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Acute Alcoholic Hepatitis: Natural History and Predictors of Mortality Using a Multicenter Prospective Study

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Abstract

Objective: To examine the natural history of acute alcoholic hepatitis (AH) and identify predictors of mortality for AH using data from a prospective multicenter observational study.

Participants and Methods: We analyzed data from 164 patients with AH and 131 heavy-drinking controls with no liver disease. Participants underwent clinical/laboratory assessment at baseline and 6 and 12 months after enrollment. Multivariable analyses were conducted to identify variables associated with mortality and examine the association between coffee drinking and risk of AH.

Results: Thirty-six patients with AH died during follow-up, with estimated 30-day, 90-day, 180-day, and 1-year survival of 0.91 (95% CI, 0.87-0.96), 0.85 (95% CI, 0.80-0.91), 0.80 (95% CI, 0.74-0.87), and 0.75 (95% CI, 0.68-0.83), respectively. In the multivariable analysis, higher serum bilirubin level (hazard ratio [HR]=1.059; 95% CI, 1.022-1.089), lower hemoglobin level (HR=1.263; 95% CI, 1.012-1.575), and lower platelet count (HR=1.006; 95% CI, 1.001-1.012) were independently associated with mortality in AH. Compared with controls, fewer patients with AH regularly consumed coffee (20% vs 44%; $P<.001$), and this association between regular coffee drinking and lower risk of AH persisted after controlling for relevant covariates (odds ratio=0.26; 95% CI, 0.15-0.46). Time-dependent receiver operating characteristic curve analysis revealed that Model for End-Stage Liver Disease; Maddrey Discriminant Function; age, serum bilirubin, international normalized ratio, and serum creatinine; and Child-Pugh scores all provided similar discrimination performance at 30 days (area under the curve=0.73-0.77).

Conclusion: Alcoholic hepatitis remains highly fatal, with 1-year mortality of 25%. Regular coffee consumption was associated with lower risk of AH in heavy drinkers.

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Excessive alcohol consumption is a growing trend in the United States, with approximately 87% of the general population older than 18 years reporting some history of alcohol consumption and approximately 25% meeting the criteria for heavy drinking.[1-3] Alcoholic hepatitis (AH) is a unique syndrome in patients with chronic and active harmful alcohol use. It is associated with poor prognosis and reported short-term mortality of 16% to 50% within 1 month of presentation, depending on initial disease severity.[4-8] Based on the National Inpatient Sample analysis, AH accounts for 0.7% of all hospital admissions in the United States, which is higher than that for myocardial infarction, acute cerebrovascular disease, or acute pancreatitis.[9,10] No recent studies have prospectively examined the natural history of AH in the United States. In addition, the lack of prospective clinical studies makes it challenging to validate existing risk stratification models, such as the Model for End-Stage Liver Disease (MELD) score; Lille score; age, serum bilirubin, international normalized ratio, serum creatinine (ABIC) score; Child-Pugh (CP) score; or Maddrey Discriminant Function

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(mDF) score, to classify disease severity and predict survival in patients with AH.[11-13]

The risk of alcoholic liver disease is related to the amount and duration of alcohol use.[14,15] However, only a small proportion of heavy drinkers develop AH, suggesting the role of host and environmental factors on the development of AH.[2,4,5,16] Recent genomic studies reported higher variants of hepatic antiapoptotic genes such as K8/K18 (keratinocytes) in white individuals or the *PNPLA3* gene in the Hispanic population, which predisposes them to liver injury.[17-19] Furthermore, several studies have suggested the benefit of regular coffee consumption in preventing liver disease, albeit limited to epidemiologic or retrospective studies involving nonalcoholic fatty liver disease and liver cancer.[20-23] There are limited data, either prospective or retrospective, that evaluate the relationship between coffee consumption and AH in heavy drinkers.

The main objectives of this study were to describe (1) the outcomes of AH in a cohort using the new diagnostic definition,[24] (2) variables associated with mortality in AH, (3) the performance of commonly used risk stratification models, and (4) the relationship between coffee consumption and the risk of AH in heavy drinkers using a multicenter prospective cohort. The data presented herein provide additional complementary analyses beyond a recent and initial publication describing this cohort.[25]

PARTICIPANTS AND METHODS

This article is concerned with an ongoing prospective, multicenter, observational study of patients with well-characterized AH (cases) and heavy drinkers without evidence of liver disease (controls) conducted by the Translational Research and Evolving Alcoholic Hepatitis Treatment (TREAT) Consortium. The TREAT Consortium, consisting of Indiana University, Virginia Commonwealth University, and Mayo Clinic, is funded by the National Institute on Alcohol Abuse and Alcoholism and its objectives are to conduct clinical research in AH and develop novel treatments.

Participants

For the most part, cases were enrolled from inpatient clinical sites associated with the respective center in the consortium, and controls were enrolled from 1 or more of the local alcohol rehabilitation facilities. However, outpatients from liver clinics were also candidates for inclusion as cases in the study, but these individuals' laboratory values were typically out of the range for inclusion as cases and, thus, they were unlikely to be enrolled. Heavy drinkers were defined as having average daily alcohol consumption greater than 40 g/d for women or greater than 60 g/d for men for the last 5 years and active drinking within the 6 weeks before study enrollment, amounts that are believed to be reasonable minimal thresholds for the development of AH.[24] Frequency-matched (for similar alcohol consumption history) heavy drinkers without liver disease were recruited to the control group. Absence of liver disease in the control group was ascertained based on history, physical examination findings, and normal liver enzyme levels. The diagnosis of AH was made by the admitting clinician based on a combination of appropriate clinical and laboratory data as per the new consensus definition of AH[24,25] criteria in the presence of heavy drinking for a minimum of 6 months and within 6 weeks before enrollment. Subsequent testing, including liver biopsy in some cases, was performed at the discretion of the managing clinician for patients in whom the diagnosis was still in question based on these criteria. Individuals with hepatitis B virus, hepatitis C virus, or human immunodeficiency virus were eligible for enrollment as cases to include the full spectrum of patients seen with AH in practice. Exclusion criteria for either cases or controls included (1) younger than 21 years; (2) evidence of other liver diseases, such as autoimmune or drug induced, hemochromatosis, or Wilson disease; (3) active intravenous drug use; or (4) comorbidities such as chronic obstructive pulmonary disease, congestive heart failure, or multiorgan failure. This study was approved by the institutional review boards at the respective institutions, and all the participants signed an informed consent form before enrollment. These cohorts were described in a recent publication by the TREAT Consortium.[24]

Detailed data were collected on (1) demographic factors (age, sex, race and ethnicity, marital status, highest educational level), vital signs, anthropometry, medical history, and concomitant medications; (2) quantity of