Total parenteral nutrition in the surgical patient: a meta-analysis

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Authors' objectives
To examine the relationship between total parenteral nutrition (TPN) and complications and death rates in surgical patients.

Searching
MEDLINE (including PREMEDLINE) was searched from 1980 to 1999 using 'parenteral nutrition, total' in combination with the following keywords: 'randomized controlled trial', 'double-blind method', 'clinical trial', 'placebo' and 'comparative study'. Additional material was located by examining the reference lists of identified studies and relevant review articles, and by searching personal files. Only articles published in the English language were eligible.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Comparisons of any form of TPN with no TPN were eligible. Studies that compared TPN with enteral nutrition or other forms of TPN were excluded. The included studies compared TPN with standard care, which was the usual oral diet plus intravenous dextrose.

Participants included in the review
Adult surgical patients were eligible. Most of the participants had undergone major gastrointestinal surgery. Other types of surgery included thoracoabdominal, spinal and genitourinary.

Outcomes assessed in the review
Studies were eligible if they assessed complications, length of hospital stay, and mortality. Studies that only assessed the impact of TPN on nutritional outcomes were excluded. The primary outcome was peri-operative death (death within 30 days of operation) or death in hospital. Major complications were defined as pneumonia, intra-abdominal abscess, sepsis, catheter-related infection, myocardial infarction, pulmonary embolism, heart failure, stroke, renal failure, liver failure, and anastomotic leak. Minor complications were defined as wound infection, phlebitis, urinary tract infection, and atelectasis.

How were decisions on the relevance of primary studies made?
Two investigators screened all citations and classified them as primary studies, review articles, or others.

Assessment of study quality
Validity was assessed and scored by awarding up to 2 points for each of the following criteria: adequacy of concealment of randomisation; degree of blinding; intention to treat analysis; method used to select sample; baseline comparability of treatment groups; extent of follow-up; description of treatment protocol; description of co-interventions; and definition of outcomes. Two investigators assessed validity, and any disagreements were resolved by consensus.

Data extraction
Two investigators extracted the following data: author and year of publication; characteristics of the patients; intervention details; and outcomes. Any disagreements were resolved by consensus. The primary investigators of studies published within the past 5 years were contacted for details and clarification of missing or ambiguous data.
Methods of synthesis
How were the studies combined?
Pooled relative risks (RR) and the 95% confidence intervals (CIs) were calculated for the outcomes of mortality and complications using a random-effects model; one-half was added to each cell to deal with sparse data. The Mantel-Haenszel method was used to test the significance of treatment effects.

How were differences between studies investigated?
An a priori decision was made to compare the following subgroups:

patients who were malnourished versus patients who were not malnourished at entry, where either the definition of malnourished used in the study was accepted or, if none was given, taken to be a weight loss greater than 10%;

studies with an overall methodological score of at least 7 versus those with a score of less than 7;

studies published no later than 1988 versus those published since 1988;

interventions including lipids versus those without lipids; and

TPN initiated pre-operatively versus TPN initiated post-operatively.

The t-test was used to assess heterogeneity between the pairs of subgroups (a p-value of less than 0.05 was considered significant). The data were also examined for evidence of heterogeneity within groups (see Other Publications of Related Interest).

Results of the review
Twenty-seven RCTs (2,907 patients) were included.

The quality scores of the studies ranged from 3 to 10. Mortality.

There was no difference in mortality rates between interventions; the RR was 0.97 (95% CI: 0.76, 1.24). The statistical test for heterogeneity was not significant, although visual inspection suggested there were differences in the treatment effect for some studies.

Major complications (22 RCTs).

There were fewer, but not significantly fewer, major complications in groups receiving TPN; the RR was 0.81 (95% CI: 0.65, 1.01, p=0.06). Evidence of significant statistical heterogeneity was found (p=0.01).

Malnourished versus non malnourished patients.

Malnourished patients showed a non significant trend towards a reduction in complication rates. but no difference in death rates, when compared with non malnourished patients.

The RR of complications was 0.52 (95% CI: 0.30, 0.91) in malnourished patients, compared with 0.95 (95% CI: 0.75, 1.21) in non malnourished patients. The heterogeneity across subgroups was just short of statistical significance (p=0.066).

The RR of mortality was 1.13 (95% CI: 0.75, 1.71) in malnourished patients. compared with 0.90 (95% CI: 0.66, 1.21) in non malnourished patients. There was no evidence of heterogeneity across subgroups (p=0.38).


Earlier studies showed a significant reduction in complication rates, and a non significant reduction in mortality, when compared with studies published after 1988. The RR of complications was 0.42 (95% CI: 0.26, 0.68) in earlier studies, compared with 1.09 (95% CI: 0.91, 1.31) in later studies. There was evidence of heterogeneity across subgroups (p=0.002).
The RR of mortality was 0.68 (95% CI: 0.43, 1.10) in earlier studies, compared with 1.11 (95% CI: 0.83, 1.48) in later studies. Heterogeneity was not significant using conventional levels of significance (p=0.10).

Studies with a methodological score of at least 7 versus those with a score of less than 7.

Studies with a lower methodology score showed a significant reduction in complication rates, and a non significant reduction in mortality, when compared with studies with a higher methodology score.

The RR of complications was 0.75 (95% CI: 0.47, 1.19) in lower-quality studies, compared with 1.08 (95% CI: 0.81, 1.43) in higher-quality studies. There was no evidence of heterogeneity across subgroups (p=0.21).

The RR of mortality was 0.50 (95% CI: 0.32, 0.76) in lower-quality studies, compared with 1.07 (95% CI: 0.86, 1.32) in higher-quality studies. There was evidence of heterogeneity across subgroups (p=0.005).

Interventions including lipids versus those without lipids. There was no difference in mortality rates or complication rates between interventions, and there was no evidence for heterogeneity between subgroups (p=0.35).

Pre-operative versus post-operative initiation of TPN. The pre-operative initiation of TPN was associated with a non significant reduction in complication rates, but no difference in mortality, when compared with post-operative initiation of TPN. The RR of complications was 0.70 (95% CI: 0.52, 0.95) for pre-operative TPN, compared with 1.01 (95% CI: 0.70, 1.46) for post-operative TPN. There was no significant difference between subgroups (p=0.15).

The use of pre- or post-operative TPN was not associated with any difference in mortality. There was no evidence for heterogeneity across subgroups (p=0.39).

Length of hospital stay (13 RCTs).

Five RCTs reported the median stay, whilst 8 RCTs reported the mean stay. In 7 RCTs the duration of hospital stay was shorter in the control group.

The authors reported the following limitations of the review: the search was restricted to articles published in the English language; it was not possible to assess the influence of the amount of TPN on the results, or whether the effect of TPN varied across different surgical populations; it was not possible to classify patients according to severity of illness or baseline co-morbidity; and there was no consistent definition of 'malnourished' used across the studies.

Authors' conclusions
TPN does not influence the death rate of surgical patients. It may reduce the complication rate, especially in malnourished patients, but study results are influenced by methodological quality and year of publication.

CRD commentary
The aims were stated and the inclusion criteria were defined in terms of study design, participants, interventions and outcomes. Details of the search strategy were reported, and the methods used to select the studies were described. By limiting the search to only one database, and only including English language publications, other relevant studies may have been omitted (the latter limitation was acknowledged by the authors).

Validity was assessed and scored using defined criteria. The results were presented and relevant information on the included studies was tabulated. The methods used to assess validity and to extract the data were described. The data were pooled in a meta-analysis, statistical heterogeneity was assessed, and sources of heterogeneity were investigated. The influence of study quality on results was assessed, and the limitations of the review were discussed. The evidence presented supports the authors' conclusion.

Implications of the review for practice and research
Practice: The authors state that, overall, there is no advantage in using TPN peri-operatively in surgical patients.
Research: The authors state that further studies are required to confirm the benefits of TPN in surgical patients.

**Bibliographic details**

**Original Paper URL**

**Other publications of related interest**

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Subject indexing assigned by NLM

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