New Insights in Nutrition in the Transplant Setting

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Transplantation creates unique nutritional demands, and optimal nutrition is needed to improve short- and long-term outcomes in patients. New insights into nutrition based on research and clinical practice in the settings of pediatric hematopoietic cell transplantation (HCT), intestinal transplantation, and liver transplantation were reviewed.

HCT creates a unique nutritional situation in children, which is influenced by their medical history, the presence of inflammation or infection, previous treatments, and toxicity to the transplant regimen or other therapies. Nutrition is a concern both during and after the transplant period, according to Lori J. Bechard, PhD, RD, Boston Children's Hospital, Boston, Massachusetts, USA.

Energy requirements, body composition, and bone health in children change during HCT. Surprisingly, in a prospective study, resting energy expenditure (REE) significantly ($P < .0001$) declined after HCT, reaching its nadir of 80% predicted REE at about 4 weeks and then increasing but not reaching pre-HCT levels in children receiving parenteral nutrition (PN) designed to supply their REE, as measured by weekly indirect calorimetry [Duggan C et al. *Am J Clin Nutr*. 2003]. A significant ($P = .03$) decrease in midarm muscle area was found and may possibly drive the reduced REE. Another study confirmed that percent body fat is increased while lean body mass is decreased, whether or not PN was titrated to REE, through day 100 post-HCT [Sharma TS et al. *Am J Clin Nutr*. 2012]. An association was found between reduced arm muscle area and reduced survival [Hoffmeister PA et al. *Biol Blood Marrow Transpl.* 2013]. These data suggest additional strategies are needed to preserve lean body mass and increase patient survival post-HCT.

Bone mineral density can be deleteriously affected after HCT [Le Meignen M et al. *Blood.* 2011], and the reductions in bone mineral density and bone mineral content occur as early as the first 30 days [Bechard LJ *Pediatr Blood Cancer*. 2015]. Vertebral compression fractures were found in about 20% of children after HCT [Taskinen M et al. *Cancer*. 2007].

The feasibility of enteral nutrition (EN) for children during HCT was shown by a retrospective study in which body weight and body mass index (BMI) were maintained and by a prospective comparison against PN in which the 77% of patients receiving EN maintained their weight, had faster platelet recovery ($P = .01$), and shorter length of stay ($P < .001$) [Azamoush S et al. *Bone Marrow Transpl*. 2012]. The children who are candidates for EN must be determined by further study.

Vitamin D deficiency is common in children after HCT [Bechard LJ *Pediatr Blood Cancer*. 2015; Campos DJ et al. *Nutr*. 2014; Duncan CN et al. *Biol Blood Marrow Transp*. 2011]. An association was found between vitamin D deficiency at baseline and outcomes (Table 1), including mortality, relapse, and transplant failure, and further research is needed to determine its role [Hansson ME et al. *Biol Blood Marrow Transplant*. 2014].

The use of parenteral lipids containing olive oil [Hartman C et al. *Clin Nutr*. 2009], fish oil [Gura KM et al. *Clin Nutr*. 2005], and a blend of soybean and fish oils

Table 1. Baseline Vitamin D Levels Associated With Outcomes Post-HCT

Risk Factor Analysis[a] for aGvHD, Mortality, Relapse, and Transplant Failure			
	HR	**95% CI**	***P* Value**
aGvHD grades II-IV, all			
Calcidiol > 50 nmol/L	1.72	.96-3.13	.065
Late disease	2.59	1.42-4.71	.002
Mortality, malignancies			
Calcidiol > 50 nmol/L	.15	.04-.57	.005
URD	3.77	1.11-12.8	.03
MDS	2.93	1.09-7.88	.03
Relapse, malignancies			
Calcidiol > 50 nmol/L	.08	.01-.63	.02
Transplant failure,[b] malignancies			
Calcidiol > 50 nmol/L	.14	.04-.50	.002
URD	3.58	1.23-10.4	.02

aGvHD, acute graft-vs-host disease; MDS, myelodysplastic syndrome; URD, unrelated donor.

Late disease indicates beyond first complete remission/first chronic phase.

[a]Corrected for differences in the characteristics, such as age, stage, and myelodysplastic syndrome.

[b]That is, relapse or death.

Adapted from *Biol Blood Marrow Transplant*, Hansson ME. Vitamin D Levels Affect Outcome in Pediatric Hematopoietic Stem Cell Transplantation, 2014;20:1537-1543. Copyright (2014) with permission from American Society for Blood and Marrow Transplantation.

Table 2. Indications From ESPEN for HPN for Intestinal Failure

Indications	Grade of Evidence
Home parenteral nutrition support should be used in patients who cannot meet their nutritional requirement by enteral intake and who are able to receive therapy outside of an acute care setting	B
Long-term PN is indicated for patients with prolonged gastrointestinal tract failure that prevents the absorption of adequate nutrients to sustain life; as it is a life-saving therapy for patients with irreversible intestinal failure, it does not require evaluation of efficacy by RCT	B
Maintaining quality of life and rehabilitation supports the indication for home treatment	C

ESPEN, European Society for Clinical Nutrition and Metabolism; HPN, home parenteral nutrition; PN, parenteral nutrition; RCT, randomized clinical trial.

Source: Staun M et al. *Clin Nutr*. 2009.

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[Baena-Gomez MA et al. *Ann Nutr Metab*. 2013] has been studied in small samples of this population.

INTESTINAL TRANSPLANTATION AND NUTRITION

Home parenteral nutrition (HPN) and ultimately intestinal transplantation are treatments for intestinal failure, defined as gut function below the minimum necessary for sufficient absorption of macronutrients, water, or electrolytes to sustain health or growth and thus requiring intravenous supplementation. The indications for HPN are shown in Table 2 [Staun M et al. *Clin Nutr*. 2009].

The major complications with HPN are catheter-related or metabolic (liver abnormalities, biliary stones, bone disease, trace element/vitamin deficiencies, manganese toxicity, impaired renal function). Others include psychological, quality of life, and rehabilitation issues, stated André Van Gossum, MD, PhD, Hôpital Erasme, Brussels, Belgium.

Recommendations to prevent HPN-related liver diseases include the following: to encourage oral food intake and a cyclical HPN regimen; to limit intestinal bacterial overgrowth; to avoid toxic factors and rapid and adequate treatment of sepsis; to limit lipid intake to < 1 g/kg/d; to protect bile salt composition supplementation with urso-deoxycholic acid; and to consider a combined liver and intestinal transplant for patients with cirrhosis and hepatic failure.

HPN dependence can result from adaptation of the colonic flora or intestinal capacities, but reversal has been shown up to 5 years after its onset [Amiot A et al. *Clin Nutr*. 2012; Pironi L et al. *Gut*. 2011]. In patients with short bowel syndrome, EN improved intestinal absorption [Joly F et al. *Gastroenterology*. 2009].

Intestinal transplants have increased in recent years and are primarily performed in North America. Five-year survival in patients on HPN who were candidates for a transplant was 73% vs 87% in those who were not candidates [Pironi L et al. *Gut*. 2011]. Other data from this study indicate the need for early referral for transplant for patients with intestinal failure and HPN-associated liver failure or invasive intra-abdominal desmoids. Indications for a pre-emptive or rehabilitative transplant are major central venous-catheter-related complications or ultra-short bowel syndrome.

IMPACT OF NUTRITION ON LIVER TRANSPLANTATION

Patients may wait for liver transplantation for years, and during this time, sarcopenia develops in half of patients [Cruz RJ Jr et al. *Transplantation*. 2013], with the prevalence decreasing with increasing BMI [Tandon P et al. *Liver Transplantation*. 2012]. Transplant outcomes are affected by body composition and malnutrition before transplantation and nutrition therapy before and after transplantation, stated Jeanette Hasse, PhD, Baylor University Medical Center, Dallas, Texas, USA.

Increased muscle wasting was associated with decreased survival in patients with sarcopenia following liver transplantation in 2 studies [Montano-Loza AJ et al. *Clin Gastroenterol Hepatol*. 2012; Englesbe MJ et al. *J Am Coll Surg*. 2010], but not in another study [Montano-Loza AJ et al. *Liver Transpl*. 2014]. In the latter study, sarcopenia influenced the length of hospitalization and the prevalence of infections; patients with sarcopenia were more likely to experience post-transplantation bacterial, viral, and fungal infections than their nonsarcopenic counterparts.

In another study, patients were grouped by tertiles of total psoas muscle area [Krell RW et al. *Liver Transpl*. 2013]. Patients with the greatest muscle wasting had >4-fold higher risk of developing a severe infection vs patients with the least muscle wasting (OR, 4.6; 95% CI, 2.25 to 9.53). Age of the transplant recipient (HR, 1.04; $P=.02$), pretransplant psoas muscle size (HR 0.38, $P<.01$), and pretransplant total bilirubin level (HR, 1.05; $P=.02$) were independently associated with the risk of developing severe infections. A severe infection was associated with a worse 1-year survival vs no infection (76% vs 92%, $P=.003$).

EN after liver transplantation has been shown to improve outcomes, including a reduction in reduced bacterial sepsis and early graft loss when initiated within 48 hours [Ikegami et al. *J Am Coll Surg*. 2012]. Perioperative immunonutrition provided to improve nutrition status before transplantation did not improve postoperative outcomes including rates of infection in a randomized study [Plank LD et al. *Hepatology*. 2015]. Continued research is needed to determine nutrition therapies to improve outcomes.