

## Perioperative Use of Arginine-Supplemented Diets: A Systematic Review of the Evidence

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### Objective:

To conduct a systematic review of all randomized clinical trials evaluating arginine-supplemented diets in elective surgical patients.

### Methods:

Meta-analysis included randomized clinical trials of elective surgical patients comparing enteral nutrition supplemented with arginine (with or without other immune-modulating agents) versus standard enteral nutrition, and reported clinical outcomes. The primary outcome of interest was number of patients with new infectious complications, and secondary outcomes included hospital length of stay (LOS) and mortality.

Subgroup analysis included (1) GI vs. non-GI surgery (2) upper GI vs. lower GI vs. both upper and lower GI surgery (3) IMPACT® formulas vs. other arginine-supplemented (non-IMPACT®) formulations and (4) pre- vs. post- vs. perioperative use of arginine-supplemented diets.

### Study Characteristics:

- 25/35 studies included elective GI surgery and 10 studies included other elective surgical procedures.

- **23 studies used IMPACT® formulas containing supplemental arginine, n-3 fatty acids and nucleotides, and 12 studies used other (non-IMPACT®) formulations supplemented with arginine and various immunonutrients. None of the non-IMPACT® formulas contained nucleotides.**

- Use of arginine-supplemented diets was exclusively reported preoperatively in 7 studies, postoperatively in 18 studies, and perioperatively in 13 studies.

### Results:

#### Infectious Complications

- Arginine-supplemented diets were associated with a 41% reduction in overall infectious complications when compared with standard formulas across elective surgeries (RR=0.59; 95% CI, 0.50-0.70; P<0.00001).

- **The use of IMPACT® formula vs. standard formula was associated with a 51% reduction in infectious complications (RR=0.49; 95% CI, 0.41-0.58; P<0.00001), compared to a 5% reduction with the use of non-IMPACT® formulations vs. standard formula (RR=0.95; 95% CI, 0.75-1.21; P=0.68). The difference between subgroups was statistically significant (P<0.0001).**

- Patients that received arginine-supplemented diets pre-, post- and perioperatively experienced fewer infectious complications compared to standard diet therapies and differences in subgroups were significant (P=0.03). The greatest treatment effect was seen with perioperative administration.
  - 54% reduction with perioperative administration (RR=0.46; 95% CI, 0.36-0.59; P<0.00001),
  - 43% reduction with preoperative administration (RR=0.57; 95% CI, 0.37-0.88; P=0.01) and
  - 22% reduction with postoperative administration (RR=0.78; 95% CI, 0.64-0.95; P=0.01).

## Results: (continued)

### Length of Stay (LOS)

- Overall hospital LOS was reduced in major elective surgical patients receiving arginine-supplemented diets when compared with patients receiving standard formulas [Weighted Mean Difference (WMD) = -2.38 days; 95% CI, -3.39 to -1.36;  $P < 0.00001$ ].

***The use of IMPACT® formula vs. standard formula was associated with a significant reduction in hospital LOS (WMD = -2.62 days; 95% CI, -3.65 to -1.59;  $P < 0.00001$ ), compared to the use of non-IMPACT® formula vs. standard formula (WMD = -0.89 days; 95% CI, -3.21 to -1.44;  $P = 0.45$ ). The difference between subgroups was statistically significant ( $P < 0.00001$ )***

- Patients fed arginine-supplemented diets post- and perioperatively experienced reduced LOS compared to standard diet therapies and differences in subgroups were significant ( $P = 0.001$ ). Again, the greatest treatment effect was seen with perioperative administration. No significant effect on LOS associated with preoperative administration was found.
  - WMD = -2.38 days with perioperative administration (95% CI, -3.44 to -1.32;  $P < 0.0001$ ),
  - WMD = -1.38 days with preoperative administration (95% CI, -3.49 to -0.73;  $P = 0.20$ ) and
  - WMD = -2.34 days with postoperative administration (95% CI, -3.80 to -0.65;  $P = 0.006$ )

### Mortality:

- Arginine-supplemented diets did not have a significant effect on mortality based on the 21 studies that reported mortality as one of the outcomes.

### Conclusion:

- Collectively, the perioperative use of arginine-supplemented nutrition therapy used in high risk elective surgical patients is associated with a substantial reduction in infection and shorter LOS.
- A sub-analysis of RCTs utilizing IMPACT® formulas shows a substantial reduction in infectious complications and LOS, whereas the aggregation of data from RCTs of other arginine-supplemented formulas shows no significant effect.

The complete study can be accessed online at:  
<http://www.ncbi.nlm.nih.gov/pubmed/21247782>