Functional Capacity and Respiratory Muscle Strength of Candidates to Hepatic Transplant

EXERCISE AND SPORTS MEDICINE CLINIC

ORIGINAL ARTICLE

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ABSTRACT

Introduction: Chronic liver disease results in large functional impact, causing loss of muscle mass and function with consequent reduction of functional capacity. Objective: To evaluate and compare the respiratory muscle strength and functional capacity of candidates for liver transplantation who are under Class B or C according to Child Pugh Score and to correlate these variables within each group. Methods - Cross-sectional study with a convenience sample of 35 patients divided into two groups based on the score obtained in the Child Pugh Score B (19 patients) and Child Pugh Score C (16 patients). All subjects were evaluated in a single moment, and the maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) as well as the distance walked during the 6-minute walk test (6MWT) were measured. Results: Individuals classified with Child Pugh Score B showed higher values in the MIP (- 86.05 vs. 23.89 - 57.94 14.14), p = 0.001, in MEP (84.16 vs. 28.26 72.00 16 1994), p = 0.142, and the distance walked in 6MWT (473.63 vs 376.13 39.00 55.276), p = 0.001. We also found a positive correlation between the values of MIP and distance walked during 6MWT in group B of the Child Pugh Score, r = 0.64 and p = 0.003. Conclusion: The progress of liver disease contributes to the onset of several complications, which together appear to contribute to the reduction of functional capacity of individuals. In our study this was evidenced by the worse performance of Child Pugh score C group. This may suggest that the wait for liver transplantation (LTx) can worsen the functional capacity of these individuals.

Keywords: liver disease, functional capacity, respiratory muscle strength, Child-Pugh score.

INTRODUCTION

Hepatic cirrhosis is characterized by the diffuse substitution of the normal hepatic structure for nodules of abnormal structure surrounded by fibrosis and is present in the final stage of a series of pathological processes derived from many causes[1]. Hepatic disease causes great nutritional impact, regardless of its etiology, since the liver performs many biochemical reactions, such as production, alteration and use of nutrients and substances metabolically important to the body [2-4].

One of the complications caused by developed hepatic disease are the metabolic alterations associated with the patients' malnutrition, since they lose great quantity of muscular mass, presenting hence, alterations in functionality, which provides a physical inactivity scenario. The association of all these factors causes negative influence in the activities of daily living (ADL) and in the quality of life of this population[5-7]. In a previous study carried out by our group, alterations in the frequency and severity of hepatic diseases, as well as in the functionality and quality of life of the individuals with severe hepatic disease and who are on the waiting list for an hepatic transplant was found (LTx)[8].

Due to the increase in the number of candidates to LTx, classification models with several clinical variables were created to determine the severity of the hepatic disease. Initially, the *Child-Pugh Score* was created and recently the *Model for End Stage Liver Disease* (MELD) has also been used in the daily practice. The former was traditionally used in the stratification of pre-surgical risks and the latter was especially used to prevent survival three months after transplant, using for its classification, serum values of bilirubin and creatinine, and coagulation proof. The MELD punctuation ranges from 0 to 40, where it is inversely proportional to the score and survival ratio[9-11]. The *Child-Pugh Score* uses variables such as bilirubin and serum albumin, prothrombin time and presence of ascites and encephalopathy. The higher the punctuation the worse the clinical status of the individual and the clinical "decompensation" status which indicates hepatic cirrhosis should be higher or equal to 7 (class B). This class is a criterion accepted for inclusion of the patients on the waiting list for the LTx[12].

Early indication to LTx made it possible to patients to reach survival rate above 70% in five years, and also reduced the treatment costs. Moreover, it is important to highlight that the patients who use medication treatment for the disease at final stage present mortality of 70% per year[13,14]. These data caused that the search for the surgical procedure for the hepatic disease solution significantly increased. Thus, many candidates spend a long period on the waiting list, which favors the onset of new complications which, on their turn, worsen the functionality of these individuals.

However, none of the models devised to grade the hepatic disease stage uses functional variables. The performance of the six-minute walking test (6MWT) is an efficient measurement of the exercise submaximal capacity which presents strong correlation with the functional capacity[15]. It has been demonstrated that individuals who complete a shorter distance in the test present increase in mortality derived from the advanced hepatic disease[16].

It is also believed that due to the presence of ascites (50% to 60% of the cases), a mechanical disadvantage in the diaphragm muscle occurs, which may possibly interfere in the length-tension of the muscle and, consequently, in the respiratory muscular strength, harming even more the functionality of the individuals[17].

Although there is great variety of studies approaching the hepatic disease and its stages, little is seen on the functional capacity of this population. We believe that the understanding on the limitations of these individuals may contribute to a more accurate approach, which enables to reach a better recovery post-LTx, reintegrating them more rapidly to their new ADL.

This study has the aim to evaluate and compare the respiratory muscle strength and functional capacity of patients candidates to LTx who are under class B or C according to the *Child-Pugh Score* and, subsequently, to correlate these variables within each group.

MATERIALS AND METHODS

This study was transversal and 35 adult patients who were under supervision in the Hepatic Transplant Service of the Santa Casa Hospital Complex of Porto Alegre between February and November,2009 have been recruited. All individuals who presented clinical conditions to perform all the proposed procedures as well as those who were on the waiting list for the hepatic transplant were included in the study. Exclusion criteria were the presence of severe encephalopathy (level III and IV), severe degenerative diseases, such as muscular dystrophy and multiple sclerosis, hemodynamic instability or any other factor which hampered the performance of the proposed procedures. No exclusion occurred during the study. The patients were selected after verification of their medical records. The *Child-Pugh Score* variables provided minimum punctuation of 1 and maximum of 3 and the final punctuation ranged between 5 and 15. Subsequently, the individuals were classified in A (from 5 to 6 points), B (from 7 to 9 points), or C (above 10 points). The entire procedure was performed by the clinical staff of the hospital. The medical records verification was performed in the maximum time of 15 days before the functional evaluation so that no difference between the medical and physiotherapeutic follow-up would occur.

The patients performed in a single moment the following evaluation: data and samples' characteristics recording through an assessment slip specifically devised, evaluation of the respiratory muscles strength through manovacuometry and the 6MWT. The measurements were always performed by the same evaluator.

The Free and Clarified Consent Form of each patient was obtained and the work was approved by the Ethics and Research Committees of the Methodist University Center at IPA and the Santa Casa Hospital Complex of Porto Alegre.

In order to measure the strength of the respiratory muscles, a digital manovacuometer MVD 500 brand name Globalmed®, which was always calibrated before each data collection was used. MIP was evaluated with the individual performing maximal expiration, until the residual volume (RV), and, after suitable positioning of the equipment in the patient's mouth, maximal forced inspiration was performed. In order to have the MEPobtained, the individual was asked to begin the maneuver from the total pulmonary capacity, which was followed by a maximal forced expiration. The maneuvers were performed with the equipment being suitably positioned in the patient's mouth so that no flaw would occur in the test. A nasal clip was used to avoid air escape and there was the drain hole in the manovacuometer. The maneuver needed to be sustained for at least one second, and a total time of it of at least two seconds, in which the peak pressure was verified. The results were obtained after performance of five maneuvers, with minimum interval of one minute between them, and at least three acceptable maneuvers were obtained; that is to say, the values did not vary from each other more than 10%. The highest pressure in water centimeters was recorded (cmH_2O), and the normality values supported by the Brazilian Pneumology and Tisiology Society were used[18,19].

The 6MWT was performed on a straight, flat, 30-meter long corridor, with not any kind of obstacle. Prior to the test beginning, all patients received instructions from the evaluator and during it standardized verbal stimuli were given at every walking minute, when the patients were encouraged to complete the longest distance possible. At the end of the test, the completed distance was measured. The patients were monitored through the respiratory rate, heart rate and oxygen peripheral saturation, using a Nonin oxymeter (9500, USA), and dyspnea sensation and fatigue in lower limbs were measured through the modified Borg's scale (0-10 scale), according to the *American Thoracic Society* (ATS)[15]. All variables previously described were measured before and after the walking test, except for the distance, which was only quantified after the 6MWT.

STATISTICAL ANALYSIS

Statistical analysis was performed in the SPSS program (*Statistical Package for Social Sciences*) version 16.0. Data normality was verified with the Kolmogorov-Smirnov test. Student's t test was used for the comparisons of the means of the muscle strength variables (MIPand MEP), distance completed in the 6MWT, anthropometric and clinical characteristics between the two groups, and for the correlations between variables, the Pearson correlation test was used. Significance level adopted was $p < 0.05$.

RESULTS

In our study, 35 patients have been evaluated and no loss or exclusion has occurred. The sample's anthropometric characteristics are described in table 1. Nineteen individuals were classified as *Child-Pugh Score* B and 16 as *Child-Pugh Score* C. Alcoholic cirrhosis diagnosis was found in nine patients from group B and in seven from group C; viral hepatitis by virus C (HVC) in seven patients from both groups; and viral hepatitis by virus B (HVB) in three patients from group B and in two from group C. The time of the disease diagnosis is not significantly different from groups B and C, 14 ± 3 *vs.* 12 ± 5 months, respectively ($p = 0.9$). There was not significant difference between groups concerning the clinical and anthropometric variables. Concerning the drug therapy in both groups, they were similar, since the use of antiretroviral medication in patients with the viral processes is usually equivalent.

Table 2 presents the comparison of the 6MWT variables of the two assessed groups. No difference has been found between the two groups in the values which preceded the test and the values after it.

Table 1. Anthropometric and clinical characteristics of the individuals.

Child-Pugh B / Child-Pugh C characteristics (p) (n = 19) / (n = 16)
Age (years) 51.05 ± 9.3 / 53.94 ± 9.53 0.3 ns
Sex – M/F 11/8 - 10/6
Weight (kg) 70.21 ± 8.13 / 73.24 ± 14.05 0.4 ns
Height (metros) 1.66 ± 0.07 / 1.64 ± 0.08 0.7 ns
BMI 24.29 ± 2.68 / 26.20 ± 3.46 0.07 ns
Abdominal perimeter - 96.95 ± 9.52 /102.81 ± 11. 75 0.1 ns
Diagnostic (n)
Alc Cirrhosis 9 / 7 ns
HCV 7 / 7 ns
HVB 3/ 2 ns

The age, weight, height, BMI and abdominal perimeter variables are described in mean and standarddeviation of the mean, respectively. M/F = male/female; BMI = body mass index; n (number of individuals); Alc Cirrhosis = alcoholic cirrhosis; HCV = hepatitis by virus C; HVB = hepatitis by virus B; ns = not significant.

Table 2. Comparison between the variable groups of the six-minute walking test.

Variables Child-Pugh B / Child-Pugh C (p) (n = 19) / (n = 16)
Distance 6MWT (meters) 473.63 ± 55.276 / 376.13 ± 39.00 - ,001*
HR bpm (initial) 73.63 ± 15.14 / 71.75 ± 17.17 0.7 ns
HR bpm (final) 89.37 ± 22.77 / 81.13 ± 16.75 0.2 ns
RR irpm (initial) 16.32 ± 2.92 / 18 ± 2 0.06 ns
RR irpm (final) 22.74 ± 3.53 / 23.38 ± 3.28 0.5 ns
SpO2 % (initial) 97. 32 ± 1.88 / 97.56 ± 2.68 0.7 ns
SpO2 % (final) 97.11 ± 2.20 / 96.38 ± 6.51 0.6 ns
Borg 1 (initial) 1 ± 1.21 / 1.31 ± 1.20 0.2 ns
Borg 1 (final) 3.17 ± 1.72 / 3.44 ± 1.93 0.6 ns
Borg 2 (beginning) 1 ± 1.22 / 1.30 ± 1.21 0.2 ns
Borg 2 (end) 3.15 ± 1.75 / 3.40 ± 1.90 0.6 ns

Variables described in mean and standard deviation. 6MWT = six-minute walking test; HR = Hear rate; SpO2 = oxygen peripheral saturation; RR – respiratory rate, Borg 1: Borg's scale modified for dyspnea; Borg 2 = Borg's scale modified for fatigue in lower limbs; n = number of individuals.

The *Child-Pugh Score* B group presented higher values in the MIP (cmH_2O), -86.05 ± 23.89 *vs.* -57.94 ± 14.14, p = 0.001 in the MEP (cmH_2O), 84.16 ± 28.26 *vs.* 72.00 ± 16.94, p = 0.142, and in the distance completed in the 6MWT (meters), 73.63 ± 55.276 *vs.* 376.13 ± 39.00, p = 0.001 (Table 3).

Positive correlation was also found between the MIP values and the distance completed in the 6MWT within the *Child-Pugh Score* B group, r = 0.64 and p = 0.003 (Figure1), a fact which was not verified in the *Child-Pugh Score* C group.

Table 3. Comparison of the respiratory muscle strength.

Variable Child-Pugh B / Child-Pugh C (p) (n = 19) / (n = 16)
MIP (cmH2O) -86.05 ± 23.89 / 57.94 ± 14.14 0.001*
MEP (cmH2O) 84.16 ± 28.26 / 72.00 ± 16.94 0.142

Variables are described in mean and standard deviation. MIP= maximum inspiratory pressure; MEP = maximum expiratory pressure; 6MWT = six-minute walking test. *Student's t test p < 0.05; n = number of individuals.

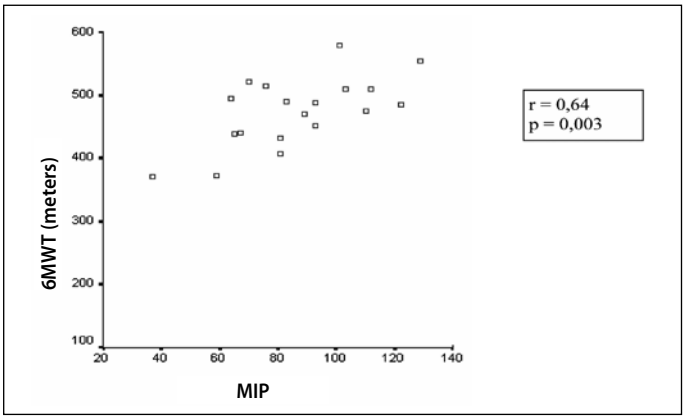

Figure 1. Correlation between the MIP and the distance completed in meters in the six-minute walking test (6MWT) in the group Child-Pugh B.

DISCUSSION

The individuals with hepatic disease develop a malnutrition scenario due to decrease in food intake, deficit in absorption and transport of nutrients and increase of the energetic cost at rest[20,21]. In our study, the patients of both groups presented mean body mass index (BMI) which does not correspond to a malnutrition and cachexia episode.

The patients of this study, classified as *Child-Pugh Score* C, presented shorter completed distance in the 6MWT and lower values in the respiratory muscle strength than those classified as *Child-Pugh Score* B. In the study performed by Leitão *et al.*[22], it was observed that the individuals who wait for an hepatic transplant complete mean of 383.8 meters in the 6MWT, which corroborates our findings here. Alameri *et al.*[16] also evaluated the functional capacity of the patients candidate to hepatic transplant through the 6MWT, and the mean completed distance was 306 meters of the *Child-Pugh Score* C patients, and these patients presented also the worst performance and survival rate when compared to the individuals classified as B and A.

The 6MWT presents good correlation with the oxygen maximal consumption ($\dot{V}O_2$)[23]. Dharancy *et al.*[24] demonstrated that majority of the cirrhotic patients presents lower peak $\dot{V}O_2$ values than the expectation. Moreover, Epstein *et al.* verified that class A patients from the *Child-Pugh Score* presented better peak $\dot{V}O_2$ values when compared to the individuals from the groups B and C[25].

Another factor which contributes to the harm in the functional capacity of this population are the abnormalities in the gas exchanges. The most relevant of these abnormalities is unsuitable oxygenation of the arterial blood, since the difference in the oxygen alveolus-arterial ratio ($P[A\text{-}a]O_2$) is increased in about 50% of the cases. Przybylowski *et al.*[26] investigated 104 patients and demonstrated that the individuals who had hepatic disease presented lower partial pressure of arterial oxygen (PaO_2), lower capacity of carbon monoxide diffusion (DL_{co}) and greater difference on the oxygen alveolus-arterial ratio ($P[A\text{-}a]O_2$) when compared to the group which did not present cirrhosis. The investigators also found positive correlation between $P(A\text{-}a)O_2$ and the *Child-Pugh Score* and negative correlation between DL_{co} and the *Child-Pugh Score*.

Regarding the respiratory musculature strength, there are few findings in the literature. Carvalho *et al.*[17] verified that those individuals with higher mortality on the waiting list to undergo an

hepatic transplant presented lower values of MIP than those in the control group. Our findings suggest that the *Child-Pugh Score* C group presents reduction in MIP when compared to the *Child- Pugh Score* B group, demonstrating that the hepatic disease progression compromises the respiratory musculature as well, either by the mass loss or by interference in the length-tension of the muscle.

When the MIP values were correlated with the completed distance in the 6MWT statistical significance was only obtained in the *Child-Pugh Score* B group. The complications already mentioned seem to have contributed so that the individuals classified as *Child-Pugh Score* C did not present correlation between variables; compromising factors, such as ascites and hepatic encephalopathy, may have disturbed their assessment.

Our study presents some limitations, especially with the control of nutritional variables. The BMI analysis may not reflect the actual nutritional aspect of the sample due to the presence of ascites in some patients. Medication administration may be a confusing variable, since at the exacerbation moment of the hepatic disease other pharmacological resources, such as corticosteroids, which negatively interfere on the musculoskeletal system, can be used. Another limitation refers to the sample size existing in both groups.

CONCLUSION

The hepatic disease progression contributes to the onset of many complications which as a set tend to reduce the functional capacity of this population. Such fact has been evidenced in our study through worse performance of the *Child-Pugh Score* C group, which presents a severe clinical status, suggesting hence that the wait for an hepatic transplant (LTx) may aggravate the functional capacity and respiratory muscle strength of these individuals.

All authors have declared there is not any potential conflict of interests concerning this article.

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