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RESEARCH ARTICLE

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Cirrhosis affects maximal oxygen consumption, functional capacity, quality of life in patients with hepatitis C

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Abstract

Objective: The aim is assess, compare, and correlate maximal oxygen consumption ($VO_{2max.}$), functional capacity and quality of life in cirrhotic patients with hepatitis C virus (HCV) and in healthy individuals.

Methods: This case–control study included 36 participants (18 patients with HCV cirrhosis and 18 healthy individuals) matched for sex and age. VO_{2max} was assessed using ergospirometry with an incremental load test on a cycloergometer. Functional capacity was measured by a 6-min walk test (6WT), and quality of life was assessed using the 36-Item Short-Form Health Survey (SF-36).

Results: Both the cirrhotic group and the control group had similar results for sex (44.4% male) and age (55.6 ± 8.31 and 55.2 ± 8.85 years, respectively). The cirrhotic group scored lower in all domains of the SF-36, on the VO_{2max} test (cirrhotic group 16.2 [11.6–18.6] ml/kg/min; control group 19.9 [16.28–26.9]; $p = 0.007$) and on the 6WT (cirrhotic group 521.5 [476.25–544.75] m; control group 618.0 [570.75–643.75] m; $p = 0.0001$). Correlations were found between the 6WT and the VO_{2max} ($r = 0.801$, $p < 0.0001$) and between the 6WT and quality of life (SF-361—functional capacity domain; $r = 0.552$, $p = 0.018$) only in the cirrhotic group.

Conclusion: Patients with cirrhosis due to HCV show changes in VO_{2max} and in functional capacity, which have a significant impact on their quality of life.

KEYWORDS
exercise, health-related quality of life, liver cirrhosis, physical therapy

1 | INTRODUCTION

Cirrhosis is a chronic and progressive hepatopathy that affects multiple systems, including the neuromuscular and cardiorespiratory systems (Marroni, Morgan-Martins, & Porawski, 2012; Dasarathy, 2012).

Metabolic alterations in the liver may cause a specific musculoskeletal impairment in which plasma amino acid levels reduce skeletal muscle protein synthesis, affecting muscle growth (Dasarathy, 2012). The association of muscle factors has a negative impact on activities of daily living for affected individuals (Younossi & Guyatt, 1998).

Abnormalities in arterial oxygenation are common in patients with liver cirrhosis. The decrease in the partial pressure of oxygen in arterial blood (PaO_2) and oxygen saturation of haemoglobin ($SatO_2$/Hb) may have a great impact on functionality and quality of life of cirrhotic patients (Maio, Dichi, & Burini, 2000; Marroni et al., 2012).

Quality of life in patients with liver diseases is measured in order to quantify the efficiency of the proposed treatments, as patients have important limitations associated with an overall motor deficit that decreases levels of physical fitness and limits the functional condition (Barcelos, Dias, Forgiarini, & Monteiro, 2008).

This study aimed to assess and compare maximal oxygen consumption ($VO_{2max.}$), functional capacity, and quality of life in cirrhotic patients with hepatitis C virus (HCV) and in healthy individuals, as well as to correlate these variables in cirrhotic patients.

2 | MATERIAL AND METHODS

This study was approved by the Ethics and Research Committee of the Clinical Hospital of Porto Alegre - HCPA, Porto Alegre - Brazil, under document number 5520, CAAE 00629712900005327. All participants provided written informed consent for participation. This case–control study comprised 36 participants (18 cirrhotic patients and 18 healthy patients). Groups were matched for sex and age. Sample size was defined based on the study by Galant et al., 2010, who investigated the functional capacity of cirrhotic patients using the 6-min walk test (Galant et al., 2010).

To be included in the study, patients had to be diagnosed with compensated liver cirrhosis due to HCV and had to be undergoing clinical follow-up at the Chronic Hepatitis Outpatient Clinic of HCPA Gatroenterology Service. We did not include patients with other etiologies of liver disease, Grade 3 or 4 esophageal varices, coinfection with other viruses, chronic renal failure, or dyspnea at rest, as well as licit or illicit drug users.

Sample loss occurred with individuals from both groups who had changes in vital signs before or during the proposed tests.

Selected patients were assessed simultaneously for physical fitness, functional capacity, and maximal oxygen consumption.

The level of physical activity was measured using the short version of the International Physical Activity Questionnaire (IPAQ). Participants answered the questionnaire with help from the researchers. IPAQ classifies the levels of physical activity into sedentary, insufficiently active, active, and very active (Matsudo et al., 2002).

Two tests were used to measure functional capacity: time up and go (TUG) and the 6-min walk test (6WT). In the TUG test, functional capacity was measured by the time the participants took to complete the test. Results were classified according to the studies by Podsialo and Richardson (1991). In the 6WT, functional capacity was measured by the distance walked in meters, in accordance with the standards of the American Toracic Society (2002).

VO_{2max} was measured using an open-circuit ergospirometry system with a gas analyser (MGC, model CPX/D). We used a cycloergometer (The Bike, Cibex, USA) for the incremental load test. A ramp protocol was applied. Initial intensity was set at 25 W min^{-2}, with an increase of 25 W every 2 min, at a cadence of 70–80 rotations per minute (rpm) (American College of Sports Medicine, 2007). Participants reported their perceived exertion using the Borg Rating of Perceived Exertion Scale. They were verbally encouraged to reach maximal exertion in the test, which lasted 8–12 min, in accordance with the recommendations of the American College of Sports Medicine. The test was concluded once the participants met one of the following conditions: (a) peak and/or plateau in oxygen consumption, (b) heart rate greater than or equal to the one predicted for age, (c) respiratory exchange rate greater than 1.15, and (c) perceived exertion greater than 18 (Dekerle, Baron, Dupont, Vanvelcenaher, & Pelayo, 2003; Wasserman & Mcilroy, 1964).

Quality of life was assessed using the 36-Item Short Form Health Survey (SF-36), which describes and measures health status by eight domains: functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects, and mental health (Ciconelli, Ferraz, Santos, Meinão, & Quaresma, 1999).

Data were analysed using the SPSS 18.0 software. Significance level was set at 5% ($p < 0.05$), and statistical power was set at 80%. To assess data distribution, we used the Shapiro–Wilk normality test. Qualitative variables were described as proportion and percentage, respectively. The chi-square test was used to compare groups. Quantitative variables were described as mean and standard deviation and median and interquartile range. Groups were compared using the independent t test and the Mann–Whitney test. For the correlation between variables, we used the Spearman's correlation test.

3 | RESULTS

The anthropometric characteristics of the sample are presented in Table 1. Both groups had similar results for age, gender, weight, height, and body mass index, with no significant differences between the participants. Most cirrhotic patients were infected with HCV Genotype 1 (50%), followed by Genotype 3 (44.4%) and Genotype 2 (5.6%).

During the TUG test, we found no significant differences for fall risk between the groups, with most cirrhotic patients having low fall risk (83.4%), followed by medium fall risk (16.7%). All patients in the control group had low fall risk (100%), as shown in Table 2.

Regarding level of physical activity, as assessed by the IPAQ, 72.3% of the cirrhotic group were insufficiently active, 22.2% were

TABLE 1 Patients' anthropometric and clinical characteristics

Variables	Cirrhotic group (n = 18)	Control group (n = 18)	p
Age (years)	55.61 ± 8.31	55.22 ± 8.85	0.893
Gender (M/F)	8 (44.4%)/10 (55.6%)	8 (44.4%)/10 (55.6%)	1.000
Weight (kg)	66.50 (57.62–73.10)	70.90 (63.85–75.62)	0.229
Height (cm)	157.45 (153.75–166.68)	163.30 (154.75–169.63)	0.261
BMI (kg/cm^2)	26.04 (21.98–28.77)	25.32 (24.13–26.70)	0.975
Genotype (HCV) 1/2/3	9(50%)/1(5.6%)/8(44.4%)		

Note. Values are expressed as mean and standard deviation, proportion and median and interquartile range. HCV: hepatitis C virus; M/F: male/female.
$^*p \leq 0.05$.

TABLE 2 Comparison of functional variables and level of physical activity between groups

Variables	Cirrhotic group (n = 18)	Control group (n = 18)	p
TUG (s)			
High risk	—	—	
Medium risk	3 (16.7%)		
Low risk	15 (83.4%)	18 (100%)	0.110
6WT (m)			
Walked distance	521.50 (476.25–544.75)	618.00 (570.75–643.75)	0.0001*
IPAQ			
Very active	1 (5.6)	2 (11.1%)	0.353
Active	4 (22.2%)	8 (44.4%)	
Insufficiently active	13 (72.3%)	8 (44.4%)	

Note. Values are expressed as proportion and percentage and as median and interquartile range. 6WT: 6-min walk test; TUG: time up and go; IPAQ: International Physical Activity Questionnaire.

*Statistical difference between groups. $p \leq 0.05$.

active, and 5.6% were very active. In the control group, 44.4% of the participants were insufficiently active, 44.4% were active, and 11.1% were very active. Distance walked in the 6WT was significantly shorter in the cirrhotic group (521.5 m; interquartile range, 476.25–544.75) than in the control group (618 m; interquartile range, 570.75–643.75; p = 0.0001), as shown in Table 2.

As for quality of life, significant differences were found in all domains assessed by the SF-36 (Table 3).

In the ergospirometry test, VO_{2max} was statistically lower in the cirrhotic group (16.20 ml/kg/min; interquartile range, 11.60–18.55) when compared with the control group (19.90 ml/kg/min; interquartile range, 16.27–26.85; p = 0.007), as shown in Figure 1.

Distance walked had a strong positive correlation with VO_{2max} (r = 0.801, p = 0.0001) in the cirrhotic group, as seen in Figure 2a, and a moderate positive correlation with the functional capacity dimension assessed by the quality of life questionnaire (r = 0.552, p = 0.018), as seen in Figure 2b. No correlations between variables were found in the control group.

TABLE 3 Comparison between groups for quality of life scores assessed by the SF-36 short-form generic quality of life assessment questionnaire

Variables	Cirrhotic group (n = 18)	Control group (n = 18)	p
SF–36-1	53.88 ± 5.50	89.16 ± 2.62	0.0001*
SF–36-2	30.55 ± 10.01	84.72 ± 5.40	0.0001*
SF–36-3	46.27 ± 5.67	82.61 ± 4.22	0.0001*
SF–36-4	45.33 ± 3.99	79.00 ± 2.62	0.0001*
SF–36-5	41.11 ± 4.95	73.33 ± 3.61	0.0001*
SF–36-6	47.91 ± 6.08	88.88 ± 3.01	0.0001*
SF–36-7	35.18 ± 10.93	85.18 ± 6.15	0.001*
SF–36-8	51.55 ± 5.40	79.11 ± 4.16	0.001*

Note. Data are expressed as mean and standard deviation. SF-36: 36-Item Short-Form Health Survey; SF–36-1: functional capacity; SF–36-2: limitation due to physical aspects; SF–36-3: pain; SF–36-4: general health status; SF–36-5: vitality; SF–36-6: social aspects; SF–36-7: mental health; SF–36-8: limitation due to emotional aspects.

*Statistical difference between groups. $p \leq 0.05$.

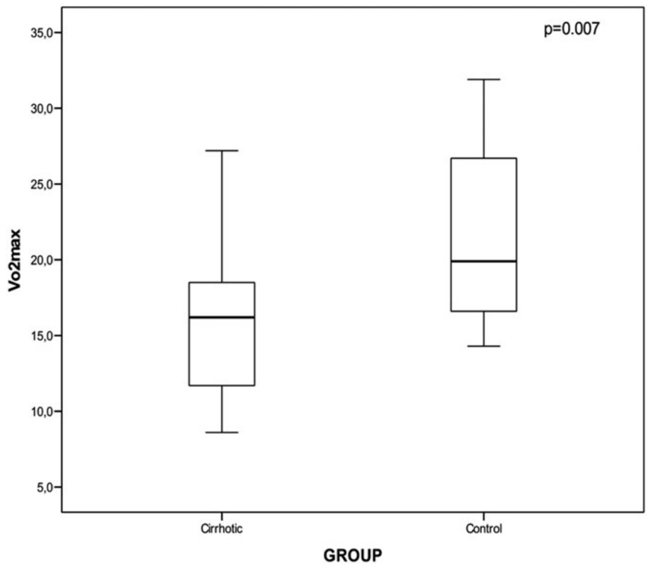

FIGURE 1 Difference between the cirrhotic group and the control group regarding maximal oxygen consumption during maximal exertion test with ergospirometry on a cycloergometer. Values are expressed as median and interquartile range (P25–P75)

4 | DISCUSSION

The main results of our study were the low scores achieved by the cirrhotic group in the eight dimensions of the SF-36 when compared with the control group (Table 3). Using SF-36, the authors compared the quality of life of patients who had undergone liver transplant with that of healthy individuals. They found that transplant patients had a lower functional capacity score, which suggests functional changes persist for some time after the transplant (Telles-Correia, Barbosa, Mega, Mateus, & Monteiro, 2009). In another study, the authors assessed the quality of life of patients on the waiting list for liver transplant and reported low scores on the functional capacity and mental health domains from the SF-36 (Barcelos et al., 2008).

In the present study, cirrhotic patients showed a significant decrease in VO_{2max} when compared with the control group (Figure 1). In 2012, a systematic review identified that the aerobic capacity of patients with compensated cirrhosis was 60% to 82% lower than that of healthy patients (Jones, Coombes, & Macdonal, 2012). Other study, evaluated 27 cirrhotic individuals and found that the ones with lower VO_{2max} had a lower survival rate (Galant, Forgiarini Junior, Dias, & Marroni, 2013).

In our study, the cirrhotic group walked a significantly shorter distance (521.5 m) than the control group (618 m). Alameri et al. (2007) and Carey et al. (2010) evaluated patients with cirrhosis, who walked between 306 and 369 m. These values are significantly lower than the ones achieved by healthy individuals.

When comparing the cirrhotic group with the control group, similar results were observed for level of physical activity and fall risk (Table 2). This is probably due to the fact that the patients in our study did not have neuromuscular impairments despite having cirrhosis.

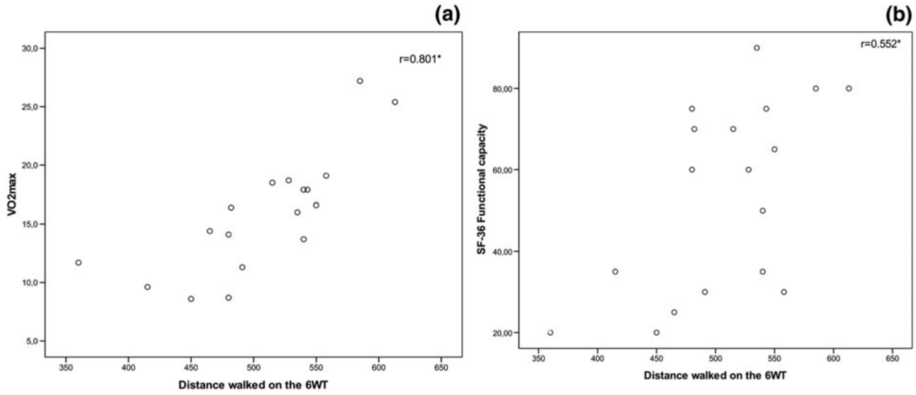

FIGURE 2 Association of maximal oxygen consumption and quality of life with functional capacity

They did not have clinical decompensation, a condition in which physical limitations and the resulting functional impairments lead to a decreased level of physical activity (Maio et al., 2000).

In the cirrhotic group, walked distance and VO_{2max} had a strong positive correlation (r = 0.801), that is, the lower the maximal oxygen consumption, the shorter the walked distance. This is explained by the fact that O_2 is required by the active muscles during exercise, and the required levels of O_2 may increase up to 20-fold during the maximal exertion test when compared with values at rest. A greater muscle power demands more energy and oxygen, because oxygen consumption increases linearly with level of exertion (Denadai, 1995).

The relationship between walked distance and functional capacity (as measured by the SF-36) in the cirrhotic group suggests a decrease in functionality, with a direct impact on quality of life. Galant et al. identified that the functional capacity of cirrhotic patients is inversely correlated with the Model End-Stage Liver Disease score, which shows that level of functional capacity is proportional to the patient's clinical status (Galant, Forgiarini Junior, Dias, & Marroni, 2012).

This study was limited by the absence of a medication use assessment and by the presence of hepatitis C comorbidities, such as insulin resistance and type 2 diabetes mellitus, because HCV may alter insulin resistance (I Consenso da Sociedade Brasileira de Infectologia para o Manuseio e Terapia da Hepatite C, 2013). The association of these factors may decrease quality of life during treatment, contributing to a poor clinical outcome (Ministério da saúde [Brasil], 2013).

We encourage future studies to investigate the neuromuscular system in order to identify the exact level of muscle mass losses, changes in muscle architecture, level of muscle activation, and levels of peripheral muscle fatigue. All these structural and functional changes determine the effectiveness of the neuromuscular system to generate strength and are therefore directly associated with functional capacity, overall physical condition and ability to perform activities of daily living. Furthermore, identification of this neuromuscular plasticity will serve as a base to identify the effects of a systematic physical activity program, which may be used to rehabilitate these patients.

5 | CONCLUSIONS

We conclude that patients with cirrhosis due to hepatitis C have lower maximal oxygen consumption and lower functional capacity, which leads to important changes in quality of life when compared with healthy individuals. We also identified associations between maximal oxygen consumption, functional capacity, and quality of life in cirrhotic patients. New studies on muscle strength, changes in muscle architecture, level of muscle activation, and peripheral muscle fatigue must be performed in order to help establish an exercise program for patients with liver cirrhosis.

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