Original Article

Assessment of muscle status and Sarcopenia in patients with liver cirrhosis

Marwa Gad, Abdelrahman Mokhtar, Adel Ibrahim, Neven Abbas

Summary

Background and objectives: *Sarcopenia characterized by progressive and generalized loss of skeletal muscle mass and function with a risk of adverse outcomes such as. There is an important relationship between cirrhosis and muscle weakness (sarcopenia), as the liver plays a major role in the metabolism of all nutrients. The Aim of this study to assess muscle status and sarcopenia among patients with liver cirrhosis and its relation to patient physical activity and dietary history as well as liver disease progression.* ***Method***: *This was a cross-sectional study conducted on 150 cirrhotic patients attending to hepatology and gastroenterology department at Specialized Medical Hospital, Mansoura University. All patients underwent through clinical evaluation, laboratory investigation, and assessment of muscle status by anthropometric parameters and grip strength. In addition, assessment of nutritional status and physical activity was done.* ***Results***: *Of included participants, 80 patients (53.3%) were diagnosed with sarcopenia and pre-sarcopenia (39.3% sarcopenic and 14% pre-sarcopenia) and 70 patients with non sarcopenia or pre-sarcopenia. Almost two-third of sarcopenic patients were men (66.4%) versus (33.6%) were women. The sarcopenia and pre-sarcopenia patients were older than non-sarcopenia patients and had lower BMI with statistically significant difference. The majority of patients with sarcopenia consumed diet with low protein, low vitamin and iron contents with statistically significant difference versus non sarcopenic patients. On other hand, excess salt and minerals intake were common among sarcopenic and pre-sarcopenic patients. Assessment of physical activity among studied group by International Physical Activity Questionnaires (IPAQ) demonstrated that, 53% of sarcopenic and pre-sarcopenic patients exerted low or no exercise with statistically significant difference compared to non-sarcopenic group (only 12%). Frequency of complications of liver cirrhosis as ascites, hepatic encephalopathy and variceal bleeding were statistically significant higher in those patients with sarcopenia and pre-sarcopenia versus those without sarcopenia. There was significant hypoalbuminemia, hyperbilurbinemia and rising serum creatinine among sarcopenic patients versus non-sarcopenic patients. Positive statistically significant association detected between Sarcopenia and progression of liver diseases assessed by Child Pugh score and MELD score versus non sarcopenic patients. The independent predictive factors of sarcopenia analysed by logistic regression were increasing age, low BMI, low protein intake and hypoalbuminemia.* ***Conclusion***: *The prevalence of sarcopenia is high in cirrhotic patients. It was highest in patients with older age, low BMI and low protein intake. Also, the worse the condition of the liver the greater the degree of muscle weakness was detected.*

Keywords: *Sarcopenia and pre-sarcopenia, liver cirrhosis, protein, vitamin variceal bleeding and hepatic encephalopathy*

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Introduction

Cirrhosis is the final stage of different chronic liver diseases characterized by hepatic cell degeneration and regeneration with fibrosis and nodular formation. Compensated cirrhosis often only slightly worsens patients′ general condition. However, morbidity and mortality are increasing rapidly if decompensation of liver cirrhosis occurs[1]. Although the most commonly known complications in cirrhotic patients are ascites, variceal bleeding, hepatic encephalopathy, and

hepatocellular carcinoma, severe muscle wasting or sarcopenia is considered one of frequent unseen complication which negatively impact survival and quality of life[2]. Sarcopenia is a disorder described by progressive loss of skeletal muscle mass and strength which associated with unfavorable outcomes such as poor quality of life, physical disability and even death[3]. Sarcopenia, as defined by muscle loss and dysfunction, is a common feature of all chronic inflammatory diseases and involve impairment of contractile, metabolic and endocrinal functions of the skeletal muscle[4]. Sarcopenia is one of the diagnostic hallmarks of malnutrition, a clinical condition that is often challenging to objectively define in patient with cirrhosis[5]. Balance between protein synthesis and protein breakdown plays important role in maintaining muscle mass. As cirrhotic patients have poor hepatic glycogen reserves due to the impaired synthetic capacity of hepatic cells, this leads to increase the utilization of amino acids as an energy source that accelerate the breakdown of skeletal muscle resulting in sarcopenia[6]. Sarcopenia is a crucial nutritional issue that is widely spread among patient with cirrhosis with prevalence 40% to 70%. Different screening procedures are used to identify sarcopenia earlier and to allow proper intervenetions[7]. Mild degree of muscle loss possibly occurs in all cirrhotic patients but the severity of sarcopenia measured by anthropometric assessment getting worse with increasing severity of liver disease measured by Child's score[8]. Diet one of the factors that may have direct effect on sarcopenia and functional status. Muscle mass weakening is related to different nutrient deficiencies including, protein, vitamin D, and antioxidant agents such as selenium and vitamins E and C especially in elderly[9]. On other hand, physical activity is an important determining factor of muscle anabolism[10]. Decreased physical activity can cause loss of skeletal muscle by a decrease in muscle protein synthesis. Conversely, loss of muscle mass and strength is associated with physical disability and it may cause patients to become disabled and stay inside[11]. The aim of our study was to assess muscle status and sarcopenia among patients with liver cirrhosis and it is relation to patient physical activity and dietary history as well as liver disease progression.

Patients and Methods

This cross-sectional study was carried out on 150 cirrhotic patients with liver cirrhosis attending to hepatology and gastroenterology unit (outpatient clinic and inpatient ward). This study conducted from January 2017 to December 2017, at specialized medical hospital in Mansoura University. **A) Inclusion criteria**: Included, patients with liver cirrhosis, age 18 -60 year and patients able to communicate. **B) Exclusion criteria**: Patients with other system failure (e.g. renal failure, heart failure and respiratory failure). Patients with other systemic, endocrinal disease that can influence the muscle status e.g., myopathies, endocrinopathies like hypothyroidism and Cushing. Patients on chronic medications that can directly affect the muscle status e.g. steroids, colchicine and hydroxychloroquine. Patients with any condition that can limit their physical activity e.g chronic arthritis, systemic neuromuscular disease. Females during pregnancy, puerperium or lactation. Patients who are bed ridden due to any cause. All selected patient were subjected to; through history taking and complete physical examination including, stigmata of chronic liver disease, nutritional status and features of any nutritional deficiencies, assessment of Child-Pugh and MELD score. Abdominal ultrasound to assess liver, spleen size, and presence of ascites.

Laboratory investigation

Including, liver function tests (serum albumin, serum bilirubin, prothrombin *time*, ALT, AST), serum creatinine, Complete blood count, serum calcium, serum CPK.

Anthropometric parameters and muscle status assessment

* Measurement of weight, height and BMI.
* Weight was sectioned into two measures: objective scale weight (kg) and subjective assessment of dry weight without ascites or pedal edema. Estimated dry weight (kg) was calculated using either the post paracentesis body weight or scale weight minus ascites weight based upon severity (mild: 5%; moderate: 10%; severe: 15 %). An additional 5% was subtracted if bilateral pedal edema was present. Body mass index (BMI) was measured using either scale or estimated dry weight divided by height (kg /m2)[12].

Assessment of muscle status

a) Measurement of muscle power by grip strength Using Jamar Hand Dynamometer (JAMARTM handgrip dynamometer; Sammons Preston, Bolingbrook, IL). The American Society of Hand Therapists (ASHT) recommended standard position to be used: the patient was seated with shoulders adducted and neutrally rotated, elbow flexed at 90 degrees, and the forearm and the wrist in neutral position. The patients were

verbally instructed to maintain their arm by their side with their shoulder in neutral position. Also, they were instructed neither extremely brace their arm against their trunk nor abduct their arm. The patients were also instructed to keep their wrists as neutral as possible although mild wrist extension is expected with power grip (0 -30 degrees of wrist extension is permissible by ASHT)[13]. Grip strength was measured from non-dominant hand. Three trials were conducted with approximately 30_s of resting time between the tests. The best attempt out of the three was recorded as the maximal result. Subjects were given verbal encouragement to maximize their effort.The scores of the hand was expressed in kilograms. Close attention was paid to make all three attempts in a similar[13].The cut off value for diagnosis of sarcopenia was reported (Ohashi et al., 2018) as < 26 kg for men and <18 kg for women[14]. **b)** Measurement of muscle mass by using mid arm circumference and skin fold thickness. Mid arm circumference was measured at the midpoint between the tip of the acromion and the olecranon process on the non-dominant side of the body using a flexible tape measure. Triceps skin fold thickness was also taken on the non-dominant side of the body, with the patients standing in a relaxed position, using skin fold caliper**.** Mid-arm muscle circumference (MAMC) was calculated using the mid-arm circumference and triceps skin fold thickness according to a standard equation[15]: **AMC (cm) = MAC (cm) - [3.14 x TSF (cm)]**. The diagnosis of sarcopenia can be established when MAMC value is below the 10^{th} percentile from a reference population[16]. According to previous methods of assessment muscle status and criteria of sarcopenia, the studied group subdivided to: **1)** Sarcopenic group (low muscle mass and strength). **2)** Pre-sarcopenic group (low muscle mass or grip strength). **3)** Non sarcopenia group (normal both muscle mass and strength). The patients diagnosed with pre sarcopenia or sarcopenia were considered as one group and compared to non sarcopenic group in this study. **I. Questionnaire for assessment of physical activity.** For assessment of physical activity we used The International Physical Activity Questionnaires (IPAQ) short version. The IPAQ short form asks about three specific types of activity include walking, moderate-intensity activities and vigorous-intensity activities. The items in the short IPAQ form were structured to provide separate scores on walking, moderate-intensity and vigorous-intensity activity. Computation of the total score for the short form requires summation of the duration (in minutes) and frequency (days) of walking, moderate-intensity and vigorous-intensity activities[17]. According to IPAQ Scoring Protocol (Short Forms), patients had one of the three level of physical activity (low or moderate or vigorous)[18]. **II. Questionnaire for Assessment of dietary history.** Assessment different types and amount of nutrient taken by the patient per week by validated questionnaire and classify these amount either more than required, less than required or as required[19]. The study protocol was approved by medical ethics research team, Faculty of Medicine in Mansoura University.

Statistical analysis

Collected data were coded, computed and statistically analyzed using SPSS (statistical package of social sciences), version 16. Data were presented as frequency and percentages (qualitative variables) and mean ± SD (quantitative continuous variables). Chi square ($\chi 2$) was used for comparison of categorical variables. Student's *t* test was used for comparison of continuous quantitative variables (two groups) and it is replaced by Mann Whitney (Z) test if the data is not normally distributed. Multiple Logistic Regression Modeling was used as multivariate analysis to find the risk priority factors. The difference was considered significant at $P \leq 0.05$.

Results

Table (1) shows that, sarcopenic and pre sarcopenic patients were elder than non sarcopenicpatients (86.2% at age above 50 year). Moreover, there is statistically significant difference regarding BMI between studied groups (p 0.001). All patients with low body weight (BMI<18) were sarcopenic. As regard obese patients (BMI≥30), 11 patients (13.8%) were sarcopenic versus 23 patients (32.9%) were non sarcopenic. On other hand, there is no significant difference as regard gender, smoking habits and different occupations between two groups. By applying multivariate analysis (Binary Logistic regression), it is found that percentage of predication of occurrence of sarcopenia or pre sarcopenia among patients with liver cirrhosis is 74.7%. The risk is significantly increased with age 50 years and above and patients with below average BMI. Table (2) shows dietary history and its relation to sarcopenia of the studied patients. Compared to non-sarcopenic patients, sarcopenic patients

had low protein intake (p<0.0001), less carbohydrate and lipids than required (p<0.001). Furthermore, as regard minerals and salt, most of sarcopenic group received amount of mineral more than required (50%) (P<0.001). In contrary, majority of sarcopenic patient take amount of iron and vitamins less than required with significant difference (p<0.0001) versus non sarcopenic group . By applying multivariate analysis (Binary Logistic regression), it is found that percentage of predication of occurrence of sarcopenia and pre sarcopenia among patients with liver cirrhosis is 74.0%. The risk is significantly increased in patients taking less protein, less iron, more minerals and added salt. Table (3) demonstrates non-significant difference as regard DM, HTN and other associated diseases (cardiac or chest or neurological diseases) between two groups. However, there is significant difference as regard diabetic treatment (p 0.004) in which insulin is the therapy for most of diabetic patients of sarcopenic group (97%). Table (4) shows, significant difference as regard serum albumin, serum bilirubin, SGOT, serum creatinine between two groups. There is no significant difference as regard INR, SGPT, HB and platelets. Although there is no significant difference in serum calcium among studied group, 66% of sarcopenic had low serum calcium. Moreover, significance association presented between elevated WBCs and sarcopenic and pre sarcopenic group (30%). By applying multivariate analysis (Binary Logistic regression), it is found that percentage of predication of occurrence of sarcopenia or pre sarcopenia among patients with liver cirrhosis is 75.3%. The risk is significantly increased in patients with low albumin and those with high serum creatinine. Table (5) shows that, sarcopenia more prevalent with progression of liver disease as (72.5) of sarcopenic group had Child Pugh C classification while most of non sarcopenic group (55.7%) had child A classification with statistically significance (p<0.0001). Also, there is significant difference as regard MELD score between two groups as it was higher in sarcopenic group (12.64 ± 4.5) than the other (19.9± 6.9). Table (6) shows statistically significant differences as regard ascites, encephalopathy, jaundice and variceal bleeding between non sarcopenic and sarcopenia and pre sarcopenia patients (P<0.05). By applying multivariate analysis (Binary Logistic regretssion), it is found that percentage of predication of occurrence of sarcopenia & pre sarcopenia among patients with liver cirrhosis is 84.7%. The risk is significantly increased in patients with moderate and severe ascites and this reporting history of encephalopathy. Table (7) shows that, the creatine phosphokinase (CPK) was significantly increased in non sarcopenic group versus sarcopenic (p= 0.001). Figure (1) shows, a significant association between sarcopenia and physical activity among studied patients (p<0.0001) as (52.5%) of sarcopenic group had low physical activity.

Table (1) Socio-demographic characteristics & BMI and their relation to sarcopenia of the studied patients.

Characters	Items	Sarcopenia& Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test	Univariate analysis Odd's Ratio (95% CI)	Multivariate* Analysis Adjusted Odd's ratio (95%CI)
		No	%	No	%			
Age (years)	<50	11	13.8	28	40.0	r		
	≥50	69	86.2	42	60.0	χ^2=13.371, P0.001	4.18(1.77-10.0)	4.1 (1.6-10.5)
Gender	Males	53	66.2	43	61.4	r		
	Females	27	33.8	27	38.6	χ^2=0.381, P0.539	0.81(0.39-1.67)	
Occupation	Manual worker	29	36.2	18	25.7	r		
	Employee	19	23.8	20	28.6	χ^2=1.46, P0.227	0.59(0.23-1.52)	
	Professionals	10	12.5	12	17.2	χ^2=1.61, P0.208	0.52(0.16-1.62)	
	HW/unemployed	22	27.5	20	28.6	χ^2=0.79, P0.375	0.68(0.27-1.73)	
Smoking habit	Never smoke	42	52.5	36	51.4	r		
	Ex-smoker	21	26.2	19	27.1	χ^2=0.02, P0.889	0.95(0.41-2.18)	
	Current smoker	17	21.2	15	21.4	χ^2=0.02, P0.887	0.97(0.39-2.40)	
BMI dry weight groups	Average (18.5-)	44	55.0	10	14.3	r		
	Below average	8	10.0	0	0.0	χ^2=3.87, P0.047	1.23(1.03-1.72)	9.8 (3.5-27.6)
	Overweight	17	21.2	37	52.9	χ^2=27.46, P0.000	9.58(3.6- 26.2)	
	Obese	11	13.8	23	32.9	χ^2=21.49, P0.000	9.2(3.08-28.5)	
***Model χ^2 =55.055, P0.000,**	**β for age ≥50 years=1.41**					**Constant**	**Percentage of predication**	
	β for BMI below average=2.279					**= 1.853**	**74.7%**	

Table (2) Dietary history and its relation to sarcopenia of the studied patients.

Diet elements	Items	Sarcopenia & Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test	Univariate analysis Odd's Ratio (95% CI)	Multivariate* Analysis Adjusted Odd's ratio (95%CI)
		No	%	No	%			
Protein	As required	23	28.8	46	65.7	r		
	< than required	49	61.2	6	8.6	χ^2=39.08, P0.000	0.06(.02-0.18)	1.88(1.12-3.16)
	>than required	8	10.0	18	25.7	χ^2=0.06, P0.812	1.13(.39-3.33)	
CHO	As required	52	65	41	58.6	r		
	< than required	17	21.2	6	8.6	χ^2=1.11, P0.242	1.74(.56-5.60)	
	>than required	11	13.8	23	32.8	χ^2=6.25, P0.012	0.36(.14-0.87)	
Lipids	As required	44	55.0	25	35.7	r		
	< than required	20	25.0	8	11.4	χ^2=0.52, P0.471	1.42(.50-4.13)	
	>than required	16	20.0	37	52.9	χ^2=13.52, P0.000	4.07(1.8-9.44)	0.49(0.32-0.76)
Minerals & added salt	As required	33	41.2	50	71.4	r		
	< than required	7	8.8	5	7.1	χ^2=1.48, P= 0.223	2.12(.54-8.55)	
	>than required	40	50.0	15	21.4	χ^2=14.43, P= 0.000	4.04(1.81-9.1)	2.3(1.52-3.46)
Iron	As required	35	43.8	51	72.9	r		
	< than required	37	46.2	12	17.1	χ^2=13.36, P0.000	4.1(1.76-9.66)	
	>than required	8	10.0	7	10.0	χ^2=1.19, P0.275	1.87(.53-6.75)	1.99(1.11-3.6)
Vitamins	As required	33	41.2	51	72.9	r		
	< than required	37	46.2	7	10.0	χ^2=23.39, P0.000	8.17(3.0-22.9)	
	>than required	10	12.5	12	17.1	χ^2=0.28, P0.599	1.29(.45-3.66)	
*Model χ^2 =39.896, P0.000,		β for protein =0.636 β for lipids = -0.706 β for Minerals= 0.831 β Iron = 0.688				Constant = -2.123	Percentage of predication 74.0%	

Table (3) Associated diseases and relation to sarcopenia of the studied patients.

Diet elements	Items	Sarcopenia & Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test	Odd's Ratio (95% CI)
		No	%	No	%		
DM	No	44	55.0	42	60.0	r	
	DM	36	45.0	28	40.0	χ^2=0.382, P= 0.537	1.23 (.61-2.48)
TTT of DM (64)	Oral	1	2.8	8	28.6	r	
	Insulin	35	97.2	20	71.4	χ^2=FET, P = 0.004	14.0 (1.55-320.6)
Hypertension	No	69	86.2	55	78.6	r	
	Yes	11	14.8	15	21.4	χ^2=1.536, P= 0.105	0.58 (.23-1.48)
Other diseases	No	70	87.5	67	95.7	r	
	Yes	10	12.5	3	4.3	χ^2=3.181, P= 0.074	3.19 (.76-15.35)

Table (4) Laboratory results and relation to sarcopenia of the studied patients.

Clinical Findings	Items	Sarcopenia & Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test	Univariate analysis Odd's Ratio (95% CI)	Multivariate* Analysis Adjusted Odd's ratio (95%CI)
		No	%	No	%			
Sr. Albumin	Normal	6	7.5	34	48.6	r		
	Low	74	92.5	36	51.4	χ^2=32.20,P= 0.000	11.65(4.12-34.21)	55.1(9.8-566.5)
Tot. Bil.	Normal	9	11.2	21	30.0	r		
	High	71	88.8	49	70.0	χ^2=8.203,P= 0.004	3.38(1.33-8.77)	
INR	Normal	7	8.8	12	17.1	r		
	High	73	91.2	58	82.9	χ^2=2.377,P= 0.123	2.16(0.73-6.54)	
SGPT	Normal	68	85.0	63	90.0	r		
	High	12	15.0	7	10.0	χ^2=0.844,P= 0.358	1.59(0.54-4.80)	
SGOT	Normal	35	43.8	48	68.6	r		
	High	45	56.2	22	31.4	χ^2=9.306,P= 0.002	2.81(1.36-5.81)	
Sr. Cr.	Normal	44	55.0	61	87.1	r		
	High	36	45.0	9	12.9	χ^2=18.376,P = 0.000	5.55(2.28-15.85)	2.9(1.2-7.1)

Sr. Ca	Normal Low	27 53	33.8 66.2	32 38	45.7 54.3	r χ^2=2.240,P=0.135	1.65(0.81-3.38)	
HB	Normal Low	14 66	17.5 82.5	21 49	30.0 70.0	r χ^2=3.261,P=0.071	2.02(0.88-4.69)	
Platelets	Normal Low	9 71	11.2 88.8	11 59	15.7 84.3	r χ^2=0.644,P=0.422	1.47(0.52-4.18)	
WBCs	Normal Low High	43 13 24	53.8 16.2 30.0	51 13 6	72.9 18.6 8.6	r χ^2=0.150,P=0.701 χ^2=10.740,P=0.001	1.19(0.46-3.08) 4.74(1.64-14.36)	
***Model χ2 =61.133, P0.000,**			**P for Albumin = 4.7010** **P for Sr. creatinine = -1.059**			**Constant = -8.07645**		**Percentage of predication 75.3%**

Table (5) Child Pugh and MELD's classifications in relation to sarcopenia of the studied patients.

Classification	Items	Sarcopenia & Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test
		No	No	No	%	
Child Pugh	A B C	9 20 51	11.3 25.0 63.7	37 23 10	52.8 32.9 14.3	χ^2=78.965, P= 0.000
MELD's score	Mean ± SD	19.95 ± 6.9		12.64 ± 4.5		t=7.550,P0.000

Table (6) Complication of cirrhosis and their relation to sarcopenia of the studied patients.

Clinical Findings	Items	Sarcopenia & Pre sarcopenia (80)		Non Sarcopenia (70)		Significance test	Univariate analysis Odd's Ratio (95% CI)	Multivariate* Analysis Adjusted Odd's ratio (95%CI)
		No	%	No	%			
Ascites	No Mild Moderate & severe	9 11 60	11.2 13.8 75.0	51 11 8	72.9 15.7 11.4	r χ^2=10.69, P0.001 χ^2=68.80, P0.000	5.7(1.7-19.75) 42 (13.9-137.9)	3.6(1.5-8.6)
Encephalopathy	No Yes	38 42	47.6 52.4	61 9	87.1 12.9	r χ^2=26.15, P0.000	7.5(3.1-18.1)	5.6(3.3-9.4)
Jaundice	No Yes	30 50	37.5 62.5	54 16	77.1 22.9	r χ^2=23.81, P0.000	5.6(2.5-12.4)	
Variceal bleeding	No Yes	39 41	48.8 51.2	48 22	68.6 31.4	r χ^2=6.020, P0.014	2.3(1.12-4.74)	
*Model χ2 =86.450, **P0.000,**			**β for Ascites =1.720** **β for Encephalopathy = -1.278**			**Constant = -2.078**		**Percentage of predication 84.7%**

Table (7) CPK and relation to sarcopenia of the studied patients (150)

Variables	Items	Sarcopenia & Pre sarcopenia (80)	Non Sarcopenia (70)	P value
CPK	Range Mean ± SD Median	22.0 – 162.0 41.400 ± 22.500 33.5	15.0 – 135.0 61.557 ± 28.227 56.5	P= 0.001

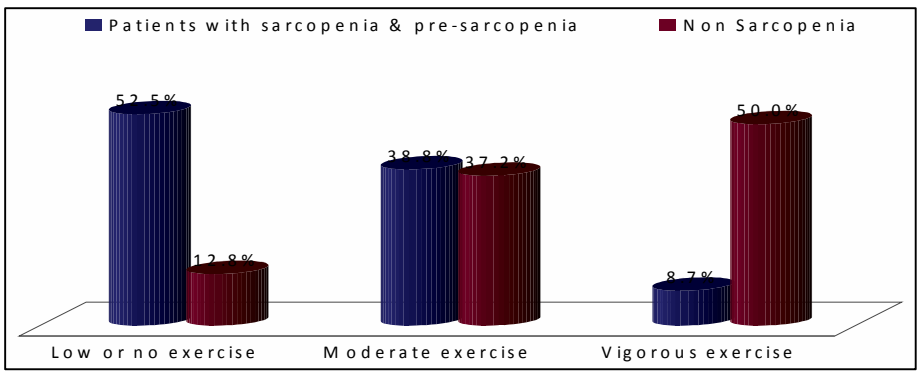

Figure (1) Comparison of percentage of physical activity levels among two groups

Discussion

The prevalence of patients with muscle affection in our study was 53.3%, sarcopenia among participants was 39.3% (n=59) and pre-sarcopenia was 14% (n=21). Close to this study, Giusto et al., found that the prevalence of sarcopenia was (51%) between studied patients[15]. However, higher result (70.3%) was reported in another study[20]. The prevalence of sarcopenia in the current study increased with age. It was 28.2% in age group <50 years and 62.2% in age group ≥50 years. Similar results were reported by another study that found the prevalence of sarcopenia increased with age in both men and women, as people aged 60 years and older having the highest prevalence rate[21]. Although there was no statistically significant difference as regard gender between sarcopenic and non sar-copenic group, the prevalence of sarcopenia tends to be more common in men than women (66.8% men versus 33.2% women of sarcopenic group). This sex difference may be related to the abundance of fat stores in females since females generate their energy more preferentially from fat stores than from skeletal muscle stores[22]. Women with sarcopenia may be at a more advanced stage of malnutrition because they have reached the point of requiring their muscle mass as an energy store. Also, the androgens deficiencies with hyperestrogenism in male patient with liver cirrhosis play a role in muscle status deterioration[23]. Also, we found that there was significant difference as regard BMI estimated by dry weight between sarcopenic and non sarcopenic patients ($p<0.001$) as all patients (100%) with low body weight (BMI<18.5) were sarcopenic. These results is in agreement with Hanai et al., who reported low body weight among sarcopenic patients. However, sarcopenia is not exclusive in under-weight patients but it constitutes a hidden condi-tion that can be present in cirrhotic patients with any BMI (55% of sarcopenia and pre-sarcopenia group had average body weight)[24]. For evaluation of nutritional status among studied patients, recent dietary intake was assessed using simple questionnaire. The protein intake was signifi-cantly lower in the sarcopenia group than in the non sarcopenic group as (61.2%) of sarcopenic patients take amount of protein less than required. This result is matched with study that detected low protein intake among patients with low skeletal muscle mass[21,25]. Nearly one-quarter of sarcopenic patients utilized low amount of carbohydrate and lipid as required compared to non sarcopenic patients who consumed amount more than required. Adequate balance among the main macronutrient (protein, carbohydrate, and lipid) is important. As excess consumption of carbohydrate and lipid with reduced protein intake may increase incidence of sarcopenic obesity[26]. On other hand low carbohydrate and lipid intake among cirrhotic patient even with normal protein intake leads negative energy balance and thus promote the wasting of the skeletal muscle mass[27]. Natural minerals and added salts were given as more than required per clinical status in almost half of sarcopenic patients (50%) while as required in (40.3%). Only (8.8%) were receiving less than required. This reflects the poor compliance of the patients with recomm-endations as following negative orders like avoid protein, avoid salt, avoid iron. Regarding iron and vitamins supplem-entation in this study, most of sarcopenic group (46.2%) received amount less than required with statistically significant difference com-pared to non sarcopenic one. These results are in agreement with previous study demonstrated low intake of iron among sarcopenic group but no significant difference regarding vitamins intake between two groups[27]. Regarding other associated medical disease, the current study found that, the prevalence of DM in sarcopenic and pre-sarcopenia group and non sarcopenic groups was (45% and 40% respe-ctively) with insignificant statistically differ-ence. Although insulin considered one of the anabolic hormones, it was the line of treatment of DM for (97.2%) of sarcopenic and pre-sarcopenia patients. This apparent paradox result may be due to majority of cirrhotic patients postpone using insulin until late stage of liver disease when they become already sarcopenic. These results matched with Hara et al., who found that, the prevalence of DM among sarcopenic and normal groups were 40% and 24% respe-ctively with insignificant statistically differ-ence[28]. On the contrary, study done by Lee et al., revealed increase incidence of DM among sarcopenic group with significant difference to non sarcopenic one[29]. Regarding complications of liver cirrhosis including

(ascites, HE, jaundice and variceal bleeding), the current study showed statistically significant difference bet- ween sarcopenic and non sarcopenic cases (p<0.001). Similar results was reported by Montano-Loza et al, as they documented increasing incidence of manifestation of hepatic decomposition among cirrhotic patients with sarcopenia with statistically significant differ-ence[30]. Ascites considered the commonest compl-ication, as it present in (88.8%) of sarcopenic and pre-sarcopenia cases versus (27%) of non sarcopenic one. This is not surprising, as the sarcopenia is one feature of protein energy malnutrition which usually associated with hypoalbuminemia the critical element in fluid retention which localized in peritoneal cavity due to portal hypertension[31]. History of hepatic encephalopathy (HE) also common among pati-ents with sarcopenia and pre-sarcopenia as, 52.7% of this group suffered from previous attack of HE versus (13%) of non sarcopenic group. This may be explained by the fact that skeletal muscles have a significant compensa-tory role in detoxifying ammonia during liver disease as it houses enzymes important for ammonia removing pathway. So, cirrhotic patients with skeletal muscle abnormalities have a higher risk of hyperammonemia and overt HE[32]. Variceal bleeding was another complication commonly presented among sarcopenia and pre-sarcopenia group in current study as almost half (51%) of sarcopenic cases had a previous attack of bleeding versus (31%) of non sarcopenic cases. Moreover study done by Ishizu et al., reported low skeletal muscle mass is one of the significant independent predictors of mortality in cirrhotic patients who have acute variceal bleeding[33]. Current study, demonstrated that, physical activity was significantly lower in the sarcopenia and pre-sarcopenia group comp-ared to in the non sarcopenic patients. 52.4% with sarcopenia and pre-sarcopenia had low or no physical activity (METS-minute/ week <600). This result is matched with Ohashi et al., who demonstrated that, the measured physical activity among sarcopenic group was METS-minute /week =369(median) and also increase time of setting and lying down among sarcopenic group compared to non sarcopenic one[14]. Regarding the biochemical measurements in this study, there were statistically significant lower values of serum albumin and CPK among sarcopenic and pre-sarcopenia group. Similar results were reported by Ohashi et al[14]. More-over, study by Hara et al., demonstrated that albumin was the only blood test measurement that showed positive correlation with changes in muscle mass. This expected as both hypoa-lbuminemia and loss of muscle mass are feat-ures of the same problem (protein deficiency)[34]. Serum bilirubin was higher in sarcopenic and pre-sarcopenia group versus non sarcopenic group with statistically sign-ificant differences (P 0.004) This is matched with Montano-Loza et al.,[35] who reported also statistically significant differences between two groups as regard to serum bilirubin level. As regard serum total calcium, the present study reported that there was a decrease of serum calcium level in sarc-openic cases related to non sarcopenic cases without statistically significant difference between both groups (P0.135). On other hand, significant higher levels of serum creatinine presented among sarcopenic and pre-sarcopenia group rather than non sarcopenic group. This is compatible with Nishikawa et al., who found increase serum creatinine and decrease estimated GFR among sarcopenic cases[35]. As regard Child Pugh score (CPS). The current study revealed that, prevalence of sarcopenia increased signif-icantly with advancing liver disease according to the CPS. In addition, the MELD score was higher in sarcopenic and pre-sarcopenia group versus non-sarcopenic group (19.95±8.67 versus 12.64±6.9) with statistically significant differences (p value <0.001). These results are matched with some studies showing positive association between sarcopenia and both Child-Pugh or MELD scores[2]. On contrary, study done by Hanai et al., reported non significant difference between two studied group as regard child Pugh score and MELD score[24]. In this study, univariate and multivariate logistic regression analysis dem-onstrated that, incr-easing age, low dry BMI, less protein intake and high salt were a predictive risk factor for sarcopenia. Hyp-oalbuminemia had the highest odds ratio 55.1(9.8-566.5) and the most risk for incre-ased incidence of sarcopenia. Furthe-rmore, the risk is significantly increased in patients with moderate and severe ascites and those reporting history of hepatic encephalopathy (OR 3.6 (1.5-8.6) and 5.6 (3.3-9.4) respectively).

Similar results were reported by Ohashi et al., as they found that independent predictive factors of sarcopenia were advanced age, low BMI and low PA[14]. The study faced multiple limitations as high financial cost of CT limits its use although it is considered the best method for diagnosis. Also, we depend on cutoff point not standardized for Egyptian populations. Finally, it was a cross-sectional study, thus we could not absolutely verify a causal relationship between PA or lifestyle and sarcopenia in patients with chronic liver disease. Future cohort studies are therefore needed.

Conclusion

Sarcopenia is one of the commonest complications of cirrhosis. The prevalence of sarcopenia was highest in patients with older age, low BMI and low protein intake. In addition, the worse the condition of the liver the greater the degree of muscle weakness was detected. Sarcopenia could be aggravated by the wrong dietary recommendations and habits. Awareness and education of the health team and patients regarding sarcopenia is of urgent need. Moreover, increase physical activity and practicing exercise can help in such situation.

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