Nutrition in Chronic Liver Disease

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Objectives

1. Describe contributing factors toward malnutrition in advanced liver disease
2. Describe the consequences/complications of malnutrition in liver disease
3. Describe methods to conduct nutritional assessment in patients with advanced liver disease
4. Describe practical nutritional interventions to improve outcomes in advanced liver disease

Question #1

Which of the following is the most important contributor to malnutrition in cirrhosis?

a) Poor Oral intake
b) Malabsorption
c) Altered Metabolism
d) None of the Above

Question 2

- What is the best way to assess nutritional status in patients with chronic liver disease?
  a) BMI
  b) Prealbumin
  c) Harris-Benedict Equation
  d) Subjective Global Assessment
  e) None of the above

Question 3

- Which of the following target goal calorie and protein requirements is the most appropriate for a patient with decompensated cirrhosis:

a) 20-25 kcal/kg ; 1.0 g/kg/protein/day
b) 25-30 kcal/kg ; 1.0 g/kg/protein/day
c) 30-35 kcal/kg; 1.2 g/kg/protein/day
d) 35-40 kcal/kg; 1.5 g/kg/protein/day

Case

- 68 y.o. male with Alcoholic Liver Cirrhosis
  - Weight 59.3 kg Ht 1.8 m BMI=18.3
  - Moderate ascites, mild pitting edema
- Is this patient malnourished? On what basis?
- What do you need to do to undertake a nutritional assessment?
- What are his calorie and protein requirements for weight maintenance?
- What else might you need to consider in the nutritional plan?

Prevalence of Malnutrition in CLD

- Rare in most ACUTE liver disease and chronic liver disease without cirrhosis
- Up to 20% with compensated disease
- 65-90% with advanced disease
- Nearly 100% in patients awaiting liver transplant

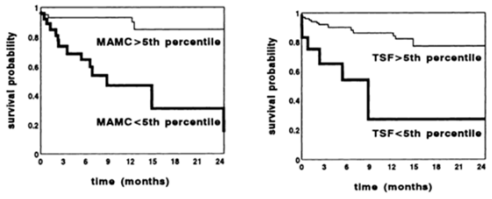
McCullough AJ et al. 1997; AJG:92:734

Consequences of Malnutrition in CLD

- Increased Rates of Portal Hypertensive Complications
- Decreased Survival Rates
- Increased rates of transplant complications
- Increased time on ventilator post-operatively
- Higher incidence of graft failure
- Decreased survival post-op

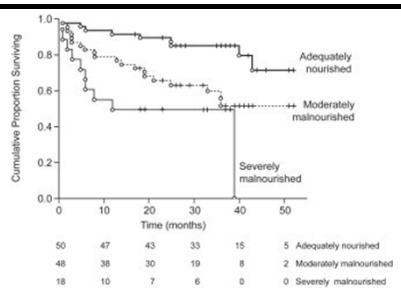
Figueirado Et al. Transplantation 2000;70:1347

Survival Probability Similar to Malignancy



Caregaro et al. Am J Clin Nutr 1996; 63: 602 - 609

Survival and Nutritional Status in Cirrhosis



Hepatology
Volume 44, Issue 4, pages 823-835, 27 SEP 2006 DOI: 10.1002/hep.21358
http://onlinelibrary.wiley.com/doi/10.1002/hep.21358/full#fig2

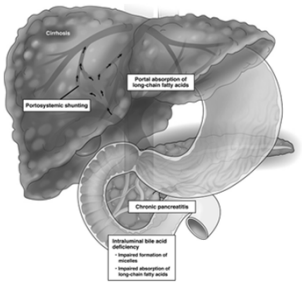
What are the contributing Factors to Malnutrition?

- Poor Oral Intake
  - Anorexia
  - Nausea, early satiety
  - Altered Taste
  - Dietary and Fluid Restriction (Taste Fatigue)
  - Low-grade encephalopathy

Contributing Factors to Malnutrition in CLD

- Malabsorption
  - Bile salt deficiency
  - Small Bowel Bacterial Overgrowth
  - Portal hypertensive enteropathy
  - Pancreatic insufficiency
  - Portosystemic Shunting

Portal causes for malabsorption



Contributing Factors to Malnutrition CLD

Metabolic Abnormalities

- Hypermetabolism
- Hypo-metabolism

• Resting Energy Expenditure (REE) is the amount of energy an individual uses to perform vital organ functions, free of activity and digestion	■ 70% of cirrhotics have a REE that is similar to predicted values ■ 15-30% of cirrhotics are hypermetabolic

Hypermetabolism

- Causes not entirely clear
  - Most recent study 268 patients did NOT associate hypermetabolism
    - Sex
    - Etiology
    - Disease severity
    - Ascites
    - Tumours
  - Inconsistent with results from older studies that reported energy expenditure increased among patients with ascites or HCC

Peng et al. Am J Clin Nutr 2007;85:1257-1266

Predisposing Factors - Hypermetabolism

- Altered Macronutrient Metabolism
  - Glucose intolerance / hyperinsulinemia / insulin resistance
  - Decreased glycogen storage
  - Increased protein catabolism
  - Decreased meal-induced protein synthesis
  - Accelerated gluconeogenesis from amino acid
  - Increased Lipid catabolism

Scolapio et al JPEN 2000;24:150

How do we assess a cirrhotic patient's nutrition status?

Subjective Global Assessment

History
- Weight loss (>5-10% in preceding 6 months)
- Changes in Food Intake
- GI symptoms
- Functional Capacity

Physical Examination
- Loss of subcutaneous fat
- Muscle Wasting (quadriceps, deltoids)
- Edema
- Sacral edema
- Ascites

SGA

A – Well nourished

B – Moderately malnourished

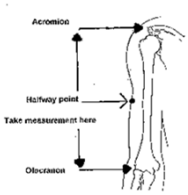
C = Severely Malnourished

Markers in Nutrition Assessment

- Merit of only using subjective measures for nutrition assessment has been questioned
- Subjective clinical evaluation of nutritional status in 260 patients with alcohol cirrhosis failed to identify “severe malnutrition” defined anthropometrically in 30% of patients
- Single objective assessment variables, weight, albumin etc. cannot be used due to innate confounding effects of fluid retention and alterations in protein metabolism

Naveau et al. J Hepatol 1995;23:234-235.

Mid-Arm Muscle Circumference



MAMC = Mid arm Circumference – (Tricep Skinfold X 0.3142)

Handgrip Strength

Table 2
Malnutrition according to patient group and method used to assess nutritional status*

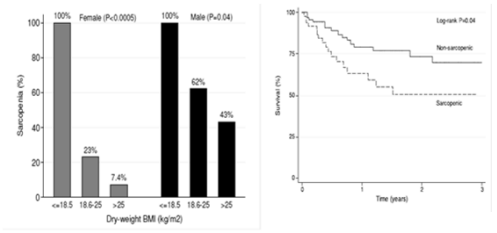
Method and nutritional status	Group 1 (cirrhosis)	Group 2 (HBP)	Group 3 (control)
SGA			
Malnourished	14 (28)	6 (13)	0 (0)
Well-nourished	36 (72)	40 (86.9)	49 (100)
PNI			
Malnourished	9 (18.8)	2 (4.35)	NP
Well-nourished	39 (81.2)	44 (95.6)	NP
HG			
Malnourished	29 (63)	10 (21.7)	2 (4.08)
Well-nourished	17 (36.9)	36 (78.3)	47 (95.9)

Table 3
Influence of nutritional status on clinical outcome in cirrhotics after a 1-y follow-up according to method of assessment*

	HG (n = 46)		PNI (n = 48)		SGA (n = 50)	
	PCM	No PCM	PCM	No PCM	PCM	No PCM
No. of patients (%)	29 (63)	17 (36.9)	9 (18.8)	39 (81.2)	14 (28)	36 (72)
Lost to follow-up	2 (6.89)	1 (5.88)	0 (0)	3 (7.69)	1 (7.14)	3 (8.33)
Major complications†	19 (65.5)	2 (11.8)	3 (33.3)	18 (46.2)	5 (35.7)	16 (44.4)
Liver transplantation	3 (10.3)	0 (0)	3 (33.3)	0 (0)	2 (14.3)	1 (2.78)
Death (without transplantation)	6 (20.7)	0 (0)	0 (0)	3 (7.69)	3 (21.4)	3 (8.33)

Alvares da Silva et al. Nutrition 2005;21(113-117)

Sarcopenia Predicts Mortality



Tandon et al. Liver Transplantation 2012 epub

Nutritional Caveats / Alternatives

- Weight / BMI
  - Fluid Retention/Ascites/Peripheral Edema
- Biochemical Tests
  - Albumin – Half Life 18 days!
  - Prealbumin –Half life 2-3 days
- Anthropometrics
  - Mid-arm muscle circumference
- Assessment of muscle function
  - Hand-grip strength

Nutritional Management of End Stage Liver Disease

Energy

- Energy expenditure: currently there are no metabolic equations which are able to estimate accurately the energy requirements of the patient with ESLD.
- Harris-Benedict, Schofields and Muller all underestimate the energy requirements of this group
- Indirect calorimetry

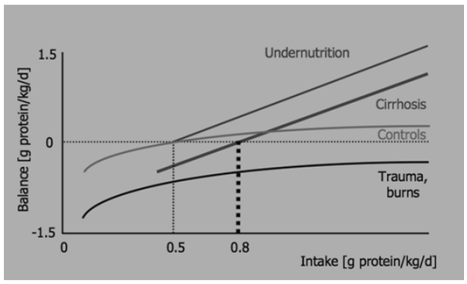
Nutritional Management of End Stage Liver Disease

Protein

- Protein turnover in cirrhotic patients is normal or increased
- Stable cirrhotics have increased protein requirements
- Stable cirrhotic patients are capable of achieving positive nitrogen balance during aggressive nutritional support regime

Kondrup J, Nellsen K et al Br J Nutr 1997; 77: 197-212
Swart, GR et all.. Clin Nutr 1989; 8: 329-336

Increased Protein Requirements



Kondrup and Nielsen. Z Gastroenterol 1996; 34 (5):26 - 31

General Nutrition Guidelines

- 6-7 small meals/day + Bedtime snack rich in CHO/Protein
- Initiate Enteral intake when oral intake is suboptimal
  - NG vs. Gastrostomy
- Identify and Correct nutrient deficiencies
  - ETOH/HCV – Thiamine/Folate
  - Cholestatic – Fat soluble Vitamin Deficiencies
- Sodium / Fluid Restriction Per Usual Criteria

Nocturnal Supplements

- Method to reduce gluconeogenesis and protein catabolism
- 12 month RCT daytime or bedtime oral supplements 700kcal
- Increased in total body stores over 3,6 and 12 months
- 2 kg of lean muscle mass
- Decreased length of overnight fast and associated progression of gluconeogenesis

Plank et al Hepatology 2008;48:557-566

General Nutrition Guidelines

Plauth M et al. Clin Nutr 1997;16-43

- Compensated Cirrhosis
  - 25-35 kcal/kg/day; 1-1.2 g/kg/d protein
- Complicated cirrhosis
  - 35-40 kcal/kg/day; 1.5g/kg/day protein
- Mild-Moderate Encephalopathy
  - 25-35 kcal/kg/day; 0.8-1.5g/kg/day protein
  - Restrict protein as briefly as possible
- Severe Encephelopathy
  - 25-35 kcal/kg; 0.5g/kg/day protein
  - Restrict protein as briefly as possible

Protein Restriction Does Not Improve HE

Cordoba et al. Je Hepatol 2004; 41: 38 - 43

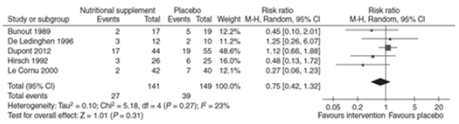
Enteral nutrition Cirrhosis

- Should be highly encouraged early if oral intake inadequate
  - Nasogastric preferred
  - Minimum 3 week trial
  - Nocturnal supplemental feeds
  - Full oral intake during daytime
- Benefits seen in severely malnourished
  - Improved in-hospital survival
  - Child's score
  - Albumin
  - Bilirubin
  - Encephelopathy
  - Infections (SBP)
  - Post-transplant infections

Cabre et al. Gastro 1990;98:715
Kearns et al. Gastro 1992;102:200

What is the impact of Nutrition Therapy on Clinical Outcomes in Cirrhosis?

Ney M, Vandermeer, van Zanten S et al. Meta-analysis: oral or enteral nutritional supplementation in cirrhosis. Aliment Pharmacol Ther 2013;37:672-679



High Risk Malnutrition Clinic

- 35 Pre-Liver Transplant Patients
- Referred for Combined MD/RD assessment
- Intervention
  - Intensive Maximization Oral Intake + Nocturnal Meals
  - Nocturnal NG feeds
  - MedGem Calorimetry
- 3 months Intervention Improvements
  - HGS
  - MAC

MedGem Indirect Calorimeter

- Measure O2 consumption and determine RMR in ambulatory patient
- Protocolized measurements
- Disposable mouthpieces

MedGem Indirect Calorimeter

- Measures RMR based on O2 production
  - Uses RQ constant 0.85
  - Modified version of Weir Equation (universal standard for conversion of gas exchange measurements into RMR)
  - RMR = [(3.941)(VO2)+(1.106)(VO2)(RQ)]
- HB underestimated REE in 21/25

(-243 ± 32.3 kcal/d)

Preliminary Data (N=24)

	Total n=24	SGA B (12, 50)	SGA C (12, 50%)	P Value
Female n, %	7 (29%)	4 (17%)	3 (12.5%)	0.653
Age, median IQR	**55.5 (48-61.5)**	**50.5 (36-59.5)**	**61 (51-64)**	**0.026**
Male Dry BMI, Median IQR	20.6 (19.8-22.4)	21.45 (20.05-25.9)	19.9 (19.35-20.95)	0.210
Female Dry BMI, Median IQR	21.2 (20.2-22)	21.29 (20.7-21.7)	20.4 (18.1-22.6)	0.858
MAC, median IQR	23 (22-26.5)	25.5 (22-28.5)	22 (22-24)	0.112
Male MAC, median IQR	24 (22-28.5)	**27.5 (23-29.5)**	**22 (22-24.5)**	0.134
Female MAC, median IQR	21 (20-25)	**23 (20.5-25.5)**	**20 (18-22)**	0.212
Male HGS, median IQR	**66 (50-77)**	**77 (70-90) (n=6)**	**52 (46.5-61) (n=8)**	**0.002**
Female HGS, median IQR	**30 (25-35)**	**34.5 (32-38.5) (n=4)**	**25 (25-26) (n=3)**	**0.032**

	Total n=24	SGA B (12, 50%)	SGA C (12, 50%)	P Value
Mean Total Calories Recommended (kcal)	2265	2453	2281	0.685
Mean Estimated total calories (kcal)	**1766**	**2185**	**1529**	**0.016**
Percent of recommended caloric intake	78%	**97%**	**67%**	
Mean Recommended Protein Intake (g)	98	109	97	0.707
Mean Estimated protein intake (g)	**72**	**90**	**61**	**0.046**

Low Protein Intake is associated with mortality

Tandon et al.

Univariable Analysis

Variable	OR (95% CI)	P value
Age (per 10 year increase)	1.4 (1.2 to 1.7)	0.0003
Male gender	1.0 (0.7 to 1.4)	0.80
Hepatocellular carcinoma	1.0 (0.6 to 1.4)	0.81
Sodium	0.9 (0.9 to 1.0)	<0.00001
Etiology of cirrhosis -HCV -Alcohol -PBC/PSC/AIH -NASH/Cryptogenic -Other	 1 0.9 (0.6 to 1.4) 0.7 (0.4 to 1.1) 0.9 (0.5 to 1.6) 0.6 (0.3 to 1.2)	 Ref 0.66 0.09 0.74 0.13
Protein intake <0.8 g/kg estimated dry weight	1.9 (1.3 to 2.7)	0.0008
SGA B/C	1.5 (1.1 to 2.2)	0.02
Child Pugh score (per 1 point increase)	1.3 (1.2 to 1.5)	<0.00001
MELD score (per 5 point increase)	1.3 (1.2 to 1.4)	<0.00001

Question #1

Which of the following is the most important contributor to malnutrition in cirrhosis?

a) Poor Oral intake
b) Malabsorption
c) Altered Metabolism
d) None of the Above

Question #2

- What is the best way to assess nutritional status in patients with chronic liver disease?
  a) BMI
  b) Prealbumin
  c) Harris-Benedict Equation
  d) Subjective Global Assessment
  e) None of the above

Question 3

- Which of the following target goal calorie and protein requirements is the most appropriate for a patient with decompensated cirrhosis:

a) 20-25 kcal/kg ; 1.0 g/kg/protein/day
b) 25-30 kcal/kg ; 1.0 g/kg/protein/day
c) 30-35 kcal/kg; 1.2 g/kg/protein/day
d) 35-40 kcal/kg; 1.5 g/kg/protein/day

Key Messages

- Expect Malnutrition in CLD
  - Protein malnutrition = poor prognosis
- Ensure adequate energy intake
  - Use indirect calorimetry
  - 35-40 kcal/kg/day
- Provide enough protein
  - 1.2 – 1.5 g/kg/day

ESPEN 2011