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Research Article

Assessment of Nutritional Status and Sarcopenia in Child Pugh A and B Cirrhosis Patients and Correlating Sarcopenia with Severity of Liver Cirrhosis.

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Introduction

The incidence of liver diseases is increasing, and it may be a severe subsequent lifestyle disease [1]. About 50-90% of patients with cirrhosis can have malnutrition. Managing this malnutrition is vital to facilitate clinical outcomes among cirrhotic patients. Sarcopenia is also associated with poor outcomes among patients with cirrhosis [2]. The pathogenesis of sarcopenia is multifactorial. Nutritional imbalances need to be treated with physical and pharmacological interventions to reverse sarcopenia and to improve their outcomes [3]. Despite the great relevance of malnutrition, its diagnosis can be troublesome in patients with cirrhosis and may go unrecognized. Sarcopenia in CLD is the most common and frequently unseen complication, has a negative impact on quality of life, survival, and response to a stressor, such as infections and surgeries in patients with liver cirrhosis [4]. Sarcopenia assessment and intervention for improving performance status should be essential in managing patients with liver cirrhosis. The clinical significance of sarcopenia and its correlation with the severity of liver disease is little explored in the Indian context. It is easier to acquire details among Child A and Child B cirrhotics and knowledge of their nutritional status and severity of liver disease can help guide early interventions and patient care.

Aims and Objectives

1. To assess the nutritional status in patients with Child-Pugh A and B cirrhosis of the liver.
2. To assess the proportion of sarcopenia in patients with Child-Pugh A and B cirrhosis of the liver.
3. To study the correlation of sarcopenia with the severity of liver cirrhosis.

Table 1 The sarcopenia-disability cascade [9]

Term	Definition	Measurement
Sarcopenia	Loss of muscle mass not because of cachexia or peripheral vascular disease	Dual-energy X-ray absorptiometry MRI/CT Ultrasound Bioelectrical impedance Midarm muscle circumference Calf circumference

Kratopenia	Loss of force, i.e., strength	Isometric (dynamometry) Isotonic
Dynapenia	Loss of power, i.e., force x velocity	Walking speed
		Walking distance Stair climbing Jebsen hand function
Frailty	Physical phenotype (fatigue, resistance, aerobic, illness, loss of weight)	CHS (fried) criteria FRAIL questionnaire Study of osteoporotic fractures criteria Canadian (Rockwood) criteria
Disability	Loss of activities of daily living (ADLs)	Katz ADLs Barthel index Functional index measure

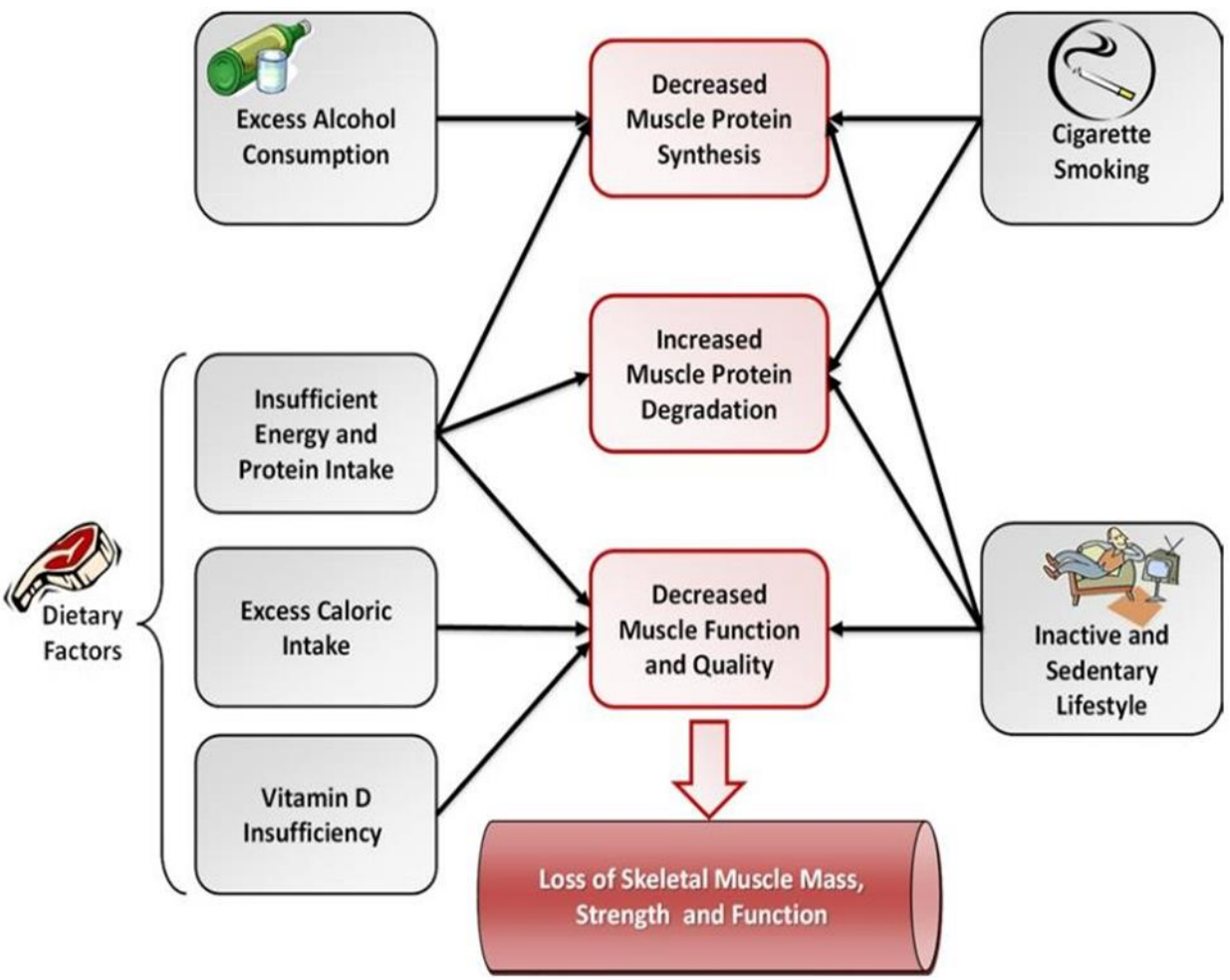

Fig 1 Lifestyle factors affecting sarcopenia [12]

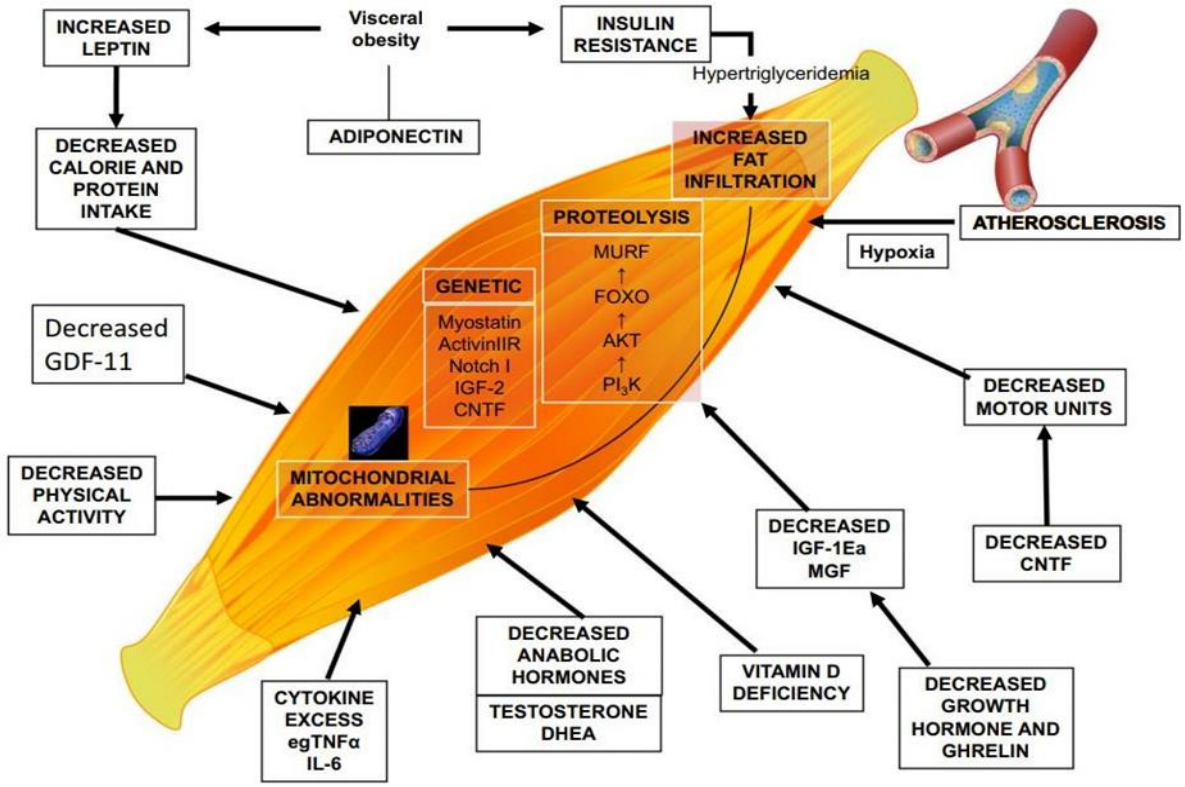

Fig 2 Factors involved in the Pathophysiology of Sarcopenia [13]

Table 2 Measurement of muscle mass, strength, and physical performance in research and practice [8]

Criteria	Clinical practice	Research
Muscle mass	BIA DEXA Anthropometry	IVNAA CT/MRI DEXA BIA Total body potassium Ultrasound
Muscle strength	Handgrip strength	Handgrip strength Knee flexion/extension Peak expiratory flow
Physical performance	SPPB Gait speed test Get-up-and-go test Stair climb power test Six-minute walk distance	SPPB Gait speed test Get-up-and-go test Sit-to-stand test Six-minute walk distance

Table 3 Characteristics of techniques for the diagnosis of sarcopenia [29]

	Anthropometry	BIA	DEXA	CT/MRI	Ultrasound
Simplicity	+++	++	+	–	+
Low cost	+++	++	+	–	+
Validity	–	+	++	+++	?
Clinical application	+	+	+	–	–
Research application	–	+	++	+++	?

Materials and Methods

Materials

Study design: Cross-sectional study

Study duration: October 2019 to December 2020

Study population: 100

Study Site: Outpatients and inpatients of the Department of Medical Gastroenterology at King George Hospital, Andhra Medical College, Visakhapatnam

Inclusion and Exclusion Criteria

Inclusion criteria

•All adult patients aged 18 - 65 years evaluated for cirrhosis of the liver and found to have Child-Pugh A and B severity

Exclusion criteria

• Liver Cirrhosis patients with Child Pugh-C

• Active comorbid disease, e.g., pulmonary, cardiovascular, renal disease (especially hepatorenal syndrome)

• Malignancy

• HIV

•Hepatic encephalopathy

• Pregnancy

• Acute hepatitis

• Refusal of consent

Methodology

• Written and informed consent of the patients was taken for the clinical examination and lab investigations. We took a detailed clinical history, and a routine physical examination was performed.

• Blood investigations like Complete blood picture, renal function tests, liver function tests were done for all the patients.

• Assessment of nutritional status by anthropometry

• Assessment of sarcopenia by Computed tomographic (CT) scan of the abdomen (Psoas muscle thickness for height value at L3 vertebra), handgrip strength, and muscle performance

• Sarcopenia was correlated with the severity of the liver disease.

Anthropometric evaluation

• Height, weight, mid-arm muscle circumference (MAMC), mid-arm circumference (MAC), and triceps skinfold thickness (TST) were measured on the right arm.

• The triceps skinfold was measured as the mean of three measurements using the skinfold caliper midpoint between the acromion and tip of the olecranon.

• TST <12.5mm for males and <18mm for females [63].

• Arm circumference was evaluated at the right arm, at a midpoint between the acromion and tip of the olecranon. The patient in the upright position, and the arm flexed at 90 degrees.

• MAMC was calculated by the formula MAMC (cm) = MAC - [3.14 * TST (cm)].[62]

• MAMC values <21.1cm for males and <19.2cm for females were considered as abnormal and patients were diagnosed to have malnutrition

• BMI values < 18.5 kg/m2 were considered abnormal [64]

Assessment of Sarcopenia

• Muscle mass - L3 Vertebral level CT scan(PMTH) <16.8mm/m is considered as abnormal) [65]

• PMTH- psoas muscle thickness/patient height -

- well correlated with Sarcopenia-used in researches.
- It does not require special software for assessment
- Digital CT scan images were accessed from the radiology department, CT slice closest to the mid-L3 vertebrae was selected, and a single observer analyzed all images.
- Psoas muscle thickness – transverse diameter of psoas muscle (left-right) perpendicular to axial diameter
- Cut-off of PMTH <16.8 mm/m2was taken for sarcopenia.

• Muscle strength – Handgrip strength (<27kg for men and < 16kg for women) [4]

• It was done using a Handgrip dynamometer (HGD)

• The patient sits comfortably on a chair advised to hold the handgrip dynamometer in the dominant hand and compress the dynamometer's handle with as much strength as possible.

• Three readings will be noted with a gap of > 30 sec. The mean of the three recordings was taken into consideration.

• Muscle performance – Gait speed [Baseline gait speed (<0.8m/sec)] [66]

The test was performed with any patient able to walk 4 meters using the instructions below:

1. Instruct the patient to walk at their average pace. Patients are advised to use an assistive device if needed.

2. The patient was asked to walk down a hallway through a 1-meter zone - acceleration, a central 4-meter

"testing" zone, and a 1-meter zone - deceleration.

3. The timer started with the first footfall after the 0-meter line of the testing zone.

4. The timer stopped with the first footfall after the 4-meter line of the testing zone.

5. SCORING: Gait speed of more than 5 seconds to walk 4 meters (<0.8 m/s) suggests poor muscle performance

Severity grading of cirrhosis

The severity of cirrhosis was graded as per Child-Turcotte Pugh score [67]

Table 7 Child Turcotte Pugh Scoring System

Factor	1 point	2 points	3 points
Total Bilirubin (mg/dL)	< 2	2-3	>3
Serum albumin (mg/dL)	>3.5	2.8-3.5	<2.8
PT INR	<1.7	1.71-2.3	>2.3
Ascites	None	Mild (or suppressed with medication)	Moderate to Severe (or refractory)
Hepaticencephalopathy	None	Grade I-II	Grade III-IV
	Class A	Class B	Class C
Total Points	5-6	7-9	10-15
1-year survival	100%	80%	45%
2-year survival	85%	60%	35%

The MELD score [68] has also been shown to predict survival in patients with cirrhosis. The estimated 3 month mortality based on MELD score is as follows.

MELD = 3.78×ln[serum bilirubin (mg/dL)] + 11.2×ln[INR] + 9.57×ln[serum creatinine (mg/dL)] + 6.43

Meld Score Mortality

40 71.3% mortality

30-39 52.6% mortality

20-29 19.6% mortality

10-19 6.0% mortality

9 or less 1.9% mortality

Ethical Justification

• Institutional ethics committee approval was taken for the study (Approval no: 184/IEC AMC/DEC/2020).

• This study involved clinical evaluation, routine lab investigations, ultrasound of the abdomen, upper gastrointestinal endoscopy, and CT scan of patients.

• All patients were given the standard of care with no changes in therapy.

• Patients were included in the study after informed consent and had the right to opt- out at any time without giving any reason.

• We conducted this study considering the Helsinki Declaration of Human Rights; the most important factors taken into account were the well-being and safety of patients.

Statistical Analysis

• The data were entered into a Microsoft Excel worksheet (Office 2016 Professional for Windows; Microsoft) and IBM Statistical Package for the Social Sciences (SPSS) for Windows [version 20, Professional] (IBM Corp., Armonk, NY, USA) was used for analysis.

• Descriptive statistics are presented in frequency, percentages, mean, standard deviation, median, and quartiles.

• When the data was following the normal distribution, a parametric test like an independent sample t-test was used to compare the means between the two groups.

• Pearson correlation test was used to find the correlation between sarcopenia and severity of the liver disease.

• Results are graphically represented where deemed necessary.

• A p-value of < 0.05 was considered to be statistically significant.

Results

A total of 100 consecutive patients with cirrhosis of the liver were enrolled over 15 months in this prospective study. The detailed characteristics and outcomes of patients are mentioned below.

Table 8 General characteristics of patients (n=100)

Parameter		**Result**
Age in years, Mean (Range)		47.9(18-65)
Gender %	Male	69
	Female	31
Ascites %	Present	50
	Absent	50

Note: Since the number of patients is 100, I have refrained from quoting numbers with percentages. As the numbers and percentage, both will be the same wherever appropriate number is mentioned with percentage.

In the present study, the age of patients ranged from 18 to 65 years. The mean ± standard deviation age of the patients was 47.9±11.5 years. The majority of the 34(34%) patients were in the age group of 41-50 years. Male predominance was seen in this study, with 69(69%) of patients being males, with a male: female ratio of 2.2:1. History of ascites was present in 50% of patients.

Table 9 Distribution of patients according to etiology of cirrhosis (n=100)

Etiology	**Number of patients**
Alcohol	51
Hepatitis B	14
Hepatitis C	10
Unknown	12
NASH	10
AIH	3

The etiology of cirrhosis was alcohol-related cirrhosis in 51% patients, NASH in 10% patients, Hepatitis B virus-related cirrhosis in 14% patients, hepatitis C virus-related cirrhosis in 10%, autoimmune hepatitis in 3%, while it was unknown in 12% of patients. No significant association was seen between various etiologies for chronic liver disease and sarcopenia (p=0.655).

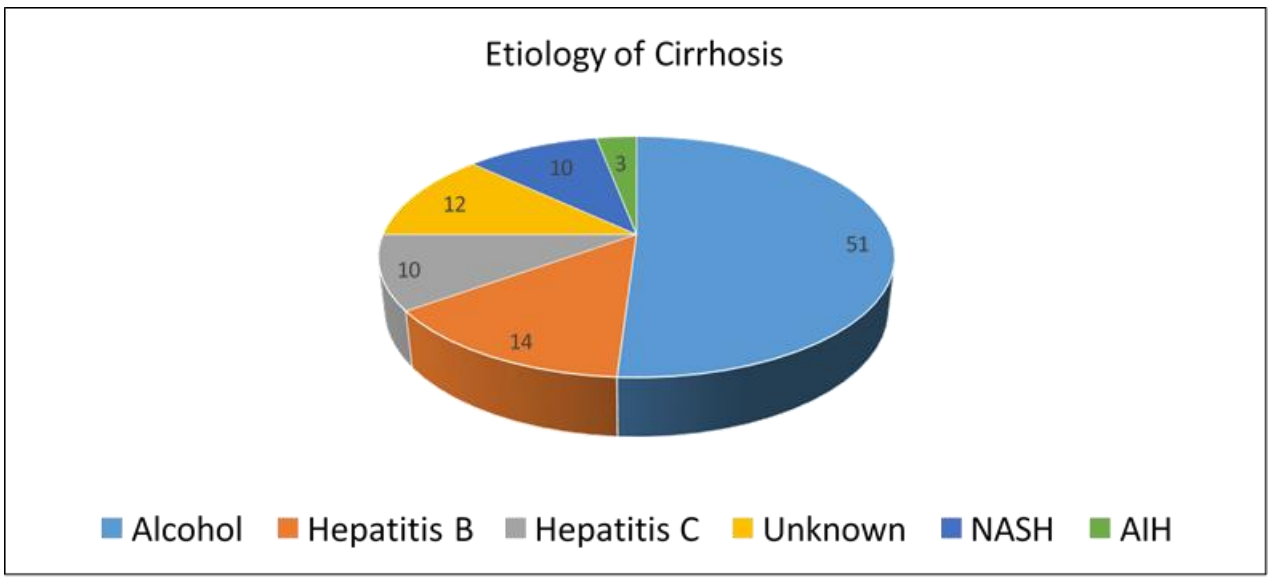

Fig 3 Etiology of Cirrhosis

Table 10 Severity grading of cirrhosis

Parameter		**Number of patients (n=100)**	**Male n(%)**	**Female n (%)**
CTP class	CTP class A	41	33(80)	8(20)
	CTP class B	59	36(61)	23(39)
MELD score	<15	72	46(64)	26(36)
	>15	28	23(82)	5(18)

The Child-Turcotte-Pugh (CTP) score was child class A in 41% of patients, while Child class B was in 59% of patients. MELD score<15 was seen in 72% of patients. The majority of the males, 23(82%), had MELD score > 15.

Table 11 Anthropometry parameters of patients

Variables	**Minimum**	**Maximum**	**Mean±SD**	**Below normal cut- off(%)**
Triceps skinfold (mm)	10	22	14.1±2.4	46
MAMC (mm)	11.1	27.3	19.9±3	45
BMI ($kg/m^{2)}$	15.4	31.3	21.4±3.1	33

Anthropometric indicators Triceps skin fold, Mid arm muscle circumference, and Body mass index were used for nutrition assessment. Mean±SD of TSF was 14.1±2.4 with the range of 10-22mm. MAMC ranged from 11.1-27.3 mm with a mean±SD of 19.9±3. BMI ranged from 15.4-31.3 kg/m2 with a mean±SD of 21.4±3.1. A total of 46 patients had below normal TSFT. MAMC was below the usual cut-off in 45 patients. BMI was low in 33 patients.

Nutritional Assessment

Table 12 Association of Triceps skinfold thickness with other parameters

Parameter		**Triceps skinfold thickness**	**P-value**
		Reduced n=46(%)	
Gender	Male	17(37)	**0.001**
	Female	29(63)	
Ascites	Present	25(54)	0.42
	Absent	21(46)	
CTP	Class A	15(32)	0.11
	Class B	31(68)	
MELD score	<15	38(82)	**0.03**
	>15	8(18)	

The Association of TSFT with gender, alcohol intake, and MELD score was significant($P<0.05$). In contrast, the association of TSFT with Ascites and CTP score was not significant.

Table 13 Association of Mid arm muscle circumference with other parameters

Parameter		**MAMC**	**P-value**
		Reduced % n=45	
Gender	Male	34(76)	0.20
	Female	11(24)	
Ascites	Present	17(38)	**0.027**
	Absent	28(62)	
CTP	Class A	22(49)	0.14
	Class B	23(51)	
MELD score	<15	33(73)	0.78
	>15	12(27)	

The association of MAMC was significant only with ascites (P<0.05), whereas it was not significant with gender, alcohol intake, CTP, and MELD score.

Table 14 Association of Body Mass Index with other parameters

Parameter		**BMI**	**P-value**
		Reduced % n=33	
Gender	Male	20(61)	0.20
	Female	13(39)	
Ascites	Present	17(51.5)	0.83
	Absent	16(48.5)	
CTP	Class A	11(33)	0.27
	Class B	22(67)	
MELD score	<15	24(73)	0.9
	>15	9(27)	

The Association of BMI was not significant with any of the above parameters.

Sarcopenia

Sarcopenia was seen in 27/100(27%) patients in the study population.

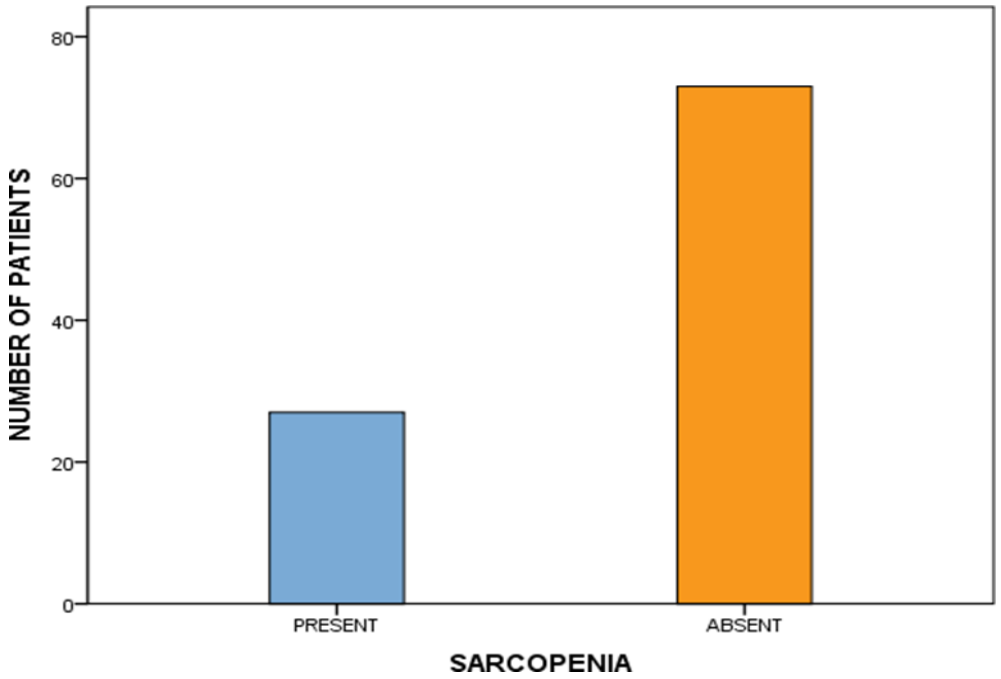

Fig 4 Bar diagram for presence of sarcopenia

Table 15 Association of age with sarcopenia

Variable	**Sarcopenia Present n=27**	**Sarcopenia Absent N=73**
Age in years, Mean ±SD	52.77±9.86	46.24±11.75

The mean age of patients with sarcopenia was 52.77±9.86 years and this was significant;p =0.012

Table 16 Sarcopenia Assessment parameters

Variables	**Mean±SD**	**Min**	**Max**	**% abnormal of total patients**
Handgrip strength (kg)	25.8±6.3	11.6	36	31
Gait Speed (m/sec)	0.87±0.19	0.6	1.3	26
CT PMTH (mm/m)	17±2.2	13.2	22.1	44

The handgrip strength was abnormal in 31/100 (31%) patients. Gait speed was reduced in 26/100 (26%) patients, and CT PMTH was abnormal in 44 patients. The mean of handgrip strength was 25.8±6.3 kg, the mean of Gait speed was 0.87±0.19 m/sec, and the mean of CT PMTH was 17±2.2 mm/m.

Table 17 Association of gender with sarcopenia

Gender	**Sarcopenia Present, n (%)**	**Sarcopenia Absent, n (%)**
Females	9 (33.3)	22(30.1)
Males	18(66.7)	51(69.9)

In females, sarcopenia was present in 9/31(33.3%) patients, while in males, sarcopenia was seen in 18/69(66.7%) patients, with no significant association between gender and sarcopenia with p= 0.759.

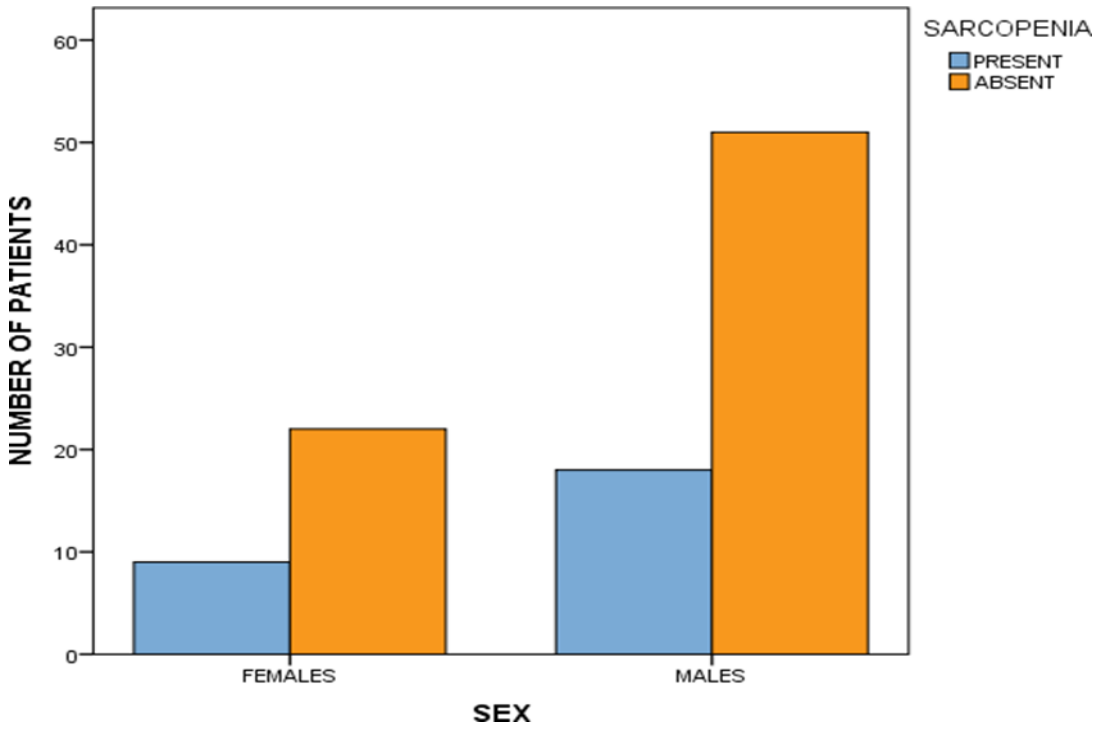

Fig 5 Bar diagram for association of gender with sarcopenia

Table 18 Association of etiology with sarcopenia

Etiology	Sarcopenia Present, n (%)	Sarcopenia Absent, n (%)
Alcohol	16(59.3)	35(47.9)
Hepatitis B virus	2(7.4)	12(16.4)
Hepatitis C virus	3(11.1)	7(9.6)
Autoimmune hepatitis	0	3(4.1)
NASH	2(7.4)	8(11)
Unknown	4(14.8)	8(11)

The proportion of sarcopenia in patients with alcohol intake was 16(59.3%), in HBV+ patients was 2(7.4%), HCV+ patients were 3(11.1%), NASH related patients was 2(7.4%), and with unknown etiology patients was 4(14.8%). None of the patients with AIH had sarcopenia.

Table 19 Association of ascites with sarcopenia

Ascites	**Sarcopenia Present, n (%)**	**Sarcopenia Absent, n (%)**
Present	21(77.8)	29(39.7)
Absent	6(22.2)	44(60.3)

In patients with ascites, 21(77.8%) patients had sarcopenia. In patients without ascites, sarcopenia was seen in 6(22.2%) patients. Presence of ascites was significantly associated with sarcopenia with p=0.001.

Table 20 Association of Child-Turcotte-Pugh class with sarcopenia

CTP	**Sarcopenia Present, n (%)**	**Sarcopenia Absent, n (%)**
A	4(14.8)	27(50.7)
B	23(85.2)	36(49.3)

In CTP class A, 4(14.8%) patients had sarcopenia. In CTP class B, sarcopenia was seen in 23(85.2%) patients. There was a significant association seen between Child- Turcotte-Pugh class and sarcopenia with p=0.001.

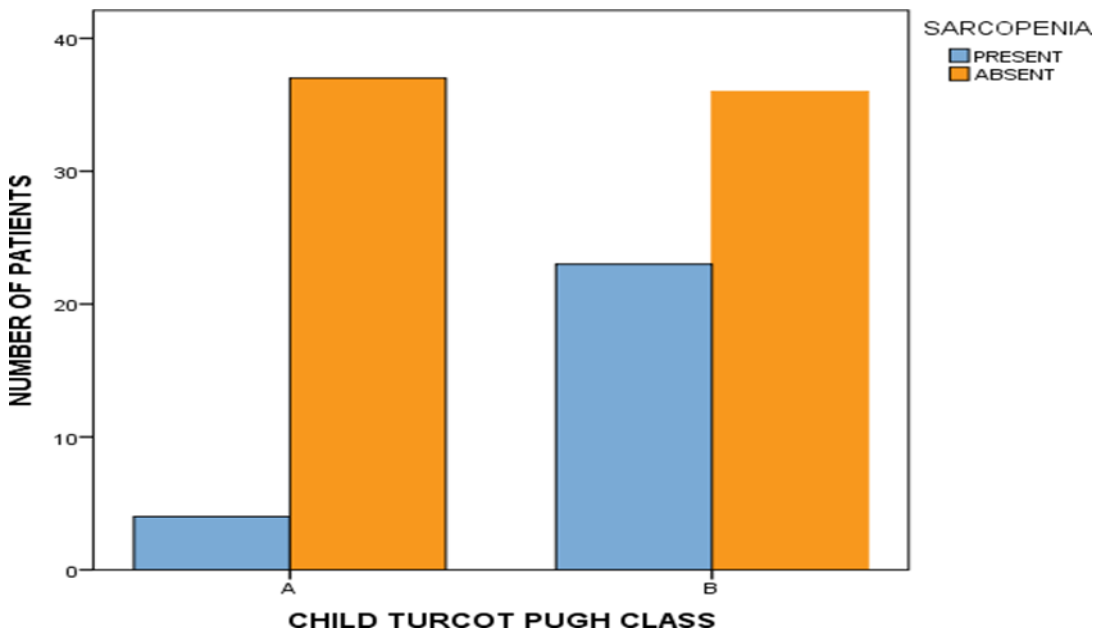

Fig 6 Bar diagram for association of Child-Turcotte-Pugh class with sarcopenia

Table 21 Association of MELD Score with sarcopenia

MELD Score	Sarcopenia Present, n (%)	Sarcopenia Absent, n (%)
< 15	15(55.6)	57(78.1)
> 15	12(44.4)	16(21.9)

In patients with a MELD score of <15, sarcopenia was seen in 15(55.6%) patients, and 12(44.4%) patients had sarcopenia with MELD >15. There was a significant association seen between MELD score and sarcopenia with p = 0.026.

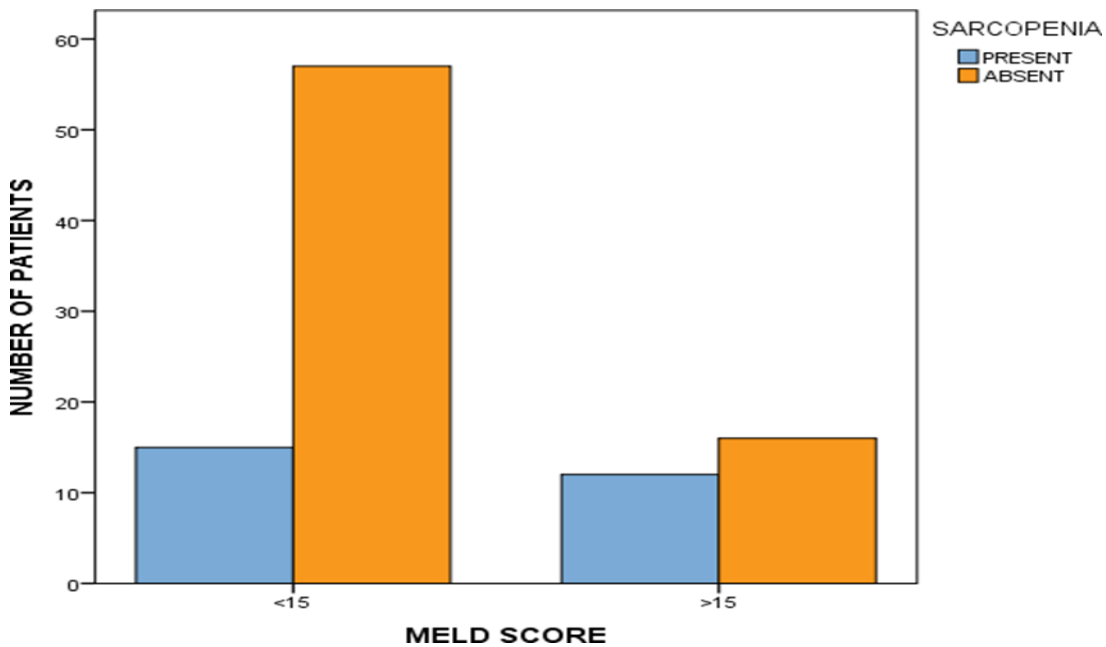

Fig 7 Bar diagram for association of MELD score with sarcopenia

Handgrip Strength

Table 22 Association of Handgrip Strength grading with sarcopenia

HGS grading	Sarcopenia Present, n (%)	Sarcopenia Absent, n (%)
Reduced	27(100)	4(5.5)
Normal	0	69(94.5)

The handgrip strength was reduced in 27(100%) patients with sarcopenia. Handgrip strength was significantly associated with sarcopenia p=0.001.

ROC of Handgrip Strength grading with sarcopenia

The ROC curve of handgrip strength for predicting sarcopenia had an area under the curve of 0.85 (excellent) with a cut-off of 27kg. It showed a sensitivity of 64% and a specificity of 100%.

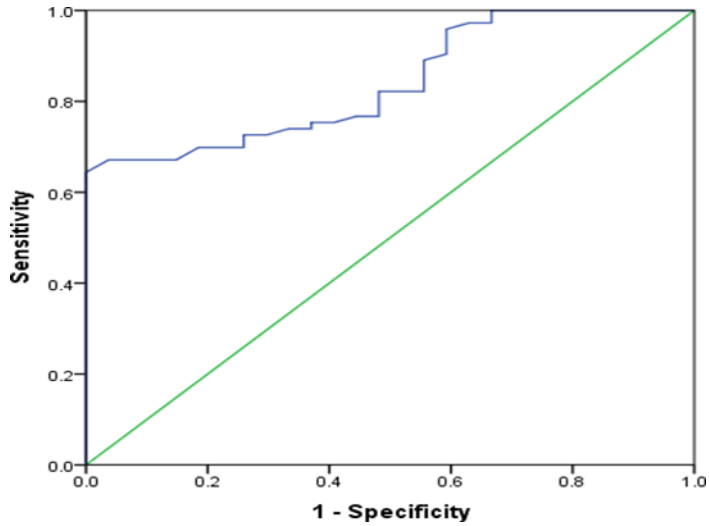

Fig 8 ROC curve of handgrip strength for predicting sarcopenia

Table 23 Association of Child-Turcotte-Pugh class with Handgrip strength

CTP	**HGS n (%) Reduced**	**HGS n (%) Normal**
A	5(16.1)	36(52.2)
B	26(83.9)	33(47.8)

The handgrip strength was reduced in 5(16.1%) patients of CTP class A and 26(83.9%) patients with CTP class B. There was a significant association between Child-Turcotte-Pugh class and handgrip strength in chronic liver disease patients with p=0.001.

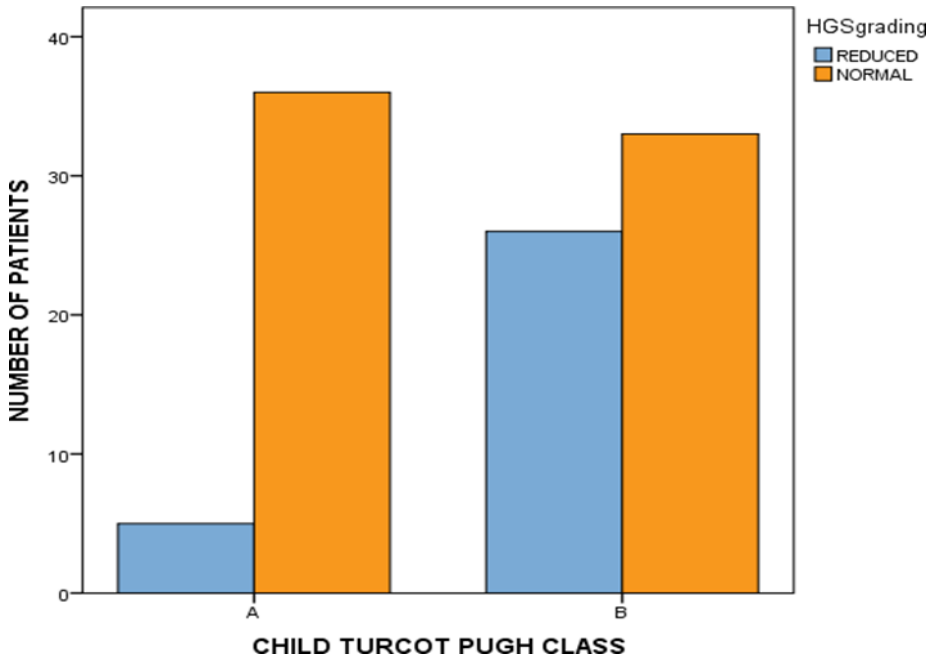

Fig 9 Bar diagram for association of Child-Turcotte-Pugh class with handgrip strength grading

Table 24 Correlation of Hand Grip Strength with MELD score, triceps skinfold thickness, mid-arm muscle circumference, Body Mass Index, Gait Speed, and Psoas Muscle thickness per height Measured with Computed Tomography

		MELD	TSFT	MAMC	BMI	Gait speed	CTPMTH
HGS	R-value	-0.170	-0.188	0.260**	0.373	0.561	0.843
	P value	0.091	0.062	0.009	0.000	0.000	0.000

A significant correlation was seen between Handgrip strength and MAMC, BMI, Gait Speed, and CT PMTH ($p<0.05$)

Gait Speed

Table 25 Association of Gait speed with sarcopenia

Gait speed (m/sec)	**Sarcopenia Present, n (%)**	**Sarcopenia Absent, n (%)**
< 0.8	18(66.7)	8(11)
> 0.8	9(33.3)	65(89)

Gait speed was reduced in 18(66.7%) patients with sarcopenia. Gait Speed was significantly associated with sarcopenia p=0.001.

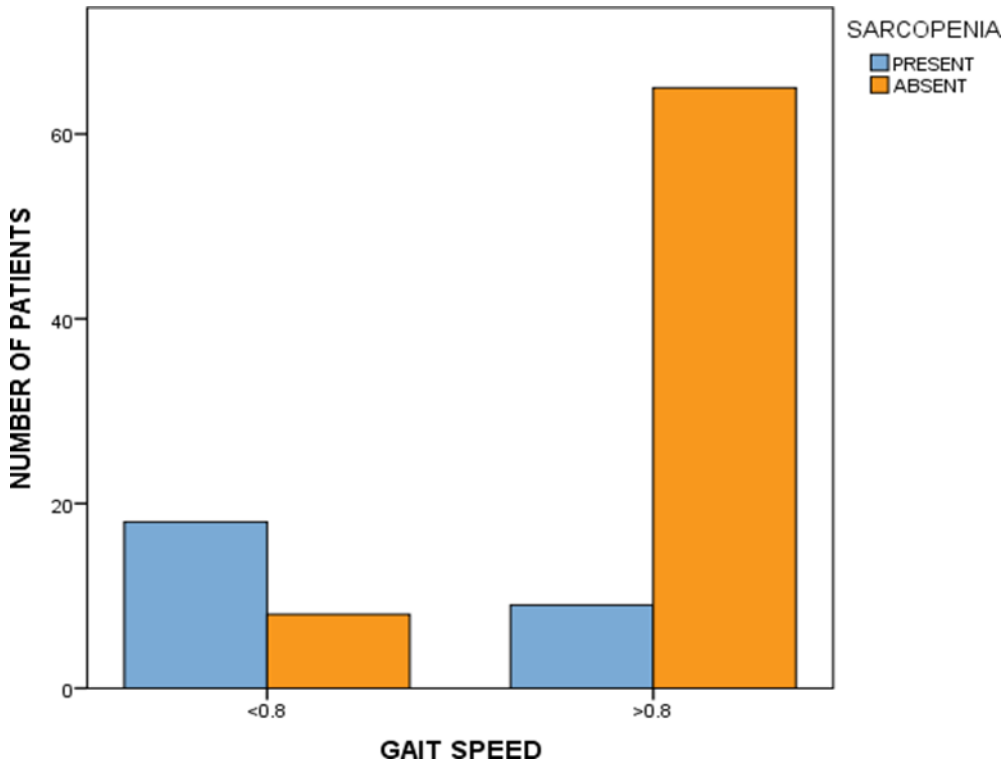

Fig 10 Bar diagram for association of Gait speed with sarcopenia

ROC of GS grade with sarcopenia

The ROC curve of gait speed for predicting sarcopenia had an area under the curve of 0.75 (acceptable) with a cut-off of 0.75 m/sec and showed a sensitivity of 89% and specificity of 67%.

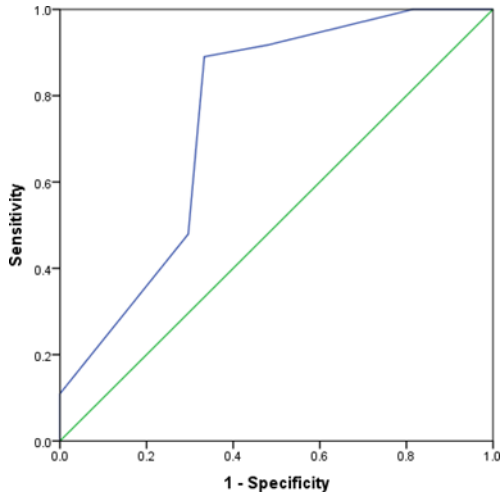

Fig 11 ROC curve of gait speed grade for predicting sarcopenia

Table 26 Association of Child-Turcotte-Pugh class with Gait Speed

CTP	**Gait speed, n (%) Reduced**	**Gait speed, n (%) Normal**
A	6(23.1)	35(47.3)
B	20(76.9)	39(52.7)

Gait speed was reduced in 6(23.1%) patients of CTP class A and 20(76.9%) patients with CTP class B. There was a significant association between Child-Turcotte-Pugh class and gait speed in chronic liver disease patients with p=0.031.

Table 27 Correlation of Gait Speed with MELD score, triceps skinfold thickness, mid-arm muscle circumference, Body Mass Index, handgrip strength, and Psoas Muscle thickness per height Measured with Computed Tomography

		MELD	TSFT	MAMC	BMI	HGS	CT PMTH
GAITSPEED	R-value	-0.222	-0.142	0.245	0.222	0.561	0.497
	P value	0.027	0.160	0.014	0.027	0.000	0.000

A significant correlation was seen between Gait speed and MELD score, MAMC, BMI, HGS, and CT PMTH ($p<0.05$).

CT PMTH

Table 28 Association of CT psoas muscle thickness per height with sarcopenia

CT PMTH	Sarcopenia Present, n (%)	Sarcopenia Absent, n (%)
<16.8mm	27(100)	17(23.3)
>16.8mm	0	56(76.7)

CT PMTH was reduced in 27(100%) patients with sarcopenia. There was a significant association between psoas muscle thickness per height and sarcopenia with p=0.001.

ROC of CT PMTH with Sarcopenia

The ROC curve of psoas muscle thickness per height measured with CT for predicting sarcopenia had an area under the curve of 0.89 (excellent) with a cut-off of 16.52mm. It showed a sensitivity of 75% and a specificity of 100%.

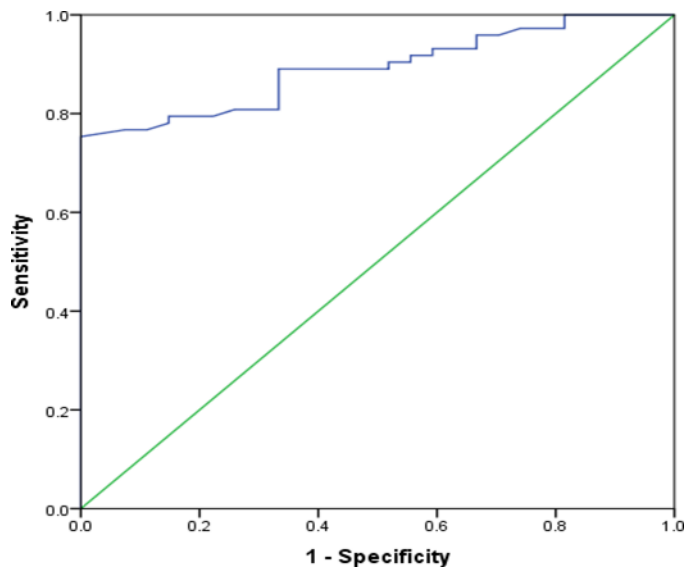

Fig 12 ROC curve of psoas muscle thickness per height measured with CT for predicting sarcopenia

Table 29 Association of CTP class with CT psoas muscle thickness per height

CTP	**PMTH n (%) Reduced**	**PMTH n (%) Normal**
A	9(20.5)	32(57.1)
B	35(79.5)	24(42.9)

PMTH was reduced in 9(20.5%) of CTP class A and 35(79.5%) with CTP class B. There was a significant association seen between Child-Turcotte-Pugh class and CT psoas muscle thickness per height in chronic liver disease patients with p=0.001.

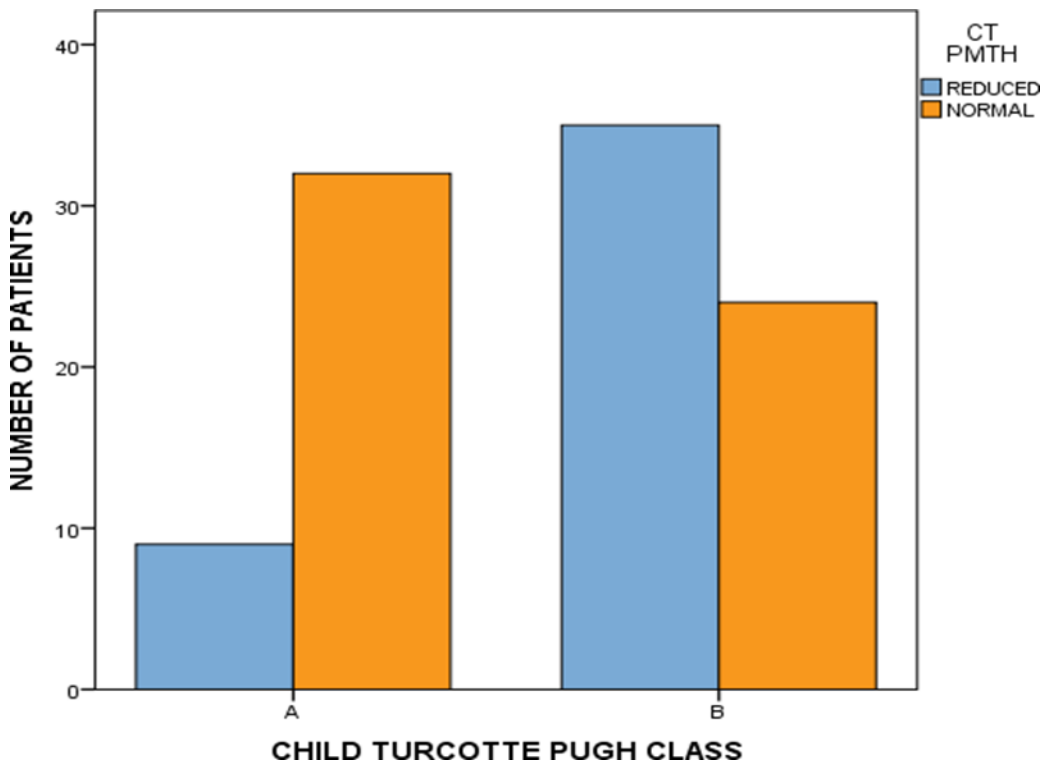

Fig 13 Bar diagram for association of Child-Turcotte-Pugh class with CT psoas muscle thickness per height

Table 30 Correlation of Psoas Muscle thickness per height Measured with Computed Tomography with MELD score, triceps skinfold thickness, mid-arm muscle circumference, Body Mass Index, handgrip strength, and Gait Speed

		MELD	TSFT	MAMC	BMI	HGS	Gait speed
CTPMTH	R- value	-0.191	-0.222*	0.238*	0.412**	0.843**	0.497**
	P value	0.056	0.026	0.017	0.000	0.000	0.000

There was a significant correlation of CT PMTH with TSFT, MAMC, BMI, HGS, and Gait Speed ($p<0.05$).

Discussion

Sarcopenia is defined as reduced skeletal muscle strength, mass, and function that often occurs in cirrhotic patients [4]. It is associated with increased mortality, a higher rate of complications and poorer outcomes in patients with hepatocellular carcinoma.

Nutritional status in patients with Child-Pugh A and B cirrhosis was assessed in this study. We also studied the proportion of sarcopenia in patients with Child-Pugh A and B cirrhosis of the liver and the correlation of sarcopenia with the severity of liver cirrhosis.

General characteristics of patients

The outcomes of 100 patients were studied. The Mean age of patients studied was 47.9±11.5 years with a range of 18-65 years. The majority of the 34(34%) patients were in the age group of 41-50 years. This means that the commonest group of individuals affected are those who were in their prime working life. Male predominance was seen in this study, with 69(69%) of patients being males, with a male: female ratio of 2.2:1. The mean ± SD of BMI was 21.4±3.1 kg/m2. The results are almost similar to those seen across the world.

Table 31 Demographic characteristics of different studies

Study	Mean age (years)	Males
Dae Hoe Gu et al., 2018 [41]	53.6	76.4%
Tae Yeob Kim et al., 2014 [70]	55	63.1%
Hari et al, 2019 [71]	63	52%

Durand et al, 2014 [65]	53	80.9%
Hou et al., 2020 [72]	62.6	51.4%
Present study	47.9	69%

Distribution of patients concerning etiology of cirrhosis

The etiology of cirrhosis was alcohol-related cirrhosis in 51% of patients; NASH in 10% of patients; Hepatitis B virus-related cirrhosis in 14% of patients; hepatitis C virus- related cirrhosis in 10%; autoimmune hepatitis in 3%. In comparison, it was unknown in 12% of patients. There was no significant association between the various etiologies for chronic liver disease and sarcopenia (p=0.655).

Table 32 Etiology of patient population across different studies

Study	Patient Population	Etiology
Dae Hoe Gu et al., 2018 [41]	Cirrhotic	49.9% Alcoholic liver disease 41% Chronic viral hepatitis
Tae Yeob Kim et al., 2014 [70]	Cirrhotic	Cirrhosis 56.9% alcohol 26.1% viral 9.3% mixed 7.7% other
Hari et al., 2019 [71]	Cirrhotic	67% alcohol 15% NAFLD 18% other
Durand et al., 2014 [65]	End-stage liver disease	42% alcohol 15% HBV, 30% HCV 5% biliary disease 8% others
Hou et al., 2020 [72]	Cirrhotic	38.3% viral 15.9% alcohol 8.4% autoimmune 37.5% other

Present study	Cirrhotic	51% Alcohol 24% Viral 10% NASH 3% Autoimmune 12% Unknown

Severity grading of cirrhosis

CTP and MELD scores have been widely used as prognostic indicators of liver disease in all the studies. The Child-Turcotte-Pugh (CTP) score was child class A in 41% of patients, while Child class B was in 59% of patients. MELD score<15 was seen in 72% of patients. The majority of the males, 23(82%), had MELD score > 15.

Table 33 Severity grading of cirrhosis (CTP and MELD) across different studies

Study	CTP	MELD (Mean)
Dae Hoe Gu et al., 2018 [41]	-	11.4
Tae Yeob Kim et al., 2014 [70]	CP A 4.6 CP B 56.9 CP C 38.5	12
Hari et al., 2019 [71]	Mean 8±2	15 (Meld Na)
Durand et al., 2014 [65]	-	20 (Meld Na)
Hou et al., 2020 [72]	CP A 41.4 CP B 44.2 CP C 14.3	11.1
Kang SH et al., 2018 [55]	CP A 47.6 CP B 44.2 CP C 8.2	9

Present study	CP A 41 CP B 59	13.03

Anthropometry parameters

We used anthropometric indicators, namely triceps skinfold thickness, mid-arm muscle circumference, and body mass index, for nutritional assessment. TSFT ranged from 10-22 mm with a mean±SD of 14.1±2.4. MAMC ranged from 11.1-27.3 mm with a mean±SD of 19.9±3. BMI ranged from 15.4-31.3 kg/m2 with a mean±SD of 21.4±3.1. A total of 46 patients had below normal TSFT (TST <12.5mm for males and <18mm for females were considered abnormal). MAMC was below the normal cut-off in 45 patients [MAMC values <21.1cm for males and <19.2cm for females were considered abnormal, and patients were diagnosed with malnutrition]. BMI was low in 33 % patients [BMI values < 18.5 kg/m2 were considered abnormal].

The Association of TSFT with gender, alcohol intake, and MELD score were significant (P<0.05). In contrast, the association of TSFT with Ascites and CTP score was not significant. The association of MAMC was significant only with ascites (P<0.05), whereas it was not significant with gender, alcohol intake, CTP, and MELD score. In contrast, the association of BMI was not significant with any of the above parameters.

As reported in the literature, patients with sarcopenia can have inadequate nutrients intake and result in muscle weakness, limiting physical exercise, and perpetuating the reduction of muscle mass [4]. In a recent north Indian study in 2018, the authors studied malnutrition in patients with liver disease. Patients with cirrhosis (n = 352), chronic hepatitis (n = 189) and healthy controls (n = 159) were enrolled in study. Malnutrition was diagnosed based on a subjective global assessment (SGA) score. According to SGA, 24% of patients with chronic hepatitis and 56% of patients with cirrhosis had malnutrition (P = 0.001). The prevalence of malnutrition according to MAMC was 12% and according to TST was 31% in chronic hepatitis patients [73].

Nunes G et al. in 2017 [74] studied nutritional assessment of CLD patients using anthropometry. A total of 130 CLD patients (80 men) aged 22-89 years (mean 60 years) were included. Most suffered from alcoholic cirrhosis (45%). Hospitalized patients presented more severe disease (P <0.001) and worst nutritional status defined by BMI (P =0.002), mid-upper arm circumference (P <0.001), mid-arm muscular circumference (P <0.001), triceps skinfold (P =0.07), and subjective global assessment (P<0.001). A third presented

deficient/low handgrip strength. Alcohol consumption (P=0.03) and malnutrition detected by BMI (P =0.03), mid-upper arm circumference (P=0.001), triceps skinfold (P =0.06), mid-arm muscular circumference (P=0.02) were associated with CLD severity. The authors concluded that triceps skinfold is the most efficient anthropometric parameter and is associated with mortality.

A study by Teiusanu A et al. in 2012 [75] studied nutritional Status in Cirrhotic Patients. In a series of 176 hospitalized patients with cirrhosis, 114 (65%) males, median age 52 years, commonest etiology of liver disease was alcohol in 98 (56%) patients. Malnutrition was correlated with the severity of liver disease. The mild-moderate malnourished patients were 88% Child B, over 58% with viral etiology. 22% of these patients were alcoholics, and 11% had Child C score ($p<0.01$). In the severely malnourished group, 43% had the alcoholic disease, and 31% were Child C classification ($p<0.01$). Triceps skinfold thickness (mm) and mid-arm circumference(cm) decreased significantly according to the Child score; a positive correlation was found between Triceps skinfold and MAMC with the severity of cirrhosis.

Sarcopenia parameters

Sarcopenia is seen in about 50% of the patients with liver cirrhosis and common among alcohol-related liver disease, ascites, and encephalopathy. The present study as well tried to evaluate these facts. Cirrhotic patients underwent abdominal computed tomography (CT) scan, including L3 and umbilical levels, to measure transverse psoas muscle thickness per height.

Table 34 Body Composition methods and outcomes of cirrhosis across different studies

Study	No of patients	Mean age	Body Composition Methods	Outcomes
Tae Yeob Kim et al., 2014 [70]	562	55	CT, L4, TPMT/height	Mortality with TPMT/height ≥14 mm/m was higher than TPMT/height <14 mm/m (HR = 5.4, p < 0.001)
Durand et al., 2014 [65]	65	53	CT at the level of umbilicus, TPMT/height	TPMT/height was an independent predictive factor of waiting list mortality (HR = 0.87, p = 0.001)

Sarcopenia was seen in 27/100(27%) patients in the present study population. The mean age of patients with sarcopenia was 52.7±9.8 years. In a South Korean study by Bae EJ et al. in 2017, the rate of sarcopenia increased with age (19.2%, 29.1%, and 42.3% among the 20–39, 40–64, and 65 and older age groups, respectively). In the 20–39 age group, the prevalence of sarcopenia was higher in men. In the 40–64 age group, the prevalence of sarcopenia was higher in women. The overall estimates of the prevalence of sarcopenia in the general population were 10% (95% CI: 8-12%) in men and 10% (95% CI: 8-13%) in women, respectively. The Sarcopenia prevalence in cirrhosis ranges from 30–70% in previous studies, depending on the diagnostic tools utilized and the severity of the liver disease, with a higher prevalence in men (61.6%) than in women (36%).

Sarcopenia and etiology

Severity and etiology of underlying liver disease, age, duration of illness, and comorbidities contribute to the sarcopenia severity [76]. Sarcopenia is a well- recognized complication of cirrhosis, and in cases of NASH and NAFLD, it can contribute to accelerating liver fibrosis to cirrhosis [77]. In this study, the proportion of sarcopenia in patients with alcohol intake was 16(59.3%), in HBV+ patients was 2(7.4%), HCV+ patients were 3(11.1%), NASH related patients was 2(7.4%), and with unknown etiology patients was 4(14.8%). None of the patients with AIH had sarcopenia.

Table 35 Prevalence of sarcopenia in cirrhosis across different studies

Study	No of patients	Males	Prevalence	Predictors
Cruz et al [78]	234	157 (67)	70% (men 76%)	-
DiMartini et al [79]	338	223 (66)	68% (men 76%, women 51%)	80% prevalence in alcoholic liver disease vs 31%-71% in other diseases 80% prevalence in normal-weight vs 62% in obese
Hanai et al [80]	130	76 (58)	68% (men 82%, women 50%)	Male gender and BMI were independent predictors of sarcopenia

Montano-Loza et al [81]	112	78 (70)	40% (men 50%, women 18%)	Sarcopenia was more frequent in men and patients with a low BMI
Montano-Loza et al [82]	248	169 (68)	5% (men 52%, women 30%)	Sarcopenia was more common in men, patients with ascites, patients with low BMI, and patients with higher CTP scores and MELD scores
Tandon et al [83]	142	85 (60)	41% (men 54%, women 21%)	Male sex, CTP class C, and BMI were independent predictors of sarcopenia.

In our study, among patients with ascites, 21(77.8%) patients had sarcopenia. In patients without ascites, sarcopenia was seen in 6 (22.2%) patients. There was a significant association between the presence of ascites and sarcopenia with p=0.001.

Association of Child-Turcotte-Pugh and MELD with sarcopenia

In CTP class A, 4(14.8%) patients had sarcopenia. In CTP class B, sarcopenia was seen in 23(85.2%) patients. There was a significant association seen between Child- Turcotte-Pugh class and sarcopenia with p=0.001. In patients with a MELD score of <15, sarcopenia was seen in 15(55.6%) patients, and 12(44.4%) patients had sarcopenia with MELD >15. There was a significant association seen between MELD score and sarcopenia with p = 0.026.

Despite certain advantages of the MELD and CTP scores, the major limitation of these scores is the lack of evaluation of the nutrition and functional status of patients with cirrhosis. However, estimation of the nutritional status in patients with cirrhosis is difficult because of fluid collection caused by impaired protein synthesis [84]. Therefore, objective assessment of nutritional status needs to be established in cirrhotic patients.

The study by Durand et al [65] showed that the MELD-sarcopenia score, which combines MELD and psoas muscle area scores, is superior to that of the MELD score. These findings suggest that sarcopenia is an attractive prognostic factor to improve organ allocation in patients with cirrhosis. However, Tandon et al noted that the impact of sarcopenia was significant in patients with low MELD scores (<15; P = .02) but not

in patients with higher MELD scores (<15; P = .59) [83]. These results are consistent with data from Merli et al, who demonstrated that muscle loss was predictive of mortality in CTP class A and CTP class B patients but not in patients with CTP class C cirrhosis [85]. Taken together, these results suggest that further validation is needed. If validated, clinical trials are warranted to explore whether transplantation in sarcopenic patients with lower MELD scores may be superior.

Romagna ES et al in 2020, found no correlation between Child-Pugh and MELD severity scores, and presence of sarcopenia [86]. Montano-Loza AJ et al, [81] studied 112 patients with cirrhosis who were consecutively evaluated for liver transplant and who had a CT scan at the third lumbar (L3) vertebrae were selected. Correlations between sarcopenia and MELD and CTP and between sarcopenia were studied. A poor correlation between sarcopenia and MELD score (r = 0.04, P .7) and Child–Pugh score (r = 0.01, P .9) was observed. Also, there was a poor correlation between sarcopenia and serum albumin (r = -0.02, P .9) and serum sodium (r = -0.11, P .2).

Association of Handgrip Strength with sarcopenia and its correlation with other parameters

The handgrip strength was reduced in 27(100%) patients with sarcopenia [<27kg for men and < 16kg for women]. Handgrip strength was significantly associated with sarcopenia p=0.001. The ROC curve of handgrip strength for predicting sarcopenia had an area under the curve of 0.85 (excellent) with a cut-off of 27kg. It showed a sensitivity of 64% and a specificity of 100%.

The handgrip strength was reduced in 5(16.1%) patients of CTP class A and 26(83.9%) patients with CTP class B. There was a significant association between Child-Turcotte-Pugh class and handgrip strength in chronic liver disease patients with p=0.001. A significant correlation was seen between handgrip strength and MAMC, BMI, Gait Speed, and CT PMTH (p<0.05).

In a prospective study from North India, the authors showed that compared to MAMC, Handgrip strength showed the highest area under curve 0.82 (95% confidence interval (CI) 0.78–0.86, P = 0.001). The authors concluded that handgrip strength is an excellent tool to assess the nutrition status in patients with cirrhosis at the bedside and has the highest diagnostic accuracy than other anthropometric tests such as MAMC and TST [73].

Association of gait speed with sarcopenia and its correlation with other parameters

We studied muscle performance in terms of Gait speed, and it was reduced in 18(66.7%) of patients with sarcopenia. Gait Speed was significantly associated with sarcopenia p=0.001. The ROC curve of gait speed for predicting sarcopenia had an area under the curve of 0.75 (acceptable) with a cut-off of 0.75 m/sec and showed a sensitivity of 89% and specificity of 67%.

Gait speed was reduced in 6(23.1%) patients of CTP class A and 20(76.9%) patients with CTP class B. There was a significant association between Child-Turcotte- Pugh class and gait speed in chronic liver disease patients with p=0.031. A significant correlation was seen between Gait speed and MELD score, MAMC, BMI, HGS, and CT PMTH ($p<0.05$).

4-m gait speed – duration <1 min - This test is one of the best predictors of disability, morbidity, mortality, and fall risk across various chronic diseases and the elderly [87,88]. It is recommended by the ACSM guidelines as a basic test of function before exercise initiation.1 In 373 patients with cirrhosis, gait speed was independently associated with hospitalization rate after adjusting for covariates such as MELD and Child-Pugh score [66]. Mean gait speed was 0.95 m/s with every 0.1 m/s decreases in gait speed associated with a 22% increase of hospital day stay with significant projected cost implications. Gait speeds of less than 0.6 to less than 0.8 m/s have been associated with poor outcomes in older adults [89].

Association of CT PMTH with sarcopenia and its correlation with other parameters

CT PMTH was reduced in 27(100%) of patients with Sarcopenia [Cut-off of PMTH <16.8 mm/m2 was taken for sarcopenia]. There was a significant association between psoas muscle thickness per height and sarcopenia with p=0.001. The ROC curve of psoas muscle thickness per height measured with CT for predicting sarcopenia had an area under the curve of 0.89 (excellent) with a cut-off of 16.52mm. It showed a sensitivity of 75% and a specificity of 100%.

PMTH was reduced in 9(20.5%) of CTP class A and 35(79.5%) with CTP class B. There was a significant association seen between Child-Turcotte-Pugh class and CT psoas muscle thickness per height in chronic liver disease patients with p=0.001. There was a significant correlation of CT PMTH with TSFT, BMI, HGS, and Gait Speed ($p<0.05$). We also found that muscle mass area measured through CT analysis correlated with the MAMC at anthropometry.

It is vital to measure the dimensions and surface area of the psoas major. It has the great advantage of being easily feasible because it does not require special software. Durand et al. [65] also found a significant association between transversal psoas muscle thickness normalized to height and mortality on the liver transplantation waiting list, independently of MELD. CT scan can identify the highest percentage of sarcopenia in cirrhosis. CT scan is the first technique that enables evaluation of the central muscle wasting, which might be less affected by sex, physical activity, and water retention. It is essential to recognize that the high cost, the possible limited access to the equipment, and the concern in terms of radiation exposure may limit the use of this technique for routine clinical practice unless the patient needs to perform a CT scan for other purposes.

A prospective observational study from South Korea in 2018 included 653 cirrhotic patients and studied the Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia [41]. The average age was 53.6 ± 10.2 years, and 499 patients (76.4%) were men. PMTH correlated well with SMI in both men and women ($P<0.001$). 241 (36.9%) patients met the criteria for SMI-sarcopenia. The best PMTH cut-off values for predicting SMI-sarcopenia were 17.3 mm/m in men and 10.4 mm/m in women, and these were defined as sex-specific cut-offs of PMTH (SsPMTH). Two hundred thirty (35.2%) patients were diagnosed with SsPMTH-sarcopenia, and 280 (44.4%) patients were diagnosed with SnPMTH-sarcopenia [41].

The present study corroborates with observations of previous studies that malnutrition is prevalent in patients with sarcopenia. There was a significant association seen between sarcopenia and Handgrip Strength, Gait Speed, and Psoas Muscle thickness per height measured with Computed Tomography. Sarcopenia represents an essential prognostic factor in cirrhotic patients and can assess the advanced liver disease. Hence, it is vital to study interventions to improve sarcopenia among cirrhotic patients in well-controlled studies.

Strengths and Limitations

Strengths

1. This is a prospective observational study with a large number of cases.

2. We assessed all possible parameters of anthropometry, including BMI, triceps skinfold thickness, mid-arm circumference, and mid-arm muscle circumference, to look for nutritional assessment.

3. Muscle strength is the measure of age-related muscle change. To assess this, we did a CT scan on all

patients. In addition to this, we studied Handgrip Strength, Gait Speed, and Psoas Muscle thickness height measured with Computed Tomography.

Limitations

1. The study results are from a single-center, with a noncomparative study design; hence, the findings cannot be generalized.

2. Being a tertiary referral center, the study includes a selected subset of referred patients; thereby, an element of referral bias might exist, the results of which may not be generalizable outside of this environment.

3. There were no interventions and follow-ups due to the limited time frame available during the study tenure. Treatment was not part of the study, so further improvement could not be assessed.

4. Quality of Life was not assessed.

5. The results perhaps would have improved if we could identify the dietary habits of these patients.

Nevertheless, we believe that the decent results obtained from this study add to the current pool of existing knowledge for future studies in India and across the world.

Conclusion

Sarcopenia is prevalent in the studied cirrhotic patients causing limitation of activities and increases the risk of fall. It was more commonly seen in middle-aged men. The commonest etiology of cirrhosis in sarcopenia was alcohol. There was a significant association seen between sarcopenia and Handgrip Strength, Gait Speed, and Psoas Muscle thickness height measured with Computed Tomography. There was a significant association shown between Child-Turcotte-Pugh class (A and B) and sarcopenia in our study, suggesting these patients may need routine surveillanceudy and early treatment to prevent future risk.

Summary

1. Sarcopenia was predominantly seen in males.

2. Presence of ascites and high MELD score was significantly seen to be associated with sarcopenia

3. Age, handgrip strength, gait speed, Psoas Muscle thickness height measured with Computed Tomography, and BMI were significantly associated with sarcopenia.

4. Middle age to elderly cirrhotic patients need a routine evaluation of gait speed and muscle strength to identify those at risk for sarcopenia.

5. Sarcopenia should be the future focus of clinical screening among Child A and Child B cirrhotic patients.

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