

AASLD 2021 Practice Guidance: Malnutrition, Frailty & Sarcopenia in Patients with Cirrhosis

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Introduction & Definitions

Cirrhosis-related factors

- Altered catabolic state & protein metabolism
- Hyperammonemia= myotoxic
- HE and ascites = strong association w/ frailty

Physical inactivity

Malnutrition

- Imbalance (deficiency or excess) of nutrients → measurable adverse effects on tissue/body form or function +/- clinical outcome (can be at any BMI)
- Royal Free Hospital Nutrition Prioritizing Tool = most consistently associated w/ malnutrition dx

Social determinants of health

Other factors

- Systemic inflammation
- Metabolic dysregulation
- Endocrine dysfunction (↓ testosterone, Δ in GH)
- Visceral fat accumulation
- Insulin resistance

Frailty

Clinical state of ↓ physiologic reserve & ↑ vulnerability to health stressors

- Physical frailty= impaired muscle contractile function
- ↓ physical function, ↓ functional performance, & disability
- Only 2 tools have evaluated the associations between longitudinal assessments & outcomes in patients with cirrhosis = Karnofsky Performance Status & Liver Frailty Index
- Compensated cirrhosis = assess q1 year
- Decompensated cirrhosis= assess q3-6 months

Etiological Factors

Clinical phenotypes

Health-related Quality of Life

↑ Decompensation

Death

Sarcopenia

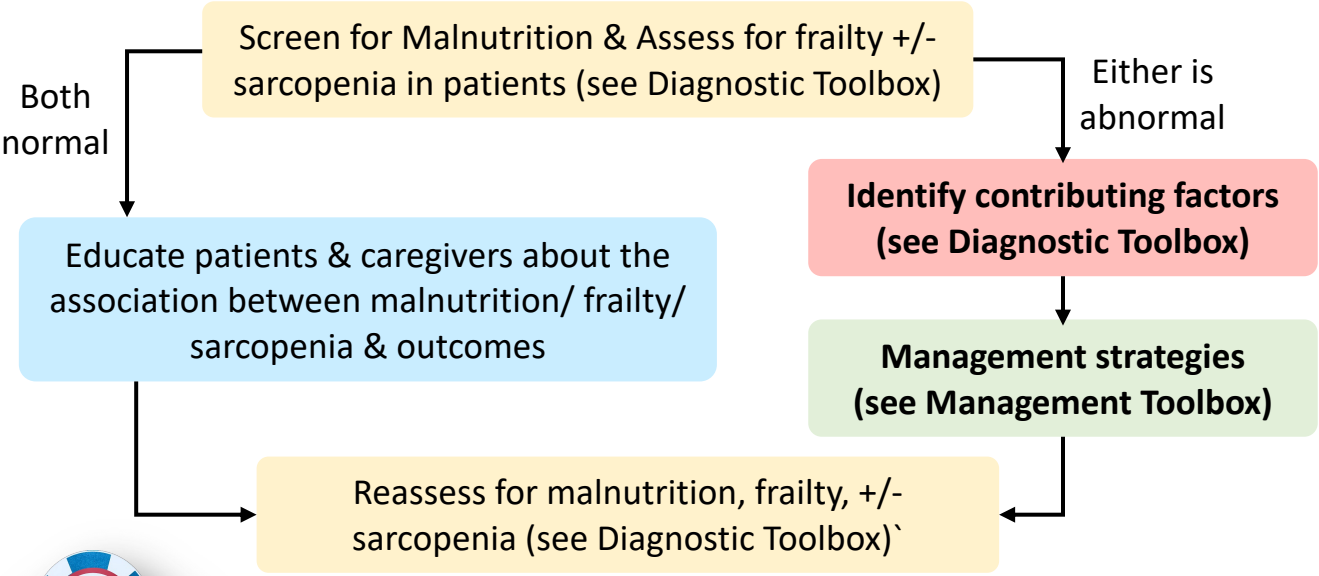
Progressive & generalized skeletal muscle disorder associated w/ ↑ likelihood of adverse outcomes including falls, fractures, disability, & mortality

- Phenotypic representation of loss of muscle mass
- CT imaging= gold standard for assessment of muscle mass (reported as SMI) in cirrhosis
 - CT not routinely ordered for this purpose
 - Most consistent & reproducible method
- Sarcopenic obesity = low sex-adjusted SMI with BMI >25 kg/m² → 20-35% prevalence
 - Independent risk factor for mortality

↑ Health care utilization

↓ Health-related quality of life

Adverse post-transplant outcomes








- Important Considerations in Management:**
- Treatment of inflammatory conditions that lead to cirrhosis (i.e. HCV, insulin resistance, obesity, ETOH use disorder)
 - TIPS placement for standard indications (i.e. ascites, acute variceal bleeding) may offer indirect benefit of improving muscle mass
 - Avoid PEG in patients with cirrhosis & ascites
 - Liver transplantation cannot be recommended specifically for the treatment of frailty or sarcopenia
 - Frailty and sarcopenia are not absolute contraindications against liver transplant

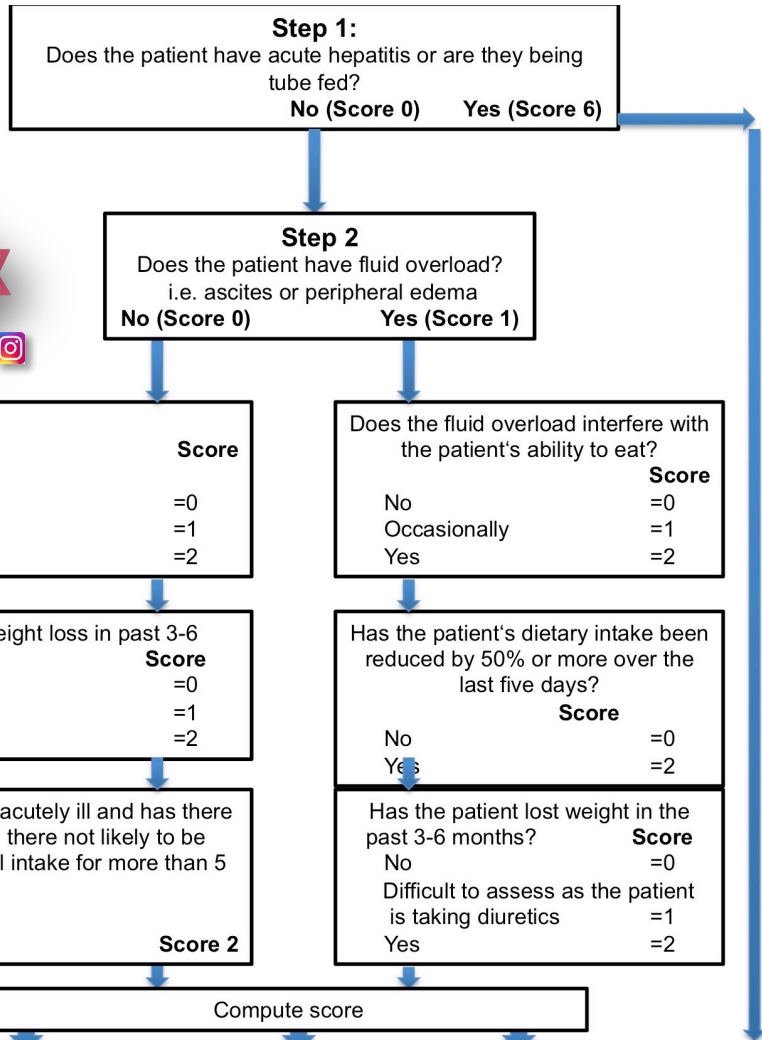


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Diagnostic Toolbox

	Clinician questions	Physical exam findings	Objective measures
<p>Screen for Malnutrition & Assess for frailty +/- sarcopenia</p>	<ul style="list-style-type: none"> ▪ Karnofsky Performance Scale ▪ Clinical Frailty Scale ▪ Activities of Daily Living ▪ Pediatric populations <p>-Royal Free Hospital-Nutrition Prioritizing Tool -Lansky play performance scale -Fried-exhaustion shrinkage, Pediatric Quality of Life Inventory</p> 	<ul style="list-style-type: none"> ▪ Muscle wasting (temples, clavicle, shoulder, scapula/ribs, quadriceps, interosseous muscles between the thumb & forefinger) ▪ Use of a walking aid ▪ Inability to stand up from chair or exam table independently, slowness 	<ul style="list-style-type: none"> ▪ CT scan LE skeletal muscle index (SMI) ▪ Liver frailty index ▪ Handgrip strength ▪ 6-minute walk test ▪ 4-meter gait speed ▪ Triceps skin-fold thickness (pediatrics) 
<p>Identify factors contributing to malnutrition, frailty, & sarcopenia</p>	<ul style="list-style-type: none"> ▪ Hunger Vital Signs (abnormal if either or both are true) -Within the past 12 months, we worried whether our food would run out before we got money to buy more -Within the past 12 months, the food we bought just didn't last and we didn't have money to get more. ▪ Physical inactivity -In the past week, on how many days have you done a total of 30 min or more of physical activity, which was enough to raise your breathing rate? 	<ul style="list-style-type: none"> ▪ Ascites ▪ Hepatic encephalopathy ▪ Poor dentition ▪ Dysgeusia 	<ul style="list-style-type: none"> ▪ MELD-Na ▪ Child Pugh Score ▪ Testosterone level (men) ▪ Data from patient's fitness tracker (e.g., daily steps, average HR) ▪ Micronutrient deficiency screen annually  

Royal Free Hospital- Nutritional Prioritizing Tool



Score 0 = Low Risk

- Routine clinical care
- Repeat screening weekly

Score 1 = Moderate Risk

- Routine clinical care
- Monitor food charts
- Encourage eating and offer snacks
- Repeat screening weekly

Score 2-7 = High Risk

- Discuss referral with dietician
- Monitor food charts
- Encourage eating and offer snacks
- Repeat screening weekly

Liver Frailty Index

Gender: Male Female

Time to do 5 chair stands: sec

Dominant hand grip strength (kg):




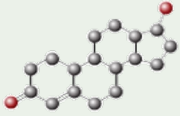
attempt 1: attempt 2: attempt 3: Avg: kg

Seconds holding 3 position balance:

Side: SemiTandem: Tandem: Total: sec

<https://liverfrailtyindex.ucsf.edu/>

Management Toolbox

Liver specific	Physical activity	Intake/Uptake	Other systems
 <ul style="list-style-type: none"> ▪ Management of disease etiology ▪ Management of ascites ▪ Management of hepatic encephalopathy (HE) 	<ul style="list-style-type: none"> ▪ Personalized activity prescription (guided by FITT): <ul style="list-style-type: none"> -<u>Frequency</u>- aerobic (4-7 d/wk); resistance (2-3 d/wk) -<u>Intensity</u>- use the talk test; 3 sets of 10-15 repetitions at a time -<u>Time</u>- Start low and build up Aerobic: 150 mins/wk Resistance: ≥ 1 day/wk -<u>Type</u>- aerobic, resistance, flexibility, & balance ▪ Consult a certified exercise physiologist or physical therapist 	 <ul style="list-style-type: none"> ▪ Calorie intake of ≥ 35 kcal/kg (non-obese) ▪ Protein intake of 1.2-1.5 g/kg body weight/d ▪ Micronutrient repletion ▪ Frequent small meals & minimize fasting (e.g., late night snack) ▪ Address barriers to intake (e.g., liberalize Na restriction as needed) ▪ Consult a registered dietician ▪ Protein intake should not be restricted in HE 	<ul style="list-style-type: none"> ▪ Testosterone replacement (men) ▪ Refer to health behavior specialist ▪ Diabetes control 

Borhofen, S.M., Gerner, C., Lehmann, J. et al. The Royal Free Hospital-Nutritional Prioritizing Tool Is an Independent Predictor of Deterioration of Liver Function and Survival in Cirrhosis. *Dig Dis Sci* 61, 1735–1743 (2016).

Lai JC, et al. Malnutrition, Frailty, and Sarcopenia in Patients With Cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021 Sep;74(3):1611-1644.

	Symptoms of Deficiency	Repletion	Comments/ Monitoring	
Fat Soluble Vitamins	Vitamin A	<ul style="list-style-type: none"> Ocular changes (eg, xerophthalmia, night blindness) Skin changes (eg, hyperkeratosis, phrynoderma, poor wound healing) Growth retardation 	Vitamin A 2,000- 20,000 IU PO QD depending on severity x 4-8 weeks	<ul style="list-style-type: none"> If not responding to replacement, consider replacing zinc Monitor levels w/ supplementation 2/2 risk significant toxicity (>120 mcg/dL)
	Vitamin D	<ul style="list-style-type: none"> Bone pain, muscle weakness, osteomalacia, anorexia, hair loss, poor wound healing Hypocalcemia, hypophosphatemia 	Vitamin D2 or D3 50,000 IU PO weekly x 8 weeks → 1,500- 2,000 IU daily maintenance	<ul style="list-style-type: none"> Goal >30 ng/mL Give calcium if low mineral bone density
	Vitamin E	<ul style="list-style-type: none"> Hemolytic anemia Neurologic deficits (eg, ataxia, peripheral neuropathy) Muscle pain 	Alpha-Tocopherol acetate 400- 800 IU PO QD	<ul style="list-style-type: none"> Less common than Vitamin A & D High doses antagonize vitamin A & adversely affect wound healing & platelet function
	Vitamin K	<ul style="list-style-type: none"> Bleeding, petechiae, purpura, ecchymosis Prolonged INR 	Phytonadione 1-10mg PO/SC/IV	<ul style="list-style-type: none"> Not stored so deficiencies occur rapidly
Water Soluble Vitamins	Thiamine (Vitamin B1)	<ul style="list-style-type: none"> Dry/ wet beriberi Wernicke encephalopathy/ Korsakoff syndrome Muscle weakness 	<ul style="list-style-type: none"> Asymptomatic: Thiamine 100 mg QD Suspected Wernicke: Thiamine 500mg IV TID x 2d → 250mg IV TID x 3d 	
	Niacin (Vitamin B3)	<ul style="list-style-type: none"> Pellagra: dry skin and bright red tongue, GI disturbance Neuro (eg, apathy, fatigue, headache, memory loss, abnormal behavior) 	Niacin 300- 1,000 mg PO QD	<ul style="list-style-type: none"> Blood levels are unreliable measures of deficiency Hepatotoxicity possible from excess dosage
	Pyridoxine (Vitamin B6)	<ul style="list-style-type: none"> Paresthesia, seizures Oral changes (eg, glossitis, ulcerations) 	Vitamin B6 100mg PO QD	<ul style="list-style-type: none"> Isolated deficiency uncommon Check vitamin B12 too High doses may reduce zinc absorption
	Folic Acid (Vitamin B9)	<ul style="list-style-type: none"> Muscle weakness, macrocytic anemia Oral changes (eg, glossitis, ulcerations) 	Folate 1-5mg PO QD	<ul style="list-style-type: none"> High doses may reduce zinc absorption
	Cobalamin (Vitamin B12)	<ul style="list-style-type: none"> Oral changes (eg, glossitis), muscle weakness Neuro (eg, peripheral neuropathy, gait disturbance, cognitive impairment) Hyperpigmentation, macrocytic/ pernicious anemia 	Vitamin B12 1,000 mcg IM q4wk or 1,000- 2,000 mcg PO daily	<ul style="list-style-type: none"> Low gastric acid secretion or s/p ileal resection= high risk for vitamin B12 deficiency and high doses may be required
	Ascorbic Acid (Vitamin C)	<ul style="list-style-type: none"> Perifollicular petechiae, keratosis, ecchymosis Impaired wound healing, anemia Oral changes (eg, gingivitis, glossitis) 	Vitamin C 500- 1,000 mg PO QD	<ul style="list-style-type: none"> Requirements increased in critical illness
Trace Elements	Zinc	<ul style="list-style-type: none"> Rash, alopecia, poor wound healing Myopathy Altered smell & taste Possible contribution to HE 	Elemental zinc 30-50 mg PO QD	<ul style="list-style-type: none"> Replacing zinc may result in normalization of vitamin A metabolism High doses can lead to copper deficiency Blood levels are only a crude index of whole-body zinc status
	Selenium	<ul style="list-style-type: none"> Cardiomyopathy, Myositis & cramps Skin changes (eg, alopecia, dry skin, erythema) 	Selenium 50- 100 mcg PO QD	<ul style="list-style-type: none"> Deficiency relatively rare
	Copper	<ul style="list-style-type: none"> Bone marrow suppression: microcytic anemia, leukopenia, pancytopenia Hypercholesterolemia, delayed wound healing Neuro (eg, neuropathies, ataxi) 	Copper 2-4 mg IV x 6d → 3-8mg PO QD until normalization of level or symptom resolution	<ul style="list-style-type: none"> Blood copper level is for screening deficiency Serum ceruloplasmin used to guide repletion, confounded by inflammation Bariatric bypass= risk factor for copper deficiency



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Table Courtesy of Tina Hang, MD
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