Early post-operative enteral or oral nutrition for patients receiving lower gastrointestinal tract surgery: Methods for a meta-analysis of randomized controlled trials.

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METHODS

This systematic review and meta-analysis was conducted and reported in compliance with established methodological guidelines (1).

Study selection, risk of bias appraisal and data abstraction will be undertaken by at least two authors. Disagreements will be settled by obtaining an opinion of a third author. Majority decisions prevailed.

Literature search

Medline (www.PubMed.org), Embase (www.EMBASE.com) and the China National Knowledge Infrastructure (www.cnki.com.cn) will be searched using appropriate statements and terms (2;3). Complete details will be reported in the Online Supplement.

Reference lists of published reviews and guidelines will be hand searched. The close out date will be documented upon completion.

Study selection

All RCTs comparing early nutrition to later nutrition published in any language will be retrieved in full text and screened for inclusion. Early nutrition is defined as oral or enteral intake initiated within 24 hours (before end of POD 1) of surgery using a drink, food or solution that contained calories *and* protein. The comparison group will be defined pragmatically, and is accepted to include any form of nutrition support commenced later than 24 h post-op.

RCTs reporting mortality conducted in adult populations who had received surgery to the lower gastrointestinal tract (distal to the ligament of Treitz) are eligible for inclusion and will be reviewed in detail.

Risk of bias

All included trials will be appraised on the reporting of three key methodological criteria: 1) the maintenance of allocation concealment; 2) the use of any form of blinding and; 3) the completeness of patient follow-up. Major methodological flaws leading to a recognized high risk of

bias are defined *a priori* as clear failure to maintain allocation concealment (4) and excessive (>10%) loss to follow-up (5).

Outcomes

The primary outcome of interest is mortality. Physical function, quality of life, duration of hospital stay, requirement for ICU admission, wound infections, clinical evidence of suspected anastomotic leak, visualization of anastomotic dehiscence, PONV, pneumonia and need for re-operation will be investigated as secondary outcomes.

Statistical analysis

Analysis is to be conducted using a fixed effects model (6) with the odds ratio (OR) metric (7). The OR metric will be calculated using the Mantel-Haenszel method unless data is sparse, in which case the Peto method will be used (4;8). The underlying assumption behind the fixed effects model will be assessed with a formal chi-square test of heterogeneity (6) and quantified using the I^2 metric (9). Important heterogeneity is defined as a P-value for the test of heterogeneity ($P_{heterogeneity}$) less than 0.10 or I^2 greater than 50% (10).

Analysis will be conducted using RevMan Version 5.3.5 for Windows (The Cochrane Collaboration®, Oxford, England, 2014). A two-tailed P-value less than 0.05 is accepted to indicate statistical significance whilst a two-tailed P-value less than 0.10 is accepted to indicate a trend towards statistical significance.

Sensitivity analysis

Focused on the primary outcome, the sensitivity analysis will consider trials with *less certainty* regarding protein content of the intervention group's early nutrition.

Heterogeneity and stratified analysis

If important heterogeneity is detected, the following *a priori* identified potential sources of heterogeneity were investigated via stratified analysis: 1) methodological quality; 2) intervention timing and dose; 3) co-interventions and comparison intervention received; and 4) measurement and timing of outcomes (11).

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