

RESEARCH NOTE

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# Dietary Approaches to Stop Hypertension (DASH) and mortality risk among patients with liver cirrhosis: a prospective cohort study

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## Abstract

**Background and purpose** The relationship between dietary patterns and cirrhosis is undeniable. The present study aimed to investigate the association between the Dietary Approaches to Stop Hypertension (DASH) diet and the risk of mortality in patients with cirrhosis prospectively.

**Methods** In this cohort study, 121 cirrhotic patients were enrolled and followed up annually for four years. Nutritional status and dietary intakes were assessed initially, and the DASH score was calculated accordingly. Crude and multivariable-adjusted hazard ratios (HR) with 95% confidence intervals (CI) were estimated using Cox proportional hazard analyses.

**Results** DASH components including fruits, vegetables, legumes, nuts and seeds, and low-fat dairy products were significantly associated with lower mortality risk in cirrhotic patients. Also, a higher DASH score was significantly associated with a reduction in the risk of mortality in patients with cirrhosis, so that after adjusting for all confounders, the risk of mortality in the upper tertile was 89% lower than the first tertile (HR = 0.11, 95% CI: 0.03–0.42,  $P$  trend < 0.001). The 4-year survival rate among patients across tertiles of DASH was 32%, 37%, and 46%, respectively ( $P = 0.005$ ).

**Conclusion** It can be concluded that a higher DASH diet score may be associated with a reduced risk of mortality in cirrhotic patients. However, larger studies are needed to confirm the findings and determine their potential mechanisms.

**Keywords** Cirrhosis, DASH, Mortality, Survival

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## Introduction

The prevalence of liver diseases is estimated at about 1.3 billion people worldwide, and Asian countries have one of the highest prevalence rates [1]. Cirrhosis is a chronic liver disease that can be resulted from various causes, including obesity, metabolic disorder-associated steatotic liver disease (MASLD), high alcohol consumption, viral hepatitis, autoimmune diseases, cholestatic diseases, and metabolic disorders [2]. This disease is characterized by the gradual replacement of healthy hepatic tissue with fibrotic tissue and nodules, which leads to portal hypertension. Cirrhosis can progress from the compensated phase, during which there are no symptoms, to a decompensated phase, during which complications such as ascites, variceal bleeding, hepatic encephalopathy, and hepatocellular carcinoma can arise [3]. These complications can significantly affect an individual's quality of life and increase the risk of mortality [4]. Cirrhosis is a major public health concern worldwide, affecting millions of people and leading to high rates of morbidity and mortality [1, 5]. While the etiology of cirrhosis is multifactorial, the underlying pathophysiology is characterized by chronic inflammation and fibrosis of the liver tissue [6].

Management of cirrhosis typically involves a combination of pharmacological and non-pharmacological interventions. A dietary modification is the cornerstone of a successful disease management program. The Dietary Approaches to Stop Hypertension (DASH) diet is a dietary pattern that has been shown to have several health benefits, including the potential to improve liver function and reduce the risk of complications in patients with cirrhosis [7]. The DASH diet mainly focuses on increasing consumption of whole grains, fruits, vegetables, low-fat dairy, lean protein sources such as fish, poultry, plant-based protein such as nuts, seeds, and legumes, and reducing consumption of fats and oils. This dietary pattern is rich in antioxidants, fiber, micro-nutrients, and nitrates while being low in sodium, saturated fats, and added sugars [7, 8].

A wide range of health benefits of the DASH diet have been demonstrated, including reductions in inflammation [9, 10], oxidative stress [11], systolic and diastolic blood pressure, body fat content, fasting blood glucose, insulin, and leptin concentrations [12, 13], and modification of serum lipid profile [14]. Therefore, according to these potential mechanisms, the DASH diet seems to be a beneficial dietary approach for the prevention and management of cirrhosis-related complications and mortality.

As far as we can discover, limited data is available regarding the association between different dietary patterns, especially DASH, and the risk of mortality in patients with cirrhosis. A knowledge gap is therefore evident in addressing the appropriate dietary intake in

order to reduce mortality in cirrhosis. In the present study, assuming the potential role of the DASH diet in improving the risk factors and reducing the mortality and complications of cirrhosis, the relationship of this dietary pattern with the risk of mortality in patients with cirrhosis has been investigated prospectively.

## Methods and materials

### Study population

This cohort study, which began in 2016 and ended on April 30, 2022, included 166 patients with cirrhosis diagnosed within the last 6 months. Cirrhosis was diagnosed by a hepatologist based on biopsy results. The patients were recruited from outpatient clinics of Ayatollah Taleghani and Shariati hospitals, which are affiliated with Shahid Beheshti University of Medical Sciences and Tehran University of Medical Sciences, respectively. After assessing the inclusion and exclusion criteria, a total of 121 cirrhotic patients were enrolled in the study and followed up annually for a duration of 4 years. 45 patients were excluded because of cancer diagnosis in the first year ( $n=2$ ), death due to other causes ( $n=4$ ), lost to follow-up ( $n=2$ ), unwillingness, missing or incomplete information ( $n=31$ ). During the follow-up period, participants were contacted annually via telephone to complete follow-up questionnaires, providing information on the occurrence of death, cause of death, medical events (such as liver transplant) or any additional morbidity. At the end of the 4-year follow-up, the survival and mortality rates were calculated.

Individuals who met any of the following criteria were excluded from the study: being pregnant or breastfeeding, having a chronic heart disease, kidney failure, pancreatic insufficiency, diabetes mellitus, chronic and severe infectious diseases such as tuberculosis or AIDS, malignancies, or acquired immunodeficiency. Additionally, participants with unusual daily calorie intake (less than 500 or more than 5000 kilocalories per day) or with a body mass index (BMI) below 15 or above 50 kg/m<sup>2</sup> were not included in the final analysis. Furthermore, individuals who were diagnosed with cancer within the first year or had incomplete dietary and basic information were also excluded from the study.

The National nutrition and Food Technology Research Institute (NNFTRI) ethics committee approved the study protocol (IR.SBMU.NNFTRI.1396.186.). All participants provided written informed consent and were informed about the study.

### Dietary assessment

At the beginning of the study, dietary intakes were assessed through face-to-face interviews using a validated and reliable food frequency questionnaire (FFQ) [15]. In this study, FFQ data was used to analyze the

dietary pattern. This is because nowadays the FFQ has become the main method of dietary assessment in large population studies. The advantages of FFQ compared to other methods are: ease of data analysis compared to open-ended dietary methods such as food records, less expensive administration of FFQ, and better access in wider populations. Another important advantage of the FFQ is that by summarizing data over a longer period of time, it can describe the usual diet better than assessments over shorter periods. This FFQ consisted of 168 items, which allowed participants to report their usual portion size, amount, and the frequency of each food item. The consumption of each food item was recorded on a daily, weekly, and monthly basis, and the data were converted to grams using a household scale. To analyze the collected dietary data, Nutritionist IV software was utilized. This software used the food composition table (FCT) of the United States Department of Agriculture (USDA) to calculate the energy and nutrient content of reported foods. However, for traditional Iranian foods that were not included in the USDA FCT, the Iranian food composition table was used as an alternative source of information.

The DASH (Dietary Approaches to Stop Hypertension) score was calculated based on the reported dietary intake data [16]. This score is a tool that assesses adherence to a diet that is rich in fruits, vegetables, whole grains, lean proteins, and low-fat dairy products, while limiting sodium, sugary beverages, and high-fat foods. First, all these eight components were converted into quintiles. Intake of whole grains, fruits, vegetables, legumes, nuts and seeds, and low-fat dairy was then scored according to the quintile of intake, i.e. 1 point for the lowest quintile and 5 points for the highest. While for sodium, red and processed meats, as well as sugar-sweetened beverages, the reverse scoring of the quintile was considered. In this way, the highest score was given to those who received the lowest quintile and the lowest score to those who received the highest quintile. Finally, the DASH score was obtained from the sum of the scores of these eight components (ranges 8–40). The DASH score was then divided into tertile, allowing for further analysis and comparison within the study population.

#### Potential confounders

The primary variables collected in this study were: age, sex, smoking and alcohol consumption, subjective global assessment (SGA), body mass index (BMI), cause of cirrhosis, model for end-stage liver disease (MELD) and Child-Pugh score at enrollment. The weight of each patient was measured using a digital scale with an accuracy of 0.5 kg. Measurement was performed with minimal clothing. Height was measured without shoes using a portable stadiometer with an accuracy of 0.1 cm. Based

on the weight and height values, the BMI was calculated by dividing the weight (in kilograms) by the square of the height (in meters). The nutritional status of each patient was estimated using the SGA, which classified patients into categories A (well-nourished), B (moderately malnourished), and C (severely malnourished), as determined by the assessment criteria developed by Detsky et al. [17]. Child-Pugh and MELD scores were used to evaluate the severity and prognosis of liver cirrhosis, respectively.

#### Statistical analysis

The study applied different statistical methods to analyze the data and explore the relationship between DASH score and mortality in patients with cirrhosis. Participants were categorized into three groups based on their DASH scores. For quantitative variables, one-way analysis of variance (ANOVA) was conducted to compare the baseline characteristics. On the other hand, chi-squared ( $\chi^2$ ) test was used for qualitative variables. To estimate the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality in patients with cirrhosis associated with DASH scores, Cox proportional hazards regression models were employed. The proportional hazard assumption was fulfilled according to Schoenfeld residuals and we found no sign of violation. The models were adjusted for potential confounding factors in a stepwise manner. Model 1 included adjustments for age (continuous) and gender (male, female). Model 2 was additionally adjusted for energy intake (continuous), BMI (continuous), smoking (yes, no), and alcohol consumption (yes, no). Model 3 was further adjusted for cause of cirrhosis (virus, autoimmune, other), MELD (continuous), SGA (A, B, C), and Child-Pugh score (A, B, and C). The *P*-trend was determined using the median of each tertile. The statistical analyses were performed using SPSS software (version 19; SPSS Inc, Chicago, IL, USA), and a significance level of  $\alpha=0.05$  was used.

#### Results

The mean age  $\pm$  standard deviation (SD) of the participants at the beginning of the study was  $54.8 \pm 9.11$  years. Out of the total participants, 31.4% were women. Also, 52.9% of cirrhosis was attributed to viral hepatitis. During the follow-up period, 43 deaths were recorded, of which 7 were women and 36 were men. The causes of these deaths were reported as follows: 47% were attributed to liver failure, 40% to cardiovascular diseases, 3% to cancers, and 10% to other causes. The participants had an average daily calorie intake of 1900 kcal. The average BMI was  $27 \text{ kg/m}^2$  with 37% classified as normal weight, 38% as overweight, and 25% as obese. Among the participants, 22% reported alcohol consumption, while

**Table 1** Characteristics of participants according to DASH score tertile

	T1	T2	T3	P value
Men, %	81	58	59	0.061
Age (y)	57.6 ± 12.7	51.1 ± 12.4	55.5 ± 10.1	0.070
Etiology of cirrhosis				0.023
Virus	66	48	50	
Autoimmune	20	32	49	
Other	14	20	1	
MELD score	13.5 ± 4.8	12.1 ± 4.6	11.3 ± 5.8	0.218
Child Pugh category (A/B/C)	%			0.497
A	70	64	78	
B, C	30	36	22	
Alcohol drinker	21	16	29	0.430
Smoker, %	47	44	26	0.176
Weight, kg	70.6 ± 12.4	72.3 ± 19.2	74.5 ± 17.2	0.617
Height, cm	166.9 ± 8.2	164.9 ± 7.6	162.7 ± 9.3	0.103
Body mass index, kg/m <sup>2</sup>	25.6 ± 4.4	26.6 ± 5.8	28.2 ± 5.5	0.113
Subjective global assessment				0.590
A	24	27	41	
B	60	54	47	
C	16	19	12	
Energy intake (Kcal/day)	2533 ± 695	2561 ± 887	2137 ± 635	0.035
Carbohydrate %	58.6 ± 5	58.5 ± 6	61.8 ± 4.2	0.004
Protein%	13.7 ± 2.3	14.7 ± 2.8	15.3 ± 2.3	0.022
Fat%	28.1 ± 4.5	26.6 ± 4.5	22.8 ± 4.8	< 0.001
DASH score	19.7 ± 2.6	24.7 ± 1.2	30.2 ± 2.2	< 0.001

Values are means ± SDs for continuous variables and percentages for categorical variables.

ANOVA for quantitative variables and  $\chi^2$  test for qualitative variables

**Table 2** Hazard ratios for total mortality, according to DASH score components

	Tertiles			P trend
	T1	T2	T3	
Fruits	1 (ref)	0.53 (0.27–1)	0.42 (0.18–0.99)	< 0.001
No. of deaths	24	15	4	< 0.001
Vegetables	1 (ref)	0.85 (0.42–1.72)	0.66 (0.31–1.42)	< 0.001
No. of deaths	22	16	5	< 0.001
Legumes, nuts and seeds	1 (ref)	0.69 (0.35–1.36)	0.26 (0.11–0.61)	0.002
No. of deaths	22	14	7	0.003
Whole grains	1 (ref)	0.80 (0.36–1.76)	1.10 (0.56–2.31)	0.599
No. of deaths	14	11	17	0.632
Low fat dairy	1 (ref)	0.58 (0.31–1.11)	0.13 (0.04–0.42)	< 0.001
No. of deaths	23	16	4	< 0.001
Red and processed meats	1 (ref)	1.60 (0.69–3.61)	2.18 (0.98–4.82)	0.054
No. of deaths	8	15	20	0.039
Sweet beverages	1 (ref)	1.61 (0.75–3.41)	1.41 (0.67–2.96)	0.363
No. of deaths	10	20	13	0.271
Sodium	1 (ref)	1.87 (0.93–3.92)	1.25 (0.56–2.77)	0.554
No. of deaths	11	18	14	0.124

Cox proportional hazards regression

39% reported smoking. The average DASH score was  $19.7 \pm 2.6$  (Table 1).

The HRs (95% CI) of the relationship between DASH score components with the risk of mortality in patients with cirrhosis are presented in Table 2. Regarding fruits consumption, the analysis revealed that individuals in the

last tertile (highest intake) had a 58% lower risk of death from cirrhosis compared to those in the first tertile (lowest intake) (HR=0.42,  $P$  trend < 0.001). Similarly, for vegetables consumption, the study found that individuals in the third tertile had a 34% lower risk of death from cirrhosis compared to those in the first tertile (HR=0.66,  $P$

trend < 0.001). Also, individuals who consumed the most seeds and legumes (third tertile) had a 74% lower risk of death from cirrhosis compared to those who consumed the least amount (first tertile) (HR = 0.26,  $P$  trend = 0.002). This association was not statistically significant for whole grains, beverages and sodium. Regarding low-fat dairy consumption, individuals in the third tertile had an 87% lower risk of mortality from cirrhosis compared to those in the first tertile (HR = 0.13,  $P$  trend < 0.001).

Table 3 presents the multivariate-adjusted hazard ratios (HRs) with a 95% confidence interval for mortality from cirrhosis in different models based on the DASH score. In general, the findings of this table indicate that a higher DASH score was significantly associated with a reduced risk of mortality in patients with cirrhosis. In Model 3, it was observed that individuals in the third tertile of the DASH score had an 89% lower risk of death from cirrhosis compared to those in the first tertile (HR = 0.11,  $P$  trend < 0.001).

The association between DASH score and risk of mortality is shown in Fig. 1. A higher DASH score was significantly associated with a reduced risk of mortality, regardless of BMI, disease severity, and malnutrition.

According to Fig. 2, which displays the Kaplan-Meier survival curve for death in cirrhotic patients categorized by the DASH score, the 4-year survival rates for patients in the first, second, and third tertiles of the DASH score were estimated as 32%, 37%, and 46%, respectively. The statistical analysis indicated a significant association ( $P = 0.005$ ) between the DASH score and survival rate.

## Discussion

Our findings demonstrated that the DASH diet was significantly associated with a reduced risk of mortality in patients with cirrhosis. Also, the examination of the components of the DASH diet indicated a significant relationship between the intake of fruits, vegetables, legumes, nuts and seeds, and low-fat dairy products with reducing the risk of mortality in patients with cirrhosis. The association of red and processed meats with increased

mortality risk was close to the significance level. The DASH diet emphasizes the intake of whole grains, fruits, vegetables, lean proteins, and low-fat dairy products, which ample of evidence of its effectiveness in improving liver function and reducing the risk of cirrhosis-related complications have been provided [18–21].

Although limited studies have investigated the relationship between DASH dietary pattern and the risk of mortality in cirrhotic patients, these findings are consistent with some previous studies. In a cohort study with 2959 patients with non-alcoholic fatty liver disease (NAFLD) (including 509 patients with cirrhosis), an inverse association between higher DASH scores and the risk of NAFLD progression was shown. Also, this association was stronger for cases of NAFLD with cirrhosis than for NAFLD without cirrhosis [22]. Furthermore, a significant relationship has been reported between DASH diet and improvement of NAFLD, reduction of BMI and degree of steatosis, aminotransferase levels, insulin level, insulin resistance, serum triglyceride and high-density lipoprotein (HDL) cholesterol levels [23]. In another study, a significant inverse relationship was observed between the DASH score and risk of NAFLD, possibly due to the reduction of inflammation, body weight, insulin resistance and fat accumulation [19, 24]. The results of some studies have indicated that antioxidants in fruits and vegetables, including carotenoids, have beneficial effects in preventing the progression of NAFLD [25, 26]. Also, in another case-control study, following the DASH diet was associated with a 30% reduction in the risk of NAFLD [27]. It is noteworthy to mention that today, the term metabolic disorder-associated steatotic liver disease (MASLD) is used instead of NAFLD, which is a more appropriate alternative for metabolic syndrome-associated steatotic liver disease [28].

In the present study, it was shown that more intake of fruits, vegetables, legumes, nuts and seeds and less intake of red and processed meats was associated with a reduced risk of mortality from cirrhosis. Fruits and vegetables, nuts and seeds and legumes, as important

**Table 3** Hazard ratios for total mortality, according to the DASH score

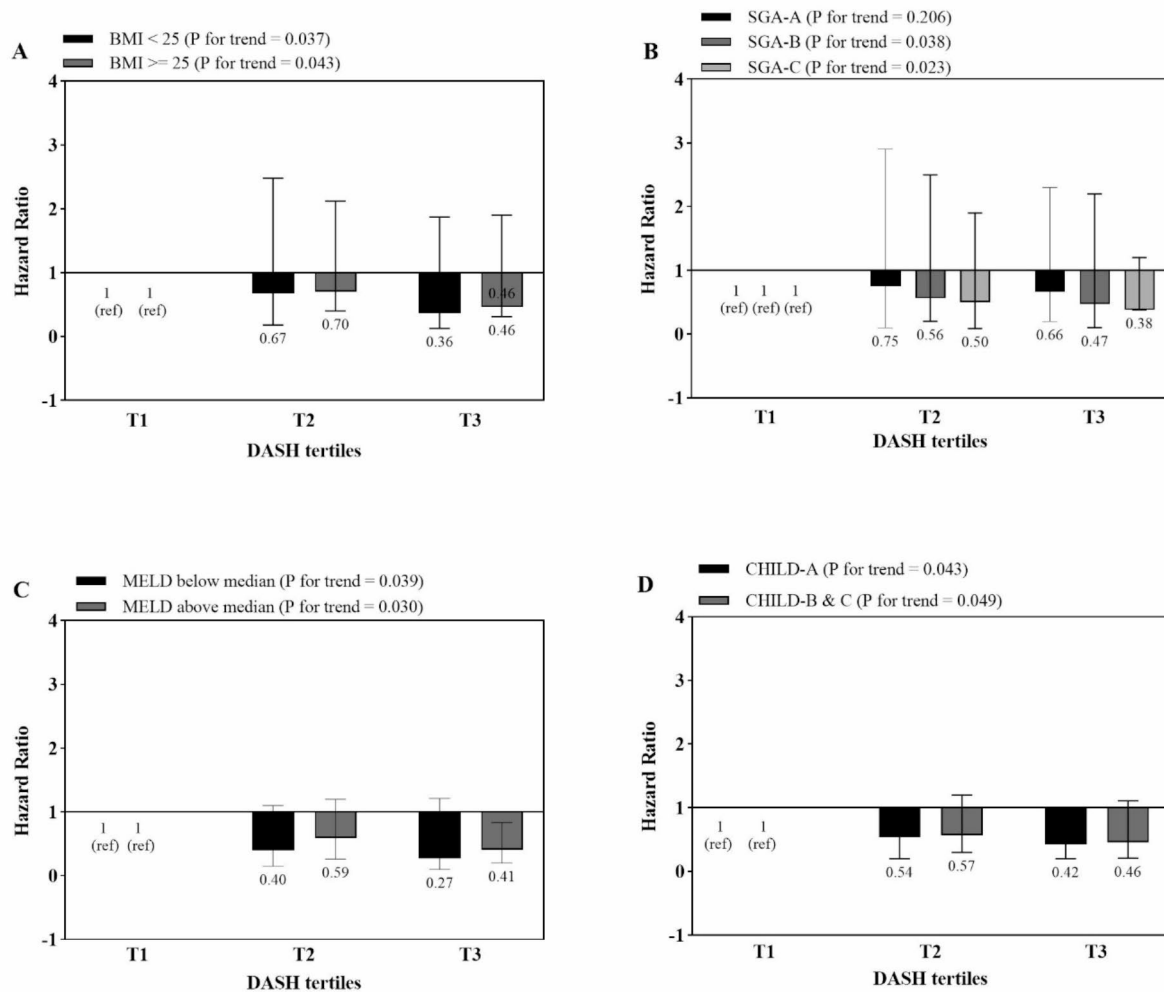
	T1 (< 22)	T2 (22–26)	T3 (> 26)	<i>P</i> trend
No. of deaths	26	12	5	
Model 1	ref	0.61 (0.30–1.32)	0.14 (0.05–0.42)	< 0.001
Model 2	ref	0.60 (0.28–1.46)	0.13 (0.04–0.43)	< 0.001
Model 3	ref	0.40 (0.12–1.33)	0.11 (0.03–0.42)	< 0.001

Cox proportional hazards regression models for estimating HRs and 95% CIs

Model 1: adjusted for age and sex.

Model 2: additionally adjusted for energy intake, BMI, smoking and alcohol

Model 3: additionally adjusted for etiology, SGA, MELD and Child-Pugh score



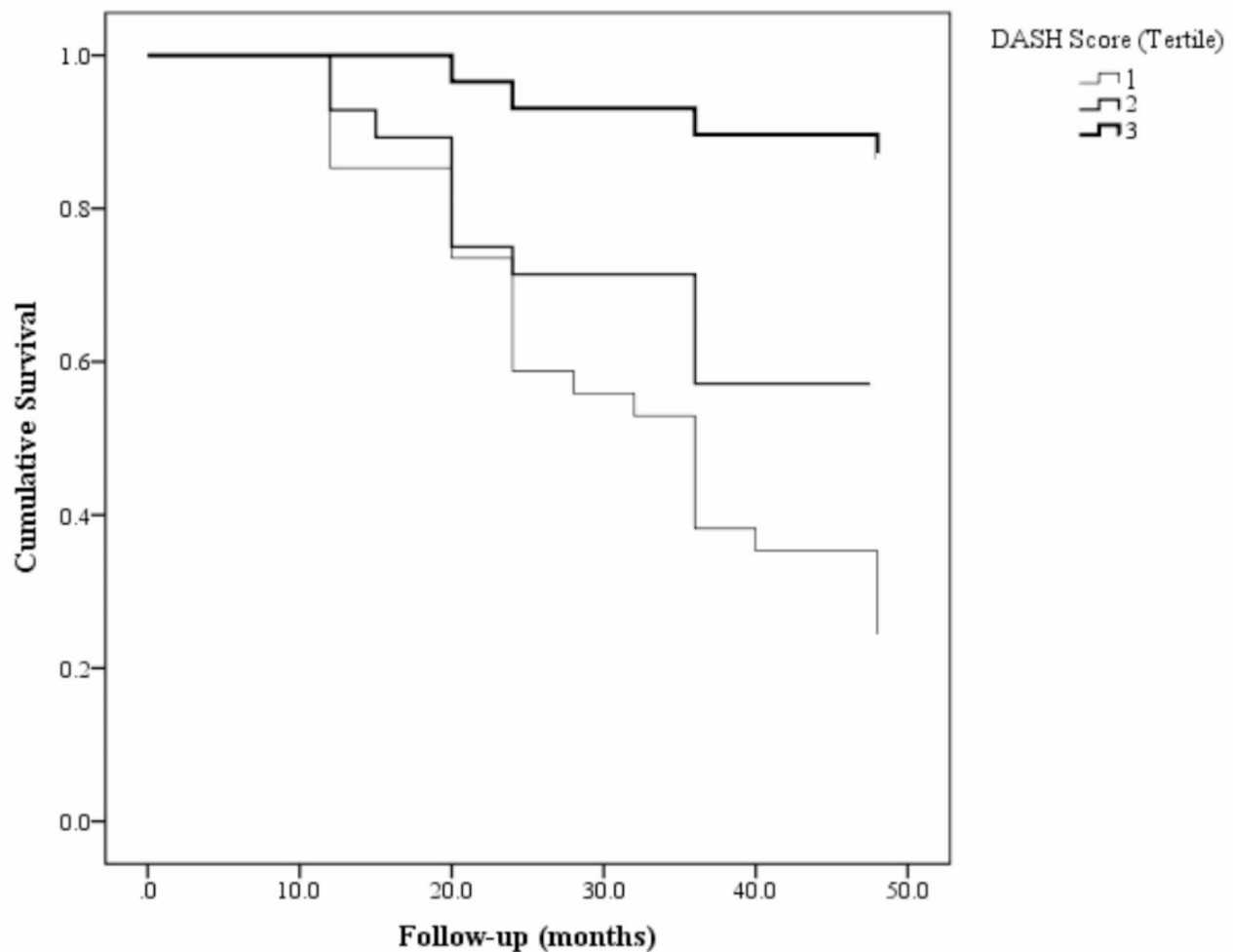
**Fig. 1** Multivariate hazard ratios of DASH tertiles for mortality in patients with cirrhosis according to risk factor status at baseline (Cox proportional hazards regression models for estimating HRs and 95% CIs, multivariable models were adjusted for sex, age, energy intake, BMI, smoking, alcohol, etiology, MELD and Child-Pugh score, except for the respective stratifying factor). Data are reported as HR (95% CI). **A**, BMI ( $P=0.018$  for interaction); **B**, SGA A vs. **B** and **C** ( $P=0.051$  for interaction); **C**, MELD score below median vs. above median ( $P=0.042$  for interaction); **D**, Child Pugh A vs. B&C ( $P=0.047$  for interaction). Ref indicates reference group

DASH: Dietary Approaches to Stop Hypertension; BMI: body mass index, SGA: subjective global assessment tool, MELD: Model for end-stage liver disease

components of the DASH diet, have been associated with liver diseases and its risk factors in previous studies due to the content of nutrients, fiber and phytochemical compounds [27, 29].

One of the main cause of death in patients with cirrhosis was found to be cardiovascular diseases (CVD) [30], cirrhosis is also associated with a broad range of cardiovascular outcomes [31]. On the other hand, previous studies have reported an inverse and significant relationship between adherence to the DASH diet and mortality in CVD patients [32]. In a study designed to determine the effect of the DASH diet on 10-year CVD risk compared with the typical American diet and a diet high in fruits and vegetables (F/V), it was found that the DASH

diet was associated with an approximately 10% reduction in 10-year CVD risk and also reduced CVD risk factors including hypertension and hypercholesterolemia more than F/V [33]. Also, in a study that evaluated the relationship between the DASH diet and cardiovascular risk factors in 2831 adults, it was found that by increasing the DASH score, there is a significant decrease in systolic blood pressure, fasting blood sugar, triglycerides, total cholesterol and its components [34]. However, in a clinical trial study, no relationship was found between the DASH diet and the risk of cardiovascular death, which may have modified the effects of the DASH diet due to the concomitant use of antihypertensive medications [35]. In addition to lowering blood pressure, the DASH



**Fig. 2** Kaplan-Meier survival curve for death among cirrhotic patients stratified by tertiles of DASH score. The 4-year survival rate among patients across tertiles was 32%, 37%, 46%, respectively (log-rank test for homogeneity,  $P=0.005$ )

diet seems to be effective in reducing other cardiovascular disease risk factors [36]. Although more studies are needed, one of the reasons for the higher survival of cirrhotic patients in the higher tertile of the DASH score may be the reduction of cardiovascular diseases and related risk factors.

The current study has several strengths. To the best of our knowledge, this study is the first cohort study to examine the association between DASH diet and mortality in patients with cirrhosis. In current study, the follow-up period of the patients was 4 years and we also used validated and reliable food-frequency questionnaires for dietary assessment. However, our study does have some limitations. The small sample size of this study limited us from deducing definitive results regarding the relationship between DASH diet and mortality in cirrhotic patients and the sample size was not estimated a priori for this cohort study. Also, despite the adjustment of

the potential confounding factors, residual confounding due to unknown or unmeasured confounders, cannot be excluded. Information about the physical activity, socioeconomic status and other demographic features of the patients was not collected, which could be confusing factors in these results. Recall bias is inevitable in completing the FFQ.

Our findings indicated that a higher DASH diet score may be associated with a reduced risk of mortality in cirrhotic patients, suggesting that greater adherence to the DASH-style dietary pattern is associated with better metabolic profiles in these patients. However, larger studies are needed to confirm the findings and determine its potential mechanisms.

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Authors have no acknowledgments to declare.

### Author contributions

Conceptualization, ZY; Formal analysis, ZY; Methodology, MS, BH, SA, FP and SK; Project administration, AZ and AH; Writing – original draft, AZ and ZY; Writing – review & editing, ZY and AH. All authors read and approved.

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### Data availability

The datasets analyzed in the current study are available from the corresponding author on reasonable request.

### Declarations

#### Ethics approval and consent to participate

National nutrition and Food Technology Research Institute (NNFTRI) ethics committee approved the study protocol (IR. SBMU. NNFTRI.1396.186). All participants provided written informed consent and were informed about the study. All procedures performed in studies involving human participants adhered to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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