

Observational Study

Malnutrition negatively impacts the quality of life of patients with cirrhosis: An observational study

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Abstract

AIM

To verify how malnutrition is related to health-related quality of life (HRQL) impairment in patients with cirrhosis.

METHODS

Data was retrospectively abstracted from medical records and obtained by direct interview. We included patients with cirrhosis from any etiology, evaluated at the Liver Clinic from Gastroenterology Department in a tertiary healthcare center, from June 2014 to June 2016. Child-Pugh score, data about complications, and demographic, clinical and anthropometric characteristics of patients were obtained. Nutritional status was evaluated by the Subjective Global Assessment (SGA). HRQL was evaluated through the Chronic Liver Disease Questionnaire. Patients were requested to assess their global HRQL with the following code: 0 = impairment

of HRQL, when it was compared with other healthy subjects; 1 = good HRQL, if it was similar to the quality of life of other healthy subjects. To compare the primary outcome between malnourished and well-nourished groups, the χ^2 test, Fisher's exact test or Student's *t*-test were used, based on the variable type. Associations between predictor variables and deterioration of HRQL were determined by calculating the hazard ratio and 95% confidence interval using Cox proportional hazards regression.

RESULTS

A total of 127 patients with cirrhosis were included, and the mean age was 54.1 ± 12.3 years-old. According to Child-Pugh scoring, 25 (19.7%) were classified as A (compensated), 76 (59.8%) as B, and 26 (20.5%) as C (B/C = decompensated). According to SGA, 58 (45.7%) patients were classified as well-nourished. Sixty-nine patients identified HRQL as good, and 76 patients (59.8%) perceived impairment of their HRQL. Multivariate analysis to determine associations between predictor variables and self-perception of an impairment of HRQL found strong association with malnutrition ($P < 0.0001$). The most important impaired characteristics in malnourished patients were: Presence of body pain, dyspnea on exertion with daily activities, decreased appetite, generalized weakness, trouble lifting or carrying heavy objects, and decreased level of energy ($P < 0.0001$).

CONCLUSION

Malnutrition is a key factor related to impairment of HRQL in patients with cirrhosis.

Key words: Malnutrition; Subjective global assessment; Health-related quality of life; Cirrhosis; Chronic liver disease questionnaire

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Core tip: Several factors, particularly the severity of disease, development of ascites, need for paracentesis and history of hospitalization for any cause, are factors that worsen the health-related quality of life (HRQL) of patients with cirrhosis. Noteworthy malnutrition is a very important factor which impacts negatively on HRQL of patients suffering cirrhosis; clinicians must recognize it promptly and search for strategies to avoid this preventable comorbidity.

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INTRODUCTION

Cirrhosis and its complications are important factors which contribute to mortality worldwide^[1]. Compared with healthy people, the patients with compensated cirrhosis have five times more risk of non-survival, and those with decompensated cirrhosis have ten times more risk of non-survival during follow-up^[2].

Malnutrition is highly prevalent in cirrhotic patients. It is related to development of complications, or even death^[3-5].

Despite new treatment options for viral hepatitis, the high frequency of undiagnosed patients with chronic viral hepatitis and the increased incidence of metabolic syndrome with non-alcoholic steatohepatitis had led to the number of individuals progressing to cirrhosis being expected to increase until about 2030^[6]. Moreover, despite increased knowledge of the pathogenesis of cirrhosis and major advances in the treatment, there remains a paucity of information related to health-related quality of life (HRQL) in these patients. Furthermore, the emotional impact of cirrhosis on individual's lives is rarely considered in clinical practice^[7].

HRQL is defined as the impact on three health domains regarding the patient's perception of their wellbeing: Physical, psychological, and social health. Measurement of HRQL requires administration of self-reported questionnaires^[8,9].

The Chronic Liver Disease Questionnaire (CLDQ) assesses HRQL in patients with chronic liver disease across diagnoses, at all stages of disease and treatment. The CLDQ is a 29-item self-reported questionnaire, with patient response options extending from 1 to 7 (all to none of the time). The CLDQ addresses the following domains that when combined give a composite score that indicates overall HRQL: Fatigue, activity, emotional function, abdominal pain, systemic symptoms, and anxiety. Mean domain scores and an overall quality of life score can be calculated, with higher scores representing better outcome^[9,10]. Previous studies have confirmed how HRQL deteriorates from compensated to decompensated cirrhosis^[11].

Our aim in this study was to verify how malnutrition is related to HRQL impairment in patients with cirrhosis.

MATERIALS AND METHODS

Study design

We designed an observational analytic study. Data were retrospectively abstracted from medical records and obtained by direct interview. All study participants provided verbal informed consent prior to study enrollment.

Patients

We included patients with cirrhosis from any etiology, who were evaluated at the Liver Clinic from Gastroenterology Department in a tertiary healthcare center,

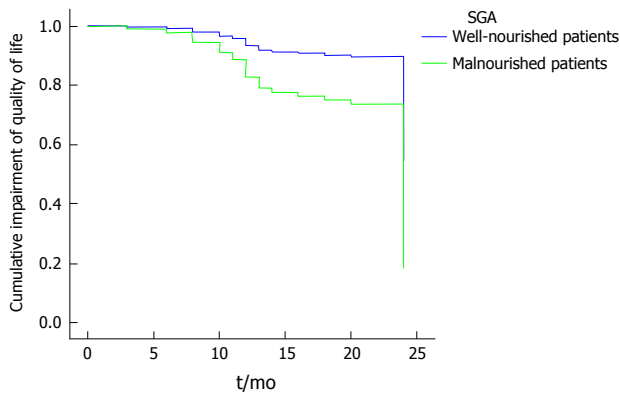


Figure 1 Kaplan-Meier curves showing the impairment of quality of life through the course of chronic liver disease, in patients with cirrhosis and malnutrition according to subjective global assessment. Malnourished patients had a worse quality of life during the follow-up in each visit to the physician, compared with those well-nourished patients. $P < 0.0001$. SGA: Subjective global assessment.

from June 2014 to June 2016. The Child-Pugh score was used to define compensated cirrhosis (Child-Pugh A) and decompensated cirrhosis (Child-Pugh B/C). We also collected data about complications of cirrhosis, including: Ascites, need of paracentesis, variceal bleeding, hepatic encephalopathy, and bacterial infection needing hospitalization. Patients with other chronic comorbidities, such as diabetes, chronic renal failure, heart or lung disease, neoplasms and acquired immunodeficiency syndrome, were excluded. We collected demographic, clinical and anthropometric characteristics of patients.

Anthropometric parameters

Weight, height, mid-arm circumference and triceps skinfold thickness were measured^[12]. Body mass index (BMI) and ideal mid-arm muscle circumference were also calculated^[13,14].

Nutritional status

Nutritional status was evaluated by the Subjective Global Assessment (SGA)^[4,5,15]. Patients were catalogued as well nourished, or moderately or severely malnourished. We chose the SGA for this study because of its being a simple bedside method recommended by the experts when other more accurate methods, such as phase angle or body cell mass measured by bioelectric impedance analysis, are not available to assess nutritional status.

HRQL

HRQL was evaluated through the CLDQ^[10]. In addition, patients were requested to assess their global HRQL with the following coding system: 0 = impairment of HRQL, when it was compared with other healthy subjects; 1 = good HRQL, if it was similar to the quality of life of other healthy subjects.

Statistical analysis

Numeric variables were stated as mean and standard deviation (SD); categorical variables were stated as

proportions and percentages. To compare the primary outcome between malnourished and well-nourished groups, the χ^2 test, Fisher's exact test or Student's *t*-test were used, as appropriate. Associations between predictor variables and deterioration of quality of life were determined by calculating the hazard ratio (HR) and 95% confidence interval (CI) using Cox proportional hazards regression. The significant variables ($P < 0.05$) in the univariate model were included in the multivariate model. Kaplan-Meier curves were constructed to compare quality of life between well-nourished and malnourished patients, and for this purpose, we identified the time when patients were diagnosed with cirrhosis and the estimated time when patients noticed impairment of their quality of life. Statistical significance was considered as a P -value < 0.05 .

RESULTS

A total of 127 patients with cirrhosis were included, 70 of which were female (55.1%) and 57 were male (44.9%); the mean age was 54.1 ± 12.3 years-old. Regarding the etiology of the cirrhosis, 68 patients (53.3%) had alcoholic cirrhosis, 23 (18.1%) had chronic hepatitis C, 21 (16.5%) had cryptogenic etiology, 11 (8.7%) had autoimmune hepatitis, 3 (2.4%) had non-alcoholic steatohepatitis, and 1 (0.8%) had chronic hepatitis B. According to Child-Pugh scoring, 25 patients (19.7%) were classified as A (compensated), 76 (59.8%) as B, and 26 (20.5%) as C (B/C = decompensated). As determined by the SGA, 58 patients (45.7%) were well-nourished and 69 (54.3%) had some degree of malnutrition, including 66 (52%) with mild to moderate malnutrition and 3 (2.3%) with severe malnutrition. A total of 51 patients (40.2%) assessed their HRQL as good quality of life or similar to other healthy subjects; on the other hand, 76 patients (59.8%) perceived impairment of their HRQL in comparison with other healthy subjects. Characteristics of patients according to their self-perception of HRQL are shown and compared in Table 1. In the univariate analysis, decompensated cirrhosis, presence of ascites, need for paracentesis, hospitalization for any cause, and malnutrition were factors significantly associated with poor HRQL.

Multivariate analysis to determine associations between predictor variables and self-perception of an impairment of HRQL is shown in Table 2. The most important factor related to poor HRQL was malnutrition ($P < 0.0001$). Also, patients with malnutrition had poorer HRQL through the time course of their chronic liver disease, when compared with the well-nourished patients ($P < 0.0001$) (Figure 1).

Finally, the comparison of characteristics evaluated through CLDQ between malnourished and well-nourished patients is shown in Table 3. The most important impaired characteristics in malnourished patients were: Presence of body pain, dyspnea on exertion with daily activities, decreased appetite, generalized weakness, trouble lifting or carrying heavy objects, and decreased

Table 1 Comparison between the patient characteristics according to the self-perception of quality of life

Characteristic	Good quality of life (<i>n</i> = 51)	Impairment of quality of life (<i>n</i> = 76)	<i>P</i>
Male	24 (47.1)	33 (43.4)	0.69
Age (yr)	54.8 ± 10.3	53.7 ± 13.5	0.61
Decompensated or Child B/C	30 (58.8)	63 (82.9)	0.003
Etiology			
Alcohol	28 (55.0)	40 (52.7)	0.83
Viral	9 (17.6)	15 (19.7)	
NASH	2 (3.9)	1 (1.3)	
Cryptogenic	8 (15.7)	13 (17.1)	
Autoimmune	4 (7.8)	7 (9.2)	
Weight in kg	65.2 ± 14.9	63.7 ± 13.4	0.55
Body mass index (kg/m ²)	26.6 ± 5.2	26.8 ± 4.0	0.32
Triceps skinfold thickness (cm)	1.4 ± 0.7	1.4 ± 0.8	0.79
Mid-arm circumference (cm)	26.4 ± 4.7	23.9 ± 3.7	0.001
Ideal mid-arm muscle circumference (cm)	22.1 ± 4.1	19.6 ± 2.8	< 0.0001
Malnourished according to SGA	14 (27.5)	55 (72.4)	< 0.0001
Presence of ascites	19 (37.3)	48 (63.2)	0.004
Need for paracentesis	7 (13.7)	25 (32.9)	0.02
Development of variceal bleeding	12 (23.5)	18 (23.7)	0.98
Development of hepatic encephalopathy	19 (37.3)	30 (39.5)	0.80
Bacterial infection requiring hospitalization	6 (11.8)	14 (18.4)	0.45
Any complication requiring hospitalization	32 (62.7)	62 (81.6)	0.02

Categorical variables are expressed as *n* (%), and compared by χ^2 or Fisher's exact test. Numeric variables are expressed as median and SD, and compared by Student's *t*-test. Statistical significance was considered as a *P*-value of < 0.05. NASH: Non-alcoholic steatohepatitis; SGA: Subjective global assessment.

Table 2 Multivariate analysis to identify factors associated with self-perception of impairment of quality of life

Characteristic	HR (95%CI)	<i>P</i>
Malnourished according to SGA	2.8 (1.6-5.0)	< 0.0001
Need for paracentesis	1.8 (1.0-3.2)	0.05
Presence of ascites	1.4 (0.7-2.7)	0.38
Any complication requiring hospitalization	1.1 (0.5-2.6)	0.82
Decompensated or Child B/C	1.8 (0.0-4.0)	0.14

Cox regression, statistical significance was considered as a *P*-value of < 0.05. HR: Hazard ratio; SGA: Subjective global assessment.

level of energy (*P* < 0.0001).

DISCUSSION

Cirrhosis represents the final stage of all chronic liver diseases. In its decompensated form, cirrhosis can result in portal hypertension and hepatic dysfunction. Cirrhosis is a leading cause of morbidity and mortality worldwide, and not only is related to decreased survival but also to poor HRQL^[16].

Quality of life is a concept that reflects the positive and negative aspects of an individual's life. The term "HRQL" specifically addresses the impact of health on patients' wellbeing^[9]. There are many factors that influence outcome and HRQL in patients with cirrhosis, however liver function clearly plays a major role affecting the HRQL of patients with cirrhosis. Patients with decompensated cirrhosis have an important impairment on HRQL^[17]. Also, many symptoms can negatively impact HRQL in patients with cirrhosis; these symptoms can include abdominal bloating, nausea, somnolence, weight

loss, weakness, fatigue and itching. All of these may interfere with patient's work, schooling, social activities, and sense of wellbeing^[18].

In our study, we found that decompensated cirrhosis (Child B/C) is a factor related to impairment of HRQL; this finding is similar to other studies. Marchesini *et al.*^[19] also reported that the severity of liver disease or the development of complications were conditions clearly related to deterioration of perception of health. Similarly, we found that the presence of ascites and need for paracentesis were associated factors related to poor quality of life. Furthermore, hospitalization for any cause was a condition related to poor HRQL in patients with cirrhosis.

In our study, interestingly we found that patients with cirrhosis and malnutrition had a poorer HRQL when compared with well-nourished patients with cirrhosis. Furthermore, malnutrition was the main factor contributing to impairment of HRQL in these patients. Cirrhosis is also associated with malnutrition, which is a complication that negatively affects cirrhotic patients, particularly those decompensated^[20-23]. In patients with cirrhosis, the prevalence of malnutrition has been reported between 20% to 60%^[24-27]. In a previous study conducted by Pérez-Reyes *et al.*^[4] in a Hispanic population, the prevalence of malnutrition was as high as 56.3%. In the present study, we also found a high frequency of malnutrition in patients with cirrhosis (54.3%). Malnutrition in cirrhosis is related to development of ascites, encephalopathy, spontaneous bacterial peritonitis, other bacterial infections and hepatorenal syndrome^[4,28-32]. But also, malnutrition deteriorates the HRQL in patients with cirrhosis^[33-35] and several other gastrointestinal and non-gastrointestinal diseases^[36,37]. Our study confirms that malnutrition is

Table 3 Chronic Liver Diseases Questionnaire items comparison according to nutritional status

CLDQ item	Well-nourished (n = 58)	Malnourished (n = 69)	P
1 How much of the time during the last 2 wk have you been troubled by a feeling of abdominal bloating?	5.72 ± 1.531	4.67 ± 2.056	0.001
2 How much of the time have you been tired or fatigued during the last 2 wk?	3.69 ± 1.366	2.94 ± 1.259	0.002
3 How much of the time during the last 2 wk have you experienced body pain?	4.14 ± 0.868	3.57 ± 0.848	0.0001
4 How often during the last 2 wk have you felt sleepy during the day?	5.05 ± 1.343	4.55 ± 1.105	0.02
5 How much of the time during the last 2 wk have you experienced abdominal pain?	5.45 ± 1.273	4.96 ± 1.529	0.05
6 How much of the time during the last 2 wk have you experienced dyspnea on exertion, being a problem for you in your daily activities?	6.16 ± 0.951	5.33 ± 1.431	0.0001
7 How much of the time during the last 2 wk have you not been able to eat as much as you would like?	6.12 ± 1.010	3.55 ± 1.549	0.0001
8 How much of the time in the last 2 wk have you been bothered by having decreased strength?	4.91 ± 1.218	2.90 ± 1.447	0.0001
9 How often during the last 2 wk have you had trouble lifting or carrying heavy objects?	5.62 ± 0.834	4.09 ± 1.391	0.0001
10 How often during the last 2 wk have you felt anxious?	5.52 ± 1.112	5.33 ± 1.379	0.41
11 How often during the last 2 wk have you felt a decreased level of energy?	5.19 ± 1.100	3.20 ± 1.491	0.0001
12 How much of the time during the last 2 wk have you felt unhappy?	5.12 ± 1.077	4.41 ± 1.527	0.003
13 How often during the last 2 wk have you felt drowsy?	4.97 ± 1.324	4.55 ± 1.051	0.05
14 How much of the time during the last 2 wk have you been bothered by a limitation of your diet?	4.14 ± 1.206	3.91 ± 1.160	0.29
15 How often during the last 2 wk have you been irritable?	5.52 ± 1.128	5.36 ± 1.175	0.45
16 How much of the time during the last 2 wk have you had difficulty sleeping at night?	5.02 ± 1.493	4.87 ± 1.444	0.57
17 How much of the time during the last 2 wk have you been troubled by a feeling of abdominal discomfort?	5.62 ± 1.437	4.77 ± 1.816	0.004
18 How much of the time during the last 2 wk have you been worried about the impact your liver disease has on your family?	5.84 ± 1.056	5.94 ± 1.371	0.66
19 How much of the time during the last 2 wk have you had mood swings?	5.50 ± 1.417	5.83 ± 1.283	0.18
20 How much of the time during the last 2 wk have you been unable to fall asleep at night?	5.10 ± 1.360	4.67 ± 1.569	0.99
21 How often during the last 2 wk have you had muscle cramps?	5.52 ± 1.047	5.39 ± 1.074	0.51
22 How much of the time during the last 2 wk have you been worried that your symptoms will develop into major problems?	4.19 ± 1.515	4.45 ± 1.586	0.35
23 How much of the time during the last 2 wk have you had a dry mouth?	5.40 ± 1.184	5.30 ± 1.192	0.66
24 How much of the time during the last 2 wk have you felt depressed?	5.33 ± 1.082	4.68 ± 1.745	0.01
25 How much of the time during the last 2 wk have you been worried about your condition getting worse?	4.05 ± 1.191	4.28 ± 1.454	0.34
26 How much of the time during the last 2 wk have you had problems concentrating?	5.34 ± 1.132	4.74 ± 1.569	0.01
27 How much of the time have you been troubled by itching during the last 2 wk?	5.71 ± 1.451	6.20 ± 1.065	0.03
28 How much of the time during the last 2 wk have you been worried about never feeling any better?	4.07 ± 1.153	4.36 ± 1.382	0.20
29 How much of the time during the last 2 wk have you been concerned about the availability of a liver if you need a liver transplant?	4.22 ± 1.312	4.23 ± 1.467	0.97

Data are expressed as median and SD, and compared with Student's *t*-test. Statistical significance was considered as a *P*-value of < 0.05. CLDQ: Chronic Liver Diseases Questionnaire.

a key factor related to impairment of HRQL in patients with cirrhosis, even when we adjusted for advanced liver disease or decompensation status, and for other major complications such as ascites, need for paracentesis and need for hospitalization for any cause.

In conclusion, cirrhosis is the end-stage of all chronic liver diseases; it contributes importantly to morbidity and mortality worldwide but also has a negative impact on HRQL that must be considered. Several factors contribute to a poor HRQL in patients with cirrhosis, however malnutrition, which is a highly prevalent comorbidity in patients with cirrhosis, represents a key factor related to poor HRQL in these patients. There is a need for developing strategies to evaluate more accurately patients with cirrhosis and to identify promptly those patients at risk of malnutrition.

COMMENTS

Background

Cirrhosis is a significant contributor to global mortality. Prevalence of malnutrition is high in patients with cirrhosis and is related to increased complications or even death. Despite increased knowledge of the pathogenesis of cirrhosis, there

remains a paucity of information related to health-related quality of life (HRQL) in these patients.

Research frontiers

The emotional impact of cirrhosis on individual's lives is rarely considered in clinical practice. The Chronic Liver Disease Questionnaire assesses HRQL in patients with chronic liver disease across diagnoses, at all stages of disease and treatment.

Innovations and breakthroughs

Cirrhosis is a leading cause of morbidity and mortality worldwide, and not only is related to decreased survival but also to poor quality of life. The term "HRQL" addresses the impact of health on a patient's wellbeing. Many factors influence HRQL in patients with cirrhosis, however the impact of comorbidities, such as malnutrition, are not well understood. The authors found that patients with cirrhosis and malnutrition had worse quality of life when compared with well-nourished patients with cirrhosis. In this study, malnutrition was the main factor contributing to impairment of quality of life in these patients.

Applications

In this study, the authors found that several factors contribute to a poor health-related quality of life in patients with cirrhosis, however malnutrition, which is a highly prevalent comorbidity in these patients, represents a key factor related to poor quality of life in these patients. There is a need for developing strategies to evaluate more accurately patients with cirrhosis and to identify promptly those patients at risk of malnutrition.

Terminology

Nutritional status was defined through the Subjective Global Assessment and patients were divided as follows: Well-nourished, or moderately or severely malnourished. The HRQL is defined as the impact on three health domains-physical, psychological, and social health-on patient perception of their wellbeing.

Peer-review

Very nice and well written paper.

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