Caring for the Critically Ill Patient

Total Parenteral Nutrition in the Critically Ill Patient

A Meta-analysis

Daren K. Heyland, MD, FRCPC, MSc; Shaun MacDonald MD, FRCSC; Laurie Keefe, RD; John W. Drover, MD, FRCSC

Context.—Nutritional support has become a standard of care for hospitalized patients, but whether total parenteral nutrition (TPN) affects morbidity and mortality is unclear.

Objective.—To examine the relationship between TPN and complication and mortality rates in critically ill patients.

Data Sources.—Computerized search of published research on MEDLINE from 1980 to 1998, personal files, and review of relevant reference lists.

Study Selection.—We reviewed 210 titles, abstracts, and papers. Primary studies were included if they were randomized clinical trials of critically ill or surgical patients that evaluated the effect of TPN (compared with standard care) on complication and mortality rates. We excluded studies comparing TPN with enteral nutrition.

Data Extraction.—Relevant data were abstracted on the methodology and outcomes of primary studies. Data were abstracted in duplicate, independently.

Data Synthesis.—There were 26 randomized trials of 2211 patients comparing the use of TPN with standard care (usual oral diet plus intravenous dextrose) in surgical and critically ill patients. When the results of these trials were aggregated, TPN had no effect on mortality (risk ratio [RR], 1.03; 95% confidence interval [CI], 0.81-1.31). Patients who received TPN tended to have a lower complication rate, but this result was not statistically significant (RR, 0.84; 95% CI, 0.64-1.09). We examined several a priori hypotheses and found that studies including only malnourished patients were associated with lower complication rates but no difference in mortality when compared with studies of nonmalnourished patients. Studies published since 1989 and studies with a higher methods score showed no treatment effect, while studies published in 1988 or before and studies with a lower methods score demonstrated a significant treatment effect. Complication rates were lower in studies that did not use lipids; however, there was no difference in mortality rates between studies that did not use lipids and those studies that did. Studies limited to critically ill patients demonstrated a significant increase in complication and mortality rates compared with studies of surgical patients.

Conclusions.—Total parenteral nutrition does not influence the overall mortality rate of surgical or critically ill patients. It may reduce the complication rate, especially in malnourished patients, but study results are influenced by patient population, use of lipids, methodological quality, and year of publication.

METHODS

Search Strategy

We conducted a computerized bibliographic search of MEDLINE (including pre-MEDLINE) for studies from 1980 to April 1998 to locate all relevant articles. The terms randomized controlled
trial, double blind method, clinical trial, placebo, and comparative study were combined with explode parenteral nutrition, total. Citations were limited to English-language studies reporting on adult patients. Reference lists of relevant review articles and personal files were also searched.

Study Selection Criteria

Initially, 2 of us (D.K.H. and S.M.) screened all citations and classified them as primary studies, review articles, or other. We then retrieved and reviewed independently all primary studies. Primary studies were selected for inclusion in this overview if the study’s (1) research design was a randomized clinical trial; (2) population consisted of surgical or critically ill human adult subjects; (3) intervention included any form of TPN (protein, source of nonprotein energy with or without lipids) compared with standard care (oral diet plus intravenous fluids); and (4) outcome measures included complications, length of stay, and mortality.

Because studies in which treatment is allocated in any method other than randomization tend to show larger (and frequently false-positive) treatment effects than do randomized trials, we elected to include only randomized trials in this review. We defined critically ill patients as those who would routinely be cared for in a critical care environment. Patients undergoing major surgery may not always be cared for in a critical care environment but share similarities in their response to illness, a hypercatabolic state characterized by weight loss, loss of body fat, and accelerated breakdown of body proteins. Previous systematic reviews have incorporated data from surgical patients and critically ill patients. Therefore, we opted to combine studies of surgical patients and critically ill patients and to explore any differences that might exist between these patients in the subgroup analysis. We excluded studies of pediatric or neonatal patients.

We included only studies that evaluated the use of supplemental TPN in patients receiving enteral feeds or studies evaluating the use of TPN in patients who were not receiving TPN or enteral nutrition. There are several randomized trials of surgical patients that examine the effect of amino acid infusion (without additional nonprotein energy or lipids) on clinical outcomes. Such therapy is not a standard of care in the critically ill patient, whereas TPN (with or without lipids) is commonly administered to critically ill patients. For the purpose of this review, we excluded studies that used only amino acid infusions as the intervention. As the scope of our review was defined by our research question, we also excluded studies that compared TPN with enteral nutrition or other forms of TPN. Finally, studies that evaluated the impact of TPN only on nutritional outcomes (ie, nitrogen balance, amino acid profile) were not included in this article. While these end points may explain underlying pathophysiology, we considered these as surrogate end points and we only included articles that reported on clinically important outcomes (morbidity and mortality).

Methodologic Quality of Primary Studies

We assessed the methodologic quality of all selected articles in duplicate, independently, using a scoring system that we have used previously (Table 1). Even in randomized trials, failure to prevent foreknowledge of treatment assignment can lead to an overestimation of treatment effect. According to the Cochrane Collaboration, we scored higher those studies that reported that their randomization schema was concealed. Given the difficulties of blinding the administration of TPN, we only awarded points for studies that blinded the adjudication of study end points. We also evaluated the extent to which consecutive, eligible patients were enrolled in the trial, whether groups were equal at baseline, if interventions were adequately described, whether objective definitions of infectious outcomes were used, and whether all patients were properly accounted for in the analysis (intention-to-treat analysis) (Table 1).

Data Extraction

Two of us (D.K.H. and S.M.) extracted data for analysis and assessment of the methodologic quality; we resolved disagreement by consensus. Not all studies reported complication rates. Some studies reported total complications per group but not on a per-patient basis. When data were missing, unclear, or not reported on a per-patient basis, we attempted to contact the primary investigators and requested them to provide further information if the article had been published in the last 5 years.

Prior Hypotheses Regarding Sources of Heterogeneity

When conducting a systematic review, heterogeneity (major differences in the apparent effect of the interventions across studies) is often found. When heterogeneity is present, it weakens inferences that can be made from the results. The possible sources of variation in study results include the role of chance or differences across studies in population, intervention, outcome, and methods. We developed several hypotheses that might explain heterogeneity of study results.

First, we considered that the premorbid nutritional status of study patients was a possible cause of variation in results. Where possible, we grouped the results of studies that included only patients who were malnourished and compared them with the results of studies that included patients who were not malnourished at entrance into the study. When possible, we used the definition of malnourished provided in each study. If none was provided, we assumed patients who had greater than 10% weight loss to be malnourished.

Second, we hypothesized that study results may be related to the methodologic quality of the study. We planned a separate analysis comparing the effect of studies with an overall methodologic quality score to those with a score less than 7 (median score, 7).

Third, since the practice of providing nutritional support and managing critically ill patients has evolved over time...
(included studies range from 1976 to 1997), we divided the studies into equal groups comparing studies published in 1998 or earlier with studies published since 1989 (halfway point of the study range).

Fourth, since some studies administered amino acids and a carbohydrate source of energy while others administered amino acids, carbohydrates, and lipids, we separated trials into those that included lipids and those without. We hypothesized that there may be adverse effects caused by lipid use.25

Finally, we speculated that differences in patient populations (surgical vs critically ill) may account for different results. To test this hypothesis, we planned a separate analysis comparing studies of surgical patients with studies of critically ill patients.

Analysis

The primary outcome was perioperative mortality (death within 30 days of operation) or mortality reported at discharge from hospital. The secondary outcome was the rate of major complications. We defined major complications as wound infection, phlebitis, urinary tract infection, pulmonary emboli, heart failure, stroke, rectal failure, liver failure, and anastomotic leak. Minor complications were defined as wound infection, phlebitis, urinary tract infection, and atelectasis. In 4 studies, the data were not portrayed in a fashion that allowed us to report major complication rates, so we reported total complication rates27-29 and total infectious complications.30 Reporting methods of individual studies did not allow us to disaggregate infectious from noninfectious complications. One study28 randomized patients to 3 groups (control vs standard TPN vs TPN with branch-chain amino acids). We only included data from the control group and the standard TPN group. Two other studies randomized patients to 3 groups (control vs TPN without lipids vs TPN with lipids), and we included both experimental groups in the analysis.32-34 One study included reports of 2 trials.34 The second trial was presumed to include patients from the first trial and was therefore excluded. We also reported on duration of hospital stay, although these data were not aggregated because of infrequent and variable reporting methods.

Agreement between reviewers on inclusion of articles was identified through a computerized bibliographic database search. Our personal files and review of reference lists yielded 57 additional articles for consideration. Initial eligibility screening resulted in 46 articles selected for further evaluation. Of these potentially eligible studies, 26 met the inclusion criteria.

We reached 100% agreement on the inclusion of articles for this systematic review. Reasons for excluding relevant randomized studies included studies not generalizable to critically ill patients49, studies that evaluated different kinds of TPN41-43, studies that evaluated amino acids only44-47, pseudorandomized studies (true randomization)48-52, studies duplicated in other publications44,45,54, studies not reporting clinically important outcomes55-57, studies available in abstract form only56, and a study that also randomized patients to anabolic steroids.50

Impact of TPN on Mortality and Complications Rates

There were 26 randomized trials involving 2211 patients that compare the use of TPN with standard care (usual oral diet plus intravenous fluids) in patients undergoing surgery.27-34,55-57 Patients with pancreatitis,56 patients in an intensive care unit,57 and patients with severe burns57 the details of each study, including the methodologic quality score, are described in Table 2. When the results of these trials were aggregated, there was no effect on mortality (RR, 1.03; 95% CI, 0.81-1.31) (Figure 1). The test for heterogeneity was not significant (P = .59), although a visual inspection of Figure 1 suggests that the treatment effects are variable.

Twenty-two studies reported major complications in study patients. Aggregation of these results revealed a trend toward reducing complication rates in patients receiving TPN (RR, 0.84; 95% CI, 0.64-1.09) (Figure 2). The test for heterogeneity was significant (P = .003).

To better understand our findings, we proceeded to examine our a priori hypotheses. We compared trials that included only malnourished patients with other trials. No difference in mortality existed (Figure 3) for studies of malnourished patients (RR, 1.13; 95% CI, 0.75-1.71) or in studies that included adequately nourished patients (RR, 1.00; 95% CI, 0.71-1.39; P = .64 for differences between subgroups). The rate of major complications was significantly lower among malnourished patients receiving TPN (RR, 0.52; 95% CI, 0.30-0.91). No difference existed in complication rates among studies of adequately nourished patients (RR, 1.02; 95% CI, 0.75-1.40). The difference in complication rates between these subgroups was of borderline significance (P = .05).

We compared trials with a methodologic quality score of less than 7 with trials with a score of 7 or better (Figure 3). Trials with the higher methods score demonstrated no effect of TPN on mortality (RR, 1.17; 95% CI, 0.88-1.56). We noted a trend toward a lower mortality rate in studies with a lower methods score (RR, 0.76; 95% CI, 0.49-1.19). The difference between these 2 subgroups was short of conventional levels of significance (P = .12). With respect to complication rates, studies with a higher methods score demonstrated no treatment effect (RR, 1.13; 95% CI, 0.89-1.50). Studies with a lower methods score showed a significant reduction in complication rates associated with TPN (RR, 0.54; 95% CI, 0.33-0.87). The difference in complication rates between these subgroups was significant (P = .02).

We next compared trials published in 1988 or earlier with trials published in 1989 or later (Figure 3). Trials published in 1988 or earlier demonstrated a trend toward a lower mortality rate associated with TPN (RR, 0.70; 95% CI, 0.44-1.13). Trials published since 1989 demonstrated no treatment effect (RR, 1.18; 95% CI, 0.89-1.57). Differences between these 2 subgroups were short of conventional levels of statistical significance (P = .07). There were significantly fewer major complications associated with TPN reported in studies that were published in 1988 or earlier (RR, 0.49; 95% CI, 0.29-0.81), while in studies published since 1989 there was no effect of TPN on complication rates (RR, 1.19; 95% CI, 0.93-1.53). The P value for the difference between these subgroups was significant (P = .005).

We then compared studies that provided intravenous lipids as a component of TPN administration with studies that did not include lipids. In studies that used lipids (RR, 1.03; 95% CI, 0.78-1.36) and studies that did not (RR, 0.98; 95% CI, 0.69-1.29).
Table 2.—Randomized Studies Evaluating Total Parenteral Nutrition (TPN) in Critically Ill Patients

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Methods Score</th>
<th>Patient Population (No.)</th>
<th>% of Malnourished Patients</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterans Affairs, 2016</td>
<td>10</td>
<td>Thoracoabdominal surgery (395)</td>
<td>100</td>
<td>TPN with lipids 14 d before surgery</td>
</tr>
<tr>
<td>Fan et al, 1989</td>
<td>10</td>
<td>Esophageal cancer surgery (40)</td>
<td>75</td>
<td>TPN with lipids 7-15 d before surgery</td>
</tr>
<tr>
<td>Figueras et al, 1988</td>
<td>7</td>
<td>Gastrointestinal surgery (49)</td>
<td>0</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Sandstrom et al, 1993</td>
<td>10</td>
<td>Major surgery/trauma (300)</td>
<td>22</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Reilly et al, 1990</td>
<td>7</td>
<td>Liver Transplant (16)</td>
<td>100</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Hwang et al, 1993</td>
<td>5</td>
<td>Gastric surgery (42)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Hwang et al, 1993</td>
<td>5</td>
<td>Gastric surgery (42)</td>
<td>...</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Moller et al, 1982</td>
<td>3</td>
<td>Gastrointestinal surgery (125)</td>
<td>60</td>
<td>TPN without lipids 10 d before surgery</td>
</tr>
<tr>
<td>Moller et al, 1986</td>
<td>4</td>
<td>Gastrointestinal surgery (105)</td>
<td>...</td>
<td>TPN with lipids 10 d before surgery</td>
</tr>
<tr>
<td>Jimenez et al, 1996</td>
<td>5</td>
<td>Gastrointestinal surgery (75)</td>
<td>100</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Brennan et al, 1994</td>
<td>8</td>
<td>Pancreatic resection (117)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Askanazi et al, 1994</td>
<td>3</td>
<td>Radical cystectomy (35)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Thompson et al, 1981</td>
<td>4</td>
<td>Gastrointestinal surgery (21)</td>
<td>100</td>
<td>TPN without lipids 5 d before surgery</td>
</tr>
<tr>
<td>Fan et al, 1994</td>
<td>7</td>
<td>Hepatocellular cancer surgery (124)</td>
<td>26</td>
<td>TPN with lipids 7 d before surgery</td>
</tr>
<tr>
<td>Abel et al, 1996</td>
<td>4</td>
<td>Cardiac surgery (44)</td>
<td>100</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Bellatone et al, 1988</td>
<td>6</td>
<td>Gastrointestinal surgery (100)</td>
<td>100</td>
<td>TPN with lipids 7 d before surgery</td>
</tr>
<tr>
<td>Smith and Hartemink, 1988</td>
<td>7</td>
<td>Gastrointestinal surgery (34)</td>
<td>100</td>
<td>TPN without lipids 10 d before surgery</td>
</tr>
<tr>
<td>Holter and Fischer, 1977</td>
<td>5</td>
<td>Gastrointestinal surgery (56)</td>
<td>100</td>
<td>TPN without lipids 3 d before surgery</td>
</tr>
<tr>
<td>Meguid et al, 1988</td>
<td>4</td>
<td>Gastrointestinal surgery (64)</td>
<td>100</td>
<td>TPN with lipids 9 d before surgery</td>
</tr>
<tr>
<td>Woolfson and Smith, 1989</td>
<td>10</td>
<td>Thoracoabdominal surgery (122)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Von Meyenfeldt et al, 1992</td>
<td>7</td>
<td>Gastrointestinal surgery (101)</td>
<td>29</td>
<td>TPN with lipids 10 d before surgery</td>
</tr>
<tr>
<td>Yamada et al, 1983</td>
<td>3</td>
<td>Gastric surgery (62)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Gys et al, 1990</td>
<td>7</td>
<td>Colorectal surgery (20)</td>
<td>0</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Freund et al, 1979</td>
<td>8</td>
<td>Gastrointestinal surgery (35)</td>
<td>0</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Sax et al, 1987</td>
<td>8</td>
<td>Pancreatitis (54)</td>
<td>...</td>
<td>TPN with lipids after admission</td>
</tr>
<tr>
<td>Chiarelli et al, 1996</td>
<td>6</td>
<td>Neurology ICU (24)</td>
<td>...</td>
<td>TPN after admission; both groups received EN (unknown lipids)</td>
</tr>
<tr>
<td>Hendon et al, 1989</td>
<td>7</td>
<td>Burns on &gt;50% of body (49)</td>
<td>100</td>
<td>TPN without lipids after admission; both groups received EN</td>
</tr>
</tbody>
</table>

*Ellipses indicate data not available; EN, enteral nutrition; ICU, intensive care unit.
†Presented as mean ± SD or (range).
‡No range was specified.
§Control group is the same for both criteria.

CI, (0.49-1.55), there was no difference in mortality. (P value for the difference between subgroups = .89). Complication rates in studies that used lipids demonstrated no effect (RR, 0.96; 95% CI, 0.69-1.34). In studies that did not use lipids, the complication rate was significantly lower (RR, 0.59; 95% CI, 0.38-0.90). The P value for the difference between these subgroups was just short of significance (P = .09).

Finally, we compared studies of critically ill patients with studies of primarily surgical patients. The mortality rate of critically ill patients was higher among those receiving TPN (RR, 1.78; 95% CI, 1.11-2.85), while studies of surgical patients showed no treatment effect (RR, 0.91; 95% CI, 0.68-1.21). The difference between these subgroups was statistically significant (P = .001). The complication rates in the studies of critically ill patients (only 2 studies reported complication rates) showed a trend toward an increase in complications (RR, 2.40; 95% CI, 0.88-6.58), while studies of surgical patients were associated with lower complication rates (RR, 0.76; 95% CI, 0.48-1.10). The P value for the difference between these subgroups was significant (P = .05).

Only 14 studies reported the effect of TPN on duration of hospital stay; 5 reported median stay and 9 reported means. In 8 studies, the duration of stay was shorter in the control group. Due to the variability in duration of stay and variability of reporting methods, we did not statistically aggregate these results, but they are displayed in Table 2.
### Table 1: Mortality, No. (%)

<table>
<thead>
<tr>
<th>Major Complications, No. (%)</th>
<th>Mortality, No. (%)</th>
<th>Mean Hospital Stay, d†</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPN Control</td>
<td>TPN Control</td>
<td>TPN Control</td>
</tr>
<tr>
<td>49/192 (25.5)</td>
<td>50/203 (24.6)</td>
<td>31/231 (13.4)</td>
</tr>
<tr>
<td>17/20 (85.0)</td>
<td>15/20 (75)</td>
<td>6/20 (30)</td>
</tr>
<tr>
<td>4/25 (16)</td>
<td>5/24 (20.8)</td>
<td>0/25 (0)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>12/150 (8)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td>0/12 (0)</td>
<td>0/16 (0)</td>
<td>0/12 (0)</td>
</tr>
<tr>
<td>0/14 (0)</td>
<td>0/16 (0)</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>11/66 (16.6)</td>
<td>19/59 (32.2)</td>
<td>3/66 (4.5)</td>
</tr>
<tr>
<td>17/46 (37)</td>
<td>19/59 (32.2)</td>
<td>10/46 (21.7)</td>
</tr>
<tr>
<td>6/60 (10)</td>
<td>3/15 (20)</td>
<td>4/60 (6.7)</td>
</tr>
<tr>
<td>27/60 (45)</td>
<td>13/57 (22.8)</td>
<td>4/60 (6.7)</td>
</tr>
<tr>
<td>1/22 (4.5)</td>
<td>2/13 (15.4)</td>
<td>0/22 (0)</td>
</tr>
<tr>
<td>2/12 (16.7)</td>
<td>1/9 (11.1)</td>
<td>0/12 (0)</td>
</tr>
<tr>
<td>22/64 (34.4)</td>
<td>33/60 (55)</td>
<td>5/64 (7.8)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>8/54 (14.8)</td>
<td>22/46 (47.8)</td>
<td>1/54 (1.9)</td>
</tr>
<tr>
<td>3/17 (17.6)</td>
<td>6/17 (35.3)</td>
<td>1/17 (5.9)</td>
</tr>
<tr>
<td>4/30 (13.3)</td>
<td>5/26 (19.2)</td>
<td>2/30 (6.7)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>1/32 (3.1)</td>
</tr>
<tr>
<td>0/29 (0)</td>
<td>5/28 (17.9)</td>
<td>0/29 (0)</td>
</tr>
<tr>
<td>0/10 (0)</td>
<td>1/10 (10)</td>
<td>0/10 (0)</td>
</tr>
<tr>
<td>0/25 (0)</td>
<td>0/10 (0)</td>
<td>0/25 (0)</td>
</tr>
<tr>
<td>4/29 (13.8)</td>
<td>1/29 (3.4)</td>
<td>1/29 (3.4)</td>
</tr>
<tr>
<td>6/12 (50)</td>
<td>3/12 (25)</td>
<td>3/12 (25)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>10/16 (62.5)</td>
</tr>
</tbody>
</table>

**Figure 3:** Results of subgroup analysis examining the effect on total parenteral nutrition (TPN) on mortality and complication rates.

### Comment

In the last 2 decades, 26 randomized trials have examined the effect of TPN on the morbidity and mortality of hospitalized patients. These studies ranged in size from 18 to 395 patients with the majority of studies including fewer than 100 patients. The mortality event rate in these studies ranged from 0% to 41% with an overall average mortality rate of 8.9%. Individually, the majority of these studies were underpowered to demonstrate a significant effect of TPN on major complications or mortality. The advantage of a meta-analysis is that it provides a method of aggregating similar studies to determine the best estimate of the treatment effect.

For this meta-analysis, we defined a specific research question, conducted a comprehensive literature search, and used explicit criteria for study selection and methodologic quality assessment. The results of our meta-analysis suggest that the adverse effects of lipids may negate any beneficial effect of nonlipid nutritional supplementation. This is consistent with the findings of a recent randomized trial of TPN with lipids compared with TPN without lipids in critically ill trauma patients that demonstrated a lower complication rate in the group that did not receive lipids.

While we set out to summarize the experimental evidence of the effect of TPN on critically ill patients, only 6 studies included patients that would routinely be admitted to the ICU as part of their care. Two of these trials evaluated the use of supplemental TPN in patients already receiving enteral nutrition, while the other 4 trials studied the use of TPN compared with patients not receiving any nutritional support. These 6 trials studied very narrowly defined ICU patient populations; there were no studies of medical ICU patients or patients with sepsis and only a limited assessment of patients with trauma. Since surgical patients and ICU patients have a similar stress response to illness, we assumed it reasonable to aggregate such studies. However, the results of our subgroup analysis suggest that both mortality and complication rates may be increased in critically ill patients.
patients receiving TPN and these treatment
effects may differ from the results in surgical patients. The results of studies
evaluating the effect of TPN in surgical patients, therefore, may not be gen-
eralizable to all types of critically ill pa-
tients. This leaves a very limited data set on which to base the practice of pro-
tviding TPN to critically ill patients.

Because some evidence shows that en-
teral nutrition is superior to TPN, en-
teral nutrition may be the preferred method of nutritional support for criti-
cally ill patients. This leaves a very limited data set on which to base the practice of pro-
tviding TPN to critically ill patients. This leaves a very limited data set on which to base the practice of pro-
tviding TPN to critically ill patients. This leaves a very limited data set on which to base the practice of pro-
tviding TPN to critically ill patients.


3. Levine GM, Deren DJ, Steiger E, Zinn R. Role of oral intake in maintenance of gut mass and disac-

4. Schroeder D, Gillanders L, Mahr K, Hill GL. Effects of immediate postoperative enteral nutri-

5. Hadfield RJ, Sinclair DG, Houlden PF, Evans TW, Evans AS. Early enteral versus parenteral nutri-

6. Moore FA, Moore EE, Jones TN, McCroskey CE, Petersen TM, TEN versus TPN following ma-

7. Moore FA, Feliciano DV, Andressy RJ, et al. Early enteral feeding compared with parenteral nutri-
tion reduces septic complications: the results of a meta-

8. Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding: effects on septic morbid-

9. Heyland DK, Cook DJ, Guyatt GH. Enteral nutri-

10. Bias in treatment assignment in controlled clinical

11. Bias in treatment assignment in controlled clinical

12. Bias in treatment assignment in controlled clinical

13. Bias in treatment assignment in controlled clinical

14. Bias in treatment assignment in controlled clinical

15. Bias in treatment assignment in controlled clinical

16. Bias in treatment assignment in controlled clinical

17. Bias in treatment assignment in controlled clinical

18. Bias in treatment assignment in controlled clinical

19. Bias in treatment assignment in controlled clinical

20. Bias in treatment assignment in controlled clinical

21. Bias in treatment assignment in controlled clinical

22. Bias in treatment assignment in controlled clinical

23. Bias in treatment assignment in controlled clinical

24. Bias in treatment assignment in controlled clinical

25. Bias in treatment assignment in controlled clinical

26. Bias in treatment assignment in controlled clinical

27. Bias in treatment assignment in controlled clinical

28. Bias in treatment assignment in controlled clinical

29. Bias in treatment assignment in controlled clinical

30. Bias in treatment assignment in controlled clinical

31. Bias in treatment assignment in controlled clinical

32. Bias in treatment assignment in controlled clinical

33. Bias in treatment assignment in controlled clinical

34. Bias in treatment assignment in controlled clinical

35. Bias in treatment assignment in controlled clinical

36. Bias in treatment assignment in controlled clinical

37. Bias in treatment assignment in controlled clinical

38. Bias in treatment assignment in controlled clinical

39. Bias in treatment assignment in controlled clinical

40. Bias in treatment assignment in controlled clinical

41. Bias in treatment assignment in controlled clinical

42. Bias in treatment assignment in controlled clinical

43. Bias in treatment assignment in controlled clinical

44. Bias in treatment assignment in controlled clinical

45. Bias in treatment assignment in controlled clinical

46. Bias in treatment assignment in controlled clinical

47. Bias in treatment assignment in controlled clinical

48. Bias in treatment assignment in controlled clinical

49. Bias in treatment assignment in controlled clinical

50. Bias in treatment assignment in controlled clinical

51. Bias in treatment assignment in controlled clinical

52. Bias in treatment assignment in controlled clinical

53. Bias in treatment assignment in controlled clinical

54. Bias in treatment assignment in controlled clinical

55. Bias in treatment assignment in controlled clinical

56. Bias in treatment assignment in controlled clinical

57. Bias in treatment assignment in controlled clinical

58. Bias in treatment assignment in controlled clinical

59. Bias in treatment assignment in controlled clinical

60. Bias in treatment assignment in controlled clinical

We would like to thank the anonymous reviewers for their helpful comments and Xiangyao Su, PhD, for his help with the statistical analysis.

References

1. Warna I, Lundholm K. Clinical significance of pro-

2. Demouey DT, Muller JL, Dubay GP. The link between

3. Demouey DT, Muller JL, Dubay GP. The link between

4. Demouey DT, Muller JL, Dubay GP. The link between

5. Demouey DT, Muller JL, Dubay GP. The link between

6. Demouey DT, Muller JL, Dubay GP. The link between

7. Demouey DT, Muller JL, Dubay GP. The link between

8. Demouey DT, Muller JL, Dubay GP. The link between

9. Demouey DT, Muller JL, Dubay GP. The link between

10. Demouey DT, Muller JL, Dubay GP. The link between

11. Demouey DT, Muller JL, Dubay GP. The link between

12. Demouey DT, Muller JL, Dubay GP. The link between

13. Demouey DT, Muller JL, Dubay GP. The link between

14. Demouey DT, Muller JL, Dubay GP. The link between

15. Demouey DT, Muller JL, Dubay GP. The link between

16. Demouey DT, Muller JL, Dubay GP. The link between

17. Demouey DT, Muller JL, Dubay GP. The link between

18. Demouey DT, Muller JL, Dubay GP. The link between

19. Demouey DT, Muller JL, Dubay GP. The link between

20. Demouey DT, Muller JL, Dubay GP. The link between

21. Demouey DT, Muller JL, Dubay GP. The link between

22. Demouey DT, Muller JL, Dubay GP. The link between

23. Demouey DT, Muller JL, Dubay GP. The link between

24. Demouey DT, Muller JL, Dubay GP. The link between

25. Demouey DT, Muller JL, Dubay GP. The link between

26. Demouey DT, Muller JL, Dubay GP. The link between

27. Demouey DT, Muller JL, Dubay GP. The link between

28. Demouey DT, Muller JL, Dubay GP. The link between

29. Demouey DT, Muller JL, Dubay GP. The link between

30. Demouey DT, Muller JL, Dubay GP. The link between

31. Demouey DT, Muller JL, Dubay GP. The link between

32. Demouey DT, Muller JL, Dubay GP. The link between

33. Demouey DT, Muller JL, Dubay GP. The link between

34. Demouey DT, Muller JL, Dubay GP. The link between

35. Demouey DT, Muller JL, Dubay GP. The link between

36. Demouey DT, Muller JL, Dubay GP. The link between

37. Demouey DT, Muller JL, Dubay GP. The link between

38. Demouey DT, Muller JL, Dubay GP. The link between

39. Demouey DT, Muller JL, Dubay GP. The link between

40. Demouey DT, Muller JL, Dubay GP. The link between

41. Demouey DT, Muller JL, Dubay GP. The link between

42. Demouey DT, Muller JL, Dubay GP. The link between

43. Demouey DT, Muller JL, Dubay GP. The link between

44. Demouey DT, Muller JL, Dubay GP. The link between

45. Demouey DT, Muller JL, Dubay GP. The link between

46. Demouey DT, Muller JL, Dubay GP. The link between

47. Demouey DT, Muller JL, Dubay GP. The link between

48. Demouey DT, Muller JL, Dubay GP. The link between

49. Demouey DT, Muller JL, Dubay GP. The link between

50. Demouey DT, Muller JL, Dubay GP. The link between

51. Demouey DT, Muller JL, Dubay GP. The link between

52. Demouey DT, Muller JL, Dubay GP. The link between

53. Demouey DT, Muller JL, Dubay GP. The link between

54. Demouey DT, Muller JL, Dubay GP. The link between

55. Demouey DT, Muller JL, Dubay GP. The link between

56. Demouey DT, Muller JL, Dubay GP. The link between

57. Demouey DT, Muller JL, Dubay GP. The link between

58. Demouey DT, Muller JL, Dubay GP. The link between

59. Demouey DT, Muller JL, Dubay GP. The link between

60. Demouey DT, Muller JL, Dubay GP. The link between

©1998 American Medical Association. All rights reserved.


