Nutrition in Cirrhosis

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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

Name:
Date:

Medical History			A	B	C
WEIGHT	Usual weight……	Current weight……			
Wt change past 6 months	Amount weight loss…….	% weight loss……			
0-<5% loss			*		
5-10% loss				*	
>10% loss					*
Weight change past 2 weeks		Amount……			
No change; normal weight			*		
Increase to within 5%			*		
Increase (1 level above)			*	*	
No change, but below usual wt				*	
Increase to within 5-10%				*	
Decrease					*
DIETARY INTAKE					
No change; adequate			*		
No change; inadequate				*	
Change	**Duration of change**……..				
Suboptimal diet				*	
Full liquid				*	
Hypocaloric liquid					*
Starvation					*
Intake borderline; increasing			*		
Intake borderline; decreasing				*	
Intake poor; no change				*	*
Intake poor; increasing				*	
Intake poor; decreasing					*
GASTROINTESTINAL SYMPTOMS					
	Frequency (never, daily, no. of times/week)	Duration (<2wk, >2wk)			
Nausea	……	……			
Vomiting	……	……			
Diarrhoea	……	……			
Anorexia	……	……			
None; intermittent			*		
Some (daily >2 week)				*	
All (daily >2 week)					*
FUNCTIONAL CAPACITY					
No dysfunction	Duration of change ……..		*		
Difficulty with ambulation/normal activities				*	
Bed/chair-ridden					*
Change past 2 week					
Improved			*		
No change				*	
Regressed					*

Physical examination	A	B	C
SUBCUTANEOUS FAT			
Under the eyes	Slightly bulging area		Hollowed look, depression, dark circles
Triceps	Large space between fingers		Very little space between fingers, or fingers touch
Biceps	Large space between fingers		Very little space between fingers, or fingers touch
MUSCLE WASTING			
Temple	Well-defined muscle/flat	Slight depression	Hollowing, depression
Clavicle	Not visible in Males; may be visible but not prominent in females	Some protrusion; may not be all the way along	Protruding/prominent bone
Shoulder	Rounded	No square look; acromion process may protrude slightly	Square look; bones prominent
Scapula/ribs	Bones not prominent; no significant depressions	Mild depressions or bone may show slightly; not all areas	Bones prominent; significant depressions
Quadriceps	Well rounded; no depressions	Mild depression	Depression; thin
Calf	Well developed		Thin; no muscle definition
Knee	Bones not prominent		Bones prominent
Interosseous muscle between thumb and forefinger	Muscle protrudes; could be flat in females		Flat or depressed area
OEDEMA (related to malnutrition)	No sign	Mild to moderate	Severe
ASCITES (related to malnutrition)	No sign	Mild to moderate	Severe
OVERALL SGA RATING	**A**	**B**	**C**

Adapted from: Detsky et al., 1994[8]; Baxter Healthcare Corporation, 1993; McCann, 1996 (Ferguson, Bauer, Banks, Capra, 1996)©

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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 1. Nutrition Recommendations

Energy requirement, based on dry weight or determined ideal body weight, for patients with ascites	25–40 kcal per d
ASPEN	
Without encephalopathy	25–35 kcal/kg per d
With acute encephalopathy	35 kcal/kg per d
Stable and malnourished	30–40 kcal/kg per d
ESPEN	
All stable cirrhosis patients	35–40 kcal/kg per d
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[a]
Zinc	Up to RDA levels[a]
Selenium	Up to RDA levels[a]
Folic acid and thiamine; patients with history of alcohol abuse	Up to RDA levels[a]
Sodium; patients with ascites and edema	Restricted to <2 g per d

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

[a]For patients without signs of deficiency.

Cheung et al. Clin Gastro Hepatol 2012; 10:120.

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

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