-Pugh Score, INR = international normalized ratio,

6 mDF = Maddrey's Discriminant Function, MELD = Model for End-Stage Liver Disease, PT =

7 prothrombin time

8

1 **Table 2. Multivariable analyses of variables associated with 30-day readmission, 30-day alcohol**
 2 **relapse and mortality**

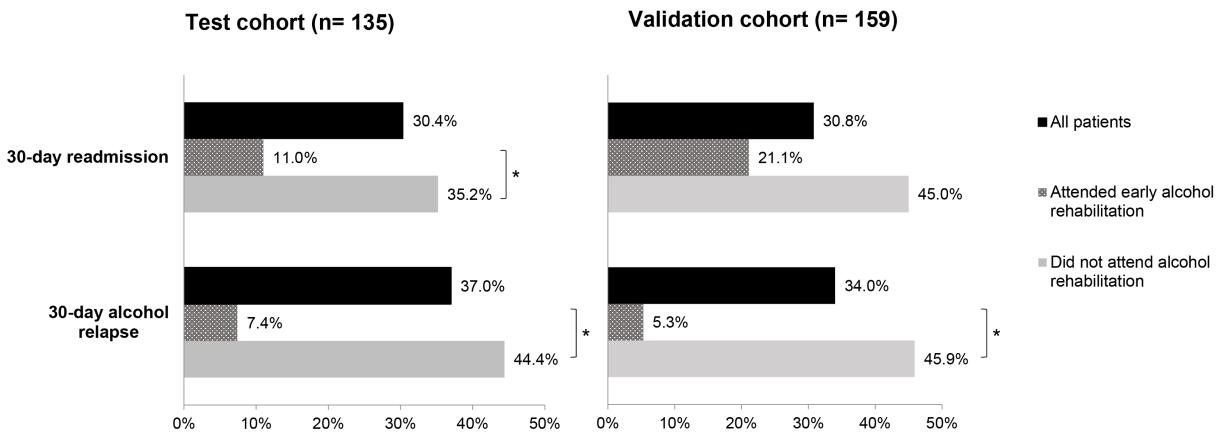
	Test cohort		Validation cohort	
	Multivariable logistic regression analysis			
30-day readmission	Adjusted Odds Ratio	P	Adjusted Odds Ratio	P
Hepatic decompensation	2.14 (0.90-5.06)	0.08	1.95 (0.87-4.38)	0.10
Total bilirubin	1.04 (1.01-1.09)	0.04	1.02 (0.99-1.06)	0.23
Attendance to alcohol rehabilitation	0.16 (0.04-0.65)	0.01	0.30 (0.09-0.98)	0.04
	Multivariable logistic regression analysis			
30-day alcohol relapse	Adjusted Odds Ratio	P	Adjusted Odds Ratio	P
College degree or above	n/a		0.74 (0.31-1.77)	0.50
MELD score	0.98 (0.89-1.07)	0.60	0.97 (0.90-1.04)	0.36
Child-Turcotte-Pugh Score	0.79 (0.53-1.17)	0.23	0.82 (0.60-1.12)	0.20
Attendance to alcohol rehabilitation	0.11 (0.02-0.53)	<0.001	0.09 (0.01-0.73)	0.02
	Multivariable Cox regression analysis			
Mortality	Adjusted Hazard Ratio	P	Adjusted Hazard Ratio	P
Age	1.01 (0.98-1.03)	0.79	1.04 (1.01-1.08)	0.04
Male	0.74 (0.41-1.32)	0.30	0.79 (0.41-1.58)	0.49
Hepatic decompensation	n/a		2.11 (1.01-4.99)	0.04
Variceal bleeding	11.1 (2.52-34.4)	0.004	n/a	
ABIC score	n/a		1.12 (0.81-1.55)	0.49
Attendance to alcohol rehabilitation	0.20 (0.05-0.56)	0.001	0.20 (0.01-0.94)	0.04

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4 n/a = variables that were not statistically significant in univariate analysis

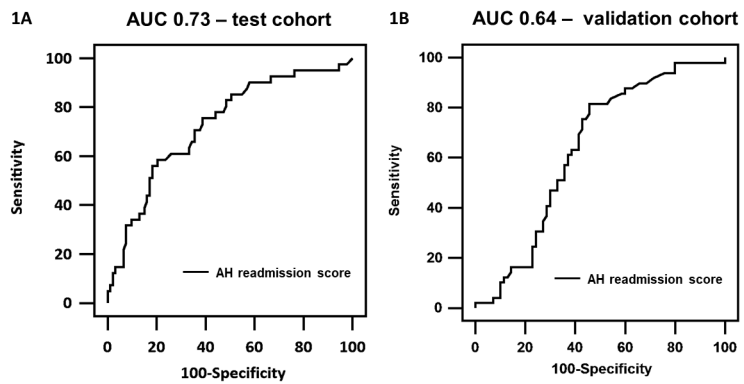
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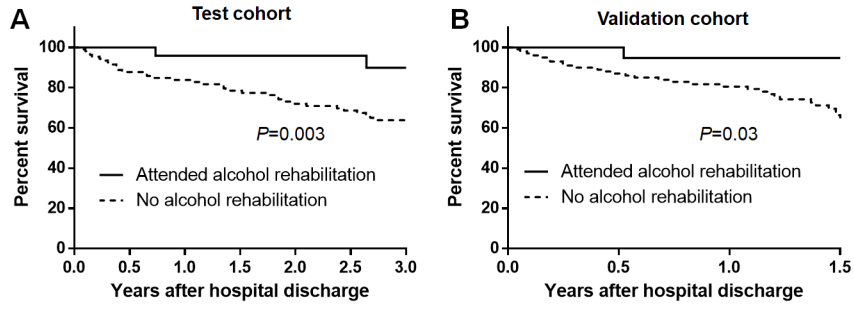
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* $P < 0.05$

ACCEPTED MANUSCRIPT





What You Need to Know

Background: Patients admitted to the hospital for alcoholic hepatitis (AH) are at increased risk of hospital readmission and death.

Findings: In two cohort of patients admitted with AH, early alcohol rehabilitation reduced risk of hospital readmission, alcohol relapse, and death.

Implications for patient care: All patients with AH should be formally evaluated by addiction specialists during hospital stay and referred for treatment within 30 days of hospital discharge.

Supplemental Table 1. Patient characteristics of those who attended vs. not attended alcohol rehabilitation

	Test cohort				Validation cohort			
	All patients (n=135)	Attended alcohol rehabilitation (n=27)	Did not attend alcohol rehabilitation (n=108)	P*	All patients** (n=119)	Attended alcohol rehabilitation (n=19)	Did not attend alcohol rehabilitation (n=100)	P***
Age, years (mean±SD)	48.0±10.2	47.6±12.1	48.1±9.7	0.84	50.0±11.0	44.7±11.3	51.7±11.3	0.02
Male (n, %)	90 (66.7%)	17 (63.0%)	73 (67.6%)	0.65	72 (60.5%)	10 (52.6%)	62 (62%)	0.44
Married or living with significant other (n, %)	42 (31.1%)	8 (29.6%)	19 (70.4%)	0.85	43 (39.5%)	9 (52.9%)	34 (37.0%)	0.22
College degree or above (n, %)	n/a	n/a	n/a		53 (48.6%)	14 (82.4%)	39 (42.4%)	0.003
Average number of drinks/day (median, IQR)	n/a	n/a	n/a		8 (5, 13)	8 (5, 20)	7 (5, 12)	0.46
Hepatic decompensation (n, %)	49 (36.3%)	39 (36.1%)	10 (37.0%)	0.93	76 (63.9%)	13 (68.4%)	63 (63.0%)	0.65
- Hepatic encephalopathy (n, %)	17 (12.6%)	3 (11.1%)	14 (13.6%)	1.00	25 (21.0%)	3 (15.8%)	22 (22.0%)	0.76
- Variceal bleeding (n, %)	3 (2.2%)	0 (0%)	3 (2.8%)	1.00	20 (16.8%)	4 (21.1%)	16 (16.0%)	0.52
- Ascites (n, %)	53 (39.3%)	12 (44.4%)	41 (38.0%)	0.54	65 (54.6%)	13 (68.4%)	52 (52%)	0.19
Severity scores								
MELD score (mean±SD)	20.5±7.2	22.6±8.9	20.0±6.6	0.17	21.8±7.2	21.8±5.8	21.6±7.2	0.88
CTP score (mean±SD)	8.9±1.5	8.9±1.7	8.9±1.5	0.87	9.5±1.8	9.5±1.9	9.4±1.7	0.84
mDF score (median, IQR)	30 (16, 50)	28 (19, 65)	31 (16, 49)	0.40	37 (15, 61)	41 (15, 69)	34 (15, 59)	0.46
mDF score≥32 (n, %)	64 (49.2%)	12 (46.2%)	52 (50.0%)	0.73	64 (54.2%)	11 (57.9%)	53 (53.5%)	0.73

Outcomes								
Hospital stay, days (median, IQR)	7 (4, 12)	7 (4, 14)	6 (4,10)	0.35	6 (3, 10)	6 (3, 13)	7 (3, 10)	0.56
Addiction medicine consult attempt	96 (71.1%)	22 (81.5%)	74 (68.5%)	0.18	n/a	n/a	n/a	
Addiction medicine consult completed	87 (64.4%)	22 (81.5%)	65 (60.2%)	0.04	n/a	n/a	n/a	

*P-value comparing those who readmitted vs. who did not readmit in test cohort

**Validation cohort in this table only include patients with available alcohol rehabilitation data

***P-value comparing those who readmitted vs. who did not readmit in validation cohort

n/a = data not available

Supplemental Table 2. Univariate logistic regression analysis for predictors of alcohol rehabilitation attendance

Variables	Test cohort		Validation cohort	
	Odds ratio	P	Odds ratio	P
Age (per 1 year)	0.99 (0.95-1.04)	0.81	0.95 (0.90-0.99)	0.01
Male	0.82 (0.34-1.96)	0.65	0.68 (0.45-0.25)	0.45
BMI	0.97 (0.91-1.03)	0.32	1.04 (0.97-1.12)	0.27
White	n/a*		0.80 (0.20-3.12)	0.75
Married or living with significant other	0.92 (0.37-2.30)	0.85	1.92 (0.68-5.44)	0.22
College degree or above	n/a		6.34 (1.70-23.6)	0.002
Average number of drinks/day	n/a		1.02 (0.96-1.08)	0.57
Hepatic decompensation	1.04 (0.43-2.95)	0.93	1.27 (0.45-3.63)	0.65
Hepatic encephalopathy	0.84 (0.22-3.16)	0.79	0.66 (0.18-2.49)	0.53
Variceal bleeding	n/a*		1.40 (0.41-4.77)	0.59
Ascites	1.31 (0.56-3.07)	0.54	2.0 (0.70-5.68)	0.18
Platelet	1.00 (0.99-1.00)	0.77	1.00 (0.99-1.01)	0.90
Albumin	1.41 (0.64-3.11)	0.39	1.86 (0.98-3.52)	0.05
Creatinine	1.63 (1.05-2.51)	0.02	0.59 (0.19-1.82)	0.25
Total bilirubin	1.11 (0.34-3.64)	0.86	1.01 (0.96-1.06)	0.68
INR	1.40 (0.71-2.78)	0.34	1.27 (0.53-3.05)	0.59
PT	1.01 (0.92-1.01)	0.86	1.03 (0.94-1.13)	0.52
MELD score	1.05 (0.99-1.08)	0.10	1.00 (0.94-1.08)	0.89
Child-Turcotte-Pugh Score	0.97 (0.73-1.30)	0.85	1.04 (0.77-1.39)	0.82
mDF score	1.01 (0.99-1.02)	0.47	1.01 (0.99-1.02)	0.49
mDF score ≥ 32	0.86 (0.36-2.03)	0.73	1.19 (0.44-3.22)	0.73
ABIC score	1.17 (0.88-1.55)	0.29	0.66 (0.43-1.01)	0.05
Addiction medicine consult completed	2.91 (1.02-8.27)	0.03	n/a	
Addiction medicine consult attempt	2.02 (0.71-5.79)	0.17	n/a	

n/a* = not enough data for analysis (only 5 patients who were non-white and only 3 patients with variceal bleeding in test cohort)

n/a = data not available

Supplemental Table 3. Multivariate logistic regression analysis for predictors of alcohol rehabilitation attendance

Variables	Test cohort		Validation cohort	
	Odds ratio	P	Odds ratio	P
Age (per 1 year)	n/a		0.95 (0.90-1.00)	0.05
College degree or above	n/a		4.62 (1.19-17.9)	0.03
Creatinine	1.53 (0.99-2.37)	0.06	n/a	
Addiction medicine consult completed	2.55 (0.88-7.37)	0.08	n/a	

Supplemental Table 4. Univariate logistic regression analysis for predictors of 30-day readmission

Variables	Test cohort		Validation cohort	
	Odds ratio	P	Odds ratio	P
Age (per 1 year)	0.99 (0.95-1.03)	0.53	0.98 (0.95-1.01)	0.21
Male	1.31 (0.59-2.90)	0.51	1.08 (0.55-2.14)	0.82
BMI	1.00 (0.95-1.05)	0.85	0.98 (0.93-1.03)	0.36
White	0.64 (0.10-4.00)	0.64	0.75 (0.29-1.92)	0.55
Married or living with significant other	1.22 (0.56-2.67)	0.62	1.32 (0.65-2.66)	0.44
College degree or above	n/a		1.23 (0.61-2.47)	0.56
Average number of drinks/day	n/a		0.95 (0.85-1.07)	0.41
Hepatic decompensation	2.87 (1.34-6.14)	0.006	1.37 (0.66-2.86)	0.40
Hepatic encephalopathy	1.73 (0.61-4.92)	0.30	0.68 (0.30-1.54)	0.36
Variceal bleeding	4.77 (0.42-54.1)	0.21	1.15 (0.45-2.89)	0.77
Ascites	1.76 (0.84-3.71)	0.14	1.16 (0.59-2.31)	0.66
Platelet	1.01 (0.99-1.01)	0.08	1.00 (0.99-1.00)	0.73
Albumin	0.60 (0.30-1.19)	0.14	0.73 (0.43-1.23)	0.22
Creatinine	0.78 (0.47-1.30)	0.31	1.14 (0.79-1.64)	0.48
Total bilirubin	1.04 (1.01-1.08)	0.009	1.01 (0.98-1.04)	0.51
INR	1.52 (0.65-3.55)	0.34	1.27 (0.69-2.33)	0.45
PT	1.02 (0.94-1.10)	0.64	1.04 (0.98-1.11)	0.20
MELD score	1.03 (0.98-1.08)	0.23	1.04 (0.99-1.09)	0.09
Child-Turcotte-Pugh score	1.26 (0.97-1.62)	0.08	1.18 (0.96-1.44)	0.10
mDF score	1.01 (1.00-1.02)	0.14	1.01 (0.99-1.02)	0.29
mDF score ≥ 32	2.18 (1.02-4.68)	0.04	1.63 (0.81-3.29)	0.17
ABIC score	1.11 (0.86-1.43)	0.41	0.97 (0.75-1.26)	0.82
Attendance to alcohol rehabilitation	0.23 (0.07-0.81)	0.02	0.33 (0.10-0.99)	0.04

n/a = data not available in test cohort

Supplemental Table 5. Univariate logistic regression analysis for predictors of 30-day alcohol relapses

Variables	Test cohort		Validation cohort	
	Odds ratio	P	Odds ratio	P
Age (per 1 year)	1.00 (0.97-1.04)	0.91	1.01 (0.98-1.04)	0.47
Male	0.54 (0.26-1.13)	0.10	0.95 (0.89-0.47)	0.89
BMI	0.99 (0.95-1.04)	0.82	0.99 (0.95-1.04)	0.82
White	n/a*		0.54 (0.19-1.49)	0.24
Married or living with significant other	1.07 (0.50-2.7)	0.86	0.62 (0.29-1.33)	0.22
College degree or above	n/a**		0.45 (0.21-0.95)	0.04
Average number of drinks/day	n/a**		0.99 (0.95-1.03)	0.54
Hepatic decompensation	0.64 (0.31-1.35)	0.24	1.20 (0.64-0.56)	0.64
Hepatic encephalopathy	0.48 (0.15-1.57)	0.20	0.48 (0.15-1.57)	0.20
Variceal bleeding	n/a*		1.78 (0.71-4.47)	0.22
Ascites	0.61 (0.29-1.27)	0.18	0.75 (0.37-1.51)	0.42
Platelet	1.00 (0.99-1.00)	0.83	0.99 (0.99-1.00)	0.41
Albumin	2.51 (1.24-5.08)	0.01	1.20 (0.74-1.96)	0.46
Creatinine	0.52 (0.27-0.98)	0.02	1.01 (0.66-1.53)	0.97
Total bilirubin	0.97 (0.93-1.00)	0.05	0.95 (0.91-0.99)	0.004
INR	0.33 (0.12-0.91)	0.02	0.43 (0.20-0.91)	0.02
PT	0.89 (0.81-0.98)	0.01	0.91 (0.84-0.98)	0.007
MELD score	0.93 (0.87-0.99)	0.01	0.92 (0.87-0.98)	0.005
Child-Turcotte-Pugh Score	0.76 (0.359-0.97)	0.03	0.78 (0.63-0.97)	0.02
mDF score	0.98 (0.97-0.99)	0.02	0.98 (0.97-0.99)	0.003
mDF score ≥ 32	0.80 (0.39-1.65)	0.55	0.36 (0.17-0.73)	0.005
ABIC score	0.80 (0.62-1.02)	0.07	0.82 (0.62-1.09)	0.16
Attendance to alcohol rehabilitation	0.10 (0.02-0.44)	0.002	0.07 (0.08-0.51)	0.009

n/a* = not enough data for analysis (only 5 patients who were non-white and only 3 patients with variceal bleeding in test cohort)

n/a** = data not available in test cohort

Supplemental Table 6. Univariate Cox regression analysis for predictors of mortality

Variables	Test cohort		Validation cohort	
	Hazard ratio	P	Hazard ratio	P
Age (per 1 year)	1.01 (0.98-1.04)	0.44	1.06 (1.03-1.09)	<0.001
Male	0.88 (0.51-1.55)	0.66	0.87 (0.45-1.75)	0.69
BMI	1.00 (0.97-1.04)	0.80	0.98 (0.94-1.03)	0.46
White	0.79 (0.24-4.84)	0.74	2.17 (0.79-8.97)	0.20
Married or living with significant other	0.60 (0.29-1.23)	0.13	1.37 (0.71-2.62)	0.34
College degree or above	n/a		0.81 (0.41-1.55)	0.52
Average number of drinks/day	n/a		0.99 (0.95-1.03)	0.60
Hepatic decompensation	1.16 (0.66-2.00)	0.59	2.05 (1.02-4.56)	0.04
Hepatic encephalopathy	0.87 (0.36-1.81)	0.72	1.39 (0.68-2.65)	0.35
Variceal bleeding	12.32 (2.92-35.44)	0.002	1.25 (0.56-2.51)	0.56
Ascites	0.90 (0.51-1.56)	0.72	1.51 (0.81-2.90)	0.20
Platelet	0.99 (0.99-1.00)	0.25	0.99 (0.99-1.00)	0.37
Albumin	0.82 (0.48-1.39)	0.47	0.88 (0.55-1.34)	0.57
Creatinine	0.75 (0.45-1.12)	0.22	0.93 (0.56-1.25)	0.69
Total bilirubin	1.00 (0.97-1.02)	0.99	0.98 (0.95-1.02)	0.36
INR	1.59 (0.84-2.81)	0.13	1.41 (0.80-2.36)	0.21
PT	1.05 (0.99-1.10)	0.05	1.02 (0.97-1.08)	0.40
MELD score	1.00 (0.96-1.04)	0.93	1.00 (0.96-1.04)	0.93
Child-Turcotte-Pugh Score	1.09 (0.91-1.32)	0.34	1.16 (0.96-1.40)	0.12
mDF score	1.01 (1.00-1.01)	0.23	1.00 (0.99-1.01)	0.66
mDF score ≥ 32	1.47 (0.85-2.57)	0.17	1.21 (0.66-2.26)	0.53
ABIC score	1.02 (0.85-1.22)	0.82	1.42 (1.13-1.78)	0.002
Attendance to alcohol rehabilitation	0.20 (0.05-0.55)	0.001	0.15 (0.01-0.68)	0.009

n/a = data not available in test cohort