

Nutrition assessment in patients undergoing liver transplant

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Abstract

Liver transplantation (LT) is a major surgery performed on patients with end stage liver disease. Nutrition is an integral part of patient care, and protein-energy malnutrition is almost universally present in patients suffering from liver disease undergoing LT. Nutrition assessment of preliver transplant phase helps to make a good nutrition care plan for the patients. Nutrition status has been associated with various factors which are related to the success of liver transplant such as morbidity, mortality, and length of hospital stay. To assess the nutritional status of preliver transplant patients, combinations of nutrition assessment methods should be used like subjective global assessment, Anthropometry mid arm-muscle circumference, Bioelectrical impedance analysis (BIA) and handgrip strength.

Keywords: Liver Transplant, Nutrition Assessment, End Stage Liver Disease

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Introduction

Liver transplantation (LT) revolutionized the management of liver disease.^[1] The most common liver diseases are: Infections such as hepatitis B, C, alcohol damage, fatty liver, cirrhosis, cancer, drug damage (especially acetaminophen also known as paracetamol) and cancer drugs. LT is the only option for those with irreversible liver failure.^[2]

According to Institute of Health Metrics and Evaluation of Global Burden of Disease, deaths from cirrhosis in all age groups is ranked 12th globally and 19th in South Asia (1990) and was ranked 12th globally and 11th in South Asia in the year 2010. Hence, an increasing death from cirrhosis is seen in South Asia over a period.^[3]

The liver is the largest and most important metabolic organ, playing a pivotal role in integrating several biochemical pathways of carbohydrate, fat, protein, and

vitamin metabolism. Protein-energy malnutrition (PEM) is common in patients with end-stage liver diseases (ESLD) and is highly prevalent in all forms of liver disease, regardless of etiology.^[4] Protein deficiency can be found in early stages of cirrhosis.^[5] PEM tends to be more frequent in advanced cirrhosis. The diagnosis of PEM in ESLD may not be that difficult to make because of marked muscle wasting and subcutaneous fat loss. The prevalence of PEM has been reported to be as high as 100% in patients undergoing LT.^[5-7]

Nutrition is an integral part of health maintenance. Progressive deterioration of nutritional status has been associated with poor outcome in cirrhotic patients.^[7] Malnutrition has been estimated to be present in 65-100% of patients with chronic hepatic diseases.^[8-10] Cause for malnutrition in liver cirrhosis includes reduction in oral intake, increased protein catabolism, insufficient protein synthesis and malabsorption/maldigestion associated with portal hypertension.^[9,11,12] Malnutrition has been associated with increased morbidity and mortality in patients undergoing LT,^[10,13,14] and the cost of the transplant are significantly higher.^[15] Increased rates of septic complications, poorer quality-of-life, and a reduced life span have all been observed in cirrhotic with poorer nutrition status when compared with well-nourished patients.^[16]

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Patients awaiting LT frequently have a number of nutritional problems. These can significantly increase the operative risk at the time of surgery. Appropriate nutrition support of these patients, both before and after surgery, can improve their outcome.^[17]

Nutrition Assessment

Malnutrition in patients with ESLD is multifactorial [Table 1]. However; major determinants are abnormal nutrient and caloric intake, decreased intestinal absorption and metabolic disturbances.^[18]

To determine the presence of malnutrition in patients with ESLD, a thorough clinical assessment must be performed as many factors contribute to malnutrition in ESLD patients.

Malnutrition is a relevant factor when determining the progress of hepatic disease, as it affects the storage of nutrients, contributes to hypoalbuminemia resulting from impaired hepatic synthesis and intensifies the hydroelectrolytic imbalance determined by renal alterations.^[19]

Accurate estimation of the nutritional status in patients with ESLD represents a major challenge due to fluid retention found in a significant number of patients and the effect of liver function on protein synthesis.^[7] Despite these challenges, PEM can be diagnosed in 20% of patients with compensated liver disease such as and in >80% of patients with decompensated liver disease – in other words, those with ascites, portosystemic hepatic encephalopathy, and portal hypertensive bleeding. PEM is more prevalent in patients hospitalized for alcoholic liver disease than in patients with nonalcoholic liver disease.^[20] PEM has been associated with adverse outcomes, including decreased patient and graft survival after LT.^[6]

However, there are difficulties and controversies regarding the identification of the best nutritional assessment method considered as the gold standard that is low cost, loyal and easy-to-apply method, and that does not affect the final result. Owing to these above said challenges, which negatively interfere in the nutritional status of the cirrhotic patient and which are part of the natural history of the disease, it is necessary to identify when malnutrition begins its course. This preventive measure applies primarily to patients on the liver transplant list, who will thus have a better quality of life until the time of the transplant. Whilst the original Child and Turcotte,^[21] classification included nutritional status, this was replaced with prothrombin

Table 1: Etiologies of malnutrition in cirrhosis^[18]

Decreased intake	Metabolic alterations
Anorexia-early satiety and nausea	Increased or decreased metabolic rate
Ascites	Glucose intolerance/insulin resistance
Altered mental status/encephalopathy	Rapid postprandial gluconeogenesis
Altered gustatory sensation	Reduced glycogen stores
Frequent hospitalizations-unpalatable diet	Elevated leptin and TNF- α
	Decreased insulin-like growth factor
	Increased resting energy expenditure
	Increased protein requirements and protein degradation
	Preference for fat oxidation
	Decreased bile salts and Increased fat malabsorption
Decreased absorption	Iatrogenic factors
Inadequate bile flow	Overzealous dietary restrictions, frequent paracentesis
Pancreatic insufficiency	Diuresis (micronutrient losses), lactulose therapy
Bacterial overgrowth	

TNF- α : Tumor necrosis factor alpha

Table 2: Parameters of Child and Turcotte 1964^[22]

Group designation	Child and Turcotte (1964)		
	A	B	C
Serum bilirubin (g%)	<2	2-3	>3
Serum albumin (mg%)	>3.5	3-3.5	<3
Ascites	None	Easily controlled	Poorly controlled
Neurological disorder	None	Minimal	Advanced (coma)
Nutrition	Excellent	Good	Poor (wasting)

Table 3: CTP classification 1972^[23,24]

Measure	CTP (1972)		
	1 point	2 points	3 points
Total bilirubin, $\mu\text{mol/l}$ (mg/dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
Serum albumin (g/dl)	>3.5	2.8-3.5	<2.8
PT INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractor)
Points	Class	1-year survival %	2-year survival %
5-6	A	100	85
7-9	B	81	57
10-15	C	45	35

CTP: Child Turcotte and Pugh; INR: International normalized ratio; PT: Prothrombin time

time (PT) in the Child Turcotte and Pugh (CTP), 1972 classification^[22,23] depicted in Tables 2 and 3. However, the presence of PEM has been shown to be associated with increased short- and long-term mortality in patients with acute and chronic liver disease.^[24]

Parameters proposed by Blackburn *et al.*,^[25] like percent ideal weight, triceps skin-fold (TSF) thickness (≥ 12.5 mm), mid arm-muscle circumference (MAMC) (≥ 25.3 cm), creatinine height index (%), albumin (≥ 3.5 g/dl), transferrin (≥ 180 mg/dl), total lymphocyte count (TLC)

(≥ 1500 cells/mm³), delayed cutaneous hypersensitivity response (≥ 5 mm induration to two or more skin tests) were used by Mendenhall *et al.*, to devise a protein-calorie malnutrition (PCM) score and classify PCM into marasmic-like or kwashiorkor-like nutrition disease by evaluating nutrition interventions in subjects with alcoholic hepatitis. The score values classified PCM as no malnutrition (PCM $\geq 100\%$), mild malnutrition (80-99.9%), moderate malnutrition (60-79.9%), and severe malnutrition ($<60\%$).^[26] According to the recommendations of Blackburn *et al.* the PCM score correlated well with mortality, clinical severity of liver disease, and biochemical liver dysfunction. Improving PCM score via hospitalization improved 6-month and 1-year survival rates, underlining the importance and prognostic significance of nutrition in chronic liver disease.^[25]

Leitão *et al.*, evaluated the physical capacity and nutritional status of patients before LT and correlated these parameters to the severity of liver function. Nutritional status was evaluated by using Mendenhall score and Blackburn classification. Low physical performance was found in 72.5% of the patients, and when the Karnofsky index was applied, malnutrition was found in 62.5% of the patients (34.37% moderately and severely malnourished and 28.13% mildly malnourished).^[27]

The role of malnutrition as it relates to patient survival after LT was evaluated by Shaw *et al.* Patients with severe muscle wasting and generalized malnutrition received a score of 2; a score of 1 was assigned to those with mild-to-moderate nutrition and 0 was assigned to normal subjects. The study developed an equation based on preoperative data that is: Risk = encephalopathy score + ascites score + malnutrition score + transfusion score + coagulopathy score. Based on the final risk score, patients were then categorized into three subgroups: Low, medium, and high risk. The Prognostic Nutritional Index (PNI) is an example: $PNI\% = 158 - 16.6 (\text{albumin}) - 0.78 (\text{TSF}) - 20 (\text{transferrin}) - 5.8 (\text{delayed hypersensitivity reaction})$, where PNI depicts the risk of developing complications. This model predicted complications in patients undergoing major surgery, but it has not been found useful in predicting complications in patients with ESLD awaiting LT.^[28]

Nutritional assessment factors (including dietary history, anthropometric and biochemical measurements, and evaluation of immunocompetence) were retrospectively reviewed in 74 patients undergoing an initial LT procedure. The patients were subdivided into four categories on the basis of the type of liver disease:

Chronic active hepatitis, primary sclerosing cholangitis, primary biliary cirrhosis, and acute or subacute hepatitis. The data indicated that malnutrition was present preoperatively in all LT groups ($\geq PNI 60\%$), but that each group had distinct characteristics. The group with primary biliary cirrhosis seemed to have the best hepatic synthetic function despite extreme wasting of muscle and fat. Based on all criteria, the group with acute hepatitis was the most malnourished of the various disease groups. It also reported the poor predictive value of the PNI in liver-failure patients which may be explained either by the rapid reversal of many of the metabolic and nutritional abnormalities by the transplanted liver or alternatively by the fact that most of the measurements included in the PNI are poor markers of malnutrition in patients with liver failure.^[8]

Malnutrition is common in patients with ESLD; hence, the ability to detect alterations in nutritional status is vital for the clinicians. Anthropometry, laboratory values, body composition analysis, subjective global assessment (SGA), and handgrip (HG) strength are tools that the clinician can use to help determine a patient's nutritional status. Early detection and interventions to correct nutritional deficits in patients with liver disease may help improve their morbidity and mortality.^[29]

Anthropometry

Anthropometry is a reasonably accurate bedside tool to detect the protein depleted status of cirrhotic patients when used by a single trained examiner.^[5,29] Measurements such as height, weight and body mass index (BMI), skin-fold thickness (triceps, biceps, subscapular, suprailiac) and MAMC are simple, quick, cheap and noninvasive methods of estimating weight-for-height, subcutaneous fat and somatic protein stores.^[14,30]

Unfortunately, most of the easily applicable methods are confounded by significant fluid retention in cirrhotics with ascites and peripheral edema. BMI in particular has been criticized for yielding falsely high values, but correction by subtracting estimated amounts of ascites and other fluid collections may compensate for this disadvantage to some extent.^[32] Anthropometric parameters to assess muscle and fat masses (FM) (arm-muscle circumference and skin-fold thickness) are simple and useful methods (when used by a trained operator) to evaluate nutritional status in those patients with chronic liver disease.^[32]

According to Italian Multicenter Cooperative Project on nutrition in liver cirrhosis (1994), patients with cirrhosis exhibited a wide range of nutritional abnormalities.

While 29% of females and 18% of males appeared to be over nourished, a significant reduction in fat stores, as estimated by the MAMC was observed in 30% of patients with cirrhosis. Measurements of mid arm circumferences (MAC) were used for the calculation of MAMC as follows: $MAMC = MAC - (3.14 \times TSF)$.^[34] The prevalence of signs of nutritional depletion increased in both sexes as liver function deteriorated. Mean values for MAMC decreased by 30% in males and by 40% in females with moderate to severe liver failure. The reduction in MAMC was more evident in males (17% decreases) than in females (9% decrease).^[33]

A study by Akerman *et al.*, showed 33% and 43% of patients were malnourished with <5th percentile of TSF and arm-muscle circumference, respectively.^[35]

A prospective study examined the effect of nutritional status, using anthropometric measurements, on outcome in 102 consecutive adult patients undergoing elective LT. Nutritional status was assessed by using MAMC. Patient outcome variables were time spent in the intensive therapy unit, total time in hospital, infective complications and mortality within 6-month. Graft outcome variables were early graft function, peak aspartate transaminase, alkaline phosphatase, bilirubin and PT. The results depicted that 79% of patients were $\leq 25^{\text{th}}$ percentile of anthropometric measurement (MAMC) and 28% were <5th percentile. These data suggest that a significant proportion of patients undergoing LT are nutritionally compromised and this has effects on patient infection, susceptibility, graft function and mortality, which may possibly be improved by nutritional intervention.^[36]

Alberino *et al.*, studied 212 hospitalized patients with liver cirrhosis who were followed clinically for 2-year or until death. Patients were evaluated by TSF and MAMC, respectively. Multivariate analysis according to Cox's model assessed the predictive power of nutritional parameters on survival. 34% of patients had severe malnutrition (MAMC and/or TSF <5th percentile and 20% had moderate malnutrition (MAMC and/or TSF, <10th percentile). Twenty-six percent of patients were over nourished (MAMC and/or TSF, >75th percentile). Severely and moderately malnourished patients had lower survival rates than normal and over nourished patients. When analyzed with Cox's regression analysis, severe depletion of muscle mass and body fat were found to be independent predictors of survival. The study also showed that inclusion of anthropometric measures in the assessment of these patients might provide better prognostic information.^[16]

A study by Figueiredo *et al.*, showed that in patients with ESLD, arm-muscle circumference and HG strength are the most sensitive markers of body cell mass (BCM) depletion. Nutritional status correlated poorly with BCM. The study suggested that a significant proportion of patients undergoing LT are nutritionally compromised and that this has effects on patient infection, susceptibility, graft function and mortality, which may possibly be improved by nutritional intervention.^[37]

Biochemical Parameters

Circulating concentrations of many visceral plasma proteins (albumin, prealbumin, retinol-binding protein) and 24-h creatinine excretion are highly affected by the presence of liver disease and inflammatory states, as these are synthesized in liver. Immune status, which is often considered a functional test of malnutrition, may be affected by hypersplenism, abnormal immunologic reactivity and alcohol abuse.^[38] At present, TLC and CD8 cell count seem to be of prognostic value in malnourished patients with alcoholic liver disease. In nutrition intervention trials, results from skin anergy test were not useful for the detection of nutritional changes. Serum transferrin has a half-life of 9 days, and can be used as a marker for malnutrition. Good correlation between transferrin levels with the CTP scores score has been demonstrated before and a reduced level of serum transferrin is additionally indicative of decreased caloric intake related to liver transplant patients.^[39]

Biochemical markers of malnutrition include serum albumin concentration and measurements of 24-h creatinine excretion related to liver transplant patients. While the former varies significantly due to hepatic function, the latter has been suggested as an indirect measure of body muscle mass, as 1 g of excreted creatinine equals 18.5 kg of muscle mass.^[40]

A study by Fukushima *et al.*, assessed the predictability of prognoses of ESLD in patients by application of nutritional index 'CONUT' for evaluating prognosis of disease. The prognoses of the patients were evaluated using the following five models: CONUT (albumin [g/dl], total lymphocyte [/ml], total cholesterol [mg/dL]), the model for end-stage liver disease (MELD) with incorporation of sodium (MELD-Na), CTP scores, Prognostic Nutritional Index (PNI), and the Japan Medical Urgency criteria of the liver. The indices were 17.74 ± 5.80 for MELD-Na, 9.21 ± 2.19 for CTP, 33.92 ± 11.16 for PNI-O, and 7.57 ± 3.09 for CONUT. Univariate analysis revealed the significance of CONUT as it showed best predictability for the distant prognoses of patients with ESLD.^[41]

It can be concluded that a poor nutritional state, as well as hypermetabolism, adversely affects survival after LT. These potentially treatable presurgical factors deserve close attention in interventional studies. Hence, multiple biochemical parameters are required to be given importance in patients undergoing LT.

Subjective Global Assessment

No gold-standard evaluation exists to determine the extent of malnutrition in patients with ESLD. Traditional nutritional parameters such as weight loss, serum protein concentrations, TLC, delayed hypersensitivity testing, urinary 3-methylhistidine excretion, and creatinine-height index may be affected by liver disease or its symptoms. Five features of the history are elicited by subjective global assessment [Figure 1]. The first is weight loss in the previous 6-month, expressed as both kilograms and proportionate loss. Weight less than 5% considered as a "small" loss, between 5% and 10% as a "potentially significant" loss, and >10% as a "definitely significant" loss. Also the rate of weight loss and its pattern are considered. The second feature of the history is dietary intake in relation to a patient's usual pattern. Patients are classified first as having normal or abnormal intake. The duration and degree of abnormal intake are also noted (starvation, hypo caloric liquids, full liquid diet, suboptimal solid diet). The third feature of the history is the presence of significant gastrointestinal symptoms (anorexia, nausea, vomiting, and diarrhea). These symptoms have persisted on virtually a daily basis for a period longer than 2 weeks. Short-duration diarrhea or intermittent vomiting is not considered significant. Daily or twice daily vomiting secondary to obstruction is considered significant. The fourth feature of the history is the patient's functional capacity or energy level (bedridden to full capacity). The last feature of the history concerns the metabolic demands of the patient's underlying disease state. There are four

features of the physical examination which are noted as either normal (0), mild (1+), moderate (2+), or severe (3+)

Therefore, the SGA is the preferred nutritional evaluation method for LT candidates.^[13,42-44] Patients are classified as being well-nourished or as having mild, moderate, or severe malnutrition.^[45] This test has shown high specificity (96%) with a very low sensitivity (22%) for diagnosing malnutrition in patients with alcoholic liver disease. However, Hasse proposed SGA as a reliable tool used to evaluate nutritional status in LT patients^[44] [Table 4].

According to Gunsar *et al.*, only SGA showed a significant association with mortality of cirrhotic. The final model included variables like urea, Royal Free Hospital-SGA, age, Child-Pugh grade and PT. The results were similar when the CTP score was replaced by the model for ESLD score, and whether a competing risks model was used.^[46] Hence, Nutritional indices add significantly to both CTP score and Model for ESLD scores when assessing the patient prognosis. The SGA demonstrated a trend towards more malnutrition in CTP C compared with CTP B liver cirrhosis.^[47] Merli *et al.*, showed SGA had 77% agreement with anthropometry. Hence, it can be has be a useful tool for screening malnutrition.^[32]

Another study showed significant relationship of SGA with clinical variables like CTP scores, presence of ascites and/or edema, and encephalopathy. Patients were nutritionally assessed by SGA, anthropometry, HG dynamometry and biochemical tests. Clinical variables were cross analyzed with the nutritional assessment methods. In the study 159 patients were followed. Malnutrition ranged from 6.3% to 80.8% according to the different methods used. Agreement among all the methods was low ($K < 0.26$). Though dynamometry showed highest percentage of malnutrition of 80.8%,

Table 4: Major studies based on SGA for nutrition assessment in patients undergoing liver transplant

Researches	Patient population %	Results
Pikul <i>et al.</i> , 1994 ^[13]	68 liver transplant patients Well-nourished: 21 Mildly malnourished: 19 Moderately malnourished: 34 Severely malnourished: 26	Moderately and severely malnourished patients had longer ICU and hospital stays Severely malnourished patients had increased incidence of tracheostomies A trend towards increased mortality in severely malnourished
Hasse <i>et al.</i> , 1998 ^[51]	1224 liver transplant patients Well-nourished: 25 Moderately malnourished: 60 Severely malnourished: 15	ICU stays were prolonged in severely malnourished 1- and 3-year patient and graft survival rates were significantly lower in severely malnourished patients
Stephenson <i>et al.</i> , 2001 ^[10]	109 liver transplant patients Mildly malnourished: 36 Moderately malnourished: 31 Severely malnourished: 33	Severely malnourished patients required more blood products ICU and hospital stays were longer in severely malnourished

ICU: Intensive care unit; SGA: Subjective global assessment

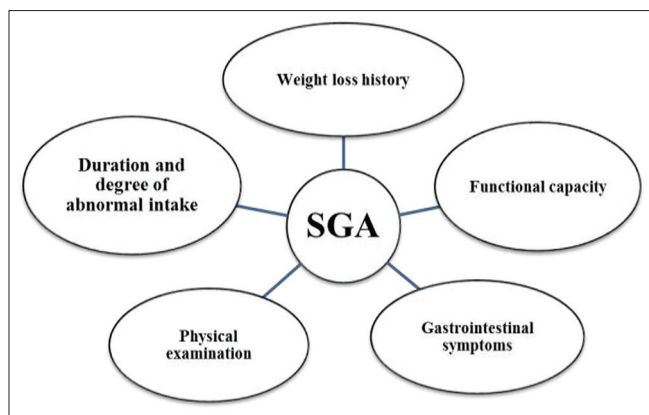


Figure 1: Components of subjective global assessment for liver transplant patients^[13,43-46]

but only SGA showed correlation with the progression of liver disease.^[48]

Subjective global assessment is a clinical tool first described >2 decades ago and has been used to assess nutritional status in patients with liver disease as well as other disease states. Figure 1 depicts five features of SGA.^[49] The SGA is an integrated tool that utilizes the clinical judgment of a practitioner to identify patients at risk of or with malnutrition. It is a clinically useful, simple, safe, and inexpensive tool allowing for widespread use by trained clinicians and remains the gold standard for new bedside assessment tools.^[50] The SGA is able to predict nutrition-associated complications that are infections, use of antibiotics, and length of hospital stay.^[49]

Subjective global assessment is an excellent independent predictor of outcome in patients undergoing LT. Severely malnourished patients require more blood products during surgery and have prolonged postoperative length of stay in hospital. Data suggest that if nutritional repletion is possible in patients with ESLD before transplantation, patient outcomes could be improved.^[10,51]

Roongpisuthipong *et al.*, aimed to determine the prevalence of PEM characteristics, and clinical importance of nutrition disorders in patients with liver cirrhosis according to severity of disease. Protein malnutrition (low albumin) and immune incompetence (abnormal response to skin tests) were found much more frequently (45% and 22%) than energy malnutrition. SGA and serum proteins correlated with the degree of liver-function impairment, but immunologic tests correlated inversely in cirrhosis patients. Mean values for creatinine- height index, hemoglobin, cholesterol, and complement C4 showed significant decreases in severe liver failure (CTP class C) only in patients with alcoholic cirrhosis. Malnutrition

was correlated with the clinical severity of liver disease. The study showed that PEM is a common complication of liver cirrhosis.^[52]

Morgan *et al.*, showed intra-observer repeatability coefficients for anthropometric variables which ranged from 0% to 8.0%. The intra-class correlation coefficient for dietary intake was 0.42 but exceeded 0.8 for all of the anthropometric variables, indicating substantial inter-observer agreement. The assessment of nutritional status was concordant in 81% of patients. Nutritional categorization was significantly associated with both relative TSF and relative MAMC, but not with BMI. Thus, the modified SGA method of nutritional assessment was reproducible between observers and was significantly associated with two of the three anthropometric variables measured.^[53]

In a study by Fernandes *et al.*, depicted, 20.2% of the patients in this study were classified as malnourished by SGA;^[54] in another study conducted by Gottschall *et al.* the SGA index achieved 38%. SGA presents sensitivity of 22% in patients with cirrhosis and underestimates the nutritional state of pretransplant patients by 57% and with overestimation of 6%.^[55] Paradoxically, some studies suggest that the benefits of SGA for the nutritional state progress of candidates for transplantation, while other studies showed that SGA detects malnutrition in only 25% of the cases. However, it should be noted that SGA is an instrument composed of quantitative and qualitative variables, subject to varied interpretations, as it is a partially subjective method.^[56,33]

Guidelines

ESPEN guidelines (1997) for nutrition in liver disease and transplantation stated that PEM impairs liver function but rarely causes morphological alterations. Quantitative liver function tests can be used as global indicators of functional impairment but are not capable of separating between malnutrition induced and disease-induced liver malfunction.^[57]

ESPEN guidelines (2006) on liver disease recommended use of simple bedside methods such as the SGA or anthropometry to identify patients at risk of undernutrition. It also recommended BCM measured by bioelectric impedance analysis to quantify undernutrition, despite some limitations in patients with ascites.^[58]

ESPEN guidelines (2006) on enteral nutrition in organ transplantation recommended use of nutritional

support in patients with severe nutritional risk for 10-14 days prior to major surgery even if surgery has to be delayed. Severe nutritional risk refers to at least one of the following: Weight loss >10-15% within 6-month, BMI < 18.5 kg/m², SGA Grade C, serum albumin <30 g/l with no evidence of hepatic or renal dysfunction.^[59]

Bioelectrical Impedance Analysis

BIA evaluates the body electrical conductivity and resistance (impedance) and has been used to determine lean body mass and fat in patients with ESLD. It is based on the principle that conduction through fat tissue tends to be decreased due to increased impedance, in contrast with a more rapid conduction through water. It is a noninvasive and inexpensive test; however, measurement of BCM in patients with edema may be inaccurate.^[60] The assessment through BIA presented a statistically significant correlation with CTP score. The use of BIA is controversial in patients with ascites,^[9,61] but caution should also be exerted in patients without clinical signs of fluid overload.^[62] In two studies, a good correlation was found between fat free mass (FFM) and BCM by BIA and BCM assessed by total body potassium counting.^[63] However, BIA was found unable to accurately reflect changes in body composition due to cirrhosis when direct methods were used.^[5]

Very little information is available on body composition in patients with cirrhosis. Difficulties arise in studying these patients because they tend to retain fluid and these results in changes in tissue density and in the hydration fraction of FFM. As the classic body composition techniques rely on the assumption that these variables remain constant, use of these methods will result in either under- or overestimates of body composition variables. Use of multi-component models (like the three-component model of water, fat and protein/mineral is based on measurements obtained from both densitometry and water dilution), employing two or more measurement techniques, will obviate the need for some of the assumptions inherent in the use of single techniques, thereby increasing the accuracy of the assessments, without loss of precision.^[64] Figueiredo *et al.*, compared the traditional two-compartment model (SGA and anthropometry and blood tests) of nutritional assessment with a multicompartmental model (body composition analysis) in patients with cirrhosis. SGA depicted 31.6% as malnourished. According to the multicompartmental model, 60.1% were malnourished, 34.4% in Child's A, 69% in B, and 94.4% in C. The use of the multicompartmental model increased the prevalence of malnutrition by >60% in Child's classes A and B patients and by >20% in Child's class C patients. Traditional nutritional assessment,

although easier, underestimated the prevalence and severity of malnutrition in patients with cirrhosis. The underestimation was more pronounced in Child's class A and B patients.^[56]

A study by Kyle *et al.*, measured BIA derived FFM among pre- and post-transplant liver, lung, and heart patients. The high correlation coefficient, small bias and small Standard estimation of error (2.3 kg) suggest that BIA using the GENEVA equation is able to predict FFM in pre- and post-transplant patients. The study showed that the lower weight seen in transplant men and women than in controls was due to lower FFM, which was partially offset by higher fat mass in men but not in women. Furthermore, the higher weights in post-transplant than in pretransplant patients were due to higher FM and % FM that was confirmed by lower FFM/FM ratio in post-transplant patients.^[65]

Kaido *et al.*, preoperatively measured BCM using a body composition analyzer and various nutritional parameters including prealbumin, branched-chain amino acids (BCAA)/tyrosine ratio, and zinc in 50 consecutive recipients undergoing Living Donor Liver Transplant for 1-year. Risk factors for post-transplant sepsis were analyzed. The incidence of postoperative severe infection and in-hospital death was significantly higher in patients with preoperative low BCM than in patients with normal or high BCM. Multivariate predictors of post-transplant sepsis included preoperative low BCM, absence of preoperative supplementation with BCAA-enriched nutrient mixture, and a model for ESLD score of 20 or above. Hence the study concluded that preoperative BCM level closely relates to the postoperative clinical course in patients undergoing LT.^[66] Selberg *et al.*, correlated BCM with MAMC and creatinine excretion. Survival analysis for all patients of the study group showed that those with a higher proportion of BCM (0.35% of body weight) tended to have better survival. A prognostic risk profile was developed on the basis of the degree of hypermetabolism and malnutrition as assessed by BCM % Body Weight.^[14]

Handgrip Strength

A cross-sectional study by Silva and Silveira (2005) evaluated nutritional status by SGA, PNI and HG strength in cirrhotic patients. Prevalence of malnutrition was 28% by SGA, 18.7% by PNI, and 63% by HG. When compared with SGA, HG lacked specificity and had a positive prediction value of only 38%. This could lead to the risk of categorizing a patient as malnourished who is not. The positive predictive value was 37.9%, and the negative value was 100%. Patients with cirrhosis were

followed for 1-year to verify the incidence of major complications, the need for transplantation, and death. There was a high prevalence of malnutrition in cirrhotic outpatients, especially when assessed by HG, which was superior to SGA and PNI in this study. HG was the only technique that predicted a significant incidence of major complications in 1-year in undernourished cirrhotic patients. HG seems to be a simple, inexpensive, and effective method to detect PCM, or at least nutritional risk, in this population because it can identify those patients who are most likely to develop complications.^[21]

A study by Figueiredo *et al.*, showed for patients with ESLD, MAMC and HG strength are the most sensitive markers of BCM depletion. It is proved that patients with depleted BCM (lowest quartile for sex) had lower HG strength. Another study by Figueiredo *et al.*, in the same year depicted the impact of nutrition status on post-transplant factors. Longer Intensive Care Unit stay was associated with lower HG strength and lower aromatic amino acid levels. Longer total hospital stay and the development of infections were associated with lower branched chain amino acid levels.^[31]

Ferreira *et al.*, aimed to study different tools used to assess the nutritional status of patients waiting for a LT. Patients were nutritionally assessed by SGA, anthropometry, HG dynamometry and biochemical tests. Clinical variables were cross analyzed with the nutritional assessment methods. Malnutrition ranged from 6.3% to 80.8% according to the different methods used. According to SGA, malnutrition was present in 74.7% of the patients, and of these, 85 patients (72%) were moderately and 33 (28%) were severely malnourished. Malnutrition in patients on the waiting list for LT according to HG was 80.8%. Only SGA showed significant relationships with clinical variables like CTP scores, presence of ascites and/or edema, and encephalopathy. Dynamometry was a more sensible method to diagnose malnutrition in cirrhotic patients.^[48] However, this parameter was not associated with CTP classes, where patients with CTP C are expected to be malnourished by definition. CTP C is associated with greater early postoperative morbidity. Advanced CTP class is also associated with diminished muscle status and parenchymal disease. Grip strength and MAMC were lower in the patients in CTP classes B and C. Parenchymal liver disease was associated with lower grip strength and MAMC when compared to cholestatic disease.^[67]

Conclusion

Nutrition assessment in LT is a crucial step which

should be performed prior to the transplant as PEM is associated with morbidity and mortality of patients. Prior nutritional assessment will help to plan nutrition intervention for patients undergoing liver transplant.

Pretransplant nutritional assessment in the patient with ESLD is problematic. The best system for nutritional assessment uses a "global" evaluation of the patient's nutritional reserves. With such a technique, the vast majority of transplant candidates have been shown to have evidence of malnutrition. Several investigators have demonstrated the risk of significant malnutrition on post-transplant outcome. An aggressive approach to nutritional repletion is necessary to improve the ESLD patient's metabolic reserves, maintain remaining hepatic function, and better the outcome after LT.^[68] Hence, timely nutrition assessment and intervention in organ transplant recipients may improve outcomes surrounding transplantation. A pretransplant nutrition assessment should include a variety of parameters including physical assessment, history, anthropometric measurements, and laboratory tests. Malnutrition compromises posttransplant survival; prolonged waiting times worsen outcomes when patients are already malnourished.^[69]

Even after considering the limitations of nutritional assessment, it is very important to obtain a more complete evaluation of a cirrhotic patient and to recognize the possible need for nutrition intervention. An appropriate nutritional evaluation will include combination of various methods like SGA, anthropometry MAMC, BIA and HG to formulate a composite score for assessment of malnutrition.

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