

Nutritional and Functional Rehabilitation in Cirrhotic Patients

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

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Received: January 20, 2021

Revised: January 31, 2021

Accepted: February 2, 2021

Published online: April 21, 2021

ABSTRACT

INTRODUCTION: Cirrhotic people often have impaired nutritional and functional status.

OBJECTIVE: To evaluate the effect of multidisciplinary rehabilitation on cirrhotic patients.

METHOD: Controlled clinical trial conducted at the Gastroenterology Ambulatory in southern Brazil, involving 33 patients with liver cirrhosis, through a multidisciplinary rehabilitation program, distributed into the groups: nutritional intervention ($n = 22$) and functional and nutritional rehabilitation ($n = 11$). Nutritional orientation according to European Society for Clinical Nutrition and Metabolism (ESPEN) Guideline. Functional intervention, during a period of 3 months, three weekly sessions of up to fifty minutes of exercise. Clinical and etiological characteristics, Child Pugh, nutritional, anthropometric and functional aspects were collected. Significant associations values were considered when $p < 0.05$.

RESULTS: Mostly male patients (60,6%), average age 58 years ($\pm 11,9$ years), prevalence of cryptogenic etiology, Child-Pugh A, well-nourished subjective global assessment (SGA). Significant changes in the parameters abdominal circumference (ABC) ($p < 0.049$), muscular arm circumference (MAC) ($p < 0.001$), six-minute walk test (6mWT) ($p < 0.001$) between the groups, with significant improvement in multidisciplinary rehabilitation. Significant improvement in the indirect parameters of sarcopenia, handshake strength (HS) ($p < 0.008$) and 6mWT ($p < 0.001$), especially in the group with functional and nutritional rehabilitation. Body composition revealed a significant change in multidisciplinary rehabilitation, in Weight ($p < 0.001$), BMI ($p < 0.001$), Phase Angle (PA) ($p < 0.036$), ABC ($p < 0.002$), MAC ($p < 0.001$) and thumb adductor muscle (TAM) ($p < 0.030$), which was not observed in the nutritional intervention group.

CONCLUSION: The multidisciplinary intervention shows positive results, as observed, where the group with the functional and nutritional rehabilitation activity was superior to the group with the isolated nutritional intervention.

Key words: Liver cirrhosis; Rehabilitation; Nutritional assessment; Sarcopenia

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Schmidt NP, Fernandes SA, Silveira AT, Rayn RG, Henz AC, Rossi D, Galant LH, Marroni CA. Nutritional and Functional Rehabilitation in Cirrhotic Patients. *Journal of Gastroenterology and Hepatology Research* 2021; **10(2)**: 3470-3477 Available from: URL: <http://www.ghrnet.org/index.php/joghr/article/view/3075>

INTRODUCTION

Protein caloric malnutrition (PCM) is a clinical *sine qua non* condition of liver cirrhosis and negatively interferes with the prognosis of these patients^[1].

In liver cirrhosis, mainly due to portal hypertension, there are pathophysiological changes related to bacterial translocation, exacerbation of pro-inflammatory cytokines, hyperammonemia, reduced growth factor, enhanced by dietary restriction, anorexia, dysgeusia, reduced protein-caloric intake, reduced metabolism and absorption of nutrients, in addition to neuroendocrine dysregulation^[2,3]. The consequences of these factors compromise body homeostasis, with reduced

protein synthesis, and gluconeogenesis, from branched-chain amino acids, increases and disrupts skeletal muscle, causing sarcopenia^[4].

Protein degradation is measured by increased oxygen consumption, measured by indirect calorimetry, where an increase in resting energy expenditure (REE) is observed in 35% of cirrhotic people compared to the healthy population. It is also possible to determine through Electrical Bioimpedance, through the Basal Metabolic Rate (BMR)^[4-6].

The nutritional and functional approach of the cirrhotic patient is fundamental in his broad clinical evaluation, as the nuances that appear are very varied and demand changes in lifestyle, habits, nutrition, activities, which can prevent or delay the natural history of the disease^[7,8].

PATIENTS AND METHODS

This is a prospective case-control study with 33 patients with liver cirrhosis treated at the Gastroenterology Outpatient Clinic of the Brotherhood of Santa Casa de Misericórdia in Porto Alegre, Rio Grande do Sul, Brazil, from June 2018 to September 2019.

Patients

The sample was for convenience, since the variables studied have not yet been described in the literature. Eleven patients were included in the Functional and Nutritional Rehabilitation Group (FNG) and twenty two participated only in the Nutritional Intervention (NI) group.

Inclusion criteria were: adults ≥ 18 years old, both sexes, diagnosed with cirrhosis by clinical evidence, laboratory, imaging and, eventually, liver biopsy. Patients on enteral diet, with some amputation of upper or lower limbs, were excluded.

Socio-demographic data, etiology of cirrhosis and disease staging using the Child-Pugh score^[9] were collected from electronic medical records during the first consultation.

Anthropometry

Weight was measured with a Filizola® anthropometric scale and height was measured with a stadiometer fixed to the wall, with the patient barefoot and in an upright position. The Body Mass Index (BMI) using the formula $BMI = \text{Weight (kg)} / [\text{Height (cm)}]^2$ and the classification was made according to the World Health Organization^[10] for adults, and the cutoff points indicated by Lipschitz, for the elderly^[11].

With the Tricipital Skinfold (TS), measured with a Cescorf plicometer, and with the Arm circumference (AC), the Muscular Arm Circumference (MAC) was calculated using the formula $MAC = AC \text{ (cm)} - 0.314 \times TS \text{ (mm)}$ ^[12]. To assess the adequation of TS and MAC, the 50th percentile of the measures proposed by Frisancho was used^[13]. The abdominal circumference (ABC) and calf circumference (CC) were measured according to Lee *et al.*^[14].

Electric Bioimpedance (EBI)

The utilized device was the Biodynamics®, model 450. The patients were instructed about the preparation protocol for the exam. Electrodes were placed at the ends of the body (hand and wrist; foot and ankle), the data of Phase Angle (PA), Lean Mass (LM), Fat Mass (FM) and Basal Metabolic Rate (BMR) were collected and classified based on reference parameters of Barbosa-Silva *et al.* study^[15].

Subjective Global Assessment (SGA)

Applied according to a document validated by Detsky *et al.*^[16].

Thumb Adductor Muscle (TAM)

A Cescorf® scientific adipometer was used, exerting continuous pressure to pinch the adductor muscle at the apex of an imaginary triangle, formed by the extension of the thumb and index finger. The procedure was done on the dominant hand three times. The result used was the average of the measurements, and the cutoff points, according to sex, proposed by González *et al.*^[17].

Handshake Strength (FS)

It was used the Baseline® branded mechanical dynamometer with adjustable handle, Smedley Spring model, manufactured in the state of New York, USA. Three evaluations were performed, with an interval of at least 30 seconds between them, with the highest value being recorded^[18]. The cutoff points used, according to sex, were those used in Álvares da Silva *et al.*^[19] study.

24-hour recall (24HR)

The 24HR questionnaire was applied on the day of the outpatient consultation, being asked what, how much and the time of the food consumed by the patient on the previous day. Afterwards, the total amount of calories consumed was calculated using the software - DietBox®.

6-minute walk test (6mWT)

The 6mWT was performed in a straight, flat corridor, 30 meters long, and without any type of obstacle. Before starting the test, all patients were instructed by the examiner and received a standardized verbal stimulus every minute of walking so that they could go through as far as possible. At the end of the test, the distance covered was measured, following the protocol by Brooks *et al.*^[20,21]. All evaluations were performed by trained professionals, nutritionists and physical therapists on the team^[22].

Nutritional Intervention

The Nutritional Intervention consisted of nutritional guidelines, over a 12-week period, in order to identify the needs for macronutrients and micronutrients, as well as the risks of malnutrition. Thus, the eating plan was calculated using the basal metabolism rate (BMR) derived from EB, respecting the Guideline of the European Society for Clinical Nutrition and Metabolism (ESPEN). The orientation was for energy intake of 25 to 35 kcal/kg of dry body weight/day to maintain body composition, and protein intake between 1.2 to 1.5 g/kg/CW/day, in order to avoid loss of muscle mass and decrease the risk of malnutrition^[4].

Functional Intervention

The patients were referred to the physiotherapy laboratory of the Federal University of Health Sciences of Porto Alegre (UFCSA) in order to perform three weekly exercise sessions for three months. The exercise program for cirrhotic patients was similar to that used for chronic cardiac and pulmonary patients, with a recommendation of aerobic physical activity of moderate intensity for a minimum of 30 minutes, five days a week or vigorous intensity for a minimum of 20 minutes, three days a week, to promote and maintain health^[23-26]. The first session consisted of 5 minutes of warm-up, followed by 30 minutes of walking on a running machine, with enough speed to reach 60% to 70% of the heart rate obtained in the peak VO₂, verified during the spirometry test. Subsequently, 2 minutes of walking time were added to each session performed, reaching up to 50 minutes of exercise, this time maintained until the end of the 8 weeks of rehabilitation.

All patients included in this study agreed and signed the Informed Consent Form (ICF), previously approved by the Research Ethics

Committees of the Brotherhood of Santa Casa de Misericórdia of Porto Alegre and the Federal University of Health Sciences of Porto Alegre (UFCSPA), under CAAE number: UFCSPA 3805918 and 3938979 ISCMPA.

STATISTICAL ANALYSIS

Quantitative variables were described by mean and standard deviation, and categorical variables by absolute and relative frequencies.

To compare means between groups, the t-student test was applied. When comparing proportions, Pearson’s chi square or Fisher’s exact tests were used.

For intra and intergroup comparisons, simultaneously, the Generalized Estimation Equations (GEE) model with Bonferroni adjustment was used.

The level of significance adopted was 5% ($p < 0.05$), and the analyzes were performed using the SPSS program version 21.0.

RESULTS

With a mean age of 58 years (± 11.9 years), 33 cirrhotic patients were evaluated, 20 (60,6%) of whom were male, subdivided into the FNG ($n = 11$) and NI ($n = 22$) groups. The clinical, etiological characteristics, associated diseases, Child Pugh score and nutritional aspects are described in Table 1.

In Table 2, data on anthropometry, EBI, baseline functional and nutritional capacity by group demonstrate a significant difference in MAC (%) and the 6mWT test between groups.

The analysis between the groups showed that there was a significant difference in AC. Regarding the MAC and the 6mWT, which already showed a difference before the intervention, they remained the same. There was a significant difference in protein intake.

Regarding intragroup differences, it was found that there were significant changes in several parameters. In the functional and nutritional rehabilitation (FNG) group, there was an improvement in weight, BMI, PA, AC, HS, TAM, 6mWT, 24HR, 24HR Kcal/Kg and protein intake ($p < 0.05$). In the nutritional intervention (NI) group, there was an improvement in the 6mWT and protein intake ($p < 0.05$).

DISCUSSION

The analyzed patients had an average of 58 years of age (± 11.9 years), similar to those found in other brazilian studies^[27,28]. The majority of patients are men (60.6%), which is also similar to the prevalence in the Indian study by Bakshi and Singh^[29] and in brazilian studies^[30,31].

The cryptogenic etiology was the most prevalent, a fact associated with the inclusion of nonalcoholic steatohepatitis (NASH), as in western and industrialized countries^[32-34], prevalence that has been increasing significantly worldwide due to nonalcoholic steatohepatitis (NASH)^[35]. This data differs from studies in which hepatitis B, C and alcohol intake are the most prevalent etiologies^[36,37].

The Child-Pugh A classification was the most prevalent, similar to the outpatient data found by Costa and collaborators^[30], Qing-HuaMeng and collaborators^[38], and Silva and collaborators^[39]. The vast majority of patients had fewer complications, absence of hepatic encephalopathy (HE) and only 9.1% with ascites.

The Subjective Global Assessment (SGA) showed that the majority had good nutritional status. The 2012 study by Fernandes and colleagues, with 129 brazilian patients, adults with liver cirrhosis, showed that SGA underestimated the prevalence and severity of malnutrition in cirrhotic patients^[40]. Vieira et al., with 78 adult brazilian patients with liver cirrhosis, advocate its use for diagnosing the

Table 1 Clinical characteristics of cirrhotic patients in the two study groups.

Variables	Total sample (n=33)	FNG (n=11)	NI (n=22)	P
Age (years) – average \pm SD	58.0 \pm 11.9	56.6 \pm 9.9	58.7 \pm 12.9	0.641
Gender - n (%)				1,000
Male	20 (60.6)	7 (63.6)	13 (59.1)	
Female	13 (39.4)	4 (36.4)	9 (40.9)	
Etiology- n (%)				0.392
Hepatitis	12 (36.4)	3 (27.3)	9 (40.9)	
Alcohol	3 (9.1)	2 (18.2)	1 (4.5)	
Autoimmune	2 (6.1)	0 (0.0)	2 (9.1)	
Cryptogenic	16 (48.5)	6 (54.5)	10 (45.5)	
Patologies- n (%)				
DM	15 (45.5)	5 (45.5)	10 (45.5)	1,000
Nephropathy	4 (12.1)	1 (9.1)	3 (13.6)	1,000
Heart disease	20 (60.6)	7 (63.6)	13 (59.1)	1,000
Dyslipidemia	10 (30.3)	5 (45.5)	5 (22.7)	0.24
Child-Pugh- n (%)				1,000
A	29 (87.9)	10 (90.9)	19 (86.4)	
B	4 (12.1)	1 (9.1)	3 (13.6)	
SGA- n (%)				0.218
Well Nourished	25 (75.8)	10 (90.9)	15 (68.2)	
Moderately Malnourished	8 (24.2)	1 (9.1)	7 (31.8)	
Ascites - n (%)	3 (9.1)	1 (9.1)	2 (9.1)	1,000

Table 2 Anthropometric characteristics, EBI, baseline functional and nutritional capacity of cirrhotic patients in the two groups under study.

Variables	Total sample (n=33)	FNG (n=11)	NI (n=22)	P
	Average \pm SD	Average \pm SD	Average \pm SD	
Weight	81.3 \pm 18.5	86.8 \pm 20.8	78.6 \pm 17.1	0.235
Height	1.63 \pm 0.11	1.63 \pm 0.11	1.64 \pm 0.11	0.823
BMI	30.3 \pm 5.4	32.4 \pm 5.1	29.3 \pm 5.4	0.128
AC	99.6 \pm 12.6	102.7 \pm 9.9	98.0 \pm 13.7	0.327
MAC (%)	75.3 \pm 22.9	61.1 \pm 6.9	82.4 \pm 24.9	0.001
CC	38.4 \pm 5.3	40.9 \pm 4.6	37.3 \pm 5.4	0.072
PA	6.08 \pm 0.89	6.19 \pm 0.60	6.02 \pm 1.01	0.616
LM (%)	65.9 \pm 7.9	64.6 \pm 7.4	66.6 \pm 8.2	0.493
FM (%)	34.1 \pm 7.8	35.4 \pm 7.4	33.5 \pm 8.1	0.502
BMR	1659 \pm 401	1731 \pm 456	1623 \pm 377	0.474
HS	38.1 \pm 27.2	42.7 \pm 32.1	35.8 \pm 24.9	0.498
TAM	14.6 \pm 7.8	13.1 \pm 7.3	15.4 \pm 8.1	0.442
6mWT	384.9 \pm 110.7	480.9 \pm 63.8	336.9 \pm 97.5	<0.001
24HR (Kcal/Kg)	23.9 \pm 5.57	25.8 \pm 5.0	23.0 \pm 5.7	0.133

nutritional status of cirrhotic patients for allowing a joint analysis of multiple variables of interest^[41]. Nunes et al., with 49 adult brazilian patients with chronic liver disease, consider that SGA should be used as a complement to other nutritional assessment techniques, since it does not have the appropriate sensitivity to identify small variations in the nutritional state^[40].

The mean BMI pointed to overweight, and showed a decrease in the total sample, in the FNG intragroup ($p < 0.05$) and not in the NI ($p = 0.285$), without varying between groups, as well as weight. This result suggests that the combination of dietary and physical behaviors can bring positive results in weight reduction. Román et al., with the 12-week physical activity program, observed muscle mass gain and, therefore, the weight was not changed^[25].

Table 3 Assessment of anthropometry, EBI, functional and nutritional capacity of cirrhotic patients, pre and post intervention by group (to be continued).

Variables	Total sample (n=33)	FNG (n=11)	NI (n=22)	p
	Media ± DP	Media ± DP	Media ± DP	
Weight				
Pre	81.3 ± 18.5	86.8 ± 20.8	78.6 ± 17.1	0.235
Post	80.2 ± 18.3	84.8 ± 20.2	77.9 ± 17.2	0.312
Difference (CI 95%)	-1.10 (-2.04 a -0.16)	-1.96 (-2.96 a -0.96)	-0.67 (-1.96 a 0.62)	0.119
p	0.022	<0.001	0.309	
BMI				
Pre	30.3 ± 5.4	32.4 ± 5.1	29.3 ± 5.4	0.128
Post	29.9 ± 5.4	31.7 ± 5.1	29.1 ± 5.5	0.161
Difference (CI 95%)	-0.41 (-0.74 a -0.07)	-0.72 (-1.07 a -0.38)	-0.25 (-0.71 a 0.21)	0.106
p	0.017	<0.001	0.285	
AF				
Pre	6.08 ± 0.88	6.19 ± 0.60	6.02 ± 1.01	0.616
Post	6.19 ± 1.09	6.50 ± 0.71	6.03 ± 1.22	0.149
Difference (CI 95%)	0.11 (-0.20 a 0.42)	0.31 (0.02 a 0.60)	0.01 (-0.43 a 0.45)	0.261
p	0.491	0.036	0.967	
LM (%)				
Pre	65.9 ± 7.9	64.6 ± 7.4	66.6 ± 8.2	0.493
Post	65.5 ± 6.5	65.0 ± 6.1	65.8 ± 6.8	0.733
Difference (CI 95%)	-0.38 (-1.72 a 0.96)	0.46 (-1.20 a 2.12)	-0.80 (-2.60 a 1.00)	0.312
p	0.579	0.584	0.385	
FM (%)				
Pre	34.1 ± 7.8	35.4 ± 7.4	33.5 ± 8.1	0.502
Post	33.9 ± 6.7	33.2 ± 6.9	34.2 ± 6.8	0.666
Difference (CI 95%)	-0.26 (-1.85 a 1.34)	-2.28 (-5.06 a 0.50)	0.76 (-1.05 a 2.56)	0.073
p	0.751	0.108	0.412	
AC				
Pre	99.6 ± 12.6	102.7 ± 9.9	98.0 ± 13.7	0.327
Post	98.9 ± 12.3	100.9 ± 10.0	97.9 ± 13.4	0.451
Difference (CI 95%)	-0.69 (-1.57 a 0.18)	-1.76 (-2.89 a -0.64)	-0.16 (-1.29 a 0.97)	0.049
p	0.122	0.002	0.782	
MAC (%)				
Pre	75.3 ± 22.9	61.1 ± 6.9	82.4 ± 24.9	0.001
Post	72.4 ± 16.3	61.6 ± 9.3	77.8 ± 16.6	<0.001
Difference (CI 95%)	-2.88 (-7.59 a 1.83)	0.57 (-2.56 a 3.71)	-4.61 (-11.4 a 2.16)	0.173
p	0.23	0.72	0.182	
CP				
Pre	38.4 ± 5.3	40.9 ± 4.6	37.3 ± 5.4	0.072
Post	38.4 ± 5.6	40.4 ± 4.8	37.4 ± 5.7	0.107
Difference (CI 95%)	-0.03 (-0.72 a 0.66)	-0.41 (-1.29 a 0.48)	0.16 (-0.77 a 1.08)	0.39
p	0.925	0.367	0.744	
HS				
Pre	38.1 ± 27.2	42.7 ± 32.1	35.8 ± 24.9	0.498
Post	42.6 ± 30.1	50.5 ± 37.2	38.7 ± 25.9	0.326
Difference (CI 95%)	4.52 (-0.44 a 9.47)	7.73 (2.04 a 13.4)	2.91 (-3.86 a 9.68)	0.285
p	0.074	0.008	0.399	
TAM				
Pre	14.6 ± 7.8	13.1 ± 7.3	15.4 ± 8.1	0.442
Post	14.4 ± 7.2	14.3 ± 7.7	14.5 ± 7.2	0.939
Difference (CI 95%)	-0.23 (-1.72 a 1.27)	1.14 (0.11 a 2.16)	-0.91 (-3.04 a 1.22)	0.09
p	0.766	0.03	0.403	
6mWT				
Pre	384.9 ± 110.7	480.9 ± 63.8	336.9 ± 97.5	<0.001
Post	433.6 ± 105.3	530.5 ± 70.0	385.2 ± 84.7	<0.001
Difference (CI 95%)	48.7 (22.4 a 74.9)	49.6 (3.71 a 95.6)	48.2 (16.2 a 80.3)	0.961

P	<0.001	0.034	0.003	
BMR				
Pre	1659 ± 401	1731 ± 456	1623 ± 377	0.479
Post	1630 ± 400	1721 ± 459	1584 ± 369	0.37
Difference (CI 95%)	-29.1 (-70.5 a 12.4)	-10.1 (-59.5 a 39.4)	-38.5 (-95.2 a 18.1)	0.458
p	0.169	0.689	0.182	
Calories (prescript %)	102 (95.9 a 108.1)	98.9 (80.1 a 117.8)	103.6 (100 a 107.2)	0.599
24HR				
Pre	1859 ± 298	1886 ± 242	1845 ± 327	0.678
Post	1751 ± 394	1708 ± 238	1772 ± 457	0.588
Difference (CI 95%)	-108 (-179 a -37.3)	-177 (-215 a -139)	-73.5 (-175 a 28.1)	0.06
p	0.003	<0.001	0.156	
24HR Kcal/Kg				
Pre	23.9 ± 5.6	25.8 ± 5.0	23.0 ± 5.7	0.133
Post	22.6 ± 5.9	23.6 ± 4.9	22.1 ± 6.5	0.433
Difference (CI 95%)	-1.3 (-2.1 a -0.5)	-2.2 (-3.0 a -1.4)	-0.9 (-2.0 a 0.2)	0.068
p	0.002	<0.001	0.117	
Protein				
Pre	1.07 ± 0.17	1.04 ± 0.19	1.09 ± 0.16	0.433
Post	1.38 ± 0.25	1.45 ± 0.29	1.35 ± 0.23	0.276
Difference (CI 95%)	0.32 (0.25 a 0.38)	0.41 (0.29 a 0.55)	0.26 (0.21 a 0.31)	0.033
p	<0.001	<0.001	<0.001	
SGA - Moderately Malnourished*				
Pre	8 (24.2)	1 (9.1)	7 (31.8)	0.085
Post	8 (24.2)	1 (9.1)	7 (31.8)	0.085
Difference (CI 95%)	0.0 (0.0 a 0.0)	0.0 (0.0 a 0.0)	0.0 (0.0 a 0.0)	**
p	**	**	**	

* Significance level $p < 0.05$ ** calculation was not possible due to lack of variability

Our data differ from those of Nishida and collaborators, whose observed an average BMI of 24.3 kg/m^2 ^[42], characterizing eutrophy, and agree with those of Chen and collaborators who found an average BMI of 30 kg/m^2 ^[43] converging to the prevalence NAFLD, in which 50 to 90% are obese^[39].

The PA of the total sample was $6.08^\circ (\pm 0.88)$ pre-intervention and $6.19^\circ (\pm 1.09)$ post-intervention and it was not different between groups, pre and post-intervention, however, it increased significantly intragroup, in the FNG, pre and post-intervention ($p = 0.036$), which was not observed in the NI. The difference may be related to physical activity in the first group. Mundstock suggests a positive association of PA with physical activity, by increasing the integrity of the cell membrane and the change in intracellular content, factors that reflect cellular and individual health^[44]. PA is dependent on tissue capacitance and is associated with quality, cell size and integrity^[45], and has been validated as a prognostic and survival indicator in critically ill patients, used as a measure of disease severity, as a functional assessment tool and as a general health indicator^[46]. According to Oliver Selberg and Daniela Selberg, patients with PA below 4.4° had shorter survival ($p < 0.01$) than those with higher PA ($6.6^\circ \pm 1.4$)^[47]. Fernandes and collaborators and Marroni and collaborators pointed out as a new parameter for the classification of the nutritional status of the cirrhotic patients the cut-off point for the PA of 5.44° ^[40,48].

The assessments of lean mass and fat mass, obtained through EBI, did not show significant differences intra and between groups, pre and post-intervention ($p = 0.579$ and $p = 0.751$, respectively). According to a study by Fernandes and collaborators, EBI has low accuracy in individual or group assessments, but it can be effective for a specific population with individuals without body changes, demonstrating that anthropometric measures may be less sensitive for

detecting changes in body composition^[40].

There was also a reduction in AC between the groups ($p = 0.049$) and intra FNG ($p = 0.002$). In studies (Spanish and Japanese), Román and collaborators and Chen and collaborators found a tendency to decrease AC in the group that performed physical activity for 12 weeks and nutritional monitoring with a contribution of 1.2 to 1.5 g/kg/day of protein^[26,43].

The MAC measurement was different, initially, between the groups ($p = 0.001$), which represents a difference in the selection, at random, and remains after the intervention, with no difference between groups ($p > 0.05$). Instead, Aby and Saab demonstrated MAC as a predictor of mortality in cirrhotic patients^[49].

Regard to CC, used in recent studies, with the objective of measuring muscle mass, estimating the prevalence of sarcopenia, predicting disability and mortality^[50,51], no significant results were found between and within groups.

FAM measures muscle strength and diagnoses the patient's nutritional status^[8]. Nishida and colleagues associated branched-chain amino acid (BCAA) supplementation and intense exercise to a significant increase in muscle strength^[43]. Similar findings, with adapted physical activity for 12 weeks with cirrhotic patients, showed a significant increase in muscle strength parameters^[52,53].

In this study, FAM was similar between the two groups ($p > 0.05$). There was a significant increase within the FNG group ($p = 0.008$), which was not found in the isolated NI ($p = 0.399$). There is a difference in the general sample, pre and post, with a significant trend ($p = 0.074$), with the increase in the number of cases. These differences emphasize the importance of physical activity as a factor in improving muscle status.

No significant change in TAM thickness was found between the

two groups in this study. However, when observing the intragroup differences, it was found that there was a significant increase in thickness in the FNG ($p = 0.030$), probably due to the physical activity developed in that branch of the study. It is noteworthy that in the literature, no studies were found relating the measurement of TAM, specifically, with the nutritional diagnosis in cirrhotic patients. Andrade and Lameu conducted a study with 150 patients with chronic clinical diseases, among which 25% were liver disease patients, and demonstrated that the TAM thickness of the dominant hand was an important prognostic indicator, associated with the evolution to infectious and non-infectious complications, infections and length of hospital stay^[54]. Budziareck, Duarte and Barboza-Silva, in a study of 300 healthy individuals, found a strong correlation between TAM thickness and FAM, concluding that the combination of these two methods may be useful for the nutritional evaluation^[55].

The 6mWT, an indirect parameter of sarcopenia, showed a significant difference ($p < 0.001$) between the groups, initially, which may represent a difference in random selection, and remained after the intervention ($p < 0.001$), with significant improvement in performance. When considering the intragroup difference of the general sample ($p < 0.001$), FNG ($p < 0.034$) and NI ($p < 0.003$), it can be seen that everyone had significant improvement in performance, valuing the intervention.

Carey and collaborators demonstrated that each increase of 100m in the 6mWT was associated with increased survival^[56]. Buchard and collaborators and Brustia, Savier and Scatton observed that the 6mWT lower than 250m in the liver pre-transplant is considered a risk factor for mortality^[57,58].

Similar to the findings of this study, Román and collaborators observed that cirrhotic patients, with physical activity three times a week, for 12 weeks, increased functional capacity and FAM^[26]. Even though anthropometric data does not correlate with changes in muscle mass, there is evidence that cirrhotic patients with low functional capacity have lower post-transplant survival rates and longer hospital stays^[43].

The offer of an adequate diet plan for patients should be based on BMR values, which can be estimated by various predictive formulas or by EBI. Most formulas are inaccurate in the presence of liver disease^[59]. In this study, the mean value (\pm SD) of BMR, by EBI, was 1659 ± 401 Kcal daily. It was found that there was no significant difference between groups or intragroup ($p > 0.05$). The percentage of calories consumed per day demonstrates the good acceptance of the guidelines, respecting the prescribed calories with the determined values, (consumption between 80.1% to 117.8% of the prescribed). There was no significant difference between groups or intragroup ($p > 0.05$).

The calculation of daily caloric intake by the 24HR showed higher values than those calculated by the EBI. Caloric data retrieved from 24HR and 24HR Kcal/Kg demonstrated consistency in the results, with no significance between groups ($p > 0.05$), which could be different if the number of patients was higher.

The 24HR presented intragroup significance, in the general sample ($p < 0.05$) and in the FNG ($p < 0.001$), with an apparent decrease in intake after the intervention, with the mean (\pm SD) in the total 24HR sample Kcal/Kg of 23.9 ± 5.6 pre-intervention and 22.6 ± 5.9 post-intervention. Considering that BMR in cirrhotic patients varies between 25 to 35 kcal/Kg of dry body weight/day^[4], it could be assumed that the patients analyzed in this study would be consuming less than recommended. Holanda and Barros questioned the use of 24HR due to its limitations and disadvantages, because it does not represent the usual intake, does not accurately estimate it, due to the variation of

the daily routine, does not evaluate portions accurately, and because it is a method dependent on the interviewed patient memory^[60].

The protein intake reported by the patients shows that there was significance between the groups ($p < 0.033$), at the same time that there was intragroup significance, in the general sample ($p < 0.001$), in the FNG ($p < 0.001$) and NI ($p < 0.001$). The mean (\pm SD) in the total protein intake sample (g/Kg/CW/day) was 1.07 ± 0.17 pre-intervention and 1.38 ± 0.25 post-intervention.

The orientation of protein intake varied between 1.2 to 1.5 g/kg/CW/day in order to avoid the loss of muscle mass^[4]. The increase in consumption is evident in the post-intervention, at all levels, which valorize the process. Nishida and collaborators evaluated that amino-acids increase liver albumin production, improve insulin resistance and quality of life in cirrhotic patients^[42] and, when combined with physical exercise, promote improvement in functional condition and quality of life, reduce malnutrition, prevent sarcopenia and loss of muscle mass, and hepatic encephalopathy^[6].

There were also significant changes in the parameters AC and 6mWT between groups and intragroup. Other parameters such as Weight, BMI, AF, TAM and FAM showed significant improvement in FNG, which was not observed in NI.

Although EBI did not present statistical significance in the percentage parameter of lean mass, it was possible to identify significant improvement in the indirect parameters of sarcopenia, FAM, MAP and 6mWT, especially in the group where there was a multidisciplinary intervention, with functional and nutritional rehabilitation.

CONCLUSION

The multidisciplinary rehabilitation program proposed in this study demonstrated that there was significance in the intervention in the functional and nutritional rehabilitation group (FNG) in relation to the nutritional intervention group (NI) in isolation in AC, in MAC, in the 6mWT and in protein intake.

The indirect parameters of sarcopenia were significant in FNG in relation to NI in the 6mWT; as well as there was a significant intragroup improvement in the FAM and 6mWT parameters.

Body composition revealed a significant change in FNG in relation to NI in AC and MAC. There was a significant improvement within the FNG group in weight, BMI, AF, CA and MAP.

The changes observed, in general, demonstrated that the functional and nutritional rehabilitation group, combining physical activity with nutritional guidance, perform better than the isolated nutritional intervention.

CONSIDERATIONS

Despite being an unprecedented work in the literature, this study is a preliminary presentation of a broader rehabilitation project in progress, and has limitations related to the small sample size.

Functional and nutritional rehabilitation with cirrhosis is difficult, since the inclusion criteria are very selective, there is low adherence to the programs, the number of patients is limited by their lack of availability, there is limited space for physical activities, and the prospective study requires multidisciplinary professionals working together, simultaneously, for a long period of time, in addition to the economic and financial difficulties for the development of the project.

From this point of view, multidisciplinary intervention is essential and shows positive results, and it is believed that by increasing the number of patients in the sample, it is possible to evidence the changes in a more expressive and consistent way, which would encourage new practices for approaching outpatient cirrhotic patients.

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