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,20 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.21 Previous systematic reviews have incorporated data from surgical patients and critically ill patients.15,22 Therefore, we opted to combine studies of surgical patients and critically ill patients 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 previously24 (Table 1). Even in randomized trials, failure to prevent foreknowledge of treatment assignment can lead to an overestimation of treatment effect.25 Accordingly, 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 1988 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 pneumonia, intra-abdominal abscess, sepsis, line sepsis, myocardial infarction, pulmonary emboli, heart failure, stroke, renal 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 rates and total infectious complications.30 Reporting methods of individual studies did not allow us to disaggregate infectious from noninfectious complications. One study31 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 measured by κ with quadratic weights. We combined data from all studies to estimate the common relative risk of mortality and complications and associated 95% confidence intervals (CIs). We summarized the treatment effect using risk ratios (RRs). To avoid the problem with bias and instability associated with RR estimation in sparse data, we added one half to each cell.25 In the meta-analysis, we used maximum likelihood methods of combining RR across all trials and examined the data for evidence of heterogeneity within groups.26 The Mantel-Haenszel27 method was used to test the significance of treatment effect. We used a random effects model to estimate the overall RR.26-28 For the test of heterogeneity across subgroups, we used the t test for the difference between the 2 subgroups. We considered P < .05 to be statistically significant.

RESULTS

Study Identification and Selection

A total of 153 citations were 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 patients98, studies that evaluated different kinds of TPN44-45, studies that evaluated amino acids only44-47, pseudorandomized studies (true randomization)99-102, studies duplicated in other publications94,95,96, studies not reporting clinically important outcomes103-105, studies available in abstract form only106, and a study that also randomized patients to anabolic steroids.30

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.27-30,107-115 Patients with pancreatitis,76 patients in an intensive care unit,76 and patients with severe burns,77 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, 0.88-1.50). 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 1988 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%
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, 1991</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, 1993a</td>
<td>5</td>
<td>Gastric surgery (42)</td>
<td>...</td>
<td>TPN with lipids after surgery</td>
</tr>
<tr>
<td>Hwang et al, 1993b</td>
<td>5</td>
<td>Gastric surgery (42)</td>
<td>...</td>
<td>TPN without lipids after surgery</td>
</tr>
<tr>
<td>Muller 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>Muller 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, 1986</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, 1986</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, 1976</td>
<td>4</td>
<td>Cardiac surgery (44)</td>
<td>...</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>...</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, 1986</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 10 d before surgery</td>
</tr>
<tr>
<td>Von Meyenfeldt et al, 1992</td>
<td>7</td>
<td>Gastrointestinal surgery (101)</td>
<td>29</td>
<td>TPN without 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>Hordon et al, 1989</td>
<td>7</td>
<td>Burns on &gt;50% of body (49)</td>
<td>...</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 = .08). 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, 0.48-1.0). 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.
trials have examined the effect of TPN on mortality and complication rates. The similarity of the subgroup results based on year of publication and methods score may be partially explained by the fact that 9 of the 13 studies that had a methods score of less than 7 also were published in 1988 or earlier. The differences between these subgroups (methods score <7 and ≥7 and published in 1988 or earlier) was significant or close to conventional levels of significance, suggesting that these subgroup results are systematically different from each other and, therefore, may explain a portion of the heterogeneity in the overall results. Indeed, if the results of studies published in 1989 or later with a methods score of more than 7 are considered the best estimate of treatment effect, TPN may do more harm than good in seriously ill patients.

There are several reports that demonstrate that lipids may adversely affect immune status and clinical outcomes.\(^{7,18}\) 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.\(^{81}\)

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.\(^{39,41,65,75-77}\) Two of these trials\(^{39,75}\) evaluated the use of supplemental TPN in patients already receiving enteral nutrition, while the other 4 trials\(^{39,41,65,75}\) 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.

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.\(^{29,70}\) In the overall analysis, we found no effect of supplemental TPN on mortality, and we found a trend toward lower complication rates associated with TPN. However, the degree of heterogeneity of the results weakens the inferences we can make from the overall results.

We performed several subgroup analyses in our attempt to explain the heterogeneity present and to understand which subgroups might benefit the most. Total parenteral nutrition was associated with significantly lower complication rates in studies of malnourished patients, although there was no mortality benefit observed. Mortality and complication rates of studies published in 1988 or earlier and studies with a lower methodologic quality score showed greater treatment effect than did later studies or studies with a higher methods score. Studies published in 1989 or later and those with a higher methods score suggest that TPN may be associated with increased mortality and no effect on complication rates.

### Complications

<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>31/231 (13.4)</td>
<td>12/150 (8)</td>
</tr>
<tr>
<td>17/20 (85.0)</td>
<td>6/20 (30)</td>
<td>0/12 (0)</td>
</tr>
<tr>
<td>4/25 (16)</td>
<td>0/25 (0)</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>0/12 (0)</td>
<td>0/16 (0)</td>
<td>2/10 (20)</td>
</tr>
<tr>
<td>0/14 (0)</td>
<td>0/16 (0)</td>
<td>0/16 (0)</td>
</tr>
<tr>
<td>0/14 (0)</td>
<td>0/16 (0)</td>
<td>0/16 (0)</td>
</tr>
<tr>
<td>11/66 (16.6)</td>
<td>3/66 (4.5)</td>
<td>1/15 (6.7)</td>
</tr>
<tr>
<td>17/46 (37)</td>
<td>10/46 (21.7)</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>4/60 (10)</td>
<td>4/60 (6.7)</td>
<td>12 ± 8</td>
</tr>
<tr>
<td>27/60 (45)</td>
<td>13/57 (22.8)</td>
<td>15 ± 6</td>
</tr>
<tr>
<td>1/22 (4.5)</td>
<td>2/13 (15.4)</td>
<td>17 ± 24</td>
</tr>
<tr>
<td>2/12 (16.7)</td>
<td>1/9 (11.1)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>22/64 (34.4)</td>
<td>33/60 (55)</td>
<td>24/20 (20)</td>
</tr>
<tr>
<td>8/54 (14.8)</td>
<td>22/46 (47.8)</td>
<td>6/16 (62.5)</td>
</tr>
<tr>
<td>3/17 (17.6)</td>
<td>6/17 (35.3)</td>
<td>6/23 (28.1)</td>
</tr>
<tr>
<td>1/10 (10)</td>
<td>1/9 (11.1)</td>
<td>17 ± 23</td>
</tr>
<tr>
<td>4/29 (13.8)</td>
<td>1/29 (3.4)</td>
<td>10 ± 3</td>
</tr>
<tr>
<td>6/12 (50)</td>
<td>3/12 (25)</td>
<td>41 ± 23</td>
</tr>
</tbody>
</table>

### Mortality

<table>
<thead>
<tr>
<th>Complications</th>
<th>Malnourished</th>
<th>Nonmalnourished</th>
<th>Quality Score &lt;7</th>
<th>Quality Score ≥7</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>P = 0.05</td>
<td>P = 0.02</td>
<td>P = 0.09</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>Quality Score</td>
<td>P = 0.05</td>
<td>P = 0.05</td>
<td>P = 0.05</td>
<td>P = 0.05</td>
</tr>
</tbody>
</table>

### Mortality

<table>
<thead>
<tr>
<th>Complications</th>
<th>Malnourished</th>
<th>Nonmalnourished</th>
<th>Quality Score &lt;7</th>
<th>Quality Score ≥7</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>P = 0.12</td>
<td>P = 0.07</td>
<td>P = 0.03</td>
<td>P = 0.01</td>
</tr>
</tbody>
</table>

### Mortality

- TPN Beneficial
- TPN Harmful

![Figure 3](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAAQAAAACwCAYAAAAUNLlKAAAABHNCSVQICAgI...)

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

**COMMENT**

The adverse effects of lipids may negatively affect 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.\(^{81}\)
patients receiving TPN and these treat-
ment effects may differ from the results in surgical patients. The results of stud-
es evaluating the effect of TPN in sur-
gical 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.15 Although the results of our meta-analysis do not support the use of TPN in critically ill patients, pro-
longed starvation (more than 14 days) is associated with poor outcomes. In a study of 300 patients undergoing major general surgical procedures, TPN was compared with prolonged glucose ad-

Levine GM, Deren JJ, Steiger E, Zinno R. Role of oral intake in maintenance of gut mass and disac-

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

Halldin EF, Sinclair DH, Houldsworth PE, Evans TW, Ffolliott MP, Sizer PO. Effect of early parenteral nutri-

Moore FA, Moore EE, Jones TN, McCrosky SL, Petersen YM, TEN versus TPN following ma-

Moore FA, Feliciano DV, Andressy RA, et al. Early enteral versus parenteral feeding: effects on septic morbid-

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

Heyland DK, Cook DJ, Guyatt GH. Enteral nu-

ASPEN Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and pedi-

Cerra FB, Benitez RB, Blackburn GL, et al. Ap-
plicated nutrition in ICU patients: a consensus state-


Detsky AS, Baker JP, O’Rourke K, Goel V. Perioperative parenteral nutrition: a meta-analy-

Sacks HS, Chalmers TC, Smith HJ. Random-
ized versus historical assignment in controlled tri-


Beale RJ, Frgyz DJ, Bihari D. Clinical effects of
immunosuppressive and enteral nutrition in critically ill patients: a meta-


Wills KE, Mikkelsen JL, Bennet B. The gut as a portal of entry for bacterial role of protein mal-

Boelhouwer RU, King WW, deVries WD, Boelhouwer RU, King WW, deVries WD. The link be-

Buchman AL, Moulkar CZ, Bhuta S, et al. Par-
enteral nutrition is associated with intestinal mor-


Deitch EA, Kimm DE, Bland G. The gut as a portal of entry for bacterial role of protein mal-


Hughes CA, Dowling RH. Speed of onset of adap-

Buchman AL, Moukarzel AA, Bhuta S, et al. Par-
terental nutrition is associated with intestinal mor-