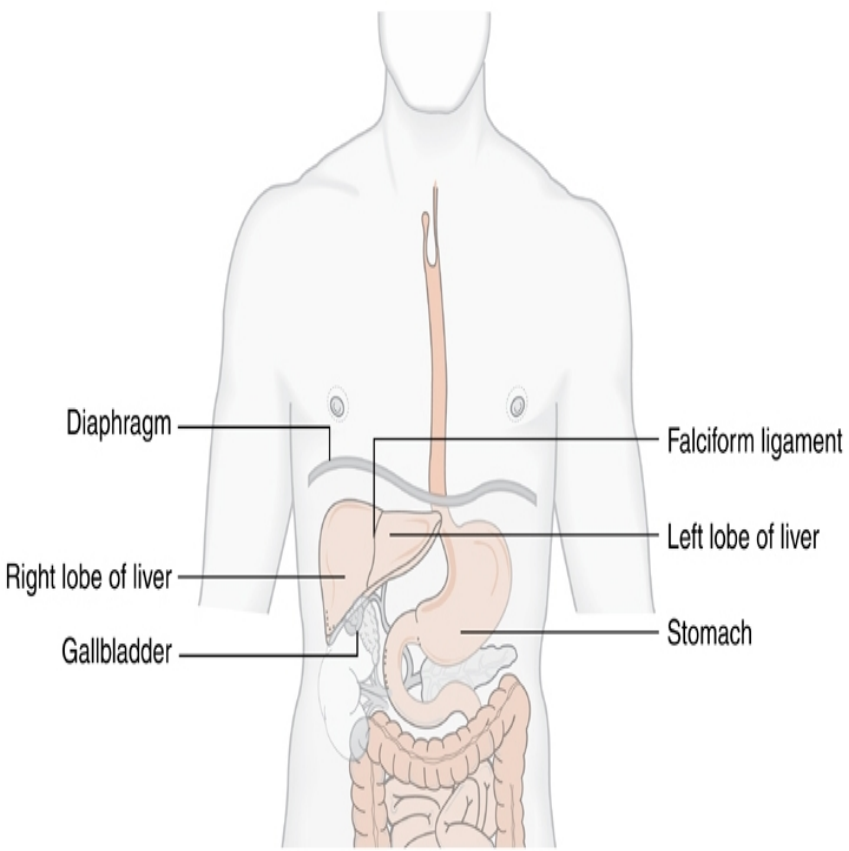
MNT for ESLSD

Presented by
AEYSHA NASIR

Where is the Liver?



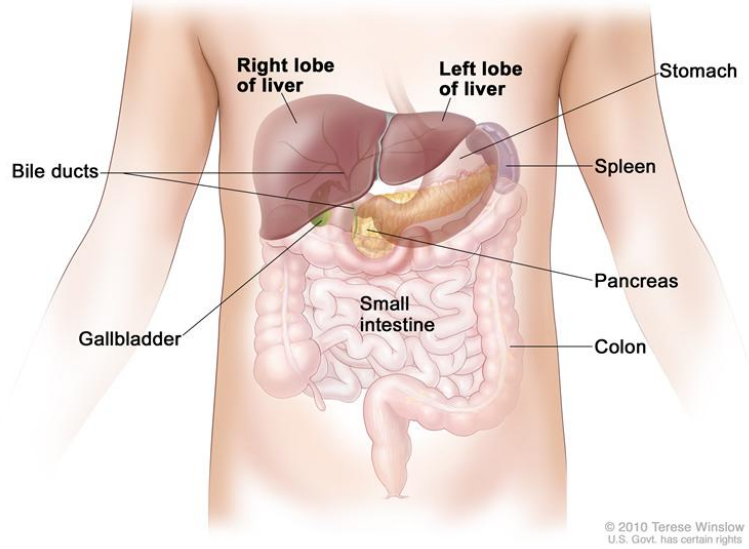
- Upper right quadrant, beneath the diaphragm
- Largest internal organ
- Weighs ~ 1500 grams

Liver Functions

- Stores glucose as glycogen or releases glycogen in response to blood sugar levels
- Break down lipids (bile)
- Break down proteins into ammonia
- Produces blood proteins (albumin, prothrombin, fibrinogen)
- Detoxifies blood of alcohol
- Secretes drugs such as antibiotics into bile
- Inactivates thyroid and steroid hormones
- Secretes bilirubin (left over pigment from break down of hemoglobin)

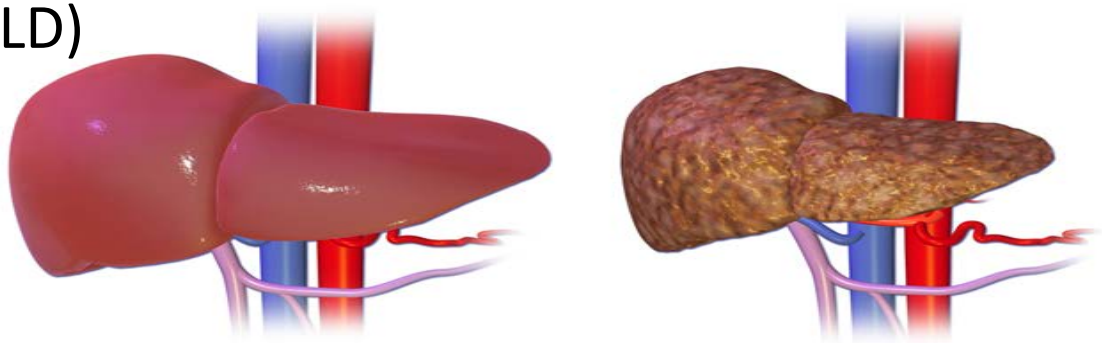
Liver Functions (cont'd)

- Stores Vitamin A, B12, D, E and K
- Stores iron and copper
- Remove old blood cells and some bacteria from blood
- Activates Vitamin D produced by the skin



ESLD

- Chronic liver failure, also called end-stage liver disease, progresses over months, years, or decades. Most often, chronic liver failure is the result of cirrhosis, a condition in which scar tissue replaces healthy liver tissue until the liver cannot function adequately. Patients with abnormal liver function who develop ascites, variceal hemorrhage, hepatic encephalopathy, or renal impairment are considered to have end-stage liver disease (ESLD)



Normal Liver

Liver Cirrhosis

Complications of ESLD

Hepatic encephalopathy

- Hepatic encephalopathy is defined as a complex neuropsychiatric syndrome marked by personality changes, intellectual impairment, and an altered level of consciousness
- Hepatic encephalopathy is associated with hepatocyte loss and dysfunction, and portosystemic shunting, which allow nitrogenous substances derived from the gut to adversely affect brain function

- It is a common and distressing complication, developing in 30% to 45% of patients with decompensated cirrhosis

- Hepatic encephalopathy resulting from cirrhosis is classified according to the severity of clinical manifestations, the time course, and the presence of precipitating factors

- In the past, a diet high in animal protein was implicated in worsening serum ammonia levels and the symptoms of HE. However, many patients with ESLD have protein-calorie malnutrition, and protein restriction is generally not recommended

(Canadian Family Physician, janvier 2016)

Spontaneous bacterial peritonitis

- Spontaneous bacterial peritonitis is defined as an ascitic fluid infection with a polymorpho nuclear cell count of 250 cell/mm3 or greater and an ascitic fluid culture positive for bacteria, in the absence of a surgically treatable source. Spontaneous bacterial peritonitis is the most common and severe infection in patients with cirrhosis: up to 30% of patients with cirrhosis develop SBP,11 with a mortality rate ranging between 30% and 50%

(canadian physician society 2016)

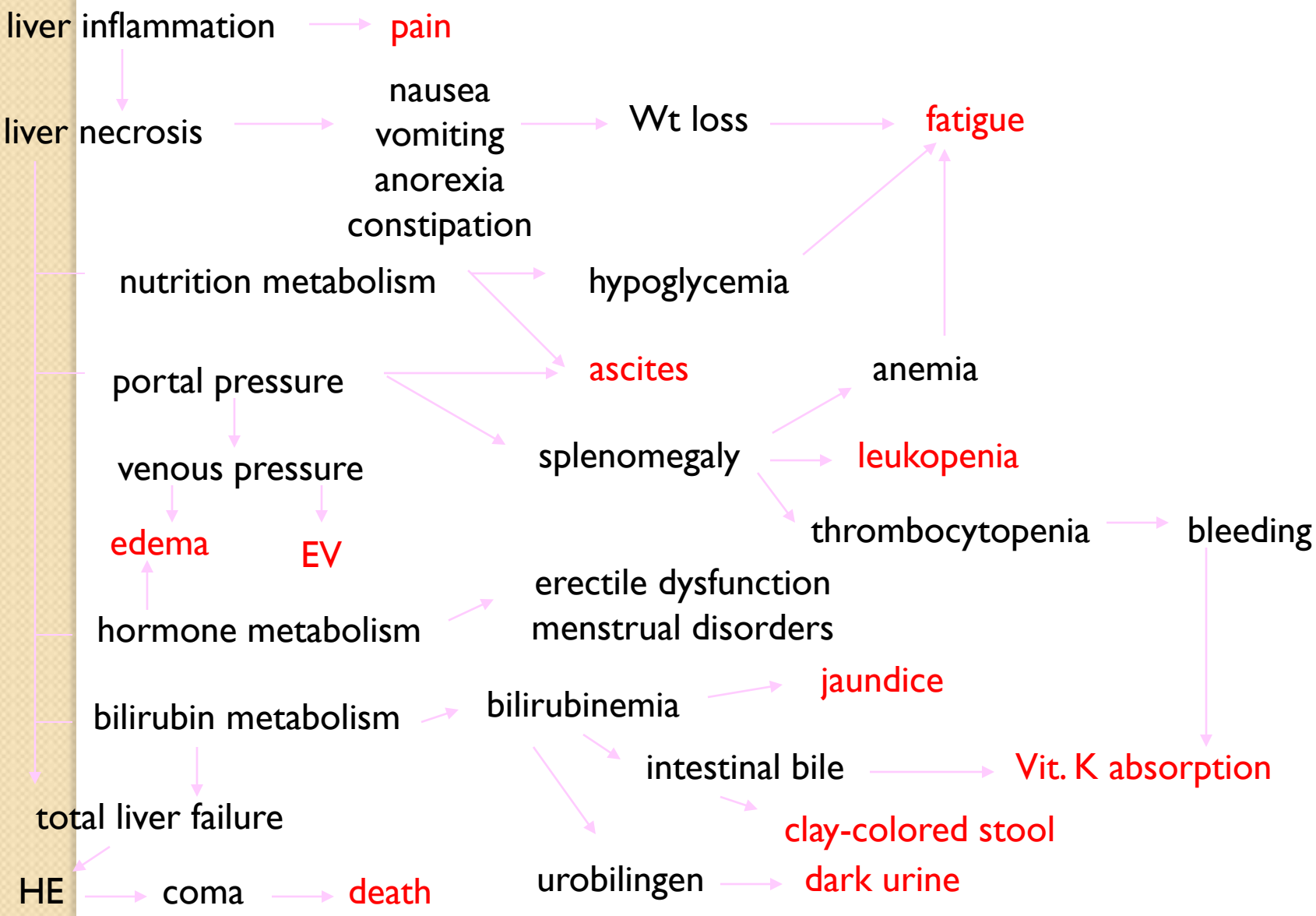
- Primary prophylaxis of SBP has been associated with a decreased risk of bacterial infection and decreased mortality in patients considered to be at high risk of SBP, which includes patients with a history of variceal bleeding or ascites fluid protein levels below 1.0 g/dL

(canadian physician society 2016)

Esophageal varices

- Esophageal varices, a direct consequence of increased portal pressure, are a common complication of cirrhosis, and their presence correlates with the severity of liver disease. Approximately 50% of patients with cirrhosis develop esophageal varices, and of these one-third will develop a variceal bleed.19 With any episode of active bleeding, there is a 30% chance of mortality and a 70% risk of hemorrhage recurrence within 1 year

(canadian physician society 2016)


liver inflammation
pain
liver necrosis
nausea
vomiting
anorexia
constipation
Wt loss
fatigue
nutrition metabolism
hypoglycemia
portal pressure
ascites
anemia
venous pressure
splenomegaly
leukopenia
edema
EV
thrombocytopenia
bleeding
erectile dysfunction
menstrual disorders
hormone metabolism
jaundice
bilirubin metabolism
bilirubinemia
intestinal bile
Vit. K absorption
clay-colored stool
total liver failure
HE
coma
death
urobilingen
dark urine

Nutritional Concerns

- In CLD there occurs a decrease in branched chain aminoacids/aromatic amino acids (BCAA/AAA) ratio, as observed in sepsis or major trauma
- During overnight fast, keto-genesis and gluconeogenesis are increased (lipids represent75% of the calories expended during this period), causing an increased AA consumption by the muscles
- This condition is also observed in healthy subjects after 3 days of fasting, but in cirrhosis, this process is accelerated

- Pancreatic dysfunction, increased lipolysis, fatty acids oxidation and ketogenesis lead to a reduction of plasma triglycerides, phospholipids, cholesterol, apoproteins and polyunsaturated fatty acids

- This decrease is proportional to the severity of the liver disease and the degree of mal-nutrition, and is associated with decreased survival and is considered an independent predictor of mortality in cirrhosis

- Micronutrient deficits are prevalent as well .Deficiency of water-soluble vitamins, especially group B vitamins, is common in cirrhosis

- Deficiency of fat-soluble vitamins has been reported, in the presence of steatorrhea associated with cholestasis and in the bile salt deficiency

- Thiamine deficiency is quite common
- Decreased intake, absorption and hepatic reserves may contribute to it

- Alcohol intake also reduces intestinal absorption of thiamine and pre-vents metabolization in its active substrate. Thiamine deficiency may lead to Wernicke encephalopathy and Korsakoff dementia

- Vitamin B12 deficiency is mainly related to the decrease of its liver reserves.
- Serum levels may be increased, but tis-sue levels are decreased
- deficiency is associated with anemia, glossitis and neurological symptoms
- Folic acid deficiency develops faster in cirrhotic patients due to decreased hepatic storage levels

Retinol deficiency is related with decreased absorption and impaired hepatic mobilization

It can cause dermatitis, night blindness or photophobia and increased risk of neoplastic disorders, including hepatocellular carcinoma

A retrospective study reported that the majority of liver disease patients being considered for liver transplantation present with vitamin A and D deficiencies

Because high doses of vitamin A are potentially hepatotoxic, care must be taken to avoid excessive supplementation

- Vitamin K deficiency is caused by decreased liver storage levels and is associated with increased risk of bleeding

- Vitamin D deficiency results from ingest reduction, decreased absorption (due to cholestatic disease or portal hypertension enteropathy)

- Since vitamin D is hydroxylated in the liver to produce calcidiol, patients with severe parenchymal or obstructive hepatic disease may have reduced production of this metabolite
- The majority of the liver must be dysfunctional before calcidiol synthesis is reduced.
- Thus, these patients rarely manifest biochemical or histological evidence of osteomalacia, unless concomitant nutritional deficiency or interruption of the enterohepatic circulation occurs.

- Extremely low serum levels of vitamin D are associated with increased mortality in patients with chronic liver disease

- Zinc and selenium deficiency have been described inpatients with alcoholic and non-alcoholic liver disease.
- Zinc deficiency is caused by intake reduction (to which contributes a diet with restriction of animal origin pro-tein), impaired intestinal absorption and treatment with diuretics
- This deficiency may increase ammonia levels in circulation, increasing the risk of HE and may also induce anorexia, dysfunction of the immune system and dysgeusia, which further decreases its intake

Vitamin and Mineral Deficits in Severe Hepatic Failure

Vitamin or Mineral	Predisposing Factors	Signs of Deficiency
Vitamin A	Steatorrhea, neomycin, cholestyramine, alcoholism	Dermatitis, night-blindness
Vitamin D	Steatorrhea, glucocorticoids, cholestyramine	Osteomalacia
Vitamin E	Steatorrhea, cholestyramine	Edema, peripheral neuropathy
Vitamin K	Steatorrhea, antibiotics, cholestyramine	Excessive bleeding; bruising
Vitamin B_6	Alcoholism	Mucous membrane lesions, dermatitis
Vitamin B_{12}	Alcoholism, cholestyramine	Megaloblastic anemia, glossitis, CNS dysfunction
Folate	Alcoholism	Megaloblastic anemia, glossitis, irritability
Niacin	Alcoholism	Dermatitis, dementia, diarrhea, inflammation of mucous membranes
Thiamin	Alcoholism, high CHO diet	Neuropathy, ascites, edema, CNS dysfunction
Zinc	Diarrhea, diuretics, alcoholism	Immunodeficiency, impaired taste acuity, wound healing, protein synthesis
Magnesium	Alcoholism, diuretics	Neuromuscular irritability, hypokalemia, hypocalcemia
Iron	Chronic bleeding	Stomatitis, microcytic anemia, malaise
Potassium	Diuretics, anabolism, insulin use	Muscular weakness, malaise, respiratory or cardiac arrest
Phosphorus	Anabolism, alcoholism	Anorexia, weakness, cardiac failure, glucose intolerance

Modified from Shronts EP: Nutritional assessment of adults with end-stage hepatic failure, *Nutr Clin Pract* 3:113, 1988.

CHO, Carbohydrate; *CNS*, central nervous system.

- Inadequate nutrients intake was seen under a variety of reasons, such as loss of appetite caused by tristimania, anorexia, drug side effects and satiety caused by less gastrointestinal peristalsis and gastric restrictive expansion caused by large volume ascites
- In addition, acute gastroesophageal varicose hemorrhage followed by long time fasting is also common in clinical practice (Plauth 2017)

- Professor Plauth pointed out in a research that many clinicians make a prescription of low protein diet to avoid encephalopathy, which leads to deterioration of nutritional status. However, it is not necessary and lack of being evidence-based in most cases (plauth 2017)

- One other important factor is the presence of impaired absorption function due to portal hypertension , which frequently accompanied with portal hypertensive gastrointestinal disease or peptic ulcer disease.

- Under this condition, there is gradually arising impaired absorption of fat-soluble vitamins such as A, D, E and K, intestinal mucosal atrophy and conditional bacterial infections, followed by hypercatabolic status and higher mortality
- Finally, iatrogenic factors such as the multiple hospitalizations, pending examinations and procedures (e.g., paracentesis) should not be ignored as well

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- **Etiologies of Malnutrition in Cirrhosis**
- **Decreased Intake**
- • Anorexia
- • Early satiety
- • Ascites
- • Altered mental status/encephalopathy
- • Frequent hospitalizations
- **Decreased Absorption**
- • Inadequate bile flow
- • Bacterial overgrowth
- • Pancreatic insufficiency
- **Metabolic alterations**
- **Iatrogenic Factors**
- • Overzealous dietary restrictions
- • Frequent Paracentesis
- • Diuresis (micronutrient losses)
- • Lactulose therapy

Used with permission from the University of Virginia Health System Nutrition Support Traineeship Syllabus

Nutritional Assessment

Assessment of nutritional status

- For complete assessment of nutritional status information, three important parameters required are:
- Energy balance
- Body composition
- Tissue function

Energy Balance

- A systematic dietary recall obtained by a skilled dietitian will provide adequate information in most cases. For hospitalized patients, a food diary should be completed, weighing the food consumed, and appropriate tables for food composition should be used for calculation of proportions of different nutrients.

Body Composition

- Body composition of cirrhotic patients is assessed by indirect techniques, such as anthropometry, urinary creatinine excretion

- It would be desirable to directly assess fat mass and fat free mass components , total body water, extracellular water and body cell or muscle mass.

- **Anthropometry** is the accurate tool to detect the protein depleted status of cirrhotic patients. Skinfold anthropometry is the best indirect method of assessing body fat stores in these patients.

- The value of **urinary creatinine excretion** also helps to estimate muscle or body cell mass as creatine is synthesized by the liver. Elevation in serum creatinine is a common laboratory finding for patients with cirrhosis and can indicate the presence of either an acute kidney injury (AKI) or chronic kidney disease (CKD)

Tissue function

- Circulating concentrations of many visceral plasma proteins (albumin, prealbumin, retin01-binding protein) are highly affected by the presence of liver disease, excessive alcohol consumption and inflammatory states
- Immune status, which is often considered a functional test of malnutrition, may be affected by hypersplenism, abnormal immunologic reactivity and alcohol abuse

- At present, total lymphocyte count and CD8 cell count seem to be of prognostic value in malnourished patients with alcoholic liver disease

- In nutrition intervention trials, results from lymphocyte PHA stimulation index or skin anergy test were not useful for the detection of nutritional changes.

(ESPEN)

History

Weight change (consider fluctuations resulting from ascites and edema)
Appetite
Taste changes and early satiety
Dietary recall (calories, protein, sodium)
Persistent gastrointestinal problems (nausea, vomiting, diarrhea, constipation, difficulty chewing or swallowing)

Physical

Muscle wasting
Fat stores
Ascites or edema

Existing Conditions

Disease state and other problems that could influence nutrition status such as hepatic encephalopathy, gastrointestinal bleeding, renal insufficiency, infection

Nutritional Rating (based on results of parameters)

Well nourished
Moderately (or suspected of being) malnourished
Severely malnourished

Subjective Global Assessment

TABLE 28-3

Factors That Affect Interpretation of Objective Nutrition Assessment Tests in Patients With End-Stage Liver Disease

Parameter	Factors Affecting Interpretation
Body weight	Affected by edema, ascites, and diuretic use
Anthropometric measurements	Questionable sensitivity, specificity, and reliability
	Multiple sources of error
	Unknown if skinfold measurements reflect total body fat
	References do not account for variation in hydration status and skin compressibility
Creatinine-height index	Affected by malnutrition, aging, decreased body mass, and protein intake
	Affected by renal function
	Creatinine is a metabolic end product of creatine synthesized in the liver; therefore severe liver disease alters creatinine synthesis rates
Nitrogen balance studies	Nitrogen is retained in the body in the form of ammonia
	Hepatorenal syndrome can affect the excretion of nitrogen
3-Methyl histidine excretion	Affected by dietary intake, trauma, infection, and renal function
Visceral protein levels	Synthesis of visceral proteins is decreased
Immune function tests	Affected by hydration status, malabsorption, and renal insufficiency
	Affected by hepatic failure, electrolyte imbalances, infection, and renal insufficiency
Bioelectrical impedance	Invalid with ascites and/or edema

Modified from Hasse J: Nutritional aspects of adult liver transplantation. In Busuttil RW, Klintmalm GB, editors: *Transplantation of the liver*, ed 2, Philadelphia 2005, Saunders.

Conclusion

- Based on expert consensus, a dry weight or usual weight be used instead of actual weight in predictive equations to determine energy and protein in patients with cirrhosis and hepatic failure, due to complications of ascites, intravascular volume depletion, edema, portal hypertension, and hypo albuminemia

- ASPEN 2016 suggest that nutrition regimens avoid restricting protein in patients with liver failure, using the same recommendations as for other critically ill patients (Aspen 2016)

Nutrition in the Management of ESLD and its Complications

Chantal Bémeur*,†, Roger F. Butterworth†

*Département de nutrition, Faculté de médecine, and †Unité de recherche en sciences neurologiques, Hôpital Saint-Luc (CHUM), Université de Montréal, Montréal, Canada

Table 1 General Recommendations for Cirrhotic Patients.

Nutriment	Recommendation
Energy	30–50 kcal/kg body weight Sufficient to restore/maintain nutritional status and enhance liver regeneration (adjust for obese patients)
Protein	1.0–1.8 g/kg body weight depending on the severity of malnutrition (adjust if renal disease present)
Carbohydrates	45–75% of caloric intake or 4–6 meals rich in carbohydrates per day
Lipids	20–30% of caloric intake (adjust if steatorrhea present)
Vitamins	B group vitamin supplements Particular attention to lipid-soluble vitamins Correct specific deficiencies
Minerals	Zinc, magnesium and selenium supplements Correct specific deficiencies

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Table 2 Nutritional Recommendations for Cirrhotic Patients with HE.

Nutrient	Recommendation
Energy	Optimal daily energy intake; 30–40 kcal/kg body weight Small meals evenly distributed throughout the day and late snack[a] of complex carbohydrates; (adjust for obese patients)
Protein	Optimal daily protein intake; 1.2–1.5 g/kg body weight Encourage diet rich in vegetables and dairy protein If patient intolerant to dietary protein, consider BCAA supplementation[b]
Fiber	25–45 g/daily
Vitamins and minerals	Multivitamin preparation in patients at increased risk of malnutrition; Correct specific deficiencies

[a]Late evening snacks allow cirrhotic patients to minimize gluconeogenesis, reduce protein utilization and favor a positive nitrogen balance.[127,128]

[b]BCAAs, which are not metabolized by the liver, provide an alternative source of proteins.

Nutrition in the complications of ESLD

- Calories (Cal)
- Fat
- Protein (PT)
- Carbohydrate (CHO)
- Sodium (Na)
- Fluid
- Vitamins

- Total Cal= 30-40 kcal/kg
- Fat=30-35% of total Cal
- PT=1g/kg/d (1 – 1.2 g/Kg) (Aspen 2016)

  ESPEN Consensus group : req. 1-1.5g/kg/d

  low PT diet may worsen HE

Plauth et al. 2017

Nutritional Management of HE

- Historical treatment theories
  - Protein Restriction
  - BCAA supplementation
- Goals of MNT
  - Treatment of PCM associated with ESLD

Historical Treatment Theories: Protein Restriction

- Studies in early 1950's showed cirrhotic pts given "nitrogenous substances" developed hepatic "precoma"
- Led to introduction of protein restriction
  - Began with 20-40g protein/day
  - Increased by 10g increments q3-5 days as tolerated with clinical recovery
  - Upper limit of 0.8-1.0 g/kg
  - Was thought sufficient to achieve positive nitrogen balance
- Lack of Valid Evidence
  - Efficacy of restriction never proven within controlled trial

Dispelling the Myth

Normal Protein Diet for Episodic Hepatic Encephalopathy

Cordoba et al. *J Hepatol*

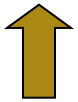
Objective: To test safety of normal-protein diets

- Randomized, controlled trial in 20 cirrhotic patients with HE
  - 10 patients subjected to protein restriction, followed by progressive increments
    - No protein first 3 days, increasing q3days until 1.2g/kg daily for last 2 days
  - 10 patients followed normal protein diet (1.2g/kg)
  - Both groups received equal calories

Dispelling the Myth

- Results
  - On days 2 and 14:
    - Similar protein synthesis among both groups
    - Protein breakdown higher in low-protein group
- Conclusion
  - No significant differences in course of hepatic encephalopathy
  - Greater protein breakdown in protein-restricted subjects

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 
- Susceptibiliy to infection increases under such catabolic conditions

Proteins

- Proteins should not be restricted in patients with liver disease unless they become protein intolerant due to encephalopathy
- Protein intake should be in the range of 1-1.5 g/kg/day

(ASPEN 2016, Plauth 2017)

Proteins. Cont

- Several studies have shown that a daily protein supply of 1.0-1.2g/kg/day may be sufficient to prevent negative N_2 balance in cirrhosis

- With mild stress, this has to increase to 1.5 g/kg/day, and with acute exacerbations of hepatitis or decompensation to 2.0g/kg/day

Proteins. Cont

- Special attention should be paid to patients on beta-blockers for prevention of variceal bleeding
- Beta-blockers increase protein oxidation (an alternative method of protein metabolism without energy production), and may increase protein requirement.
- patients on propranolol should be placed on the higher end of the protein intake.

BCAA Supplementation
Effective or Not?

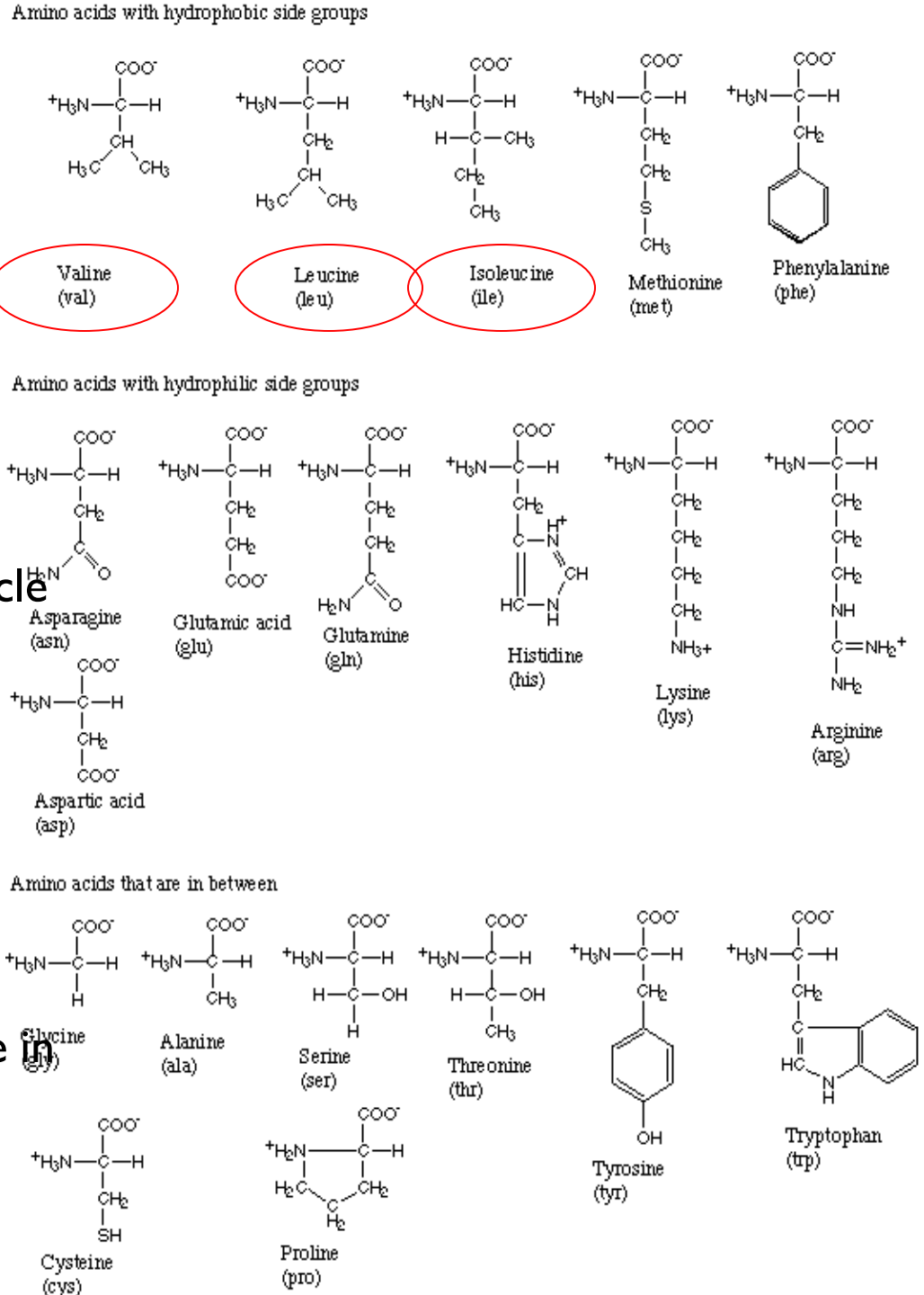
Branched Chain Amino Acids (BCAA)

Valine
Leucine
Isoleucine

- Important fuel sources for skeletal muscle during periods of metabolic stress
- Metabolized in muscle & brain, not liver

-promote protein synthesis
-suppress protein catabolism
-substrates for gluconeogenesis

Catabolized to L-alanine and L-glutamine in skeletal muscle



BCAAs in cirrhosis with acute encephalopathy

- 7 controlled studies
- BCAAs group v.s. glucose or non selective AA soln. or lipid groups
- BCAAs was gave for 2-6 d
- Post treatment observation period : 4-16 d
- 201(BCAAs) v.s. 179(isocaloric group)
- No statistically significant in survival

Riggio et al. 1982
Wahren et al. 1983
Michel et al. 1985
Cerra et al. 1985
Fiaccadori et al. 1985
Strauss et al. 1986
Vilstrup et al. 1990

- Certainly BCAAs don’t worsen encephalopathy and may be safely used to maintain an adequate PT intake in subjects at risk of altered mental state

- BCAAs may be easily used as energy sources, thus improving nitrogen balance and have a beneficial on anorexia.

Plauth et al. 2017

- A multicenter, randomized study, > 1 yr, 174 p't
- (a) BCAA supplementation group
- (b) maltodextrins group (equicaloric)
- (c) lactoalbumin gro

Non-BCAA group

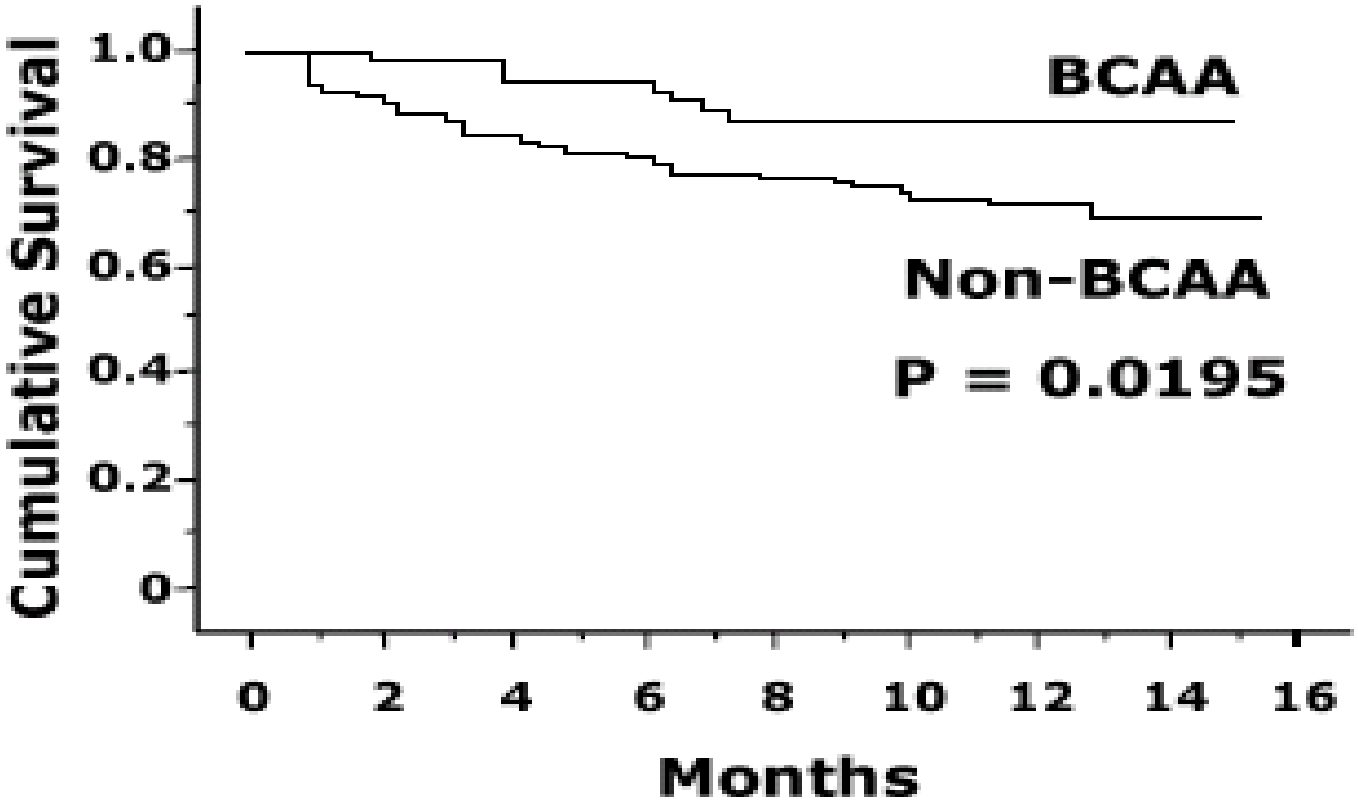


Figure 1 Kaplan-Mejer survival curve in patients with cirrhosis treated with BCAA and in the combined control group (maltodextrins and lactoalbumin, non-BCAA). Subjects dying for non-liver-related causes were excluded from the intention-to-treat analysis.

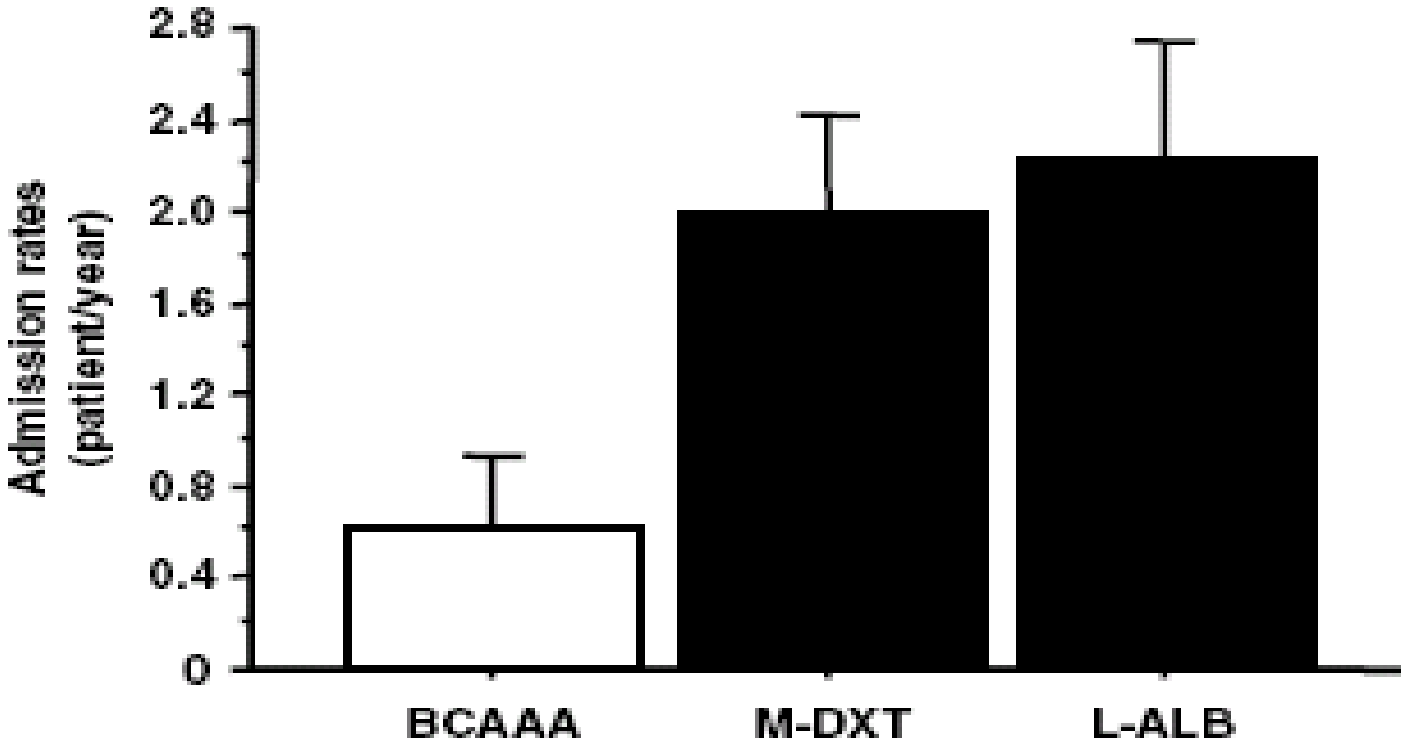


Figure 2 Admission rates in cirrhosis treated with BCAA (open b
dextrins
and = 0

Long term BCAA supplementation increases survival time and prevents to decrease hospital admission rates.

- BCAA-enriched formulations can be useful in p't who are intolerant to PT and malnourished, which can improve PT synthesis and reduce post injury catabolism.

Nompleggi and Bonkovsky 2014

- BCAA-enriched soln. increased serum alb. also reduced morbidity and improved the quality of life.

Poon et al, 2014

- BCAAs strongly activate mTOR signaling in liver, which is the cellular nutrition sensor for PT translation initiation.

Nishitani et al, 2014

ASPEN 2016

- There is no evidence to suggest that a formulation enriched in BCAA improves patient outcomes compared with standard whole-protein formulations in critically ill patients with liver disease.
- The rationale for use of BCAAs in the treatment of hepatic encephalopathy in liver failure is based on their reduced concentrations in liver failure, competing for binding sites in the central nervous system with aromatic amino acids, and their stimulatory effect on ammonia detoxification to glutamine

- Findings from randomized outpatient trials suggest that long-term (12 and 24 months) nutrition supplementation with oral BCAA granules may be useful in slowing the progression of hepatic disease and/or failure and prolonging event-free surviva

- In patients with hepatic encephalopathy already receiving first-line therapy (antibiotics and lactulose), there is no evidence to date that adding BCAAs will further improve mental status or coma grade

(ASPEN 2016)

Caffeine's Effect

- Caffeine is present in coffee, tea, chocolate, cola, and some over-the-counter medications
- Caffeine is metabolized through the liver. However caffeine itself is not directly harmful to the liver
- Some people may experience a rapid heartbeat and/or palpitations from caffeineconsumption
- Excessive intake of caffeine in patients with chronic liver disease at increased risk for osteoporosis and bone fractures

Na Restriction

- For mobilization of ascites, Na has to be restricted to less than the daily losses. If patients have high urinary Na and are able to excrete a water load, they will respond to Na restriction alone, and will lose 200-250 g fluid for every gram Na deficit.

- A no added salt regimen together with avoiding salty food will result in a diet containing 50 mEq Na daily

Fluid Restriction

- Fluid restriction of all patients with ascites is inappropriate.

- Patients should drink, but not toexcess.
- Water restriction to treat hyponatremia is indicated only if this is severe.

- Fluid restriction to less than 1 liter daily is justified only in hyponatremic patients, and only when the serum Na drops below 120 mEq/L.

Drug	Purpose	Nutrient Interaction
TUMS,	Antacid	Increases Calcium uptake, take at different times than Calcium
Zantac	Antiulcer/ AntiGERD	Decreases iron and B12 absorption
Lisinopril	Treats hypertension and CHF	Do not take with alcohol, decrease sodium and calcium intake
Lactulose	Treats constipation, laxative, decrease portal systemic encephalopathy	Take with high fiber and 1500-2000ml of water to prevent constipation. Don't take with antacid (TUMS) medication, Ca, or Mg supplement.
Octreotide	Antidiarrheal	Decrease fat intake to help improve GI function
Vitamin K	Help to coagulate blood	Maintain constant intake
Compazine	Treats severe N&V, antipsychotic	Take Mg supplement by 2 hr, limit caffeine.
Morphine	Treats moderate to severe pain, narcotic	Take with food to help GI function, may increase thirst, dehydration
albumin iv	Help to replace blood protein loss	Do not mix with other protein solutions or solutions with alcohol
furosemide iv	Treats fluid retention	Take on empty stomach or with milk if GI distress occurs

The management of perioperative nutrition in patients with end stage liver disease undergoing liver transplantation

- The prevalence of glucose intolerance and insulin resistance is seen in the population of ESLD patients. Many could develop the hepatic diabetes. Overnight fasting, hepatic glycogen stores are depleted in patients with ESLD, presenting increased gluconeogenesis from amino acids and increased lipid peroxidation. At this time, fat becomes their main substrate for energy. As the result, the mobilization of amino acids from the skeletal muscles and visceral proteins is active, demonstrating muscle depletion and decrease in subcutaneous fat

- Perioperative maintenance of normoglycemia is frequently emphasized to improve surgical outcomes and may be quite important factor to prevent surgical site infection . A research found that surgical site infections were reduced in patients whose HbA1c was <7% (10)

HepatoBiliary Surg Nutr 2015

- adequate preoperative nutritional support (≥7 d) is beneficial to patients with a nutrition risk score (NRS) score at least 5
- The ability of oral intake is connected with postoperative mortality. In addition, body mass index (BMI) should be obtained from patient's height and weight.
- BMI of <18.5 kg/m^2 or the 15th percentile for arm anthropometric measurements often were considered be malnutrition in this population. However, BMI can be inaccurate in the condition of fluid retention or edema

- Surgery has been associated with hypermetabolism in reported literatures and guidelines
- The formula of 25 kcal/kg ideal body weight provides an approximate estimate of daily energy requirements. Under conditions of severe stress, requirements may approach 30 kcal/kg ideal body weight and a protein intake of 1.5 g/kg ideal body weight (or approximately 20% of total energy requirements) is generally effective to limit nitrogen losses .
- Some studies suggest that the degree of hypermetabolism is on average not more than 110-120% of predicted , and should not be furnished more than 20-25 kcal/kg daily in the acute phase of critical severe illness

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- mixed-fuel system of both carbohydrate and fat is suggested to provide energy in post-OLT period. Usually, 70% of non-protein calories are given as carbohydrates during this phase .
- In a study of patients in a surgical critical care unit, either 30 kcal/kg adjusted body weight or the REE calculated from the Harris Benedict equation multiplied by 1.5 adequately predicts the nutritional requirements of critically ill surgery

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- Additional several meta-analysis show more clearly the evidence of feeding started within 24-48 h of surgery. Recent clinical trial performed in 346 liver transplant patients has gotten a conclusion that Bacterial sepsis occurred in 5.9% of patients who received tube feeding within 48 hours of surgery compared with 21% in patients who started tube feeding after 48 hours

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- for those patients in hemodynamic instability requiring vasopressor agents , once the hemodynamic is stable for more than 24 hours and bowl function is in recovery, feeding should commence from at 10-20 mL/h rate with a progressive increase to reach the full goal within 2-3 days of post-operation exception of contraindication for enteral nutrition

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Table 2 Summary of nutrients post liver transplantation

Nutrient	Author, year	Population [N]	General conclusions
Synbiotic (four lactic acid bacteria and fibers)	Rayes *et al*., 2005 (64)	Post LT [66]	Bacterial infection was 3% *vs*. 48%
Whey-hydrolyzed peptide	Kaido *et al*., 2010 (2)	Post LDLT [30]	Post-transplant bacteremia was 10% *vs*. 50%
BCAA	Shirabe *et al*., 2011 (65)	Post LDLT [236]	Absence of BACC was independent risk factor for post-transplant bacteremia
BCAA	Yoshida *et al*., 2012 (66)	Post LDLT [25]	Improved nutritional disorders and shortened the post-transplant catabolic phase after LDLT
Alanyl-glutamine	Qiu *et al*., 2009 (67)	Post LT [65]	TPN with Ala-Gln helped to improve synthetic function and to reduce the injury to a transplanted liver
Omega-3 fatty acid	Zhu *et al*., 2012 (68)	Post LT [66]	mitigated the liver injury, reduced the infectious morbidities and shortened the post-transplant hospital stay
Arginine	Drover *et al*., 2010 (69)	35 RCTs [>1,000]	Reduction in infectious complications and shorter hospital LOS, with no overall effect on mortality compared with standard supplemented diets

LT, liver transplantation; LDLT, living donor liver transplantation; BCAA, branched-chain amino acid; LOS, length of stay.

Thank you