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Assessment of Sarcopenia with 30 and 90 Days Morbidity and Mortality Outcomes in Child-Turcotte-Pugh (CTP) B and C Cirrhosis

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Abstract

Background: Sarcopenia is defined as progressive loss of skeletal mass, strength and physical performance. Our study focused on evaluation of sarcopenia as an independent factor to predict with 30 and 90 days morbidity and mortality outcomes in CTP B and C cirrhosis.

Methods: Sarcopenia was assessed by muscle mass, strength and physical performance and each parameter was individually scored.

Results: 50 patients with confirmed cirrhosis CTP B and C were included and assessed for sarcopenia. 27(54%) patients were CTP grade B and 23 (46%) were CTP grade C with a mean age of 45.26 ± 12.731 years. Sarcopenia was present in 36 (72%) patients; 12 (24%) had moderate and 24 (48%) had severe sarcopenia. CTP C group (63%) had more significant sarcopenia than CTP B group (82.6%) (p = 0.01). Significant morbidity at 30 (p = 0.03) and 90 days (p = 0.01) was seen. The association of 30 and 90 days mortality is also significant (p <0.01).

Conclusion: Sarcopenia can be considered as a good indicator of morbidity and mortality in the patients of cirrhosis and has a high concordance with the CTP score.

Key words: Sarcopenia; Child-Turcotte-Pugh (CTP); cirrhosis; morbidity; mortality.

Abbreviations: CTP: Child-Turcotte-Pugh; BIA: Bioimpendance analysis; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; SPPB: Short Physical Performance Battery; MELD: Model for end-stage liver diseases; MDCT: Multi-Detector Computed Tomography; PI: Psoas Index; RPA: Right Psoas Area; LPA: Left Psoas Area; HU: Hounsfield Unit; HUAC: Hounsfield Unit Average Calculation; PTMT/H: Psoas Muscle Thickness for Height; CLDQ: Chronic Liver Disease Questionnaire; HE: Hepatic encephalopathy; UGIB: Upper gastrointestinal bleed; HRS: Hepato-renal syndrome; TPMT: Transverse psoas muscle thickness; SMI: Skeletal muscle index; BCCA: Branched-chain amino acid.

Introduction

Sarcopenia as a term was devised by Irwin Rosenberg in 1989 and derived from two Greek words-'Sarx' which means flesh and 'Penia' which means loss[1]. It is defined as progressive loss of skeletal mass, strength and physical performance[2-4]. It is categorised as primary and secondary[4]. Primary sarcopenia is age related while secondary sarcopenia is due to disease, nutrition and decreased activity. Muscle mass can be calculated by radiological and conventionally accepted methods including bioimpendance analysis (BIA) and anthropometry. Radiological methods like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) have the advantage of direct visualisation and measurements of tissue compartments and are not affected by fluid accumulation (ascites) as well as simultaneous evaluation of the liver is done[5]. Muscle strength is assessed with hand grip, knee flexion/extension, peak expiratory flow. Physical performance is assessed by usual gait speed, timed get-up-and-go test, stair climb power test and Short Physical Performance Battery (SPPB)[6].

Cirrhosis is a hypercatabolic state and is associated with sarcopenia and malnutrition[7,8]. The possible reasons cited for hypercatabolic state are hyperdynamic circulation, systemic inflammation and subclinical endotoxaemia related to intestinal bacterial translocation. Sarcopenia in cirrhosis is due to inadequate dietary intake, metabolic disturbances, hypercatabolism and associated clinical or subclinical malabsorption.

Sarcopenia and poor nutrition is associated with adverse outcomes in cirrhosis[7-13]. The prevalence of sarcopenia in cirrhotics is reported to be between 40 - 68%[10,12]. It is an independent risk factor for mortality in patients with cirrhosis[9-13]. However, traditional scores like modified Child-

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Turcotte-Pugh (CTP) or the model for end-stage liver diseases (MELD) do not include sarcopenia as a criterion for prognosis. Various other tools have been used over time for the assessment of the nutritional status in patients with cirrhosis but there has been a lack of reproducibility, objectivity, and prognostic performance which limits their wider application[7].

Hence, sarcopenia quantified by an objective method along with other commonly used prognostic tools has the potential to improve prognostication in patients with cirrhosis. There is paucity of data on sarcopenia and its correlation with cirrhosis in India. Our study focused on evaluation of sarcopenia as an independent factor to predict with 30 and 90 days morbidity and mortality outcomes in CTP B and C cirrhosis.

Material and Methods

This study was conducted in a tertiary care facility at Government Medical College and Hospital, Chandigarh, India. All patients over 18 years of age diagnosed with cirrhosis due to various aetiologies belonging to CTP class B and C were included. CTP A cirrhotics and patients having associated malignancy were excluded. Cirrhosis was confirmed by clinical and radiological methods. Sarcopenia was assessed by muscle mass, strength and physical performance and each parameter was individually scored (as indicated in Table I)[4]. The tests were done by one blinded investigator to avoid bias.

Table I: Parameters to assess sarcopenia.

S.No.	Parameter	Methods	Points
1.	Muscle mass	CT scan abdomen done at two levels; one at L3 vertebral level and the other at umbilical level[14].	1
2.	Muscle strength	Done with hand held Jamar dynamometer[15].	1
3.	Physical performance	Done with Short Physical Performance Battery (SPPB).[6]	1

For muscle mass, CT scan of abdomen on 64 slice Multi-Detector Computed Tomography (MDCT) scanner (Inbuilt software) was done at two levels; two axial images were taken; one at L3 vertebral level and the other at umbilical level to look for psoas muscle parameter[14]. One point was given to reduced muscle mass, if all the 3 criteria of CT abdomen were fulfilled as given below:

1. At L3 vertebral level, Psoas Index (PI) was measured normalising by the square of the height.

   PI = [Right Psoas Area (RPA) + Left Psoas Area (LPA)]/ height^2 in cm^2/m^2

   PI $\leq$7.77 cm^2/m^2 in males and $\leq$4.75 cm^2/m^2 in females was significant and indicated reduced muscle mass[14].

2. At L3, Hounsfield Unit Average Calculation (HUAC) was done after taking mean of three values on each side[14].

   HUAC = [(Right mean psoas HU density x RPA) + (Left mean psoas HU density x LPA)]/(Total Psoas Area).

   HUAC $\leq$38.5 Hounsfield unit was significant indicating reduced muscle mass[14].

3. At umbilical level, Psoas Muscle Thickness for Height (PMTH/H) was done after normalising the patient's height[10].

   PMTH/H <16.8 mm was taken as significant indicating reduced muscle mass[10].

Muscle strength was assessed with hand held Jamar dynamometer. An average of three values was taken. A cut-off value of $\leq$30 Kg in males and $\leq$20 Kg in females was considered significant for reduced muscle strength and one point was given[15].

Physical performance was assessed using the Short Physical Performance Battery (SPPB) which is a battery of tests used to check mobility and physical performance. A final score of $\leq$8 indicates reduced physical performance and one point was given if the score was met[6].

Then patients were stratified into various categories namely pre-sarcopenia, moderate sarcopenia, and severe sarcopenia; although literature categorises moderate sarcopenia as sarcopenia[4] (Table II).

Table II: Criteria based categorisation of Sarcopenia[4].

Groups	Categorisation of sarcopenia	Criteria	Points
Non-Sarcopenia group	No Sarcopenia	No criteria fulfilled	0 out of 3
	Pre-Sarcopenia	Reduced muscle mass only	1 out of 3
Sarcopenia group	Moderate Sarcopenia	Reduced muscle mass + Reduced muscle strength/ reduced physical performance	2 out of 3
	Severe Sarcopenia	Reduced muscle mass + Reduced muscle strength + Reduced physical performance	3 out of 3

Patients meeting minimum 2 out of 3 criteria are defined as sarcopenic. These are subcategorised into moderate (if 2/3 criteria fulfilled) and severe (if 3/3 criteria fulfilled). Pre-sarcopenia was defined if 1/3 criteria met. So there were two groups- Non-Sarcopenia group and Sarcopenia group (Table II).

The patients followed up after discharge at day 30 and 90 and the data was analysed for association with sarcopenia. Morbidity was assessed by using Chronic Liver Disease Questionnaire (CLDQ), a validated score used to assess

quality-of-life and consists of 29 items on a seven-point Likert scale, with higher scores indicating a better quality-of-life. Out of a total of 7, a cut-off at <3.5 was considered as significant. Mortality was recorded along with the immediate cause of death.

Results

Baseline demographic and clinical characteristics of 50 patients included in the study are presented in Table III; 39 (78%) patients were males and 11 (22%) females. The mean age of the patients was 45.26 ± 12.731 years (Range 19 - 76 years). 27 (54%) patients were CTP grade B and 23 (46%) were CTP grade C. Various aetiologies identified were alcohol in 26 (52%), hepatitis B in 8 (16%), hepatitis C in 7 (14%), NASH in 4 (8%) and cryptogenic in 5 (10%) patients. Co-morbid illnesses like diabetes mellitus present in 4 (8%) and hypertension in 6 (12%) were also recorded and these patients belonged to sarcopenia group. There were no other co-morbidities.

Table III: Baseline characteristics of study population

Characteristics	n (%)
Age	45.26 ± 12.731 (Range 19 - 76 years)
Males	39 (78%)
Females	11 (22%)
Aetiologies	
– Alcohol	26 (52%)
– Hepatitis B	8 (16%)
– Hepatitis C	7 (14%)
– NASH	4 (8%)
– Cryptogenic	5 (10%)
Co-morbidity	
– Diabetes mellitus	4 (8%)
– Hypertension	6 (12%)
– None	40 (80%)
CTP	
– CTP B	27 (54%)
– CTP C	23 (46%)
Sarcopenia	36 (72%)
Categorisation of Sarcopenia	
– No Sarcopenia	5 (10%)
– Pre-Sarcopenia	9 (18%)
– Moderate Sarcopenia	12 (24%)
– Severe Sarcopenia	24 (48%)
Total Morbidity	
– 30 day	22/35 (62.85%)
– 90 day	15/26 (57.69%)
Total Mortality	
– 30 day	15 (30%)
– 90 day	24 (48%)

Sarcopenia was present in 36 (72%) patients; 12 (24%) had moderate and 24 (48%) had severe sarcopenia. Both moderate and severe sarcopenia together constituted the sarcopenia group while no sarcopenia and pre-sarcopenia were in non-sarcopenia group (Table III). Sarcopenia was present in 6 (54.5%) females and 30 (76.9%) males but the correlation with gender was statistically insignificant (p = 0.15). CTP C group had more significant sarcopenia than CTP B group, i.e., 17 (63%) out of 27 patients of CTP B and 19 (82.6%) out of 23 patients of CTP C had sarcopenia (p = 0.01).

Significant morbidity at 30 days was seen in 22 patients - 16 belonged to sarcopenia group and 6 to pre-sarcopenia group (p = 0.03). Significant morbidity at 90 days was seen in 15 patients - 10 belonged to sarcopenia group and 5 to pre-sarcopenia group (p = 0.01). No morbidity was seen in no sarcopenia group at both 30 and 90 days (Table IV).

At 30 days 15 (30%) patients died - all belonging to sarcopenia group (p <0.01), and at 90 days 24 (48%) patients died - 22 belonging to sarcopenia group and 2 to pre-sarcopenia group (p <0.01). (cause of mortality as mentioned in Table IV).

Morbidity and mortality were then compared with moderate and severe sarcopenia. In moderate sarcopenia group, 3 patients died at 30 days (p = 0.06) and 5 patients at 90 days (p = 0.01) (Table V). Significant morbidity at 30 days was seen in 7 patients (p = 0.26) while at 90 days 5 patients had significant morbidity (p = 0.32).

In severe sarcopenia group, 12 patients died at 30 days (p = 0.002) and 17 patients died at 90 days (p = 0.001). Significant morbidity at 30 days was seen in 9 patients (p = 0.38) and at 90 days 5 patients had significant morbidity (p = 0.18).

Other parameters assessed like ascites, which was present in 45 (90%) patients (p = 0.05). Out of which, 9 (18%) had mild, 17 (35%) had moderate and 19 (38%) had gross ascites. Hepatic encephalopathy (HE) was present in 20 (40%) patients (p = 0.42). 8 (16%) had grade I HE, 7 (14%) had grade II HE, 3 (6%) had grade III and only 2 (4%) had grade IV HE. Patients with sarcopenia had lower mean albumin level of 2.5, as compared to non-sarcopenia group with 2.9 (p = 0.01). Mean serum bilirubin in non-sarcopenia group was 3.4, while in sarcopenia group it was 6.0 (p = 0.29). Mean INR in patients with sarcopenia was 1.72 while in non-sarcopenia group it was 1.49 (p = 0.15).

Table IV: Characteristics of sarcopenia and non-sarcopenia group

Characteristics	Non-Sarcopenia Group (no and pre-sarcopenia)	Sarcopenia Group (moderate + severe sarcopenia)	p value
Gender			0.15
– Males	9	30	
– Females	5	6	
CTP (Average = 9.74 ± 2.02)			0.01
– B	10	17	
– C	4	19	
Aetiologies			
– Alcohol	6	20	<0.01
– Hepatitis B	4	4	0.20
– Hepatitis C	3	4	0.20
– NASH	0	4	0.20
– Cryptogenic	1	4	0.20
Morbidity			
– At 30 day	6	16	0.03
– At 90 day	5	10	0.01
Mortality			
– 30 day	0	15	<0.01
– 90 day	2	22	<0.01
Cause of Mortality			
– At 30 day			
UGIBHE	0	5	0.14
Sepsis	0	1	053
Shock	0	3	0.27
HRS	0	1	0.53
Others	0	0	1.5
– At 90 day			
UGIB	0	8	0.05
HE	1	7	0.10
Sepsis	0	2	0.37
Shock	1	3	0.27
HRS	0	1	0.53
Others	0	1	0.53

**CTP: Child-Turcotte-Pugh Score, UGIB: upper gastrointestinal bleed, HE: hepatic encephalopathy, HRS: hepato-renal syndrome.*

Table v: Categorisation of sarcopenia and correlation with morbidity and mortality - 30 and 90 days

	Total patients	30 day Morbidity	P value	90 day Morbidity	P value	30 day Mortality	P value	90 day Mortality	P value
No Sarcopenia	5	0	0.02	0	0.02	0	0.02	0	0.02
Pre-sarcopenia	9	5	0.34	5	0.34	0	0.03	2	0.09
Moderate Sarcopenia	12	7	0.26	5	0.32	3	0.06	5	0.01
Severe Sarcopenia	24	9	0.38	5	0.18	12	0.002	17	0.001

Discussion

Sarcopenia has been observed to be an emerging prognostic factor in determining mortality in patients with cirrhosis[9-13]. We assessed sarcopenia in CTP B and C cirrhotic patients and it's correlation with 30 and 90 days morbidity and

mortality. We found a prevalence of sarcopenia in 72% patients (36/50), which is higher than the data available in existing literature (40 - 68%)[10,12]. We excluded CTP A patients who are relatively less sick, while the other studies did not exclude them.

In a study conducted by Montano loza *et al* sarcopenia was observed in 40% patients (45/112)[12]. Hanai *et al* observed sarcopenia in 68% patients (89/130)[10]. Various methods for studying muscle mass have been used in different studies namely PMTH/H, PI, HUAC, TPMT (transverse psoas muscle thickness), SMI (skeletal muscle index). There is no study which has compared these parameters with each other. However, all these parameters do indicate the muscle mass and measurements have been defined for each parameter indicating sarcopenia. Montano lazo *et al* and Hanai *et al* calculated sarcopenia using SMI at L3 level while we estimated psoas muscle at two levels; PMTH/H at umbilical level and PI and HUAC at L3 level. Durand *et al* calculated TPMT at the level of umbilicus[9]. Though the study did not calculate sarcopenia like our study but there was a 15% increase in mortality risk per unit decrease in TPMT/height and it was significantly associated with mortality, independent of the MELD and MELD-Na scores[9].

In our study sarcopenia has been categorised into pre-sarcopenia, moderate sarcopenia and severe sarcopenia. We did not come across any study categorising sarcopenia; hence the results cannot be compared. The patients were followed up for morbidity with CLDQ questionnaire at 30 and 90 days and higher morbidity was seen in sarcopenic patients at both 30 and 90 days. The correlation of sarcopenia in cirrhosis has not been studied though CLDQ questionnaire for assessing the morbidity in past and we have done it for first time and hence the results cannot be compared. Janani *et al* observed health related quality-of-life in cirrhosis patients using CLDQ questionnaire and did not correlate it with sarcopenia[17]. There were 149 patients (44-CTP A, 49-CTP B and 56-CTP C) studied, out of which CTP C cirrhotics had significantly higher complications as compared to CTP A and B indicating poor quality-of-life.

The association of at 30 and 90 days mortality in patients with CTP B and C cirrhosis with sarcopenia is significant ($p < 0.01$). Patients with severe sarcopenia had higher mortality as compared to pre and no sarcopenia. Montano Loza *et al* also observed shorter median survival time in patients with sarcopenia, i.e., 19 ± 6 months compared with 34 ± 11 months among non-sarcopenia patients ($p = 0.005$)[12]. Hanai *et al* also identified significantly higher mortality in sarcopenic patients ($p = 0.01$)[10]. Hanai *et al* also determined the outcomes of branched-chain amino acid (BCCA) supplementation and it improved the survival in sarcopenic patients ($p < 0.01$)[10]. Our study was an observational study and no intervention in form of nutritional supplements was studied.

Hence, sarcopenia can be considered as a good indicator of morbidity and mortality in the patients of cirrhosis and has a high concordance with the CTP score. Therefore, quantification of sarcopenia by an objective method along with commonly used prognostic systems may improve prognostication in patients with cirrhosis and larger studies are needed to evaluate these aspects.

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