Liver Disease

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Functions of the Liver: A Brief overview

- Largest organ in body, integral to most metabolic functions of body, performing over 500 tasks
- Only 10-20% of functioning liver is required to sustain life
Function of Liver

1. **Metabolic function**
   • Carbohydrate, protein, fat, vitamin and mineral metabolism

2. **Excretory function**
   • Bile pigment and bile salt excretion

3. **Protective function**
   • ammonia detoxify
   • clearances of hormones
The liver performs more than 500 functions

http://mygohealthy.com/liver-function-in-human-body
Liver Diseases

Classifications

• Duration
  – Acute vs Chronic
• Pathophysiology
  – Hepatocellular vs Cholestatic
• Etiology
  – Viral
  – Alcohol
  – Toxin
  – Autoimmune
• Stage/Severity
  – ESLD
  – Cirrhosis

- Viral hepatitis A, B, C, D, E (and G)
- Fulminant hepatitis
- Alcoholic liver disease
- Non-alcoholic liver disease
- Cholestatic liver disease
- Hepatocellular carcinoma
- Inherited disorders
Nutrition Assessment

- Assessment of nutrition, history and energy intake
- Assessment of body composition
- Biochemical assessment
- Micronutrients
Table 1. Causes of Malnutrition in Advanced Liver Disease.\textsuperscript{1,2,10-15}

<table>
<thead>
<tr>
<th>Inadequate oral intake of nutrients due to</th>
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<tbody>
<tr>
<td>• Anorexia</td>
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<tr>
<td>• Nausea/ emesis</td>
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<tr>
<td>• Bloating/ abdominal distention</td>
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<tr>
<td>• Abdominal discomfort</td>
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<tr>
<td>• Ascites</td>
</tr>
<tr>
<td>• Encephalopathy</td>
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<tr>
<td>• Delayed gastric emptying</td>
</tr>
<tr>
<td>• Restrictive diet (low sodium, low protein, fluid restriction)</td>
</tr>
<tr>
<td>• Dysgeusia (zinc deficiency)</td>
</tr>
<tr>
<td>• Alcohol intake</td>
</tr>
<tr>
<td>• Socioeconomic status</td>
</tr>
<tr>
<td>• Increase in leptin</td>
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<table>
<thead>
<tr>
<th>Metabolic disturbances (catabolism)</th>
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</thead>
<tbody>
<tr>
<td>• Alterations in glucose, lipid, and protein metabolism</td>
</tr>
<tr>
<td>• Altered pattern of energy consumption</td>
</tr>
<tr>
<td>• Insulin resistance</td>
</tr>
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<thead>
<tr>
<th>Malabsorption</th>
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<tbody>
<tr>
<td>• Bile acid deficiency (cholestasis)</td>
</tr>
<tr>
<td>• Small bowel bacterial overgrowth</td>
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</tbody>
</table>

| Decreased capacity of the liver to store nutrients |
Nutritional Implications: PCM associated Liver Dz

• Malnutrition reported in 65%-90% cirrhotic pts

• Poor Dietary Intake
  – Anorexia
  – Dietary Restrictions
  – Ascites
  – Gastroparesis
  – Zinc Deficiency
  – Increased proinflammatory cytokines

• Nutrient malabsorption/maldigestion
  – Cholestatic & non-cholestatic liver disease
  – Excessive protein losses
  – Pancreatic insufficiency

• Abnormal Metabolism
  – Hypermetabolism
  – Hyperglucagonemia
  – Increased protein metabolism
  – Increased lipid oxidation
  – Osteopenia
Causes of Malnutrition in Liver disease

- Inadequate oral intake
- Metabolic disturbances
- Malabsorption
- Decrease capacity of the liver to store nutrients
# Assessment of nutrition, history and energy intake

## Table 2. Tools for Assessing Oral Protein-Energy Intake in End Stage Liver Disease.

<table>
<thead>
<tr>
<th>Assessment Tool</th>
<th>Method</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-Hour recall</td>
<td>Participant recalls all foods and beverages consumed over the previous 24 hours</td>
<td>Low cost, Quick, No equipment required</td>
<td>May be inaccurate in those with poor memory or encephalopathy, Underreporting of portions and food items consumed may occur in women, those with body issues, or those who are overweight</td>
</tr>
<tr>
<td>Food frequency questionnaire</td>
<td>Participant is given a list of foods/beverages and indicates how frequently these foods are consumed</td>
<td>Low cost, Quick</td>
<td>May not represent foods typically consumed, High level of participant literacy required, Does not provide data on portion sizes or actual protein-energy intake</td>
</tr>
<tr>
<td>Calorie count</td>
<td>A healthcare professional calculates protein-energy intake based on foods consumed</td>
<td>Does not rely on patient’s recall, Low cost, No equipment required</td>
<td>Subjective, Portion sizes may not be standard or well documented, Often relies on nursing staff to complete</td>
</tr>
<tr>
<td>Food diary</td>
<td>Patient or caregiver records foods eaten</td>
<td>Low cost, Does not require special equipment, Can be very accurate</td>
<td>Requires instruction by provider, Requires a higher level of literacy, Subjectivity may lead to inaccuracies, Typically underestimates energy intake</td>
</tr>
</tbody>
</table>
# Assessment of body composition

<table>
<thead>
<tr>
<th>Tool</th>
<th>Method</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (BMI)(^2^7)</td>
<td>Weight (kg)/height (m(^2))</td>
<td>• Easy to perform • No equipment required • Cost free • Easily accessible • Low cost • Component involved in diagnosing metabolic syndrome</td>
<td>• Inaccurate in patients with ascites or edema unless dry weight is available • Not accurate in patients with ascites</td>
</tr>
<tr>
<td>Waist circumference(^2^8,2^9)</td>
<td>Measures abdominal visceral adiposity</td>
<td>• Low cost • Quick • Requires minimal equipment • Useful for assessing changes in muscle mass over time</td>
<td>• Not a strong predictor of malnutrition</td>
</tr>
<tr>
<td>Mid-arm circumference (MAC)(^2^7)</td>
<td>Mid-arm is measured to assess muscle mass</td>
<td>• Low cost • Quick • Requires minimal equipment • Number of sites tested improves accuracy</td>
<td></td>
</tr>
<tr>
<td>Skin fold(^2^0)</td>
<td>Skin folds are measured using a caliper at various points of the body • Used to assess body fat</td>
<td>• Low cost • Requires minimal equipment • Number of sites tested improves accuracy</td>
<td>• Requires training for proper use • Conflicting reports of accuracy in predicting malnutrition in cirrhosis • Was not found to correlate with Child-Pugh score</td>
</tr>
<tr>
<td>Hand grip strength (HGS)(^2^8,3^1)</td>
<td>A hand dynamometer is used to assess grip strength • Decreased grip strength is associated with malnutrition</td>
<td>• Low cost • Requires a hand-grip dynamometer • Found to better predict complications of cirrhosis over the Subjective Global Assessment, BMI, skin fold, MAC, and BIA</td>
<td></td>
</tr>
<tr>
<td>Body cell mass (BCM)(^2^4)</td>
<td>Validated marker used to assess body composition in the cirrhotic patient</td>
<td>• Very accurate even in the fluid-overloaded patient</td>
<td>• Expensive • Not readily available for clinical use and is typically used as a validation tool when analyzing other anthropometric assessments</td>
</tr>
<tr>
<td>Dual-energy X-ray absorptiometry (DEXA)(^3^0)</td>
<td>Assesses body composition through a low-dose X-ray</td>
<td>• Gold-standard test • Easily accessible • Correlates well with Child-Pugh score • Accurate in patients without ascites</td>
<td>• Expensive • Not readily available • Not accurate in patients with ascites</td>
</tr>
<tr>
<td>Bioelectrical impedance analysis (BIA)(^2^7,3^2,3^3)</td>
<td>Measures body composition via an electrical current that estimates total body water, fat-free mass, and body fat</td>
<td>• Noninvasive • Quick, convenient • Requires minimum compliance • Reliable • No water submersion</td>
<td>• Varies among men and women • Limited availability</td>
</tr>
<tr>
<td>Air plethysmography(^3^4,3^5)</td>
<td>Measures whole body density and subsequent calculation of body composition</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Anthropometric Assessment in End Stage Liver Disease.
Biochemical assessment

- Prealbumin (transthyretin) and albumin are produced in liver
- Due to location of their synthesis and response to inflammation, value of prealbumin and albumin is not an indicator for nutritional status
- Prealbumin and albumin are markers of prognosis, morbidity and mortality
- Prealbumin and albumin – correlate with Child-Pugh score
### Micronutrients in Liver Disease

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Relation to Liver Disease</th>
<th>Signs of Deficiency</th>
<th>Recommended Daily Intake</th>
<th>Normal Serum Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamine (Vitamin B&lt;sub&gt;1&lt;/sub&gt;)&lt;sup&gt;50,51&lt;/sup&gt;</td>
<td>Increased requirements with alcohol and larger carbohydrate (CHO) meals</td>
<td>Neurological (dry beriberi) Cardiovascular (wet beriberi) Ophthalmoplegia</td>
<td>1-2 mg</td>
<td>70-180 nmol/L</td>
</tr>
<tr>
<td>Folic acid&lt;sup&gt;50,51&lt;/sup&gt;</td>
<td>Increased requirements in alcoholism</td>
<td>Atrophic lingual papillae</td>
<td>0.4 mg</td>
<td>≥ 4 mcg/L</td>
</tr>
<tr>
<td>Pyridoxine (Vitamin B&lt;sub&gt;6&lt;/sub&gt;)&lt;sup&gt;50&lt;/sup&gt;</td>
<td>To prevent peripheral neuropathy and deficiency due to decreased intake</td>
<td>Cheilitis Weakness Seborrheic dermatitis Glossitis Angular stomatitis</td>
<td>2 mg</td>
<td>Pyridoxal 5-phosphate: 5-50 mcg/L Pyridoxic Acid: 3-30 mcg/L</td>
</tr>
<tr>
<td>Vitamin A&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Increased risk of deficiency due to malabsorption</td>
<td>Skin: scaling, follicular hyperkeratosis Night blindness Conjunctival xerosis</td>
<td>25,000 IU for 4-12 weeks (Repletion)</td>
<td>32.5-78 mcg/DL</td>
</tr>
<tr>
<td>Vitamin D&lt;sup&gt;48,49,50,51&lt;/sup&gt;</td>
<td>Increased risk of deficiency due to malabsorption and decreased UV light exposure Hepatic dysfunction</td>
<td>Osteomalacia Rickets Tetany</td>
<td>600-800 IU Vitamin D and 1200-1500 mg calcium</td>
<td>Total 25-Hydroxyvitamin D2 and D3 25-80 ng/mL</td>
</tr>
<tr>
<td>Vitamin E (α-tocopherol)&lt;sup&gt;56,58&lt;/sup&gt;</td>
<td>Increased risk of deficiency due to malabsorption</td>
<td>Neuropathy</td>
<td>400-1200 IU</td>
<td>5.5-17 mg/L</td>
</tr>
<tr>
<td>Vitamin K&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Necessary for blood clotting</td>
<td>Purpura Bleeding</td>
<td>90 mcg</td>
<td>0.13-1.19 ng/mL</td>
</tr>
<tr>
<td>Zinc&lt;sup&gt;56-61&lt;/sup&gt;</td>
<td>Deficiency may be a factor in hepatic encephalopathy</td>
<td>Nasolabial seborrhea Thinning hair Slow wound healing Dyseusia</td>
<td>50 mg elemental zinc (220 mg zinc sulfate)</td>
<td>0.66-1.1 mcg/mL</td>
</tr>
<tr>
<td>Selenium&lt;sup&gt;61,62&lt;/sup&gt;</td>
<td>May be deficient with alcoholism Supplement only if deficient; excess iron is toxic to the liver</td>
<td>Cardiomyopathy (rare)&lt;sup&gt;63&lt;/sup&gt; Pale skin Brittle finger nails Weakness, fatigue</td>
<td>45 mcg</td>
<td>70-150 ng/mL Males: 50-150 mcg/dL Females: 35-145 mcg/dL</td>
</tr>
<tr>
<td>Iron&lt;sup&gt;59&lt;/sup&gt;</td>
<td>May be deficient with alcoholism</td>
<td>Loss of appetite Stomachache Diarrhea, Confusion Depression, Weakness Vomiting, Nausea</td>
<td>6-8 mg</td>
<td>1.7-2.3 mg/dL</td>
</tr>
<tr>
<td>Magnesium&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Magnesium decreases with liver disease progression; often deficient with alcoholism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choline&lt;sup&gt;64&lt;/sup&gt;</td>
<td>Deficiency contributes to liver scarring and worsening liver disease</td>
<td>Impairment of verbal &amp; visual memory, hepatic steatosis</td>
<td>425-550 mg</td>
<td>7-20 umol/L</td>
</tr>
</tbody>
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Nutrition intervention

- Estimated protein and energy requirements
- Carbohydrate and fat requirements
- Fluid needs
Table 5. Protein-Energy Requirements in End Stage Liver Disease.

<table>
<thead>
<tr>
<th>A.S.P.E.N./ESPEN&lt;sup&gt;10,83&lt;/sup&gt;</th>
<th>25–40 kcal/kg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy requirement based on dry weight or determined ideal body weight if ascites is present</td>
<td></td>
</tr>
<tr>
<td>A.S.P.E.N.&lt;sup&gt;10&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Stable and malnourished</td>
<td>$\text{REE} \times 1.2–1.4$</td>
</tr>
<tr>
<td>Without encephalopathy</td>
<td>$\text{REE} \times 1.2–1.4$</td>
</tr>
<tr>
<td>1.0–1.5 g/kg/d protein</td>
<td></td>
</tr>
<tr>
<td>Acute encephalopathy</td>
<td>$\text{REE} \times 1.2–1.4$</td>
</tr>
<tr>
<td>0.6–0.8 g/kg/d protein</td>
<td></td>
</tr>
</tbody>
</table>
Estimated protein and energy requirements

<table>
<thead>
<tr>
<th></th>
<th>ESPEN$^{86}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stable cirrhosis patients</td>
<td>35–40 kcal/kg/d</td>
</tr>
<tr>
<td></td>
<td>1.0–1.5 g/kg/d protein</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Critically Ill$^{88}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU malnourished patients at risk for refeeding</td>
<td>15–20 kcal/kg/d</td>
</tr>
<tr>
<td>ICU for maintenance caloric support</td>
<td>1.2 g/kg/d protein</td>
</tr>
<tr>
<td>Catabolic</td>
<td>25–30 kcal/kg/d</td>
</tr>
<tr>
<td>Critically ill obese$^{89-92}$ (body mass index &gt;30)</td>
<td>1.5 g/kg/d protein</td>
</tr>
<tr>
<td></td>
<td>35–50 kcal/kg/d</td>
</tr>
<tr>
<td></td>
<td>Mifflin–St Jeor equation$^a$</td>
</tr>
<tr>
<td></td>
<td>Indirect calorimetry for comorbidities</td>
</tr>
<tr>
<td></td>
<td>1.5–2.0 g/kg/d protein ideal body weight</td>
</tr>
</tbody>
</table>
A fluid intake of 30–40 mL/kg/d maintains fluid balance in the average adult. An alternate method of determining fluid requirements is to provide 1 mL/kcal/d. In general, fluid gains (intake) should be in balance with fluid losses (output). Excess
Fluid needs

- Fluid loss
  - Diarrhea
  - Wound
  - Surgical drainage
  - Nasogastric tube drainage chest tubes
  - Ostomy output
  - Pancreatic secretion
  - Urine output
Table 6. Summary of Nutrition Management in End Stage Liver Disease.

Oral diet
- Small/frequent meals\(^{95}\)
- Bedtime snack or late evening meal\(^{96}\)
- High protein\(^{87,97}\)
- Avoidance of skipping meals\(^{95}\)
- ≤2000 mg sodium daily if ascites/edema present\(^{84,94,98,99}\)

Enteral nutrition
- Initiate if unable to meet protein-energy needs via PO diet\(^{83-85}\)
- Standard, energy-dense formula\(^{90}\)
- Nasoenteral tube\(^{86,101}\)
- Percutaneous gastrostomy tube relatively contraindicated\(^{101}\)
- Aspiration precautions\(^{102,103}\)

Parenteral nutrition
- Indicated only if nutrition needs cannot be met via oral and enteral routes\(^{10}\)
- Monitor glucose levels closely\(^{83}\)
- If hyperglycemia present, limit glucose to 2–3 g/kg/d
- ≤1 g/kg/d lipids\(^{104}\)
- Limit manganese and copper in setting of cholestasis\(^{10}\)
- Cyclic regimen recommended\(^{105}\)
- Concentrated solution to prevent fluid overload\(^{76}\)
Nutrition challenges in the cirrhotic patient

Optimizing Intake to Meet Nutrient Needs

Protein Supplementation and Hepatic Encephalopathy

Nutrition Support

Fluid Imbalance, Ascites, and Hepatorenal Syndrome
Optimal intake to meet nutrients needs

- Meal frequency and timing is upmost important
- Intake of 4-6 small portion sized meal daily is recommended to promote
  - protein-kcal intake
  - prevent longer periods of fasting
  - muscle sparing effect
Protein supplementation and hepatic encephalopathy

- BCAAs to AAAs
- Glutamine
- Prebiotics, prebiotic, synbiotic
Pathogenesis Theories:
False Neurotransmitter Hypothesis

- Liver cirrhosis characterized by altered amino acid metabolism
  - Increased Aromatic Amino Acids in plasma and influx in brain
  - Decrease in plasma Branched Chain Amino Acids
  - Share a common carrier at blood-brain barrier
  - BCAAs in blood may result in AAA transport to brain
Goals of MNT for HE

• Treatment of PCM associated with Underlying Liver Disease
  – Suppression of endogenous protein breakdown to reduce stress placed on de-compensated liver
  – Achieve positive nitrogen balance without exacerbating neurological symptoms
    • PCM associated with morbidity and mortality in cirrhosis (65-90% with PCM)
    • Severity of pcm positively correlated with mortality

• PCM associated with morbidity and mortality in cirrhosis (65-90% with PCM)
Treatment of Hepatic Encephalopathy

• Various measures in current treatment of HE
  – Strategies to lower ammonia production/absorption
    • Nutritional management
      – Protein restriction ???
      – BCAA supplementation
    • Medical management
  – Medications to counteract ammonia’s effect on brain cell function
    • Lactulose
    • Antibiotics
  – Devices to compensate for liver dysfunction
  – Liver transplantation
Nutritional Management of HE

• Historical treatment theories
  – Protein Restriction
  – BCAA supplementation

• Goals of MNT
  – Treatment of PCM associated with ESLD
Protein and HE Considerations

• Presence of malnutrition in pts with cirrhosis and ESLD clearly established
• No valid clinical evidence supporting protein restriction in pts with acute HE
• Higher protein intake required in CHE to maintain positive nitrogen balance
• Protein intake < 40g/day contributes to malnutrition and worsening HE
  – Increased endogenous protein breakdown   NH3
• Susceptibility to infection increases under such catabolic conditions
Other Considerations

• Vegetable Protein
  – Beneficial in patients with protein intolerance <1g/kg
    • Considered to improve nitrogen balance without worsening HE
  – Beneficial effect d/t high fiber content
    • Also elevated calorie-to-nitrogen ratio

• BCAA Supplementation
  – Effective or Not?
Protein supplementation and hepatic encephalopathy

- BCAAs to AAAs
- *Glutamine*
- Prebiotics, prebiotic, synbiotic
Glutamine has been touted by the dietary supplement industry as an amino acid that promotes muscle development. However, glutamine is metabolized into ammonia and may increase plasma ammonia levels in cirrhotic patients.\textsuperscript{116} Therefore, despite the unclear significance of an elevated ammonia level, it may be advisable for cirrhotic patients to avoid glutamine supplements until more information is available.
Protein supplementation and hepatic encephalopathy

- BCAAs to AAAs
- Glutamine
- Prebiotics, prebiotic, synbiotic

ASPEN 2013
In 2 recent randomized controlled studies involving patients with HE, participants were treated with a synbiotic preparation containing a *Bifidobacterium* species plus fructo-oligosaccharide (FOS). A reduction in serum ammonia levels plus an improvement in protein tolerance and neurological symptoms was seen in the synbiotic group.\textsuperscript{117,118} Another study showed similar improvements in patients receiving a probiotic yogurt without FOS.\textsuperscript{119}
Fluid imbalance, ascites

- sodium restriction in addition to diuretic therapy.
- Sodium is commonly restricted to 2 g/day
- More severe limitations may be imposed; however, caution is warranted because of the limited palatability of these diets.
- Adequate protein intake is also important when a patient undergoes frequent paracenteses
Hyponatremia

- Fluid intake is usually restricted to 1 to 1.5 L/day, depending on the severity of the edema and ascites.
- A moderate sodium intake should be continued because excessive sodium intake will worsen fluid retention and the dilution of serum sodium levels.
Glucose alterations

- Patients with diabetes should receive standard medical and nutrition therapy to achieve normoglycemia
- Patients with hypoglycemia should eat frequently to prevent this condition
Fat malabsorption

• If significant steatorrhea is present, replacement of some of the long-chain triglycerides (LCTs) or dietary fat with medium-chain triglycerides (MCTs) may be useful.

• Because MCTs do not require bile salts and micelle formation for absorption, they are readily taken up via the portal route.

• Some nutrition supplements contain MCTs, which can be used in addition to liquid MCT oil.
Relax

ขอบคุณค่ะ

Relax !!!

ขอบคุณค่ะ