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【 ORIGINAL ARTICLE 】

A Comparison of the Effects of Alcohol Abstinence and Drinking Habit on the Survival of Patients with Alcohol-related Cirrhosis: A Retrospective Observational Study

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Abstract:

Objective Abstaining from alcohol improves the outcome of alcohol-related cirrhosis. This study evaluated the effect of alcohol abstinence on the outcomes of patients with alcohol-related cirrhosis recruited from a core hospital in Boso Peninsula, Japan.

Methods This single-center retrospective study recruited 116 patients with alcohol-related cirrhosis who were admitted to our department between April 2014 and October 2022. Taking the day of discharge as day 0, the patients were divided into two groups based on their subsequent behavior (abstinence/non-abstinence from alcohol). The study analysis included 98 patients after excluding 13 who died during hospitalization and 5 for whom follow-up at our hospital ended after discharge. We evaluated differences in the patient survival between the abstaining and drinking groups.

Results The abstaining and drinking groups comprised 57 and 41 patients, respectively. We excluded from the analysis 10 and 6 patients with viable hepatocellular carcinoma in the abstaining and drinking groups, respectively. The findings revealed that the survival rate plateaued in the abstaining group from the third year onward, whereas the survival rate in the drinking group gradually decreased with time.

Conclusion Our findings suggest that at least two years of alcohol abstinence is required to sustain the survival of patients with alcohol-related cirrhosis. The data collected by our hospital retrospectively demonstrated the importance of abstinence on a timescale of years of sustained abstinence.

Key words: alcohol abstinence, drinking habit, alcohol-related cirrhosis, MELD score, survival

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Introduction

Unhealthy consumption of alcohol is a significant public health issue that caused 3 million deaths globally in 2016 (1). Among digestive disorders, which were the second major cause of death, 95% occurred due to liver cirrhosis. Alcohol-associated liver diseases include fatty liver, alcoholic hepatitis, steatohepatitis with or without fibrosis, alcohol-related cirrhosis, and their complications, including hepatocellular carcinoma (HCC). With the increase in per capita alcohol consumption in the Asia-Pacific region, the burden of liver disease is likely to increase (2). An increase in alcohol intake leads to an increase in alcohol-related cirrhosis.

Excess alcohol consumption is a risk factor for cirrhosis, and the associated HCC risk occurs in a dose-dependent manner (3). Previous studies have reported a high mortality rate in patients with alcohol-related cirrhosis (4). The mortality rates of patients with alcohol-related cirrhosis in a previous study were 71%, 84%, and 90% at 5, 10, and 15 years, respectively, and most patients had decompensated

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cirrhosis (5). Many factors, such as alcohol abstinence, Child-Pugh class, clinical parameters, and biochemical parameters, affect the survival of patients with alcohol-related cirrhosis (6). However, the effect of alcohol abstinence on the survival of patients with alcohol-related cirrhosis remains controversial.

While some studies have found a better rate of survival following abstinence, others have found that survival of abstinent patients is not significantly better than that of alcoholics who have continued drinking (6-9). These contradictory findings reflect differences in parameters among these studies, such as patient characteristics, diagnostic criteria for excessive alcohol consumption, proportion of alcoholic patients who stopped drinking after their diagnosis, severity of liver disease, and follow-up duration.

The present study therefore evaluated the effect of alcohol abstinence on outcomes in patients with alcohol-related cirrhosis recruited from a core hospital in Boso Peninsula, Japan, an area with relatively little demographic variation and thus less patient selection bias than other regions.

Materials and Methods

Study design and patients

This retrospective single-center study was conducted at the Eastern Chiba Medical Center in Chiba, Japan. Consecutive patients with alcohol-related cirrhosis admitted between April 2014 and October 2022 were included in this study. The patients were administered general treatment in accordance with the guidelines of the Japanese Society of Gastroenterology and Japan Society of Hepatology (10).

Ethics approval

This study was approved by the Ethics Committee of the Eastern Chiba Medical Center on January 13, 2023 (approval no. 205). The requirement for informed consent was waived because of the retrospective design of the study. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Categorization of patients

Considering the day of discharge, i.e., the day of recovery of general health following the first admission, as day 0, patients were divided into two groups (abstaining and drinking) based on their subsequent habit of alcohol consumption. The abstaining group comprised patients who did not resort to alcohol consumption after discharge from the hospital. Abstinence was determined based on medical record information provided by the attending physician and self-reported information from the patients and their families. The drinking group comprised patients who continued to consume alcohol after hospital discharge. Since the information was collected based on medical records, we were unable to examine alcohol consumption, genetics, or mental health.

Primary endpoints

The primary endpoint of this study was the evaluation of the differences in the patient prognosis between the abstaining and drinking groups.

Follow-up

As this was a retrospective study, the frequency and duration of follow-up were not standardized.

Statistical analyses

The characteristics of the two groups were compared using the Pearson chi-square test for categorical variables and Mann-Whitney U test for continuous variables. Cumulative survival rates were compared using a Kaplan-Meier analysis and log-rank tests. The significance level was set at $p<0.05$. No data were missing. All data were analyzed using the SPSS Statistics software program, version 24 (IBM, Armonk, USA).

Results

Patients' baseline characteristics

In total, 116 patients with alcohol-related cirrhosis were admitted to our department. We excluded 13 patients who died during hospitalization and 5 who did not continue follow-up at our hospital after discharge. The final analysis included a total of 98 patients. The median follow-up duration was 501.5 (range: 3-2,903) days. The abstaining group included 57 patients, and the drinking group included 41 patients. The baseline characteristics of the patients in both groups are presented in Table 1. Patients in the drinking group were younger, had a lower body mass index, a lower model for end-stage liver disease (MELD) score, lower serum creatinine levels at baseline, and more frequently had gastrointestinal bleeding as the reasos for the first admission than those in the abstaining group (Table 2). Viable HCC was observed in 10 and 6 patients in the abstaining and drinking groups, respectively.

Cumulative survival rates in the abstaining and non-abstaining groups

The cumulative survival rates of patients in both groups were calculated after excluding patients with viable HCC. There were no missing data for the other patients. No new HCC cases developed during the observation period. The causes of death in the abstaining group were liver failure in 15 cases and pancreatic cancer in 1 case, while the causes of death in the drinking group were liver failure in 8 cases, suicide in 1 case, and death at home in 2 cases. The survival curves of the patients in the abstaining and drinking groups are shown in Figure, and their survival rates at 1, 2, 3, 4, 5, and 6 years after the first discharge are shown in Table 3. The survival rate in the drinking group was significantly higher (56.2%) than that in the abstaining group (51.1%) af-

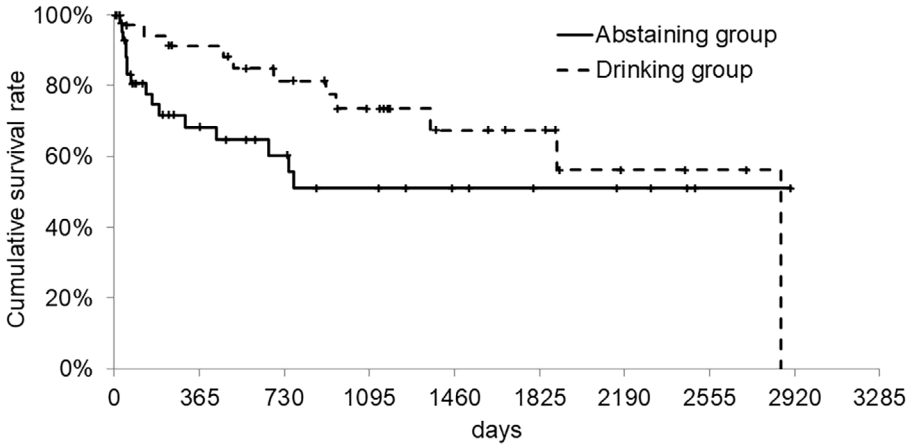
Table 1. Patients' Baseline Characteristics in Abstaining and Drinking Groups.

Parameters	Abstaining group (n=57)	Drinking group (n=41)	p value
Age (years)	61.4±13.8	56.2±11.3	0.043*
Men, n (%)	51 (89.5%)	36 (87.8%)	1.000
Body mass index (kg/m^2)	23.4±4.7	21.0±2.9	0.002*
Presence of viable hepatocellular carcinoma, n (%)	10 (17.5%)	6 (14.6%)	0.701
Child-Pugh score	8.9±2.4	8.3±2.1	0.239
MELD[a] score	12.7±5.1	10.8±3.8	0.043*
Albumin level (g/dL)	2.8±0.7	2.9±0.6	0.406
Total bilirubin level (mg/dL)	2.7±3.2	1.8±1.6	0.292
Creatinine level (mg/dL)	1.0±0.5	0.8±0.4	0.039*
Prothrombin time-international normalized ratio	1.28±0.27	1.23±0.24	0.332

[a]MELD: model for end-stage liver disease

Table 2. Reasons for the First Admission.

Parameters	Abstaining group (n=57)	Drinking group (n=41)	p value
Treatment of complications of cirrhosis, n (%)	26 (45.6%)	13 (31.7%)	0.165
Gastrointestinal bleeding, n (%)	10 (17.5%)	21 (51.2%)	<0.001*
Infection, n (%)	8 (14.0%)	2 (4.9%)	0.255
Treatment of hepatocellular carcinoma, n (%)	6 (10.5%)	3 (7.3%)	0.851
Others, n (%)	7 (12.3%)	2 (4.9%)	0.370



	1 year	2 year	3 year	4 year	5 year	6 year	7 year
Abstaining group	20	15	11	8	6	5	2
Drinking group	30	24	18	11	9	4	3

Figure. Survival curves of patients in the abstaining and drinking groups. The numbers below the curve indicate the numbers of patients who continued follow-up at those time points.

ter 6 years (p=0.021). In addition, the survival rate plateaued in the abstaining group from the third year onward, whereas the survival rate in the drinking group continued to decrease gradually over time.

Discussion

This study elucidated the effects of alcohol abstinence on the cumulative survival of patients with alcohol-related cirrhosis. Only a few studies have evaluated the effects of alcohol abstinence on the cumulative survival in Japan. Fifty-

Table 3. Cumulative Survival Rates in the Abstaining and Drinking Groups.

Duration	Abstaining group (n=47)	Drinking group (n=35)
1 year	68.2%	91.3%
2 years	60.3%	81.3%
3 years	51.1%	73.6%
4 years	51.1%	67.4%
5 years	51.1%	67.4%
6 years	51.1%	56.2%

eight percent of patients abstained from alcohol consumption following discharge from the hospital, a much more promising value than the 80% of people who resort to alcohol consumption following addiction treatment in the general alcohol-dependent population (11). There are some apparent differences between patients with alcohol-related liver disease and the overall population of alcohol-dependent individuals. Many patients with alcohol-related liver diseases may never experience the psychosocial effects of binge drinking or receive a referral for alcohol abuse.

In our study, the survival rate in the abstaining group plateaued from the third year onward, whereas the survival rate in the drinking group continued to decrease gradually over a period of six years. However, the cumulative survival rates were more favorable in the drinking group than in the abstaining group, which may reflect the significant differences in the baseline MELD scores between the groups. The drinking group had a significantly lower MELD score than the abstaining group at baseline, suggesting that the abstaining group may have included patients who wanted to consume alcohol but were not allowed to drink because of their poor health status. A follow-up study on abstinence in patients with alcohol-related liver cirrhosis revealed that patients did not stop consuming alcohol until their cirrhosis had advanced, most likely because of severe cirrhosis-related morbidities (9). Therefore, it is possible that patients with severe alcohol-related cirrhosis were too ill to consume alcohol and might have been included in the abstaining group, whereas those with less severe illnesses were more capable of consuming alcohol and included in the drinking group. In the follow-up study mentioned above, short-term mortality was found to be associated with only cirrhosis severity, expressed as the MELD score, and patient participation in alcohol abuse treatment (9). Thus, the degree of liver disorders tends to affect abstinence and the survival. This supports the introduction of more effective interventions to encourage alcohol abstinence among patients with alcohol-related liver diseases as early as possible during the course of illness, ideally avoiding the development of cirrhosis.

A meta-analysis of 7 cohort studies revealed that alcohol abstinence had no significant effect on the 0.5- or 1-year survival rates but had a significant effect on the 1.5-, 2-, 2.5-, 3-, 3.5-, 4-, and 5-year survival rates (4). Alcohol abstinence for at least 1.5 years was required before a statistically significant difference in the survival could be observed between the abstinent and drinking groups. This is also supported by the findings of our study, wherein the survival rate plateaued in the abstaining group from the third year onward, whereas it continued to decline in the drinking group. The findings of the meta-analysis mentioned above[4] also showed that at least four and three years of alcohol abstinence were required for compensated and decompensated cirrhotic patients, respectively, before a statistically significant difference in the survival could be observed. Furthermore, there may be a threshold effect of alcohol consumption on mortality due to alcohol-related cirrhosis, as suggested by the findings of earlier research, which indicate that persistent heavy drinking, rather than binging or moderate drinking, has a substantial impact on the survival in patients with alcohol-related cirrhosis (12). A previous study in patients with decompensated alcohol-related cirrhosis also reported that moderate drinkers had a similar survival to abstainers and a substantially better prognosis than heavy drinkers (4). Thus, the amount of alcohol consumed appears to affect the survival of patients with cirrhosis. We cannot rule out the possibility that patients with daily alcohol intake below the threshold were included in the drinking group, as no attempt was made to measure alcohol consumption in the current investigation.

Several limitations associated with the present study warrant mention. First, based on the sample size calculation while considering significance (95% confidence level), power (80%), predicted effect size, and variability in the data, the estimated minimum sample size was 110; however, our analyses included data from 98 participants only, which might have affected the findings of our study, potentially rendering them not representative of the general population. Second, abstinence was determined based on self-reported information from patients and their families; therefore, we could not ensure that the abstinence or drinking status was accurate. Third, the patients were enrolled from the Boso Peninsula, Japan. Therefore, our findings may not be generalizable to all patients with alcohol-related LC. Fourth, the patients had different follow-up durations. The median follow-up duration was 501.5 days but varied widely from 3 to 2,903 days. Fifth, our study lacked data regarding the alcohol intake.

In conclusion, the data collected by our hospital retrospectively demonstrated the importance of abstinence on a timescale of years of sustained duration. Our findings suggest that at least two years of alcohol abstinence is required to sustain the survival of patients with alcohol-related cirrhosis.

The authors state that they have no Conflict of Interest (COI).

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