Research Article

Sarcopenia in Chronic Liver Diseases

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Abstract

Background: Sarcopenia is defined as a muscle mass two standard deviations below the healthy young adult mean, and although it is associated with aging, it can also be present as a result of chronic diseases and malignancy, and it ultimately leads to decreased functional capacity and higher risk of morbidity and mortality in different groups of patients. **Aim of The work:** The aim of this study is to investigate the frequency of sarcopenia in HCV induced chronic liver diseases. **Subjects and Methods:** This case control hospital based study recruited patients with HCV-induced chronic liver disease of different functional grades according to Child-Pough and Meld scores and a group of healthy subjects as controls. All participants were assessed for demographic, hematological, and biochemical liver and renal profiles. Radiological diagnostic parameters of sarcopenia were determined by subjecting all participants to MDCT abdominal scan at the level of psoas muscle. **Results:** Using computed tomography measurement of psoas muscle thickness/height as a diagnostic validated test for sarcopenia, sarcopenia was detected in 52.5% of our liver cirrhosis patients. **Conclusion and future recommendations** In conclusion, sarcopenia is a common complication of cirrhosis and adversely affects survival, quality of life, and response to stress including infection and surgery.

Keywords: Sarcopenia, HCV, Cirrhosis.

Introduction

Sarcopenia is defined as a muscle mass two standard deviations below the healthy young adult mean[1], and although it is associated with aging, it can also be present as a result of chronic diseases and malignancy[2], and it ultimately leads to decreased functional capacity and higher risk of morbidity and mortality in different groups of patients[3]. Severe muscle wasting or sarcopenia is one of the most common and frequently hidden complications in patients with cirrhosis, which negatively impact survival, quality of life, and response to stressor, such as infections and surgeries[4] . The etiology of this condition is more complex than simple protein and calorie malnutrition. Cirrhosis also results in depleted glycogen stores and metabolic alternations that cause excessive protein catabolism, increased activation of the ubiquitin-proteasome pathway and inappropriate muscle autophagy. Satellite cell differentiation and proliferation is also reduced due to a combination of elevated myostatin level, reduced IGF-1 and hypogonadism[5]. Although alterations in body composition in cirrhosis have been reported using a number of methods, radiographic image analysis is believed to be the most precise technique to quantify muscle mass and define sarcopenia[6]. Computed tomography with one of the image analysis programs is being increasingly used since skeletal muscle can be directly viewed and quantified [7]. Measurements of psoas and abdominal muscle mass on CT images at L3 or L4 vertebra are used due to their relative independence from the activity level[8].

Aim of the work

The aim of this study is to determine the frequency of sarcopenia in HCV induced chronic liver diseases.

Patients and methods

This case control hospital based study was conducted in Internal Medicine department

and outpatient clinic at Minia University Hospital from March 2018 to October 2018.
The criteria for inclusion in this study: This study included cirrhotic patients post hepatitis C with Child Pugh classification A and B compared to a group of healthy subjects as controls.
The criteria for exclusion in this study: 1) Patients with DM. 2) Chronic kidney disease. 3) Age>50 years old. 4) Malignancy. 5) Rheumatologically- induced diseases. 6) Neurological diseases affecting muscles.
Ethical aspects: All patients and control subjects signed informed consent before participating in this study. Furthermore, this study was approved by the IRB of faculty of Medicine, Minia University. The study protocol is consistent with the 1975 Helsinki guidelines.

Methods: All patients and controls were subjected to the following: -
Thorough history taking: personal, current and past history with emphasis on historical features of the Subjective global assessment SGA such as the amount of weight loss through the previous 6 months, the patient's dietary intake and the presence of gastrointestinal symptoms experienced daily for at least 2 weeks (Gimenes et al., 2017).

Clinical Examination:
Anthropometric measures including Body weight and height with calculation of body mass index, mid-arm circumference, triceps skin fold thickness with calculation of mid-arm muscle circumference (MAMC), waist and hip circumferences and calculation of waist-to-hip ratio (WHR).

Examination of the physical performance using 4 meter walk gait speed test and physical assessment part of (SGA) including Subcutaneous fat, muscle wasting and fluid retension.

Laboratory investigations:-
Routine laboratory investigation including random blood glucose, liver and renal function tests were done by auto-analyzer, complete blood picture was determined by automated cell counter, prothrombin time was done using kits and viral markers including HBs Ag, HBC IGG, anti HCV antibodies ,and anti HIV antibodies were performed by ELISA.

Through history and laboratory tests patients were confirmed to have liver fibrosis using Fibrosis- 4 score = (Age (years) x AST level (U/L))/(platelets count (10 /L)x√ ALT level (U/L)). And severity of cirrhosis was assessed by Child-Turcotte-Pugh (CTP) Class and Score.

Radiological investigation
Abdominal ultrasonography.
CT scan of abdomen and determining markers of sarcopenia which are:
Psoas muscle thickness measured on CT to diagnose sarcopenia: transverse psoas muscle thickness, defined as diameter of the psoas muscle perpendicular to the longest axial diameter of the muscle at the umbilical level was measured, and then the value was normalized to the patient's height by dividing transverse psoas muscle thickness by height. This psoas muscle thickness/height (PMTH) was easily calculated as muscle mass. Psoas muscle density: lower density reflecting higher fat infiltration of muscles

Results
The study included a total of 180 subjects, 120 post hepatitis C virus liver cirrhotic patients that were reclassified functionally into 60 Child Pugh classifications A and 60 Child Pugh classification B. Sixty age and sex matched healthy subjects were also included as a control group. Using computed tomography measurement of psoas muscle thickness/height (PMTH) as a diagnostic validated test[9] for sarcopenia, it revealed detection of sarcopenia in 52.5% of our liver cirrhosis patients.

Analysis of data between the sarcopenic and non sarcopenic groups:
There were statistically significant differences between the sarcopenic and non-sarcopenic patients as regard weight, BMI, MAC, MAMC, MCC, WC and HC . The Sarcopenic patients had significantly lower BMI, MAC, MAMC, MCC, WC and HC with p value <0.001. The Sarcopenic patients compared to non sarcopenic group had highly statistically significant differ-

ence as regard the 4 meters walking test (4M W T) and subjective global assessment (SGA). There were statistically significant differences between patients with sarcopenia and those without it as regard mean psoas muscle density and psoas muscle thickness; p value < 0.001; for both.

Table [1]: The sarcopenic and non sarcopenic groups as regard CT findings.

		Sarcopenia		P value
		No	Yes	
		N=57	N=63	
RT P D (HFU)	*Range* *Mean ± SD*	(41-74) 53.5±6.5	(34-58) 47.3±6.7	**<0.001***
LT P D (HFU)	*Range* *Mean ± SD*	(41-64) 54.2±5.8	(27-59) 46.8±7.5	**<0.001***
Mean PD (HFU)	*Range* *Mean ± SD*	(42.5-67) 53.9±5.1	(36.5-57) 47.2±6	**<0.001***
PMT (Mm)	*Range* *Mean ± SD*	(23-43) 32.4±4.6	(15-30) 21.6±5.2	**<0.001***

- Independent samples T test for parametric quantitative data between the two groups
- Chi square test (if expected values within cell > 5) and Fisher exact test (if expected values within cell < 5). – *: Significant difference at P value < 0.05.

Table [2]: Comparison between three groups as regard anthropometric measures

		Control (Group C)	Child A (Group A)	Child B (Group B)	P value		
		N=60	N=60	N=60			
Weight	***Range*** ***Mean ± SD***	(53-98) 65.6±10.6	(54-90) 72.7±10.5	(45-87) 67.2±11.7	*0.001**		
					C vs A	*C vs B*	*A vs B*
					*0.001**	*0.708*	*0.018**
Height	***Range*** ***Mean ± SD***	(156-184) 169.5±7.5	(154-180) 168.2±7.2	(155-180) 164.7±6.5	*0.001**		
					C vs A	*C vs B*	*A vs B*
					0.565	*0.001**	*0.022**
BMI	***Range*** ***Mean ± SD***	(19.3-23.9) 20 ±1.6	(20.3-31.6) 25.7±3.6	(17.6-29.8) 24.7±3.4	*<0.001**		
					C vs A	*C vs B*	*A vs B*
					*<0.001**	*0.007**	*0.194*
BMI interpretation	***Under weight*** ***Normal*** ***Over weight*** ***Obese***	0(0%) 60(100%) 0(0%) 0(0%)	0(0%) 27(45%) 21(35%) 12(20%)	3(5%) 21(35%) 36(60%) 0(0%)	*<0.001**		
					C vs A	*C vs B*	*A vs B*
					*<0.001**	*<0.001**	*<0.001**
MAC	***Range*** ***Mean ± SD***	(25-36) 31.7±3	(18-36) 29.2±4	(20-38) 28.7±4.6	*<0.001**		
					C vs A	*C vs B*	*A vs B*
					*0.002**	*<0.001**	*0.700*
TSF	***Range*** ***Mean ± SD*** ***Median***	(4.5-25) 13.8±6.2 13.4	(12-30) 17.5±4.7 16.7	(15.6-38) 23.6±6.7 23			
					C vs A	*C vs B*	*A vs B*
					*0.001**	*<0.001**	*<0.001**
MAMC	***Range*** ***Mean ± SD***	(23.2-32.2) 27.4±2.8	(12.4-28.1) 23.7±3.7	(12.2-29.7) 21±4	*<0.001**		
					C vs A	*C vs B*	*A vs B*
					*<0.001**	*<0.001**	*<0.001**

Discussion

Our data indicated that the PMT and the more indicative PMTH ratio are significantly lower in patients compared to matched healthy controls, (p<0.0001). Our

study has found that sarcopenia is present in 52.5% of 120 Egyptian liver cirrhosis patients after hepatitis C virus infection by using computed tomography imaging according to sex specific PMTH measurement. Sarcopenia was detected in 50% of our study patients when sex specification is not considered.

Our data showed that in our patient population, the PMTH at 16mm/m is indicative of sarcopenia. Based on this mean of PMTH in all patient groups, sarcopenia was detected in 50% of all patients without sex specification.

Albeit, when relying upon sex specific PMTH mean, PMTH < 17.6 for males and PMTH < 11.56 for females, as indicative of sarcopenia, it was found that 52.5% of our patients are sarcopenic.

In our study, sarcopenia was detected in 28.5% in child A patients and 75% of our child B patients by SsPMTH index; while Sarcopenia was diagnosed in 24.4% of those with Child-Pugh A, 37.7% of those with Child-Pugh B, according to published criteria [10].
This finding promotes the fact that sarcopenia in chronic liver disease is progressively increased in severity with advancement in the stage of liver disease and has been associated with progression of chronic liver diseases (CLD).
MAC and TSF were obtained for all subjects and accordingly MAMC was calculated for all subjects and we found that MAC was significantly lower in patients than in control, however, TSF is higher in patients than in control.

Among the other indicators of sarcopenia are the tests for muscle strength which include the 4 MWT and the SGA which in our results were significantly more worse in patients compared to control (p<0.0001).
The prolonged 4 MWT has been reported by many authors [11], [12] and [13] to be a reliable accurate test to indicate sarcopenia.
The 4 MWT was significantly prolonged in our patients compared to control (*Mean* ± *SD*=4.9±1.2 versus 3.2±0.3 seconds P value <0.001). This may reflect the sarcopenia associated decreased muscle strength with chronic liver diseases.

Similarly, our data concerned with SGA indicated that all our control were in grade A, while in patients grade A was found in in 47.5%, grade B in 32.5% and grade C in 20% with significant difference, (P value <0.001), between patients and controls.
According to simple logistic regression analysis, the presence of sarcopenia was found, among other laboratory variables, to be a significant predictor for morbidity (Odds ratio:7, 95% CI : 3.1-15.6, P value <0.001). This finding was observed by many authors [7], [9] and [14].

Other authors[15], found that sarcopenia not only correlates with the clinical outcomes and survival of patients undergoing liver transplant, but also serves as a prognostic factor for candidates of liver transplantation and patients with hepatocellular carcinoma.
Dasarathy, S,[16], concluded that sarcopenia is a major complication of cirrhosis and adversely affects outcomes during the entire course of a cirrhotic patient's life.
Sarcopenia is associated with an increased hospital length of stay both pre- and post-transplant, [17].

Our data indicate that some of the simple anthropometric tests can be utilized to indicate the presence of sarcopenia as diagnosed by PMTH. These tests include MAC, MAMC, MCC which significantly correlated with the more technically CT consumed index (PMTH ratio), with P values <0.001. Furthermore, the prolonged 4 MWT can also indicate the presence of sarcopenia but the power of significance was low as indicated by linear regression analysis for prediction of PMTH.

Conclusion and future recommendations
In a conclusion, sarcopenia is a common complication of cirrhosis and adversely affects survival, quality of life, and response to stress including infection and surgery. Sarcopenia is a significant predictor for morbidity and chronic disease progression.. Based on our findings we recommend the following:

- Screening for malnutrition and sarcopenia in cirrhotic patients even using simple

anthropometric measures rather than using costly imaging modalities.

- Long-term studies to confirm relation between sarcopenia and mortality in chronic liver diseases.

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