L-Arginine Supplemented Immunonutrition and Associated Health Outcomes in Critically Ill Patients

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Background

- L-arginine supplemented immunonutrition (IM) enteral formulas are designed to optimize outcomes in critically ill patients, and routine use is suggested post-operatively in the surgical intensive care unit (ICU).[1]
- Additional research is needed on the healthcare resource utilization (HCRU) between IM enteral formulas in a broad cohort of severely ill hospitalized patients.

Objectives

- The primary objective of this retrospective observational study was to compare health outcomes between IMPACT® Peptide 1.5, a higher L-arginine IM formula (HAF), and Pivot® 1.5 Cal, a lower L-arginine containing IM formula (LAF) in the ICU setting using real-world evidence.

Methods

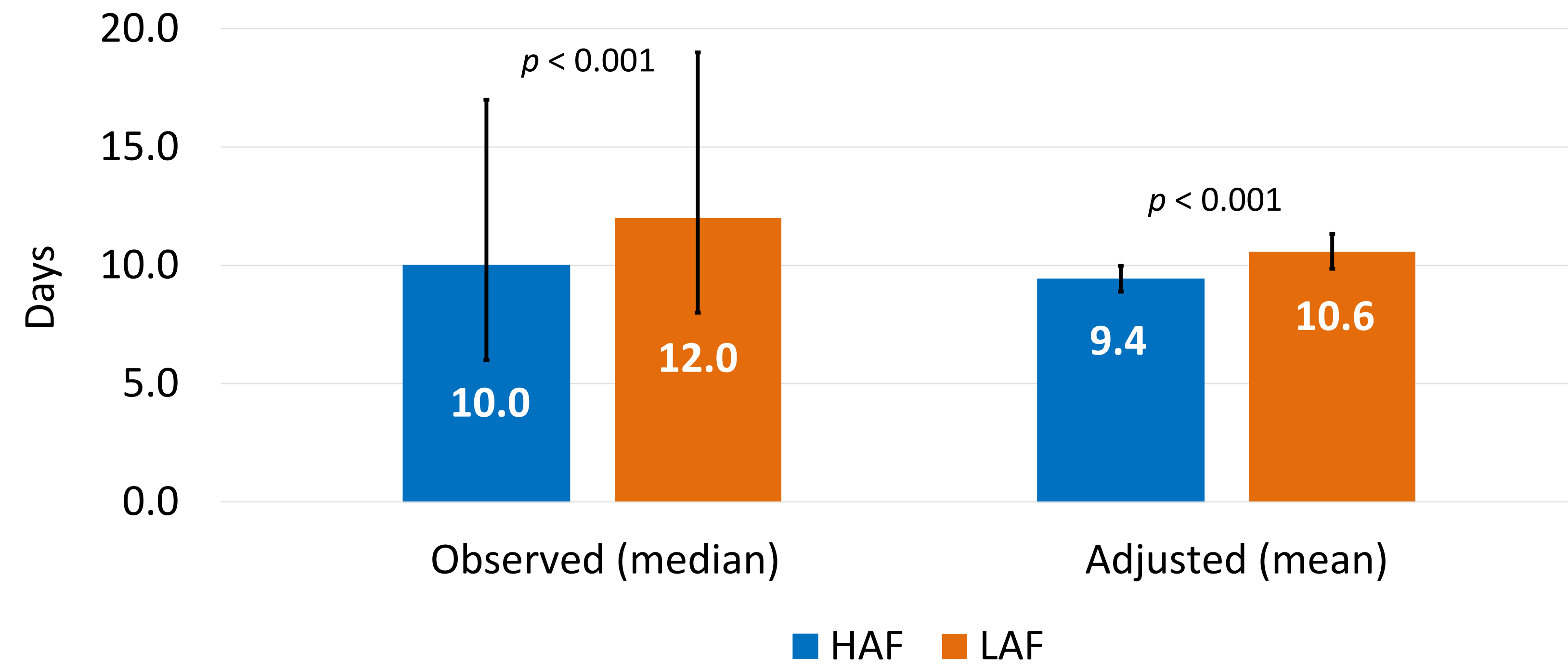- The PINC AI™ Healthcare Database (PHD, formerly known as Premier Healthcare Database) was reviewed from Oct 2015 – Feb 2019 for adult patients with an ICU stay and at least 3 out of 5 days exclusive use of either HAF (18.7 g/L) formula, or LAF (11 g/L) formula.
- Patient demographics, clinical and visit characteristics, comorbidities, severity of illness, and outcomes were examined.
- Multivariable generalized linear model (GLM) regression was used to study associations between formulas and ICU length of stay (LOS), controlling for demographics, hospital and visit characteristics, severity of illness, and comorbid conditions.
- Adjusted ICU LOS was calculated using least square means estimated from the GLM regression.
- All analyses were conducted using SAS version 9.4. An a priori alpha of 0.05 and a value of $p < 0.05$ defined significance.

Enteral formula containing higher L-arginine is associated with reduced ICU length of stay vs. LAF

Figure 1. HCRU Comparisons by IM Formula Group

Error bars are 25th & 75th percentiles for median and 95% confidence intervals for mean
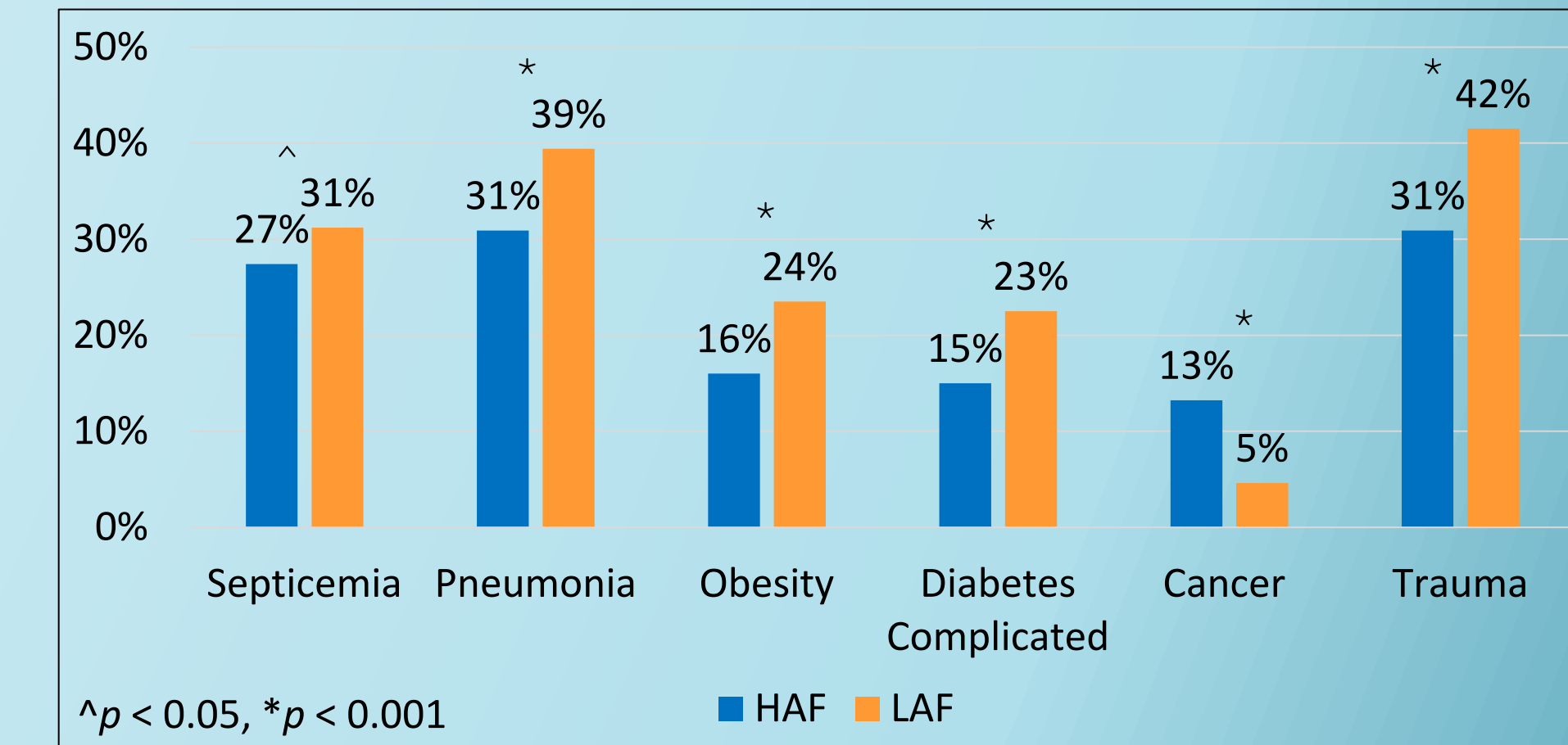
Results

- 3,284 patients (75% surgical; 78% mechanical ventilation) were included from 21 hospitals, with 2,525 receiving HAF and 759 LAF.
- No significant difference in median age (59 y), 3M™ All Patient Refined™ Diagnosis Related Group (APR-DRG) severity of illness (87% severe/extreme) or malnutrition (29%) was observed between groups.
- Both HAF and LAF contained 1500 calories and 94 g protein per liter. Median formula use was 7 days, with more formula billed in the HAF vs LAF group (9L vs 8L; $p = 0.002$).
- Inpatient mortality (19.4%) did not differ between groups, but 30-day all-cause readmission rate was lower in HAF compared to LAF patients (11.6% vs. 15.3%, $p = 0.01$).
- Patients receiving HAF had less rectal catheterization (9% vs. 19%; $p < 0.001$), and groups differed in other clinical characteristics and comorbid diagnoses **(Figure 2)**.
- After adjusting for demographics, visit, severity of illness, and clinical characteristics, associated ICU LOS for patients in the HAF group was 11% shorter [exponentiated coefficient = 0.89 (95% CI: 0.84, 0.94; $p < 0.001$)] compared to patients in the LAF group **(Table 1)**.
- **Adjusted mean ICU LOS was 9.4 days (95% CI: 8.9, 10.0 days) for the HAF group compared to 10.6 days (95% CI: 9.9, 11.3 days) for the LAF group ($p < 0.001$) (Figure 1).**

Table 1. Multivariable Regression Showing Associations with ICU LOS

Variables*	Exponentiated Estimate	95% CI Lower, Upper	p-value
HAF (ref. LAF)	**0.89**	**0.84, 0.94**	**< 0.001**
Wound dehiscence/disruption	1.27	1.14, 1.41	< 0.001
Surgery	1.29	1.22, 1.35	< 0.001
Trauma	0.98	0.93, 1.03	0.4205
ECMO or tracheostomy	1.61	1.54, 1.69	< 0.001
Mechanical ventilation	1.36	1.29, 1.44	< 0.001
Rectal catheterization	1.22	1.15, 1.30	< 0.001
Nutrition liters billed per day	0.97	0.91, 1.02	0.236

Also in model: septicemia, pneumonia, renal failure, malnutrition, antidiarrheal medications, male, nutrition pattern, discharge status, hospital region (each $p < 0.05$, associated with longer ICU LOS); complicated diabetes, cancer, APR-DRG severity of illness severe (vs. mild/moderate), age 65+ (vs. 18-34 y), other race (vs. White), hospital beds ($p < 0.05$, shorter ICU LOS); and congestive heart failure, obesity, APR-DRG severity of illness extreme (vs. mild/moderate) and risk of mortality, admission type, age 35-64 (vs 18-34), Black (vs. White), payer ($p > 0.05$).

Figure 2. Clinical Characteristics and Comorbid Diagnoses by IM Formula Group

^$p < 0.05$, *$p < 0.001$

HAF= higher L-arginine formula; LAF = lower L-arginine formula

Conclusions

- Despite formulas having equivalent calories and protein, HAF use was associated with significantly reduced ICU LOS, compared to LAF.
- The difference observed in ICU LOS was sustained after controlling for a comprehensive list of clinical and visit characteristics as well as comorbidities.
- These results demonstrate the potential role of higher L-arginine supplemented IM in improving health outcomes in critically ill patients.
- Other differences between IM formulas may also contribute to these results and suggest the need for further study in ICU patients.

1. Taylor BE et al. CCM 2016; 44(2): 390-438.

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