

# Nutritional Status and Liver Transplantation

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**Chronic liver disease has a profound effect on nutritional status and undernourishment is almost universally present in patients with end-stage liver disease undergoing liver transplantation. In the last decades, due to epidemiological changes, a trend showing an increase in patients with end-stage liver disease and associated obesity has also been reported in developed countries. Nutrition abnormalities may influence the outcome after transplantation therefore, the importance to carefully assess the nutritional status in the work-up of patients candidates for liver transplantation is widely accepted. More attention has been given to malnourished patients as they represent the greater number. The subjective global nutritional assessment and anthropometric measurements are recognized in current guidelines to be adequate in identifying those patients at risk of malnutrition. Cirrhotic patients with a depletion in lean body mass and fat deposits have an increased surgical risk and malnutrition may impact on morbidity, mortality and costs in the post-transplantation setting. For this reason an adequate calorie and protein intake should always be ensured to malnourished cirrhotic patient either through the diet, or using oral nutritional supplements or by enteral or parenteral nutrition although studies supporting the efficacy of nutritional supplementation in improving the clinical outcomes after transplantation are still scarce. When liver function is restored, an amelioration in the nutritional status is expected. After liver transplantation in fact dietary intake rapidly normalizes and fat mass is progressively regained while the recovery of muscle mass can be slower. In some patients unregulated weight gain may lead to over-nutrition and may favor metabolic disorders (hypertension, hyperglycemia, hyperlipidemia). This condition, defined as 'metabolic syndrome', may play a negative role on the overall survival of liver transplant patients. In this report we review data on nutrition and liver transplantation. (J CLIN EXP HEPATOL 2011;1:190-198)**

**L**iver transplantation (LT) has dramatically changed the prognosis of end-stage liver disease. The amelioration in the immunosuppressive regimens and surgical techniques has progressively improved the outcome of these patients and survival after LT is nowadays 70–80% at 5 years.<sup>1</sup> From 2002, the introduction of the model for end-stage liver disease (MELD) for prioritization of the patients in need of a new liver has led to a significant reduction in mortality in the waiting list, favoring the transplantation of the sickest patients;<sup>2–4</sup> at the same time, it has been clearly demonstrated that there is no transplant benefit when patients are transplanted with a MELD score below 15.<sup>5</sup> As a consequence in the past years, patients submitted to liver transplant are likely to have a more compromised clinical status, and complications of cirrhosis, such as malnutrition, are expected to be even more

prevalent in liver recipients than before. Those patients with a more advanced liver insufficiency are in fact known to experience a higher prevalence of severe protein/calorie malnutrition.<sup>6</sup> The possible impact of malnutrition on the outcome of LT and the need of dietary counseling and nutritional supplementation in patients with end-stage liver disease has become therefore a subject of growing interest and debate. From another point of view, countries with an increasing prevalence of overnutrition have recently reported that the number of obese patients in the waiting list for LT is increasing and there is a concern that also severe obesity may affect the morbidity and mortality after transplantation.<sup>7</sup>

The purpose of this review was to examine the recent literature to estimate the prevalence of malnutrition in advanced liver disease, evaluate the possible methods to recognize nutritional alterations in these patients, consider the role of nutritional status in liver transplant, and underline the main recommendation and guidelines for nutritional support in advanced liver disease.

## METHODS

Bibliographic searches were performed in MEDLINE for the following words (all fields): 'nutrition' (MeSH) or 'malnutrition' (MeSH) or 'obesity' (MeSH) or 'nutritional status' (MeSH) and 'liver transplantation' (MeSH) or 'liver transplant' (MeSH) or 'cirrhosis' (MeSH) or 'end-stage liver disease' (MeSH). Reference lists of the studies

*Keywords:* Body weight, cirrhosis, end stage liver disease, malnutrition, nutritional assessment, nutritional support or nutritional therapy, obesity, outcomes

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*Abbreviations:* BCAA: branched chain amino acids; BMI: body mass index; LT: liver transplantation; MELD: model for end-stage liver disease; SGA: subjective global assessment for nutrition

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identified during electronic searching were also hand-searched to identify the additional relevant studies for the inclusion. Studies eligible for the review were those published between 1990 and 2011; however, older studies were utilized, when needed, to support the information about the physiopathology of malnutrition in liver disease. Studies published in abstract form only, or in non-English language, were excluded. Preference was given to studies presenting original data than to review studies.

### Prevalence and Consequences of Nutritional Alterations in Patients With End-stage Liver Disease

Malnutrition is frequently associated with chronic liver disease: the prevalence may range from 20% to 80% depending on the methods used for the nutritional assessment and the severity of liver disease.<sup>6,8,9</sup> A large multicenter study has shown that the prevalence of malnutrition is considerably higher in patients with a more severe liver impairment (20–25% in Child A–B patients but >50% in Child C).<sup>6</sup> The correlation between malnutrition and the origin of liver cirrhosis is controversial. Some authors have suggested a higher prevalence of malnutrition in patients with postalcoholic disease;<sup>10</sup> alcohol abuse may in fact represent a cause of malnutrition per se due to the replacement of nutrient foods with empty calories, or secondary to the conditions of maldigestion and malabsorption, induced by the reduction of the bile and pancreatic enzyme secretion, which can lead to increase nutrient losses.<sup>11,12</sup> Malnutrition, however, is not limited to post-alcoholic cirrhosis and a number of studies have demonstrated that the prevalence of malnutrition is similar in patients with non-alcoholic liver disease.<sup>6,8,13,14</sup> Concerning the gender, a more pronounced loss of body fat has been described in woman while men experience more frequently a depletion in the lean body mass. This alteration may be present even in the early stages of liver cirrhosis and is further accelerated in the advanced stages of the disease.<sup>15–17</sup>

In the past decade, a new scenario with a higher prevalence of overweight/obese cirrhotic patients has been pointed out. Data from the United Network of Organ Sharing have shown that, in the past decade, obesity-associated liver disease has become an increasing indication for LT. At the same time, the prevalence of obese patients in the waiting list has been reported to be as high as 20%.<sup>18</sup> Although these data mainly refer to the United States where a high prevalence of overnutrition exists, a similar trend could also involve other developed countries in the near future. Data on the nutritional status of patients with end-stage liver disease in other populations are not always available. It is expected in fact that in countries in developing transition, both under-nutrition and obesity may coexist.<sup>19</sup> The impact of these double burden in cirrhotic patients is unknown and data about the nutritional status

of patients awaiting for LT in developmental countries is still scarce. In a recent study on Malaysian patients with decompensated cirrhosis, the prevalence of malnutrition was as high as 50%.<sup>20</sup> In our unit, which is a tertiary referral center, among 205 cirrhotic patients consecutively hospitalized in the year 2010, a mid-arm muscular circumference <5th percentile was detected in 35%. After correcting body weight for ascites and edema (estimated dry weight), body mass index (BMI) ( $\text{Kg}/\text{m}^2$ ) <18, denoting malnutrition, was reported in 21% of patients and BMI >35, denoting obesity, was found in 5%.

Malnutrition in cirrhotic patients is known to be associated with a higher prevalence of complications, such as hepatic encephalopathy, ascites, hepatorenal syndrome, and bacterial infections;<sup>21,22</sup> furthermore, malnourished patients may experience a deterioration in the quality of life. The independent role of malnutrition on survival in patients with liver disease has been extensively documented; patients comparable for the severity of liver insufficiency show a higher rate of mortality when nutritional status is severely impaired.<sup>23–25</sup>

### Main Causes of Malnutrition and Methods to Recognize Nutritional Alterations in Patients With End-stage Liver Disease

A variety of mechanisms are considered to be responsible for malnutrition in patients with chronic liver disease and usually two or more may coexist (Table 1). All these abnormalities may precede protein-calorie malnutrition which arises when the diet does not provide adequate calories and proteins to maintain the nutritional status or when the body is unable to fully absorb or utilize the food eaten secondary to the liver disease. The most common findings in cirrhotic patients are a reduction in the muscle mass and function and a depletion in fat deposits;<sup>6,8,17,23,26</sup> the body composition profile may be modified in cirrhotic patients even in the initial stages.<sup>15,16</sup> These changes may, however, be masked due to fluid retention which increases both intra- and extracellular water even before ascites and edema become clinically apparent.<sup>27</sup>

Considering the predictive role of malnutrition for the patient's outcome, an accurate assessment of the nutritional status in patients with advanced liver disease is mandatory. However, the methods to be used for the assessment of the nutritional status in liver cirrhosis are controversial.<sup>28</sup> Malnutrition in these patients may develop insidiously and is frequently jeopardized by multiple confounding factors (Tables 2 and 3). The main tools commonly used to investigate the nutritional status can be inappropriate in the setting of chronic liver disease: body weight and BMI can be misleading because of edema and ascites, although one study has validated BMI in cirrhotic patients using an appropriate cut-off;<sup>29</sup> plasma protein concentration is influenced by the functional reserve of the

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