Nutrition in Cirrhosis

Angela D. Salvaña, MD
Nutritional Status in Liver Disease

- Predictor of morbidity and mortality
- Worsens as Child-Pugh status advances
- 50-90% prevalence of malnutrition among cirrhotics
- Greater incidence of complications such as ascites, hepatorenal syndrome, hepatic encephalopathy, infections, compromised respiratory function
- Associated with longer hospital stays
Etiology of Malnutrition

- Anorexia, poor oral intake
- Hypercatabolic state
- Malabsorption
- Altered macronutrient metabolism
Anorexia

- Nausea, bloating, fatigue, vomiting
- Dysgeusia associated with zinc deficiency
- Mechanical compression from ascites
- Increased TNF-alpha
- Increased leptin
- Dietary restrictions- sodium, preoperative fasting, protein restriction in hepatic encephalopathy
- Poor and irregular feeding among alcoholics
Hypercatabolic State

- From concurrent infection, sympathetic overactivity, inflammatory phenotype of liver disease, neural dysregulation

- Harris Benedict Equation/ Resting Energy Expenditure (REE)

Male = 66.5 + (13.75 x weight in kg) + (5.003 x height in cm) - (6.775 x age)

Female = 655.1 + (9.563 x weight in kg) + (1.85 x height in cm) - (4.676 x age)

Stress Factor 1.1-2.0

- Hypermetabolism is a REE > 120% of predicted

- 15-30% of cirrhotics are hypermetabolic
Malabsorption

- Portosystemic shunting causes nutrients to bypass liver
- Chronic pancreatitis in alcoholics
- Intraluminal bile acid deficiency, impairing micelle formation
- Alternate route for fat absorption via portal vein bypasses lymphatics, resulting in excess hepatic fat storage
Altered Macronutrient Metabolism

- Reduced ability to synthesize, store and break down glycogen
- Increased gluconeogenesis from fats and protein
- Insulin resistance with higher fasting plasma insulin, further depleting hepatic glycogen reserves
- Increased plasma glucagon, increasing gluconeogenesis
- Increased protein catabolism
Altered Macronutrient Metabolism

- Increased cytokines activate proteolysis causing muscle cell breakdown
- Cytokines also increase oxidation of branched chain aromatic acids
- Using oxidative fuels increases lipid oxidation
Micronutrient Deficiencies

- Zinc
- Magnesium
- Vitamin A
- Vitamin D
- Vitamin B6 and folate in HCV
- Vitamins B1 and B2 in patients undergoing therapy with pegylated interferon and ribavirin
Nutrition Assessment

- Subjective Global Assessment
- Anthropometric measurements
- Bioelectric impedance analysis
- Handgrip strength test
Subjective Global Assessment

- Simple, cost-effective bedside tool
- Information on intake, weight change, GI symptoms
- Examination for subcutaneous fat loss, muscle wasting, edema, ascites
- May underestimate frequency and severity of malnutrition
- Not predictive of outcome
### Subjective Global Assessment

<table>
<thead>
<tr>
<th>Medical History</th>
<th>A</th>
<th>B</th>
<th>C</th>
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<tbody>
<tr>
<td><strong>WEIGHT</strong></td>
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<tr>
<td>Wt change past 6 months</td>
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<td>0–6% loss</td>
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<td>5–10% loss</td>
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<td>&gt;10% loss</td>
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<td>Weight change past 2 weeks</td>
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<td>Amount...........</td>
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<tr>
<td>Increase to within 5%</td>
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<tr>
<td>Increase (1 level above)</td>
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<tr>
<td>No change, but below usual wt</td>
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<td>Increase to within 5–10%</td>
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<td>Decrease</td>
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<tr>
<td><strong>DIETARY INTAKE</strong></td>
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<td>No change; adequate</td>
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<tr>
<td>No change; inadequate</td>
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<tr>
<td>Change</td>
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<td>Suboptimal diet</td>
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<td>Full liquid</td>
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<tr>
<td>Hypocaloric liquid</td>
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<tr>
<td>Starvation</td>
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<tr>
<td>Intake borderline; increasing</td>
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<tr>
<td>Intake borderline; decreasing</td>
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<tr>
<td>Intake poor; no change</td>
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<td>Intake poor; increasing</td>
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<tr>
<td>Intake poor; decreasing</td>
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<tr>
<td><strong>GASTROINTESTINAL SYMPTOMS</strong></td>
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<tr>
<td>Frequency (never, daily, no. of times/week)</td>
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<tr>
<td>Duration (&lt;2wk, &gt;2wk)</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Vomiting</td>
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<tr>
<td>Diarrhoea</td>
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<tr>
<td>Anorexia</td>
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<tr>
<td>None; intermittent</td>
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<tr>
<td>Some (daily &gt;2 week)</td>
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<tr>
<td>All (daily &gt;2 week)</td>
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<tr>
<td><strong>FUNCTIONAL CAPACITY</strong></td>
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<tr>
<td>No dysfunction</td>
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<tr>
<td>Difficulty with ambulation/normal activities</td>
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<tr>
<td>Bed/chair-ridden</td>
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<td>Change past 2 week</td>
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<tr>
<td>Improved</td>
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<tr>
<td>No change</td>
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<tr>
<td>Riggressed</td>
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<table>
<thead>
<tr>
<th>Physical examination</th>
<th>A</th>
<th>B</th>
<th>C</th>
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</thead>
<tbody>
<tr>
<td><strong>SUBCUTANEOUS FAT</strong></td>
<td></td>
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<tr>
<td>Under the eyes</td>
<td>Slightly bulging area</td>
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<tr>
<td></td>
<td>Hollowed look, depression, dark circles</td>
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<tr>
<td>Triceps</td>
<td>Large space between fingers</td>
<td>Very little space between fingers, or fingers touch</td>
<td></td>
</tr>
<tr>
<td>Biceps</td>
<td>Large space between fingers</td>
<td>Very little space between fingers, or fingers touch</td>
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<tr>
<td><strong>MUSCLE WASTING</strong></td>
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<tr>
<td>Temple</td>
<td>Well-defined muscle/flat</td>
<td>Slight depression</td>
<td>Hollowing, depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Protruding/prominent bone</td>
</tr>
<tr>
<td>Clavicle</td>
<td>Not visible in Males; may be visible but not prominent in females</td>
<td>Some protrusion; may not be all the way along</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Square look; bones prominent</td>
<td></td>
</tr>
<tr>
<td>Shoulder</td>
<td>Rounded</td>
<td>No square look; acromion process may protrude slightly</td>
<td></td>
</tr>
<tr>
<td>Scapula/ribs</td>
<td>Bones not prominent; no significant depressions</td>
<td>Mild depressions or bone may show slightly; not all</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bones prominent; significant depressions</td>
<td></td>
</tr>
<tr>
<td>Quadriceps</td>
<td>Well rounded; no depressions</td>
<td>Mild depression</td>
<td>Depression; thin</td>
</tr>
<tr>
<td>Calf</td>
<td>Well developed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee</td>
<td>Bones not prominent</td>
<td></td>
<td>Thin; no muscle definition</td>
</tr>
<tr>
<td>Interoseous muscle between thumb and forefinger</td>
<td>Muscle protrudes; could be flat in females</td>
<td>Flat or depressed area</td>
<td></td>
</tr>
<tr>
<td><strong>OEDEMA</strong> (related to malnutrition)</td>
<td>No sign</td>
<td>Mild to moderate</td>
<td>Severe</td>
</tr>
<tr>
<td><strong>ASCITES</strong> (related to malnutrition)</td>
<td>No sign</td>
<td>Mild to moderate</td>
<td>Severe</td>
</tr>
</tbody>
</table>

### OVERALL SGA RATING

Adapted from: Detsky et al., 1994; Baxter Healthcare Corporation, 1993; McCann, 1996 (Ferguson, Bauer, Banks, Capra, 1996) ©
Tools for Assessing Oral Intake

- 24-hour recall - inaccurate with encephalopathy
- Food frequency questionnaire - no data on portion sizes
- Calorie count - subjective
- Food diary - time-consuming, assumes high level of literacy
Anthropometric Measures

- Men lose 20% of total body protein, women lose 11%
- Women lose a greater proportion of fat
- Muscle wasting more evident in temporal, clavicular, scapular areas
- Weight- affected by ascites
- Body mass index- need dry weight
- Mid-arm circumference- not a strong predictor of malnutrition
- Waist circumference
- Triceps skin-fold thickness
Bioelectric Impedance Analysis

- Estimates total body water, body fat, fat-free mass
- Phase angle alpha - relative contribution of fluid (resistance) and cellular membranes (capacitance)
- Lower phase angles indicate cell death
- Inaccurate with ascites
Handgrip Strength Test

- Malnourished if grip strength < 2 SD from mean of age and sex
- Predictor of uncontrolled ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome
- Needs dynamometer
Other Measures of Nutritional Status

- Albumin and prealbumin/transthyretin reflect severity of underlying illness and inflammation rather than nutrition status
- 24-hour creatinine excretion
Other Measures of Nutritional Status

- Total body potassium count
- Dual-energy x-ray absorptiometry - expensive
- In-vivo neutron activation analysis
- Isotope dilution
- Air plethysmography
- Body cell mass - validation tool
Cochrane Review of Nutritional Support in Liver Disease 2012

- 37 trials from studies collected over 3 decades
- Trials had a high risk of bias and potentially overestimated benefits
- Most analyses showed no significant differences
- Medical patients had improvements in ascites, infection and encephalopathy on oral nutrition
- Medical patients had improved nitrogen balance on enteral nutrition
- Medical patients had reduced bilirubin on parenteral nutrition
- Surgical patients had reduced ascites
Caloric Requirements

- ASPEN: 25-35 kcal/kg/day without encephalopathy, 35 kcal/kg/day with acute encephalopathy
- ESPEN: 35-40 kcal/kg/day for all patients with stable cirrhosis
- ESPEN: oral supplements or overnight enteral feeds as needed
- Caloric requirements based on dry weight or on ideal body weight if with ascites
- Large amount of calories lost from large-volume paracentesis
<table>
<thead>
<tr>
<th>Table 1. Nutrition Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Energy requirement, based on dry weight or determined ideal body weight, for patients with ascites</strong></td>
</tr>
<tr>
<td>ASPEN</td>
</tr>
<tr>
<td>Without encephalopathy</td>
</tr>
<tr>
<td>With acute encephalopathy</td>
</tr>
<tr>
<td>Stable and malnourished</td>
</tr>
<tr>
<td>ESPEN</td>
</tr>
<tr>
<td>All stable cirrhosis patients</td>
</tr>
</tbody>
</table>

**Macronutrients**

| Carbohydrate | 45%–65% of daily caloric intake per DRI |
| Protein |
| All patients, except acute encephalopathy | 1.0–1.5 g/kg per d |
| Acute encephalopathy | 0.6–0.8 g/kg per d |
| Fat | 25%–30% of daily caloric intake per DRI |

**Micronutrients**

| Fat-soluble vitamins (vitamins A, D, E, and K); all patients with compensated liver disease | Up to RDA levels<sup>a</sup> |
| Zinc | Up to RDA levels<sup>a</sup> |
| Selenium | Up to RDA levels<sup>a</sup> |
| Folic acid and thiamine; patients with history of alcohol abuse | Up to RDA levels<sup>a</sup> |
| Sodium; patients with ascites and edema | Restricted to <2 g per d |

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DRI, daily recommended intake; RDA, recommended dietary allowance.

<sup>a</sup>For patients without signs of deficiency.
Protein Intake

- High-protein diets well-tolerated by cirrhotics
- High-protein diets improve prognosis and mental status
- Protein restriction 0.5g/kg/day leads to increased protein catabolism
- Recommended protein intake 1-1.5g/kg/day
- Use dry weight or estimated dry weight
- Whole protein formulas generally recommended
Protein Intake and Hepatic Encephalopathy

- High protein diets well-tolerated by patients with moderate hepatic encephalopathy

- Temporary protein restriction in acute encephalopathy 0.6-0.8 g/kg/day until cause is eliminated

- ESPEN does not recommend even transient protein restriction
Carbohydrate Intake

- Carbohydrate restriction not recommended
- Carbohydrates should make up 45-65% of caloric intake
- Frequent meals and snacks reduce hypoglycemic episodes
Fat Intake

- 25-35% of calories from fat
- Medium-chain triglyceride supplementation only if abnormal 72-hour 100g fecal fat test
Fluid Balance

- Fluid intake 30-40mL/kg/day maintains fluid balance
- Dilutional hyponatremia develops due to decreased renal blood flow and greater free water accumulation
- Fluid restriction of 1.5L/day only if with ascites and hyponatremia <120mEq/L
Nutritional Supplementation

- In early cirrhosis normal food intake with nutritional counseling is adequate
- Vitamin A deficiency associated with increased risk of progression to hepatocellular carcinoma
- Association between vitamin D deficiency and Child-Pugh score
- Improved zinc levels associated with improvement in liver function
Nutritional Supplementation

- Vitamins A, D, E, and K, zinc and selenium supplementation for all cirrhotics
- If with chronic cholestasis, check serum levels of vitamin A and 25(OH)-D annually
- B12 levels falsely elevated due to inactive cobalamin analogues
- Alcoholics need folate and thiamine supplements
- Glutamine supplements metabolized to ammonia, avoid for now
Sodium Restriction

- Limit sodium to <2g/day if with edema and ascites
- More severe restriction will lead to poor compliance
Probiotics

- 25% of cirrhotics have small intestinal bacterial overgrowth
- Probiotics decrease intestinal pH, inhibiting growth of pathogenic bacteria
- Probiotics with fructo-oligosaccharides equal to lactulose for hepatic encephalopathy
- Generally safe and well-tolerated
- Strain and dose unknown
Branched-Chain Amino Acids

- Cirrhotics have lower concentrations of leucine, isoleucine, valine
- Cirrhotics have a low ratio of branched-chain amino acids (BCAAs) to aromatic amino acids (AAAs)
- AAAs increased due to impaired deamination
- BCAAs decreased due to use by skeletal muscle as an energy substrate
- Brain uptake of AAA tryptophan increased, causing neurotransmitter synthesis
BCAA Supplementation

- Reduces ammonia levels
- Inhibits muscle proteolysis
- Improves manifestations of recurrent hepatic encephalopathy
- Heterogeneity in clinical trials in mode of administration and methods of assessing hepatic encephalopathy
- Recommended by ESPEN because of increased albumin, and lower combined rates of decompensation and death
- Dose 0.25g/kg
- Long-term effects unlikely after stopping treatment
Nocturnal Supplements

- To decrease length of overnight fast
- To reduce gluconeogenesis and protein catabolism
- BCAA-rich snacks improve albumin
Feeding Methods

- 4-6 small meals per day
- If >10 hour fast, start IVF with 2-3g/kg/day glucose
- Nasoenteral tube if enable to meet energy goals orally
- If with gastroparesis advance tube beyond pylorus
Feeding Methods

- If hyponatremic use concentrated calorie dense feedings 1.5cal/mL
- Renal/low electrolyte formulas may be useful in hepatorenal syndrome
- Enteral nutrition may improve liver function, reduces complications and prolongs survival
Feeding Methods

- Parenteral feeding only if oral and enteral feedings are contraindicated or caloric intake is inadequate despite best efforts

- Proteins 1.2g/kg/day for compensated cirrhosis, 1.5g/kg/day for decompensated cirrhosis

- CHO 50-60%, lipids 40-50% of nonprotein energy requirements

- Lipid emulsions should provide 1g/kg/day or less of fat
Parenteral Nutrition

- Risk of catheter-related infections
- Parenteral feeding requires strict glucose monitoring
- Cyclic parenteral infusion if liver enzymes worsen with continuous infusion
- Do not overfeed
Obesity

- Obese cirrhotic patients are often protein depleted

- If BMI>25, gradual weight loss of 5-10% improves insulin sensitivity

- Weight loss achieved by creating deficit of 500-1000 calories/day

- Rapid weight loss with bariatric surgery or weight loss medications may cause decompensation

- Maintain intake during illness or hospitalization
Summary

- Malnutrition is common among cirrhotics
- Malnutrition is multifactorial
- Malnutrition has prognostic implications
- Bedside assessment tools can be useful
- Cirrhotics require more protein and calories
- Vitamin supplementation is a reasonable option
- Probiotics and BCAAs may be useful adjuncts
- More research is needed using hard endpoints in adequately powered studies


