



## Temporal Trends in the Use of Parenteral Nutrition in Critically Ill Patients

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**Background:** Clinical practice guidelines recommend enteral over parenteral nutrition in critical illness and do not recommend early initiation. Few data are available on parenteral nutrition use or timing of initiation in the ICU or how this use may have changed over time.

**Methods:** We used the Project IMPACT database to evaluate temporal trends in parenteral nutrition use (total and partial parenteral nutrition and lipid supplementation) and timing of initiation in adult ICU admissions from 2001 to 2008. We used  $\chi^2$  tests and analysis of variance to examine characteristics of patients receiving parenteral nutrition and multilevel multivariate logistic regression models to assess parenteral nutrition use over time, in all patients and in specific subgroups.

**Results:** Of 337,442 patients, 20,913 (6.2%) received parenteral nutrition. Adjusting for patient characteristics, the use of parenteral nutrition decreased modestly over time (adjusted probability, 7.2% in 2001-2002 vs 5.5% in 2007-2008,  $P < .001$ ). Enteral nutrition use increased simultaneously (adjusted probability, 11.5% in 2001-2002 vs 15.3% in 2007-2008,  $P < .001$ ). Use of parenteral nutrition declined most rapidly in emergent surgical patients, patients with moderate illness severity, patients in the surgical ICU, and patients admitted to an academic facility ( $P \leq .01$  for all interactions with year). When used, parenteral nutrition was initiated a median of 2 days (interquartile range, 1-3), after ICU admission and  $> 90\%$  of patients had parenteral nutrition initiated within 7 days; timing of initiation of parenteral nutrition did not change from 2001 to 2008.

**Conclusions:** Use of parenteral nutrition in US ICUs declined from 2001 through 2008 in all patients and in all examined subgroups, with the majority of parenteral nutrition initiated within the first 7 days in ICU; enteral nutrition use coincidentally increased over the same time period.

*CHEST 2014; 145(3):508-517*

**Abbreviations:** MPM<sub>0</sub>-III = mortality probability model III score at ICU admission; PPN = partial parenteral nutrition; TPN = total parenteral nutrition

Critical illness often results in impaired nutritional intake, either due to anorexia or an inability to eat secondary to altered mental status,<sup>1</sup> the need for invasive mechanical ventilation,<sup>2</sup> or disease processes that disrupt normal GI function.<sup>3</sup> Lack of adequate nutrition may lead to nosocomial infections, poor wound healing, and delayed recovery.<sup>4-7</sup> Therefore, guidelines recommend early institution of nutritional support, within 24 to 48 h of presentation, as part of the care of critically ill patients who are unable to eat.<sup>8,9</sup>

Parenteral nutrition is one option to meet these nutritional goals. Use of parenteral nutrition may result in higher caloric intake than enteral nutrition alone<sup>10,11</sup>; but is also associated with mucosal atrophy, overfeeding, hypervolemia, hyperglycemia, and infection.<sup>12</sup> Results of studies investigating the utility of parenteral nutrition in patients who cannot tolerate full

enteral feeds are inconsistent, suggesting, in turn, both benefit and harm.<sup>11,13,14</sup> In reconciling these studies, clinical practice guidelines published over the past decade emphasize that use of enteral nutrition is preferable to parenteral nutrition whenever possible in the critically ill patient with a functional GI tract.<sup>8,9,15</sup> Some experts even suggest abandoning parenteral nutrition in critically ill patients altogether, except in rare circumstances, such as for patients with anatomic abnormalities of the GI tract in whom enteral nutrition is not possible.<sup>16</sup> American guidelines recommend initiation of parenteral nutrition only after 7 days without nourishment in previously healthy patients.<sup>9</sup>

In the context of this debate, information on the actual frequency of use and timing of initiation of parenteral nutrition in the care of critically ill patients is lacking. Therefore, we sought to characterize the

epidemiology of parenteral nutrition use in critically ill patients in the United States using a large, multi-center database. Given increased advocacy in support of early enteral nutrition and increased awareness of the risks of parental nutrition,<sup>17</sup> we hypothesized that the use of parenteral nutrition declined and the time to initiation increased over time.

## MATERIALS AND METHODS

We performed a retrospective cohort study of adult ICU admissions using the Project IMPACT database. Project IMPACT is a voluntary, fee-based ICU registry that, when in operation, provided regular performance audits and feedback to participating ICUs. Data were collected at each institution by on-site data collectors who were certified in advance by Project IMPACT to assure standardization and uniformity in data definitions and entry.<sup>18</sup> We used data from 2001 to 2008, the last full year of data available.

### *Patients and Variables*

For each ICU, data were collected from either consecutive admissions or a random sample of admissions. Sites using the latter method collected information on either 50% or 75% of patients; the percentage was determined quarterly before data collection commenced. We excluded patients < 18 years of age. We also excluded patients admitted to neurologic ICUs, neurosurgical ICUs, or cardiac surgery ICUs, as these units were few and highly specialized, with patient populations that do not generalize to other study ICUs. Only the initial ICU admission for a given hospital stay was included.

For each ICU admission, Project IMPACT collected patient-level data on demographics (age, race, sex), chronic comorbidities from a predefined set of up to 16 conditions, severity of illness on admission as assessed by the mortality probability model at ICU admission (MPM<sub>0</sub>-III),<sup>19</sup> admission diagnosis, admission type (medical, emergent surgical, elective surgical), and location prior to ICU admission (ED, operating room/postanesthesia care unit, general ward, other). Project IMPACT also collected ICU- and hospital-level data including the type of ICU (surgical, including trauma/burn ICUs; medical, including coronary care units; and mixed medical-surgical), ICU structure ("closed model" physician staffing and/or required mandatory critical care consultation for all admissions vs those that did not), hospital teaching status (academic vs nonacademic [community or government run]), and hospital location (urban, suburban, or rural).

Manuscript received July 11, 2013; revision accepted October 17, 2013.

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**Funding/Support:** Financial support for this project was provided by the National Institute on Aging [K08AG038477] to Dr Wunsch.

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**DOI: 10.1378/chest.13-1597**

Project IMPACT contains data on the start and stop dates for each of various categories of supplemental feeding for individual patients. Categories included total parenteral nutrition (TPN), TPN with lipids, partial parenteral nutrition (PPN), PPN with lipids, PPN that was a fat emulsion only, and enteral nutrition. We defined receipt of parenteral nutrition as having received TPN, PPN, lipids, or any combination for at least 1 day during the ICU stay. We considered parental nutrition as intended to be supplemental to enteral feeding when a patient was receiving enteral nutrition on the day of initiation of parenteral nutrition; for patients receiving parental nutrition for > 1 day, it was considered supplemental parenteral nutrition only if enteral feeding was provided on both days 1 and 2 (as patients with only 1 day of overlap may represent a switch from enteral to parenteral nutrition rather than use as supplementation).

### *Analysis*

We described the hospital and ICU characteristics of the cohort using standard summary statistics. To assess trends in parenteral nutrition use over time, we first examined the unadjusted percentage of patients who received parenteral nutrition in 2-year time periods: 2001 to 2002, 2003 to 2004, 2005 to 2006, and 2007 to 2008. Two-year time periods were used to increase group size and power to detect statistically significant differences. We then assessed differences in patient-, ICU-, and hospital-level characteristics of patients receiving parenteral nutrition in each time period, using  $\chi^2$  tests and analysis of variance, as appropriate. To account for possible changes in the case mix of patients over time, we built a multilevel multivariable logistic regression model to determine the adjusted odds of receiving parenteral nutrition over time. We converted the coefficients of these models into predicted probabilities using marginal standardization.<sup>20</sup> All available patient-, ICU-, and hospital-level variables were included in a base model without interaction terms. To understand the degree to which temporal trends in parenteral nutrition were potentially related to trends in enteral nutrition use, we fit a similar multivariable model using receipt of enteral nutrition as the dependent variable.

We then assessed whether trends in parenteral nutrition use over time varied for specific subgroups of interest. The subgroups were selected based on the medical literature to be stratified based on factors that may either impact parenteral nutrition use or cessation in use of ICU therapies.<sup>10,21-23</sup> Patient-level subgroups of interest included patient type (medical, elective surgical, emergent surgical), age (grouped as < 50, 50-64, 65-84,  $\geq$  85 years), severity of illness (MPM<sub>0</sub>-III  $\leq$  5%, 6%-25%, 26%-50%, > 50%), and admission diagnosis (categorized by level of baseline use of < 2%, 2%-15%, or > 15% during the 2001-2002 study period) (Table 1). ICU- and hospital-level subgroups of interest included ICU type (medical, surgical, or combined), ICU structure (closed or mandatory critical care consultation vs possible or no critical care consultation), and academic affiliation of the hospital. For these analyses, we constructed separate multilevel models that included an interaction term between each of the subgroups of interest and admission year to determine whether there was variation by group in changes over time. We assessed statistical significance of the interaction term using the likelihood ratio test.

We defined the timing of parenteral nutrition as the number of days between ICU admission and initiation of the first episode of parenteral nutrition administration. For the patients who received parenteral nutrition, we used Kaplan-Meier analysis and the log-rank test for equality to compare changes in length of time until initiation of parental nutrition over time. We then assessed whether trends in timing of initiation of parenteral nutrition varied over time for the whole cohort and the subgroups (both patient level and ICU/hospital level) using Cox proportional-hazard regression with interaction terms; shared frailty was used to allow for

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