**Name of Journal: *World Journal of Hepatology***

**ESPS Manuscript NO: 29425**

**Manuscript type: Original Article**

***Observational Study***

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

Rojas-Loureiro G *et al*. Malnutrition impacts quality of life in cirrhosis

**Gabriela Rojas-Loureiro, Alfredo Servín-Caamaño, Elizabeth Pérez-Reyes, Luis Servín-Abad, Fátima Higuera-de la Tijera**

**Gabriela Rojas-Loureiro, Elizabeth Pérez-Reyes, Fátima Higuera-de la Tijera,** Liver Clinic, Gastroenterology Department, Hospital General de México. “Dr. Eduardo Liceaga”, Mexico City 06720, Mexico

**Alfredo Servìn-Caamaño,** Internal Medicine Department, Hospital General de México “Dr. Eduardo Liceaga”, Mexico City 06720, Mexico

**Luis Servín-Abad,** Gastroenterologist at Lakeland Regional Medical Center, Lakeland, FL 33803, United States

**Author contributions:** Higuera-de la Tijera F was the guarantor and designed the study; Rojas-Loureiro G, Servín-Caamaño A and Pérez-Reyes E participated in the acquisition, analysis, and interpretation of the data; Higuera-de la Tijera F wrote the manuscript; Servín-Abad L reviewed the final manuscript, and revised the article critically for important intellectual content. All the authors read and approved the final manuscript.

**Institutional review board statement:** The study was reviewed and approved by The Coordination of Research from Gastroenterology Department from Hospital General de México.

**Informed consent statement:** All study participants, provided verbal informed consent prior to study enrollment.

**Conflict-of-interest statement:** The authors involved in this manuscript [Gabriela Rojas-Loureiro, Alfredo Servín-Caamaño, Elizabeth Pérez-Reyes, Luis Servín-Abad, Fátima Higuera-de la Tijera] have no conflicting commercial, personal, political, intellectual, or religious interests.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Correspondence to: Fátima Higuera-de la Tijera, MD, MSc,** Gastroenterology and Hepatology Department, Hospital General de México “Dr. Eduardo Liceaga”, Dr. Balmis 148, Mexico City 06726, Mexico. fatimahiguera@yahoo.com.mx

**Telephone:** +52-55-27892000**-**30047

**Received:** August 13, 2016

**Peer-review started:** August 14, 2016

**First decision:** September 2, 2016

**Revised:** October 28, 2016

**Accepted:** December 7, 2016

**Article in press:**

**Published online:**

**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 by a direct interview. We included patients with cirrhosis from any etiology, evaluated at the Liver Clinic from Gastroenterology Department in a tertiary health-care center, from June 2014 to June 2016. Child-Pugh score, data about complications, demographic, clinical and anthropometric characteristics of patients were obtained. Nutritional status was evaluated with the Subjective Global Assessment (SGA). HRQL was evaluated through the Chronic Liver Disease Questionnaire (CLDQ).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 chi-square 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 Hazard Ratio and 95%CI calculated using Cox proportional hazards regression.

***RESULTS***

A total of 127 patients with cirrhosis were included, the mean age was 54.1 ± 12.3 years old. According to Child-Pugh score, 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, and 69 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, anddecreased level of energy (*P* < 0.0001).

***CONCLUSION***

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

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

**© The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Several factors, particularly the severity of the disease, development of ascites, need for paracentesis, 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 searching for strategies to avoid this preventable comorbidity.

Rojas-Loureiro G, Servín-Caamaño A, Pérez-Reyes E, Servín-Abad L, Higuera-de la Tijera F. Malnutrition negatively impacts the quality of life of patients with cirrhosis: An observational study. *World J Hepatol* 2016; In press

**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 of new treatment options for viral hepatitis, due to high frequency of undiagnosed patients with chronic viral hepatitis, and increased incidence of metabolic syndrome with non-alcoholic steatohepatitis; the number of individuals progressing to cirrhosis is expected to increase until about 2030[6]. 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: Physical, psychological, and social health on patient perception of their wellbeing. 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 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 by a 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 health-care center, from June 2014 to June 2016. 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: ascites, need of paracentesis, variceal bleeding, hepatic encephalopathy, bacterial infection needing hospitalization. Patients with other chronic comorbidities, such as diabetes, chronic renal failure, heart or lung disease, neoplasms, acquired immunodeficiency syndrome, were excluded. We collected demographic, clinical and anthropometric characteristics of patients.

***Anthropometric parameters***

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

***Nutritional status***

Nutritional statuswas evaluated with the Subjective Global Assessment (SGA)[4,5,15]. Patients were catalogued as well nourished, moderately or severely malnourished. We chose the SGA for this study because of it is 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***

HRQLwas evaluated through the CLDQ[10].Also patients were requested 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.

***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 chi-square 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 Hazard Ratio and 95%CI calculated 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, 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 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%) chronic hepatitis C, 21 (16.5%) cryptogenic etiology, 11 (8.7%) autoimmune hepatitis, 3 (2.4%) non-alcoholic steatohepatitis, and 1 (0.8%) chronic hepatitis B. According to Child-Pugh score, 25 (19.7%) were classified as A (compensated), 76 (59.8%) as B, and 26 (20.5%) as C (B/C = decompensated). As stated by the SGA, 58 patients were assessed as well-nourished (45.7%), and 69 (54.3%) patients had some degree of malnutrition: 66 with mild to moderate malnutrition (52%), and 3 patients with severe malnutrition (2.3%). A total of 51 patients (40.2%) assessed their HRQL as good quality of life or similar to other healthy subjects, in 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 well-nourished patient (*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, anddecreased level of energy (*P* < 0.0001).

**DISCUSION**

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 is related 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 address 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, itching. All of them may interfere with patient´s work, school, 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. In this study, malnutrition was the main factor contributing to impairment of HRQL in these patients. Cirrhosis also is 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 in Hispanic population by Pérez-Reyes *et al*[4], the prevalence of malnutrition was as high as 56.3%.In the present study, we found also 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, hepatorenal syndrome[4,28-32]. But also, malnutrition deteriorates the HRQL in patients with cirrhosis[33-35], and other several gastrointestinal and non-gastrointestinal diseases[36,37]. Our study confirms that malnutrition is 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. It 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 (CLDQ) 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 is related to poor quality of life. The term HRQL addresses the impact of health on 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 (SGA)and patients were divided as follows: well nourished, moderately or severely malnourished; Health related quality of life (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.

**REFERENCES**

 1 **Tucker ME.** Global burden of liver disease substantial. Available from: URL: http: //www.medscape.com/viewarticle/813788#1

2 **Fleming KM**, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: a population-based cohort study. *Liver Int* 2012; **32**: 79-84 [PMID: 21745279 DOI: 10.1111/j.1478-3231.2011.02517]

3 **Maharshi S**, Sharma BC, Srivastava S. Malnutrition in cirrhosis increases morbidity and mortality. *J Gastroenterol Hepatol* 2015; **30**: 1507-1513 [PMID: 25974421 DOI: 10.1111/jgh.12999]

4 **Pérez-Reyes E,** Rivera-Sánchez J, Servín-Caamaño AI, Pérez-Torres E, Abdo-Francis JM, Higuera-de la Tijera F. Malnutrition is related to a higher frequency of serious complications in patients with cirrosis. *Rev Med Hosp Gen Méx* 2016; **79:** 11-16 [DOI: 10.1016/j.hgmx.2015.04.003]

5 **Landa-Galván HV**, Milke-García MP, León-Oviedo C, Gutiérrez-Reyes G, Higuera-de la Tijera F, Pérez-Hernández JL, Serralde-Zúñiga AE. [Nutritional assessment of alcoholic liver cirrhotic patients treated in the liver Clinic of the Mexico's General Hospital]. *Nutr Hosp* 2012; **27**: 2006-2014 [PMID: 23588452 DOI: 10.3305/nh.2012.27.6.6070]

6 **Davis GL**, Albright JE, Cook SF, Rosenberg DM. Projecting future complications of chronic hepatitis C in the United States. *Liver Transpl* 2003; **9**: 331-338 [PMID: 12682882 DOI: 10.1053/jlts.2003.50073]

7 **Anthony PP**, Ishak KG, Nayak NC, Poulsen HE, Scheuer PJ, Sobin LH. The morphology of cirrhosis. Recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. *J Clin Pathol* 1978; **31**: 395-414 [PMID: 649765]

8 **Les I**, Doval E, Flavià M, Jacas C, Cárdenas G, Esteban R, Guardia J, Córdoba J. Quality of life in cirrhosis is related to potentially treatable factors. *Eur J Gastroenterol Hepatol* 2010; **22**: 221-227 [PMID: 19794311 DOI: 10.1097/MEG.0b013e3283319975]

9 **Loria A**, Escheik C, Gerber NL, Younossi ZM. Quality of life in cirrhosis. *Curr Gastroenterol Rep* 2013; **15**: 301 [PMID: 23250701]

10 **Younossi ZM**, Guyatt G, Kiwi M, Boparai N, King D. Development of a disease specific questionnaire to measure health related quality of life in patients with chronic liver disease. *Gut* 1999; **45**: 295-300 [PMID: 10403745]

11 **Younossi ZM**, Boparai N, McCormick M, Price LL, Guyatt G. Assessment of utilities and health-related quality of life in patients with chronic liver disease. *Am J Gastroenterol* 2001; **96**: 579-583 [PMID: 11232711 DOI: 10.1111/j.1572-0241.2001.03537.x]

12 **Lohman TG,** Roche AF, Martorell R. Anthropometric standardization reference manual. Champaign, IL: Human Kinetic Books; 1988

13 **Ratib S**, Fleming KM, Crooks CJ, Walker AJ, West J. Causes of death in people with liver cirrhosis in England compared with the general population: a population-based cohort study. *Am J Gastroenterol* 2015; **110**: 1149-1158 [PMID: 26169512 DOI: 10.1038/ajg.2015.191]

14 **Frisancho AR**. New norms of upper limb fat and muscle areas for assessment of nutritional status. *Am J Clin Nutr* 1981; **34**: 2540-2545 [PMID: 6975564]

15 **Morgan MY**, Madden AM, Soulsby CT, Morris RW. Derivation and validation of a new global method for assessing nutritional status in patients with cirrhosis. *Hepatology* 2006; **44**: 823-835 [PMID: 17006918 DOI: 10.1002/hep.21358]

16 **Nusrat S**, Khan MS, Fazili J, Madhoun MF. Cirrhosis and its complications: evidence based treatment. *World J Gastroenterol* 2014; **20**: 5442-5460 [PMID: 24833875 DOI: 10.3748/wjg.v20.i18.5442]

17 **Heidelbaugh JJ**, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. *Am Fam Physician* 2006; **74**: 756-762 [PMID: 16970019]

18 **Grattagliano I**, Ubaldi E, Bonfrate L, Portincasa P. Management of liver cirrhosis between primary care and specialists. *World J Gastroenterol* 2011; **17**: 2273-2282 [PMID: 21633593 DOI: 10.3748/wjg.v17.i18.2273]

19 **Marchesini G**, Bianchi G, Amodio P, Salerno F, Merli M, Panella C, Loguercio C, Apolone G, Niero M, Abbiati R; The Italian Study Group for Quality of Life in Cirrhosis. Factors associated with poor health-related quality of life of patients with cirrhosis. *Gastroenterology* 2001; **120**: 170-178 [PMID: 11208726 DOI: 10.1053/gast.2001.21193]

20 **Tessari P**. Protein metabolism in liver cirrhosis: from albumin to muscle myofibrils. *Curr Opin Clin Nutr Metab Care* 2003; **6**: 79-85 [PMID: 12496684 DOI: 10.1097/01.mco.0000049044.06038.30]

21 **Bianchi G**, Marzocchi R, Agostini F, Marchesini G. Update on nutritional supplementation with branched-chain amino acids. *Curr Opin Clin Nutr Metab Care* 2005; **8**: 83-87 [PMID: 15586005]

22 **Bilbao I**, Armadans L, Lazaro JL, Hidalgo E, Castells L, Margarit C. Predictive factors for early mortality following liver transplantation. *Clin Transplant* 2003; **17**: 401-411 [PMID: 14703921 DOI: 10.1034/j.1399-0012.2003.00068.x]

23 **Alvares-da-Silva MR**, Reverbel da Silveira T. Comparison between handgrip strength, subjective global assessment, and prognostic nutritional index in assessing malnutrition and predicting clinical outcome in cirrhotic outpatients. *Nutrition* 2005; **21**: 113-117 [PMID: 15723736 DOI: 10.1016/j.nut.2004.02.002]

24 **Peng S**, Plank LD, McCall JL, Gillanders LK, McIlroy K, Gane EJ. Body composition, muscle function, and energy expenditure in patients with liver cirrhosis: a comprehensive study. *Am J Clin Nutr* 2007; **85**: 1257-1266 [PMID: 17490961]

25 **Alberino F**, Gatta A, Amodio P, Merkel C, Di Pascoli L, Boffo G, Caregaro L. Nutrition and survival in patients with liver cirrhosis. *Nutrition* 2001; **17**: 445-450 [PMID: 11399401 DOI: 10.1016/S0899-9007(01)00521-4]

26 **Campillo B**, Richardet JP, Bories PN. Enteral nutrition in severely malnourished and anorectic cirrhotic patients in clinical practice. *Gastroenterol Clin Biol* 2005; **29**: 645-651 [PMID: 16141996]

27 **Plauth M**, Schütz ET. Cachexia in liver cirrhosis. *Int J Cardiol* 2002; **85**: 83-87 [PMID: 12163212 DOI: 10.1016/S0167-5273(02)00236-X]

28 **Kalaitzakis E**, Simrén M, Olsson R, Henfridsson P, Hugosson I, Bengtsson M, Björnsson E. Gastrointestinal symptoms in patients with liver cirrhosis: associations with nutritional status and health-related quality of life. *Scand J Gastroenterol* 2006; **41**: 1464-1472 [PMID: 17101578 DOI: 10.1080/00365520600825117]

29 **Kalaitzakis E**, Olsson R, Henfridsson P, Hugosson I, Bengtsson M, Jalan R, Björnsson E. Malnutrition and diabetes mellitus are related to hepatic encephalopathy in patients with liver cirrhosis. *Liver Int* 2007; **27**: 1194-1201 [PMID: 17919230 DOI: 10.1111/j.1478-3231.2007.01562.x]

30 **Huisman EJ**, Trip EJ, Siersema PD, van Hoek B, van Erpecum KJ. Protein energy malnutrition predicts complications in liver cirrhosis. *Eur J Gastroenterol Hepatol* 2011; **23**: 982-989 [PMID: 21971339 DOI: 10.1097/MEG.0b013e32834aa4bb]

31 **Merli M**, Lucidi C, Giannelli V, Giusto M, Riggio O, Falcone M, Ridola L, Attili AF, Venditti M. Cirrhotic patients are at risk for health care-associated bacterial infections. *Clin Gastroenterol Hepatol* 2010; **8**: 979-985 [PMID: 20621200 DOI: 10.1016/j.cgh.2010.06.024]

32 **Merli M**, Giusto M, Gentili F, Novelli G, Ferretti G, Riggio O, Corradini SG, Siciliano M, Farcomeni A, Attili AF, Berloco P, Rossi M. Nutritional status: its influence on the outcome of patients undergoing liver transplantation. *Liver Int* 2010; **30**: 208-214 [PMID: 19840246 DOI: 10.1111/j.1478-3231.2009.02135.x]

33 **Poupon RE**, Chrétien Y, Chazouillères O, Poupon R, Chwalow J. Quality of life in patients with primary biliary cirrhosis. *Hepatology* 2004; **40**: 489-494 [PMID: 15368455 DOI: 10.1002/hep.20276]

34 **Kalaitzakis E**. Gastrointestinal dysfunction in liver cirrhosis. *World J Gastroenterol* 2014; **20**: 14686-14695 [PMID: 25356031 DOI: 10.3748/wjg.v20.i40.14686]

35 **Shiraki M,** Nishiguchi S, Saito M, Fukuzawa Y, Mizuta T, Kaibori M, Hanai T, Nishimura K, Shimizu M, Tsurumi H, Moriwaki H. Nutritional status and quality of life in current patients with liver cirrhosis as assessed in 2007–2011. *Hepatol Res* 2013; **46:** 106-112 [DOI: 10.1111/hepr.12004]

36 **Norman K**, Kirchner H, Lochs H, Pirlich M. Malnutrition affects quality of life in gastroenterology patients. *World J Gastroenterol* 2006; **12**: 3380-3385 [PMID: 16733855 DOI: 1007-9327/12/3380.asp]

37 **Noman K,** Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. *Clin Nut* 2008; **27:** 5-15 [DOI: 10.1016/j.clnu.2007.10.007]

**P- Reviewer:** Ali,A Dina I, El-Karaksy HM, Facciorusso A, Gallo P, Sharma V

 **S- Editor:** Song XX **L- Editor: E- Editor:**



**Figure 1 Kaplan Meier curves showing the impairment of quality of life through the course of them 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.

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

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic | Good quality of life (*n* = 51) | Impairment of quality of life (*n* = 76) | *P* |
| Male gender | 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:AlcoholViralNASHCryptogenicAutoimmune | 28 (55.0)9 (17.6)2 (3.9)8 (15.7)4 (7.8) | 40 (52.7)15 (19.7)1 (1.3)13 (17.1)7 (9.2) | 0.83 |
| Weight (kg) | 65.2 ± 14.9 | 63.7 ± 13.4 | 0.55 |
| Body mass index (kg/m2) | 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 with *χ*2 or Fisher´s exact test. Numeric variables are expressed as media and SD, and compared with t Student´s test. Statistical significance was considered as a *P* value < 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) | *P* |
| 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. -4.0) | 0.14 |

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

**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 two weeks have you been troubled by a feeling of abdominalbloating? | 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 two weeks? | 3.69 ± 1.366 | 2.94 ± 1.259 | 0.002 |
| 3 How much of the time during the last two weeks have you experienced body pain? | 4.14 ± 0.868 | 3.57 ± 0.848 | 0.0001 |
| 4 How often during the last two weeks 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 two weeks have you experienced abdominal pain? | 5.45 ± 1.273 | 4.96 ± 1.529 | 0.05 |
| 6 How much of the time during the last two weeks 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 two weeks 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 two weeks have you been bothered by having decreased strength? | 4.91 ± 1.218 | 2.90 ± 1.447 | 0.0001 |
| 9 How often during the last two weeks 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 two weeks have you felt anxious? | 5.52 ± 1.112 | 5.33 ± 1.379 | 0.41 |
| 11 How often during the last two weeks 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 two weeks have you felt unhappy? | 5.12 ± 1.077 | 4.41 ± 1.527 | 0.003 |
| 13 How often during the last two weeks have you felt drowsy? | 4.97 ± 1.324 | 4.55 ± 1.051 | 0.05 |
| 14 How much of the time during the last two weeks 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 two weeks have you been irritable? | 5.52 ± 1.128 | 5.36 ± 1.175 | 0.45 |
| 16 How much of the time during the last two weeks 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 two weeks have you been troubled by a feeling of abdominaldiscomfort? | 5.62 ± 1.437 | 4.77 ± 1.816 | 0.004 |
| 18 How much of the time during the last two weeks 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 two weeks have you had mood swings? | 5.50 ± 1.417 | 5.83 ± 1.283 | 0.18 |
| 20 How much of the time during the last two weeks 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 two weeks have you had muscle cramps? | 5.52 ± 1.047 | 5.39 ± 1.074 | 0.51 |
| 22 How much of the time during the last two weeks have you been worried that your symptoms willdevelop into major problems? | 4.19+1.515 | 4.45 ± 1.586 | 0.35 |
| 23 How much of the time during the last two weeks 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 two weeks have you felt depressed? | 5.33 ± 1.082 | 4.68 ± 1.745 | 0.01 |
| 25 How much of the time during the last two weeks 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 two weeks 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 two weeks? | 5.71 ± 1.451 | 6.20 ± 1.065 | 0.03 |
| 28 How much of the time during the last two weeks 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 two weeks 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 media and SD, and compared with *t* Student´s test. Statistical significance was considered as a *P* value < 0.05. CLDQ: Chronic Liver Diseases Questionnaire.