Nutrition and Alcoholic Liver Disease

Effects of Alcoholism on Nutrition, Effects of Nutrition on Alcoholic Liver Disease, and Nutritional Therapies for Alcoholic Liver Disease

Srinivasan Dasarathy, MD*

KEYWORDS

• Alcoholic liver disease • Malnutrition • Sarcopenia • Skeletal muscle loss
• Myostatin • Molecular pathways • Mitochondria • Reactive oxygen species

KEY POINTS

- Malnutrition is the most frequent complication in alcoholic liver disease, adversely affects the clinical consequences and includes loss of skeletal muscle mass or sarcopenia and perturbations in energy metabolism.
- Among the different etiologies of liver disease, malnutrition and sarcopenia are believed to be most severe in alcoholic liver disease.
- Very recent data show that alcohol is directly metabolized in the skeletal muscle and contributes to loss of muscle mass but the contribution of skeletal muscle ethanol metabolism to other organ injury is not known.
- There are no effective therapies for malnutrition and sarcopenia in alcoholic liver disease primarily because treatments used to date have focused on improved dietary intake and nutrient supplementation.
- Targeting myostatin, molecular signaling pathways that regulate protein synthesis and autophagy, and mitochondrial protective agents are exciting novel therapeutic strategies that are likely to reverse sarcopenia in ALD.

INTRODUCTION

The term malnutrition is defined as a condition when the body does not receive enough nutrition to maintain health. Malnutrition can also be defined as a loss of muscle and/or fat mass. In addition to skeletal muscle loss, another component

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Departments of Gastroenterology, Hepatology and Pathobiology, Lerner Research Institute, NE4 208, 9500 Euclid Avenue, Cleveland, OH 44195, USA
* Corresponding address: Department of Gastroenterology and Hepatology, Lerner Research Institute, NE4 208, 9500 Euclid Avenue, Cleveland, OH 44195.
E-mail address: dasaras@ccf.org

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of malnutrition is an alteration in energy metabolism with accelerated starvation.[1,2] Malnutrition is the most frequent complication in liver disease and cirrhosis; however, there are no standardized definitions, which makes comparisons across studies difficult. It is necessary to accurately define nutritional status in alcoholic liver disease (ALD) so that published data are interpreted appropriately and the use of standardized terminology allows comparisons of results from different studies.[3] The term malnutrition has been used to define loss of body weight, muscle mass, fat mass, muscle strength, visceral protein levels, immune function, and poor oral intake of nutrients.[4–6] Each of these measures suffers from significant limitations. Visceral protein concentrations in blood including albumin, prealbumin, and retinol binding proteins have been used extensively but are truly measures of hepatic synthetic function.[4] Immune function is directly altered by alcohol and viral infection and cannot be truly considered measures of hepatic effects on the skeletal muscle or nutritional indices.[7] Anthropometric measures including skinfold thickness that measures fat mass and arm muscle area are used as nutritional indices but suffer from intraobserver and interobserver variability.[8] Nitrogen balance studies are difficult and suffer from imprecision in the clinical setting, long-term accurate dietary intake studies are difficult, and retrospective studies suffer from recall bias. The term malnutrition is increasingly used to refer to the phenotype of loss of skeletal muscle mass with/without fat loss and not dietary intake, digestion, and absorption of nutrients even though the latter contribute to muscle and fat loss and disordered energy metabolism.

The term sarcopenia refers to muscle loss in patients with chronic diseases.[2,9–11] Even though micronutrient deficiencies are common in alcoholic hepatitis and cirrhosis,[12,13] the focus of this article is on skeletal muscle loss and how it is integrated with the disordered energy metabolism in patients with ALD.

Most publications refer to malnutrition in cirrhosis and ALD without specifying if the effects are caused by sarcopenia, loss of fat mass, or a combination of both. Careful analyses of published studies show that sarcopenia is the major component of malnutrition[4,5,14,15] and liver injury and alcohol contribute to muscle loss. The role of nutritional deficiencies on progression of liver injury is not known. Myokines are proteins secreted by the skeletal muscle including interleukin-6 and -15, which may alter hepatic metabolism and fibrosis, but a muscle-liver axis has not yet been established.[16,17] This article focuses on prevalence and methods to quantify malnutrition, specifically sarcopenia; the mechanisms of muscle loss in ALD including the liver-muscle axis; and potential therapies including novel, molecular targeted treatments. The impact of disordered energy metabolism is discussed in the context of its contribution to sarcopenia. Micronutrient deficiencies including zinc are common in patients with ALD, and their impact on outcomes in ALD has been reviewed elsewhere and is not discussed in detail here.[12,13,18] The effect of different nutrient supplements on hepatic histology and liver function in ALD is also not discussed and the interested reader is referred to reviews published on this topic.[19,20] For more information on nutritional therapy for acute alcoholic hepatitis, see Phillips PK, Lucey MR: Acute Alcoholic Hepatitis – Therapy, in this issue.

PREVALENCE AND METHODS TO QUANTIFY MALNUTRITION IN ALCOHOLIC LIVER DISEASE

Malnutrition is present in 20% to 90% of patients with liver disease and sarcopenia in nearly 70% of these patients.[2,4,5,21,22] We have recently reported that the prevalence of alcoholic cirrhosis is likely to be the major form of liver disease in the