Nutritional problems in liver transplantation

Patients presenting at the extreme ends of the nutritional spectrum often raise the most concern with regard to liver transplantation. However, they are not excluded from the procedure as there is currently no international consensus regarding nutritional status and liver transplantation.

Protein energy malnutrition (PEM) in chronic liver disease (CLD) is multifactorial. Causes include decreased nutrient intake, malabsorption and maldigestion, abnormal fuel metabolism and energy expenditure alterations, as reviewed by Patton and Aranda-Michel (2002). This editorial will highlight that while we already know a lot about the aetiology of malnutrition and substrate metabolism in CLD, in everyday clinical practice we are unable to answer the simple question: Does nutritional support provided pre- and post-transplant have any effect on post-transplant outcome?

PROTEIN ENERGY MALNUTRITION

PEM is common in all forms of CLD, regardless of aetiology. It can be identified in 20% of patients with compensated disease and more than 80% of decompensated patients. Studies in liver transplant patients have shown increased mortality in the most malnourished. In one study mortality was nearly doubled and in another 6-month survival was only 87% compared with 100% in the well nourished. Other studies have noted increased requirement for ventilatory support and tracheostomies, and an increased overall length of stay in the malnourished. These studies are reviewed by Hasse (2001).

However, despite PEM being acknowledged as an independent risk factor for morbidity and mortality, it is not considered an absolute contraindication to liver transplantation and there are currently no guidelines recommending below what body mass index (BMI) a transplant should not be considered. In the author's centre a BMI of less than 18 kg/m^2, combined with a mid arm muscle circumference (MAMC) of less than the fifth percentile, would raise definite concerns.

OBESITY

Another group of patients with CLD potentially at increased risk of mortality and morbidity from liver transplantation are the severely obese. With the current view that a large number of cryptogenic cirrhotics have progressed from non-alcoholic steatohepatitis, combined with the increasing prevalence of obesity in the general population, this may become a more common issue in patients presenting for consideration of liver transplantation.

The potential complications with the severely obese are early death, a more technically difficult operation, primary non-graft function, wound infection and dehiscence, and increased length of stay.

Studies have given conflicting results, with the majority showing wound infection as the main complication and only one revealing increased mortality. However, a study by Nair et al (2002) addressed the small sample size and inconsistent definition of severe obesity in these earlier studies by looking at the post-1988 United Network for Organ Sharing database of 18 172 post liver transplant patients. They defined obesity as BMI 30.1–35.0 kg/m^2, severe obesity as BMI 35.1–40.0 kg/m^2, and morbid obesity as BMI 40.1–50.0 kg/m^2. They found no differences in rates of infection, operative mortality and cerebrovascular events. However, all three obesity groups showed a significantly higher cardiovascular mortality, with the severely and morbidly obese having a poorer 5-year survival.

In addition primary non-graft function and immediate, 1-year and 2-year mortality were significantly higher in the morbidly obese. They concluded that patients with a BMI greater than 40 kg/m^2 should be listed on a highly individual basis and that all patients with a BMI greater than 35 kg/m^2 awaiting transplant should be actively encouraged to lose weight to a target BMI of less than 30 kg/m^2, because of the likelihood of post-transplant weight gain. So, despite there being no international consensus above which BMI liver transplant should not be considered, there is at least now some clinical guidance regarding patients at this end of the nutritional spectrum.

NUTRITIONAL ASSESSMENT

It is the norm for patients to have a dietetic assessment as part of a liver transplant assessment, however, there is no gold standard for nutritional assessment in CLD. In this group of patients body weight alone cannot be relied upon as an accurate measure of nutritional status. Fluid retention (ascites and oedema) can mask weight loss and even in patients not retaining fluid, an apparently stable weight can mask deterioration in body protein stores.

Body composition can be determined by dual-energy X-ray absorptiometry (DEXA), total body potassium, 24-hour urinary creatinine excretion and four site skinfold measurement, but cost and time implications mean these are mostly restricted to research purposes.

Bioelectrical impedance analysis is likely to now be available to the clinician but its use in CLD is controversial because of body fluid shifts. Others use a subjective global assessment technique adapted for CLD. However, the techniques most widely used by dietitians in the UK liver transplant centres are upper arm anthropometric measurements of subcutaneous fat and muscle mass and hand grip strength to measure muscle function. These physical assessments are combined with an assessment of nutrient requirements and current intake to formulate a pre-

operative treatment plan to improve or maintain nutritional status.

With malnutrition identified as an independent, 'potentially reversible' risk factor for liver transplant, it would seem that the effectiveness of pre-transplant nutritional support should have been well studied. It is a potentially reversible risk factor but the provision of preoperative nutritional support is controversial, with some believing that this is futile as the 'sick' liver is unable to appropriately process nutrients and recommending early transplant rather than prolonged nutritional support. Others believe PEM is reversible but requires aggressive nutritional support to achieve it.

Intervention studies so far have been of oral supplementation only. Le Cornu et al (2000) found oral supplementation improved MAMC and grip strength, but had no effect on outcome. However, daily energy intake was similar in both control and study groups, perhaps because the study group ate less compensating for the oral supplement. In another study Hasse et al (1997) compared diet alone with diet and either a casein or hepatic supplement. The supplemented groups consumed more energy and protein but there was no effect on nutritional status. Patients on the hepatic formula spent fewer days in hospital pre-transplant.

Clearly, what are needed are large multicentre randomized controlled trials of aggressive nutritional support pre-transplant. Subjectively, the author has had good results using overnight nasogastric (NG) feeding, resulting in overall weight gain and increase in MAMC. This may be because the patients are actually receiving their increased requirements, but may also be partly because overnight feeding reduces fasting time, reducing gluconeogenesis and thereby reducing muscle breakdown. Cirrhosis has been termed a disease of 'accelerated starvation', as there is an accelerated transition from the fed to the fasting state because of inadequate glycogen stores.

NG feeding is the normal route for preoperative nutritional support as percutaneous gastrostomies are contraindicated in ascites because of the risk of infection. Parenteral nutrition (PN), as with all other areas, should be reserved for true bowel obstruction or ileus.

There have also been limited studies of feeding in the postoperative liver transplant patient, as reviewed by Hasse (2001). Two studies compared enteral feeding with PN. One showed that ileus occurred less often in a jejunostomy-fed group than a PN group. Another study compared nasojejunal tube (NJT) feeding with PN and found no significant differences in length of stay, ventilatory days or infection rates. A further study compared nasojejunal feeding with standard intravenous fluids. Feeding had no effect on ventilator requirements and length of stay but did result in significantly less viral infections. The authors reported a drawback in this study was the high dropout rate mainly resulting from surgeons forgetting to place feeding tubes during surgery.

In the authors' clinical practice, this is also the major drawback to postoperative feeding as patients often return from theatre without any feeding access, despite NJT placement being requested for all malnourished patients. Placement is not currently requested for well-nourished patients, but there is an argument for NJT placement in all patients, as it is impossible to determine if there will be postoperative complications requiring an extended nil by mouth period. At present, patients not receiving NJTs intraoperatively who go on to have postoperative complications may end up on inappropriate PN if gastric dysmotility prevents NG feeding, unless there is easy access to endoscopic NJT placement.

CONCLUSIONS

It is clear that there is a lack of research in this area. Large multicentre randomized controlled trials are needed to assess whether or not pre- and postoperative nutritional support affects post-transplant outcome. With the shortage of organs and the wish to see the 'best life' for each organ, more studies may also allow identification of good transplant candidates and identify the points at the ends of the BMI spectrum which sufficiently affect outcome to constitute a contraindication to liver transplantation. HM

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KEY POINTS

- Protein energy malnutrition adversely affects morbidity and mortality post-liver transplant.
- There is currently no international consensus as to the body mass index (BMI) below which liver transplant is contraindicated.
- Nasojejunal tubes can be placed intraoperatively to allow early postoperative enteral feeding.
- Morbid obesity affects morbidity and mortality post-liver transplant.
- Patients with BMIs greater than 35 kg/m^2 awaiting liver transplant should be actively encouraged to lose weight.
- More multicentre randomized controlled trials are needed on the impact of pre- and post-transplant nutrition support on clinical outcome.