Nutritional support in liver diseases

M. Plauth (DE)
ESPEN Guideline
Nutrition in Liver Disease

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ESPEN Guideline Liver Disease
Working Group

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1. General (*sarcopenia*)
2. Acute Liver Failure ALF
3. Alcoholic Steatohepatitis ASH
4. Non-alcoholic Steatohepatitis NASH (*expanded*)
5. Liver Cirrhosis LC
6. Transplantation & Surgery
7. Nutrition Associated Liver Injury NALI (*new topic*)
**Recommendation 3:**
In NASH, LC and LT patients, the presence or absence of sarcopenia should be assessed since sarcopenia is a strong predictor of mortality and morbidity.
Grade of recommendation B – Strong consensus (100 % agreement)

**Recommendation 5:**
Radiologic methods (DXA or when CT/MRT images are available for other reasons) should be used to diagnose sarcopenia. (BM)
Grade of recommendation B – Strong consensus (100 % agreement)
112 patients with cirrhosis, skeletal muscle index (SMI): normalized muscle area [cm$^2$/m$^2$] at L3 low level of correlation with MELD or CPS

Montano-Loza et al, Clin Gastroenterol Hepatol 2012, 10:166-173
112 patients with cirrhosis, skeletal muscle index (SMI): normalized muscle area [cm²/m²] at L3 cut-off ♂ 52.4 cm²/m², ♀ 38.5 cm²/m²

Montano-Loza et al, Clin Gastroenterol Hepatol 2012, 10:166-173
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Cirrhosis Specific Cut-off Values for SMI at L3 Level

396 wait listed patients, multicenter, retrospective analysis
new proposed cut-off values for cirrhosis

♂ 50 cm$^2$/m$^2$
♀ 39 cm$^2$/m$^2$

→ Poster MON-P157

396 wait listed patients, multicenter, retrospective analysis
new proposed cut-off values for cirrhosis $\sigma$ 50 cm$^2$/m$^2$, $\varphi$ 39 cm$^2$/m$^2$
wait list mortality (death or removal for deterioration)

**Statement 10:**
Phase angle (measured by bioelectrical impedance analysis) or handgrip strength allow assessment of mortality risk. (BM)
Strong consensus (93% agreement)
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Phase Angle (BIA) – Low PA Predicts Mortality

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Frailty (Muscle Function) Predicts Wait-List List Mortality

309 OLT wait-list candidates, MELD $\geq$ 12 at enrolment, 20 % HCC median follow-up 13.7 (8.0-22.8) mo, median BMI 29 (25-33) kg/m$^2$

46 (15 %) dead or delisted
85 (28 %) OLT
155 (50 %) still waiting

HR (95 % CI)

<table>
<thead>
<tr>
<th>Measure</th>
<th>HR (95 % CI)</th>
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<tbody>
<tr>
<td>Grip strength per kg increase</td>
<td>0.89 (0.83-0.95)</td>
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<tr>
<td>Gait speed per 1m/sec increase</td>
<td>0.72 (0.62-0.84)</td>
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<tr>
<td>Chair stands per 1 sec increase</td>
<td>1.17 (1.09-1.25)</td>
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<tr>
<td>SPPB score &lt; 10</td>
<td>1.45 (1.15-2.20)</td>
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adjusted for baseline physical function, HCC, baseline albumin, baseline MELD-Na, longitudinal trajectory of MELD-Na

Lai et al, Hepatology 2016, 63: 574-580
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Topics

1. General
2. Acute Liver Failure ALF
3. Alcoholic Steatohepatitis ASH
4. Non-alcoholic Steatohepatitis NASH
5. Liver Cirrhosis LC
6. Transplantation & Surgery
7. Nutrition Associated Liver Injury NALI
**Recommendation 15:**

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.

Grade of recommendation B – Strong consensus (100% agreement)

**Recommendation 16:**

ONS should be used when patients with severe ASH cannot meet their caloric requirements through normal food in order to improve survival.

Grade of recommendation B – Strong consensus (100% agreement)

**Recommendation 18:**

EN should be used when patients with severe ASH cannot meet their caloric requirements through normal food and/or oral nutritional supplements in order to improve survival and infectious morbidity. Grade of recommendation B – Strong consensus (100% agreement)
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ASH – Underfeeding Associated with Mortality

n = 138, severe ASH
tube feeding and methylprednisolone vs oral nutrition and methylprednisolone

Moreno et al, Gastroenterology 2016, 150:903-910
<table>
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<td>6. Transplantation &amp; Surgery</td>
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<td>7. Nutrition Associated Liver Injury NALI</td>
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**Recommendation 29:**

In overweight / obese NAFLD / 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.

Grade of recommendation A – Strong consensus (96% agreement)

**Recommendation 30:**

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.

Grade of recommendation A – Strong consensus (100% agreement)
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NASH – Weight Loss Improves NASH

Vilar-Gomez et al, Gastroenterology 2015, 149:367-378
Effect of 48 weeks of life-style intervention aiming at improvement of at least 3 NAS points (red shaded area) on liver biochemistry and histology.

Promrat et al, Hepatology 2010, 51:121-129
Recommendation 32:
Overweight and obese NAFLD / NASH patients shall follow a weight reducing diet to reduce the risk of comorbidity and to improve liver enzymes and histology (necroinflammation).
Grade of recommendation A – Strong consensus (100% agreement)

Recommendation 33:
In order to achieve weight loss, a hypocaloric diet shall be followed according to current obesity guidelines irrespective of the macronutrient composition.
Grade of recommendation A – Strong consensus (93% agreement)
Effect of low carb vs low fat diet on intrahepatic triglyceride content and visceral adipose tissue mass

Haufe et al, Hepatology 2011, 53:1504-1514
Intrahepatic lipid content ($^1$H-MRS) before and after 6 weeks isocaloric protein-rich diet (30 % calories)

Markova et al, Gastroenterology 2017, 152:571-585
Recommendation 31:
In normal weight NAFLD / NASH patients, increased physical activity to improve insulin resistance and steatosis can be considered. (BM)
Grade of recommendation GPP – Strong consensus (100% agreement)
Effect of 12 weeks weight-neutral exercise on intrahepatic triglyceride content and visceral adipose tissue mass

Recommendation 45:
In otherwise eligible obese NAFLD / NASH patients without cirrhosis, after weight reduction diets and intensive lifestyle interventions have failed, bariatric surgery should be considered.
Grade of recommendation B – Strong consensus (100% agreement)

Recommendation 46:
In obese NAFLD / NASH patients, the efficacy of bariatric surgery regarding weight reduction and improvement in hepatic steatosis and necroinflammation including fibrosis as well as insulin resistance shall be considered.
Grade of recommendation A – Strong consensus (100% agreement)
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NASH – Bariatric Surgery can Improve NASH & Fibrosis

Remission of NASH and improvement of fibrosis
1 year after surgery

Remission of NASH

Improvement of fibrosis

Lasailly et al, Gastroenterology 2015, 149:379-388
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**Recommendation 52:**
In cirrhotic patients, an increased energy intake is not recommended in overweight, obese patients.
Grade of recommendation GPP – Strong consensus (100% agreement)

**Recommendation 57:**
In obese patients with cirrhosis lifestyle intervention aiming for beneficial effects of weight reduction should be implemented, which include reduced portal hypertension.
Grade of recommendation B – Strong consensus (100% agreement)
ESPEN Guidelines Liver Disease
Sarcopenic Obesity - Prognosis

678 patients with cirrhosis, SMI at L3

Montano-Loza et al, J Cachexia Sarcopenia Muscle 2016, 7:126-135
n = 161, compensated cirrhosis, trajectory until decompensation
BMI independent predictor, HR 1.06 (1.01-1.12), p=0.02

Berzigotti et al, Hepatology 2011, 54:555-561
... is a driver of portal hypertension

*Berzigotti et al, Hepatology 2017, 65:1293-1305*
**Recommendation 59:**

Periods of starvation should be kept short by consuming 3 to 5 meals a day and a late evening snack are recommended to improve total body protein status. (BM)

Grade of recommendation B – Strong consensus (100% agreement)
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Cirrhosis – Nocturnal ONS Improve Protein Status Better

**Recommendation 61:**

Long-term oral BCAA supplements (0.25 g·kg⁻¹·d⁻¹) should be considered in patients with advanced cirrhosis in order to improve event-free survival or quality of life (BM)

Grade of recommendation B – Consensus (89% agreement)
Sarcopenia in Liver Cirrhosis
Prognosis and Treatment with BCAA

130 patients with cirrhosis, skeletal muscle index at L3 (slice-O-matic) cut-off $\sigma \leq 52.4 \text{ cm}^2/\text{m}^2$ or $\varphi \leq 38.5 \text{ cm}^2/\text{m}^2$

subgroup on BCAA (3 x 4 g p.o.) for $\geq$ 1 year (BCAA indication: albumin $< 35 \text{ g/L}$)

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Recommendation 73:
In adults, for preoperative nutrition standard nutrition regimens should be used since specialised regimens (e.g. BCAA-enriched, immune-enhancing diets) were not superior to standard regimens regarding morbidity or mortality. (BM)

Grade of recommendation B – Strong consensus (100% agreement)
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OLT – No Effect of Pre-OP Immune Enhancing Diet

120 OLT wait list patients, double-blind RCT, follow-up until 360 d post-OP oral immune enhancing vs isocaloric standard diet
8 (IED) and 11 (Con) patients died or delisted

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OLT – No Effect of Pre-OP Immune Enhancing Diet

120 OLT wait list patients, double-blind RCT, follow-up until 360 d post-OP oral immune enhancing vs isocaloric standard diet

8 (IED) and 11 (Con) patients died or delisted

→ no difference in total body protein, grip strength, infections, LOS

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Survival after OLT – Effect of Perioperative Nutrition Nutrition

124 living donor transplant recipients

Kaido et al, Am J Transplant 2013, 13: 1549-1556
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7. Nutrition Associated Liver Injury NALI
Statement 15:
In infants and children, parenteral nutrition can cause cholestasis, therefore named parenteral nutrition-associated cholestasis (PNAC). Strong consensus (92% agreement)

Recommendation 84:
In infants, children and adults, specialised nutrition protocols making optimal use of enteral nutrition should be implemented. Grade of recommendation B – Strong consensus (92% agreement)

Recommendation 85:
In case of PNAC in infants and children, the use of lipid emulsions enriched with omega-3-fatty acids can be considered. Grade of recommendation 0 – Strong consensus (100% agreement)
Statement 16
In adults it is difficult to differentiate between the role of the underlying condition (extensive small bowel resection, sepsis) and that of parenteral nutrition in the pathogenesis of parenteral nutrition associated liver disease. (PNALD).
Strong consensus (100% agreement)

Recommendation 86:
In adults with suspected PNALD, the use of lipid emulsions with a reduced n6/n3 ratio may be considered.
Grade of recommendation 0 – Strong consensus (92% agreement)
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