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Abstinence from alcohol improves survival in decompensated cirrhotic patients

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ABSTRACT A critical appraisal and clinical application of Alvarez MA, Cirera I, Solà R, Bargalló A, Morillas RM, Planas R. Long-term clinical course of decompensated alcoholic cirrhosis. *Journal of Clinical Gastroenterology*. 2011;45(10):906-911. doi: 10.1097/mcg.0b013e3182284e13.

Keywords: *alcoholic cirrhosis, abstinence, survival, decompensation*

Clinical Context

M.W. is a 45-year-old Caucasian female with a history of alcohol abuse and liver cirrhosis, who presented to the emergency department with a one-day history of abdominal pain, ascites, and vomiting. On physical exam, patient was found to be jaundiced, with abdominal distension, diffuse abdominal tenderness, asterixis, and altered mental status. The patient reported drinking five beers per day prior to the episode despite physician recommendations to abstain. Liver studies were obtained: AST 146, ALT 16, total bilirubin 26.2, alkaline phosphatase 161, INR 2.23. Creatinine was 1.8. We diagnosed her with acute alcoholic hepatitis, and she was managed conservatively. Her MELD score at baseline was 19, but on admission was calculated to be 34, which put her at a high risk of death from liver failure.2 Child-Pugh score was 13 (Class C). She understood that alcohol use was damaging her liver but because cirrhosis is ultimately incurable, she did not believe abstinence would drastically affect her prognosis.

Clinical Question

Does abstinence from alcohol improve survival rates in patients with alcoholic cirrhosis?

Research Article

Alvarez MA, Cirera I, Solà R, Bargalló A, Morillas RM, Planas R. Long-term clinical course of decompensated alcoholic cirrhosis. *Journal of Clinical Gastroenterology*. 2011;45(10):906-911. doi: 10.1097/mcg.0b013e3182284e13

Related Literature

PubMED database was searched for articles containing the keywords “alcoholic cirrhosis” AND “abstinence” AND “survival”. 68 articles were retrieved on 11/1/17; a majority of which focused on survival rates of liver transplantation patients. Since our patient was not a candidate for liver transplantation due to her active alcohol abuse, these were found to be irrelevant. Several prospective cohort studies were found. A meta-analysis by Xie et al. on seven such cohort studies concludes that alcohol abstinence does improve the survival of patients with alcoholic cirrhosis, but that it takes at least 1.5 years before a statistically significant difference in survival can be observed.[1]

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After further comparing the study designs of those seven articles, it is necessary to quantify alcohol consumption. M.W. reported having 5 drinks per day, and assuming 14 grams of alcohol in a standard drink, M.W.'s intake was 70g/day. Five of the seven studies set a cut-off of at least 80g/day.[4-8] Since our patient would not qualify for those studies, we can exclude them. Of the remaining two studies, Powell et al. only specifies that subjects had a history of chronic alcoholism, and Alvarez et al. specifies at least 80g/day in men and 60g/day in women.[3,9] Furthermore, it is important to distinguish between compensated and decompensated cirrhosis. Our patient's condition is classified as decompensated cirrhosis, because of her symptomatic presentation. Patients with decompensated cirrhosis are found to have significantly lower survival rates compared to those with compensated cirrhosis.[2] Thus, it would be more precise to select a study concentrating on decompensated patients. Damico et al.'s 1986 study mixed compensated and decompensated patients, which would likely produce higher survival rates and decreased impact of abstinence than expected in a purely decompensated population. Alvarez et al. and Soterakis et al. were the only two studies that solely involved decompensated cirrhotic patients. However, the former study is much more recent, following patients from 1998 to 2010, while the latter's 1973 study is more outdated.

A decision was made to critically appraise Alvarez et al.'s 2011 study because of its stringent criteria and exclusion of patients with underlying liver disease such as hepatocellular carcinoma and hepatitis B and C. It was most relevant to our patient context and the clinical question.

Critical Appraisal

The article by Alvarez et al. is a prospective cohort study following 165 patients for 12 years, monitoring the long-term course of alcoholic cirrhosis (AC). Subjects were those hospitalized in University Hospitals in Barcelona between 1998 and 2001. Inclusion criteria were "(1) the possibility of performing a prospective follow-up in the same referral hospital; (2) no known hepatocarcinoma; and (3) age between 18 and 80 years." Cirrhosis was diagnosed by liver biopsy in 15% of subjects, and the rest were diagnosed by means of biochemical and ultrasonographic features, which corresponds with the guidelines set forth by the American Association for the Study of Liver Diseases (AASLD).[11] Decompensated cirrhosis was defined by ascites, hepatic encephalopathy, portal hypertensive gastrointestinal bleeding, severe bacterial infection, and/or severe alcoholic hepatitis. Follow-ups took place at least twice a year in which patients underwent clinical assessment and standard liver biochemical tests. All patients were encouraged to abstain from alcohol. Administrators evaluated abstinence participation by either querying patients and their relatives, or with urine alcohol tests when abuse was suspected. However, the authors do not explicitly define the time frame for abstinence and how relapses may factor in.

A total of 23 clinical and biological variables were analyzed in relation to survival rate. During follow-up, 99 patients practiced abstinence and 66 did not. 116 patients died overall: 93 liver-related and 23 non-liver-related. Overall survival was significantly higher for abstinent patients (78 vs 32 months, $p<0.0001$). These patients had higher survival rates at 1 year (95% vs 63%), 5 years (61% vs 36%), and 10 years (31% vs 11%) of follow-up, although this difference cannot be considered statistically significant because no statistical testing was performed, hence no p-values. But from a patient's perspective, these differences would likely be considered substantial.

There are several dissimilarities between our 45-year-old female patient and the study subjects, who are 86% male with median age of 56 years and baseline MELD of 13.8. While Alvarez et al. found age and MELD score to be independently correlated with survival, the coefficient of regression for those two categories (1.07, $p<0.001$ and 1.05, $p=0.03$, respectively) are drastically lower than that for alcohol use (2.68, $p<0.001$). So even if age and MELD score may distinguish M.W. from the study population, the influence of abstinence is still applicable to our patient.

Based on the Strength of Recommendation Taxonomy (SORT) criteria, this study is a level 1A study because it is a prospective cohort study with good follow-up.[10] It is important to note that 5% of patients dropped out, which may be low but the authors did not discuss the details of the drop-outs or how they fit in the data, leading to potential reporting bias. Furthermore, the authors did not delineate the characteristics of the two groups; we do not know how the abstinent and drinking groups differ in age, gender, cause of death, etc. This sort of data would be useful; for example, 23 patients died from non-liver-related causes such as accidents but we do not know the distribution, and results could be skewed if all 23 were found in the non-abstinent group. Confirming abstinence is also essential. The authors claim that urine alcohol tests were only performed when "excessive use was suspected." This ambiguity

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casts suspicion on whether the abstinent group was truly abstinent. It is also difficult to believe that all 99 patients who stopped drinking on first follow-up maintained abstinence through 10-12 years.

Because the cohort study does not randomize or blind, there exists the possibility of confounding factors, as well as performance bias in case the physicians provide better health care for one group over the other. Similarly, participation bias should be considered, as well, seeing as how patients who choose to abstain are making a more conscious effort to improve health. An additional issue of the cohort study design is the exploratory nature of its statistical analyses. Despite the potential pitfalls, the study does attempt to minimize other biases. Lead-time bias is mitigated by defining day 1 as the first date of decompensation symptoms rather than date of diagnosis. Indication bias is avoided as all patients were encouraged to abstain from alcohol. And because the hospitals sampled consecutive AC patients, sampling bias is controlled for.

Overall, this study was a well-designed prospective cohort. The decompensated population is carefully defined, and multiple variables were evaluated in relation to overall survival—of which alcohol intake was found to be most significant.

Clinical Application

Abstinence from alcohol is universally encouraged for patients with alcoholic cirrhosis. The AASLD posits “in patients with evidence of alcohol-induced liver disease, strict abstinence must be recommended, because continued alcohol use is associated with disease progression (Class 1, level B).” The patient of interest was hesitant to give up alcohol because she considered her disease to already be incurable. While this is true, Alvarez et al. shows significantly increased survival rates for cirrhotic patients who quit drinking. She fits within the criteria for this study, as a decompensated AC patient with no underlying liver disease.

Alcohol use as a risk factor is entirely modifiable and abstinence produces no harm upon the patient aside from possible withdrawal, which should be carefully monitored. On discharge, she vowed to quit drinking and was placed in a subacute rehabilitation facility, where she would work towards recovery.

Learning points:

1. Abstinence significantly increases survival rate in decompensated cirrhotic patients.
2. Alcoholic cirrhosis carries a poor prognosis and high mortality rate.
3. Decompensated cirrhosis includes complications such as jaundice, hepatic encephalopathy, ascites, and variceal bleeding.

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