Correlation between Serum Irisin Concentration and Sarcopenia in Patients with Liver Cirrhosis

Mohammed Alaa El- Din Nouh[1], Moamena Said Elhamouly[1], Rania Mohammed Azmey El-Shazely[2], Mahmoud Mohamed Ahmed Moawad[3], Heba El said Mohammed Nagy[1], Ahmed Abo-zaid Ahmed Teima[1].

[1]Tropical Medicine Department, Faculty of Medicine, Menoufia University, Shebin Elkom, Menoufia, Egypt.
[2]Biochemistry Department, Faculty of Medicine, Menoufia University, Shebin Elkom, Menoufia, Egypt.
[3]Radiology Department, Faculty of Medicine, Menoufia University, Shebin Elkom, Menoufia, Egyp.

Corresponding Author
Heba E Nagy
Mobile: 01061163058
E-mail: drhebanagy39@gmail.com
Postal address; 32511

Receive date:26/9/2024
Revise date:13/12/2024
Accept date:13/1/2024
Publish date:15/1/2024
Keywords: Cirrhotic sarcopenic, Cirrhotic non-sarcopenic, Irisin, Liver cirrhosis, Skeletal muscle index.

Background and study aim: Liver cirrhosis is an end-stage liver disease that occurs due to exposure of the liver to damage and inflammation for a prolonged time. It is characterized by replacing normal liver tissue with nonfunctional scar tissue. Sarcopenia is a muscle disorder that is seen in about 70% of patients with advanced liver disease and is characterized by progressive loss of all skeletal muscle mass and function. Our study assessed the correlation between serum irisin concentration and sarcopenia in cirrhotic patients. **Patients and Methods:** This case-control cohort study was conducted on three groups, group I (cirrhotic sarcopenic group of 40 patients), group II (cirrhotic nonsarcopenic group of 40 patients), and group III included 20 healthy control subjects. Serum level of irisin and Skeletal muscle index (SMI) at the level of the third lumbar vertebra (L3) were measured for all groups.

Results: Our study revealed that serum irisin concentrations were lower in cirrhotic sarcopenic than cirrhotic non-sarcopenic patients than control group with mean values (of 9.51 ng/ml, 31.40 ng/ml, and 58 ng/ml) respectively and there was a statistical significant decrease in skeletal muscle index (SMI) in cirrhotic sarcopenic than cirrhotic non-sarcopenic and control group with mean values (36 cm2/m2, 45.9 cm2/m2, 52.3 cm2/m2) respectively. **Conclusion:** Serum irisin is a useful marker in the diagnosis of sarcopenia in cirrhotic patients. Irisin can be an independent predictor of sarcopenia in patients with liver cirrhosis.

INTRODUCTION

Sarcopenia is a type of muscle disorder that affects skeletal muscles and leads to a progressive decrease of all skeletal mass and strength [1]. End-stage liver disease patients are more frequently exposed to muscle wasting that causes many fatal complications such as decreased quality of life, difficulty in daily physical activity, and death [2]. Several factors such as decreased protein and energy intake, decreased protein synthesis in the liver, increased proteolysis, reactive oxygen species, and cytokines of inflammation in cirrhotic patients lead to the development of muscle wasting [3]. Irisin is a protein produced by muscles, its formation occurs through cleavage of its precursor fibronectin type III domain-containing protein 5 (FNDC5) [4]. Also, irisin is produced from fatty tissue, so it seems to work as a myokine and an adipokine [5]. The first discovery of irisin was in 2012 and from that time the importance of irisin was noted as it helps in the diagnosis of metabolic diseases, such as obesity, type 2 diabetes mellitus (T2DM), fat metabolism, heart disease, non-alcoholic fatty liver disease (NAFLD), polycystic ovary syndrome and metabolic bone diseases [6]. Irisin is also important for many vital functions of muscles such as the process of muscle synthesis, and mitochondrial biogenesis, and protects muscle from atrophy and wasting. Increased irisin level in the body encourages the proliferation of several cell types [7].

Being a muscle-wasting process, sarcopenia leads to a decrease in plasma irisin levels in cirrhotic patients as irisin is a myocyte-secreted protein, and sarcopenia is frequently seen in cirrhotic patients [8].

DOI: 10.21608/aeji.2024.323922.1418

It was discovered that the rate of occurrence of muscle wasting was 2.2% per year in patients with liver cirrhosis. According to the Child-Pugh classification, it was found that skeletal muscle mass declines by 1.3% in Child-Pugh A patients, 3.5% in Child-Pugh B patients, and 6.1% in Child-Pugh C patients in year in patients with liver cirrhosis. With the worsening of liver function, there is a significant decrease in plasma irisin concentration in sarcopenic patients with liver cirrhosis [9].

In this study, we aimed to assess the correlation between serum irisin concentration and sarcopenia in cirrhotic patients.

METHODS

Study design: a case-control cohort study.

This study was conducted on 80 patients presented with liver cirrhosis in the Tropical Medicine Department in the Faculty of Medicine, Menoufia University in the period between January 2023 to September 2023 included 49 males and 31 females aged from 40 years old to 72 years old in addition to 20 healthy volunteers 10 males and 10 females in the age from 45 to 69 years old as a control group.

Sample size:

The sample size calculation using statistical software (Sample Size Pro version 6), it was determined that the least sample size required for this study was 100 subjects, with 40 subjects in each of the two groups (sarcopenic vs. non-sarcopenic) and 20 subjects for the control group. The statistical power of the study was set at 80%, and the confidence level at 95%.

Inclusion criteria were patients with liver cirrhosis diagnosed clinically, laboratory, and radiological their age >18 years, and no pregnancy.

The exclusion criteria were patients with malignant diseases in their terminal stage other than hepatocellular carcinoma, acute generalized inflammation, acute infectious disease, history of drug abuse, and chronic renal failure which are the causes of sarcopenia.

All participants were classified into 3 groups, group 1: a cirrhotic sarcopenic group that included 40 patients, group 2 cirrhotic nonsarcopenic group that included 40 patients and each group was sub-classified according to Child-Pugh classification into three groups A, B, and C [10], group 3, included 20 healthy volunteers as a control group.

All patients and controls were subjected to the following: History taking, general examination with stress on the manifestations of liver cell failure as conscious level, jaundice, pallor, lower limb edema, and flapping tremors, local abdominal examination with stress on hepatomegaly, splenomegaly, ascites. The Child-Pugh score was calculated for all patients to assess the severity of liver disease. This scoring system uses bilirubin, albumin, INR, the presence and severity of ascites, and encephalopathy. It classifies patients into class A, B, or C. Class A has a favorable prognosis, while class C is at a high risk of death [10].

Laboratory investigations included: liver function tests (serum albumin, prothrombin time and concentration and INR, total and direct bilirubin), serum aminotransferases, complete blood count, hepatitis C virus antibody, and hepatitis B surface antigen. Radiological examinations included: abdominopelvic ultrasound which showed liver size, spleen size, ascites, and focal lesions. CT which indicated skeletal muscle area of psoas muscle at the level of L3 vertebra to detect sarcopenia.

Measurement of irisin: to assess irisin; blood samples were taken under complete aseptic condition and centrifuged for 5 min at 3000 rpm/min. Then serum was stored at −20°C. Serum irisin was determined by the principle of competitive enzyme immunoassay according to ELIZA kits, normal level of irisin in a range of (4ng/ml–60 ng/ml).

Assessment of sarcopenia: Clinically by measurement of body weight in (kilogram), mid-arm muscle circumference (MAMC), radiological by CT at the level of L3 vertebra to detect SMI. Hand grip strength was examined using a dynamometer with three repetitions for each hand. We recorded the average of three measures. The cutoff points for hand grip strength were 26 kg for men and 18 kg for women [3]. Body mass index (BMI) was defined as body weight (kg) / height squared (m2). BMI for healthy weight ranges from (18.5 – 24.9 kg/ m2) [11].

We measured the arm circumference (AC) at the middle distance between the top of the shoulder

DOI: 10.21608/aeji.2024.323922.1418

and the elbow joint using a flexible and non-stretchable tape. We measured the thickness of the triceps skin fold (TSFs) using a skin fold caliper.

Measurement steps of skin fold caliper by a specific caliper: First, we grasped a fold of skin and subcutaneous fatty tissue 2.0 cm above the mid-arm circumference point. Second, we put the tips of the caliper jaws on the skin fold and then released the handle of the caliper to make a complete tension on the skin fold. The thickness of the closest to 0.1 mm was red. Each TSF must consist of a double thickness of skin and underlying fat for the measurements to be true. The average of three measures was taken. The average TSF thickness was 18.7 ± 8.5 mm. Females have much higher TSF thickness than males (23.6 ± 7.5 mm vs 14.3 ± 6.8 mm) [12].

The mid-arm muscle circumference (MAMC) was calculated as follows:

MAMC (cm) = AC (cm) − (π × triceps skin fold thickness [cm]) [13].

AC in males = 29.9 (28.3–32.0) cm and in females =27.7 (25.8–29.4) cm.

MAMC in males = 27.4 (26.0–29.2) cm and in females = 24.2 (23.0–25.6) cm.

Measurement of skeletal muscle index: SMI is the most common method used to measure sarcopenia, based on the current guidelines, SMI is defined as skeletal muscle area (SMA) cm2/height squared (m2), where SMA is measured using computed tomography (CT) and sarcopenia in patients with liver cirrhosis is less than 52.4 cm2/m2 for males and less than 38.5 cm2/m2 for females [3].

Statistics

All patient details and study variables were entered in a predesigned data collection sheet. Data was analyzed by using the statistical software SPSS 13.0. All the quantitative data was expressed as mean ± SD. Qualitative data was analyzed by Chi-square test and quantitative data by Student's t-test or Mann-Whitney's U test. The correlation study was done by using Spearman's correlation coefficient test. The performance of the test was assessed by sensitivity and specificity. The receiver operating characteristic (ROC) curve was used to assess the usefulness of the test and performance at different cutoff values. A 'p' value of <0.05 was taken as statistically significant and a 'p' value of <0.001 was taken as highly statistically significant.

RESULTS

When comparing demographic characteristics and skeletal muscle assessment in the studied groups, there was no statistically significant difference in age and gender (p-value> 0.05) and statistically significant difference in body mass index (BMI), SMI, hand grip strength, mid-arm muscle circumference, and irisin concentration among the studied groups (p-value <0.001) (Table 1).

The current study revealed that there was a statistically significant difference in the presence of anorexia, lower limb swelling, abdominal enlargement, vomiting, fatigue, and jaundice among the studied patient groups (p-value <0.05) (Table 2).

The laboratory investigations in the studied patient groups showed that there was a statistically significant difference in albumin concentration, bilirubin (total and direct), INR, urea, creatinine (p-value <0.05), hemoglobin concentration, and platelet count (p-value <0.001) and no statistically significant difference in ALT, AST, white blood cell count among the studied patient groups (p-value>0.05) (Table 3).

The current study showed the association between Child-Pugh score with irisin concentration and SMI and found that patients with Child-Pugh score 5-A had the highest mean irisin level (32.50±9.44 ng/ml) and SMI (50.01±6.26 cm2/ m2), both with (p-value <0.001).

Conversely, patients with a Child-Pugh score of 12-C had the lowest mean irisin level (5.00±1.48 ng/ml) and SMI (39.03±5.52 cm2/m2). Overall, higher Child-Pugh scores were generally associated with lower irisin and SMI, indicating a significant correlation between liver disease severity and irisin and SMI (Table 4).

The current study showed that the diagnostic accuracy of irisin in the diagnosis of sarcopenia in cirrhotic patients had a sensitivity of 93%, specificity 63%, cutoff point 12.35 and AUC= 0.700, (95% CI of AUC=0.592-0.807) and SMI has a sensitivity 87%, specificity 67%, cutoff point 27 and AUC= 0.783, (95% CI of AUC=0.694-0.872), (p-value <0.001) (Table 5) (Figure 2). This study showed a positive correlation between serum irisin concentration

DOI: 10.21608/aeji.2024.323922.1418

and SMI in the studied patient groups (r=0.537, 95% CI= 0.381-0.664 and (p-value <0.001) (Figure 3).

Table (1). Demographic characteristics and skeletal muscle assessment in the studied groups

Variable	Cirrhotic sarcopenic (n=40)		Cirrhotic non-sarcopenic (n=40)		Control group (n=20)		Test of sig.	p-value
	No	%	No	%	No	%		
Gender Male Female	 25 15	 65.5 37.5	 24 16	 60.0 40.0	 10 10	 50 50	χ2= 0. 05	0.818 (NS)
Age (years) Mean ±SD Range	53.75 ±7.66 42-72		53.50 ±8.98 40-71		52.7±9.32 45-69		t=0 .165	0.510 NS
BMI (Kg/ m^2) Mean ±SD Range	21. 12±3.74 23-33		24.11±2.73 25.8- 32.5		24.62 ±2.51 22-27.7		t=0.56	< 0.001
Mid-arm muscle circumference (cm) Normal Decreased	6 34	15 85	37 3	92.5 7.5	100 0	100 0	t=45.49	< 0.001
Hand grip strength(kg) Normal Decreased	9 31	22.5 77.5	38 2	95 5	100 0	100 0	T=57.00	< 0.001
SMI (cm^2/ m^2) Mean ±SD Range	36.15±5.77 28.5-44.3		45.92 ±7.81 30-56.2		52.3 ±7.53 41-58		F=154.78	<0.001*
Irisin (ng/ml) Mean ±SD Range	9.51 ±2.63 2.5-14		31.40 ±12.1 10.5-45		58 ±2.52 38-59		K=77.32	<0.001*

*: Statistically significant, NS: Non-significant, χ2: Chi-squared test, t: Student t-test, FE: Fisher exact test, BMI: body mass index, SMI: Skeletal muscle index, SD: Standard deviation.

Table (2). Clinical findings in the studied patient groups (n=80)

Variable	Cirrhotic sarcopenic (n=40)		Cirrhotic non-sarcopenic (n=40)		Total (n=80)		χ^2	p-value
	No	%	No	%	No	%		
Anorexia								
Present	22	55	10	25	32	40	7.01	0.007*
Absent	18	45	30	75	48	60		
LL swelling								
Present	24	60	14	35	38	47.5	10.92	0.025*
Absent	16	40	26	65	42	52.5		
Abd enlargement								
Present	23	57.5	14	35	37	46.25	10.01	0.024
Absent	17	42.5	26	65	43	53.75		
Vomiting								
Present	15	37.5	7	17.5	22	27.5	4.01	0.045*
Absent	25	62.5	33	82.5	58	72.5		
Fatigue								
Present	33	82.5	11	27.5	44	55	7.27	0.007*
Absent	7	17.5	29	72.5	36	45		
Jaundice								
Present	25	62.5	12	30	37	46.25	7.02	0.004*
Absent	15	37.5	28	70	43	53.75		

*: Statistically significant, NS: Non-significant, χ2: Chi-squared test, t: Student t-test, LL: lower limb

DOI: 10.21608/aeji.2024.323922.1418

Table (3). laboratory investigations in the studied patient groups (n=80)

Variable	Cirrhotic sarcopenic (n=40)	Cirrhotic non sarcopenic (n=40)	Test of sig.	p-value
ALT (u/l) Mean±SD Range	62.13±39.93 15-200	51.90 ±21.02 23-116	U=0.13	0.893 (NS)
AST (u/l) Mean±SD Range	65.30 ±36.56 24-190	49.43 ±18.83 14-120	U=1.90	0.058 (NS)
Albumin (g/dl) Mean±SD Range	2.86 ±0.54 1.7-3.1	3.26 ±0.66 2.8-4.6	t=3.86	0.004
Biliruben (total) (mg/dl) Mean±SD Range	2.63 ±1. 79 1.4-10.2	1.79 ±1.77 0.9-4.3	U=2.56	0. 010
Biliruben (direct) (mg/dl) Mean±SD Range	1.9 ±0.64 1.4-10.2	1.12 ±1.58 0.4-4.2	U=3.41	0.01
INR Mean±SD Range	2.11±0.50 1.5-3.4	1.54±0.4 1.09-2.9	F =24.345	<0.001
Urea (mg/dl) Mean±SD Range	92.40 ±55.85 20-160	63.93 ±42.53 26-90	U=2.41	0.016*
Creatinin (mg/dl) Mean±SD Range	2.22 ±1.09 0.7-3.6	1.65 ±0.94 0.5-2.2	U=2.60	0.009*
Hemoglobin (%) Mean ±SD Range	10.06 ±1.27 6.9-12	11.34 ±1.22 9-14	t=4.62	<0.001
WBCs (×103/UL) Mean ±SD Range	12.88 ±7.26 1.8-34.4	11.02 ±3.76 3.4-19.5	U=1.16	0.246 (NS)
Platelets(×103/UL) Mean ±SD Range	86.10 ±21.64 39-125	179.73 ±80.87 90-370	U=6.08	<0.001

*: Statistically significant, NS: Non-significant, $\chi 2$: Chi-squared test, t: Student t-test, F: One Way ANOVA test, U: Mann-Whitney U test, ALT: Alanine Transaminase, AST: Aspartate Transaminase, International Normalized Ratio (INR), white blood count (WBC).

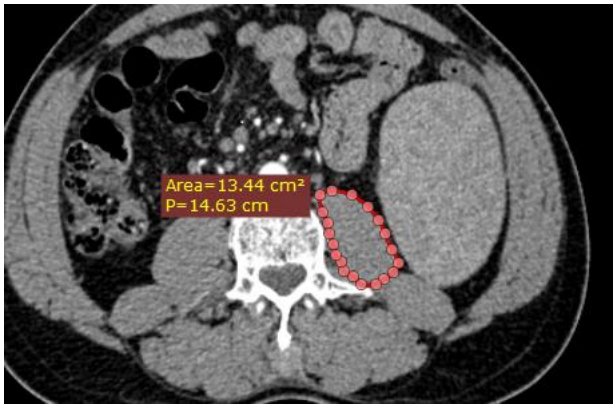

Figure (1). CT image: Skeletal muscle area at the level of L3

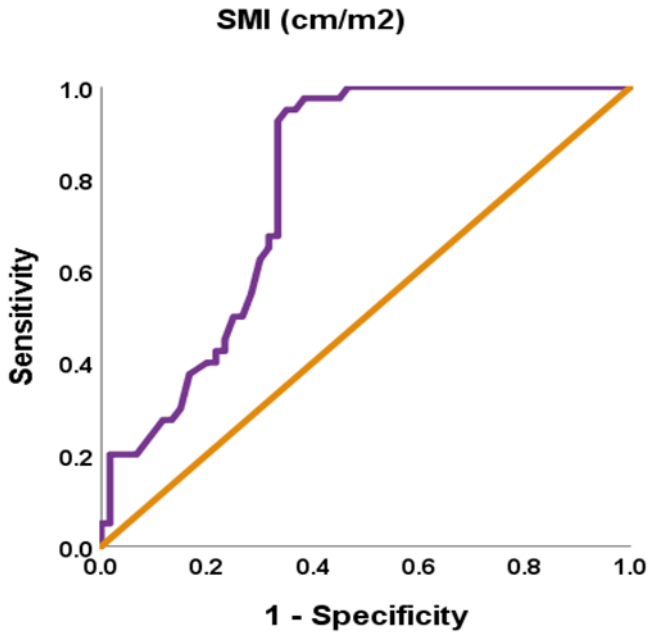

Figure (2). ROC curve analysis of the accuracy of SIM in the diagnosis of sarcopenia in cirrhotic patients

Table (4). Association between child Pugh with irisin and SMI in the studied patient groups

		Irisin (ng/ml)	P-value	SMI(cm²/ m²)	p-value
		Mean± SD		Mean± SD	
Child-Pugh	5-A	32.50±9.44	<0.001	50.01±6.26	<0.001
	6-B	14.24±7.20		39.74±7.98	
	7-B	34.67±7.94		48.22±7.85	
	8-B	9.97±3.19		39.70±6.32	
	9-B	11.66±5.82		40.57±6.94	
	10-C	26.00±9.52		45.65±7.78	
	11-C	36.00±11.31		49.20±7.86	
	12-C	5.00±1.48		39.03±5.52	
	13-C	5.90±2.07		35.02±7.37	

Skeletal muscle index (SMI), Standard deviation (SD).

DOI: 10.21608/aeji.2024.323922.1418

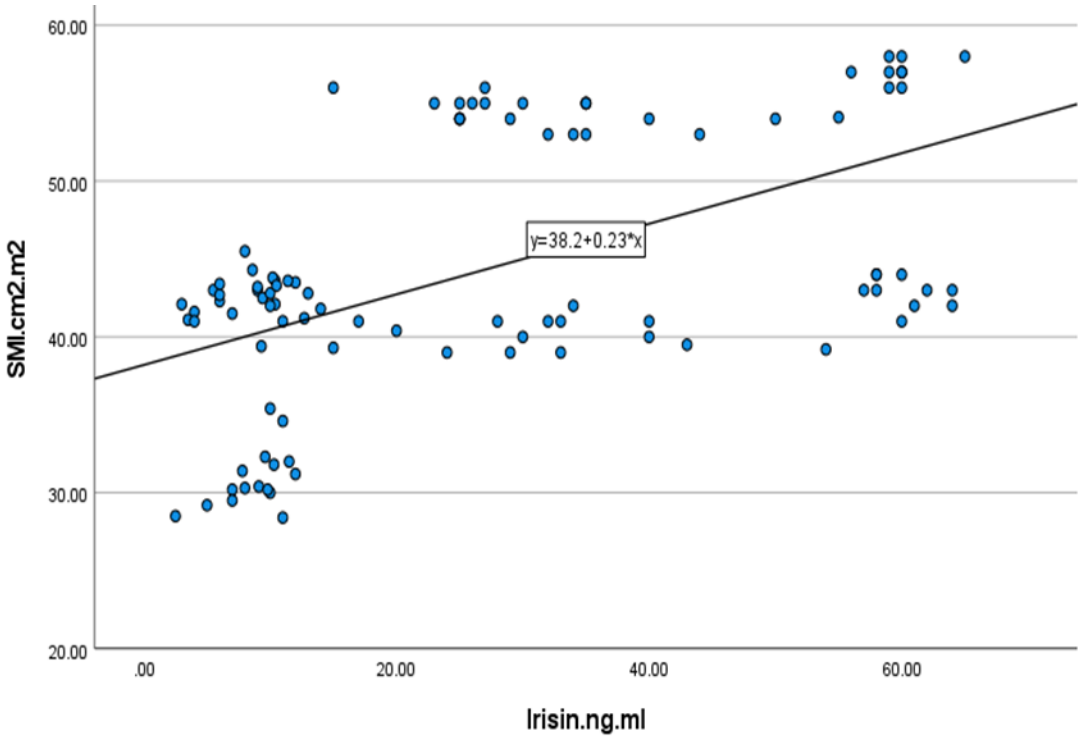

Figure (3). Correlation between serum irisin and SMI in the studied cirrhotic patients (n=80).

Table (5). Diagnostic accuracy of irisin and SMI in the diagnosis of sarcopenia in cirrhotic patients.

	Irisin (ng/ml)	**SMI (cm^2/ m^2)**
Cutoff point	12.35	27
Sensitivity	93%	87%
Specificity	63%	67%
AUC	0.700	0.783
95% CI of AUC	0.592-0.807	0.694-0.872
p-value	<0.001	<0.001

Skeletal muscle index (SMI), Area under the curve (AUC), CI: confidence interval.

DISCUSSION

Several studies showed that there is a strong association between liver disease severity and a decrease in skeletal muscle mass and function. Many clinical studies have been carried out in this field in a trial to prove that. It is not easy to illustrate the cause of this complicated phenomenon in sarcopenia, so many factors are involved. Irisin has an important role in metabolic diseases, aging, inflammation, and neurogenesis. Irisin concentration in plasma is affected by many factors such as diet, obesity, exercise, drugs, and different pathological conditions [3].

Many studies have shown that irisin and sarcopenia are closely correlated with some chronic diseases such as sarcopenic obesity, sarcopenia in postmenopausal women, sarcopenia in dialysis patients, and sarcopenia in those with myotonic dystrophies [14].

The current study revealed that BMI was decreased in cirrhotic sarcopenic than in cirrhotic nonsarcopenic and control groups with mean values (21.12±3.74kg/m^2, 24.11±2.73 kg/m^2, 24.62±2.51kg/m^2) respectively.

This is in line with Hanai et al., and Sinclair et al., who reported that the main cause of sarcopenia in liver cirrhosis is increased muscle protein breakdown, and this is the cause of a decrease in BMI in liver cirrhosis patients [8] and [15].

Bhaskaran et al. reported that BMI is not an ideal method for measuring body composition from muscles, subcutaneous and visceral fatty tissue, and their distributions in the body as the presence of ascites in decompensated cirrhotic patients

may mask accurate body weight. So, the prognostic impact of BMI may be false or inaccurate [16].

The current study proved that mid-arm muscle circumference and hand grip strength were decreased in the cirrhotic sarcopenic than non-sarcopenic group.

Plauth et al., shared the same result as they found that cirrhotic sarcopenic patients have a decrease in mid-arm muscle circumference (in cm) and triceps skin fold thickness (in mm) [17]. Also, Nishikawa et al., reported that cirrhotic sarcopenic patients have an increased rate of decrease in hand grip strength three times or more than in patients without sarcopenia, so they considered the decrease in hand grip strength to be the most prominent factor in the diagnosis of sarcopenia in patients with LC [3].

When comparing SMI, the current study showed a marked decrease in SMI between cirrhotic sarcopenic, cirrhotic non-sarcopenic patients and the control group with mean values (36 cm^2/m^2, 45.9 cm^2/m^2, 52.3 cm^2/m^2) respectively.

Sarcopenia is characterized by loss of skeletal muscle mass and power. Ebadi et al., discovered that patients with liver cirrhosis are more prone to this progressive and generalized loss of mass and power as it is reported to occur in a range from 30 to 70 % [18].

When serum irisin concentrations were measured, we found a decrease in its concentration in cirrhotic sarcopenic than in cirrhotic non-sarcopenic patients than control group with mean values (of 9.51 ng/ml, 31.40 ng/ml, and 58 ng/ml) respectively.

Polyzos et al., and Park et al., reported from their studies on cirrhotic patients where they classified them into sarcopenic and nonsarcopenic groups, found that serum irisin concentrations were decreased in the first than in the second group [6] and [14]. Lee et al. also reported the same result when measuring serum irisin concentration, they found lower irisin concentration in cirrhotic sarcopenic patients compared to nonsarcopenic [19].

This is in contrast with Kukla et al., who found no significant difference in the levels of irisin in cirrhotic patients either compensated or not, having ascites or not, or between early and end-stage LC and when they measured muscle mass by CT or anthropometry, they found no relation between irisin levels and the muscle mass [20].

The current study revealed that there was a decrease in albumin concentration and elevation in bilirubin, INR, urea, and creatinine and no significant difference in ALT and AST levels among the studied patient groups.

The current study showed that patients with Child-Pugh score 5-A had the highest mean irisin level (32.50±9.44 ng/ml) and SMI (50.01± 6.26 cm^2/m^2). Conversely, patients with a Child-Pugh score of 12-C had the lowest mean irisin level (5.00±1.48 ng/ml) and SMI (39.03±5.52 cm^2/m^2). Overall, higher Child-Pugh scores were generally associated with lower irisin and SMI, indicating a significant correlation between liver disease severity and (irisin and SMI).

Waluga et al., reported also that the mass of skeletal muscle decreases by 1.3% in Child-Pugh A patients, 3.5% in Child-Pugh B patients, and 6.1% in Child-Pugh C patients annually and they reported that as liver functions impaired gradually, there was a significant decrease in plasma irisin concentrations in sarcopenic patients with liver cirrhosis [21].

The current study showed that the diagnostic accuracy of irisin in diagnosis of sarcopenia in cirrhotic patients had a sensitivity 93%, specificity 63%, cutoff point 12.35 And AUC=0.700, (95% CI of AUC=0.592-0.807), and the diagnostic accuracy of SMI in diagnosis of sarcopenia in cirrhotic patients had sensitivity 87%, specificity 67%, cutoff point 27 And AUC=0.783, (95% CI of AUC=0.694-0.872).

Park et al., and Zhao et al., showed in their study that, when comparing patients with sarcopenia and pre-sarcopenia with the control group, there was a decrease in serum irisin concentration in sarcopenic and pre-sarcopenic patients than control [22] and [23]. Hanai et al., clarified in their study on patients with cirrhosis that skeletal muscle mass decreased by 2.2% per year in cirrhotic patients [8].

Woo et al., agreed with this result as they found that when serum irisin concentration decreased by 1 ng/mL, there was a 95% higher risk of having sarcopenia. In addition, they reported that circulating irisin with a concentration of 8.46 ng/ml has a sensitivity of 68% and a specificity of 69% is recommended as a cut-off value for sarcopenia [24].

DOI: 10.21608/aeji.2024.323922.1418

This study showed a positive correlation between irisin and SMI in the studied cirrhotic patients.

A positive correlation between serum irisin levels with both appendicular lean mass and hand grip strength in both sexes was reported by Chang et al., and also they confirmed the decrease in serum irisin concentration in sarcopenic patients compared with a normal group [25]. Similar results were presented by Lee et al., who reported that there was a positive correlation between measured serum irisin concentrations and mid-arm muscle circumference and thigh circumference in cirrhotic patients. This positive correlation confirmed the significant association between irisin and muscle mass [7]. Due to the strong association between irisin and sarcopenia, Park et al., suggested that irisin may serve as a biomarker for sarcopenia [14].

Also, Hanai et al. found a statistically positive correlation between irisin concentrations and L3 SMI values ($r = 0.516$) in all patients with liver cirrhosis. Owing to the frequent presentation of sarcopenia in most cirrhotic patients and the irisin is a myocyte-secreted protein, it can be concluded that sarcopenia directly leads to lower irisin levels [8]. Chang et al. proved in their study that a lower serum irisin level is associated with muscle weakness and atrophy [25].

Zhao et al. shared the same opinion as they found that irisin levels were lower in sarcopenic compared to non-sarcopenic patients with cirrhosis. In addition, they found a positive correlation between irisin levels and SMI measured by CT [23].

Choi et al. have a different opinion as they did not find any differences in irisin levels when compared with muscle mass. They argue this finding to the difference in the basic characters of the studied patient group [26]. Our study has some limitations; this study had approved a strong association between irisin concentrations and sarcopenia in cirrhotic patients, but it was unable to put a conclusion about the cause of this association due to a lack of confidence in the randomized interventional study design. The sample size was small. The effect of irisin on outcomes in cirrhotic sarcopenic patients should be more obvious in future studies. Power and mass of the muscles can predict outcomes in cirrhotic sarcopenic patients, but we cannot prove if the grip strength test that we used on these patients was affected by subjective factors of the patients. We did not comment on malnutrition, which is a major complication in cirrhotic patients and affects patient outcomes and recovery. There is a positive relation between malnutrition and irisin levels. Although this study had limitations, we believe that this study provides useful information about the association between irisin concentrations and sarcopenia in cirrhotic patients.

CONCLUSION

So finally, it can be concluded that: Serum irisin concentration is a useful marker in the diagnosis of sarcopenia in cirrhotic patients. Irisin levels can be an independent predictor of sarcopenia in patients with liver cirrhosis.

Ethical approval: A written informed consent was obtained from all participants and approval from the ethics committee was obtained (IRP 3/2022-TROP 13).

Conflict of Interest: None

Funding Sources: None.

Availability of data and materials:The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions: MAN revised the results and shared them in manuscript writing and editing. MSE established the concept of the study and analyzed data. RMA constructed the idea, shared in interpreting the results, and revised the manuscript. MMA provided the study design and conducted data analysis. HEMN applied clinical studies, collected data, and shared in writing the manuscript. AAAT collected data, analyzed results, and prepared manuscripts. All authors read, revised, and approved the final manuscript.

HIGHLIGHTS

- The importance of recognizing and addressing sarcopenia in cirrhotic patients, as it appears to be associated with more severe liver dysfunction and poorer overall health status.
- 2-Early identification and intervention for sarcopenia could potentially improve outcomes and quality of life for these patients.
- 3-Serum irisin concentration is a useful marker in the diagnosis of sarcopenia in cirrhotic patients.

Abbreviations:

Skeletal muscle index (SMI), Third lumbar vertebra (L3), Fibronectin type III domain-containing protein 5 (FNDC5), Diabetes mellitus type 2 (T2DM), Nonalcoholic fatty liver disease (NAFLD), International Normalized Ratio (INR), Computed tomography (CT), Mid-arm muscle circumference (MAMC), Body Mass Index(BMI), Arm-circumference (AC), Triceps skin fold thickness (TSF), Skeletal muscle area (SMA), Alanine Transaminase (ALT), Aspartate Transaminase (AST), White blood count (WBC).

REFERENCES

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age and Ageing*. 2019 Jan 1; 48(1):16-31.
2. Bhanji RA, Takahashi N, Moynagh MR, Narayanan P, Angirekula M, Mara KC, et al. The evolution and impact of sarcopenia pre and post-liver transplantation. *Alimentary Pharmacology & Therapeutics*. 2019 Mar; 49(6):807-813.
3. Nishikawa H, Nishiguchi S, Hiramatsu A, Moriya K, Hino K, Nishiguchi S. Sarcopenia in Liver Disease. *The Evolving Landscape of Liver Cirrhosis Management*. 2019: (46): 951–963.
4. Munoz IYM, Romero EDSC, Garcia JJG, Mihalache L, Covasa M, Nguyen TT. Irisin a novel metabolic biomarker: present knowledge and future directions. *International Journal of Endocrinology*. 2018; 1:8.
5. Ma EB, Sahar NE, Jeong M, Huh JY, Pochec E, Mazur-Biały A. Irisin exerts an inhibitory effect on adipogenesis through regulation of Wnt signaling. *Frontiers in Physiology*. 2019 Aug 22; 10:1085.
6. Polyzos SA, Anastasilakis AD, Efstathiadou ZA, Makras P, Perakakis N, Kountouras J, et al. Irisin in metabolic diseases. *Endocrine*. 2018 Feb; 59:260-274.
7. Lee MJ, Lee SA, Nam BY, Park S, Lee SH, Ryu HJ, et al. Irisin, a novel myokine is an independent predictor for sarcopenia and carotid atherosclerosis in dialysis patients. *Atherosclerosis*. 2015 Oct 1; 242(2):476-482.
8. Hanai T, Shiraki M, Ohnishi S, Miyazaki T, Ideta T, Kochi T, et al. Rapid skeletal muscle wasting predicts worse survival in patients with liver cirrhosis. *Hepatology Research*. 2016 Jul; 46(8):743-751.
9. Waluga M, Kukla M, Kotulski R, Zorniak M, Boryczka G, Kajor M, et al. Omentin, vaspin, and irisin in chronic liver diseases. *Journal of Physiology & Pharmacology*. 2019 Apr 1; 70(2); 277–285.
10. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Ridgway G, Williams R. Transection of the esophagus for bleeding oesophageal varices. *British Journal of Surgery*, 1973 Aug; 60(8):646-649.
11. Rosengren A, Edqvist J, Rawshani A, Sattar N, Franzén S, Adiels M, et al. Excess risk of hospitalization for heart failure among people with type 2 diabetes. *Diabetologia*. 2018 Nov; 61(11):2300-2309.
12. Nickerson BS, Fedewa MV, Cicone Z, Esco MR, Iwata M, Hasegawa J. The relative accuracy of skin folds compared to four-compartment estimates of body composition. *Clin Nutr*. (2020) ; 39:1112–6.
13. Kopple JD, Cohen AH, Wang H, Qing D, Tang Z, Fournier M, et al. Effect of exercise on mRNA levels for growth factors in skeletal muscle of hemodialysis patients. *Journal of Renal Nutrition*, 2006 Oct 1; 16(4):312-324.
14. Park HS, Kim HC, Zhang D, Yeom H, Lim SK, Alnaami A.M. The novel myokine irisin: clinical implications and potential role as a biomarker for sarcopenia in postmenopausal women. *Endocrine*, 2019 May 15; 64:341-348.
15. Sinclair M, Gow PJ, Grossmann M, Angus PW, Kambadur R, Grassi B. sarcopenia in cirrhosis–etiology, implications, and potential therapeutic interventions. *Alimentary Pharmacology & Therapeutics*, 2016 Apr; 43(7):765-777.

DOI: 10.21608/aeji.2024.323922.1418

16. Bhaskaran K, dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L, Kang TH. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3· 6 million adults in the UK. *The lancet Diabetes & Endocrinology*, 2018 Dec 1; 6(12):944-953.
17. [17] Plauth M, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, et al. ESPEN guideline on clinical nutrition in liver disease. *Clinical Nutrition*. 2019 Apr 1; 38(2):485-521.
18. Ebadi M, Bhanji RA, Mazurak VC, Montano-Loza AJ, Alen, KH, Herzig S. Sarcopenia in cirrhosis: from pathogenesis to interventions. *Journal of Gastroenterology*, 2019 Oct; 54(10):845-859.
19. Lee J, Park J, Kim YH, Lee NH, Song KM, Song KM, D'Souza C. Irisin promotes C2C12 myoblast proliferation via ERK-dependent CCL7 upregulation, *PLoS One*, 2019 Sep 13; 14(9): e0222559.
20. Kukla M, Skladany L, Menżyk T, Derra A, Stygar D, Skonieczna M, et al. Irisin in liver cirrhosis. *Journal of Clinical Medicine*, 2020 Sep 29; 9(10):3158.
21. Waluga M, Kukla M, Kotulski R, Zorniak M, Boryczka G, Kajor M, et al. Omentin, vaspin, and irisin in chronic liver diseases. *Journal of Physiology & Pharmacolog*, 2019 Apr 1; 70(2):277–285.
22. Park SH, Plank LD, Suk KT, Park YE, Lee J, Choi JH, et al. Trends in the prevalence of chronic liver disease in the Korean adult population, 1998–2017. *Clinical and Molecular Hepatology*, 2020 Apr; 26 (2): 209–215.
23. Zhao M, Zhou X, Yuan C, Li R, Ma Y, Tang X. Association between serum irisin concentrations and sarcopenia in patients with liver cirrhosis: A cross-sectional study. *Scientific Reports*, 2020 Sep 30; 10 (1):16093.
24. Woo J, Leung J, Morley JE, Rolland SM, Schneider E, Topinkova M. Validating the SARC-F: A Suitable Community Screening Tool for Sarcopenia? J. Am. Med. Dir. Assoc. 2014; 15 (9): 630–634.
25. Chang JS, Kim TH, Nguyen TT, Park KS, Kim N, Kong ID. Circulating irisin level as a predictive biomarker for sarcopenia: A cross-sectional community-based study; *Geriatrics & Gerontology international.* 2017 Nov; 17(11):2266-73.
26. Choi HY, Kim S, Park JW, Lee NS, Hwang SY, Huh JY, et al. Implication of circulating irisin levels with brown adipose tissue and sarcopenia in humans, *The Journal of Clinical Endocrinology & Metabolism*. 2014 Aug 1; 99(8):2778-2785.

Cite as: Nouh, M., Elhamouly, M., Mohammed Azmey El-Shazely, R., Moawad, M., Nagy, H., Teima, A. Correlation between Serum Irisin Concentration and Sarcopenia in Patients with Liver Cirrhosis. *Afro-Egyptian Journal of Infectious and Endemic Diseases*, 2025; (): -. doi: 10.21608/aeji.2024.323922.1418