ASSESSMENT OF NUTRITIONAL STATUS AND MANAGEMENT OF SARCOPENIA IN CHRONIC LIVER DISEASE

by
Dr Sipho Nkandlalalana

Facilitator
Prof C. Wendy Spearman

12-06-2023

Outline

- Introduction
- Pathophysiology
- Nutritional assessment
- Management
- Take home message

Introduction

- Sarcopenia is a term that was first described by Irwin Rosenberg in 1989, derives its origin from the Greek phrase sarco- meaning flesh/muscle and penia meaning loss.

- Sarcopenia is a muscle wasting syndrome that is defined by a reduction in muscle mass.

- It is often accompanied by a decreased muscle strength and function.

Clinical Medicine 2020 Vol 20, No 5: 489–92

Sarcopenia in Chronic liver disease

- It is an underappreciated complication of end stage liver disease, occuring with similar frequency as HE and more common than refractory ascites or variceal bleeding.

- Estimated to affect 30-70% of patients with end stage liver disease and over 300 000 people in the USA.

Aliment Pharmacol Ther 2016; 43: 765–777

Table 1 Classification of sarcopenia

Primary sarcopenia	
Age-related sarcopenia	When there is no other clear cause other than age
Secondary sarcopenia	
Activity-related sarcopenia	When the cause is being bedridden, an inactive lifestyle, ataxia (life), or weightless states
Disease-related sarcopenia	When there is severe organ failure (heart, lung, liver, kidneys, or brain), inflammatory disease, malignant tumor, or endocrine disease
Nutrition-related sarcopenia	When there is a lack of calorie and/or protein intake due to malabsorption, gastrointestinal disease, drugs that cause lack of appetite, or other reasons

Adapted from Age Aging 2014; 43: 748–59.

Malnutrition

- Malnutrition affects 20% of patients with compensated cirrhosis and 50% of adults with decompensated cirrhosis.
- According to clinical practice guidelines its synonymous with undernutrition.
- Malnutrition and sarcopenia are associated higher rates of complications such susceptibility to infections, hepatic encephalopathy and ascites.
- They are independent predictors of lower survival in cirrhosis and in patients undergoing liver transplantation.

World J Hepatol 2022 September 27; 14(9): 1694-1703

Pathophysiology of Sarcopenia in CLD

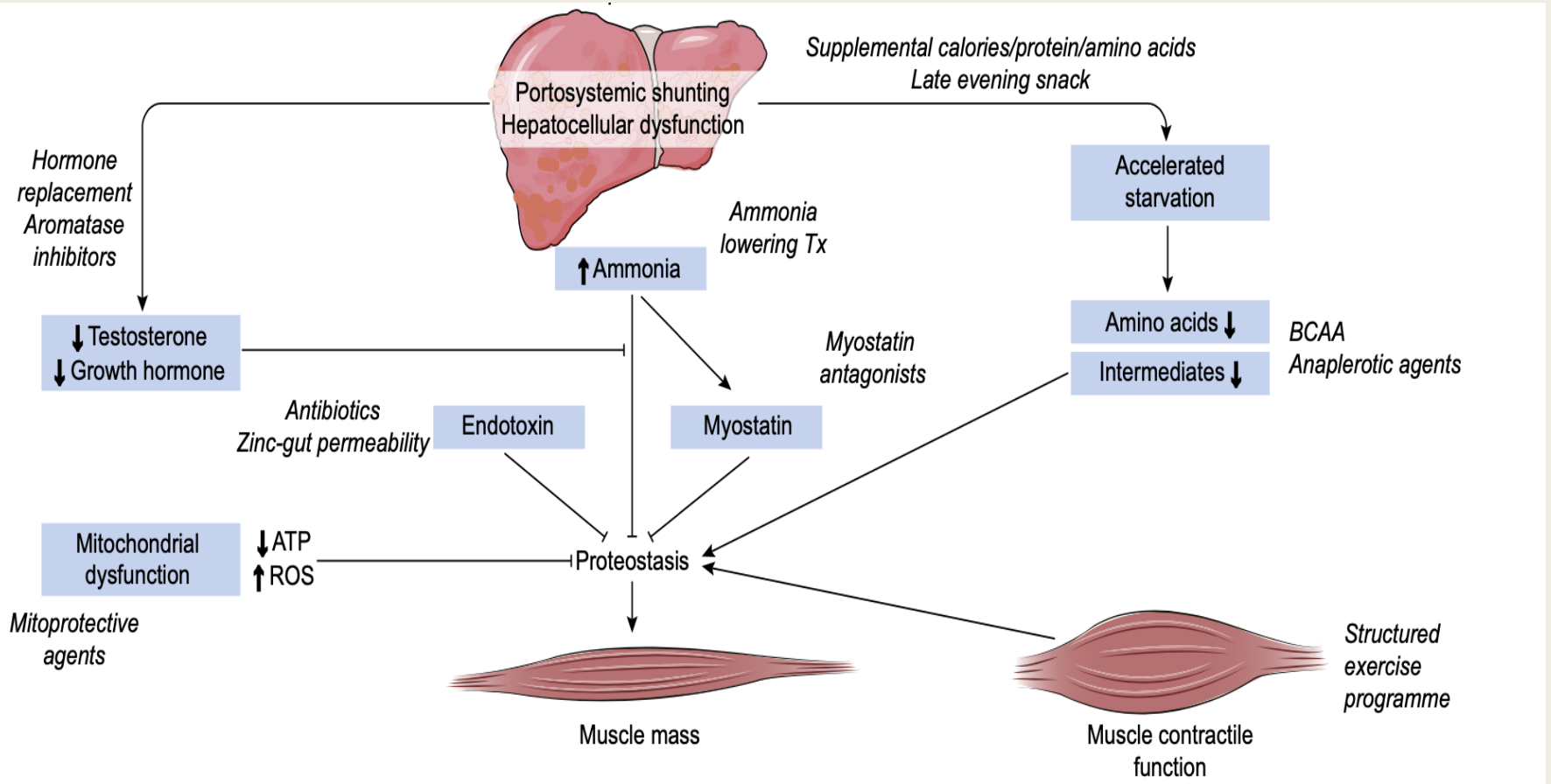

Fig. 2. Mechanisms and potential targets for anabolic resistance and dysregulated proteostasis resulting in sarcopenia and/or failure to respond to standard supplementation. Adapted from Dasarathy S. et al. 2016.[65] BCAA, branched chain amino acid; ROS, reactive oxygen species; Tx, treatment.

Journal of Hepatology **2019** vol. 70 | 172–193

Pathophysiology of Sarcopenia in CLD

- Due to multifactorial processes such as impairment in protein turnover, dysbiosis, malnutrition, hyperammonemia and chronic inflammation .
- Liver cirrhosis causes an accelerated state of starvation with increased gluconeogenesis, fat oxidation, ketogenesis and catabolic state.
- Also associated with alterations in the endocrine system such hypotestosteronemia and impaired insulin/IGF-1 pathway.

Life **2021**, *11*, 250. https://doi.org/10.3390/life11030250

DOI: 10.4254/wjh.v14.i9.1694

Figure 1 Factors contributing to malnutrition and sarcopenia in liver cirrhosis.

Nutritional assessment in cirrhosis

- Two criteria stratify patients as high risk for malnutrition- underweight (BMI <18.5 kg/m2) and advanced cirrhosis (child-Pugh C).
- The above criteria should have detailed nutritional assessment.
- All patients with advanced chronic liver disease not meeting above criteria should undergo nutritional screening.
- This is to identify patients at risks, confirm presence and severity of malnutrition.

Journal of Hepatology **2019** vol. 70 | 172–193

EASL™ The Home of Hepatology

Nutritional screening

- There are two liver disease specific nutritional screening tools:

The Royal Free Hospital-nutritional prioritizing tool (RFH-NPT) score and the liver disease under-nutrition screening tool.

- At risk for malnutrition during screening should undergo a detailed nutritional assessment.

- Detailed nutritional assessment include evaluation of muscle mass, global assessment tools and a detailed dietary intake assessment.

Nutritional assessment

- Detailed dietary intake includes a three day food diary or a 24 h dietary recall.

- Global assessment tools in cirrhosis include:

subjective global assessment (SGA) and the Royal Free Hospital-global assessment (RFH-GA).

- which are subjective, inaccurate and underestimates the prevalence of sarcopenia in cirrhosis.

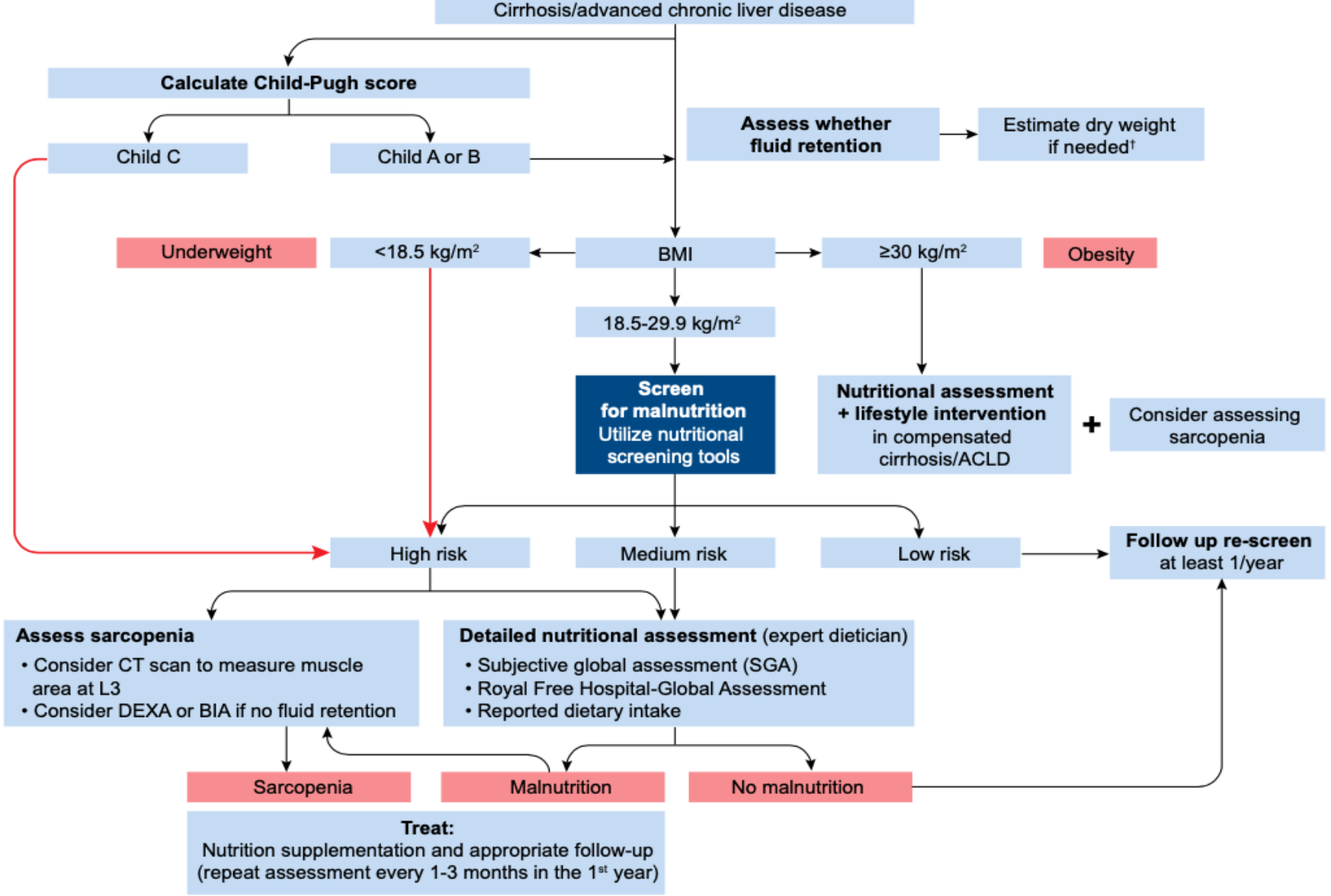

Fig. 1. Nutritional screening and assessment in patients with cirrhosis. All patients should undergo a rapid screening of malnutrition using validated, accepted tools. A liver specific screening tool which takes into consideration fluid retention may be advisable (Royal Free Hospital Nutritional Prioritizing Tool (RFH-NPT). Patients found to be at high risk of malnutrition should undergo a detailed nutritional assessment, and based on the findings they should receive either supplementation or regular follow-up. †In a case of fluid retention, body weight should be corrected by evaluating the patient's dry weight by post-paracentesis body weight or weight recorded before fluid retention if available, or by subtracting a percentage of weight based upon severity of ascites (mild, 5%; moderate, 10%; severe, 15%), with an additional 5% subtracted if bilateral pedal oedema is present. BIA, bioelectrical impedance analysis; BMI, body mass index; CT, computed tomography; DEXA; dual-energy X-ray absorptiometry.

Assessment of sarcopenia in CLD

- CT imaging is the gold standard for assessment of muscle mass in cirrhosis.
- Analyses cross-sectional area of abdominal skeletal muscles at L3 vertebrae, normalised to height to calculate the skeletal muscle index (cm2/m2).
- Standardized cut-off values of SMI are < 50 cm2/m2 in males and < 39 cm2/m2 in women to define sarcopenia.

HEPATOLOGY, Vol. 74, No. 3, 2021

Skeletal Muscle Index

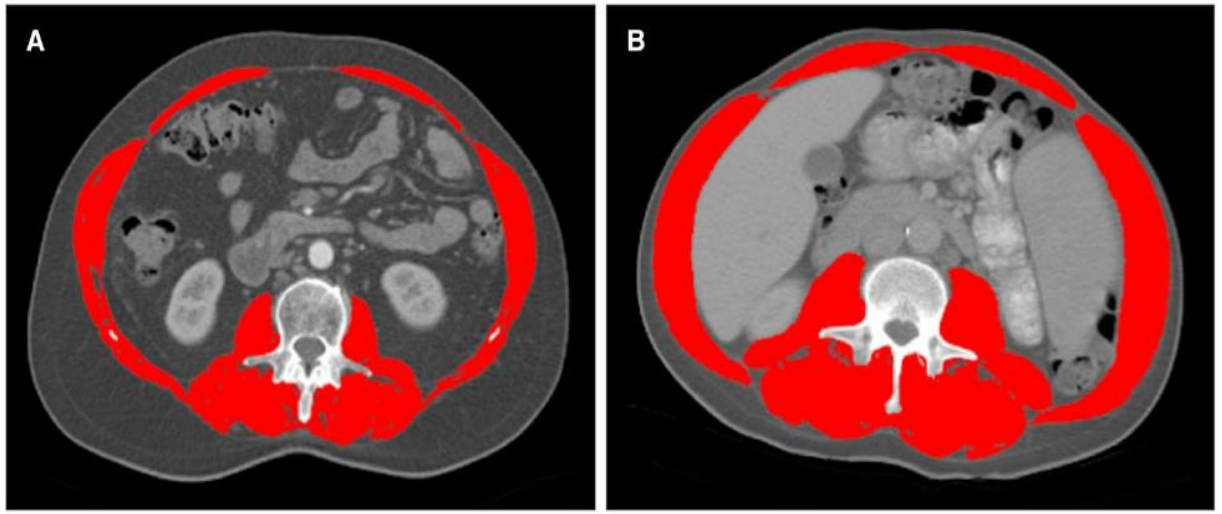

FIG. 1. Total muscle area quantification at the level of third lumbar vertebra using abdominal CT images from two male patients with cirrhosis. (A) and (B), respectively, present a patient who had low SMI (46 cm^2/m^2) and high SMI (60 cm^2/m^2) as indicated by the red shading.

Assessment of sarcopenia in CLD

- Cost and exposure to ionizing radiation limits routine use of CT *solely for the purpose of detecting sarcopenia* in many clinical settings.
- Other modalities include BIA , DEXA scan, Anthropometry and muscle ultrasound.
- Bioimpedance analysis (BIA) is affected by Fluid retention affecting the reliability of lean body mass estimates.
- Anthropometric measurements including BMI and MAMC are poor indicators of nutritional status due to inability to differentiate fat from muscle mass and fluid retention.

HEPATOLOGY, Vol. 74, No. 3, 2021

- Dual energy x-ray absorptiometry (DEXA) is unable to differentiate water from muscle , as result edema falsely elevates muscle mass measurements.

- Laboratory tests for evaluating nutritional status in the general population such as serum albumin are generally affected hepatic dysfunction.

Table 1. Summary of tests used to assess sarcopenia (muscle mass, strength, function)

Muscle mass	Muscle function	Muscle strength
Computed tomography (CT) L3 skeletal muscle index	Short physical performance battery test (SPPB)	Handgrip strength (HGS)
Magnetic resonance imaging (MRI)	Gait speed	Knee flexion/extension peak
Mid-arm muscle circumference (MAMC)	Timed get-up-and-go test[a]	torque strength[c]
Dual-energy X-ray absorptiometry (DEXA)	Liver Frailty Index (LFI)	Liver Frailty Index (LFI)
Muscle ultrasound	Aerobic exercise capacity:[b]	
Bioimpedance analysis (BIA)[a]	6-minute walk distance (6MWD)	
	Cardiopulmonary exercise testing (CPET)	

[a] = less frequently used tests; [b] = separate entity but relies on muscle function; [c] = research-based tests that are not yet validated in clinical practice.

Clinical Medicine 2020 Vol 20, No 5: 489–92

Micronutrient deficiency

- Assessment of micronutrients is recommended at least annually in decompensated cirrhosis.

- If assessment cannot be performed, an empiric course of oral multivitamins is advised

- These include fat soluble vitamins (Vit A, B, E,K), water soluble vitamins (folate and vitB12) and trace elements (magnesium, selenium and zinc).

Nutritional management principles in CLD

- Management should be done by multidisciplinary including a trained dietician.
- Approach with specific focus on lifestyle, nutrition, exercise and pharmacotherapy.
- Aim to achieve adequate caloric and protein intake.
- Adopted in sarcopenic obese patients with cirrhosis to achieve weight loss without compromising protein stores.

Journal of Hepatology **2019** vol. 70 | 172–193

EASL™
The Home of Hepatology

Nutrition

- Evidence suggests that high-energy, high protein diet improves nitrogen balance.
- Daily energy intake should aim for 35 kcal/kg. actual BW/day
- Daily protein intake should be 1.2-1.5 g/kg. actual BW/day to replenish sarcopenic state.
- The daily intake should be divided into frequent small meals and/or snacks 5-6 times a day.

Journal of Hepatology **2019** vol. 70 | 172–193

EASL™
The Home of Hepatology

Nutrition

- Preferable be split to three main meals: breakfast, lunch, dinner and three snacks: mid morning, mid afternoon, late evening.
- A late evening snack containing > 50 g of complex carbohydrates has been shown to improve nitrogen balance in end stage liver disease.
- Some studies support the use of BCAAs supplements in management of cirrhosis, especially when adequate nitrogen intake is not achieved.
- Recommended long-term oral BCAA supplement of 0.25 g/kg/d in advanced cirrhosis improves event free survival and quality of life.

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Nutrition

- Protein intake should not be restricted in patients with cirrhosis and Hepatic encephalopathy.
- Optimal daily protein intake should not be lower than the general recommendations in HE.
- Enteral nutrition via a nasogastric or parenteral feeding is permitted in patients with grade III-IV HE, also in those unable to take orally diet.
- A moderately hypocaloric diet (500-800 kcal/d) with adequate protein (> 1.5g/kg. ideal BW/d) in obese cirrhotics is recommended to achieve weight loss without compromising protein stores.

- Micronutrients such fat soluble vitamins , water soluble vitamins and trace elements should be repleted if deficient and reassessed after repletion.

- Sodium intake of 80 mmol day = 2g of sodium that corresponds to 5g of salt added to the diet is permitted.

Exercise

- A combination of aerobic exercise and body weight resistance is recommended to improve sarcopenia and exercise capacity.
- A recommendation of 30-60 min supervised walk and light weights lifting such as hand weights, two to three times per week.
- Aiming for a total of 150-200 minutes per week.
- There is no specific evidence supporting that physical therapy alone reverses sarcopenia.

Journal of Hepatology **2019** vol. 70 | 172–193

EASL™
The Home of Hepatology

Pharmacotherapy

- Use of testosterone replacement is recommended in man with cirrhosis and sarcopenia who have low testosterone to improve muscle mass.

- Relative contraindications to use of testosterone include a history HCC, malignancies or thrombosis.

- Experimental agents include ammonia lowering agents, myostatin antagonists, which are current topics of research with no human trials yet.

Journal of Hepatology **2019** vol. 70 | 172–193

- Other proposed interventions include reversal of portal HTN with TIPSS, liver transplantation.

- Baseline sarcopenia is a strong risk factor for failure to improve muscle mass after TIPS and worsening HE.

- There is no evidence for use of TIPS and liver transplant primarily for the management of sarcopenia or frailty.

Take home message

- Sarcopenia and malnutrition are underappreciated complications of chronic liver disease.
- All patients with advanced cirrhosis should undergo nutritional screening during admission or in the outpatient setting (1- 6 months).
- Early intervention is important to decrease waitlist morbidity and mortality and improves post transplant outcomes.
- There is still more research needed for pharmacological therapies for management sarcopenia in chronic liver disease.

- THANK YOU.

References

- Amritpal Dhaliwal and Matthew J Armstrong et al. Clinical Medicine 2020 Vol 20 No 5: 489-92. Sarcopenia in cirrhosis: A practical overview
- M. Sinclair, P. J. Gow, M. Grossmann et al. Aliment Pharmocol Ther 2016; 43: 765-777: Sarcopenia in cirrhosis- aetiology, implications and potential therapeutic interventions
- Chalermrat Bunchorntavakul, K. Rajender Reddy et al. Alimentary Pharmacol Ther. 2020;51:64-77: malnutrition/sarcopenia and frailty in patients with cirrhosis
- Puneeta Tandon, Maitreyi Raman et al. HEPATOLOGY, VOL. 65; NO. 3, 2017: A Practical Approach to Nutritional Screening and Assessment in Cirrhosis
- Sara Haj Ali, Awni Abu sneineh et Al. World J Hepatol 2022 September 27; 14(9): 1694-1703: Nutritional assessment in patients with liver cirrhosis
- EASL Clinical Practice Guidelines on nutrition in chronic liver disease. Journal of Hepatology 2019 vol. 70| 172-193