



Study of Prevalence of Sarcopenia in Chronic Liver Disease and its Impact on Outcomes

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Abstract

Background: Sarcopenia is the most common feature of chronic liver disease characterized by progressive loss of muscle mass and function and increases the mortality and morbidity rates among cirrhosis patients. The purpose of this study was to investigate the prevalence of sarcopenia in patients with chronic liver disease and its impact on outcome. **Methods:** This prospective observational study was conducted at institute of Medical Gastroenterology, Madras Medical college Chennai from September 2021 to May 2022 and included patients with chronic liver disease, graded by severity based on CTP and MELD Na scores. Sarcopenia was assessed according to EWGSOP 2 criteria. The association of lab parameters with Sarcopenia was studied. The outcomes of Sarcopenia were studied. **Results:** A total of 114 patients were enrolled in the study, 78.07% were male. The major etiology of Chronic liver disease was alcohol consumption (54.4%). The prevalence of sarcopenia was 54.3 %, with no significant differences between the male and female groups. Albumin, haemoglobin, Sodium, Handgrip, TPMT & Gait speed were significantly associated with sarcopenia. Mean CTP and MELD Na scores are high in sarcopenia group. Among the outcomes, we found that Ascites, Hepatic Encephalopathy & death are significantly associated with Sarcopenia. **Conclusion:** Sarcopenia is a common complication of liver cirrhosis and associates with adverse outcomes and poor survival rates.

Keywords: Sarcopenia, clinical outcomes, survival, handgrip strength, Psoas muscle thickness

Introduction

Sarcopenia is the loss of skeletal muscle mass, quality, and strength. It is a major sign of malnutrition in cirrhosis [1,2]. The number of people with chronic liver disease (CLD) who have sarcopenia is estimated to be between 25% and 70%, with higher rates in men [3]. The presence of sarcopenia causes serious clinical problems and has been linked to an increased risk of death [4], a lower quality of life (QoL) [5], longer hospital stays [6], and problems like infections and death before and after a liver transplant (LT) [7]. In the end, sarcopenia is a big economic problem because patients with sarcopenia who are waiting for LT have higher health care costs than patients who don't have sarcopenia [8]. The present study was done to evaluate the prevalence of sarcopenia in patients with chronic liver disease and investigate the association of lab parameters with sarcopenia and also to study the impact of outcomes associated with Sarcopenia.

Materials and Methods

Type of Study

Prospective Observational study

Locus of Study

Institute of Medical Gastroenterology, Madras Medical college, Chennai

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Study period

From September 2021 to May 2022

Study population

All patients attending the MGE outpatient department and inpatients fulfilling inclusion & exclusion criteria.

Inclusion criteria:

- Patients within the age group 18-65 with chronic liver disease of all etiologies.

Exclusion criteria:

- Cirrhosis with active comorbid diseases e.g: Pulmonary, Renal disease.
- Malignancy - HCC, Extrahepatic cancers
- Hepatic encephalopathy
- Patients with neurological diseases.
- Patients who are not willing to give consent

Sampling technique

purposive sampling technique

Sample size: 114

Data collection

All patients included in the study were subjected to blood investigations and various test for sarcopenia assessment. Subjects are graded by severity based on CTP and MELD Na scores. Sarcopenia diagnosis was made using the EWGSOP2 criteria and cut-offs [9]. In accordance with the EWGSOP2 algorithm, those with normal muscle strength were considered as having no sarcopenia, those with low muscle strength but normal muscle mass were categorised as probable sarcopenia, and those who had low muscle strength, low muscle mass, and poor physical performance were categorized as having severe sarcopenia [1,9]. Measurement of transverse psoas muscle thickness (TPMT) for muscle quantity assessment: TPMT was defined as the distance between the right psoas muscle's cross-sectional diameter and its longest axial diameter at the L3 end plate [10]. In men, the cut-off value for predicting sarcopenia was 17.3 mm/m (sensitivity: 65.3%; specificity: 76.3%), and in women, it was 10.4 mm/m (sensitivity, 31.2 % ; specificity, 90.6 %). Handgrip Strength: A handheld dynamometer will be used to measure the isometric hand grip strength. With an accuracy of 0.1 kg, the device measures strength in kilograms. The task will need to be done twice by each participant with each hand. For these analyses, the best result from each hand will be used as a measure. According to the consensus report of the Asian Working Group for Sarcopenia, low grip strength was defined as 26 kg for men and 18 kg for women. Gait Speed Assessment 4-meter walk test. The route is laid out in a straight, well-marked manner. Participants are given instructions to walk at their normal pace from a still standing posture behind the starting line using a timer. Timing begins with the first foot movement and finishes with a foot crossing the finish line entirely. Canes and walkers are permitted if the individual utilises them regularly in his or her

everyday life. Gait speed is set at 0.8 m/sec as the cut-off value. After the diagnosis of Sarcopenia, patients have been followed up for 6 months to assess its impact on outcomes. Days until the date of last follow-up or date of death/decompensation were calculated from the time of the CT scan.

Outcomes

- Development or worsening of ascites
- Development of hepatic encephalopathy
- Variceal bleeding
- SBP or other infections
- Death

Statistical analysis

The data was imported into a Microsoft Excel spreadsheet and analysed with the SPSS 22 programme. Frequencies and proportions were used to represent categorical data. For qualitative data, the Chi-square test was utilised as a significance test. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to determine if the continuous data was normal. The mean and standard deviation were used to describe continuous data. For quantitative data, the ANOVA (Analysis of Variance) test of significance was used to determine the mean difference between more than two groups. After adopting all statistical principles, a p value (probability that the result is true) of 0.05 was judged statistically significant. To analyse the data, MS Excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) were used.

Results

Table 1: Prevalence of Sarcopenia

| | | Count | % |
|------------|-----------|-------|--------|
| Sarcopenia | Confirmed | 28 | 24.6% |
| | Severe | 10 | 8.8% |
| | Probable | 24 | 21.1% |
| | Absent | 52 | 45.6% |
| | Total | 114 | 100.0% |

In the study 24.6% had confirmed sarcopenia, 8.8% had severe, 21.1% had probable and 45.6% had No Sarcopenia.

Table 2: Age and Gender distribution with respect to Sarcopenia

| | | Sarcopenia | | | | | | | | Total | P value |
|-------------|----------|------------|------|--------|------|----------|------|--------|------|-------|---------|
| | | Confirmed | | Severe | | Probable | | Absent | | | |
| | | n | % | n | % | n | % | n | % | | |
| Age (years) | <40 | 3 | 15 | 2 | 10 | 2 | 10 | 13 | 65 | 20 | 0.030* |
| | 41 to 50 | 9 | 23.1 | 1 | 2.6 | 7 | 17.9 | 22 | 56.4 | 39 | |
| | 51 to 60 | 9 | 23.7 | 3 | 7.9 | 11 | 28.9 | 15 | 39.5 | 38 | |
| | >60 | 7 | 41.2 | 4 | 23.5 | 4 | 23.5 | 2 | 11.8 | 17 | |
| Sex | Female | 3 | 12 | 4 | 16 | 6 | 24 | 12 | 48.0 | 25 | 0.247 |
| | Male | 25 | 28.1 | 6 | 6.7 | 18 | 20.2 | 40 | 44.9 | 89 | |

In the study there was significant association between Sarcopenia and age distribution. Highest confirmed sarcopenia cases were seen in the age group >60 years (41.2%).

There was no significant association between Gender and Sarcopenia.

Table 3: Association between Sarcopenia and Child-Turcotte-Pugh (CTP)

| | | Sarcopenia | | | | | | | | P value |
|-----|------------------------|------------|---------|--------|---------|----------|---------|--------|---------|---------|
| | | Confirmed | | Severe | | Probable | | Absent | | |
| | | Count | Row N % | Count | Row N % | Count | Row N % | Count | Row N % | |
| CTP | Child Class A (5 to 6) | 4 | 9.8% | 4 | 9.8% | 8 | 19.5% | 25 | 61.0% | 0.104 |
| | Child Class B (7 to 9) | 13 | 35.1% | 2 | 5.4% | 7 | 18.9% | 15 | 40.5% | |
| | Child Class C (≥10) | 11 | 30.6% | 4 | 11.1% | 9 | 25.0% | 12 | 33.3% | |

In the study there was no significant association between CTP and sarcopenia. Among subjects with Child Class A, 9.8% had confirmed sarcopenia, 9.8% had severe sarcopenia, 19.5% had probable sarcopenia. Among subjects with Child Class B, 35.1% had confirmed sarcopenia, 5.4% had severe sarcopenia, 18.9% had probable sarcopenia. Among subjects with child Class C, 30.6% had confirmed sarcopenia, 11.1% had severe sarcopenia, 25% had probable sarcopenia. There was no significant association between CTP and sarcopenia.

Table 4: Association between Sarcopenia and MELD Score

| | | Sarcopenia | | | | | | | | P value |
|------------|-----|------------|------|--------|-----|----------|------|--------|------|---------|
| | | Confirmed | | Severe | | Probable | | Absent | | |
| | | n | % | n | % | n | % | n | % | |
| MELD Score | >15 | 15 | 30 | 6 | 12 | 12 | 24 | 17 | 34 | 0.162 |
| | ≤15 | 13 | 20.3 | 4 | 6.2 | 12 | 18.8 | 35 | 54.7 | |

In the study among subjects with MELD Score >15, 30% had confirmed sarcopenia, 12% had severe sarcopenia, 24% had probable sarcopenia and among subjects with ≤15 MELD Score, 20.3% had confirmed, 6.2% had severe, 18.8% had Probable sarcopenia. There was no significant association between MELD score and sarcopenia.

Table 5: Etiology and findings distribution with respect to Sarcopenia

| | | Sarcopenia | | | | | | | | P value | |
|------------------|---------------|------------|------|--------|------|----------|------|--------|------|---------|--------|
| | | Confirmed | | Severe | | Probable | | Absent | | | Total |
| | | n | % | N | % | n | % | n | % | | |
| Cause of CLD | AIH | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 100 | 1 | 0.249 |
| | Cryptogenic | 1 | 6 | 1 | 6 | 2 | 13.3 | 11 | 73.3 | 15 | |
| | Ethanol | 19 | 27.9 | 4 | 5.9 | 14 | 20.6 | 31 | 45.6 | 68 | |
| | HBV | 1 | 16.7 | 0 | 0 | 3 | 50 | 2 | 33.3 | 6 | |
| | HBV+Ethanol | 1 | 25 | 0 | 0 | 1 | 25 | 2 | 50 | 4 | |
| | HCV | 1 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | |
| | HCV + Ethanol | 1 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | |
| | NAFLD | 4 | 23.5 | 5 | 29.4 | 4 | 23.5 | 4 | 23.5 | 17 | |
| Wilson's | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 100 | 1 | | |
| Ascites grade | Grade 1 | 7 | 29.2 | 1 | 4.2 | 6 | 25 | 10 | 41 | 24 | 0.005* |
| | Grade 2 | 9 | 30 | 3 | 10 | 7 | 23.3 | 11 | 36.7 | 30 | |
| | Grade 3 | 9 | 47.4 | 4 | 21.1 | 3 | 15.8 | 3 | 15.8 | 19 | |
| | No | 3 | 7.3 | 2 | 4.9 | 8 | 19.5 | 28 | 68.3 | 41 | |
| History of bleed | Absent | 15 | 36.6 | 3 | 7.3 | 10 | 24.4 | 13 | 31.7 | 41 | 0.073 |
| | Present | 13 | 17.8 | 7 | 9.6 | 14 | 19.2 | 39 | 53.4 | 73 | |
| History of HE | Absent | 26 | 24.1 | 9 | 8.3 | 22 | 20.4 | 51 | 47.2 | 108 | 0.519 |
| | Present | 2 | 33.3 | 1 | 16.7 | 2 | 33.3 | 1 | 16.7 | 6 | |
| Comorbidities | DM | 8 | 34.8 | 4 | 17.4 | 5 | 21.7 | 6 | 26.1 | 23 | 0.034* |
| | No | 20 | 22.5 | 5 | 5.6 | 19 | 21.3 | 45 | 50.6 | 89 | |
| | RA | 0 | 0 | 1 | 100 | 0 | 0.0% | 0 | 0 | 1 | |
| | Thyroid | 0 | 0 | 0 | 0 | 0 | 0.0% | 1 | 100 | 1 | |

In the study there was no significant association between Ascites Grade and Sarcopenia, highest confirmed cases of sarcopenia were seen in Grade 3 Ascites patients.

There was significant association between Comorbidities and Sarcopenia, among DM subjects, 34.8% had sarcopenia.

There was no significant association between Cause of CLD, History of bleed and History of HE with Sarcopenia.

Table 6: Laboratory parameters with respect to Sarcopenia

| | Sarcopenia | | | | | | | | | | P value |
|----------------|------------|---------|--------|---------|----------|---------|---------|---------|---------|---------|---------|
| | Confirmed | | Severe | | Probable | | Absent | | Total | | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | |
| Hb - gms/dl | 9.09 | 1.91 | 9.43 | 2.14 | 9.33 | 1.53 | 10.43 | 2.62 | 9.78 | 2.27 | 0.043* |
| TC-cells/c.mm | 6769.64 | 3471.61 | 7188.0 | 3009.71 | 6822.08 | 3460.98 | 5878.88 | 3163.03 | 6411.07 | 3287.27 | 0.457 |
| PLT in lakhs | 1.43 | 1.08 | 1.13 | .55 | 1.12 | .59 | .99 | .55 | 1.14 | .74 | 0.078 |
| MCV | 87.57 | 14.28 | 86.90 | 11.10 | 87.04 | 9.56 | 88.03 | 10.98 | 87.61 | 11.48 | 0.983 |
| TB-mg/dl | 4.24 | 4.82 | 2.82 | 2.46 | 3.92 | 4.85 | 3.19 | 5.35 | 3.57 | 4.90 | 0.761 |
| DB-mg/dl | 2.20 | 3.02 | 1.83 | 1.92 | 1.99 | 2.71 | 1.36 | 2.45 | 1.74 | 2.61 | 0.536 |
| AST-U/L | 57.89 | 37.87 | 52.10 | 28.95 | 55.58 | 37.97 | 48.12 | 33.33 | 52.44 | 34.96 | 0.649 |
| ALT-U/L | 29.75 | 18.49 | 29.50 | 13.34 | 24.58 | 9.36 | 26.42 | 11.01 | 27.12 | 13.12 | 0.481 |
| ALP-U/L | 138.89 | 54.46 | 117.40 | 54.33 | 113.46 | 42.21 | 108.17 | 57.71 | 117.64 | 54.47 | 0.111 |
| TP-gm/dl | 6.49 | 1.00 | 6.47 | .64 | 6.47 | .82 | 6.66 | .81 | 6.56 | .85 | 0.743 |
| Albumin-gm/dl | 2.81 | .71 | 2.99 | .70 | 2.85 | .64 | 3.31 | .78 | 3.06 | .76 | 0.012* |
| PT | 18.21 | 5.87 | 17.22 | 3.16 | 18.90 | 6.47 | 17.46 | 5.20 | 17.92 | 5.49 | 0.717 |
| INR | 1.50 | .59 | 1.44 | .32 | 1.59 | .63 | 1.42 | .44 | 1.48 | .51 | 0.553 |
| Urea-mmol/l | 23.43 | 12.25 | 32.40 | 20.65 | 27.13 | 15.11 | 22.67 | 12.50 | 24.65 | 13.99 | 0.166 |
| Creatine-mg/dl | .86 | .36 | 1.10 | .65 | .93 | .34 | .84 | .26 | .89 | .35 | 0.149 |
| Na-mEq/l | 134.71 | 4.66 | 131.80 | 6.89 | 134.96 | 4.89 | 136.58 | 4.16 | 135.36 | 4.85 | 0.023* |
| K-mEq/l | 5.17 | 6.84 | 4.20 | .76 | 4.14 | .51 | 3.97 | .48 | 4.32 | 3.41 | 0.503 |
| CTP | 8.82 | 2.13 | 8.80 | 2.82 | 8.33 | 2.26 | 7.25 | 2.20 | 8.00 | 2.33 | 0.013* |
| MELD-Na | 17.29 | 6.79 | 19.30 | 8.23 | 17.50 | 7.48 | 14.33 | 5.80 | 16.16 | 6.79 | 0.052 |
| Hand Grip(kg) | 19.78 | 4.09 | 15.48 | 6.07 | 21.09 | 4.50 | 29.92 | 6.07 | 24.30 | 7.50 | <0.001* |

| | | | | | | | | | | | |
|------------------|-------|------|-------|------|-------|------|-------|------|-------|------|---------|
| TPMT at L3(mm) | 12.63 | 2.99 | 12.50 | 3.62 | 18.37 | 3.40 | 21.72 | 5.04 | 17.97 | 5.77 | <0.001* |
| Gait speed (sec) | 4.05 | .66 | 6.69 | 1.02 | 4.03 | .63 | 3.45 | .64 | 4.00 | 1.11 | <0.001* |

In the study there was significant difference in mean Hb, albumin, sodium, CTP score, Hand Grip, TPMT and Gait speed with respect to Sarcopenia.

- Mean Hb, Albumin was low in Confirmed Sarcopenia group
- Mean Na was low in Severe Sarcopenia group
- Mean CTP was high in Confirmed Sarcopenia group
- Mean MELD score was high in Confirmed Sarcopenia group
- Mean TPMT at L3 was lowest in Confirmed Sarcopenia group
- Mean Gait speed was highest in Confirmed Sarcopenia group

There was no significant difference in other parameters with respect to Sarcopenia

Table 7: Association between Sarcopenia and outcome at Follow up

| Follow up | | Sarcopenia | | | | | | | | | | P value |
|-----------|---------|------------|------|--------|----|----------|------|--------|------|-------|------|---------|
| | | Confirmed | | Severe | | Probable | | Absent | | Total | | |
| | | n | % | n | % | n | % | n | % | n | % | |
| Ascites | Grade 1 | 1 | 3.6 | 1 | 10 | 0 | 0 | 2 | 3.8 | 4 | 3.5 | <0.001* |
| | Grade 2 | 2 | 7.1 | 1 | 10 | 3 | 12.5 | 4 | 7.7 | 10 | 8.8 | |
| | Grade 3 | 15 | 53.6 | 7 | 70 | 6 | 25 | 5 | 9.6 | 33 | 28.9 | |
| | No | 10 | 35.7 | 1 | 10 | 15 | 62.5 | 41 | 78.8 | 67 | 58.8 | |
| Bleed | No | 21 | 75 | 7 | 70 | 19 | 79.2 | 49 | 94.2 | 96 | 84.2 | 0.053 |
| | Yes | 7 | 25 | 3 | 30 | 5 | 20.8 | 3 | 5.8 | 18 | 15.8 | |
| HE | No | 25 | 89.3 | 5 | 50 | 20 | 83.3 | 50 | 96.2 | 100 | 87.7 | 0.001* |
| | Yes | 3 | 10.7 | 5 | 50 | 4 | 16.7 | 2 | 3.8 | 14 | 12.3 | |
| Death | No | 23 | 82.1 | 5 | 50 | 21 | 87.5 | 50 | 96.2 | 99 | 86.8 | 0.001* |
| | Yes | 5 | 17.9 | 5 | 50 | 3 | 12.5 | 2 | 3.8 | 15 | 13.2 | |

In the study among subjects with confirmed sarcopenia, 3.6% had grade 1, 7.1% had grade 2 and 53.6% had grade 3 ascites. Among subjects with Sever Sarcopenia, 10% had grade 1 and Grade 2 and 70% had grade 3 ascites, among subjects with probable, 12.5% had grade 2, 25% had grade 3 ascites and among subjects with 3.8% had grade 1, 7.7% had grade 2 and 9.6% had grade 3 ascites. There was significant association between Ascites and sarcopenia.

In the study among subjects with confirmed sarcopenia, 25% had Bleeding. among subjects with sever sarcopenia, 30% had Bleeding, among subjects with probable sarcopenia, 20.8% had bleeding and among subjects without sarcopenia, 5.8% had bleeding. significant association was not found between Bleeding and sarcopenia.

In the study among subjects with confirmed sarcopenia, 10.7% had Hepatic encephalopathy, among subjects with sever sarcopenia, 50% had Hepatic encephalopathy, among subjects with probable sarcopenia, 16.7% had Hepatic encephalopathy and among subjects without sarcopenia, 3.8% had Hepatic encephalopathy. There was significant association between Hepatic encephalopathy and sarcopenia.

In the study among subjects with confirmed sarcopenia, 17.9% had mortality, among subjects with sever sarcopenia, 50% had mortality, among subjects with probable sarcopenia, 12.5% had mortality and among subjects without sarcopenia, 12.5% had mortality. There was significant association between mortality and sarcopenia.

Discussion

In our study, by applying the EWGSOP2 criteria and cut-offs, sarcopenia was diagnosed in 54.4% of the patients, which was also found in previous studies [11-13]. Given that the majority of our patients were Child-Pugh B and C, and the most common etiology was alcohol. In this study we found a significant difference in mean Hb, albumin, sodium, CTP score, Hand Grip, TPMT and Gait speed with respect to Sarcopenia. Even though other studies [13,14] say that sarcopenia is more common in men with chronic liver disease, our study shows that there is no statistical difference between men and women when it comes to sarcopenia. Women have more fat stores than men, and they use fat stores more often than muscle stores [15].

So, fat reserves are more depleted in women, while skeletal muscle mass is more depleted in men [16]. Also, differences in sex hormones may affect how skeletal muscle is turned over [17]. Some studies did not find any link between sarcopenia and the level of hepatic dysfunction (Child-Pugh and MELD), which are used to predict death [18,19,20]. Others, however, found a link and suggested that including sarcopenia assessment in Child-Pugh and MELD scores could make it easier to predict a patient's death when they have cirrhosis [19,20,21]. In this study, the sarcopenic group had a higher mean CTP and MELD score, but there wasn't a strong link between the two. The prognosis of sarcopenic cirrhotic patients is significantly worse than that of non-sarcopenic patients, with a higher mortality rate [14]. In our study, there was a statistically significant difference between the sarcopenic and non-sarcopenic patients. In the current study, we also found a significant association between sarcopenia and hypoalbuminemia, hyponatremia, Similar differences were found in the study of Montano-Loza et al. [20]. In our study it was found that Ascites, and Hepatic encephalopathy were significantly associated with sarcopenia. Similar findings were observed by the previous studies [22,23].

Limitations

This study has been done with a small sample size -114 and follow up time to check for the impact of sarcopenia is short.

Conclusion

The present study indicated that there was a high prevalence of Sarcopenia among individuals with chronic liver disease and it has associated with worsened clinical outcomes and reduced survival. Identification of probable sarcopenia provides a therapeutic window where early interventions would be beneficial and lead to prevention of complications like hepatic encephalopathy, ascites and reduced mortality.

Statement of Ethics

This study was conducted after approval by the institutional ethics committee, madras medical college and performed in accordance

with the Helsinki declaration. Written informed consent was obtained from all subjects.

Financial support and sponsorship

Nil

Conflicts of interest

Nil

List of abbreviations

CLD: Chronic Liver Disease
CTP: Child Turcotte Pugh
DM: Diabetes Mellitus
EWGSOP: European Working Group on Sarcopenia in Older People
HE: Hepatic Encephalopathy
LT: Liver Transplant
MELD: Model for End Stage Liver Disease
QoL: Quality of Life
TMPT: Transverse Psoas Muscle Thickness

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