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Study to ascertain the incidence of sarcopenia among end stage liver disease patients awaiting liver transplant in south Indian population

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Abstract

Background: Malnutrition is least highlighted in general population but interestingly found to have an adverse impact on outcomes following gastrointestinal surgeries. It is all the more important in prolonged ailments like chronic liver disease. With the current surge in liver diseases, prompt screening and nutritional planning will ensure well-being of the patient during the waiting period and will improve the outcome following liver transplantation. Apart from the routine screening methods using anthropometric measurements, computed tomography analysis of sarcopenia has facilitated precise and objective evaluation of nutritional status in a given patient.

Methods: A cross sectional study in which we have enrolled 40 end stage liver disease (ESLD) male patients who underwent CT abdomen and level of nutrition was assessed by subjective global assessment (SGA) along with standard anthropometry measurements and hand grip strength (HGS) was checked by digital dynamometer. The value at 2SD below mean of the mean psoas muscle mass of young healthy reference population was used to define sarcopenia and HGS to define low muscle strength cut off was also taken as per

the Asian Working Group of Sarcopenia (AWGS) 2019 guidelines.

Results: The mean psoas muscle area index and mean psoas muscle density index at 2SD below mean were 151.56 mm^2/m^2 and 0.28 Hu/kg respectively. The mean HGS was 27.16 (6.28). We have observed that the incidence of sarcopenia is 2.5% (95% CI:0%, &.3%) and all our ESLD patients had low muscle strength.

Conclusion: To ascertain incidence of sarcopenia among ESLD patients is of utmost importance to prevent malnutrition and its associated consequences. This is one of the few studies conducted for determining sarcopenia among patients from rural South India and the mean muscle area and muscle density index in our study were in concordance with the mean value of north Indian population. However, we strongly recommend early nutritional intervention and supervised diet therapy during the treatment process to improve the clinical outcome.

Keywords: End stage liver disease, liver transplantation, Psoas muscle index, Subjective global assessment

Introduction

Nutritional assessment plays a pivotal role in treatment planning, more so in patients suffering from chronic ailments. The traditional methods of nutritional assessment have been widely subjective, while the objective measurement techniques, especially using computed tomography (CT scan) has been in vogue lately. As per the initial reports, the term sarcopenia signifies an age-associated depletion in muscle mass [1] probably due to the occurrence in older individuals with reduced physical activity; hence sarcopenia was interchangeably used with frailty syndrome. Recent consensus has revised the definition, very specifically to address causes other than aging such as the chronic inflammatory disease process [2,3]. Sarcopenia represents a significant reduction of skeletal muscle mass and function. The presence of sarcopenia has been linked with adverse outcomes in patients like increased risk of falls, functional impairment, increased hospital stays, readmission rates thereby escalating morbidity and mortality [4-7]. In patients with ESLD, the imbalance between protein turnover and breakdown is red-flagged, from the beginning of treatment. In patients waitlisted for LT, measurement of sarcopenia serves as a tool to prevent complications in the pre-transplant period and sarcopenia predict the outcomes following LT [8-14].

Currently, some of the researchers are trying to address the issue of standardising region-specific cut-off for sarcopenia to recommend intervention protocols for sarcopenia. In this study, we propose to ascertain the incidence of sarcopenia by measuring psoas muscle area indices and muscle strength in patients diagnosed with ESLD waiting for LT.

Materials & methods

This is a cross sectional study performed from a prospective database maintained for patients diagnosed with ESLD considered for liver transplantation from May 2018 till May 2021. Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) is a tertiary care hospital catering to patients mainly with low socioeconomic status. Forty male patients with ESLD underwent nutritional screening using subjective global assessment (SGA) and HGS assessment using digital dynamometer. The components of the SGA assessment were (i) related to the medical history of the patients, such as recent changes in weight (in one month), food intake during one-month, gastrointestinal symptoms for the past two weeks, changes in functional capacity for one month, and

metabolic demand; (ii) based on physical examination, namely loss of subcutaneous fat and muscle wasting, oedema, and ascites. Patients are classified as normal, being grade A (score 7–14), moderately malnourished as grade B (score 15–28), and severely malnourished as grade C (score 29–35). HGS was checked on the dominant hand, using a digital hand dynamometer (Camry Model: EH101), and an average of three measurements has been taken, and the results were expressed in kilogram. As a part of the ESLD workup, all patients underwent cross-sectional imaging in the form of CT scan abdomen at least once and these scans were used for assessment of mean psoas muscle area (mm^2/m^2) and psoas muscle density (HU/kg). The mean muscle area was normalized to height to calculate muscle area index in mm^2/m^2, while the mean of muscle density was normalized to patient weight in kilograms to arrive at muscle density index expressed in Hounsfield unit / Kilogram (HU/kg) at both vertebral levels at L3 and L4. It is well known that muscle mass declines in the older age group and fat replacement can be assessed using the muscle density [6]. The psoas muscle area and density indices were measured at L3 and L4 vertebral levels as shown in Figures 1 and 2.

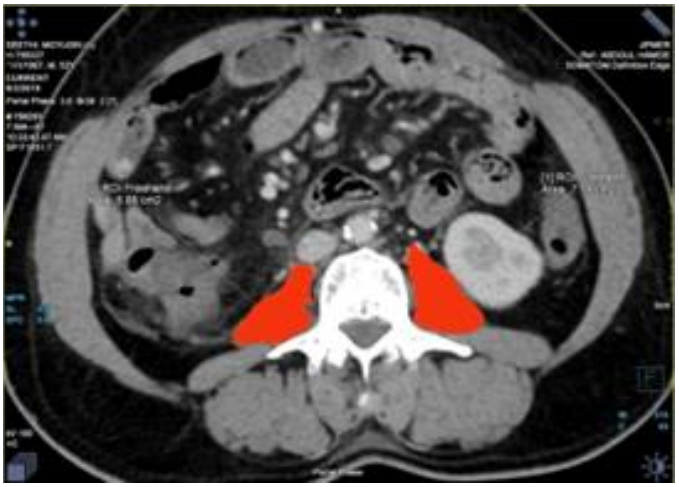

Fig 1: CT scan depicting psoas muscle mass area (cm^2) at L3 level

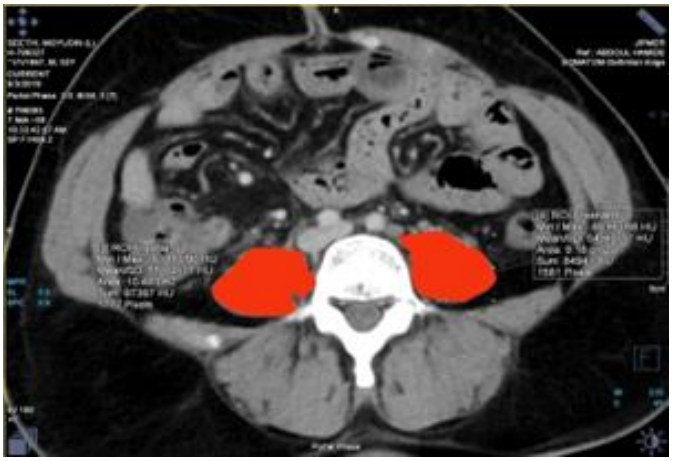

Fig 2: CT scan depicting psoas muscle density (Hu/u) at L4 level

Our study focuses on the aspect of sarcopenia in patients diagnosed with ESLD and compared psoas muscle indices in general population to define sarcopenia specific to our population, as taken from one Indian published study [5]. As per the definition of ASGS [3] values less than 2SD below the mean are considered abnormal.

Statistical Analysis

All the categorical variables were summarized using frequency and percentages. Incidence of sarcopenia was reported along with 95% confidence intervals. Continuous variables were summarized using mean (SD)/median (IQR) depending upon the normality of the data. Shapiro-Wilk's test was used for checking normality of the data. The statistical analysis was carried out using SPSS software (SPSS for Windows, version 19.0. Chicago: SPSS Inc.)

Results and discussion

A total of 40 male patients were included in the study. In order to compare with the general population to define sarcopenia, reference cut off was taken from previous published Indian study [5]. The distribution of demographic and clinical characteristics of patients with ESLD were shown in Table 1,2. In our current study, all

the ESLD patients were males. This is due to the high prevalence of alcoholism and resultant ESLD in males compared to females in India. More than 57.5% of patients were alcoholic, 27.5% were cryptogenic and 12.5% had hepatitis (B&C) and around 2.5% were due to other reasons. Mean age at presentation was 47.8 (11.04) years. The liver disease severity of the patients was categorized as per the Child-Pugh's score.12 (30%) patients belonged to Child A, 18 (45%) belonged to Child B and 10 (25%) were belonged to Child C. The mean MELD - Na score among the patients was 14.8 (4.8). Comorbidity was present in 22.5% of patients. 7 (17.5%) of patients were smokers. Among these patients, 28 (70%) had ascites and 27 (67.5%) had edema. Among the patients, 19 (47.5%) had normal BMI, and 3 (7.5%) had mild to severe thinness as per the World Health Organization (WHO) BMI classification. The mean mid upper arm circumference (MUAC) and mid arm muscle circumference (MAMC) were 26.63 cm (4.91) and 22.21 (3.14) cm, respectively. The mean triceps skinfold thickness (TST) and HGS were 14.08 (7.74) mm and 27.16 (6.28) kg, respectively. The HGS of all patients were in the <10th percentile range with low muscle strength. The mean nutritional score assessed by SGA was 14.95 (4.2). The nutritional score was further categorized as SGA-A normal, SGA-B moderately malnourished, and SGA-C severely malnourished. Among the patients, 21 (52.5%) were identified as moderately malnourished, and the remaining 19 (47.5%) were normal, and none had severe malnutrition as per nutritional assessment by SGA.

Table 1: Distribution of demographic and clinical characteristics of patients with ESLD (Categorical variables) (n=40)

Clinical characteristics	Category	Number (%)
Gender	Males	40 (100.0)
	Females	0 (0.0)
Etiology	Alcoholism	23 (57.5)
	Cryptogenic	11 (27.5)
	Hepatitis (B&C)	5 (12.5)
	Others	1(2.5)
Child-Pugh class	A	12 (30.0)
	B	18 (45.0)
	C	10 (25.0)
BMI	Normal	19 (47.5)
	Mild to Severe Thinness	3 (7.5)
	Over weight	10 (25.0)
	Obese	8 (20.0)
Co-morbidity	Yes	9 (22.5)
	No	31 (77.5)
Alcoholism	Yes	24 (60.0)
	No	16 (40.0)
Smoking	Yes	7 (17.5)
	No	33 (82.5)
Edema	Yes	27 (67.5)
	No	13 (32.5)
Ascites	Yes	28 (70.0)
	No	12 (30.0)
Nutritional score		
Nutritional status, SGA	A	19 (47.5)
	B	21 (52.5)

Table 2: Distribution of demographic and clinical characteristics of patients with ESLD (Quantitative variables) (n=40)

Clinical Characteristics	Mean (SD)/ Median (Q1, Q3) [$]
Age in years	47.8 (11.04)
Duration of alcoholism in years [$] (n=24)	9 (6,15)
Abstinence of alcoholism in months [$] (n=24)	12 (10, 22.5)
MELD-Na score	14.80 (4.79)
Weight (Kg)	72.19 (17.95)
Height (cm)	168.28 (5.50)
BMI	25.46 (5.76)
MUAC (cm)	26.63 (4.91)
MAMC (cm)	22.21 (3.14)
TST (mm)	14.08 (7.74)
HGS (kg)	27.16 (6.28)
Nutritional score (SGA)	14.95 (4.2)
Nutritional score (SGA)	14.95 (4.2)

[$]Expressed as Median (Q1, Q3)

The distribution of biochemical parameters of ESLD patients were expressed as mean (SD) and median (Q1, Q3) and is shown in Table 3. Most of the parameters were in normal range except total bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT). Erythrocyte sedimentation rate (ESR) was elevated with a median value of 29 (26, 38) and the mean PT/ INR was prolonged in these patients.

Table 3: Distribution of biochemical parameters of patients with ESLD (n=40)

Biochemical parameters	Mean (SD) / Median (Q1, Q3) [$]
Random blood sugar (RBS)[$] mg/dL	97 (83, 151.25)
Urea[$] mg/dL	18.5 (14, 23.75)
Creatinine[$.] mg/dL	0.72 (0.60, 0.94)
Sodium (n=34) [$.] mEq/dL	134 (132, 137.25)
Potassium (n=11) mEq/dL	4.41 (0.54)
Calcium (n=37) mg/dL	8.90 (0.80)
Phosphorous (n=35) mg/dL	3.15 (0.73)
Uric acid (n=32) mg/dL	4.05 (1.17)
Total Bilirubin mg/dL	2.70 (1.64)
Direct Bilirubin[$] mg/dL	0.75 (0.32,1.29)
Total Protein g/dL	7.34 (0.80)
Albumin g/dL	3.30 (0.80)
Aspartate transaminase (AST) IU/L	60.25 (23.07)
Alanine transaminase (ALT) [$] [IU]/L	31.50 (23.25,43.50)
Alanine phosphatase (ALP) IU/L	152.43 (59.48)
Gamma glutamyl transferase (GGT) (n=39) [$] [IU]/L	36.0 (25.0,71.0)
Iron (n=27) mcg/dL	108.96 (56.17)
Unsaturated iron binding capacity (UIBC) (n=25)	206.88 (134.71)
Total iron binding capacity (TIBC) (n=26) mcg/dL	307.50 (96.61)
T Transferrin saturation (TSAT) (n=24)	36.74 (24.78)
Prothrombin time (PT) (n=39) Sec	17.23 (4.57)
INR (n=39) [$]	1.38 (1.17,1.59)
Hemoglobin (g/dL)	11.87 (2.19)
Red blood cells (RBC) million/mm^3	3.96 (0.77)
White blood cells (WBC) 10^3	5.60 (1.76)

/mm^3	
Neutrophil[$]	61.3 (46.93, 65.95)
Lymphocyte[$]	25.8 (20.68, 31.95)
Neutrophil Lymphocyte ratio (NLR)[$]	2.4 (1.5, 3.1)
ESR (n=39) mm/hr	29 (26, 38)

[$] Expressed as Median (Q1, Q3)

The mean psoas muscle area index and the mean muscle density index in ESLD patients were 264.80 (56.62) and 0.74 (0.23) respectively and details has been provided in table 4. The mean muscle area and mean muscle density index of reference value of young organ donors from Indian published study were [378.8 (102.5) and 0.76 (0.14)]. As per the definition of AWGS 2019 guidelines [15], values less than 2SD below the mean are considered abnormal. However, only one patient was sarcopenic among ESLD patients when compared with 2 SD below the mean of the reference population; might be due to majority of the ESLD patients were moderately malnourished (52.5%) and 47.5% of patients were well nourished as per SGA score. The incidence of sarcopenia was found to be 2.5% (95% CI: 0%,7.3%) among male patients with ESLD.

Table 4: Psoas muscle area index (mm^2/m^2) and psoas muscle density index (Hu/kg) among ESLD patients with reference to Indian population

Parameter	Muscle area index (mm^2/m^2) in ESLD patients	Muscle density index (mm^2/m^2) in ESLD patients	Muscle area index (mm^2/m^2) Kapoor D et. al 2020 [5]	Muscle density index (mm^2/m^2) Kapoor D et. al 2020 [5]
n	40	40	160	160
Mean (SD)	264.80 (56.62)	0.74 (0.23)	378.8 (102.5)	0.76 (0.14)
1.64 SD below mean	171.94	0.36	210.7	0.53
2 SD below mean	151.56	0.28	173.8	0.48
5th percentile	196.56	0.43	220.7	0.56
10th percentile	202.23	0.47	239.05	0.58

The mean HGS of ESLD patients were 27.16 (6.28). As per AWGS 2019 and EWGSOP 2019 guidelines [15,16] for HGS depicted that mean HGS value less than 28 kg and 27 kg respectively were considered to be having low muscle strength. Hence, all ESLD patients in our study had low muscle strength (Table 5).

Table 5: HGS (Kg) among ESLD patients with reference to Indian population

Parameter	HGS in ESLD patients	AWGS 2019 Men [15]	EWGSOP 2019 Men [16]
N	40		
Mean (SD)	27.16 (6.28)	<28 kg	<27 kg
5th percentile	15.53		
10th percentile	20.20		

Discussion

Ever since the first report in 1989, sarcopenia has been extensively evaluated as a tool for nutritional assessment. Despite multiple consensus definitions and

diagnostic criteria, regional and ethnic factors tend to obscure their universal application, and hence it is imperative to establish region-specific cut-off values. Although it was comprehensive, it was not universally accepted and the AWGS in 2014 proposed a definition that is now being accepted worldwide [3]. The Foundation for the National Institutes of Health Sarcopenia Project proposed that sarcopenia should be defined based on muscle mass adjusted by the body mass index (BMI) with cut off values of (< 0.789 kg/m^2 men and < 0.512 kg/m^2 women) and HGS (< 26 kg men and < 16 kg women) [4]. In our study, the mean HGS was 27.16 (6.28) kg and all our patients had low muscle strength. A recent research publication analysing the normal patient population visiting a tertiary care hospital in North India, reported mean values for psoas muscle mass area index of 367.8 mm^2/m^2 for males. Similarly, the psoas muscle density index of 0.76 Hounsfield units/kg for males [5]. Although not standardized, a report published by Dodd's et al, suggests handgrip strength <27 kgs for males and <16 kgs for ladies as suggested as cut-offs for low muscle strength [7]. Another study by Carey et al [17] suggested cut off as <50 cm2/m2 and <39 cm2/m2 in males and females with chronic liver disease respectively. Both the studies have adopted the definition proposed by the AWGS, using the 2SD below mean as sarcopenic. Our study findings also showed low muscle mass and strength as per the AWGS 2019 guidelines [15].

The EWGSOP definition is based on specific parameters [2,16] The presence of low muscle mass and function along with gait speed and grip strength using handheld dynamometry were used to define Sarcopenia. The handgrip strength less than 0.8 m/sec was used as cut-off, which was confirmed with computerized tomography findings. Patients were stratified into 3 categories as pre sarcopenic means reduced muscle mass with normal strength and physical performance, sarcopenic have reduced muscle mass with less strength or performance and severely sarcopenic have reduced muscle mass with less strength and performance.

In addition, Sarcopenia is a valuable tool in the prediction of mortality at 1 year by multiple studies [18-22]. In a recent single centre study, the sarcopenia prevalence was reported to be 10%, 34% and 54% in child classes A, B and C respectively [11] and in our study 30% in child A, 45 % in child B and 25% in child C classes. High incidence of mortality is reported in sarcopenic patients awaiting LT in contrast to patients without sarcopenia [17]. Many nutritional tools are used to evaluate malnutrition among cirrhotic. Earlier research had related higher Child-Pugh scores and MELD scores with undernourished patients [23]. Our study also revealed a considerably higher rate of malnourishment in the higher Child-Pugh class (B) by SGA and MELD-Na scores.

Our study has focused to identify the incidence of sarcopenia and muscle strength in ESLD patients. Although, the study was done in 40 patients, significant conclusion can't be derived from this with respect to incidence of sarcopenia and the risk of malnutrition.

Conclusion

As opposed to the previously published data, our patient population is mostly from rural South India from a low socio-economic background. This is one of the few studies to assess sarcopenia among ESLD patients from Indian population. Incidence of severe malnutrition is minimal among our study population and hence the low observed incidence of sarcopenia. As half of the patients suffer from moderate to severe malnutrition, we strongly

recommend early nutritional planning and supervised nutritional support among ESLD patients in order to improve the outcome of LT.

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