HEPATOLOGY

A clinical textbook

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20. Nutrition and liver diseases

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Abbreviations

Branched-chain aminos acids (BCAA)
Hepatic encephalopathy (HE)
Aromatic aminod acids (AAA)
End stage liver disease (ESLD)

Abstract

The liver, as the central metabolic organ, is essentially responsible for nutrient homeostasis. Therefore, nutrition is a central aspect in liver diseases. On the one hand, patients with advanced liver diseases often suffer from malnutrition and sarcopenia, which have an important impact on the mortality and morbidity in these patients and affect the outcome after liver transplantation. Hence, early screening and implementation of nutritional therapy are crucial for these patients. On the other hand, malnutrition can also cause liver diseases such as fatty liver disease or parenteral nutrition-associated liver diseases.

In conclusion, nutrition and nutritional therapy is an important part in the field of hepatology.

Introduction

Patients with advanced liver disease, such as cirrhosis, often suffer from malnutrition and loss of muscle mass and functionality, which is referred to as sarcopenia. The prevalence of malnutrition is very high, affecting up to 80% of patients with cirrhosis. Numerous studies have shown that malnutrition and sarcopenia promote disease progression and worsen prognosis. This has been attributed to the increased rate of complications such as infections, hepatic encephalopathy, ascites, and hepatorenal syndrome. In addition, the outcome of liver transplantation is also significantly influenced by preoperative nutritional status (Bischoff 2020, EASL 2019, Plauth 2019).

In contrast, overweight or obesity in metabolic diseases is not only causally related to liver disease but also increases morbidity and mortality (Plauth 2024).

While malnutrition is usually obvious in advanced liver cirrhosis,

the risk of malnutrition in early liver disease and especially overweight sarcopenia is not perceived. In the final stage of liver cirrhosis, however, it is difficult to influence the nutritional status. Therefore, a structured assessment of the nutritional status at the first diagnosis of liver disease is crucial. It allows early detection of malnutrition and initiation of targeted nutritional therapy to prevent late complications and improve prognosis (Bischoff 2020, EASL 2019, Plauth 2019, Plauth 2024).

Screening and assessment of nutritional status

Screening and baseline assessment for malnutrition and obesity

In addition to the diagnosis and the stage of the presenting liver disease, the detailed history should include nutritional aspects (e.g. weight history, nausea, vomiting, reported dietary intake, digestive symptoms).

In addition to the physical examination, the basic assessment begins with the collection of the body mass index (BMI; body weight kg / body length m^2). According to the generally accepted rules, a BMI ≤18.5 is considered underweight (for patients older than 65 years a BMI ≤20) and a BMI ≥25 is considered overweight, a BMI ≥ 30 is considered obesity. However, when assessing BMI, it is important to keep in mind that ascites and oedema may confound the significance, and that malnutrition and sarcopenia may also be present in overweight or obese patients. A simple estimation correction formula can be used for patients with ascites: subtract 5% of body weight for small amounts of ascites, 10% for medium amounts, and 15% for large amounts of ascites (Plauth 2024).

Laboratory chemistry parameters can complement the examination and should be determined according to the underlying disease. For nutritional status, determination of liver synthesis parameters such as albumin, prealbumin, transferrin, minerals, and vitamins may be helpful.

Nutrition screening tools

All patients with chronic liver disease should be systematically screened for the presence of malnutrition using a validated tool at the time of diagnosis. This evaluation should then be repeated every 3-6 months according to the dynamics of the disease course (Lai 2021, Plauth 2024).

In clinical practice, the Nutritional Risk Score (NRS 2000) according to Kondrup is primarily used in addition to the Subjective Global Assessment Score (SGA) according to Detsky. Although both scores are clinically well established and the NRS has gained acceptance due to its relatively simple and examiner-independent collection, neither score has been evaluated in patients with liver disease. An NRS ≥3 indicates an increased risk of malnutrition (Bischoff 2020, Plauth 2024).

Two tools have been developed for liver-specific screening for malnutrition: the Royal Free Hospital Global Assessment (RFH-Ga) or Royal Free Hospital Nutritional Prioritising Tool (simplified form RFH-NPT), which has also been validated in patients with chronic liver disease, and the Liver Disease Undernutrition Screening Tool (LDUST). Both tools are recommended. The RFH-NPT is investigator-independent and correlates with cirrhosis severity, progression, and complication rate. The LDUST is relatively easy to collect due to the 6 questions asked of the patient, but is of limited value due to the patient's subjective assessment (Georgiou 2020, Boulhosa 2020, Plauth 2024).

Expanded nutritional assessment

All patients with alcohol-associated hepatitis (ASH), metabolic dysfunction-associated steatohepatitis (MASH), cirrhosis, and those listed for transplantation should be screened for the presence of sarcopenia, as it is a strong predictor of morbidity and mortality. Several methods can be used for this purpose (Plauth 2024, Lai 2021).

Radiologic methods should be used to quantify muscle mass and quality as a prognostically important subcriterion of sarcopenia (e.g., when performed for other indications). Special software could be used to measure the area of the psoas and paravertebral muscles at the level of LWK 3 and relate it to body surface area. Skeletal muscle index values of < 50 in men and < 39 cm2/m2 can be used as cutoff values for the diagnosis of sarcopenia (Plauth 2024, Carey 2017).

Anthropometric measurements such as mid-arm circumference and triceps skinfold (TZF) are easy to obtain. All that is needed is a tape measure or, for TZF, a skinfold caliper. The TZF correlates with the body fat mass. These tests are of particular prognostic importance in disease progression. Matching with percentile tables taking into account sex and age allows assessment of nutritional status (malnutrition <15th percentile) (EASL 2019).

Since not only muscle mass is important for prognostic assessment but quite significantly muscle function, handgrip strength, walking speed, or chair stand-up test should be performed for quantification (Lai 2021, Plauth 2024).

To assess frailty as a multidimensional construct, a standardised instrument should be used that also allows graduation such as the Karnofsky Index and the Liver Frailty Index (Lai 2021, Plauth 2024).

One method for determining compartments is bioelectrical impedance analysis (BIA). In addition to determining body compartments, phase-sensitive devices in mono-frequency mode allow determination of the phase angle (PhA). PhA is of prognostic importance and represents an integral measure of cell mass and cell integrity. A PhA < 5 correlates with increased mortality (Ruiz-Margáin 2021, Plauth 2019, Plauth 2024).

- All patients with advanced liver disease should be screened for malnutrition and sarcopenia.
- NRS screening could be used for basic screening.

Nutritional management

Therapy of malnutrition

As the central metabolic organ, the liver is primarily responsible for nutrient homeostasis. Accordingly, advanced liver dysfunction results in catabolism due to increased gluconeogenesis and decreased ability to release glucose from glycogen during fasting periods.

Nutritional therapy should first consider the causes and incorporate individual needs into nutritional counseling. A helpful basis for expert nutritional counseling is the preparation of a food diary for at least 3 days. In any case, the nutritional therapy should be carried out by a nutrition expert (registered dietitian, ecotrophologist, bachelor of science dietitian).

If patients are unable to achieve their nutritional energy and protein goals through oral dietary intake even after all measures have been exhausted, there should be no hesitation to prescribe artificial nutrition. Here, sip feeds are available for oral nutrition supplementation (ONS), but enteral nutrition via tubes as well as parenteral nutrition (PE) should also be used to overcome the period of malnutrition as well as permanent home nutritional support (Bischoff 2020, Plauth 2019, Plauth 2024).

Energy requirements

Energy requirements are best determined by measuring resting energy expenditure (REE) using indirect calorimetry; if this method is not available, energy requirements can be estimated using formulas (Bischoff 2020, EASL 2019, Plauth 2019). The ideal weight or dry weight should be used as a reference. It should be taken into account that in liver cirrhosis patients the measured REE may differ from the estimated one by ± 500 kcal/d. Energy requirements depend on the underlying disease or stage of the disease and physical activity. Approximately 35% of patients with liver cirrhosis exhibit hypermetabolism, while up to 30% exhibit hypometabolism (Müller 1999, Limon-Miro 2022). Patients with acute liver failure have an 18-30% increased REE compared to healthy individuals (Walsh 2000). Sustained alcohol consumption increases REE by 26%, which decreases rapidly with abstinence (Levine 2000). Patients with metabolic dysfunction-associated steatotic liver disease (MASLD) are more complex to assess because overweight or obesity, inflammatory activity, and pre-existing cirrhosis affect energy expenditure.

Thus, the recommendation can be derived to set the energy requirements for patients (without unusual physical activity) with liver cirrhosis, acute liver failure, ASH, and after liver transplantation (LT) at 1.3 times the dietary REE, which corresponds to 30 kcal/kgKG/d; for patients with MASLD without inflammation, 20-25 kcal/kgKG/d (Bischoff 2020, EASL 2019, Plauth 2019). For obese patients with MASLD an energy-restricted diet with exercise therapy should be implemented for weight loss, which can also be implemented with formulary diets *(see MASLD chapter)*.

Obese patients with chronic liver disease who are critically ill or facing surgery or liver transplantation should be fed hypocaloric, high-protein diet. The energy and protein targets are based on the recommendations for critically ill patients; for BMI 30-50, 22-25 kcal/kg/d and protein intake of 1.5 g/kg/d (amino acids 1.8 g/kg/d) are recommended; for BMI > 50, energy intake of 11-14 kcal/kg and protein intake of 1.5 g/kg (amino acids 1.8 g/kg/d) are calculated at ideal weight (Elke 2019).

Nutrient requirements

When calculating the macronutrients protein, carbohydrates and fats, the increased requirement in cirrhosis should be taken into account. Meals can be enriched with energy- and protein-dense additives (EASL 2019). Protein restriction even in encephalopathy is not recommended, except for severe encephalopathy with severely elevated ammonia, and then only for 24-48 hours. Early nutritional support should be provided to accelerate resolution of encephalopathy (Nardelli 2019). Thus, protein intake of 1.2-1.5 g/kgKG/d is recommended (EASL 2019, Plauth 2019, Plauth 2024). This is to stabilise the catabolic metabolic state that is often aggravated by protein losses. Plant proteins have a more favourable amino acid profile than animal products. Branched-chain amino acid (BCAA) supplementation in decompensated patients has been shown to have a positive effect in some studies (Dam 2018).

Carbohydrate intake is recommended at 50-60% of non-protein dependent energy requirements with a fat intake of 1g/kgKG/d. In cases of

fat malabsorption, such as chronic cholestasis, modification with medium-chain fatty acids may have a stabilising effect on malnutrition.

For patients with MASLD, the Mediterranean diet with whole grain products is particularly recommended *(see MASLD chapter)*. Patients with advanced liver disease should avoid alcohol altogether. Alcohol has a high energy density with no nutritional value and at the same time inhibits energy turnover, making it counterproductive for both weight loss and malnutrition. In addition, the risk of hepatocellular carcinoma and osteoporosis is increased (Bischoff 2020, EASL 2019) *(see ASH chapter)*.

Patients with advanced liver disease should generally be urged to eat 3 main meals and 3 snacks to avoid fasting periods longer than 4 hours. This can be implemented by a late-night snack (protein, carbohydrate) or anONS.

Salt-restricted diets are not recommended, because they increase the risk of worsening malnutrition. The EASL guideline recommends 5 g of salt added to the diet daily in cirrhotic patients with ascites (EASL 2019).

Certain micronutrients are critical in chronic liver disease especially with increased alcohol consumption and diseases associated with maldigestion-absorption (Llibre-Nieto 2021). If a deficiency exists or a high risk can be assumed, supplementation should be added to the diet. This concerns the fat-soluble vitamins, specifically the vitamin D (target > 30 ng/mL), and the water-soluble vitamins, namely folic acid and vitamin B1. The latter play a pathogenetic role for Wernicke's encephalopathy in alcohol dependence (Plauth 2024).

For minerals and trace elements, timely zinc and magnesium supplementation should be prescribed (Bischoff 2020, EASL 2019).

Protein supplementation

One the one hand, patient with end-stage liver disease and malnutrition have the need for a hypercaloric, high-protein diet, but on the other hand, they have a high risk for hyperammonaemia and hepatic encephalopathy (HE).

Branched-chain amino acids (BCAA), including leucine, isoleucine and valin are essential amino acids, which are mostly metabolised in the muscles, therefore they could be utilised even in end-stage liver disease (ESLD). In contrast, aromatic amino acids (AAA) could not sufficiently be metabolised any more in ESLD and accumulate. Therefore, the ratio between BCAA and AAA (BCAA to AAA ratio), which is normally 3.5:1, is altered, which seems to worsen HE. Furthermore, there is evidence that BCAA support the ammonia detoxification and have ammonia lowering effect (Plauth 2024). Clinical studies could demonstrate that BCAA reduce hepatic encephalopathy in ESLD and improve the incidence of post-LTc bacteremia and sepsis (Dam 2018). Besides these beneficial effects of BCAA, there is also some discussion about potential negative side effects. BCAA could impair liver fat content and insulin resistance (Plauth 2011). However, further studies are needed to confirm these data.

In conclusion, the current ESPEN guidelines recommend the use of BCAA in patients with HE and need for additional enteral nutrition (Bischoff 2020, Plauth 2019).

- Median energy requirement in patients with advanced liver disease is around 30 kcal/kgKG/d
- Energy requirement in patients with MASLD should be around 20-25 kcal/kgKG/d
- Protein intake should be 1.2-1.5 g/kgKG/d
- BCAA are recommended for patient with risk for clinical HE

Nutrition and liver transplantation

Before Liver transplantation

Malnutrition and sarcopenia are associated with an increased risk of morbidity and mortality in patients with end stage liver disease (Kim 2017). Furthermore, this is associated with increased mortality in patients on the waiting list and even affects the outcome after liver transplantation (Kalafateli 2017). A small pilot study showed that pre- and perioperative nutritional support may improve posttransplant outcomes (Plank 2005).

Therefore, it is recommended that patients on the waiting list should be carefully screened for malnutrition and sarcopenia. Early nutritional support should be implemented according to the current nutrition status and the recommended nutrition guidelines for patients with end stage liver disease. In short, a total energy intake of 30 kcal/kg/d and a protein intake of 1.2-1.5 g/kg/d are recommended (Bischoff 2020, Plauth 2019). Oral nutrition is preferred and should be accompanied by nutritional counseling. However, if the required energy intake cannot be achieved orally, further support with enteral or parenteral nutrition support should be provided at an early stage. In this case, enteral nutrition is the preferred route because it preserves the gut barrier and may therefore reduce the risk of bacterial translocation. However, this might be often challenging due to ascites. Therefore, parenteral nutrition is also recommended.

As obesity is an epidemic burden, it is an increasing problem also in the transplant setting. Diet and exercise are important treatment options, even in patients already on the waiting list. Weight loss in this group of patients should be achieved by reducing calories from carbohydrates and fat content, while maintaining a high amount of protein intake (2,0g/kg/ideal body

weight) to avoid sarcopenia (Moctezuma-Velazquez 2019). Total energy intake should be around 25 kcal/kg of ideal body weight. In the specific setting of liver transplantation, the use of BCAA is not recommended. In addition, the use of specific immunonutrition is not recommended.

After liver transplantation

With a new functional liver, nutritional and metabolic dysfunctions are expected to improve. However, the normalisation of malnutrition and sarcopenia may be prolonged and some alterations in body composition may persist. On the other hand, there is the risk for the development of other kind of malnutrition, such as obesity. Therefore, nutritional therapy is an important tool in terms of long-term outcome after LT (Hammad 2017a, Hammad 2015). Shortly after transplantation, enteral nutrition should be implemented after LT within 12-24 h as it could reduce the rate of infections (Hasse 1995). After the acute postoperative period, a total energy intake of about 30-35kcal/kg body weight with at least 1.2-1.5/kg body weight of protein is recommended in the current ESPEN guidelines (Bischoff 2020).

Recent studies have shown a significant reduction of infections by administration of pre- and probiotics such as Lactobacillus spp. (Plank 2005, Rayes 2002, Sugawara 2006). Specifically, the addition of synbiotics (combination of pro- and prebiotics) have been shown to restore macrophage function and modulate lymphocyte function, mainly through Lactobacillus. Furthermore, improving the intestinal barrier could prevent bacterial translocation from the gut. Therefore, the additional use of synbiotics after LT is recommended in the current guidelines.

Immunosuppression

The main change in lifestyle after LT is due to the lifelong intake of immunosuppression. Common immunosuppression after LT compromise steroids, calcineurin inhibitors such as cyclosporin or tacrolimus, and mycophenolat-mofetil. This therapy affects the diet by changing the metabolism, immune function and by food-drug interactions.

Metabolism

Corticosteroids could lead to overweight, as they increase appetite. Furthermore, they promote insulin resistance and dyslipidaemia and also influence the fat distribution (Noppe 2016). Their use is also associated with increased risk for liver steatosis (Sprinzl 2013). Calcineurin inhibitors, such as cyclosporin or tacrolimus, are associated with prediabetes (Perito 2017) and with significant weight gain after LT (Hammad 2017b). Furthermore, tacrolimus was associated with increased liver steatosis after LT. Therefore, weight gain is a current problem after LT. Obesity and new onset of diabetes are important risk factors for graft steatosis and increase the cardiovascular risk (Campos-Murguia 2024, Galvin 2019). Patients should be advised to aim for a normal body weight and avoid obesity. On the other hand, everolimus and sirolimus are associated with decrease in muscle mass (Hammad 2017a), which should be prevented by physical activity and sufficient protein intake.

Calcineurin inhibitors are known to affect the insulin secretion (Heit 2006, Vincenti 2007). Corticosteroids lead to insulin resistance with consecutive impaired hepatic glycogen metabolism and increased gluconeogenesis. As obesity further increases the risk of diabetes after LT (Chang 2018), obesity should be prevented.

While zincs deficiency regress in most cases, hypomagnesaemia often occurs after transplantation as a side effect of calcineurin inhibitors. Therefore, the intake of magnesium-rich food is encouraged, such as whole grain, nuts and seeds. In addition, steroids lead to hypocalcaemia and vitamin D deficiency, so vitamin D and optional Calcium substitution is recommended.

Immunosupression and food interaction

Food-drug interactions are mainly due to modification in the CYP3A4 and CYP 450 metabolism, which affects the immunosuppressive metabolism and therefore the blood concentration. The most important food is grapefruit, as it significantly increases calcineurin inhibitor levels in particular (Chan 2001). Particularly, the components bergamottin and naringenin act on the CYP3A4 pathway, which are also present in pomelo. One study showed that pomelo affected the cyclosporin levels (Grenier 2006). In addition, pomegranate juice has been shown to modulate CYP3A4 in animal models and *in vitro* (Mansoor 2023). However, a recent study in humans showed no significant alterations in cyclosporin levels (Anlamlert 2020). Another study further demonstrated, that all citrus fruits might affect the CYP3A4 pathway in a dose-dependent manner (Fujita 2008), as they all contain at least bergamottin or naringenin. In conclusion, patients should avoid eating grapefruit and should be educated about the potential risk of pomelo, cranberry and pomegranate to modify immunosuppressant levels in a dose-dependent manner.

Furthermore, St. John's wort affects the CYP4A3 and p-glycoprotein pathways and therefore affects the levels of tacrolimus and cyclosporine (Mannel 2004).

Immune systeme

Due to the immunosuppression, the transplant recipient is more susceptible to infections, especially food-borne infections, such as Shigella, Yersinia, Norovirus or Rotaviruses (Fagiuoli 2014). It is therefore important to avoid raw meat, fish, eggs and unpasteurised dairy products. Furthermore, vegetables and fruits should be washed thoroughly. In addition, food should be stored at appropriate temperatures and the kitchen should be hygienic and clean.

Furthermore, hepatitis E virus infection in liver transplant recipients is a serious infection because it can lead to chronic hepatitis with rapid progression to cirrhosis. Besides transmission via blood products, hepatitis E virus is mainly transmitted via undercooked meat and fish (Behrendt 2014). Meat should be cooked properly for at least 20 minutes.

In summary, good kitchen and food preparation hygiene is recommended to prevent food-borne infections.

Conclusion

In conclusion, nutritional therapy is an essential module in the treatment of patients before and after liver transplantation. Pre-operative malnutrition has a significant impact on the post-transplant outcome and should be treated as early as possible. Furthermore, nutritional therapy can prevent many side effects and complications after liver transplantation.

- Malnutrition and sarcopenia in patients on the liver transplant waiting have a significant impact on short- and long-term outcomes after liver transplantation and should be treated as early as possible.
- After liver transplantation, normal weight should be achieved, overweight should be avoided.
- As Immunosuppression influences the immune system, foodborne infections should be prevented.
- Due to interaction with immunosuppression, especially grapefruit and St. John´s wort intake should be avoided.

Nutrition-associated liver injury (NALI)

Severe malnutrition, such as in anorexia nervosa, can lead to liver damage and even acute liver failure due to the lack of protein in the diet. The reduced synthesis of apoproteins with fatty degeneration of the liver plays an important pathophysiological role. In addition, malnutrition also impairs other important liver functions and is able to induce hepatocellular autophagy processes (Bitetto 2010, Plauth 2019). It is not known whether fatty liver can progress to chronic liver disease because of malnutrition.

If nutrition resumes, there is a risk of acute liver damage from refeeding syndrome. This develops with a maximum rise in transaminases around day 27 and normalises in more than 80% of patients after 1 month (Rosen 2017).

Of increasing importance is liver damage up to acute liver failure due to malnutrition after bariatric surgery (Addeo 2019). Studies indicate that liver failure occurs at a median of 20 months. The incidence is highly dependent on the surgical procedure used and is highest with jejunoileal bypass and Scopinaro biliopancreatic diversion procedure. The cause is multifactorial, with bacterial overgrowth in the small intestine and severe protein amino acid deficiency thought to play an important role. In addition, it should be noted that the affected patient population already has a very high predisposition to MASLD. Therefore, in addition to monitoring nutritional status and liver function parameters, it is necessary to implement an adapted nutritional concept perioperatively. A nutritionist should accompany patients in this regard.

For information on liver damage due to hyperalimentation, see the chapter on MASLD.

Liver damage caused by medical nutrition

Parenteral nutrition (PE) can cause liver disease, which also manifests varies depending on the age of the patient and the type of intestinal failure. In infants and children, cholestatic liver disease called *Parenteral Nutrition Associated Cholestasis (PNAC)* may occur in addition to steatosis. Premature infants with low birth weight are particularly affected. Due to their different presentation and pathophysiology, PNAC in infants should be distinguished from PE-associated liver disease in adults (PNALD) (Koletzko 2010).

Adult PNALD is defined as a complication of PE administered for more than 14 days, which is usually biochemically associated with a 1.5-fold increase in the upper limit of normal or at least 2 of the following liver enzymes: AST, ALT, alkaline phosphatase. Often, this enzyme increase, which occurs 1-3 weeks after the onset of total PE, is accompanied by an increase in conjugated bilirubin of > 2 or 3 mg/dL (Żalikowska-Gardocka 2020). Histologically, there is predominantly evidence of small-mixed droplet fatty degeneration without nuclear shift, which is fundamentally different from classic MASLD. Progression is via steatohepatitis with periportal lymphocytic infiltration and hepatocellular necrosis to fibrosis and bile duct hyperplasia to cirrhosis (Buchman 2017). Prevalence and

disease progression depend on the duration of PE and the remaining length of the small bowel after bowel resection. Analyses showed that remaining small bowel length < 50 cm and fat administration > 1.0 g/kgKG/d were significantly associated with liver failure. Thus, pathophysiologically, liver damage is not only a consequence of PE but also of intestinal failure, which is why the literature often refers to "intestinal failure-associated liver disease" (IFALD), which is very difficult to differentiate in the clinic.

Prevention and treatment of NALI

For the prevention of NALI, specific nutritional protocols should be implemented in infants and children as well as adults with the aim of promoting enteral feeding patterns and intestinal rehabilitation in the best possible way (Bischoff 2020). The involvement of a qualified nutritionist is imperative in addressing these issues. Energy and nutrient intake must be individually adjusted to avoid both deficiencies as well as hyperalimentation. In addition, the adaptation and absorption capacity of the intestine should be promoted to the maximum (Pironi 2023). In most cases, an individual formulation (compounded) will be required as part of a long-term PE. Lipid intake has been focused on as a critical nutrient parameter in studies, with lipid emulsions containing fish oil being attributed a protective effect (Koletzko 2010). However, few basic rules can be derived from these studies. Accordingly, for the prevention of PE-associated liver damage in both children and adults, mixed lipid emulsions, which may contain omega-3 fatty acids in addition to MCT, oleic acid, should be used rather than pure soybean oil emulsions (Pironi 2023). If PNALD is suspected, the lipid emulsion should be changed to a reduced ratio of omega-6/omega-3 fatty acids (Lapillonne 2018).

- Parenteral nutrition may cause liver disease (PNALD).
- PNALD may manifest as a cholestatic or steatotic liver disease.
- Omega-3 fatty acids may be used to treat PNALD.

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