ESPEN Guideline on Clinical Nutrition in Liver Disease

- In patients with cirrhosis, a high prevalence of malnutrition, protein depletion and trace element deficiency should be anticipated.
- In acute liver failure (ALF), a severe derangement of carbohydrate, protein and lipid metabolism should be anticipated characterized by impaired hepatic glucose production and lactate clearance as well as protein catabolism associated with hyper-aminoacidemia and hyper-ammonemia.

- In LC, a stage dependent progressive impairment of carbohydrate, protein and lipid metabolism characterized by hepatic glycogen depletion, impaired non-oxidative glucose metabolism and reduced albumin synthetic rate should be anticipated

- In ALF, alcoholic hepatitis (ASH) and cirrhosis
- resting energy expenditure (REE) is usually increased
- patients with nonalcoholic fatty liver disease (NAFLD) have a normal REE
- In adults with liver disease, REE should be measured using indirect calorimetry, if available.
- Patients with chronic liver disease and a sedentary lifestyle should receive a total energy supply of 1.3 x REE. (BM)

- After LT for LC, prolonged incomplete recovery of total body nitrogen status should be anticipated.
- After LT, the risk of developing sarcopenic obesity and metabolic syndrome should be taken into account and nutritional rehabilitation should aim for an earlier and faster recovery of total body protein and muscle function

- Liver disease patients should be screened for malnutrition
- In malnourished ALF patients enteral nutrition (EN) and/or parenteral nutrition (PN) should be initiated promptly, as in other critically ill patients.
- ALF patients without malnutrition should be provided with nutritional support (preferentially EN) when they are considered unlikely to resume normal oral nutrition within the next five to seven days, as in other critical Illness

- In patients with severe hyper-acute disease with hepatic encephalopathy and highly elevated arterial ammonia who are at risk of cerebral edema, nutritional protein support can be deferred for 24–48 hours until hyper-ammonemia is controlled.
- When protein administration is commenced, arterial ammonia should be monitored to ensure no pathological elevation occurs.

- Patients suffering from only mild HE can be fed orally as long as cough and swallow reflexes are intact.
- In patients with mild HE oral nutritional supplements (ONS) should be used when feeding goals cannot be attained by oral nutrition alone
- Current clinical practice adopted in many European liver units demonstrates the safety and feasibility of EN in ALF patients.

- ALF patients who cannot be fed orally should receive EN via nasogastric / nasojejunal tube
- EN should be performed by starting with low doses independent of the grade of HE.
- PN should be used as second line treatment in patients who cannot be fed adequately by oral and/or EN

- Standard enteral formulas can be given, as there are no data regarding the value of a disease specific composition
- Nutrition therapy should be offered to all patients with severe ASH who cannot meet requirements by spontaneous food intake in order to improve survival, infection rate, liver function and resolution of encephalopathy.
- ONS should be used when patients with severe ASH cannot meet their caloric requirements through normal food in order to improve survival (BM)

- EN should be used when patients with severe ASH cannot meet their caloric requirements through normal food and/or ONS in order to improve survival and infectious morbidity.
- PN shall be commenced immediately in moderately or severely malnourished patients with severe ASH who cannot be nourished sufficiently by oral and/or enteral route.

- PN should be considered in patients with unprotected airways and HE when cough and swallow reflexes are compromised or EN is contraindicated or impracticable.
- For ONS or EN in patients with severe ASH standard formulas should be used, preferably formulas with high energy density (≥1.5 kcal·ml−1)

- In patients with severe ASH trace element and vitamin deficiency should be anticipated.
- Water soluble and fat-soluble vitamins as well as electrolytes and trace elements shall be administered daily from the beginning of PN in order to cover requirements

- Individualized nutrition counselling should be used in order to improve food intake.
- ONS shall be used as first line therapy when feeding goals cannot be attained by oral nutrition alone and should be given as a late evening or nocturnal supplement
- EN can be used in severe ASH to ensure adequate energy and protein intake without increasing the risk of HE.

- EN should be used in severe ASH, because EN has been shown to be as effective as steroids alone and, in survivors of the first four weeks, to be associated with a lower mortality rate in the following year
- Patients with severe ASH who can be fed sufficiently either by oral or enteral route but who have to abstain from food temporarily (including nocturnal fasting!) for more than twelve hours, should be given i. v. glucose at 2–3 g·kg−1·d−1. When this fasting period lasts longer than 72 hours total PN is required.
- In patients with severe ASH, PN should be delivered like in other critically ill patients.

- In overweight / obese NAFL / NASH patients a 7–10 % weight loss shall be aimed for to improve steatosis and liver biochemistry; a weight loss of > 10 % shall be aimed for in order to improve fibrosis.
- In overweight / obese NASH patients, intensive life style intervention leading to weight loss in conjunction with increased physical activity shall be used as first-line treatment.

- In normal weight NAFL / NASH patients, increased physical activity to improve insulin resistance and steatosis can be recommended.
- Overweight and obese NAFL / NASH patients shall follow a weight reducing diet to reduce the risk of comorbidity and to improve liver enzymes and histology (necroinflammation).

- In order to achieve weight loss, a hypocaloric diet shall be followed according to current obesity guidelines irrespective of the macronutrient composition.

- NAFL / NASH patients shall be advised to exercise in order to reduce hepatic fat content, but there are no data regarding the efficacy of exercise in improving necroinflammation.

- Vitamin E (800 IU α-tocopherol daily) should be prescribed to non-diabetic adults with histologically confirmed NASH aiming for improvement of liver enzymes and histology.
- Until further data regarding their efficacy are available, antioxidants (e.g. vitamin C, resveratrol, anthocyanin, bayberries) cannot be recommended to treat NAFL / NASH.
- Until further data regarding their efficacy are available, omega-3- fatty acids cannot be recommended to treat NAFL / NASH.

- Nutritional supplements containing selected probiotics or synbiotics can be used to improve liver enzymes in NAFL / NASH patients.
- EN or PN shall be administered in NAFL / NASH patients during severe intercurrent illness, when oral nutrition alone is inadequate or impossible or contraindicated

- In NAFL / NASH patients with a BMI < 30 kg/m2 EN and/or PN should be done as recommended for ASH patients
- Obese NAFL / NASH patients with intercurrent illness should be given EN and/or PN with a target energy intake of 25 kcal▪kg−1 IBW▪d−1 and an increased target protein intake of 2.0–2.5 g▪kg−1 IBW▪d−1.

- Specific nutritional counselling should be implemented in cirrhotic patients using a multidisciplinary team to improve patients' long-term outcome/ survival.
- Multidisciplinary nutrition care should include monitoring of nutritional status and provide guidance for achieving nutritional goals.

- Cirrhotic patients in conditions of increased energy expenditure (i. e. acute complications, refractory ascites) or malnutrition, should ingest an increased amount of energy.
- In cirrhotic patients, an increased energy intake is not recommended in overweight or obese patients. (BM)

- Non-malnourished patients with compensated cirrhosis should ingest 1.2 g▪kg−1▪d−1 protein.
- To replenish malnourished and/or sarcopenic cirrhotic patients the amount of 1.5 g▪kg−1▪d−1 protein should be ingested.
- Protein intake should not be restricted in cirrhotic patients with HE as it increases protein catabolism.

- In cirrhotic patients, micronutrients should be administered to treat confirmed or clinically suspected deficiency.
- Oral diet of cirrhotic patients with malnutrition and muscle depletion should provide 30–35 kcal▪kg−1▪d−1 and 1.5 g protein▪kg−1▪d−1.
- Periods of starvation should be kept short by consuming three to five meals a day and a late evening snack should be recommended to improve total body protein status.

- In cirrhotic patients who are protein “intolerant”, vegetable proteins or BCAA (0.25 g·kg−1·d−1) should be used by oral route to facilitate adequate protein intake.
- Long-term oral BCAA supplements (0.25 g·kg−1·d−1) should be prescribed in patients with advanced cirrhosis in order to improve event-free survival or quality of life

- In cirrhotic patients, who cannot be fed orally or who do not reach the nutritional target through the oral diet, EN should be performed.
- Esophageal varices are no absolute contraindication for positioning a nasogastric tube
- PEG placement is associated with a higher risk of complications, due to ascites or varices, and thus, can only be used in exceptional cases.

- PN should be used in cirrhotic patients in whom oral and/or EN are ineffective or not feasible.
- LC patients scheduled for elective surgery or listed for transplantation should be screened and assessed for malnutrition timely in order to treat malnutrition prior to surgery and thereby improve body protein status. (BM)

- In the immediate preoperative period LC patients should be managed according to the ERAS approach in order to prevent unnecessary starvation
- In LC patients scheduled for elective surgery nutrition management should proceed as recommended for cirrhosis.

- Preoperatively, a total energy intake of 30–35 kcal▪kg−1▪d−1 (126–147 kJ▪kg−1▪d−1) and a protein intake of 1.2–1.5 g▪kg−1▪d−1 should be aimed for. These ranges cover recommended intakes depending on treatment goals, i.e. maintenance or improvement of nutritional status
- Obese patients can be given EN and/or PN with a target energy intake of 25 kcal ▪kg−1 IBW ▪d−1 and an increased target protein intake of 2.0–2.5 g▪kg−1 IBW ▪d−1.

- In adults, for preoperative nutrition standard nutrition regimens shall be used, since specialized regimens (e. g. BCAA-enriched, immune-enhancing diets) were not superior to standard regimens regarding morbidity or mortality.
- After LT, normal food and/or EN should be initiated within 12–24 hours postoperatively to reduce infection rate. (BM)

- After scheduled surgery, chronic liver disease patients should be managed according to the ERAS protocol.
- PN should be preferred to no feeding in order to reduce complication rates and length of mechanical ventilation and length of stay in ICU, when oral nutrition or EN is impossible or not practicable.
- PN should be used in patients with unprotected airways and HE when cough and swallow reflexes are compromised or EN is contraindicated or impracticable.

- After the acute postoperative phase an energy intake of 30–35 kcal▪kg−1▪d−1 (126–147 kJ▪kg−1▪d−1) and a protein intake of 1.2–1.5 g▪kg−1▪d−1 should be aimed for
- For early EN nasogastric / nasojejunal tubes should be used as in non-liver disease surgery.
- After transplantation, enteral formula together with selected probiotics should be used to reduce infection rate.
- BCAA-enriched formulas can be used in patients with HE in need of EN

- No recommendations can be made regarding donor or organ conditioning by use of specific nutrition regimens, such as i. v. glutamine or arginine, with the object of minimizing ischemia/reperfusion damage

- Overnutrition can cause NAFLD or NASH which is a precursor condition for LC. Recommendations for the nutritional management of this condition are given in the section on NAFLD and NASH of these guidelines

- In infants and children, PN can cause cholestasis, therefore named parenteral nutrition-associated cholestasis (PNAC)
- In adults, it is difficult to differentiate between the role of the underlying condition (extensive small bowel resection, sepsis) and that of PN in the pathogenesis of PNALD.

- In case of PNAC in infants and children, lipid emulsions enriched with omega-3-fatty acids can be used.
- Recommendation 85—In adults with suspected PNALD, lipid emulsions with a reduced
- n6/n3 ratio can be used. (BM)

- Abbreviations
- ALF acute liver failure
- ASH alcoholic steatohepatitis
- BCAA branched chain amino acids
- CT computed tomography
- DXA dual energy X-ray absorptiometry
- EN enteral nutrition
- GL guideline
- HCC hepatocellular carcinoma
- HE hepatic encephalopathy
- ICU intensive care unit
- IFALD intestinal failure associated liver disease
- LC liver cirrhosis
- LT liver transplantation
- MCT medium-chain triglyceride
- MEDD Mediterranean diet
- MRT magnetic resonance tomography
- NAFL non-alcoholic fatty liver
- NAFLD non-alcoholic fatty liver disease
- NASH non-alcoholic steatohepatitis

- OLT orthotopic liver transplant
- ONS oral nutritional supplements
- PEG percutaneous endoscopic gastrostomy
- PN parenteral nutrition
- PNAC parenteral nutrition-associated cholestasis
- PNALD parenteral nutrition associated liver disease
- REE resting energy expenditure
- RFH-NPT Royal Free Hospital Nutrition Prioritizing Tool
- RFH-SGA Royal Free Hospital SGA
- SGA subjective global assessment
- SMOF soy-bean based lipid and olive oil and MCT-lipid and fish oil
- UDCA ursodeoxycholic acid
- VA study Veteran Affairs study