Journal of
*Gastroenterology and Hepatology Research*

Online Submissions: http: //www.ghrnet.org/index./joghr/
doi: 10.17554/j.issn.2224-3992.2019.08.823

Journal of GHR 2019 June 21; **8(3)**: 2896-2902
ISSN 2224-3992 (print) ISSN 2224-6509 (online)

ORIGINAL ARTICLE

# Low Adherence To Nutritional Recommendations In Patients With Cirrhosis: A Prospective Observational Study

*Francesco Palmese[1], *Ferdinando Antonino Giannone[2], Ilaria Bolondi[1], Maurizio Baldassarre[1,3], Giacomo Zaccherini[1], Manuel Tufoni[1], Silvia Boffelli[1], Sonia Berardi[4], Franco Trevisani[1], Paolo Caraceni[1,2,3]

1 Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Italy
2 Support Services and People Care, General Direction, S.Orsola-Malpighi University Hospital, Bologna, Italy
3 Center for Applied Biomedical Research (C.R.B.A.), Alma Mater Studiorum University of Bologna, Italy
4 Department of Care of Organ Failures and Transplants, Internal Medicine for the Treatment of Severe Organ Failures, Sant'Orsola-Malpighi University Hospital, Bologna, Italy
*these authors equally contributed to the work

Conflict-of-interest statement: The authors declare that there is no conflict of interest regarding the publication of this paper.



Correspondence to: Paolo Caraceni, MD, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Via Massarenti 9, 40138 Bologna, Italy.
Email: paolo.caraceni@unibo.it
Telephone: +39-051-2142919
Fax: +39-051-2142930

Received: April 1, 2019
Revised: May 7, 2019
Accepted: May 10, 2019
Published online: June 21, 2019

## ABSTRACT

**AIM:** The aim of the study was to evaluate patients' adherence to the current nutritional recommendations adapted to the individual clinical status.

**MATERIALS AND METHODS:** 192 outpatients with cirrhosis were prospectively evaluated. 161 were considered at risk of impaired nutrition as they present at least one of the following factors: altered body mass index score, non-volitional body weight changes, ascites, peripheral edema, hepatic encephalopathy, or diabetes.Patients at risk were offered a nutritional assessment by a nutritionist, including a 3-days food diary and hand-grip strength (HGS) test. Only 78 patients returned the diaries properly filled in.

**RESULTS:** The analysis of food diaries showed a low-level adherence to the nutritional recommendations: caloric intake was insufficient, in excess or adequate in 75%, 13% and 12% of cases, respectively. An appropriate consumption of carbohydrates, protein and fibers was found only in 10-15% of cases, while the intake of simple sugars, lipids, and water resulted adequate in up to 55%. The protein intake was more frequently insufficient in patients with more advanced disease. HGS test was altered in 49% of patients. 27 subjects (17%) refused the nutritional assessment: these patients presented a significantly less severe disease and a lower number of risk factors.

**CONCLUSIONS:** Patients with cirrhosis have inadequate nutritional intake and poor adherence to the recommendations provided during the normal path of care. Therefore, a multidisciplinary approach with a nutritionist should be recommended, starting in the early stage of the disease when the awareness of patients regarding the importance of nutrition appears to be lower.

**Key words**: Malnutrition; Liver Cirrhosis; Diet records; Energy Intake; Patient compliance



Palmese F, Giannone FA, Bolondi I, Baldassarre M, Zaccherini G, Tufoni M, Boffelli S, Berardi S, Trevisani F, Caraceni P. Low Adherence To Nutritional Recommendations In Patients With Cirrhosis: A Prospective Observational Study. *Journal of Gastroenterology and Hepatology Research* 2019; **8(3)**: 2896-2902 Available from: URL: http://www.ghrnet.org/index.php/joghr/article/view/2552

**Data share:** data described in the manuscript, code book, and analytic code will be made available upon request pending approval by the authors.

**List of abbreviations**: HGS: hand-grip strength; NASH: non-alcoholic steatohepatitis; HE: hepatic encephalopathy; NYHA: New York Heart Association; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HCC: hepatocellular carcinoma; BMI: body mass index; FD: food diary; MELD: model for end stage liver disease; INR: international normalized ratio.

## INTRODUCTION

Patients with cirrhosis frequently present a state of malnutrition, term which refers both to deficiencies (undernutrition and sarcopenia) and to excesses of nutrients (obesity). These disorders can occur alone or, more frequently, in combination. While the association between undernutrition and sarcopenia is expected, the loss of skeletal muscle mass with simultaneous gain of adipose tissue, a condition termed "sarcopenic obesity", has been spreading in last years as a result of the growing number of patients with cirrhosis caused by non-alcoholic steato-hepatitis (NASH)[1-4].

The global prevalence of malnutrition, regardless the different types, is high in patients with cirrhosis and usually progresses in parallel with the severity of the disease, being 40-90% in those with decompensated cirrhosis (Child classes B and C)[5]. However, its prevalence is relatively frequent (25%) also in patients in the earlier stage of the disease (Child class A)[6]. Furthermore, it has been described that malnutrition is an independent predictor of morbidity and mortality in patients with cirrhosis including those undergoing liver transplantation[7].

Patients with cirrhosis, especially in the advanced stage of the disease, suffer from complications, such as ascites, hepatic encephalopathy (HE), renal failure, and diabetes, which require nutritional interventions as part of their global management[5]. Unfortunately, some of these interventions can adversely influence the already altered nutritional status of these patients: examples are represented by the low-protein diet given to prevent HE recurrence, which can aggravate sarcopenia[3], or the low-sodium diet prescribed to better manage the water balance and control ascites, even if it makes the food less palatable thus favoring a further reduction of the already compromised caloric intake[5].

Based on all the above considerations, it appears evident that patients with cirrhosis represent a very heterogeneous population in terms of nutritional requirements, which can be determined only through a personalized assessment of the complex interaction between their nutritional status and clinical condition.

With this background, we performed an observational prospective study in patients with cirrhosis attending the outpatient clinic with the aim to determine the level of their adherence, in terms of both caloric and macronutrients intake, to the current nutritional recommendations adapted to their individual clinical status.

## METHODS

### Study design

The Nutrition in Cirrhosis (NutriCIRR) is a prospective observational study performed at the outpatient clinic for the management of patients with cirrhosis of the O.U."Semeiotica Medica" at the S. Orsola-Malpighi Hospital, University of Bologna, Italy, a third-level referral center for patients with liver diseases. The study endpoint was to determine the level of adherence, in terms of both caloric and macronutrients intake, to the current nutritional recommendations in a cohort of patients with cirrhosis.The inclusion criteria were: age above 18 years, diagnosis of liver cirrhosis made by clinical, laboratory and imaging techniques, stable clinical conditions, and obtaining the informed consent. The main exclusion criteria were the evidence of an ongoing acute decompensation of cirrhosis, diagnosis of heart failure (NYHA ≥ II class) and respiratory failure (GOLD III and IV), hepatocellular carcinoma (HCC) exceeding Milan criteria or other extra-hepatic malignancies, and previous liver transplantation. The research was not considered as a clinical trial and therefore not registered as such.The Emilia-Romagna ethic committee (CE-AVEC) reviewed and approved the study.

### Procedures and data collection

Patients were evaluated during an outpatient visit planned according their normal care path and were considered at risk of impaired nutrition in case they presented at least one of the following conditions: (1) altered body mass index (BMI) score (> 30 and < 22); (2) non-volitional body weight change within 6 months (at least 5%); (3) ascites and/or peripheral edema; (4) recurrent or persistent HE, 5. diabetes. Patients found at risk were offered a nutritional assessment including the examination by a clinical nutrition specialist, who required to fill in a 3-days food diary (FD), and the performance of the hand-grip strength (HGS) test to evaluate muscular strength.

At the time of inclusion, clinical and laboratory data were collected for each patient. The severity of cirrhosis was evaluated by the Model for End Stage Liver Disease[8] and Child-Pugh[9] scores.

### Nutritional assessment

Nutritional assessment was performed by a certified nutritionist (F.A.G.) trained to manage patients with liver diseases. The first step of the analysis consisted in providing all the indications on how to fill in properly the 3-days FD. For each meal, the patient was asked to specify the quantity and origin of the food and the amount of water and other drinks consumed. It was also requested to indicate the distribution of meals during the day and to specify any physical activity carried out and the hours of sedentariness.Once the FD were returned by the patients, the following items were calculatedto assess the nutritional intake: (1) daily caloric intake; (2) carbohydrates intake specifying the proportion of simple sugars; (3) lipid intake; (4) protein intake; (5) fibers intake; (6) water and other liquids intake (including soups); (7) physical activity performed; (8) meals distribution.

The calculation was made by using the nutritional tables of commercial products, when indicated, or the Food Composition Database for Epidemiological Studies in Italy[10]. In case of incorrect or lacking report of the weight of the portions, we have referred to the Portion Quantitative Standards (LARN) of the Italian Human Nutrition Society (SINU)[11] or to a photographic food atlas for portion sizes. Then, the average daily intake of the 3 days was determined for each specific parameter.

To assess the level of adherence, the average daily intake of each patient was compared to what is recommended by the most recent nutritional guidelines[12,13]. Specifically, energy and protein intakes were compared with the standards proposed by the European Society for the Study on the Liver (EASL)[12], while the intake of water, carbohydrates, fibers and lipids were compared with those provided by the European Society for Clinical Nutrition and Metabolism (ESPEN) (Table 1)[12-14].

To estimate the adequacy of nutrients, we referred to the actual body weight for patients who did not show signs of fluid retention. Otherwise, in case of ascites or peripheral edemas, we calculated the dry body weight according to three different methods: (1) using post-paracentesis body weight; (2) using ones registered before the retention of liquids; or (3) calculating it by subtracting a weight

percentage (5, 10 or 15% based on the clinical assessment of the severity of fluid retention)[12]. In obese patients, the ideal body weight was used considering the ideal BMI of 25 kg/m$^2$ [12].

Finally, for each parameter, the patient intake was considered adequate if included within the reference range indicated by the guidelines, while inadequate if outside the range. The degree of inadequacy from the reference range was also estimated. A daily distribution in 4-5 meals was considered adequate, except for patients with HE for whom we considered 6 meals including a late evening snack of complex carbohydrates[13].

### Hand-grip strength test

At the time of nutritional evaluation, muscle function was evaluated by the HGS test. Each patient was asked to perform three times the HGS test using a hand-dynamometer, first with the dominant hand and then with the other hand with an interval of one minute between measurements. The mean value of three attempts was calculated for each hand and the results were compared with the standard values of the healthy Caucasian adults stratified by age and gender[17].

### Statistical analysis

Continuous variables were expressed as mean and standard deviation or median and interquartile range (IQR) according to their distribution. Categorical parameters were expressed as absolute frequency and percentage. Comparisons between categorical variables were made using the $\chi^2$ test or Fisher's exact test in case of comparison between two dichotomous variables.

Continuous data were compared by means of Student's t test or Mann-Whitney U test according to their distributions. When more than two groups were analyzed, the One-way Analysis of Variance (ANOVA) or the Kruskal-Wallis test were used. Pairwise comparisons were made using the Bonferroni correction method. All tests were two-sided and $p$ values < 0.05 were considered statistically significant. Analyses were performed using the Statistical Package for Social Sciences version 25 (SPSS, IBM Corporation, New York, USA).

## RESULTS

### Study population

From March 6, 2015, to March 3, 2017, 192 patients with cirrhosis were screened (Figure 1) and 161 of them resulted at risk of impaired nutrition, according to the presence of at least one of the pre-established criteria (BMI abnormalities, non-volitional changes in body weight, ascites, HE, diabetes). All these 161 patients were offered to receive a specialized nutritional assessment, which was accepted by 134 (83%) patients. However, only 78 (48%) successfully returned the FD thus representing the study population.

The demographic and anthropometric data, the etiology of cirrhosis, the main clinical data and the prognostic scores of the study population are summarized in Table 2. Median age was 61 years and 67% were male. Mean BMI was 27. Alcohol (23%) was the most frequent etiological factor, followed by alcohol plus hepatotropic viral chronic infection (19%). Mean MELD score and mean Child-Pugh score were 12 ± 4 and 7 ± 2 respectively, with a distribution in Child-Pugh classes A/B/C of 38, 51 and 11%, respectively. Regardless clinical features, HCC within Milan criteria was present in 17 patients (22%), HE in 18 (23%), diabetes in 35 (44%) and ascites in 36 (46%).

### Adherence to the nutritional recommendations

As shown in Table 3, the adherence to guidelines on macronutrients and caloric intake was globally low. Among macronutrients, the intake of lipids and simple sugars was adequate in more than half of patients, being 54% and 53% respectively. However, only 9-20% of patients turned to be adherent to the nutritional guidelines regarding the intake of total calories, protein, carbohydrates, and fibers. Indeed, an insufficient intake was found in the vast majority ranging between 77 to 88% of the total cohort, while less than 10% presented an excessive intake.

Interestingly, the greater level of adherence was found for the intakes of liquids and water, which were appropriated in 63% and 55% of cases, respectively. Finally, the daily meal distribution was

**Table 1** Nutritional recommendations for patients with cirrhosis based on international guidelines

| | Values of reference |
|---|---|
| Energy | 30-35 kcal/kg body weight [§] |
| Protein | 1.2-1.5 g/kg body weight [†] |
| Carbohydrates | 45-75% of caloric intake |
| Simple Carbohydrates | 10-15% of caloric intake |
| Fibers | 25-45 g/daily |
| Lipids | 20-30% of caloric intake |

[§] actual body weight in non-obese patients, actual body weight - 650 Kcal in obese patients, dry body weight in case of fluid retention[12]. [†] actual body weight in non-obese patients, ideal body weight in obese patients, dry body weight in case of fluid retention[12].

**Table 2** Demographic, anthropometric, clinical and laboratory features of study population.

| Anthropometrics characteristics | n = 78 |
|---|---|
| Age (years) | 61 (54-65) |
| Male sex | 52 (67%) |
| Weight (kg) | 79 (63-94) |
| Mean BMI | 27 (22-31) |
| BMI | n = 78 |
| < 18.5 kg/m$^2$ | 3 (4%) |
| 18.5-24.9 kg/m$^2$ | 24 (31%) |
| 25.0-29.9 kg/m$^2$ | 22 (28%) |
| ≥ 30.0 kg/m$^2$ | 29 (37%) |
| Cause of cirrhosis | n = 78 |
| Viral | 15 (19%) |
| Alcohol | 18 (23%) |
| Alcohol + Viral | 15 (19%) |
| Alcohol + NASH | 8 (10%) |
| Alcohol + Viral + NASH | 2 (3%) |
| NASH | 8 (10%) |
| NASH + Viral | 6 (8%) |
| Other | 6 (8%) |
| Prognostic scores | n = 73 [†] |
| Mean MELD score | 12 (±4) |
| Mean Child-Pugh score | 7 (±2) |
| Child-Pugh classes (A/B/C) | 28/37/8 (38% - 51% - 11%) |
| Clinical features | n = 78 |
| Ascites | 36 (46%) |
| Hepatic encephalopathy | 18 (23%) |
| Diabetes | 35 (44%) |
| Hepatocellular carcinoma within Milan criteria | 17 (22%) |
| Renal failure (serum creatinine > 1.5 mg/dl) | 4 (5%) |

[†] in 5 patients MELD and Child-Pugh scores were not calculated due to the fact the INR values were altered by the ongoing oral anticoagulant therapy. Abbreviations: BMI: body mass index; NASH: non-alcoholic steatohepatitis; MELD: model for end stage liver disease (8).

adequate in 53% of patients, while less than one-third of patients reported daily physical activity.

Figure 2 shows the degree of inadequacy from the range of normal intakes based on what indicated by international guidelines for all variables[12,15]. When the study population was divided according to the tertile of inadequacy, patients were distributed homogeneously among the tertiles. More importantly, it appears that a considerable part of them had a macronutrient intake very distant from the level of adequacy. As examples,about one-third of patients present a deficit of caloric intake of about 1000 kcal or a deficit of carbohydrates intake of approximately 150 grams/day.

No clear correlations were found between macronutrient intakes and complications or prognostic scores. However, the protein intake was more frequently insufficient in patients with higher MELD score: mean MELD was 12.9 ± 4.1 in patients with insufficient protein intake and 8.7 ± 4.5 in those with regular intake ($p < 0.037$).

### HGS test

HGS test was altered (at least 20% less than the age and sex reference values) in 37/76 (49%) patients at risk (2 patients were not able to perform the HGStest). No significant correlations were found between HGS test and macronutrient intakes.

### Compliance of patients

Twenty-seven patients (17%) did not accept the nutritional assessment when offered with the regular care plan. Interestingly, these patients had lower MELD, Child-Pugh score and a lower number of risk factors for malnutrition (Table 4).

## DISCUSSION

The major finding of the present study is represented by the low level adherence of patients with cirrhosis to the nutritional recommendations provided by the current international guidelines[12,15], in terms of inadequate intake of daily total calories and different macronutrients. Indeed, caloric intake was within the expected normal range only in 12% of patients, being insufficient in about 75% of cases and in excess in 13% of cases. Similarly, an adequate consumption of carbohydrates, protein and fibers was found in only 10-15% of cases, with almost all patients having an insufficient intake. A higher degree of adherence up to about 55% was documented with regard to simple sugars, lipids, and daily drinking water.

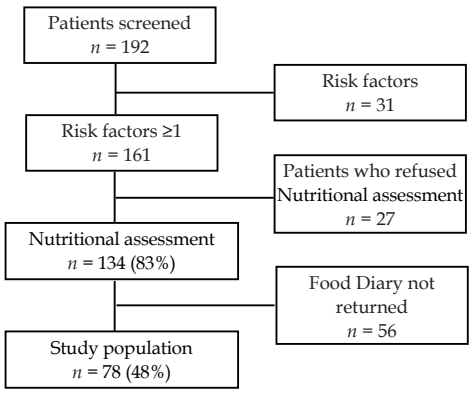


**Figure 1** Study profile.

These patients were all included in an out-patient program of our service specifically dedicated to patients with cirrhosis. Within their regular planned path of care, the hepatologist in charge provides patients with general recommendations on food and liquid consumption with the support of simple written material. Until the beginning of the study, a specialized nutritional assessment was not performed. Thus, these data prompt questions on why diet of these patients appears to be so far distant from what is recommended and how we can improve their nutritional intake. This should be considered an important goal of the global patient management since malnutrition (undernutrition, sarcopenia and obesity) has been now accepted as a major independent risk factor for mortality and morbidity[11].

A possibility to explain this high level of inadequacy can be related to our process of selection of patients at risk and subsequent nutritional assessment. Although we did not apply the screening tools previously validated in patients with cirrhosis, such as the Royal Free Hospital - Global Assessment or the Royal Free Hospital - Prioritizing Tool[19], we considered as risk factors several items already included in these tools (i.e., BMI, weight change, ascites, and peripheral edema). We also decided to insert complications or frequent comorbidities of cirrhosis as predisposing conditions for inadequate food and liquid intake, since their management also includes nutritional recommendations by the physician (i.e., ascites, HE, renal failure, and diabetes). As a result, it is not surprising that more than 80% of our patients were considered at risk of malnutrition. Interestingly, about 25% of those carried at least 3

**Table 3** Adherence of patients to nutritional intakes according to international guidelines and recommendations (n = 78).

| | Adequate | Inadequate (reduced) | Inadequate (excessive) |
|---|---|---|---|
| Caloric intake | 9 (12%) | 60 (76%) | 9 (12%) |
| Carbohydrates intake | 9 (12%) | 69 (88%) | 0 (0%) |
| Simple carbohydrates intake | 41 (53%) | 18 (23%) | 19 (24%) |
| Protein intake | 7 (9%) | 65 (83%) | 6 (8%) |
| Fibers intake | 16 (20%) | 60 (77%) | 2 (3%) |
| Lipids intake | 42 (54%) | 24 (31%) | 12 (15%) |

**Table 4** Prognostic scores, risk factors and complications distribution according to the patient compliance of performing the 3-days FD

| | Patients who returned FD (*n* = 78) | Patients who did not returned FD (*n* = 56) | Patients who refused the nutritional assessment (*n* = 27) | P value |
|---|---|---|---|---|
| Child-Pugh classes (A/B/C) | 38% - 51% - 11% | 29% - 44% - 16% | 74% - 18% - 4% | 0.002 |
| Child-Pugh Score | 7 (6-8) | 8 (6-9) | 6 (5-6) | 0.006 |
| MELD Score | 12 (8-15) | 13 (9-15) | 9 (7-13) | 0.014 |
| Risk factors (1/2/≥3) | 32% - 37% - 31% | 39% - 36% - 25% | 48% - 37% - 15% | 0.532 |
| Ascites | 46% | 44% | 35% | 0.189 |
| Hepatic encephalopathy | 23% | 24% | 15% | 0.587 |
| Diabetes | 44% | 38% | 37% | 0.795 |
| BMI (kg/m$^2$) | 27 (22-31) | 28 (17-40) | 27 (19-40) | 0.559 |

Abbreviations: FD: 3-days food diaries; MELD: model for end stage liver disease (8); BMI: body mass index.

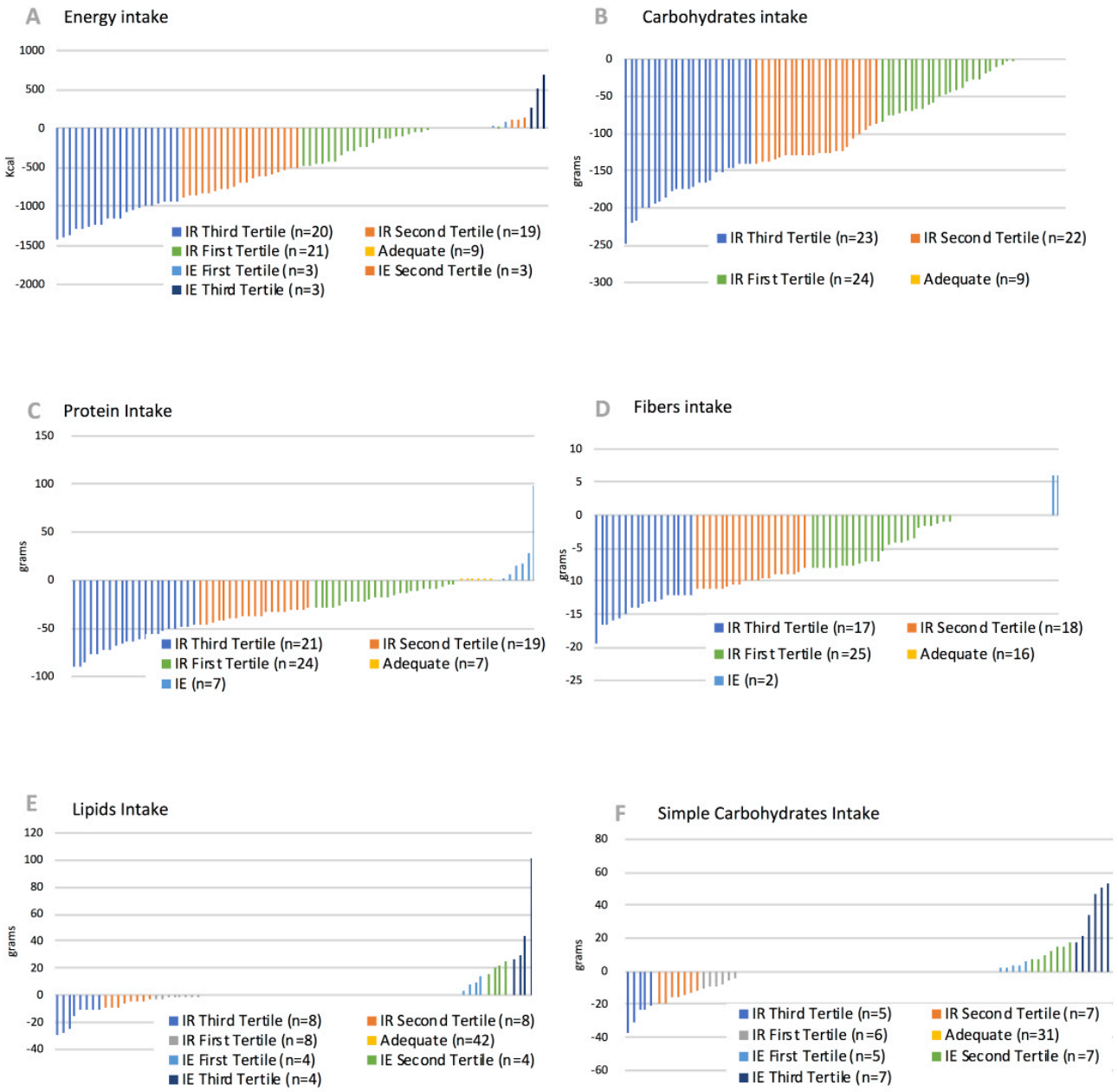


**Figure 2** Level of adherence of macronutrient intakes from the normal ranges indicated by international guidelines (12,14). The distribution of the degree of inadequacy from the range of normal intake is shown in tertiles ($n$ = 78). IR: inadequate reduced. IE: inadequate in excess.

concomitant risk factors. Therefore, the patients evaluated in our study represented a quite heterogeneous population reflecting, however, what the hepatologist encounters in his daily clinical practice.

The second step of the assessment was instead a more tailored approach to the patient, based on the analysis of the personal eating habits and its evaluation by a certified nutritionist with long-experience in managing patients with liver diseases.Thus, it appears reasonable that this approach, which matches the nutritional requirements to the clinical features at the individual patient level, could have contributed to unveil the lack of adherence to the international recommendations.

A potential limitation of the study is the use of a 3-day FD that implies a certain degree of subjectivity. We tried to minimize this risk with an accurate information by the nutritionist on the proper reporting of food and liquid intake with the support of a photographic food atlas for portion size, while the analysis of FD was based, whenever possible,on the nutritional tables of commercial products and alternatively on the Food Composition Database for Epidemiological Studies in Italy[10]. Furthermore, although time-consuming and requiring patient cooperation and skilled personnel, 3-days FD is considered the best method that relies the least on patient recall by international guidelines[12].

There are several reasons to explain the very low-level adherence to the nutritional recommendations, such as both patients' and physicians' poor knowledge of the content of food and drinks, low socio-economic conditions, cultural habits, lack of family support, low awareness of patients on how nutrition can help the management of their disease, limited time to explain accurately dietary recommendations by the physicians in their routine clinical practice, and the general poor compliance with prescribed diets[20,21]. Several indirect findings of our study are in line with the above considerations. First, almost 20% of patients refused the nutritional assessment offered by their hepatologist. Interestingly, these patients

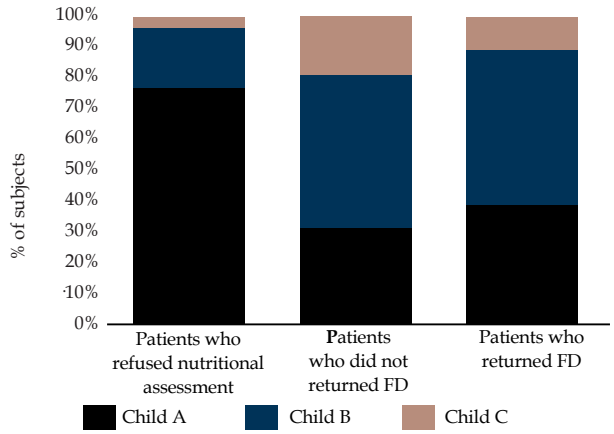


**Figure 3** Distribution of the Child-Pugh classes among patients who refused nutritional assessment, patients who did not returned FD and patients who returned FD.

were less severely ill, as indicated by the lower MELD and Child-Pugh scores, and presented a lower number of risk factors as compared to those who accepted (Figure 3).

Second, about 40% of patients did not return the FD at all or it was too incomplete to be analyzed. Third, it appears reasonable that the conventional wisdom that consumption of "sweet and fat foods" are bad habits may have contributed to the higher adherence of the intake of lipids and simple sugars. Similarly, the relatively acceptable adherence to the water daily intake may reflect both the historical importance given by physicians to fluid balance management for the controlof ascites and the quite easy quantification by the patients of the water amount allowed every day.

Some other aspects on patient adherence deriving from our study deserve a comment. First, the distance from the normal range of macronutrients intake established by recommendations was quite wide in many patients, as additional proof of the overall underestimation of the importance of nutrition in the global care path. Second, the distribution of meals during the day was also not adequate in 44% of patients, although they were invited to divide the daily caloric intake, especially in the presence of HE which requires the consumption of a late-evening snacks[3]. Third, although our study was not designed to analyze the type and extent of daily physical activity, only 28% of patients reported to perform any type of physical activity during the day. At last, it is important to underline that inadequate food intake wasquite frequent also in the early disease stage, as up to 40% of patients with Child-Pugh class A cirrhosis were not adherent to nutritional recommendations. At this regard, HGS was suggestive for sarcopenia in about 35% of Child-Pugh A patients (data not shown).

In conclusion, this observational study clearly shows that patients with cirrhosis present a very poor adherence, both in terms of caloric and macronutrient intakes, to the recommendations of international guidelines, despite the indications provided by physicians as part of the normal path of care. This can be explained both by the limited knowledge of foods and their nutritive principles, and by the lack of an effective educational program on nutrition. Thus, these results highlight the importance of a nutritional intervention tailored to the specific needs of the individual patient, provided possibly by certified nutritionists or dieticians, as part of a multidisciplinary approach directly involving the physicians who have in charge the patients. Finally, this comprehensive nutritional intervention should start from the initial stage of the disease, when lower is the awareness of patients and higher the probability of success in positively influencing patient's prognosis and quality of life.

## ACKNOWLEDGMENTS

No benefits in any form have been received or will be received from a commercial party related to the subject of this article. All authors have read and approved the final manuscript.

## REFERENCES

1. Zamboni M, Mazzali G, Fantin F, Rossi A, Di Francesco V. Sarcopenic obesity: A new category of obesity in the elderly. *Nutr Metab Cardiovasc Dis*. 2008; **18**: 388-395. [PMID: 18395429]; [DOI: 10.1016/j.numecd.2007.10.002].
2. Montano-Loza AJ, Angulo P, Meza-Junco J, Prado CMM, Sawyer MB, Beaumont C, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. *J Cachexia Sarcopenia Muscle*. 2016; **7**: 126-135. [PMID: 27493866]; [DOI: 10.1002/jcsm.12039].
3. Amodio P, Bemeur C, Butterworth R, Cordoba J, Kato A, Montagnese S, et al. The nutritional management of hepatic encephalopathy in patients with cirrhosis: International society for hepatic encephalopathy and nitrogen metabolism consensus. *Hepatology*. 2013; **58(1)**: 325-36. [PMID: 23471642]; [DOI: 10.1002/hep.26370].
4. 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].
5. Tsiaousi ET, Hatzitolios AI, Trygonis SK, Savopoulos CG. Malnutrition in end stage liver disease: Recommendations and nutritional support. *J Gastroenterol Hepatol*. 2008; **23**: 527-533. [PMID: 18397483]; [DOI: 10.1111/j.1440-1746.2008.05369.x].
6. Guglielmi FW, Panella C, Buda A, Budillon G, Caregaro L, Clerici C, et al. Nutritional state and energy balance in cirrhotic patients with or without hypermetabolism. Multicentre prospective study by the "Nutritional Problems in Gastroenterology" Section of the Italian Society of Gastroenterology (SIGE). *Dig Liver Dis*. 2005; **37**: 681-688. [PMID: 15978878]; [DOI: 10.1016/j.dld.2005.03.010].
7. Italian Multicentre Cooperative Project on nutrition in liver cirrhosis. Nutritional status in cirrhosis. J Hepatol. 1994; **21**: 317-325. [DOI: 10.1016/S0168-8278(05)80308-3].
8. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology*. 2001; **33**: 464-470. [PMID: 11172350]; [DOI: 10.1053/jhep.2001.22172].
9. Pugh RNH, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973; **(60)**: 646-649. [PMID: 6367015]; [DOI: 10.1002/bjs.1800600817].
10. Gnagnarella P, Salvini S PM. Food Composition Database for Epidemiological Studies in Italy. 2015. [Available from: URL: http:// www.bda-it/].
11. Società Italiana di Nutrizione Umana (SINU). Livelli di Assunzione di Riferimento di Nutrienti ed energia per la popolazione italiana. IV Rev. 2014; [Available from: URL: http://www.sinu.it/html/pag/tabelle_larn_2014_rev.asp].
12. Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L, et al. EASL Clinical Practice Guidelines on nutrition in chronic liver disease. *J Hepatol*. 2019; **70(1)**: 172-93. [PMID: 30144956]; [DOI: 10.1016/j.jhep.2018.06.024].
13. Bémeur C, Butterworth RF. Reprint of: Nutrition in the Management of Cirrhosis and its Neurological Complications. *J ClinExpHepatol*. 2015; **5**: S131-S140. [PMID: 25755550]; [DOI: 10.1016/j.jceh.2015.02.004].
14. Plauth M, Merli M, Kondrup J, Weimann A, Ferenci P, Muller MJ. ESPEN guidelines for nutrition in liver disease and transplantation. *ClinNutr*. 1997; **16**: 43-55. [PMID: 16844569]; [DOI: 10.1016/S0261-5614(97)80022-2].
15. Plauth M, Cabré E, Riggio O, Assis-Camilo M, Pirlich M, Kondrup

J, et al. ESPEN Guidelines on Enteral Nutrition: Liver disease. *ClinNutr.* 2006; **25**: 285-294. [PMID: 16707194]; [DOI: 10.1016/j.clnu.2006.01.018].
16. Plauth M, Schütz T. ESPEN-Guidelines-Parenteral-Hepatology. ClinNutr. 2011; 30: 132. [DOI: 10.1016/j.clnu.2010.07.018].
17. Günther CM, Bürger A, Rickert M, Crispin A, Schulz CU. Grip Strength in Healthy Caucasian Adults: Reference Values. *J Hand Surg Am.* 2008; **33(4)**: 558-565. [PMID: 18406961]; [DOI: 10.1016/j.jhsa.2008.01.008].
18. Plauth M, Cabré E, Riggio O, Assis-Camilo M, Pirlich M, Kondrup J, et al. ESPEN Guidelines on Enteral Nutrition: Liver disease $ Summary of statements: Alcoholic steatohepatitis Subject Recommendations Grade 55 Number. *ClinNutr.* 2006; **25**: 285-294. [PMID: 16707194]; [DOI: 10.1016/j.clnu.2006.01.018].
19. Borhofen SM, Gerner C, Lehmann J, Fimmers R, Görtzen J, Hey B, et al. The Royal Free Hospital-Nutritional Prioritizing Tool Is an Independent Predictor of Deterioration of Liver Function and Survival in Cirrhosis. *DigDis Sci.* 2016; **61(6)**: 1735-1743. [PMID: 26725059]; [DOI: 10.1007/s10620-015-4015-z].
20. Burra P, Giannini EG, Caraceni P, GinanniCorradini S, Rendina M, Volpes R, et al. Specific issues concerning the management of patients on the waiting list and after liver transplantation. *Liver Int.* 2018; **38(8)**: 1338-62. [PMID: 28096056]; [DOI: 10.1111/liv.13755].
21. Ney M, Gramlich L, Mathiesen V, Bailey RJ, Haykowsky M, Mang M, et al. Patient-perceived barriers to lifestyle interventions in cirrhosis. *Saudi J Gastroenterol*. 2017; **23(2)**: 97-104. [PMID: 28361840]; [DOI: 10.4103/1319-3767.203357].