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Retrospective Analysis of demographic and laboratory characteristics of patients with liver cirrhosis: A single center experience

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Abstract

Liver cirrhosis is a progressive, irreversible disease constituted by a decrease in normal hepatocytes, diffuse fibrosis, and regeneration nodules due to liver damage developed by the chronic inflammation process. This study aims to evaluate patients with liver cirrhosis who applied to Çanakkale Onsekiz Mart University (COMU) Hospital and met the criteria in terms of demographic, etiological, and laboratory values. Patient data were recorded from the hospital data recording system that was admitted to COMU hospital between January 1, 2013, and January 01, 2022. A total of 199 patients with liver cirrhosis were included in the study. Of these patients, 38.2% were female, and 61.8% were male. Their mean age was 63.43±10.73 years. When the patients were evaluated with regard to etiological distribution, the top three etiological causes of cirrhosis were cryptogenic, alcohol-induced, and HBV in 27.6%, 27.1%, and 25.1% of patients, respectively. In terms of complications, ascites were detected in 43.2% of the patients, esophageal varices in 56.3%, splenomegaly in 69.3% and hepatic encephalopathy in 7%. Over the years, the number of patients with cirrhosis due to viral hepatitis has decreased due to an increase in viral hepatitis vaccination campaigns and the spread of antiviral treatments. However, due to the rise in chronic alcohol use, alcohol appears more frequently as a significant risk factor for the etiology of liver cirrhosis.

Keywords: Cirrhosis, etiology, demographic factors, MELD score

Introduction

Hepatic cirrhosis is a progressive and irreversible disease characterized by a decrease in normal hepatocyte count, diffuse fibrosis, and formation of regeneration nodules due to hepatic damage developing from chronic inflammation [1,2]. Clinical symptoms and findings of hepatic cirrhosis are hepatic cell dysfunction, portosystemic shunts, and portal hypertension. Hepatic cirrhosis is the 10th–15thleading cause of mortality globally. The mortality rate increases with age. Additionally, hepatic cirrhosis is the most common cause of hepatic cancer. It has been demonstrated that 3–4% of all deaths are caused by hepatic cirrhosis when calculated together with hepatic cancer [3,4].

A review of the Turkish Statistical Institute's (TÜİK) 2017 data reports a mortality rate of 0.5¬–1% due to chronic liver disease among all mortalities in Turkey. In developing countries like ours, the most common etiology of hepatic cirrhosis is chronic viral hepatitis [5,6]. In our country, the incidence of hepatic cirrhosis due to chronic hepatitis B, C, and delta is 50–55%, followed by alcohol-induced, cryptogenic, and others: 15–20%, 15–20%, and 9–10%, respectively [7,8].

The expected complications in hepatic cirrhosis are as follows: ascites and spontaneous ascites infections, portal hypertension (esophageal variceal hemorrhages), hepatic failure, hepatic encephalopathy, hepatocellular carcinoma,

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hypersplenism, hepatorenal syndrome, hepatopulmonary syndrome, hematological disorders, infections, gastrointestinal complications, endocrine disorders [9,10]. Many scoring systems have been developed in patients diagnosed with hepatic cirrhosis for the identification of patients with poor prognosis, involving clinical and laboratory tests for follow-up. The most commonly used scoring systems are the Child-Pugh classification and the MELD score.

The main objectives in treating cirrhosis are to slow or revert the progression of the disease, prevent and treat complications, and establish the compatibility and timing of liver transplantation. Liver transplantation is the most effective treatment method for hepatic cirrhosis.This study aims to evaluate the demographic, etiological, and laboratory values of patients with hepatic cirrhosis who presented to COMU Hospital.

Material and Methods

Design and Settings

The study includes 199 patients who presented to COMU Faculty of Medicine Hospital between January 1, 2013, and January 01, 2022, and were diagnosed with hepatic cirrhosis. This study excluded patients who lacked information in their files and were under 18 years of age. Ethics committee approval of number 04-12, dated March 2, 2022, was received from the COMU Clinical Trials Ethics Committee.

The etiological subtype of hepatic cirrhosis was categorized and recorded as hepatitis B, hepatitis C, alcohol-induced, cryptogenic, autoimmune PBS, Budd-Chiari, Non-Alcoholic SteatoHepatitis (NASH), and splenic vein thrombosis. The following information from the patients' initial applications was recorded: age, gender, tobacco use, alcohol use, Child-Pugh, MELD scores, presence of complications due to hepatic cirrhosis (ascites, splenomegaly, esophageal varices, HCC development, etc.), transplantation status, fatality, and laboratory values. Possible causes and available examinations were investigated to evaluate the patients regarding etiological factors. Initially, the patients were evaluated for HBV and HCV using the ELISA technique to test HBsAg, HBV-DNA, anti-HCV, and HCV-RNA in serum. Autoimmune hepatic cirrhosis in patients with negative viral parameters was investigated by testing ANA, ASMA, and LKM-1 antibodies in serum. In patients presenting symptoms suggestive of alcoholic cirrhosis, their history of alcohol use for the past 10 years was investigated in detail. Patients with no alcohol use were investigated for NASH, presence of diabetes, and metabolic syndrome. Moreover, their abdominal USG results were reviewed. In patients with symptoms suggestive of Budd-Chiari syndrome, portal vein doppler USG results were reviewed retrospectively. Finally, 55 patients with negative test results and no etiological cause were accepted as having cryptogenic cirrhosis.

A flow-cytometry devicewith a hematology system, the Shenzhen Mindray (Bio-Medical Electronics Co, Ltd. / China), was used to analyze whole blood count parameters. In addition, the Japanese Roche Cobas 8000 auto-analyzer was used to analyze the biochemical parameters (sodium, potassium, creatinine, urea, total bilirubin, direct bilirubin, albumin, ALT, AST, and CRP).

Statistical Analysis

The data of the study were transferred to the SPSS 26.0 statistics program, where data control and analysis were performed. Frequency, percentage, mean, standard deviation, median, and minimum and maximum values were used in the presentation of descriptive data. The chi-square test was used in statistical comparisons. Statistical significance was accepted as $p<0.05$.

Results

The study included 199 patients: 76 (38.2%) females and 123 (61.8%) males. Out of 199 patients, 97 (48.7%) were under 65 years, and 102 (51.3%) were above 65 years; 116 (58.3%) were smokers, while 83 (41.7%) were non-smokers; 79 (39.7%) used alcohol, and 120 (60.3%) did not use alcohol. Table 1 demonstrates the distribution of sex, age, tobacco, and alcohol use.

Table 1. Demographic analysis of patients with cirrhosis

Variables	Number	%
Gender		
Female	76	38.2
Male	123	61.8
Age (Year)		
Under 65	97	48.7
65 years and older	102	51.3
Tobacco		
Smoker	116	58.3
Non-smoker	83	41.7
Alcohol consumption		
Alcoholic	79	39.7
Non-alcoholic	120	60.3
Total	**199**	**100**

When the patients were evaluated with regard to etiological distribution, the top three etiological causes of cirrhosis were cryptogenic, alcohol-induced, and HBV in 55 (27.6%), 54 (27.1%), and 50 (25.1%) patients, respectively. Figure 1 demonstrates the etiological distribution of patients diagnosed with cirrhosis.Table 2 demonstrates the laboratory valuesof patients diagnosed with cirrhosisat the time of first presentation.

When complications were investigated, the development of esophageal varices, HE, HRS, splenomegaly, SBP, ascites, and HCC was observed in 112 (56.3%), 14 (7%), 37 (18.6%), 138 (69.3%), 8 (4%), 86 (43.2%), and 16 (8%) patients, respectively. Figure 2 demonstrates the distribution of complications.

This study evaluated the distribution of cirrhosis complications by gender: the number of patients with splenomegaly, esophageal varices, and ascites was 84 males and 54 females, 67 males and 45 females, and 49 males and 37 females, respectively. Additionally, complications and gender were evaluated with the chi-square testin patients diagnosed with cirrhosis; however, there was

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no statistically significant difference. Table 3 demonstrates the evaluation of the distribution of complications and gender with a chi-square test.

Table 2. Laboratory values at the time of first presentation in patients diagnosed with cirrhosis

	Average	Std Deviation	Minimum	Maximum	Median
Hgb (g/dl)	11.79	2.33	5	17.2	12
Wbc (x10³/ul)	6.11	4.92	1.5	56	5.5
Plt (x10³/ul)	131.19	90.46	14	810	104
Na (mmol/l)	138.91	4.07	125	149	139
K (mmol/l)	4.5	0.51	2.78	5.8	4.57
Creatinine (mg/dl)	0.98	0.54	0.4	4.7	0.84
Urea(mg/dl)	38.87	28.07	7	222	30
Total Bilirubin (mg/dl)	1.79	1.82	0.2	18	1.3
Albumin (g/dl)	3.59	0.7	1.9	5	3.64
ALT (U/L)	30.06	24.02	5	129	23
AST (U/L)	46.34	40.58	8	273	34
INR	1.28	0.27	0.7	2.82	1.21
CRP (mg/dl)	1.97	6.91	0.1	91	0.5

(Hgb: Haemoglobin, Wbc: White Blood Cell, Plt: Platelet, Na: Sodium, K: Potassium, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, INR: International Normalized Ratio, CRP: C-Reactive Protein)

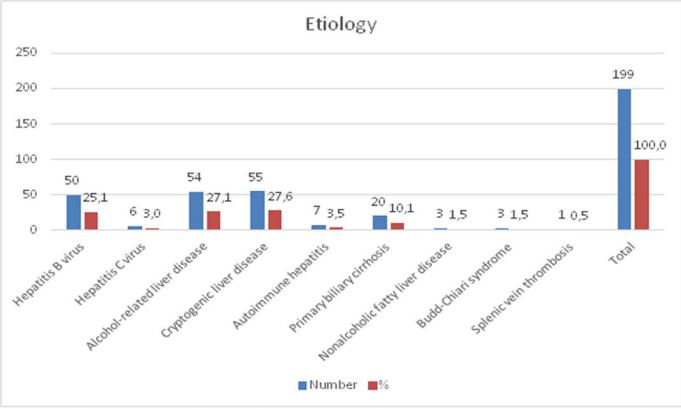

Figure 1. Distribution of etiology in patients diagnosed with cirrhosis

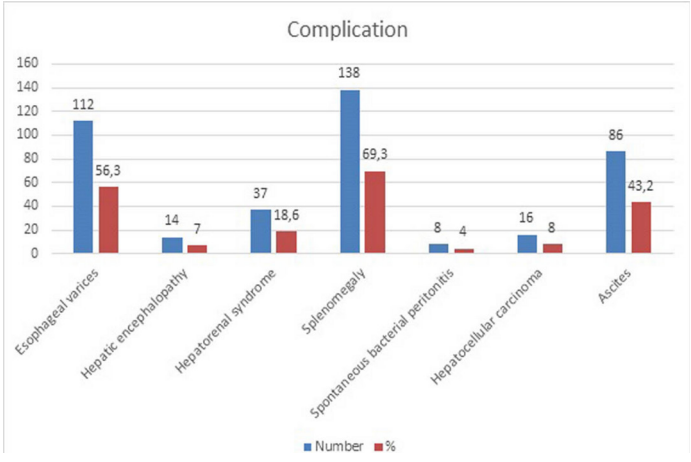

Figure 2. Distribution of complications in patients diagnosed with cirrhosis

Table 3. Distribution of complications and gender in patients diagnosed with cirrhosis

Complication	Male	Female	Total	p
Esophageal varices	67	45	112	0.513
Hepatic encephalopathy	11	3	14	0.109
Hepatorenal syndrome	19	18	37	0.147
Splenomegaly	84	54	138	0.682
Spontaneous bacterial peritonitis	12	4	16	0.375
Hepatocellular carcinoma	7	1	8	0.099
Ascites	49	37	86	0.413

p: chi-square test

Patients were evaluated in terms of mortality, transplantation, and HCC frequency in our study.Out of 199 patients,liver transplantation was performed on 11 (6%), the frequency of HCC was 8%, and the mortality rate was 7%. Table 4 demonstratesthe frequency of mortality, transplantation, and HCC.

Table 4. Frequency of mortality. transplantation and hcc in patients diagnosed with cirrhosis

Mortality	Number	%
Live	185	93
Exitus	14	7
Total	199	100
Transplantation		
Transplanted	11	5.5
Non-transplanted	188	94.5
Total	199	100
Hepatocellular carcinoma		
HCC	16	8
Non-HCC	183	92
Total	199	100

(HCC: Hepatocellular carcinoma)

When classified according to Child-Pugh score and groups, which help determine the course of the disease and estimated life expectancy in patients with hepatic cirrhosis, 114 (57%) were evaluated as Child A, 66 (33%) as Child B, and 19 (9%) as Child C. Figure 3 shows the Child-Pugh classification according to the etiology of hepatic cirrhosis.

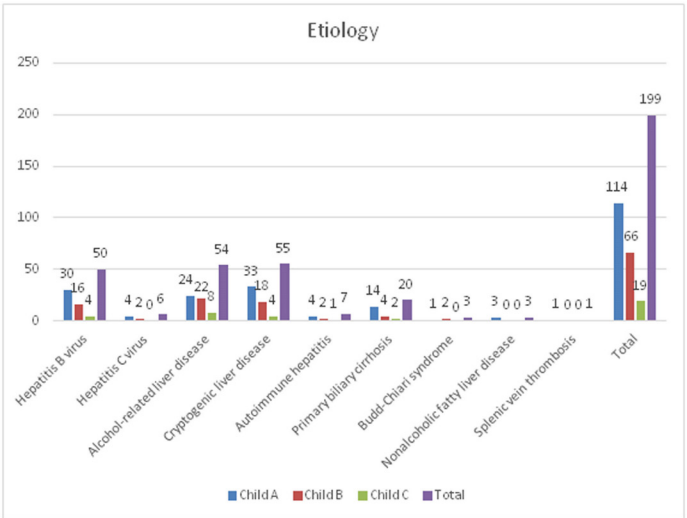

Figure 3. Distribution of child-pugh classification by etiology in patients diagnosed with cirrhosis

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Discussion

This study investigated the etiology, demographic characteristics, and laboratory parameters of 199 patients who were admittedto ÇOMÜ Faculty of Medicine Hospital between January 1, 2013, and January 01, 2022, with a hepatic cirrhosis diagnosis.

The mean age of the patients in our study was 63.43±10.73. In a study conducted by Sajja KC et al. in the USA, involving 2,048 patients between 2001 and 2011, the mean age of the patients was 52±11 [11].In another study conducted on 57,769 patients between 2011 and 2018 in Japan, the mean age of the patients was 69.2±12.4 [12]. In a study conducted in our country by Karakütük on 505 patients between 2000 and 2014, the mean age of the patients was 60.8±10.8 [13]. These studies show that even though the average age of cirrhosis varies between 60 and 65 years, the onset may occur earlier due to geographical conditions and an increase incases of alcoholic cirrhosis. Although there were many patients with alcoholic hepatic cirrhosis in our study, there was no significant difference in the age of onset.

This study included 199 patients: 76 (38.2%) were females, and 123 (61.8%) were males. In a multi-center cohort study in the USA, the distribution of hepatic cirrhosis by gender was evaluated.This study observed that, in centers included in the study, the distribution of patients by gender was between 59.3% and 70%, in favor of male gender [14]. Zatonski et al. conducted a broad evaluation of European studies, including more than 100,000 patients between 1959 and 2002.This study also demonstrated a predominance of hepatic cirrhosis in the male gender [15].

In our study, we think that the male gender predominance is due to the high rates of alcohol intake in the Çanakkale region, similar to the findings of studies conducted in Europe and the USA. Gender distributions appear to be more balanced in regions where viral hepatitis is a more common etiology than other types. In a study conducted by Toz et al. in our country, the ratio of men and women was shown as balanced [16].

In addition, we think that in regions where viral hepatitis is high in etiology and where the socioeconomic development level is low, the gender distribution is more evenly distributed.The top three causes in the etiology of patients included in our study were alcohol-induced, HBV, and cryptogenic cirrhosis in 54 (27.1%), 50 (25.1,and 55 (27.6%) patients, respectively. The first factor in European- and American-based studies is alcohol consumption and NASH. However, in the Middle East, Far East, Africa, and in our country, viral hepatitis is the leading etiology due to lower socioeconomic development, less alcohol consumption, and fewer routine liver biopsiesthan on the European and the American continents.

Michiataka et al. (2009) compiled data from 58 hospitals and 33,379 patients in Japan. They found viral hepatitis 74.5%, alcohol 13.6%, and PBS 2.4% to be the top three leading etiological causes [17]. Based on these results, we think that even though the main cause of hepatic cirrhosis in Japan and Far Eastern countries like Japan, continues to be viral hepatitis, socioeconomic changes, increase in early diagnosis, and treatment of viral hepatitis and the increase in alcohol consumption may cause changes in etiological causes over time.

In a study conducted by Mendez et al. in Mexico, in 1,486 patients, the top three leading etiological factors were found to be alcohol at 39.5%, HCV at 36.6%, and cryptogenic at 10.4% [18]. In a study conducted by Scaglione et al. between 1999 and 2010 in the United States, the top three leading causes were found to be alcohol, HCV, and NASH [19]. An evaluation was performed in 2003 by Ökten et al. in our country in 573 patients: viral hepatitis, cryptogenic cirrhosis, and alcohol were evaluated as 55%, 16.4%, and 12.4%, respectively [20]. Furthermore, a study was conducted in 2015 by Karakütük et al. in Aydın involving 505 patients: viral hepatitis, cryptogenic cirrhosis, and alcohol were evaluated as 41%, 23%, and 20.3%, respectively [13]. In a study conducted in Erzurum by Topdağı et al. in 2012 involving 100 patients, viral hepatitis, cryptogenic cirrhosis, and alcohol were evaluated as 63%, 26%, and 2%, respectively [21].

Being a developing country with a low socioeconomic level compared to Europe and the USA, in our country, viral hepatitis remains the leading etiology. However, as observed in these studies, we see various differences between the eastern and western parts of the country. We think that the reason is thatsocioeconomic development and alcohol consumption are higher in the country's western part than in the eastern part. In our study, even though the incidence of viral hepatitis is high in accordance with the literature, we demonstrated that alcoholic cirrhosis is more common in our region. We consider that this is due to the higher level of socioeconomic development and high alcohol consumption in Çanakkale and its surroundings.

In our study, splenomegaly, esophageal varices, and ascites were observed in 69.3%, 56.3%, and 43.2% of the patients, respectively, as the top three complications of cirrhosis. In a study conducted in 2020 by Yanaş et al. in our country involving 270 patients in Istanbul, esophageal varices were found in 72% of patients, ascites in 40%, and hepatic encephalopathy in 13%, which were listed as the top three complications [22]. In Germany, in a study conducted in 2014 by Sivanathan et al. involving 236 patients, esophageal varices were found in 60%, ascites in 49%, and hepatic encephalopathy in 25% of patients [23]. Thus, in terms of complication rates, our study revealssimilar results to other similar studies.

Studies have shown that the incidence of NASH in the general population ranges from 1.2%–4.8%. However, it increases by up to 74% in populations with a high prevalence of obesity and diabetes [24]. Although diabetes and obesity rates are high in the general population in our country, the rate of NASH has been found to be 1.5% in our study. One reason this rate is lower than expected at our hospital may be due to not performing routine biopsies on patients with hepatic cirrhosis. Therefore, we think

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that some patients in our study evaluated with cryptogenic cirrhosis have NASH.

In our study, the rate of cryptogenic hepatic cirrhosis was determined as the etiologyin 27.6% of cases. According to the studies performed, we think this rate is higherdue to the lack of performance of routine liver biopsies. Some studies demonstrate that some of these cases occur due to NASH, autoimmune hepatitis, and occult ethanol use [25].

Child-Pugh scores and group classification help determine the course of the disease and the estimated life expectancy in patients with hepatic cirrhosis.In our study, 57% of the patients were evaluated as Child A, 33% as Child B, and 9% as Child C. In a study conducted in 2015 by Karakütük in Aydın, 38% of the patients were determined to be Child A, 39%were Child B, and 22% were Child C (13). The literaturehas demonstrated 52% of patients to be Child A, 36% Child B, and 12% Child C, similar to our study [26].

The patients participating in this study were evaluated by MELD scoring as a prognostic indicator during transplantation: 59.8%, 32.7%, 5.5%, and 2% of the patients had a MELD score of <10, 11–18, 19–24, and >25, respectively. The MELD scores of our study participants are similar.

Patients with hepatic cirrhosis are 60–70% likely to develop esophageal varices. The detection rate of esophageal varices at the time of diagnosis is around 50% [27]. Esophageal variceal bleeding is the most fatal complication of hepatic cirrhosis, with a 20–30% mortality rate. Therefore, it is very important to detect esophageal varices at the time of the first presentation ofhepatic cirrhosis and to start prophylactic treatment. In a study conducted by Madhotra et al. involving 184 patients in the USA, the rate of esophageal varices at the time of first presentation was shown to be 51% [28]. In the study conducted in 2017 by Dinçer Aydın involving 510 patients in Malatya, this rate was 47.7% [29] and in a study conducted in 2020 by Yanaş involving 270 patients in Istanbul, the rate was 72% [22]. In our study, the frequency of esophageal varices at the time of the first presentation was determined as 56.3%. This rate is similar to the studies in the literature.

Hepatocellular carcinoma is the most common primary liver malignancy and one of the leading causes of cancer-related deaths worldwide. According to the literature, the frequency of HCC development is considered to be between 10–12% [30]. As the years progress, this rate increases due to the development of diagnostic techniques and the longer duration of patient follow-up [31]. In our study, the rate of patients with hepatic cirrhosis with HCC was determined as 8%. This rate is lower than in the literature.

Hepatic encephalopathy is a cirrhosis complication that has a high mortality rate and shows that the disease has progressed to decompensation. Approximately 25–30% of patients diagnosed with hepatic cirrhosis die due to hepatic encephalopathy. The most common factors leading to hepatic encephalopathy include gastrointestinal bleeding, infections, dehydration, and other complications [32]. Grattagliano et al. reviewed the relevant literature between 1985 and 2010, demonstrating in their 2011 study that the incidence of hepatic encephalopathy at the time of initial diagnosis was 10–14% and, during the follow-up, 15–21% [33].

In our study, the frequency of hepatic encephalopathy was determined to be 18.6%. In our country, the situation was determined as follows at the time of the first application. In a study conducted by Karakütük in 2015 involving 505 patients in Aydın, this rate was found to be 17% and 13% in a 2020 study conducted by Yanaş involving 270 patients in Istanbul. In our study, the frequency of hepatic encephalopathy is consistent with the literature, and our findings indicate that a higher rate of hepatic encephalopathy was observed at the time of the first presentation compared to other studies in our country.

In our study, ascites development rate was determined to be 43.2%. In a study conducted by Moore et al. in the USA, the rate of ascites development was shown to be 50% [34]. In our country, in a study conducted in 2021 by Demirbaş et al. involving 85 patients in Rize, the rate of ascites development was found to be 56.6% [35]. In a 2022 study conducted in Konya involving 120 patients, this rate was found to be 45.8% [36]. This reveals that the rate of ascites development in our study is similar to the literature.

Currently, liver transplantationis an effective treatment of hepatic cirrhosis. Of the 199 patients who participated in our study, 11 patients (6%) underwent liver transplantation. In a2017 study conducted by Dinçer Aydın involving 510 patients in Malatya, this rate was found to be 33.3%. In our study, the reason for the low rate of liver transplantation is due to the fact that liver transplantation is not yet performed in our center, and the number of cadaveric transplants is low because of COVID-19.

Conclusion

In summary, although viral hepatitis is still considered the most common etiology of hepatic cirrhosis in our country, it is being replaced by alcoholic hepatic cirrhosis due to early diagnosis and advancements in antiviral therapies. These top two reasons in etiology are followed by NASH. Since hepatic cirrhosis is a disease with high morbidity and mortality rates, early diagnosis of the disease would reduce morbidity and mortality.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Ethics Board aproval was obtaine from Canakkale Onsekiz Mart University Ethical Board (Date: 02.03.2022; No: 2022-04).

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