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The impact of nutritional supplementation on quality of life in patients infected with hepatitis C virus

R. S. S. B. Boulhosa,* L. P. M. Oliveira,*† R. P. Jesus,† L. N. Cavalcante,*‡ D. C. Lemaire,§ L. Vinhas,¶ L. G. C. Lyra‡ & A. C. Lyra*‡

*Medicine and Health Post-Graduation Program, Federal University of Bahia, Salvador, Brazil
†Nutrition Science Department, Federal University of Bahia, Salvador, Brazil
‡Gastro-Hepatology Unit, Hospital São Rafael, Salvador, Brazil
§Laboratory of Immunology, Health Science Institute, Federal University of Bahia, Salvador, Brazil
¶Center for Treatment and Surgery of Obesity, Salvador, Brazil

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Correspondence
R. Souza da Silva Baqueiro Boulhosa, R. Álvaro Cova, 4 – Ribeira, Salvador, Bahia 40420-560, Brazil.
Tel.: +55 71 3316 7643; +55 71 99674891
Fax: +55 71 3283 7700
E-mail: ramonabaqueiro@hotmail.com

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Abstract

Background: The present study aimed to evaluate the impact of animal and vegetable protein supplementation on health-related quality of life (HRQL) in patients with hepatitis C virus (HCV) and to investigate clinical and nutritional variables related to quality of life in these patients.
Methods: One hundred and forty patients infected with HCV were randomly assigned to one of two groups: the Soy Group (SG; $n = 72$), where patients received a soy supplement diet and the Casein Group (CG; $n = 68$), where patients received casein as a supplement. Anthropometric, biochemical and clinical assessments were performed in all patients, and the Short-Form Health Survey was applied at baseline and 12 weeks after study initiation.
Results: Before supplementation, poor HRQL scores were associated with female sex ($P = 0.004$) and advanced fibrosis (F3/F4; $P = 0.04$). Reduced HRQL scores were correlated with age ($r = -0.263$; $P = 0.002$), serum albumin levels ($r = 0.245$; $P = 0.004$), lean mass ($r = 0.301$; $P < 0.0001$) and body fat percentage ($r = -0.262$; $P = 0.002$). After 12 weeks of intervention, patients in both supplementation groups showed significantly increased HRQL scores, with no difference being observed between the SG and the CG.
Conclusions: Nutritional therapy with either soybean or casein supplementation improved quality of life in patients infected with HCV. Quality of life was influenced by anthropometric, biochemical, clinical and sociodemographic factors in patients with HCV before nutritional supplementation.

Introduction

Chronic hepatitis C virus (HCV) infection is a significant public health problem and is estimated to affect 170 million persons worldwide [World Health Organization (WHO), 1999; Lavanchy, 2008]. Approximately 10–20% of chronically infected HCV patients will progress to liver cirrhosis after two decades (Freeman *et al.*, 2001; Harris *et al.*, 2006). Once cirrhosis has developed, patients may go on to develop liver failure or hepatocarcinoma, often becoming potential candidates for liver transplantation (Ferenci *et al.*, 2007; Jacobson *et al.*, 2010).

Patients with HCV have more impaired health-related qualities of life than the general population (Bayliss *et al.*,1998; McHutchison *et al.*,2001; Younossi *et al.*, 2005). These decrements in functioning and well-being have been linked to several factors, including the severity of their liver disease, sex and drug abuse, as well as manifestations, such as fatigue, depression and cognitive impairment (Strauss & Teixeira, 2006; Foster, 2009).

Targeted nutritional assistance that aims to promote healthy lifestyles and appropriate nutrition in patients with chronic liver disease (CLD) can minimise or prevent the comorbidities associated with HCV. Therefore, nutri-

tional treatment may reduce the progression of liver disease and decrease related metabolic complications, such as insulin resistance, nonalcoholic fatty liver disease and diabetes mellitus type II, all of which confer a poor prognosis in CLD (Okita, 2004). Although the impact of different nutritional therapies has been described previously, no studies to date have assessed specific nutritional interventions in patients infected with HCV and the influence of interventions on the quality of life of these individuals.

Therefore, the present study aimed to evaluate the impact of animal and vegetable protein supplementation on quality of life in patients with chronic HCV and to investigate clinical and nutritional variables associated with quality of life in these subjects.

Materials and methods

Subjects

Nondiabetic patients with chronic HCV were recruited from a reference outpatient unit of the Federal University of Bahia's Hospital between June 2008 and December 2009. The diagnosis of HCV infection was made by the presence of serum anti-HCV, which was confirmed by qualitative determination of HCV RNA. Inclusion criteria were: patients aged >18 years patients with ethanol consumption <20 g day^{-1}; patients with normal liver function (Child-Pugh A), and patients who were not undergoing antiviral therapy or who had discontinued antiviral therapy for at least 6 months.

Patients co-infected with HIV and/or HBV, patients with renal failure and patients with heart disease, decompensated cirrhosis, pregnancy, any malignancy, diabetes mellitus or obesity [body mass index (BMI) > 30 kg m^{-2}] were excluded. The subjects provided their written informed consent before participating in the study. The Ethics Committee of the Federal University of Bahia approved the study.

Management protocol

The present study is a branch of a randomised, prospective and single-blinded clinical trial that was published previously (Oliveira *et al.*, 2012). One hundred and sixty patients were divided into two groups: the Casein Group (CG; $n = 80$), where patients were supplemented with 32 g per day of animal protein (casein), and the Soy group (SG; $n = 80$), where patients were supplemented with 32 g per day of vegetable protein (soy). Both supplements were powder and all patients were instructed to dissolve them in water, juice, soup, porridge or to consume then with fruit three times per day. In the present study, we evaluated only 140 patients and 20 patients (12 from the CG and 8 from the SG) were not included because they did not answer the health-related quality of life (HRQL) questionnaire 3 months after the supplementation.

Based on their nutritional status and dietary habits, patients received verbal and written dietary advice to promote healthy eating and weight control. Diet counselling aimed to promote the ingestion of a normocaloric, normoglycaemic and high-protein (1.5 g kg^{-1} per day) diet in both groups (Plauth *et al.*, 1997). Patients returned on a monthly basis to receive their supplements.

Patients underwent follow-up visits once a month with registered dietitians to evaluate adherence to the diet prescription and protein supplementation. Schedule monitoring also included weekly telephone calls in the first month and biweekly thereafter.

Quality of life assessment

Health-related quality of life was assessed with the 36-item Short Form Health Survey (SF-36), a 36-item, self-administered questionnaire encompassing eight physical and mental health domains, including physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health, as well as two physical and mental summary scales, namely, the physical component summary (PCS) and mental component summary (MCS) (Ware *et al.*, 1994). Raw scores were recorded, aggregated and transformed onto a 0–100 scale, with higher scores indicating better health; this metric was adjusted for values of the American general population (Ware & Gandek, 1998). The SF-36 has demonstrated consistently high reliability and validity in a variety of patient populations (McHorney *et al.*, 1993, 1994) and has been translated and validated in the Brazilian population (Ciconelli *et al.*, 1999). Measurements of HRQL were obtained at baseline and after 12 weeks of nutritional supplementation.

Data collection

Complete demographic and social history data (sex, age, educational level, occupation and lifestyle) were obtained from all patients. Clinical data, such as clinical diagnosis, viral genotype, necro-inflammatory activity index and fibrosis (Metavir classification), were collected directly from medical records.

Anthropometrics and body composition

Anthropometric data, including body weight and height, were measured according to standardised procedures (CDC, 2000) at the baseline and after 12 weeks of supplementation. Additionally, Multi-Compartment Bioimpedance (Inbody 520; Biospace, Cerritos, CA, USA) was performed in accordance with the standardised instruc-

tions (Eickemberg *et al.*, 2011) before and after 12 weeks of supplementation.

Biochemical analysis

At the baseline, after a 12-h fast, blood samples were collected for the determination of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (γGT), serum albumin, plasma glucose and insulin.

Before supplementation, the insulin resistance index was predicted according to the homeostasis model assessment (HOMA-IR) method. The formula was: insulin resistance [HOMA-IR = fasting insulinaemia (microU mL^{-1}) × fasting glycemia (mML^{-1})/22.5) (Matthews *et al.*, 1985).

Statistical analysis

Descriptive analysis was performed to characterise the study population. The Mann–Whitney *U*-test and Wilcoxon's rank sum tests were used to compare the quality of life values in both groups and to evaluate the differences obtained at baseline and after intervention. Spearman's correlation coefficient was calculated to assess the relationship between variables.

$P < 0.05$ was considered statistically significant. Statistical analysis was performed with the R, version 2.12 (R Development Core Team, 2010).

Results

A total of 160 patients were randomised to the CG or SG. Twenty patients were excluded because they had not responded to the SF-36 questionnaire before or after nutritional therapy. Thus, 140 patients completed the study, consisting of 68 patients from the CG and 72 patients from the SG.

Demographic, clinical, biochemical, histological and anthropometric characteristics of all 140 patients are summarised in Table 1. Most patients were aged <60 years (87.9%) with a mean (SD) age of 52.55 (10.47) years; 61.4% were male. The prevalence of HCV genotype 1 and non-1 infected subjects was 85.7% and 14.3%, respectively; advanced fibrosis (Metavir F3/F4) was detected in 41.8% of patients. The median (SD) PCS and MCS scores were 46.47 (5.68) and 51.09 (5.19), respectively.

At baseline, there were no statistically significant differences in the sociodemographic characteristics or clinical, anthropometric, biochemical or quality of life summary components between the CG and SG (Table 1).

The median SF-36 values for the PCS and MCS were significantly lower in female patients with chronic HCV compared to males ($P = 0.004$ and 0.014, respectively), revealing a difference in quality of life between the two sexes at baseline (Table 2).

We verified a stage-dependent reduction of the physical summary score in patients with chronic HCV, although there was no corresponding significant association with the MCS. Thus, PCS was significantly impaired in patients with advanced fibrosis (F3/F4) compared to patients showing a lower stage of fibrosis ($P = 0.04$). Moreover, PCS was reduced among patients with systemic arterial hypertension ($P = 0.024$). Other clinical variables were not associated with domains of quality of life at baseline (Table 2).

Worse PCS but not MCS scores were correlated with elevated γGT ($r = -0.187$; $P = 0.031$) and low serum albumin levels ($r = 0.245$; $P = 0.004$). Furthermore, fasting glucose was negatively correlated with MCS ($r = -0.228$; $P = 0.007$). No significant correlation was found between the SF-36 scores and AST, ALT and HOMA-IR levels. However, we observed a trend toward a negative correlation between PCS and AST ($r = -0.146$; $P = 0.088$) and HOMA-IR ($r = -0.152$; $P = 0.074$).

Body composition, as determined by multi-compartmental bioimpedance, and BMI were compared with components of the SF-36 questionnaire. According to this analysis, there was a significant positive correlation between lean mass with seven domains of SF-36 and two summary components: PCS ($r = 0.301$; $P < 0.0001$) and MCS ($r = 0.198$; $P = 0.019$). Body fat percentage demonstrated an inverse correlation with physical functioning ($r = -0.32$; $P < 0.0001$), body pain ($r = -0.212$; $P = 0.012$) and PCS ($r = -0.262$; $P = 0.002$). Negative correlations were also observed between BMI and general health ($r = -0.198$; $P = 0.019$), social function ($r = -0.167$; $P = 0.048$) and MCS ($r = -0.2$; $P = 0.018$). After 12 weeks of supplementation, most of the SF-36 domains maintained a positive correlation with lean mass, and a negative correlation with body fat percentage and BMI (Table 3). Notably, over the 12-week treatment period, a significant increase in lean mass was observed in both groups (CG: from 45.16 kg to 46.27 kg, $P = 0.033$; SG: from 46.32 kg to 48.43 kg, $P = 0.002$).

The effect of nutritional intervention in all patients on HRQL is shown in Fig. 1. After 12 weeks of intervention, independent of the protein source, we observed a significant improvement in the domains: physical functioning ($P = 0.008$), role physical ($P < 0.0001$), bodily pain ($P = 0.004$), general health ($P < 0.0001$), social functioning ($P = 0.009$), mental health ($P < 0.0001$) and the PCS ($P < 0.0001$) and MCS ($P = 0.001$) scores (Fig. 1a). In the group supplemented with casein, we verified an improvement in the domains: physical functioning ($P = 0.023$), role physical ($P = 0.026$), bodily pain ($P = 0.008$), general health ($P = 0.001$), mental health ($P < 0.0001$), and the

PCS ($P = 0.001$) and MCS ($P = 0.014$) scores (Fig. 1b). Significant increases in scores for role physical ($P = 0.005$), general health ($P < 0.0001$), social functioning ($P = 0.01$), mental health ($P < 0.0001$), PCS ($P = 0.01$) and MCS ($P = 0.018$) were seen in the SG (Fig. 1c).

Table 4 shows that there were no significant differences between the groups after supplementation. Therefore, supplementation improved quality of life independently of the protein source.

Discussion

In the present study, we evaluated the impact of protein supplementation on the HRQL of patients with chronic HCV. To the best of our knowledge, the present study is the first to have evaluated the effect of nutritional supplementation on the quality of life of this patient population. Previous studies in different clinical populations have shown that malnourishment is related to a poor quality of life and that different nutritional interventions are effective in improving both nutritional status and quality of life (Wanden-Berghe *et al.*, 2009).

The results of the present study show that nutritional intervention with protein supplementation, independently of the type of protein (either casein or soy protein), caused a significant increase in quality of life scores in both groups; however, this increase was not significantly different between the two groups. It is probable that the

Table 1 Characterization of the study population

	All, *n* (%)	Casein group, *n* (%)	Soy group, *n* (%)	*P*-value
Demographics				
Age				
Adult	123 (87.9)	57 (83.4)	66 (91.7)	0.16
Elderly	17 (12.1)	11 (16.6)	6 (8.3)	
Gender				
Male	86 (61.4)	40 (58.8)	46 (63.0)	0.538
Female	54 (38.6)	28 (41.2)	26 (36.1)	
Clinical data				
Genotype				
1	114 (85.7)	58 (90.6)	56 (81.2)	0.12
2 and 3	19 (14.3)	6 (9.4)	13 (18.8)	
Degree of fibrosis				
0/1/2	64 (58.2)	29 (52.7)	35 (63.6)	0.246
3/4	46 (41.8)	26 (47.3)	20 (36.4)	
Biochemical data	Median (IQR)	Median (IQR)	Median (IQR)	*P*-value
Fasting glucose (mg dL^{-1})	91.00 (84.00–99.00)	90.50 (84.00–97.00)	91.50 (83.25–99.75)	0.573
HOMA-IR	2.28 (1.4–3.19)	2.25 (1.4–3.1)	2.30 (1.32–3.28)	0.822
AST (U L^{-1})	59.50 (39.00–79.25)	60.50 (42.80–78.25)	58.00 (36.50–79.50)	0.174
ALT (U L^{-1})	81.00 (56.00–88.00)	80.50 (56.75–104.3)	81.00 (53.50–108.50)	0.435
γGT (U L^{-1})	92.00 (51.00–136.00)	109.00 (58.00–161.00)	77.00 (48.00–106.00)	0.325
Albumin (mg dL^{-1})	4.00 (3.6–4.35)	3.90 (3.70–4.10)	4.00 (3.60–4.40)	0.11
Anthropometric data	Mean (SD)	Mean (SD)	Mean (SD)	*P*-value
Body Mass Index (kg m^{-2})	24.69 (3.26)	24.75 (3.54)	24.63 (3.54)	0.827
Body fat (%)	27.21 (9.71)	27.75 (9.92)	26.69 (9.92)	0.521
Lean mass (kg)	45.76 (9.02)	45.16 (9.39)	46.31 (8.69)	0.298
Quality of life component summary	Median (IQR)	Median (IQR)	Median (IQR)	*P*-value
Physical component summary	46.47 (40.79–52.15)	44.50 (36.54–52.46)	46.99 (41.83–52.15)	0.71
Mental component summary	51.09 (45.90–56.28)	52.57 (47.5–57.58)	48.86 (42.37–55.35)	0.11

AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGT, gamma glutamyl aminotransferase; HOMA-IR, homeostasis model assessment of insulin resistance; IQR, interquartile range; SD, standard deviation.

Table 2 Relationship between demographics, clinical and biochemical data to physical and mental components scores on SF-36-item Short Form Health Survey (SF-36)

	Physical component summary				Mental component summary			
	Median (IQR)	*P*-value*	Correlation coefficient	*P*-value†	Median (IQR)	*P*-value*	Correlation coefficient	*P*-value†
Demographics								
Age			−0.263	0.002			0.051	0.552
Gender								
Male	48.49 (41.50–55.47)	0.004			52.36 (44.09–60.8)	0.014		
Female	41.02 (34.23–48.28)				45.95 (36.42–55.43)			
Clinical and histological data								
Degree of fibrosis								
F0/F2	48.72 (39.97–57.19)	0.04			51.09 (40.23–61.92)	0.816		
F3/F4	44.00 (33.80–54.2)				51.31 (39.68–62.94)			
Genotype								
1	46.08 (36.11–56.05)	0.184						
2 or 3	46.96 (42.13–51.09)							
Systemic arterial hypertension								
Yes	39.71 (28.88–50.54)	0.024			51.28 (41.43–61.13)	0.728		
No	47.73 (40.90–54.58)				50.08 (40.03–50.08)			
Biochemical data								
AST			−0.146	0.088			−0.045	0.598
ALT			0.039	0.652			−0.021	0.806
γGT			−0.187	0.031			0.02	0.816
Fasting glucose			−0.93	0.275			−0.228	0.007
HOMA-IR			−0.152	0.074			−0.06	0.48
Albumin			0.245	0.004			0.054	0.531

Results of bivariate analysis.

*Mann–Whitney *U*-test.

†Spearman's correlation coefficient.

AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGT, gamma glutamyl aminotransferase; HOMA-IR, homeostasis model assessment of insulin resistance; IQR, interquartile range.

increase in quality of life scores was related to a combination of better body composition with a higher lean mass and continuous and individualised nutritional care offered to both groups of patients, which promoted changes in diet and life habits; the quality of the protein did not appear to be an important issue. In a previous study with patients with head and neck cancer, nutritional counselling promoted improvement in patients' nutritional and nonnutritional outcomes, such as nutritional status, overall intake, radiotherapy-related symptoms and quality of life, as evaluated by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire, version 3.0 (Ravasco *et al.*, 2005). In that study, both groups had higher scores after intervention than baseline in all functional domains and symptoms scales during the radiotherapy; the group of patients that received their usual diet plus nutritional supplements without counselling had the domains scores increased by 52% but, in the medium term, these changes were not maintained and returned to baseline. Subjects who received nutritional advice had their scores increased by 56% and, in the medium term, these changes were maintained over time (Ravasco *et al.*, 2005).

In the present study, using multi-compartment bioimpedance, we observed that adequate body composition with greater lean mass and a lower percentage of body fat correlated with a better quality of life at baseline, showing that nutritional status is an important aspect to quality of life, even in patients with compensated liver disease. Protein malnutrition in patients with liver cirrhosis, as measured by arm muscle circumference, is associated with a lower survival rate compared to patients without nutritional deficits (Alberino *et al.*, 2001). Two previous studies have evaluated the relationship between nutritional indicators and quality of life in patients with HCV. Bonkovsky *et al.* (2007) observed higher mean BMI values in patients with worse PCS and no association between BMI and MCS (Bonkovsky *et al.*, 2007). Córdoba *et al.* (2003) did not find an association between PCS and BMI and mid-arm muscle circumference, although their study did show a positive correlation between hand grip strength, a functional indicator of protein depletion and malnutrition, and PCS (Córdoba *et al.*,

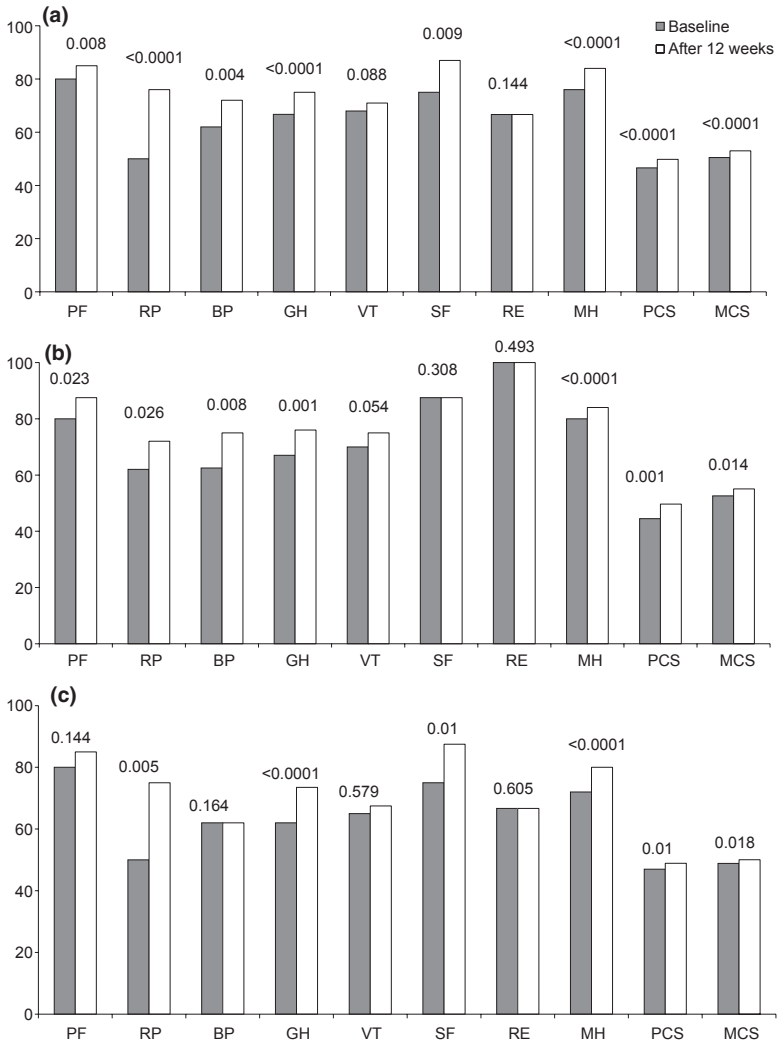

Figure 1 The 12-week changes from baseline in the health-related quality of life scores of patients supplemented with both animal and vegetal protein (a), animal protein only (b) and soy protein only (c). Grey bars: baseline; white bars: after 12 weeks. Results of the Wilcoxon test ($P < 0.05$). BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; RE, role emotion; RP, role physical; SF, social functioning; VT, vitality.

2003). However, both studies included subjects with decompensated liver disease. The present study is first to evaluate the influence of body composition in the HRQL of compensated patients infected with HCV.

One previous study reported that the spontaneous dietary intake of protein is lower than recommended in patients with HCV-related liver cirrhosis and, after intervention with adequate oral diet prescribed by a dietitian, there was a synergistic improvement of dietary intake of protein and mid-arm muscle circumference (Manguso *et al.*, 2005). In the present study, diet supplementation promoted an increase in the content of lean mass in both intervention groups, as expected, and a similar increase was observed in HRQL scores. Similarly, another study showed an increase in quality of life scores after a nutritional supplementation that increased fat-free mass in patients with liver cirrhosis (Plank *et al.*, 2008), thereby confirming the relationship between body composition and quality of life and emphasising the importance of nutritional care in these patients.

We also evaluated the relationship between fibrosis and quality of life. We found a significant association between the impairment of the physical aspects of quality of life and the stage of fibrosis in patients infected with HCV. Several studies have previously shown a deterioration of HRQL scores in proportion to the severity of liver disease; however, most of these studies included decompensated chronic HCV patients (Córdoba *et al.*, 2003; Bonkovsky *et al.*, 2007; Teuber *et al.*, 2008). Several studies compared compensated patients with chronic HCV with healthy controls or the general population and showed an influence of HCV in impairments of HRQL (Bayliss *et al.*, 1998; Bonkovsky & Woolley, 1999; McHutchison *et al.*, 2001; Gallego-Orozco *et al.*, 2003; Younossi *et al.*, 2005; Teixeira *et al.*, 2006; Kallman *et al.*, 2007). The present study showed that patients with HCV and advanced but

Table 3 Correlation between anthropometric variables and 36-item Short form Health Survey (SF-36) domains and summary scores at baseline and after 12 weeks of nutritional therapy

	Baseline						After 12 weeks					
	Lean mass (kg)		Body fat (%)		Body mass index (kg m^{-2})		Lean mass (kg)		Body fat (%)		Body mass index (kg m^{-2})	
	*r**	*P*-value	*r**	*P*-value	*r**	*P*-value	*r**	*P*-value	*r**	*P*-value	*r**	*P*-value
SF-36 components												
Physical functioning	0.294	<0.0001	−0.32	<0.0001	−0.1	0.238	0.401	<0.0001	−0.351	<0.0001	0.06	0.479
Role physical	0.172	0.042	−0.119	0.16	−0.68	0.423	0.183	0.03	−0.109	0.199	−0.144	0.09
Bodily pain	0.295	<0.0001	−0.212	0.012	−0.52	0.545	0.241	0.004	−0.253	0.003	−0.05	0.557
General health	0.264	0.002	−0.088	0.302	−0.198	0.019	0.241	0.03	−0.018	0.836	−0.259	0.002
Vitality	0.21	0.011	−0.149	0.08	−0.77	0.368	0.219	0.009	−0.144	0.089	−0.115	0.175
Social function	0.156	0.066	0	0.997	−0.167	0.048	0.223	0.008	−0.144	0.09	−0.144	0.09
Role emotional	0.236	0.005	−0.145	0.088	−0.103	0.227	00.126	0.137	−0.136	0.109	−0.112	0.187
Mental health	0.235	0.005	−0.082	0.338	−0.163	0.055	0.262	0.002	−0.151	0.074	−0.199	0.019
Physical component summary	0.301	<0.0001	−0.262	0.002	−0.013	0.88	0.3	<0.0001	−0.24	0.004	−0.141	0.098
Mental component summary	0.198	0.019	−0.033	0.702	−0.2	0.018	0.192	0.023	−0.129	0.13	−0.18	0.02

Results of bivariate analysis.

*Spearman's correlation coefficient. Lean mass and body fat evaluated by multi-compartment bioimpedance.

Table 4 Median quality of life scores at baseline and after 12 weeks of nutritional therapy

	Baseline			After 12 weeks		
	Soy group median (IQR)	Casein group median (IQR)	*P*-value	Soy group median (IQR)	Casein group median (IQR)	*P*-value
PF	80.00 (61.50–88.5)	80.00 (51.25–90.00)	0.92	85.00 (66.25–100.00)	87.50 (65.00–100.00)	0.93
RP	50.00 (0–100.00)	62.50 (25.00–100.00)	0.47	75.00 (50.00–100.00)	75.00 (50.00–100.00)	0.97
BP	62.00 (41.25–83.00)	62.00 (40.00–82.00)	0.98	62.00 (51.00–63.00)	72.00 (60.00–83.00)	0.26
GH	62.00 (47–78.00)	67.00 (47.25–86.75)	0.62	73.50 (60.00–80.00)	76.00 (62.00–88.00)	0.64
VT	65.00 (50.00–80.00)	70.00 (55.00–85.00)	0.42	67.50 (50.00–82.00)	75.00 (60.00–93.00)	0.08
SF	75.00 (53.12–88.00)	87.50 (52.50–100.00)	0.19	87.50 (65.5–100.00)	87.50 (75.00–100.00)	0.95
RE	66.67 (0–88.87)	100.00 (0–100.00)	0.38	66.67 (33.37-100.00)	100.00 (33.37–100.00)	0.07
MH	72.00 (52.00–90.00)	80.00 (64.00–96.00)	0.06	80.00 (60.00–100.00)	84.00 (72.00–100.00)	0.17
PCS	46.99 (41.83–52.15)	44.50 (36.54–52.46)	0.71	48.90 (43.10–54.69)	49.67 (45.67–54.30)	0.92
MCS	48.86 (42.37–55.35)	52.57 (47.5–57.58)	0.11	50.06 (43.30–56.78)	55.08 (51.04–59.30)	0.11

Results of Mann–Whitney *U*-test ($P < 0.05$).

BP, bodily pain; GH, general health; IQR, interquartile range; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; RE, role emotion; RP, role physical; SF, social functioning; VT, vitality.

compensated fibrosis presented a reduction in the physical domain of HRQL compared to subjects with HCV and mild or moderate fibrosis; this result suggests a progressive reduction of HRQL with worsening fibrosis.

In the present study, analyses by sex revealed that women had lower SF-36 scores, as reported in other studies. Some studies used SF-36 and noted a significant reduction in the physical domains of quality of life (Hussain *et al.*, 2001; Córdoba *et al.*, 2003; Teixeira *et al.*, 2006; Kallman *et al.*, 2007). Other studies have verified an impairment of the mental domains of HRQL in woman with HCV with the same tool (Teixeira *et al.*, 2006; Teuber *et al.*, 2008). The reasons for lower quality of life scores in female patients are not totally understood, although a number of qualitative studies have pointed out that social problems, including stigma, discrimination and prejudice against patients infected with HCV, affect women disproportionately. Furthermore, women express greater fears about their sexual and reproductive life, mainly because of the potential risk of virus transmission to partners and children (Gifford *et al.*, 2003). Uncertainties about the future and the ability to take care of family are also a source of anxiety that is more pronounced in women than in men (Crockett & Gifford, 2004).

A possible limitation of the present study is that we used a generic questionnaire instead of a specific tool to evaluate quality of life. Currently, there is only one specific liver disease questionnaire validated in the Brazilian population: the Liver Disease Quality of Life (Teixeira *et al.*, 2005). However, this instrument is adequate only in patients with decompensated liver disease, which was not the population investigated in the present study. There are other specific liver-disease questionnaires designed for compensated liver disease subjects, such as the Hepatitis Quality of Life Questionnaire (Ware *et al.*, 1999) and the Chronic Liver Disease Questionnaire (Younossi *et al.*, 1999), however these questionnaires have not been validated in our population.

Although SF-36 is a generic questionnaire, it is a reliable instrument that has been extensively previously tested and validated in many populations of healthy and diseased subjects, including patients with chronic liver disease. Therefore, SF-36 appears to be suitable for evaluating and comparing different studies and therapeutic protocols. Additionally, our studied population comprised patients with compensated liver disease without complications related to cirrhosis.

Conclusions

The combination of nutritional supplementation with casein or soy protein and an individualised and continuous nutritional care protocol for 12 weeks promoted a better quality of life in patients infected with HCV. Additionally, physical and mental aspects of quality of life were correlated with lean mass and body fat percentage.

Conflicts of interest, sources of funding and authorship

The authors declare that there are no conflicts of interest.
No funding is declared.
LPMO, RPJ, ACL, DCL, LGCL conceived and designed the study. LPMO, RPJ, RSSBB, LNC and ACL were involved in the acquisition of data and evaluated and assisted the patients. LPMO, RPJ and RSSBB conducted the research. RSSBB analysed the data and performed the statistical analysis. RSSBB, LPMO, RPJ, ACL and LGCL drafted the article and revised it critically for important intellectual content. All authors critically reviewed the manuscript and approved the final version submitted for publication.

References

Alberino, F., Gatta, A., Amodio, P., Merkel, C., Pascoli, L., Boffo, G. & Caregaro, L. (2001) Nutrition and survival in patients with liver cirrhosis. *Nutrition* **17**, 445–450.

Bayliss, M.S., Gandek, B., Bungay, K.M., Sugano, D., Hsu, M.A. & Ware, J.E. Jr. (1998) A questionnaire to assess the generic and disease-specific health outcomes of patients with chronic hepatitis C. *Qual. Life Res.* **7**, 39–55.

Bonkovsky, H.L., Woolley, J.M. & The Consensus Interferon Study Group (1999) Reduction of health-related quality of life in HCV and improvement with interferon therapy. *Hepatology* **29**, 264–270.

Bonkovsky, H.L., Snow, K.K., Malet, P.F., Madruga, C.B., Fontana, R.J., Sterling, R.K., Kulig, C.C., Di Bisceglie, A.M., Morgan, T.R., Dienstag, J.L., Ghany, M.G., Gretch, D.R. & HALTC-C Trail Group. (2007) Health-related quality of life in patients with chronic hepatitis C and advanced fibrosis. *J. Hepatol.* **46**, 420–431.

Centers for Disease Control and Prevention (CDC). (2000) *National Health and Nutrition Examination Survey (NHANES). Anthropometry Procedures Manual*. Available at: http://www.cdc.gov/nchs/data/nhanes/bm.pdf (accessed on 6 October 2008).

Ciconelli, R.M., Ferraz, M.B., Santos, W., Meinão, I. & Quaresma, M.R. (1999) Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). *Rev. Bras. Reumatol.* **39**, 143–150 [in Portuguese].

Córdoba, J., Flaviá, M., Jacas, C., Saudela, S., Esteban, J.I., Vargas, V., Esteban, R. & Guardia, J. (2003) Quality of life and cognitive function in hepatitis C at different stages of liver disease. *J. Hepatol.* **39**, 231–238.

Crockett, B. & Gifford, S.M. (2004) 'Eyes wide shut': narratives of women living with hepatitis C in Australia. *Woman Health* **39**, 117–137.

Eickemberg, M., Oliveira, C.C., Roriz, A.K.C. & Sampaio, L.R. (2011) Bioimpedância elétrica e sua aplicação em avaliação nutricional. *Rev. Nutr. Campinas.* **24**, 873–882 [in Portuguese].

Ferenci, P., Ferenci, S., Datz, C., Rezman, I., Oberaigner, W. & Strauss, R. (2007) Morbidity and mortality in paid Austrian plasma donors infected with hepatitis C at plasma donation in the 1970s. *J. Hepatol.* **47**, 31–36.

Foster, G.R. (2009) Quality of life considerations for patients with chronic hepatitis C. *J. Viral Hepatitis* **16**, 605–611.

Freeman, A.J., Dore, G.J., Law, M.G., Thorpe, M., Von Overbeck, J., Lloyd, A.R., Marinos, G. & Kaldor, J.M. (2001) Estimating progression to cirrhosis in chronic hepatitis C virus infection. *Hepatology* **34**, 809–816.

Gallego-Orozco, J.F., Fuentes, A.P., Argueta, J.G., Pérez-Pruna, C., Hinojosa- Becerril, C., Sixtos-Alonso, M.S., Cruz-Castellanos, S., Gutiérrez-Reyes, G., Olivera- Martinez, M.A., Gutiérez-Ruiz, M.C. & Kershenobich, D. (2003) Health-related quality of life and depression in patients with chronic hepatitis C. *Arch. Med. Res.* **34**, 124–129.

Gifford, S.M., O'Brien, M.L., Bammer, G., Banwell, C. & Stoové, M. (2003) Australian women's experiences of living with hepatitis C virus: results from a crosssectional survey. *J. Gastroenterol. Hepatol.* **18**, 841–850.

Harris, H.H., Ramsay, M.E. & Andrews, N.J. (2006) Survival of a national cohort of hepatitis C virus infected patients, 16 years after exposure. *Epidemiol. Infect.* **134**, 472–477.

Hussain, K.B., Fontana, R.J., Moyer, C.A., Su, G.L., Sneed-Pee, N. & Lok, A.S. (2001) Comorbid illness is an important determinant of health-related quality of life in patients with chronic hepatitis C. *Am. J. Gastroenterol.* **96**, 2737–2744.

Jacobson, I.M., Davis, G.L., El-Serag, H., Negro, F. & Trépo, C. (2010) Prevalence and challenges of liver diseases in patients with chronic hepatitis C virus infection. *Clin. Gastroenterol. Hepatol.* **8**, 924–933.

Kallman, J., O'Neil, M.M., Larive, B., Boparai, N., Calabrese, L. & Younossi, Z.M. (2007) Fatigue and health-related quality of life (HRQL) in chronic hepatitis C virus infection. *Dig. Dis. Sci.* **52**, 2531–2539.

Lavanchy, D. (2008) Chronic viral hepatitis as a public health issue in the world. *Best Pract. Res. Clin. Gastroenterol.* **22**, 991–1008.

Manguso, F., D'Ambra, G., Menchise, A., Sollazzo, R. & D'Agostino, L. (2005) Effects of an appropriate oral diet on the nutritional status with HCV-related liver cirrhosis: a prospective study. *Clin. Nutr.* **24**, 751–759.

Matthews, D.R., Hosker, J.P., Rudenski, A.S., Naylor, B.A., Treacher, D.F. & Turner, R.C. (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* **28**, 412–419.

McHorney, C.A., Ware, J.E. Jr & Raczek, A.E. (1993) The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med. Care* **31**, 247–263.

McHorney, C.A., Ware, J.E. Jr, Lu, J.F. & Sherbourne, C.D. (1994) The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med. Care* **32**, 40–66.

McHutchison, J.G., Ware, J.E. Jr, Bayliss, M.S., Pianko, S., Albrecht, J.K., Cort, S., Yang, I., Neary, M.P. & Hepatitis Interventional Therapy Group. (2001) The effects of interferon alpha-2b in combination with ribavirin on health related quality of life and work productivity. *J. Hepatol.* **34**, 140–147.

Okita, M. (2004) Chronic hepatic disease and dietary instruction. *Hepatol. Res.* **30**, 90–93.

Oliveira, L.P.M., Jesus, R.P., Boulhosa, R.S.S.B., Mendes, C.M.C., Gnoatto, M.C., Cavalcante, L.N., Lemaire, D.C., Toralles, M.B.P., Lyra, A.C. & Lyra, L.G.C. (2012) Effect of soy protein supplementation on insulin resistance, fatty liver disease and biochemical markers in patients with chronic hepatitis C. *World J. Gastroenterol.* **18**, 2203–2211.

Plank, L.D., Gane, E.J., Peng, S., Muthu, C., Mathur, S., Gillanders, L., McIlroy, K., Donaghy, A.J. & McCall, J.L. (2008) Nocturnal nutritional supplementation improves total body protein status of patients with liver cirrhosis: a randomized 12-month trial. *Hepatology* **48**, 557–566.

Plauth, M., Merli, M. & Kondrup, J. (1997) ESPEN guidelines for nutrition and liver disease and transplantation. *Clin. Nutr.* **16**, 43–55.

R Development Core Team. (2010) *R: A Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing. Available at: http://www.R-project.org (accessed on 30 October 2010).

Ravasco, P., Monteiro-Grillo, I., Vidal, P.M. & Camilo, M.E. (2005) Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head Neck* **27**, 659–668.

Strauss, E. & Teixeira, M.C.D. (2006) Quality of life in hepatitis C. *Liver Int.* **26**, 755–765.

Teixeira, M.C.D., Ribeiro, M.F.S. & Strauss, E. (2005) A new insight into differences among non-cirrhotic patients using the liver disease quality of life instrument (LDQOL). *Ann. Hepatol.* **4**, 264–271.

Teixeira, M.C.D., Ribeiro, M.F.G.S., Gayotto, L.C.C., Chamone, D.A.F. & Strauss, E. (2006) Worse quality of life in volunteer blood donors with hepatitis C. *Transfusion* **46**, 278–283.

Teuber, G., Schafer, A., Rimpel, J., Paul, K., Keicher, C., Scheurlen, M., Zeuzem, S. & Kraus, M.R. (2008) Deterioration of health-related quality of life and fatigue in patients with chronic hepatitis C: association with demographic factors, inflammatory activity, and degree of fibrosis. *J. Hepatol.* **49**, 923–929.

Wanden-Berghe, C., Sanz-Vakero, J., Escribà-Aguir, V., Castelló-Botia, I. & Wanden- Berghe, R.G. (2009) Evaluation of quality of life related to nutritional status. *Br. J. Nutr.* **181**, 950–960.

Ware, J.E. & Gandek, B. (1998) Overview of the SF-36 health survey and the international quality of life assessment (IQOLA) project. *J. Clin. Epidemiol.* **51**, 903–912.

Ware, J.E., Kosinski, M. & Keller, S.D. (1994) *SF-36 Physical and Mental Summary Scales: A User's Manual*. Boston, MA: The Health Institute, New England Medical Center.

Ware, J.E., Bayliss, M.S., Mannocchia, M., Davis, G.L. & The International Hepatitis Interventional Therapy Group. (1999) Health-related quality of life in chronic hepatitis C: impact of disease and treatment response. *Hepatology* **30**, 550–555.

WHO. (1999) Global surveillance and control of hepatitis C - report of a WHO consultation organized in collaboration with the Viral Hepatitis Prevention Board, Antwerp, Belgium. *J. Viral Hepatitis* **6**, 35–47.

Younossi, Z.M., Guyatt, G., Kiwi, M., Boparai, N. & King, D. (1999) Development of a disease specific questionnaire to measure health related quality of life in patients with chronic liver disease. *Gut* **45**, 295–300.

Younossi, Z.M., McCullough, A.C., Barnes, D.S., Post, A., Ong, J.P., O'Shea, R., Martin, L.M., Bringman, D., Farmer, D., Levinthal, G., Mullen, K.D., Carey, W.D., Tavill, A.S., Fergusaon, R. & Gramlich, T. (2005) Pegylated Interferon a-2b, ribavirin and amantadine for chronic hepatitis C. *Dig. Dis. Sci.* **50**, 970–975.

