


# Adequate Home Parenteral Nutrition Does Not Improve Lean Body Mass in Bone Marrow Transplantation Patients with Graft Versus Host Disease.

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## Abstract

**Rationale:** Severe graft-versus-host disease (GVHD) following bone marrow transplantation may require home parenteral nutrition (HPN). The aim of this study was to examine changes in body composition in patients receiving HPN.

**Methods:** This historic cohort study compared HPN patients with and without GVHD. All patients in the adult HPN database from 1991 to 2002 with a baseline nutrition assessment (NA) and a repeat between 4 and 52 weeks were eligible. Those receiving HPN for < 5 days/week were excluded. 20 of 69 GVHD patients met these criteria. 20 of 575 controls without GVHD were matched for gender, BMI and days between NA. Results were analyzed by paired t-tests, Wilcoxon signed rank tests and analysis of covariance adjusting for age.

**Results:** The mean age of GVHD and control patients was 38 ±12 y vs 55 ±18 y (p=0.001); days between NA were 80 ±38 vs 81 ±40 (p=0.56); energy kcal/kg/d was 37 ±10 vs 33 ±10 (p=0.004); and protein g/kg/d was 1.8 ±0.3 vs 1.7 ±0.4 (p=0.14). There were 12 men in each group. Baseline albumin (g/dL) was the same (2.6 ±0.5 vs 2.6 ±0.6) and only improved in controls (2.6 ±0.5 vs 3.0 ±0.8, p=0.09). Fat stores decreased in controls and increased in GVHD patients. Somatic proteins improved in controls and declined in GVHD subjects, with the difference in repeat values remaining significant after adjusting for age (p=0.0001).

**Conclusions:** GVHD patients developed worsening protein nutriture despite adequate HPN. These findings suggest that GVHD and related therapies result in a hypermetabolic and hypercatabolic state.

	GVHD*	Control*	P- value
BMI Baseline	23.7 ± 4.9	24.7 ± 7.5	ns
Repeat	23.3 ± 5.4	25.3 ± 6.2	0.02
TSF Baseline	15.4 ± 8.7	16.1 ± 10	ns
Repeat	17.4 ± 8.8	14.7 ± 7.6	ns
MUAMC Baseline	23.3 ± 3.7	23.6 ± 3.6	ns
Repeat	20.8 ± 3.6	24.2 ± 4.1	0.001

\*mean ± SD; TSF:Triceps skinfold, MUAMC: Mid-upper arm muscle circumference

## Background & Aim

Patients with Graft versus Host Disease (GVHD) of the gastrointestinal tract are at high risk for the development of severe protein-calorie malnutrition (PCM) as a result of anorexia, nausea, vomiting, diarrhea and abdominal pain.<sup>1</sup>

The pathogenesis of PCM in GVHD of the gastrointestinal tract is attributed to limited oral intake, maldigestion and malabsorption, protein losing enteropathy, and increased protein and energy requirements. It has been suggested that daily macronutrient requirements of adults with GVHD range from 1.5-2.0 g/kg for protein and 30-40 kcal/kg for energy.<sup>2,3</sup>

While PN has been shown to improve survival in BMT,<sup>4</sup> little is known about the long-term effect of this therapy on body composition in GVHD. We have observed that it is very difficult to normalize visceral proteins despite the provision of intensive nutrition support to these patients.

The aim of this study was to describe the nutritional outcomes in a cohort of adult bone marrow transplant (BMT) patients with GVHD of the gut requiring home parenteral nutrition (HPN).

## Methods

An historic cohort study using data obtained from a computerized database of all adult patients who receive HPN between 1991 and 2002 at the Cleveland Clinic Foundation.

Information maintained in the database includes age, gender, diagnosis, indication for HPN, start and end date of therapy, nutrient composition of the parenteral nutrition formula and all laboratory studies.

Nearly all patients have a comprehensive nutrition assessment at the start of HPN and many, but not all, have a repeat value during a subsequent clinic or hospital encounter.

The nutrition assessment consists of the following measures:

- Height
- Weight
- Body mass index (BMI)
- Triceps skin fold (TSF)
- Mid upper arm muscle circumference (MUAMC)
- Serum albumin and transferrin

Patients are closely monitored and the parenteral nutrient formula is adjusted to improve the nutritional status of the patient. Monitoring includes the evaluation of daily weights, intake and output records, and laboratory studies that are sent to the HPN office once each week. Clinic visits are scheduled at 1, 3, 6 and 12 months after discharge from the hospital to assess clinical and nutritional progress.

The nutrient composition of the HPN prescription with the greatest energy content given within 8 weeks of the HPN start date was chosen as the representative formula for each patient.

Patients on HPN for GVHD of the gastrointestinal tract were matched to one control subject by gender, BMI and +/- 15 days between the 1st and 2nd nutrition assessment.

### Inclusion Criteria

Study patients: those who received HPN for GVHD following allogeneic BMT.

Control patients: those who received HPN for malabsorption secondary to short bowel syndrome as a result of intestinal resection for benign disease or radiation enteritis.

HPN five (5) or more nights per week for at least four (4) weeks.

A comprehensive nutrition assessment performed at the initiation of HPN and a subsequent measure performed between 4 and 52 weeks following hospital discharge.

### Exclusion Criteria

HPN <4 weeks.

Age <20 years.

Incomplete or absent nutrition assessment at start of HPN or between 4 and 52 weeks of treatment.

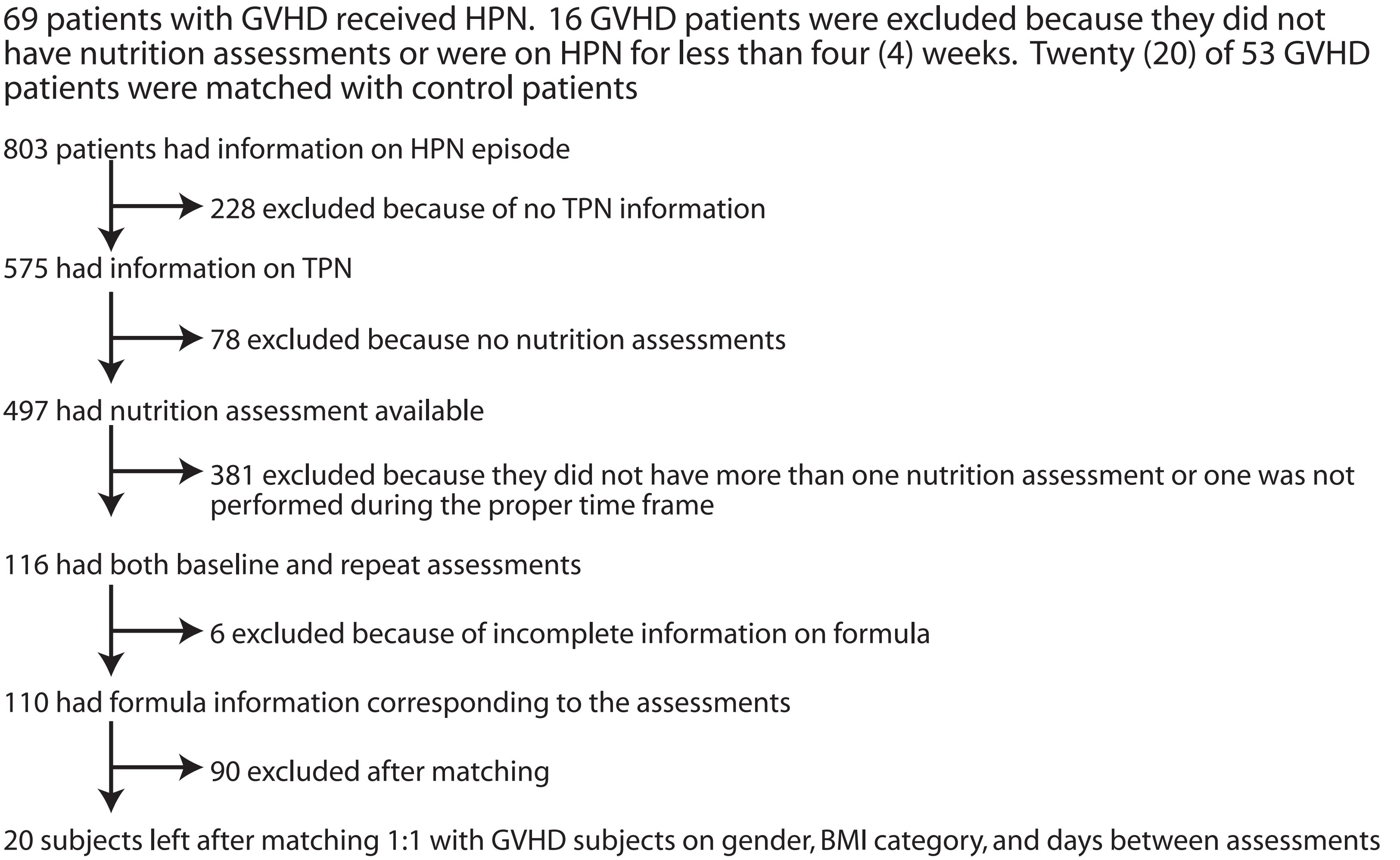
Underlying cancer or abdominopelvic infection that might negatively impact body composition and visceral proteins.

### Statistical methods

Results were analyzed by paired t-tests and Wilcoxon signed rank tests as appropriate. Repeated measures analysis of covariance was used to study possible differences between both groups while adjusting for age and duration of HPN. Spearman's correlation coefficients were calculated to study the association between feeding patterns and BMI category for both of the groups. A significance level of 0.05 was used for all analyses. SAS 9.0 software, SAS Institute Inc., Cary, NC was utilized to carry out all analyses.

## Results

### Patient Characteristics



**Table 1** shows the distribution of gender, BMI and time interval between the initial and follow up nutrition assessment between the two groups. Patients in the GVHD group were younger and used HPN for a shorter length of time compared to the controls. These differences are not unexpected.

**Table 1: Patient Characteristics.**

Criteria Matched		GVHD n=20		Controls n=20	
Gender	Male	12		12	
	Female	8		8	
BMI (kg/m <sup>2</sup> )					
	< 20	30%		30%	
	20-24.9	20%		20%	
	25-29.9	40%		40%	
	≥ 30	10%		10%	
Days between assessments (Mean ± SD)		80 ± 38		81 ± 40	P <sup>†</sup> = 0.56*
Criteria Not Matched		GVHD n=20		Controls n=20	
Age at HPN start		38 ± 12		55 ± 18	P <sup>†</sup> = 0.001
Duration of HPN		88.6 ± 69.6		303.0 ± 390.8	P <sup>†</sup> = 0.001*

<sup>†</sup>P-values correspond to Paired t-test and Wilcoxon signed rank tests (latter denoted by \*)

### Analysis

The results of univariable analysis is shown in **Table 2** and revealed that:

- GVHD patients were given higher total energy per kg (P=0.004);
- control patients had a higher BMI at the second nutrition assessment (P=0.02) and a higher baseline transferrin (P=0.002) compared to GVHD patients;
- control patients had a higher MUAMC at the second nutrition assessment (P=0.001) compared to GVHD patients; and control patients had a slight increase in MUAMC between the first and second nutrition assessment (+0.6 mm), while GVHD patients had a mean decrease (-2.5 mm). This change was significantly different between both groups (P=0.0001).

**Table 2: HPN Formula and Nutrition Assessment**

		GVHD	Controls	P-value <sup>†</sup>
Energy (kcal/kg/d)		37 ± 10	33 ± 10	0.004
Protein (g/kg/d)		1.8 ± 0.3	1.7 ± 0.4	0.14
BMI	Baseline	23.7 ± 4.9	24.7 ± 7.5	0.60*
	Repeat	23.3 ± 5.4	25.3 ± 6.2	0.02
TSF	Baseline	15.4 ± 8.7	16.1 ± 10.0	0.50*
	Repeat	17.4 ± 8.8	14.7 ± 7.6	0.15
MUAMC	Baseline	23.3 ± 3.7	23.6 ± 3.6	0.95*
	Repeat	20.8 ± 3.6	24.2 ± 4.1	0.001*
Albumin	Baseline	2.6 ± 0.5	2.6 ± 0.6	0.63
	Repeat	2.6 ± 0.5	3.0 ± 0.8	0.09
Transferrin	Baseline	126.0 ± 28.1	171.6 ± 51.8	0.002
	Repeat	155.6 ± 36.5	175.5 ± 72.2	0.27

<sup>†</sup>P-values correspond to Paired t-test and Wilcoxon signed rank tests (latter denoted by \*)

Multivariable analysis adjusting for age at start of HPN also confirmed that the change in MUAMC between the first and second nutrition assessment was significantly different between the groups (P=0.001); the baseline transferrin was higher in the controls (P=0.002); and albumin increased significantly in the controls (P=0.01).

**Table 3** shows that the feeding pattern expressed as energy per kg highly correlated with BMI category for both GVHD and control patients.

**Table 3: Energy Prescription vs. BMI**

BMI (kg/m2)	GVHD		Controls	
	n	Mean ± SD	n	Mean ± SD
< 20	6	47.7 ± 9.0	6	45.6 ± 5.2
20 - 24.9	4	38.2 ± 5.1	4	33.2 ± 3.9
25 - 29.9	8	31.7 ± 2.6	8	29.0 ± 4.7
≥ 30	2	25.4 ± 8.4	2	16.6 ± 7.2
Correlation coefficient (95% CI)*		- 0.88 (- 1.00, - 0.64)		- 0.85 (- 1.00, - 0.58)

\*95% Confidence Interval for the correlation coefficient

## Discussion

- Protein, energy and feeding pattern based on BMI appeared to be clinically appropriate, even though energy requirements and nitrogen balance was not measured.
- The improvement in BMI and visceral and somatic proteins in control patients suggests that the nutrient prescription was adequate in this group.
- The increase in TSF in the GVHD patients, though not statistically significant, suggests that adequate energy was provided to this group. The change in TSF may alternatively reflect an expansion of the extracellular fluid compartment.<sup>5</sup>
- The decline in BMI and somatic proteins, negligible change in visceral proteins, and increase in fat stores suggests that, despite provision of more energy to the GVHD patients, this group of patients is hypermetabolic and hypercatabolic.
- Measurements of MUAMC have been shown to correlate to body cell mass and lean body mass in post-BMT patients, therefore our somatic protein data in the GVHD group can be considered to be reliable.<sup>5</sup>
- Patients with GVHD are often treated with high-dose corticosteroids that can lead to muscle wasting and elevation in resting energy expenditure. These patients are profoundly immunosuppressed from both GVHD and its therapy and most develop ongoing infectious complications, which can contribute to their hypermetabolic and hypercatabolic state.
- While the nutritional status of patients with GVHD of the gut did not improve with HPN, the clinical stability that HPN provides allows these patients to safely receive aggressive GVHD treatment and affords them the opportunity for positive long-term results.

## References

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