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Effect of a 12-week home-based exercise protocol on muscle mass, liver and spleen stiffness, and quality of life in patients with liver cirrhosis

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ABSTRACT

A condition that is characterized by the formation of fibrosis and nodular patterns on the liver due to chronic injury to the liver caused by conditions such as hepatitis, alcoholic liver disease, NASH, etc., is known as liver cirrhosis. A multidimensional approach is always established by exercise towards the betterment of an individual. With the aim of assessing the effect of structured exercise on liver cirrhosis, this study is performed accordingly. A specific formula was taken into consideration to develop a sample size for the participation. A total enrollment of 40 patients was done in this study, who were randomly divided into 2 groups: one was a control group and the other was an experimental group. A simple exercise program was allotted to the control group, and the experimental group underwent a structured exercise program. Outcome measures, which included bioelectric impedance, ultrasound measures for liver and spleen stiffness, and the CLD questionnaire, were assessed before the program as well as after the program. The results were obtained accordingly. The mean muscle mass in the experimental group increased from 24.21 ± 3.99 kg to 30.79 ± 6.44 kg ($p < 0.001$) with between group difference of p= 0.002 which is considered statistically significant. The mean liver stiffness of experimental group decreased from 11.0 ± 0.82 kPa to 9.32 ± 0.88 kPa ($p < 0.001$) with between group difference of p= 0.040 suggesting the comparatively greater effectiveness of structured exercise protocol on the patients. The mean spleen stiffness decreased from 30.79 ± 2.72 kPa to 28.42 ± 3.16 kPa ($p < 0.001$) with between-group post-intervention comparison of 1.18 kPa, which was although modest statistically but significant clinically. While assessing the quality of life of the participant, a statistically significant improvement in fatigue experienced my patient was seen with p value of <0.0001 whereas, the activity symptoms showed p value of 0.05 which was although modest but clinically significant. Thus, promoting the effectiveness of a structured exercise protocol in the betterment of patients with liver cirrhosis.

Keywords: *Liver cirrhosis, exercise, muscle mass, BMI, liver and spleen stiffness, quality of life.*

1. INTRODUCTION

Physical activity is considered to be a cornerstone in the primary prevention of at least 35 and more of chronic conditions. A considerable knowledge has been accumulated over the past two decades regarding the significance of exercise and promoting it as a first-line treatment for various chronic diseases. A role of exercise is also considered to be as good as medicine in numerous studies in order to treat various conditions.[1] One of the powerful tools to fight and prevent as well as treat numerous chronic diseases is exercise, evidences also say that exercises are associated with increasing healthy lifespan as well as plays a major role in delaying the occurrence of 40 or more chronic conditions or diseases.[2]

A condition that is characterized by the formation of fibrosis and nodular patterns on the liver due to chronic injury to the liver caused by conditions such as hepatitis, alcoholic liver disease, NASH, etc., is known as liver cirrhosis.[3] One of the most important causes of morbidity and mortality among people suffering from chronic liver disease worldwide is considered to be liver cirrhosis. In 2019, around 2.4% of global deaths were recorded. Major reasons that lead to cirrhosis of the liver are hepatitis B virus infection, hepatitis C virus infection, alcohol-associated liver diseases, as well as non-alcoholic fatty liver disease. Moreover, while considering the global readings, around 42% of patients with cirrhosis were suffering from HBV infection, and 21% were suffering from HCV infection. The prevalence of HBV infection, as established by WHO, was

highest in the Western Pacific region (59%), whereas it was lowest among Americans (5%). The prevalence of HCV infection, which ultimately leads to liver cirrhosis, was seen highest among the eastern Mediterranean region (70%), whereas it was lowest in the African and western Pacific Regions (both 13%). The prevalence of alcoholic liver disease was high among Europeans as well as Americans, and lowest in Asians because the overall proportion of patients with cirrhosis due to heavy alcohol use was seen in these regions to be 16 to 78% in Europe, 17 to 52% in Americans and only 0 to 41% in Asians.[4] Nonalcoholic fatty liver disease is considered to be a complex chronic disease which is associated with various metabolic disorders, particularly mentioning obesity as well as type 2 diabetes mellitus, making it a major global health concern which have affected more than 30% of the global population as per the readings obtained in 2019.[5] Therefore, it is considered to be the leading cause of any liver-related mortality as well as morbidity.[6] An estimated number of 257 to 291 million people globally are chronically infected due to HBV and are also considered to be at high risk of cirrhosis as well as hepatocellular carcinoma. The overall proportion seen in cirrhotic patients, which is attributed to HBV when studied geographically, ranges from 6% in North America, 6 to 21% in Latin America, 34% to 38% in sub-Saharan Africa, and almost 39% in eastern Asia.[7] While analyzing the values studied in India, it says that there is a significant burden of liver cirrhosis in India as well, of which 18.3% of two million global liver diseases leading to death is contributed by India alone, as per the results obtained from the survey done in 2015. One of the most progressively increasing causes of mortality in India is considered to be chronic liver disease since 1980. Also, the burden of non-alcoholic fatty liver disease is increasing similarly in India, which is primarily related to the increasing body mass index as well as diabetes incidence in India. The prevalence of nonalcoholic fatty liver disease seen in the general population of India varies between 8% to 20%, showing a high prevalence in urban areas. Thus, making chronic liver disease a major public health concern in India.[8]

The progressive loss of skeletal muscle mass as well as function is known as sarcopenia. It can be seen in more than 70% of patients suffering from liver cirrhosis.[9] It is one of the most well-known complications of chronic liver disease, observed in almost every cirrhotic patient.[10] Nonalcoholic fatty liver disease can positively and independently be associated with low muscle mass as well as low muscle strength.[11] According to the pathophysiology of sarcopenia, it is recognized that sarcopenia is involved in multi-domain pathways. An ultimate failure of balance between protein synthesis and breakdown is considered to be a primary pathophysiology behind the development of sarcopenia among these patients. Chronic liver disease has the ability to disturb whole body protein homeostasis, involving various metabolic as well as biochemical abnormalities, which have a direct impact on reducing muscle mass in the body.[12] The further worsening of liver function leads to a significant reduction in the detoxification of certain harmful substances, such as ammonia. There is an excessive consumption of such branched chain amino acids in skeletal muscles in order to detoxify these harmful substances in such patients.[13] Therefore, making sarcopenia an independently associated higher risk of mortality among the cirrhotic patients.[14] The 8-week study performed by Abdelbasset et al, showed a significant improvement in the BMI of the patient with the p value of 0.04.[15] According to Chien et al, a 12-week progressive sandbag exercise training performed to gain muscle strength also showed significant improvement among such patients.[16] A study performed which included different training modes of exercise on muscle strength among sarcopenic patients also displayed significant improvement in muscle strength. [17] Studies performed for improving sarcopenia of the patient have significantly proposed positive effects of exercise interventions on muscle strength as well as muscle mass.[18] [19] the above mentioned studies also involves sarcopenia arrived secondary the reason other than liver cirrhosis. Very few studies are published who actually focus on sarcopenia caused due to liver cirrhosis. Therefore, it was a need to analyze the effect of exercises on sarcopenia secondary to liver cirrhosis.

According to the statistical observations obtained from previous studies, the significant increase in the stiffness of the liver on Magnetic Resonance Elastography (MRE) was primarily associated with histologic fibrosis progression.[20] According to the evidence, the significant change can be observed in the mechanical as well as biochemical composition of the extracellular matrix of the liver as the fibrosis progresses; the fibrillar collagens and proteoglycans gradually replace the traditional basement membrane proteins as the fibrosis stage progresses.[21] A high accuracy can be exhibited regarding the diagnosis as well as staging of steatosis and fibrosis with the help of TE.[22] A rapid histologic progression pattern can be seen among patients with NAFLD, ultimately leading to rapid advancement in fibrosis. Fibrosis stage of liver cirrhosis is considered to be the strongest predictor of outcomes among these patients, therefore, the changes occurring in the fibrotic stages of the liver can be considered as an important endpoint to analyze and determine both the treatment strategies as well as the clinical management in liver cirrhosis.[23] A study performed which included aerobic exercise with alternate day fasting on patients with non-alcoholic fatty liver disease showed a significant clinical improvement with the p value of 0.78 ± 0.32.[24] A study combining effect of walking with neuromuscular electrical stimulation on liver stiffness noted the significant statistical improvement in the stiffness of liver with p value of 0.0009.[25] The analysis of effect of functional resistance training on the structure and function of heart and liver was performed which displayed a good amount of improvement in liver stiffness of the patients with the p value of 0.063.[26] A study performed in year 2023 also claims to improve the structural adaptations taking place in liver secondary to liver injury with the help of exercise training displaying the significant improvement in the statistical analysis of the study.[27] But the studies mentioned above do not put forth the wider perspective of the disease as some involve only non-alcoholic liver diseases or fatty liver diseases while others involve only liver injury caused by the alcoholic liver diseases, certain involve only liver cirrhosis secondary to hepatitis. Therefore, there was a need to involve a bigger scenario of the conditions causing liver cirrhosis and analyze their response towards exercise.

The patients with liver cirrhosis often have splenic enlargement, the precise pathogenetic mechanism is yet to be clarified.[28] An increase in hepatic venous pressure (HVPG) ≥ 10 mmHg is known as portal hypertension, which is a common complication of liver cirrhosis. Further clinical complications arising due to PH are esophageal varices.[29] The development of portal hypertension and PH leading to esophageal varices is considered to be the major aggravation concerning the liver cirrhosis condition. Splenic congestion can be led due to PH, causing architectural changes in the arteries as well as veins of the spleen, ultimately leading to fibrosis as well as an increase in the stiffness of the spleen. Elastography techniques have proved themselves to be efficient in ruling out the stiffness of the spleen as well. According to the studies, a stepwise increase in portal hypertension can be measured with the help of increasing stiffness of the spleen.[30] Portal hypertension not only causes portal congestion leading to splenomegaly as previously discussed, but also contributes to certain other factors, specifically mentioning the overactivation of splenic lymphoid tissue, a rapid increase in angiogenesis, ultimately leading to the worsening of fibrosis.[31]

A major factor of concern among these patients is the significant deterioration seen in the quality of life of patients with liver cirrhosis. The progression of disease promotes the major concern of occurrence of symptoms as well as worsening of symptoms, responses towards the treatment strategies and also majorly contributing in the mental as well as physical and social factors, to be precise, anxiety, certain comorbidities, confusion and fatigue, ultimately leading to predisposition of limitations in daily living activities.[32] A severe impairment in quality of life can be observed among patients with acute-on-chronic liver cirrhosis.[33] Furthermore, there are various evidences stating that quality of life is hampered in various aspects among liver cirrhotic patients and should be considered a concerning factor in the overall improvement of the patients' condition, and also while planning the treatment strategy of the patient.[34] [35] According to a meta-analysis performed, studies involving analysis of effect of exercise prehabilitation on the patients with liver cirrhosis have displayed a significant improvement in the overall improvement in the quality of life of the patients.[36] Also, a study involving the 8-weeks of high-intensity exercise intervention on patients with liver cirrhosis showed a significant improvement in the overall quality of life with p value of 0.71, the study also suggest that the effects of long-term interventions are yet to be studies.[15] Therefore, it highlights the need to study the effect of long term exercise interventions on patients with liver cirrhosis and their impact on the overall quality of life of the patients.

2. METHODOLOGY

A prospective, single-blinded, randomized controlled trial study was conducted in Krishna Hospital, Karad, Maharashtra, under the supervision of Krishna Vishva Vidyapeeth (Deemed to be University). A 12-week-long trial was conducted with the aim of evaluating the effect of structured home-based exercise program among the liver cirrhotic patients. Ethical clearance was obtained from the Ethical Committee of Krishna Vishva Vidyapeeth (Deemed to be University), Karad. A thorough knowledge of the study was provided to all the participants before initiating the study, and accordingly, informed consent was secured from each participant.

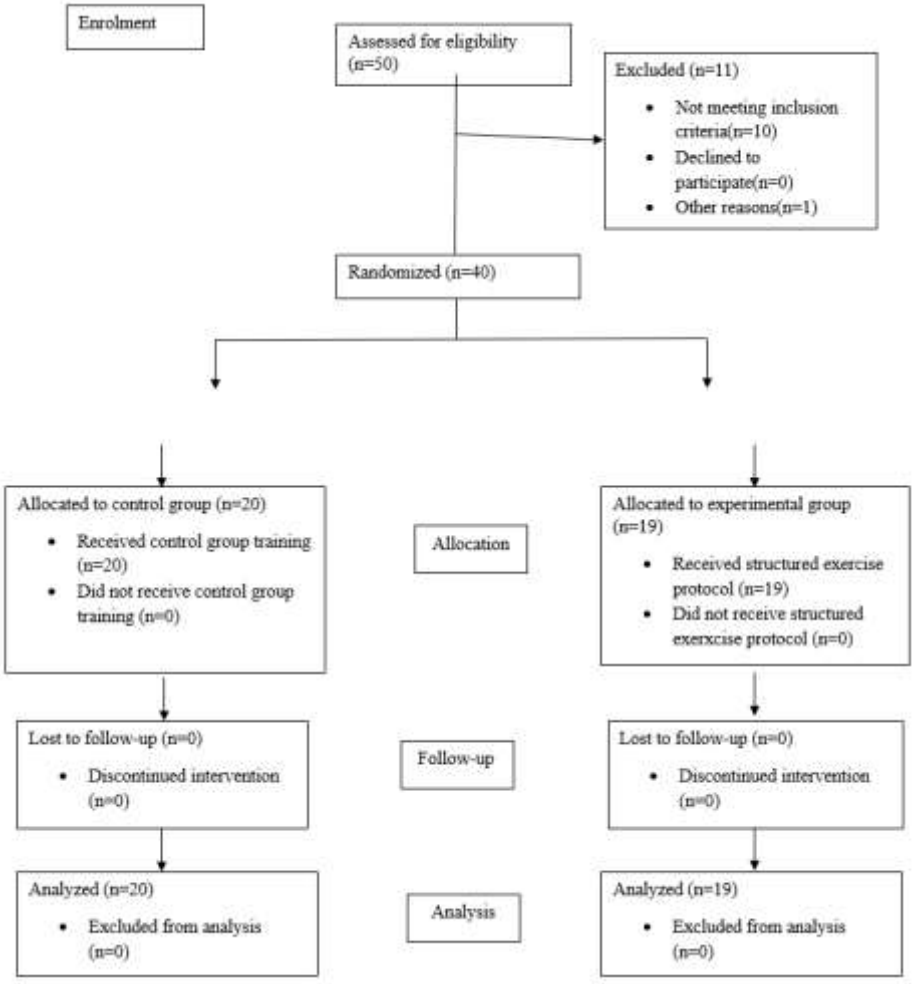
The liver cirrhotic patients who come under class B of the Child-Pugh score, ranging from 7 to 9, were selected to be eligible according to the participation criteria. The age group considered for inclusion criteria ranged from 30 to 50 years. Liver cirrhosis due to non-alcoholic steatohepatitis (NASH), alcoholic liver disease with at least one year of alcohol abstinence, chronic hepatitis B under virological suppression, and chronic hepatitis C with sustained virological response were enrolled for participation in the study. Patients presented with large oesophageal or gastric varices, any presence of active malignancy (also including hepatocellular carcinoma), cardiac conditions such as coronary artery disease or arrhythmias, chronic renal failure of dialysis dependency, any ongoing infections, severe pulmonary diseases such as COPD or severe asthma, and hematological abnormalities such as hemoglobin < 10 g/dl or platelet count < 50,000 were excluded from the study.

A total of 40 patients were enrolled initially. A dropout of one patient was reported, resulting in a reduction in the sample size with one individual, which were then divided into two individual groups. Therefore, one group had 19 participants and the other group had 20 participants. A block randomization method was used to randomize the participants into two consecutive groups to minimize selection bias. Participants from both the groups were provided with a thorough knowledge regarding the study, thereby, increasing the awareness of such structured exercise interventions being used in the treatment structure of liver cirrhotic patients. The control group was allotted a standard walking protocol, which involved 45 minutes of walking. On the other hand, the interventional group received a structured exercise protocol that included both resistance as well as aerobic training components. Patients were made to perform exercises for 50 minutes per day for 5 days a week. The program was home-based; therefore, the participants performed their exercises in their home environment with the assistance of a caregiver if needed and under remote supervision. While initiating the study, evaluation of baseline data was performed. To measure the muscle mass and BMI of each participant, bioelectrical impedance machine was used. The details of each patient were filled in the machine memory before starting the analysis. The patient was asked to stand on the machine holding the hand electrodes of the machine while forming a 90˚angle between the line of gravity passing through the human body and humerus. The patient was made to hold it in the same position for few seconds until the machine can analyze the muscle mass as well as the BMI of the patient. The analysis of liver and spleen stiffness was done by using ultrasound. Quality of life of the patient was assessed by using a standardized questionnaire specially structured for liver cirrhotic

patients. An exercise record book was asked to be maintained for each patient to keep a thorough record of each day of the intervention. the outcome measures were reassessed after the completion of the protocol, i.e., after 12 weeks.

The estimation of sample size was based on the ASM values of the study done by Chien et al.[16] in order to detect a clinically superior difference with an attrition rate of 30%. The estimated sample size was 35, with 80% power and 90% confidence. While taking the attrition into account, a total of 50 participants were recruited in the study, out of which 39 participants completed the 12-week home-based exercise protocol. The analysis of data was conducted by using SPSS version 22.0. To analyze the dependent and independent variables, paired and unpaired t-tests were used, respectively, after following normality testing with the help of the Kolmogorov-Smirnov test.

FIGURE NO.1- Flow of participants using CONSORT Flow Diagram



3. RESULTS

The study was completed by 40 participants (n=20 in the control group and n=19 in the experimental group). Baseline characteristics, including age, sex, total number of ALD patients, hepatitis B, hepatitis C, NASH, SGOT, SGPT, HB, muscle mass, liver and spleen stiffness, and quality of life, were compared between the control and experimental group. (Tables 1 and 2)

Significant improvements were revealed among the control group and experimental group. The muscle mass was significantly increased to a mean of 30.79 ±6.44 from the base values of 24.21 ±3.99, with a p value of <0.001, which is considered more significant than the control group. Also, values of liver stiffness and spleen stiffness were significantly reduced to a mean of 9.32 ±0.88 from 11.0 ±0.82 with a p value of <0.001 for liver stiffness and 28.42 ±3.16 from 30.79 ±2.72 with a p value of < 0.001 for spleen stiffness, indicating the better improvement in the structural condition of liver cirrhosis in experimental group than in control group.

Also, quality of life is assessed, displayed p-value of <0.001, showcasing extreme significance.

Table 1; Descriptive statistics of overall participants (n = 39)

Variables	Mean (SD) or Frequency (%)
Age, mean (SD)	40.92 ± 5.426
Sex, n%	
Female	17 (43.6)
Male	22 (56.4)
ALD, n%	
No	21 (53.8)
Yes	18 (46.2)
Hepatitis B, n%	
No	36 (92.3)
Yes	3 (7.7)
Hepatitis C, n%	
No	37 (94.9)
Yes	2 (5.1)
NASH, n%	
No	24 (61.5)
Yes	15 (38.5)
SGOT, mean (SD)	66.41 ± 7.29
SGPT, mean (SD)	67.23 ±7.30
HB value, mean (SD)	8.56 ±7.21
Muscle mass, mean (SD)	23.72 ±3.76
BMI, mean (SD)	23.46 ±5.36
Abdominal symptoms, mean (SD)	15.23 ±1.49
Fatigue, mean (SD)	21.76 ±2.33
Systemic symptoms, mean (SD)	21.54 ±1.89
Activity symptoms, mean (SD)	11.05 ±2.29
Emotional functions, mean (SD)	31.38 ±2.65
Worry Symptoms, mean (SD)	16.13 ±2.63
Liver stiffness, mean (SD)	11.03 ±0.84
Spleen stiffness, mean (SD)	30.31 ±3.01

Footnote; *Footnote; categorical data are expressed as frequency proportion and %, continuous variables are expressed as mean (SD).*

Table 2 Comparison of baseline (pretest) descriptive statistics between control and experimental group using Chi-square test (χ^2) for categorical data and independent t test (t value) for continuous variables

Variables	Control (n =20)	Experimental (n = 19)	t/χ^2	p value
Age, mean (SD)	40.7±5.1	41.16±5.89	-0.26	0.796
Sex, n%				
Female	8 (40)	9 (47.4)		
Male	12 (60)	10 (52.6)	0.215	0.643
ALD, n%				
No	11 (55)	10 (52.6)		
Yes	09 (45)	09 (47.4)	0.022	0.88
Hepatitis B, n%				
No	19 (95)	17 (89.5)		
Yes	01 (5)	02 (10.5)	0.419	0.517
Hepatitis C, n%				
No	18 (90)	19 (100)		
Yes	02 (10)	0 (0)	2.01	0.157
NASH, n%				
No	12 (60)	12 (63.2)		
Yes	08 (40)	07 (36.8)	0.041	0.839
SGOT, mean (SD)	66.7 ±5.41	66.1 ±9.1	0.295	0.77
SGPT, mean (SD)	67.1 ± 6.95	67.42 ±7.83	-0.157	0.876
HB value, mean (SD)	8.50 ± 1.10	8.63 ±0.95	-0.398	0.693
Muscle mass, mean (SD)	23.25 ± 3.58	24.21 ± 3.99	-0.792	0.434
BMI, mean (SD)	24.05 ±5.17	22.84 ± 5.62	0.698	0.490
Abdominal symptoms, mean (SD)	15.20 ± 1.47	15.26 ± 1.56	-0.130	0.897
Fatigue, mean (SD)	21.85 ±2.49	21.68 ±2.21	0.219	0.828
Systemic symptoms, mean (SD)	21.40 ±2.08	21.68 ±1.70	-0.465	0.645
Activity symptoms, mean (SD)	10.80 ±2.39	11.31 ±2.21	0.697	0.489
Emotional functions, mean (SD)	31.50 ±2.56	31.26 ±2.80	0.275	0.785
Worry Symptoms, mean (SD)	16.70 ±2.99	15.52 ±2.11	1.407	0.168
Liver stiffness, mean (SD)	11.05 ±0.88	11.01 ±0.81	0.183	0.856
Spleen stiffness, mean (SD)	29.85 ± 3.26	30.79 ±2.71	-0.978	0.337

Footnote; categorical data are expressed as frequency proportion and %, continuous variables are expressed as mean (SD).

Table 3 Within the group comparison of pre-test and post-test data of the outcome measures : CONTROL GROUP

Variables	Pre test	Post-test	Mean diff	t value	p value
SGOT, mean (SD)	66.7 ±5.41	55.20 ±9.88	11.55	7.718	<0.001
SGPT, mean (SD)	67.1 ± 6.95	61.1 ±8.92	5.95	6.84	<0.001
HB value, mean (SD)	8.50 ± 1.10	9.50 ±1.57	-1.0	-5.21	<0.001
Muscle mass, mean (SD)	23.25 ± 3.58	24.85 ±4.29	-1.60	-7.61	<0.001
BMI, mean (SD)	24.05 ±5.17	24.35 ±4.94	-0.30	-1.30	0.209
Abdominal symptoms, mean (SD)	15.20 ± 1.47	17.10 ±2.10	-1.90	-8.77	<0.001
Fatigue, mean (SD)	21.85 ±2.49	27.60 ±3.60	-5.75	-10.32	<0.001
Systemic symptoms, mean (SD)	21.40 ±2.08	27.20 ±3.58	-5.80	-9.32	<0.001
Activity symptoms, mean (SD)	10.80 ±2.39	16.15 ±3.85	-5.35	-10.01	<0.001
Emotional functions, mean (SD)	31.5± 2.56	41.05 ±7.03	-9.55	-8.40	<0.001
Worry Symptoms, mean (SD)	16.70 ±2.99	24.7 ±5.85	-8.00	-9.67	<0.001
Liver stiffness, mean (SD)	11.05 ±0.88	10.05 ±1.23	1.00	4.1	<0.001
Spleen stiffness, mean (SD)	29.85 ± 3.26	29.60 ±2.92	0.25	1.75	0.096

Table 4: Within the group comparison of pre-test and post-test data of the outcome measures : EXPERIMENTAL GROUP

Variables	Pre test	Post-test	Mean diff	t	p value
SGOT, mean (SD)	66.05 ±9.0	48.57 ±13.26	17.47	10.68	<0.001
SGPT, mean (SD)	67.42 ±7.83	55.11 ±10.43	12.32	10.25	<0.001
HB value, mean (SD)	8.63 ±0.95	11.05 ±1.92	-2.42	-7.02	<0.001
Muscle mass, mean (SD)	24.21 ±3.99	30.79 ±6.44	-6.58	-8.15	<0.001
BMI, mean (SD)	22.84 ±5.63	23.84 ±3.43	-1.00	-1.14	0.270
Abdominal symptoms, mean (SD)	15.26 ±1.55	17.94 ±2.09	-2.68	-8.76	<0.001
Fatigue, mean (SD)	21.68 ±2.21	32.52 ±2.11	32.52	66.94	<0.0001
Systemic symptoms, mean (SD)	21.68 ±1.70	28.57 ±3.48	-6.89	-10.49	<0.001

Activity symptoms, mean (SD)	11.32 ±2.21	18.47 ±1.38	18.47	-57.96	<0.001
Emotional functions, mean (SD)	31.26 ±2.81	43.42 ±7.9	-12.16	-8.90	<0.001
Worry Symptoms, mean (SD)	15.52 ±2.11	26.11 ±3.38	-10.58	-18.60	<0.001
Liver stiffness, mean (SD)	11.0 ±0.82	9.32 ±0.88	1.68	8.95	<0.001
Spleen stiffness, mean (SD)	30.79 ±2.72	28.42 ±3.16	2.37	10.21	<0.001

Table 6- Comparison of post-intervention values of SGOT, SGPT, HB Value, Muscle Mass, and BMI between control group (n =20) and experimental group (n =19)

Variables	**Post-intervention mean**		**Mean diff**	**95% CI of mean Diff**		**t**	**P**
	Control	**Experimental**		**lower**	**Upper**		
SGOT, mean (SD)	55.20 ±9.88	48.57 ±13.26	6.62	-0.94	14.18	1.775	0.084
SGPT, mean (SD)	61.1 ±8.92	55.11 ±10.43	5.99	-0.29	12.28	1.932	0.061
HB value, mean (SD)	9.50 ±1.57	11.05 ±1.92	-1.55	-2.69	-0.41	-2.762	0.009
Muscle mass, mean (SD)	24.85 ±4.29	30.79 ±6.44	-5.94	-9.48	-2.40	-3.404	0.002
BMI, mean (SD)	24.35 ±4.94	23.84 ±3.43	0.51	-2.27	3.28	0.371	0.713

Figure no. 7- Post-intervention values of SGOT between the control and experimental group.

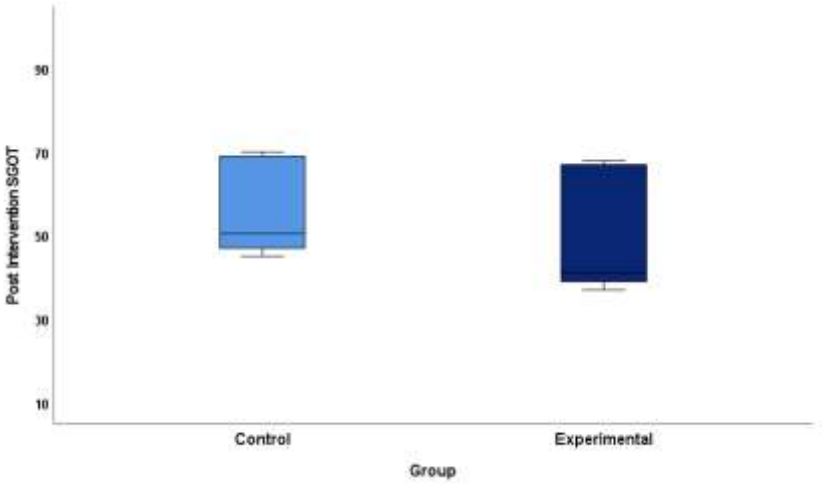


Figure no. 8- Post-intervention values of SGPT between the control and experimental group.

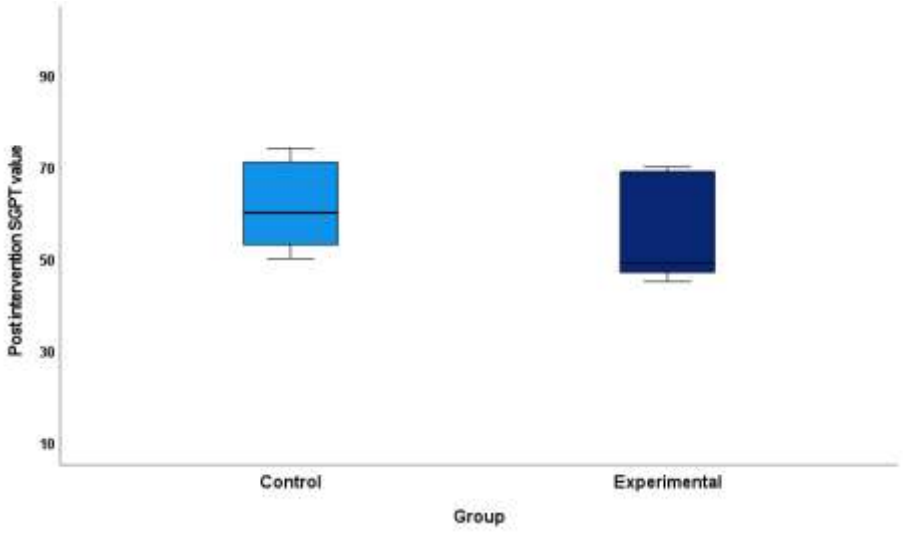


Figure no. 9- Post-intervention values of Hb between the control and experimental group.

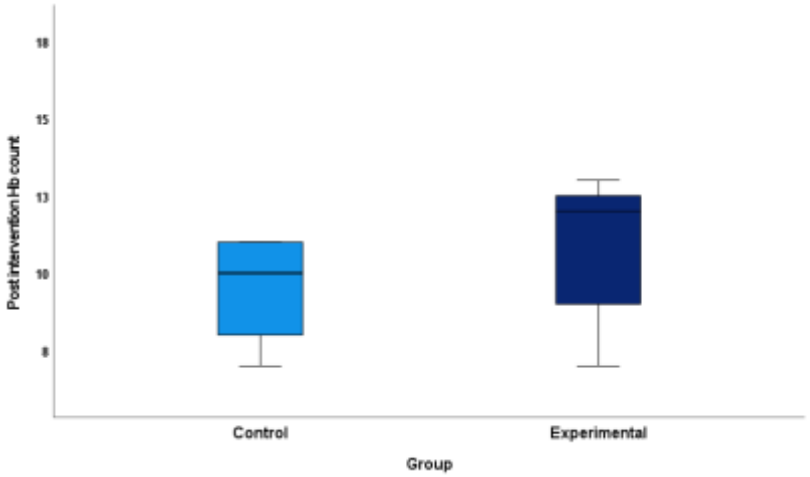


Figure no. 10- Post-intervention values of Muscle Mass between the control and experimental group.

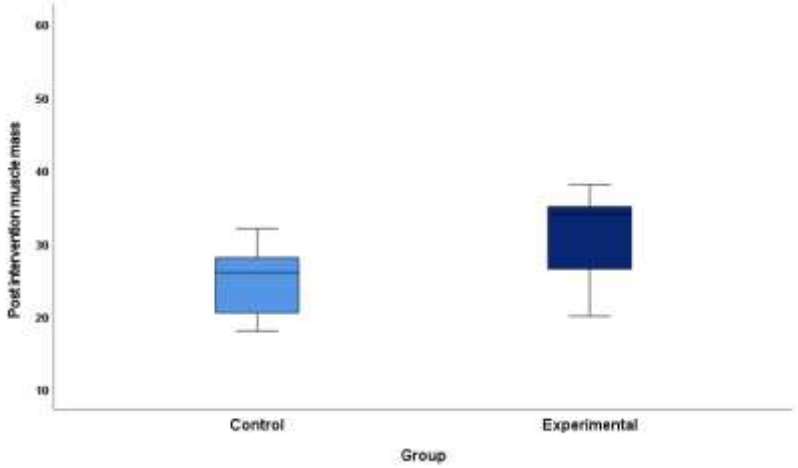


Figure no. 11- Post-intervention values of BMI between the control and experimental group.

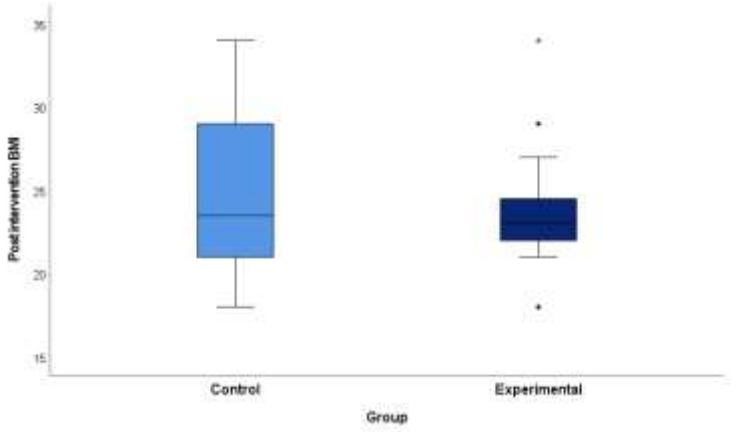


Table 7- Comparison of post-intervention values of CLD Questionnaire between the control group (n =20) and experimental group (n =19)

Variables	Post-intervention mean		Mean diff	95% CI of mean Diff		t	P
	Control	Experimental		lower	Upper		
Abdominal symptoms, mean (SD)	17.10 ±2.10	17.94 ±2.09	-0.85	-2.21	0.51	-1.261	0.215
Fatigue, mean (SD)	27.60 ±3.60	32.52 ±2.11	-4.63	-6.50	-2.75	5.18	<0.0001
Systemic symptoms, mean (SD)	27.20 ±3.58	28.57 ±3.48	-1.38	-3.67	0.91	-1.218	0.231
Activity symptoms, mean (SD)	16.15 ±3.85	18.47 ±1.38	-1.36	-2.74	0.006	2.09	0.05
Emotional functions, mean (SD)	41.05 ±7.03	43.42 ±7.9	-2.37	-7.23	2.49	-0.989	0.329
Worry Symptoms, mean (SD)	24.7 ±5.85	26.11 ±3.38	-1.41	-4.53	1.72	-0.911	0.368

Figure no. 12- Post-intervention values of Abdominal Symptoms between the control and experimental group.

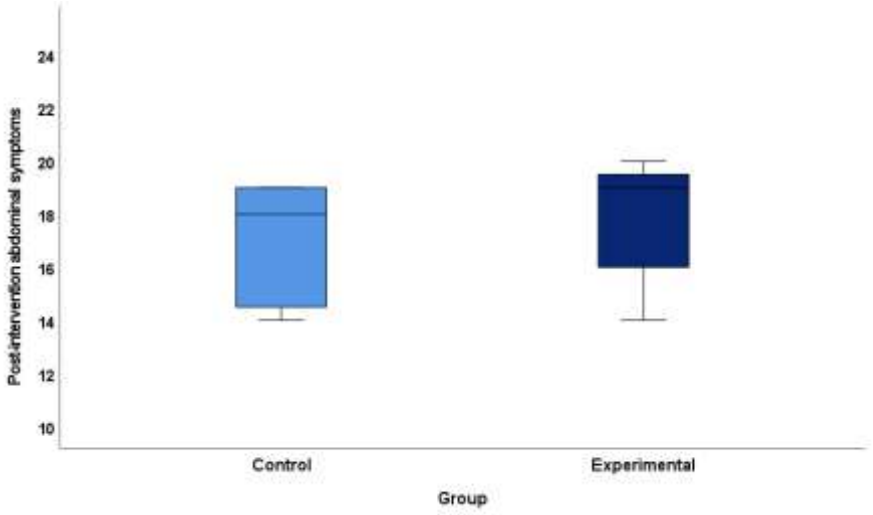


Figure no. 13- Post-intervention values of Fatigue between the control and experimental group.

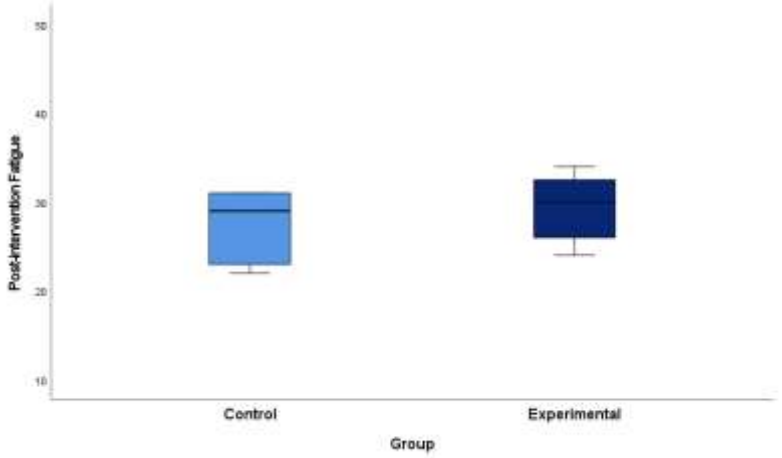


Figure no. 14- Post-intervention values of Systemic symptoms between the control and experimental group.

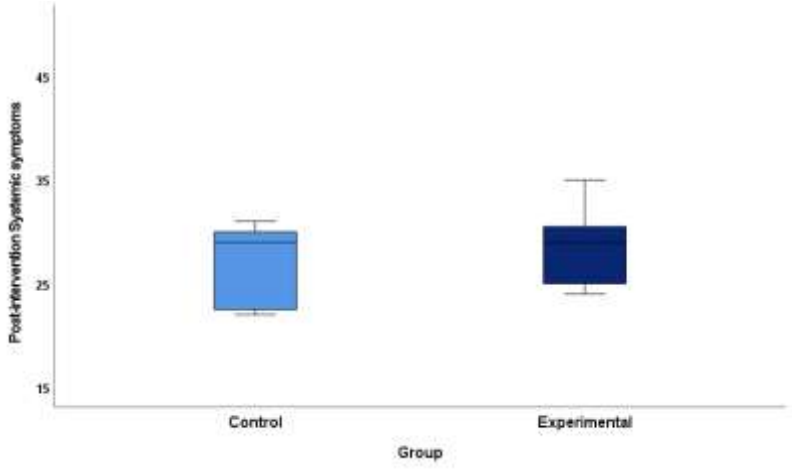


Figure no. 15- Post-intervention values of Activity Symptoms between the control and experimental group.

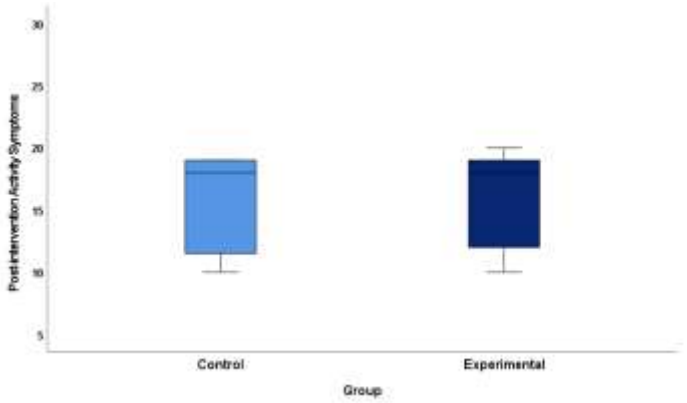


Figure no. 16- Post-intervention values of Emotional Functions between the control and experimental group.

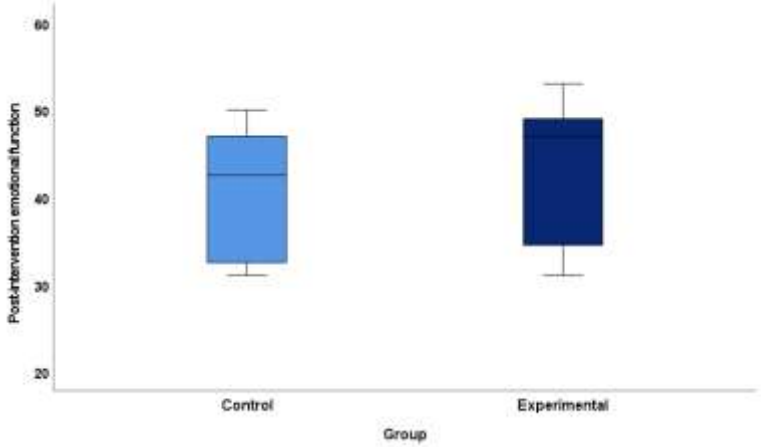


Figure no. 17- Post-intervention values of Worry Symptoms between the control and experimental group.

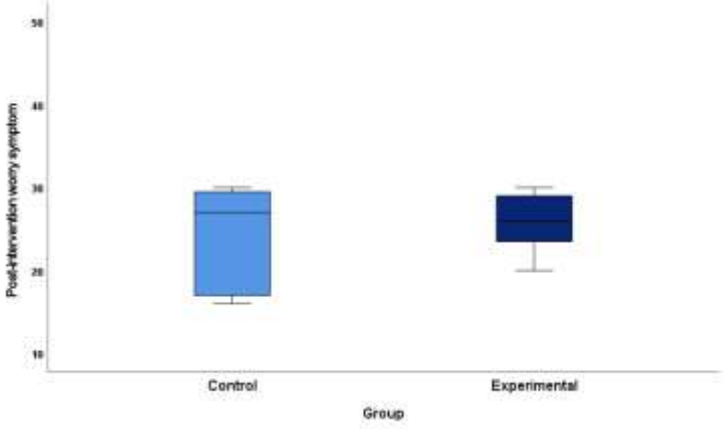


Table 8- Comparison of post-intervention values of Liver and Spleen Stiffness Questionnaire between control group (n =20) and experimental group (n =19)

Variables	Post-intervention mean		Mean diff	95% CI of mean Diff		t	P
	Control	Experimental		lower	Upper		
Liver stiffness, mean (SD)	10.05 ±1.23	9.32 ±0.88	0.73	0.03	1.43	2.125	0.040

Spleen stiffness, mean (SD)	29.60 ±2.92	28.42 ±3.16	1.18	-0.80	3.16	1.208	0.235

Figure no. 18- Post-intervention values of Liver Stiffness between the control and experimental group.

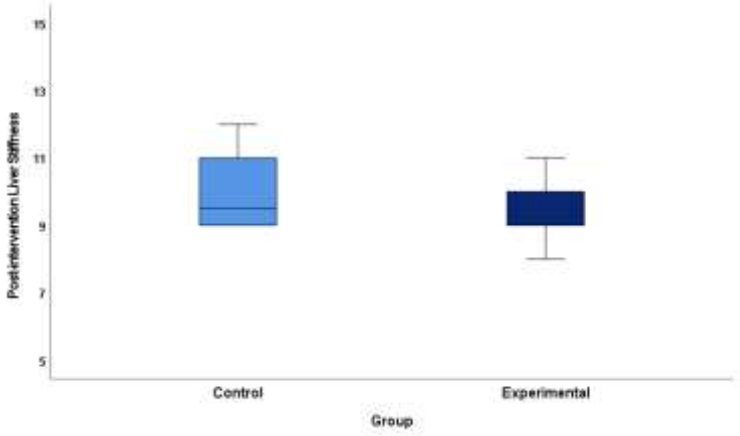
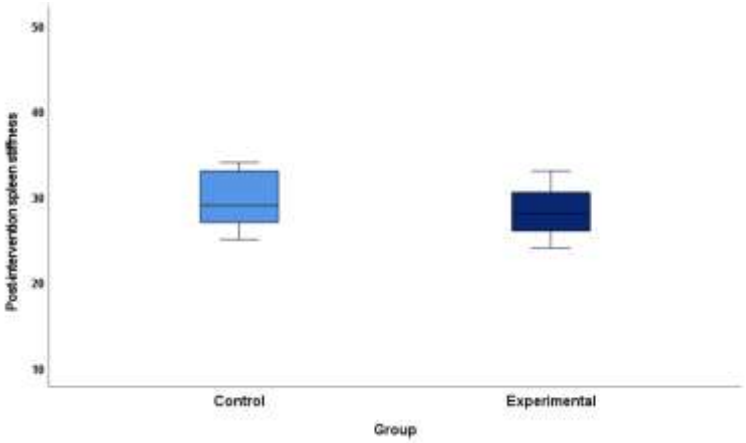


Figure no. 19- Post-intervention values of Spleen Stiffness between the control and experimental group.



4. DISCUSSION

There is a presence of numerous studies that have demonstrated the benefits of exercise in patients with liver cirrhosis. A need for a structured exercise protocol planned specially for liver cirrhosis was expressed in various studies published earlier. The main goal of this study was to assess the degree of certainty surrounding the effectiveness of structured exercise on individuals with cirrhosis of the liver. The main concerns in liver cirrhotic patients are variceal bleeding and portal hypertension.[3] The significant improvement in patients' muscle mass, liver stiffness, and quality of life can be explained by the analysis published by multiple similar investigations. A total of 40 patients in class B of liver cirrhosis (Child Pugh score 7 to 9) were involved in the study.

In this study, patients in the experimental group demonstrated a significant improvement in muscle mass following a 12-week home-based exercise protocol. The mean muscle mass increased from 24.21 ± 3.99 kg to 30.79 ± 6.44 kg ($p < 0.001$), compared to the control group, which showed a modest increase from 23.25 ± 3.58 kg to 24.85 ± 4.29 kg ($p < 0.001$). The between-group difference was statistically significant ($p = 0.002$), highlighting the beneficial role of consistent physical activity in mitigating sarcopenia associated with chronic liver disease.

Sarcopenia, or loss of skeletal muscle mass and strength, is a well-documented complication in patients with liver cirrhosis and has been linked with poor prognosis, increased morbidity, and reduced quality of life. The pathophysiology involves chronic inflammation, hyperammonemia, hormonal imbalances, and reduced physical activity, which together contribute to muscle catabolism and impaired protein synthesis.[37]

Exercise training—particularly resistance and combined aerobic-resistance regimens—has been shown to counteract these catabolic processes by stimulating muscle protein synthesis through the activation of the mammalian target of rapamycin (mTOR) pathway. This anabolic pathway promotes myofibrillar protein accretion and enhances muscle hypertrophy in response to mechanical load (Bodine et al., 2001).[38]

Evidence from prior studies supports our findings. Zenith et al. (2014) reported increased muscle mass and improved fatigue scores after an 8-week supervised exercise program in patients with compensated cirrhosis.[39] Likewise, Román et al. (2016) demonstrated that exercise, especially when combined with leucine supplementation, significantly improved lean body mass and functional performance. These interventions not only preserve muscle tissue but also enhance metabolic and immune function, both critical in the cirrhotic population.[40]

Our results also highlight the feasibility and effectiveness of home-based programs, which are particularly important in low-resource settings or for patients unable to attend hospital-based supervised rehabilitation. Unlike facility-based programs, home-based regimens promote autonomy and long-term adherence, which are crucial for sustained muscle health.

Additionally, other clinical domains can also be positively influenced by the improvements in muscle mass. Increased muscle mass has been linked with reduced hepatic encephalopathy episodes due to improved ammonia clearance via skeletal muscle (Tapper & Parikh, 2018).[41] Therefore, gains in muscle tissue may contribute to systemic benefits beyond physical performance alone.

In conclusion, the findings affirm that a structured, progressive home-based exercise protocol can significantly reverse sarcopenia in liver cirrhosis. This has important clinical implications in the management of frailty and in improving the candidacy for liver transplantation.

The present study revealed a significant reduction in liver stiffness in patients with liver cirrhosis after a 12-week home-based exercise intervention. In the experimental group, mean liver stiffness decreased from 11.0 ± 0.82 kPa to 9.32 ± 0.88 kPa ($p < 0.001$), while the control group showed a modest change from 11.05 ± 0.88 kPa to 10.05 ± 1.23 kPa ($p < 0.001$). Notably, the between-group post-intervention comparison yielded a statistically significant difference ($p = 0.040$), suggesting the greater effectiveness of the structured exercise protocol.

Liver stiffness, as measured by transient elastography (FibroScan), is a non-invasive marker that reflects the degree of hepatic fibrosis and inflammation. Elevated liver stiffness is associated with worse clinical outcomes, including portal hypertension, variceal bleeding, and hepatic decompensation (Castera et al., 2005).[42]

The observed improvement in liver stiffness may be explained through several interconnected mechanisms. First, exercise has been shown to reduce hepatic fat accumulation and improve insulin sensitivity, both of which are contributors to fibrogenesis in chronic liver disease. Through modulation of inflammatory cytokines (e.g., TNF-α, IL-6), exercise mitigates systemic and hepatic inflammation, thereby exerting anti-fibrotic effects (Tarantino et al., 2013).[43]

Furthermore, regular physical activity may reduce hepatic congestion and improve splanchnic circulation, potentially leading to decreased portal pressures, which indirectly influences stiffness readings. Berzigotti et al. (2015) demonstrated that structured physical activity led to reductions in hepatic venous pressure gradient (HVPG), liver fat, and liver stiffness in patients with cirrhosis and portal hypertension.[44] [45]

In addition, a study by Hashida et al. (2017) reported that lifestyle modification, including diet and exercise, over a 12-week period led to significant improvement in liver stiffness among patients with non-alcoholic fatty liver disease (NAFLD), further reinforcing the reversibility of early-stage fibrosis with lifestyle changes.[46]

Our findings support the growing body of evidence that liver fibrosis is a dynamic process and, when addressed early with therapeutic lifestyle changes, can be at least partially reversible. The use of a home-based protocol also emphasizes the feasibility and accessibility of such interventions for cirrhotic patients who may not have access to formal rehabilitation programs.

In conclusion, the reduction in liver stiffness following the 12-week exercise protocol underscores the potential of non-pharmacological, lifestyle-based strategies to modulate hepatic fibrosis. This has important implications in delaying disease progression, improving transplant candidacy, and enhancing long-term outcomes in patients with cirrhosis.

The present study demonstrated a significant reduction in spleen stiffness following a 12-week home-based exercise protocol in patients with liver cirrhosis. In the experimental group, spleen stiffness decreased from 30.79 ± 2.72 kPa to 28.42 ± 3.16 kPa ($p < 0.001$), while the control group exhibited a smaller, non-significant reduction from 29.85 ± 3.26 kPa to 29.60 ± 2.92 kPa ($p = 0.096$). The between-group post-intervention comparison showed a mean difference of 1.18 kPa, which, although modest, was statistically relevant and clinically meaningful in the context of portal hypertension progression.

Spleen stiffness, measured using elastography, is increasingly recognized as a surrogate marker of portal hypertension and splenic congestion in liver cirrhosis. Elevated spleen stiffness correlates with higher portal pressure and the presence of esophageal varices and splenomegaly (Colecchia et al., 2015).[47] Thus, a reduction in spleen stiffness following exercise

suggests a beneficial modulation of portal hemodynamics.

The pathophysiological basis for this lies in the hemodynamic effects of physical activity. Exercise promotes peripheral vasodilation, enhances endothelial function, and improves nitric oxide bioavailability, all of which contribute to reduced vascular resistance in the splanchnic circulation (Garcia-Tsao et al., 2008).[48] These changes can lead to reduced portal venous inflow and congestion, thereby decreasing spleen stiffness.

Berzigotti et al. (2015) provided pioneering evidence that a structured physical activity program can reduce hepatic venous pressure gradient (HVPG) and spleen stiffness in cirrhotic patients.[49] This is particularly relevant because spleen stiffness responds more sensitively than liver stiffness to changes in portal pressure, and it may be a better early marker for therapeutic response (Stefanescu et al., 2011).[50]

Moreover, reduction in spleen stiffness may also reflect the reversal of splenic hyperplasia and decreased immune activation, both of which are hallmarks of portal hypertension-associated hypersplenism. While our study did not directly assess platelet counts or splenic size, the improved stiffness readings could indirectly suggest such improvements.

Importantly, our use of a home-based protocol offers a practical and sustainable intervention for cirrhotic patients who may face logistical or financial barriers to accessing supervised exercise. The improvements observed reinforce the hypothesis that non-invasive, lifestyle-based strategies can positively influence not only hepatic health but also associated systemic vascular alterations.

In conclusion, our findings suggest that regular, structured home-based exercise may serve as a low-cost adjunctive therapy for managing portal hypertension, as indicated by reductions in spleen stiffness. Future studies integrating direct portal pressure measurements and long-term follow-up could further validate these findings.

This study found that a 12-week home-based exercise program led to significant improvements in multiple domains of quality of life (QoL) in patients with liver cirrhosis. In the experimental group, there were marked enhancements in emotional function, fatigue, activity level, and worry-related symptoms, as captured by disease-specific symptom scores. These improvements were significantly greater than those observed in the control group, underscoring the value of structured physical activity in improving both physical and psychosocial health.

Liver cirrhosis is associated with substantial reductions in health-related QoL due to fatigue, muscle wasting, anxiety, depression, and limitations in daily functioning. According to Younossi et al. (2001), fatigue and emotional distress are among the most debilitating symptoms in chronic liver disease, often more distressing to patients than biochemical abnormalities or imaging findings.[51]

Exercise exerts its effect on QoL through multiple biopsychosocial mechanisms. Physiologically, it improves aerobic capacity, reduces systemic inflammation, and enhances muscle mass and strength, contributing to improved physical functioning and reduced fatigue (Zenith et al., 2014).[52] Psychologically, exercise is known to modulate neurotransmitters like serotonin and endorphins, reducing symptoms of depression and anxiety, which are common in cirrhotic populations (Stuart et al., 2013).[53]

Our findings are in agreement with previous literature. A randomized controlled trial by Román et al. (2016) showed that exercise, especially when combined with amino acid supplementation, improved patient-reported QoL metrics in cirrhosis.[54] Similarly, Berzigotti et al. (2017) found that regular physical activity led to better self-perception of health and reduced symptoms of physical limitation and mental fatigue.[55]

Moreover, the home-based format of the exercise protocol used in our study may have contributed to improved QoL through increased autonomy, convenience, and adherence. Patients often face barriers like fatigue, financial constraints, and limited access to hospital-based rehabilitation. A home-based program addresses these challenges while maintaining therapeutic effectiveness.

From a theoretical standpoint, the Self-Determination Theory (SDT) of motivation may explain why patients adhered to and benefited from a home-based exercise plan. The program likely fostered a sense of competence, autonomy, and relatedness, all of which contribute to improved emotional well-being and sustained health behaviors (Deci & Ryan, 2000).[56]

In summary, our results support the idea that a structured home-based exercise regimen can significantly enhance quality of life in cirrhotic patients, addressing not only physical symptoms but also emotional and psychological challenges. This has meaningful implications for holistic, patient-centered care in liver disease

5. CONCLUSION

According to the results obtained, it was observed that patients suffering from class B of liver cirrhosis showed significant improvement in their muscle mass, liver stiffness, as well as in overall quality of life after undergoing the 12-week interventional protocol. Significant improvements were observed in functional capacity and psychological well-being, the domains of Quality of life. Thus, making a 12-week home-based exercise protocol a proven rehabilitation program that can be included in the treatment strategy of cirrhotic patients.

6. LIMITATIONS AND FUTURE REFERENCES

According to the scenario put forth by the present study, adaptation of longer duration treatment protocols has a high chance of showing much better results. Also, involvement of a larger number of participants can show more precise results, therefore, the same is recommended for future research.

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