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GUIDELINE

Nutritional Management in Chronic Liver Diseases and Liver Transplantation

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Abstract

Prevalence of malnutrition is most common in patients with chronic liver diseases. Malnutrition is associated with frequent infections, inflammations, long duration of hospitalisation and cause deep negative impact on disease progression and outcomes. Early screening and identifying the levels of malnutrition may help in initiating timely and focused care to prevent further complications.

Keywords: Nutrition; Malnutrition; Assessment

Introduction

Advanced liver disease patients are more prone to malnutrition and nutritional deficiencies. Prevalence of malnutrition increases with liver disease severity and raises the risk of mortality even in patients with Model for End-Stage Liver Disease – Sodium (MELD-Na) < than 15[(1)]. Hospitalisation and risk of malnutrition elevates in malnourished patients than the well-nourished, and in some patients, malnutrition is masked by obesity. Hence, regular nutritional screening and diet therapy helps in identifying and treating malnutrition and improves the disease condition and quality of life of the patient[(2)]. But intake of food is affected in liver disease patients due to various factors like feeling of fullness, decreased appetite, unpalatable food due to diet restrictions[(3)], ascites and long hours of fasting for certain medical procedure Figure 1. Diet for chronic liver diseases (CLD) patients should be a normal standard diet with supplements if necessary. Goals of diet therapy are to improve the status of malnutrition, to supply recommended macro and micronutrients, to correct nutritional deficiency diseases or clinical signs if any, to achieve positive nitrogen balance, to prevent muscle depletion, complications and to avoid hepato-toxic elements through diet[(4)].

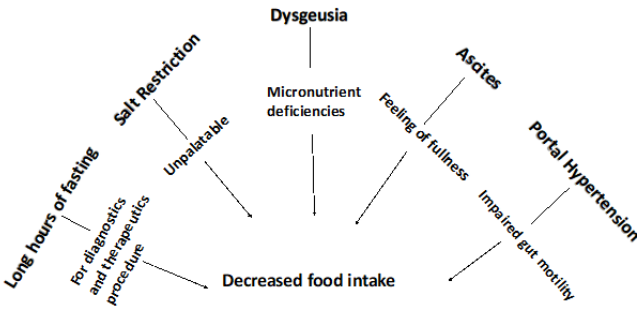

Fig 1. Factors affecting food intake in chronic liver disease

Methodology

This paper addresses the guidelines on nutrition in chronic liver diseases and liver transplantation. Practical guidelines recommendations were initiated after critical evaluation of previous guidelines. Search was done for systematic reviews, randomized controlled clinical trials and original articles. These guidelines focus on the practical and feasible considerations in Indian scenario and after many deliberations by our expert group, these final recommendations were framed.

Recommendation 1

- **Malnutrition has many negative impacts in patients with CLD, hence nutritional assessment is required.**
  - Malnutrition is a serious issue of concern in liver diseases, often undiagnosed and is associated with worse outcomes. Prevalence of malnutrition is around 5-92% in patients with liver diseases [3].
  - Malnutrition is associated with loss of subcutaneous fat, muscle mass and muscle strength, increased risk of bacterial infections and complications, nutritional deficiency diseases, longer periods of hospitalization and/or ventilation.
  - Malnutrition affects the overall survival and prognosis prior to and after liver transplantation (LT) [5].
  - High risk for malnutrition is also assumed if body mass index (BMI) <18.5 kg/m^2, or >40kg/m^2 or Child Turcotte Pugh (CTP)-C.
  - Detailed nutritional screening must be performed once in every three months for outpatients and on a monthly basis for those who are at risk for malnutrition and on a weekly basis for hospitalized patients.
  - Detailed nutritional screening includes global assessment tools viz., subjective global assessment (SGA), Royal Free Hospital Nutrition Prioritizing Tool (RFHNT), Nutrition Risk Screening (NRS)-2002 and Malnutrition Universal Screening Tool (MUST); anthropometry assessment like mid-arm muscle circumference (MAMC), mid-arm circumference (MAC), triceps skinfold thickness (TSF), BMI and muscle mass evaluation.
  - NRS-2002 and MUST are validated tools to screen the risk of malnutrition in hospitalised patients and recommended by ESPEN [6].
  - NRS-2002 is helpful in identifying malnutrition among liver cirrhosis patients with Hepatocellular carcinoma (HCC) [6].
  - RFH-NPT is considered the validated gold standard for malnutrition screening and to identify those at risk of malnutrition. It is considered more sensitive than NRS-2002 [7].
  - Dual-energy X-ray absorptiometry (DEXA) and Bioimpedance analysis (BIA) can also be used to estimate skeletal muscle mass. However, this leads to overestimation due to water retention [2].
  - Physical frailty is a good predictor of adverse clinical outcomes in chronic liver diseases (CLD). Patients referred for liver transplantation should be assessed both at baseline and during follow-up using objective performance frailty tools like liver frailty index.

Recommendation 2

- **Patient with chronic liver diseases requires high calorie diet to reverse malnutrition.**
  - High calorie intake of about 30-35kcal/kg/day (1.2-1.3 times the REE) is recommended to improve their nutritional status, prevent catabolism and enhance liver regenerationFigure 2.
  - Calorie intake can be achieved by increasing the frequency of meals i.e. 5-7 small meals per day than three big meals a day.
  - 50-60% of total calories should be provided from carbohydrates mainly complex carbohydrates, 20-30% of calories from fat, preferably MUFA and PUFA (saturated fat intake should be limited) and 20-30% of calories from proteins [8].
  - Excess intake of calories leads to lipogenesis and liver dysfunction.

Recommendation 3

- **Optimal intake of protein, carbohydrate and fats are beneficial in cirrhotic patients.**
  - Protein requirement in CLD patients who are not malnourished is 1.2 g/kg/day and in the presence of malnutrition 1.5g/kg/day is recommended [8] to prevent muscle loss, reduce lethargy and gain

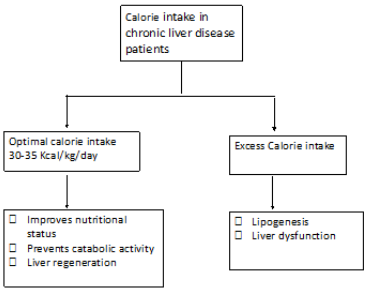

Fig 2. Effect of calorie intake in chronic liver disease patients

muscle mass[9].

- Inadequate protein intake of less than 0.8g/kg/day increases the risk of morbidity and mortality in cirrhotic patients[10].
- Milk protein and vegetable proteins are well tolerated by cirrhotic patients, in addition, animal protein improves the protein quality and is well absorbed[4].
- Branched-chain amino acids (BCAA) are a combination of dairy and plant protein, which helps in increasing appetite, restoring muscle mass, synthesizing skeletal muscle and maintaining Fischer ratio[11].
- Limitation in glycogen storage increases the risk of hypoglycemia hence a liberal intake of carbohydrate is required to increase the glycogen stores to improve liver function.
- 300-400g/day of high complex and simple carbohydrates is suggested and can be obtained through 4-6 carbohydrate rich foods[12].
- 60-70% of calories should be obtained from carbohydrates to prevent ammonia accumulation[13].
- Fat restriction is not advisable until slow gastric emptying and steatorrhea are reported[14].
- Short chain and medium chain fatty acids can be supplemented as it does not require bile salts for absorption.
- Omega-3 fatty acids supplementations delay disease progression and are beneficial especially in the post-transplant period[15].

Recommendation 4

- **Obesity increases the risk of morbidity and mortality, irrespective of its etiology, hence hypo-calorie diet with high protein is recommended in patients with obesity.**
  - 20-35% of CLD patients are obese irrespective of its etiology**.** Increased obesity is observed in Non-alcoholic steatohepatitis (NASH) related cirrhosis.
  - Obesity in end-stage liver disease (ESLD) patient is associated with increased infection.
  - A target of 5-10% weight loss can be achieved by reducing 500-800 kcal from their daily requirements.
  - High protein diet of greater than 1.5g/kg/day is recommended.
  - Hypocaloric can be maintained by reducing the food portion size and the frequency of eating.
  - High protein intake helps in preventing muscle loss and promoting weight loss.
  - Physical activity should be increased gradually and avoid hypomobility.

Recommendation 5

- **All patients with CLD should be identified for potential micronutrient status and if any deficiencies should be treated.**
  - Micronutrient deficiencies are very common among patients with liver diseases due to poor intake, depleted stores of nutrients and malabsorption and dysbiosis.
  - Fat soluble vitamin deficiencies are common due to inadequate bile secretion and decreased storage[16].
  - Inadequacies also occur due to less intake, malabsorption, and decreased synthesis of binding proteins (retinol binding protein for Vitamin A and Vitamin D binding proteins).
  - Daily oral supplementation of 2000-2,00,000 IU of vitamin A is suggested if serum retinol levels are <10 μg/dL which reflects vitamin A deficiency[17].
  - Serum calcidiol (25-hydroxy vitamin D [25(OH)D]) reflects vitamin D levels. The Endocrine society considers serum calcidiol levels between 20 - 30 ng/mL as insufficient and <10 ng/mL as a risk factor for hepatic decompensation and mortality[18].
  - Endocrine society also suggests oral dosage of 6000 IU/day or 50,000 IU/week to be supplemented during deficiency and oral maintenance dose of 1500-2000 IU/day can be continued until the normal serum levels are achieved[19].
  - Vitamin E deficiency can cause hemolytic anaemia, platelet aggregation and peripheral neuropathy. During deficiency 400-800 IU/day is recommended as initial supplementation.
  - Vitamin K is common in decompensated disease mainly due to malabsorption and gut dysbiosis. Injection with the dosage of 10mg of Vitamin K for 3 days is helpful in treating the deficiency.
  - Due to malabsorption and gut dysbiosis, oral supplement will not be beneficial in these patients.

- In alcoholic liver disease, vitamin B deficiency cause Wernicke's encephalopathy and Korsakoff's dementia. Oral supplementation of 30-100 mg of thiamine twice/ thrice/day treats this condition [20].
- Folic acid deficiency causes microcytic anaemia. Intravenous supplementation of 400-1000 μg for 3days and 400 μg/day orally until normal levels of erythrocyte folate is achieved (140ng/ml) [21].

Recommendation 6

- **Malnutrition and sarcopenia are associated with increased risk of morbidity and mortality.**
  - Due to the limited capacity of hepatocytes to synthesize, store and breakdown of glycogen, carbohydrate utilization is reduced and fat depletion is increased for energy utilization. As the disease progresses, scarcity of fat leads to pronounced muscle protein breakdown that further leads to skeletal muscle loss contributing to sarcopenia [22].
  - Prevalence (47% - 84%) of malnutrition and sarcopenia in cirrhosis is higher among the Indian population [8].
  - Sarcopenia in cirrhotic patients have an increased chance of developing hepatic encephalopathy (HE), refractory ascites and complications due to infection and inflammation.
  - Sarcopenia in Non-alcoholic fatty liver disease (NAFLD) patients likely increases the chance of steatohepatitis or advanced fibrosis.
  - In HCC patients, sarcopenia is associated with poor survival, tumor recurrence and mortality.
  - Sarcopenia and malnutrition, during pre-transplant period increase the risk of decompensation, morbidity and mortality.
  - Sarcopenia in post-transplant period increase post operative infections, increase the duration of hospitalisation and poor outcomes.

Recommendation 7

- **Bone disease should be identified and treated mainly in cholestatic liver disease and liver transplantation waiting patients.**
  - Patients with liver damage are more prone to hepatic osteodystrophy, which includes osteoporosis and osteomalacia.
  - Osteoporosis is loss of muscle mass causing fragility fractures; Osteomalacia is demineralization of bone due to Vitamin D deficiency.
  - Higher prevalence of osteoporosis (30%) is noticed in cholestasis including primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) and in patients waiting for liver transplantation.
  - A balanced diet with optimal nutrient intake is suggested in addition to 1000-1500 mg/d calcium supplements and 400-800 IU/day of 25-hydroxy vitamin D/calcidiol until the normal levels are reached.
  - Lifestyle changes like increased physical activity, exercise and cessation of alcohol and tobacco are helpful.

Recommendation 8

- **Fluid restrictions is not required in patients with chronic liver disease.**
  - As a rule, fluid intake is not restricted until the sodium levels are <125mEq/L, or in the presence of uncontrolled ascites or the patient also have renal failure.
  - Fluid accumulates since the blood vessels lose the capabilities to retain fluids due to impaired protein synthesis and albumin synthesis [12].
  - Sodium intake is restricted to 2g/day to prevent fluid build-up especially in ascites.

Recommendation 9

- **Timings and mode of feeding is also a vital component in reducing malnutrition and sarcopenia.**
  - Long hours of fasting in CLD patients affects protein synthesis, increases muscle proteolysis and gluconeogenesis (especially from amino acids) thus increasing the risk for sarcopenia.
  - Long fasting hours should be avoided, and frequent intake of small meals prevent catabolic state. Long hours of starvation are usually possible during night hours and hence nocturnal supplementation rich in carbohydrates and proteins are beneficial.
  - Multigrain bread or nut bread sandwich may be a healthy option for late evening snacks (LES), this provides 700 calories and 25g protein, helps in preventing catabolism and maintaining muscle mass [23].
  - LES enriched with BCAA improves serum albumin levels, glucose tolerance and Fischer ratio thus reducing the mortality among cirrhotic patients.
  - LES helps in reversing anabolic resistance and sarcopenia.
  - In gastrointestinal bleeding, early feeding within 24 hours after the bleed reduces the risk of rebleeding [24].
  - Enteral nutrition may be the preferable route to deliver the nutrients since it maintains the integrity of gastric mucosa and gut barrier function, and less expensive with very few complications [25].

- Parenteral route is indicated to patients unable to achieve optimal nutritional requirement orally for more than 12 h or in moderate or severe malnutrition.
- Long term use of parenteral nutrition may also worsen liver function.
- Parenteral nutrition carries the risk of infection, electrolyte imbalance and fluid over-load. Hence it is important to initiate enteral or oral nutrition during the early recovery period [25].

Recommendation 10

- **Physical activity and exercises are recommended to improve muscle contractile function and muscle mass in patients with CLD**
  - Physical inactivity and sedentary lifestyle are associated with frailty, sarcopenia and mortality in CLD patients [26]. Physical activity and exercise are physiological anabolic stimuli that can reverse protein synthesis and increase muscle mass [26].
  - Exercises increase plasma testosterone concentrations which stimulate amino acid uptake and protein synthesis and inhibits protein degradation [27].
  - In adults, 150-300min / week of moderate-intensity of physical activity or 75-150 mins of vigorous-intensity of physical activity is recommended [28].

Disease specific recommendation

- **HE**
  - Protein restriction does not benefit in HE, as it worsens, HE outcomes.
  - Intake of 1.2g/kg/day of protein reduces lethargy and is safe in cirrhotic patients with episodic encephalopathy but should not be restricted beyond 0.8g/kg/day as it imposes the risk of mortality and morbidity [29].
  - 25-45 g/ day of fibre intake (non- digestible carbohydrate) alters gut microbiota, prevents bacterial translocation, increases ammonia excretion via stools and prevents constipation [4,30].
  - Intake of probiotics, BCAA, fibre and supplements for vitamins and minerals should be ensured for patients' wellbeing Impact of SARS CoV-2 /COVID-19 infection on the course of advanced chronic [31].
- **NAFLD**
  - High protein intake of 2-2.5 g/kg/day help in reducing weight loss. Majority of calories should be contributed by proteins [32].
  - Hypo-caloric, high fibre, high protein diet significantly reduced liver fat content, liver stiffness, GGT and serum lipids [33].
  - Food intake should be once in every 2-3 hours; hence 5-6 meals/ day is recommended [32] .
  - Boiled, steamed, and baked foods are allowed and avoid soft drinks, fried and fast foods.
  - Regular coffee consumption decreases the risk of NAFLD by 29%, liver fibrosis by 30-39% and cirrhosis by 39% [34].
- **NASH**
  - Weight loss is encouraged, targeting a reduction of 7-10% weight loss improves liver fat content, inflammation and fibrosis. A reduction in 5% of BMI is associated with 25% relative reduction in liver fat [35].
  - 20-25kcal/kg/day is recommended and helps in reducing 5-10% of body weight.
  - Alcohol abstinence helps in decreasing the comorbidity risk and improves liver biochemistry and histology [36].
  - Vitamin E supplementation of 400-800 IU / day improves liver enzymes, steatosis, and inflammation as well [37].
  - Water soluble vitamin deficiencies are common in alcoholic hepatitis and NASH.
- **HCC**
  - Vitamin A and D deficiency are contributing factors of HCC development.
  - The endocrine society warns that serum calcidiol concentrations <10 ng/mL is a high risk for HCC patients.
  - Vitamin D has to be supplemented until the normal range is achieved (normal serum calcidiol concentrations >30 ng/mL) [19].
  - BCAA supplementation improves nutritional status, prevents reduction in residual liver function, and prevents recurrence.

Conclusion

Malnutrition is very commonly observed in chronic liver disease. Assessing the nutritional status, timely identification of risks and deficiencies, and proper planning of diet in addition to treatment have a positive impact on the prognosis of health condition of decompensated liver failure patients. Proper care during the liver transplant waiting period helps in improving their nutritional status, improves survival, decrease morbidity, and improves the quality of life.

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References

1) Atiemo K, Skaro A, Maddur H, Zhao L, Montag S, Vanwagner L. Mortality Risk Factors Among Patients With Cirrhosis and a Low Model for End-Stage Liver Disease Sodium Score (</=15): An Analysis of Liver Transplant Allocation Policy Using Aggregated Electronic Health Record Data. *Am J Transplant*. 2017;17(9):2410–2419. Available from: https://www.amjtransplant.org/article/S1600-6135(22)25134-X/fulltext.
2) Reber E, Gomes F, Vasiloglou MF, Schuetz P, Stanga Z. Nutritional Risk Screening and Assessment. *J Clin Med*. 2019;8(7). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6679209/pdf/jcm-08-01065.pdf.
3) Traub J, Reiss L, Aliwa B, Stadlbauer V. Malnutrition in Patients with Liver Cirrhosis. *Nutrients*. 2021;13(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7915767/pdf/nutrients-13-00540.pdf.
4) Silva M, Gomes S, Peixoto A, Torres-Ramalho P, Cardoso H, Azevedo R, et al. Nutrition in Chronic Liver Disease. *GE Port J Gastroenterol*. 2015;22(6):268–76. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5580118/pdf/main.pdf.
5) Sakamoto N, Suda G, Morikawa K, Ogawa K. Nutrition is often ignored in management of chronic liver diseases. *J Gastroenterol Hepatol*. 2019;34(7):1127–1135. Available from: https://doi.org/10.1111/jgh.14776.
6) Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. *Lancet*. 2019;393:2312–2333. Available from: https://doi.org/10.1016/S0140-6736(18)32776-4.
7) Traub J, Bergheim I, Horvath A, Stadlbauer V. Validation of Malnutrition Screening Tools in Liver Cirrhosis. *Nutrients*. 2020;12(5). Available from: https://doi.org/10.3390/nu12051306.
8) Puri P, Dhiman RK, Taneja S, Tandon P, Merli M, Anand AC. Nutrition in Chronic Liver Disease: Consensus Statement of the Indian National Association for Study of the Liver. *J Clin Exp Hepatol*. 2021;11(1):97–143. Available from: https://doi.org/10.1016/j.jceh.2020.09.003.
9) Molfino A, Johnson S, Medici V. The Challenges of Nutritional Assessment in Cirrhosis. *Curr Nutr Rep*. 2017;6(3):274–80. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5703218/pdf/nihms894240.pdf.
10) Ney M, Abraldes JG, Ma M, Belland D, Harvey A, Robbins S, et al. Insufficient Protein Intake Is Associated With Increased Mortality in 630 Patients With Cirrhosis Awaiting Liver Transplantation. *Nutrition in Clinical Practice*. 2015;30(4):530–536. Available from: https://dx.doi.org/10.1177/0884533614567716.
11) Ruiz-Margain A, Macias-Rodriguez RU, Rios-Torres SL, Roman-Calleja BM, Mendez-Guerrero O, Rodriguez-Cordova P, et al. Effect of a high-protein, high-fiber diet plus supplementation with branched-chain amino acids on the nutritional status of patients with cirrhosis. *Rev Gastroenterol Mex*. 2018;83(1):9–15. Available from: https://pubmed.ncbi.nlm.nih.gov/28408059/.
12) Sidiq T. Nutrient Requirements of Patients with Liver Cirrhosis. *Curr Trends Biomedical Eng & Biosci*. 2017;4(4):73–75. Available from: https://juniperpublishers.com/ctbeb/pdf/CTBEB.MS.ID.555645.pdf.
13) Campos AC, Matias JE, Coelho JC. Nutritional aspects of liver transplantation. *Curr Opin Clin Nutr Metab Care*. 2002;5(3):297–307. Available from: https://journals.lww.com/co-clinicalnutrition/abstract/2002/05000/nutritional_aspects_of_liver_transplantation.10.aspx.
14) Hammad A, Kaido T, Uemoto S. Perioperative nutritional therapy in liver transplantation. *Surg Today*. 2015;45(3):271–83. Available from: https://link.springer.com/article/10.1007/s00595-014-0842-3.
15) Bakshi NS, Singh K. Nutrition profile of a liver transplant recipient. *Hepatoma Res*. 2016;2:98–102. Available from: https://www.oaepublish.com/articles/2394-5079.168958.
16) Saeed A, Hoekstra M, Hoeke MO, Heegsma J, Faber KN. The interrelationship between bile acid and vitamin A homeostasis. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2017;1862(5):496–512. Available from: https://doi.org/10.1016/j.bbalip.2017.01.007.
17) Kumar N. Neurologic presentations of nutritional deficiencies. *Neurol Clin*. 2010;28(1):107–70. Available from: https://doi.org/10.1016/j.ncl.2009.09.006.
18) Finkelmeier F, Kronenberger B, Koberle V, Bojunga J, Zeuzem S, Trojan J, et al. Severe 25-hydroxyvitamin D deficiency identifies a poor prognosis in patients with hepatocellular carcinoma - a prospective cohort study. *Aliment Pharmacol Ther*. 2014;39(10):1204–1216. Available from: https://doi.org/10.1111/apt.12731.
19) Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96(7):1911–1941. Available from: https://doi.org/10.1210/jc.2011-0385.
20) Frank LL. Thiamin in Clinical Practice. *Journal of Parenteral and Enteral Nutrition*. 2015;39(5):503–520. Available from: https://doi.org/10.1177/0148607114565245.
21) Flannery AH, Adkins DA, Cook AM. Unpeeling the Evidence for the Banana Bag: Evidence-Based Recommendations for the Management of Alcohol-Associated Vitamin and Electrolyte Deficiencies in the ICU. *Crit Care Med*. 2016;44(8):1545–52. Available from: https://journals.lww.com/ccmjournal/abstract/2016/08000/unpeeling_the_evidence_for_the_banana_bag_.14.aspx.
22) Allen SL, Quinlan JI, Dhaliwal A, Armstrong MJ, Elsharkawy AM, Greig CA, et al. Sarcopenia in chronic liver disease: mechanisms and countermeasures. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2021;320(3):G241–G257. Available from: https://dx.doi.org/10.1152/ajpgi.00373.2020.
23) Marchesini G, Bianchi G, Merli M, Amodio P, Panella C, Loguercio C, et al. Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind, randomized trial. *Gastroenterology*. 2003;124(7):1792–1801. Available from: https://dx.doi.org/10.1016/s0016-5085(03)00323-8.
24) Hébuterne X, Vanbiervliet G. Feeding the patients with upper gastrointestinal bleeding. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2011;14(2):197–201. Available from: https://dx.doi.org/10.1097/mco.0b013e3283436dc5.
25) Tandon P, Ney M, Irwin I, Ma MM, Gramlich L, Bain VG, et al. Severe muscle depletion in patients on the liver transplant wait list: its prevalence and independent prognostic value. *Liver Transpl*. 2012;18(10):1209–1225. Available from: https://doi.org/10.1002/lt.23495.
26) Lai JC, Tandon P, Bernal W, Tapper EB, Ekong U, Dasarathy S, et al. Malnutrition, Frailty, and Sarcopenia in Patients With Cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;74(3):1611–1644. Available from: https://dx.doi.org/10.1002/hep.32049. doi:10.1002/hep.32049.
27) Riachy R, McKinney K, Tuvdendorj DR. Various Factors May Modulate the Effect of Exercise on Testosterone Levels in Men. *Journal of Functional Morphology and Kinesiology*. 2020;5(4):81–81. Available from: https://dx.doi.org/10.3390/jfmk5040081.
28) Powell KE, King AC, Buchner DM, Campbell WW, DiPietro L, Erickson KI, et al. The Scientific Foundation for the Physical Activity Guidelines for Americans, 2nd Edition. *Journal of Physical Activity and Health*. 2019;16(1):1–11. Available from: https://dx.doi.org/10.1123/jpah.2018-0618.
29) Córdoba J, López-Hellín J, Planas M, Sabín P, Sanpedro F, Castro F, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. *Journal of Hepatology*. 2004;41(1):38–43. Available from: https://dx.doi.org/10.1016/j.jhep.2004.03.023.
30) Kieffer DA, Martin RJ, Adams SH. Impact of Dietary Fibers on Nutrient Management and Detoxification Organs: Gut, Liver, and Kidneys. *Advances in Nutrition*. 2016;7(6):1111–1121. Available from: https://dx.doi.org/10.3945/an.116.013219.

31) Pazgan-Simon M, Kucharska M, Górka-Dynysiewicz J, Simon K. Impact of SARS CoV-2 /COVID-19 infection on the course of advanced chronic liver disease and hepatocellular carcinoma. *Pharmacological Reports*. 2022;74(6):1306–1314. Available from: https://dx.doi.org/10.1007/s43440-022-00434-4.
32) Ramachandran G, Pottakkat B. Nutritional therapy to cirrhotic patients on transplantation waiting lists. *Journal of Liver Transplantation*. 2022;5:100060–100060. Available from: https://dx.doi.org/10.1016/j.liver.2021.100060.
33) Arslanow A, Teutsch M, Walle H, Grünhage F, Lammert F, Stokes CS. Short-Term Hypocaloric High-Fiber and High-Protein Diet Improves Hepatic Steatosis Assessed by Controlled Attenuation Parameter. *Clinical and Translational Gastroenterology*. 2016;7(6):e176–e176. Available from: https://dx.doi.org/10.1038/ctg.2016.28.
34) Liu F, Wang X, Wu G, Chen L, Hu P, Ren H, et al. Coffee Consumption Decreases Risks for Hepatic Fibrosis and Cirrhosis: A Meta-Analysis. *PLOS ONE*. 2015;10(11):e0142457–e0142457. Available from: https://dx.doi.org/10.1371/journal.pone.0142457.
35) Patel NS, Doycheva I, Peterson MR, Hooker J, Kisselva T, Schnabl B, et al. Effect of Weight Loss on Magnetic Resonance Imaging Estimation of Liver Fat and Volume in Patients With Nonalcoholic Steatohepatitis. *Clinical Gastroenterology and Hepatology*. 2015;13(3):561–568.e1. Available from: https://dx.doi.org/10.1016/j.cgh.2014.08.039.
36) Åberg F, Byrne CD, Pirola CJ, Männistö V, Sookoian S. Alcohol consumption and metabolic syndrome: Clinical and epidemiological impact on liver disease. *Journal of Hepatology*. 2023;78(1):191–206. Available from: https://dx.doi.org/10.1016/j.jhep.2022.08.030.
37) Sanyal AJ, Chalasani N, Kowdley KV, McCullough A, Diehl AM, Bass NM, et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. *New England Journal of Medicine*. 2010;362(18):1675–1685. Available from: https://dx.doi.org/10.1056/nejmoa0907929.