Oral L-arginine supplementation in acute myocardial infarction therapy: a meta-analysis of randomized controlled trials

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CRD summary
The authors concluded that oral L-arginine supplementation had no effect on clinical outcomes in patients with acute myocardial infarction. Given the absence of a fully-reported review process, the inclusion of only two trials and the restriction to reporting results only for mortality, the conclusion is unlikely to be reliable.

Authors' objectives
To evaluate the effect of oral L-arginine supplementation in patients with acute myocardial infarction.

Searching
PubMed and EMBASE were searched from 1966 to January 2009. The Cochrane Library was also searched. Reviews and reference lists from selected articles were scanned for additional studies. Search terms were reported.

Study selection
Published randomised controlled trials (RCTs) of patients with acute myocardial infarction receiving oral L-arginine in addition to standard post infarction therapy were eligible for inclusion in the review. The outcomes evaluated were all-cause mortality, myocardial reinfarction, successful resuscitation, shock/pulmonary oedema, recurrent myocardial ischaemia, hospitalisation for heart failure, and adverse events.

The included trials were placebo-controlled. The average age of included patients was between 60 and 64 years; the total dose of L-arginine was 9g per day (administered in three doses), and treatment duration ranged from 30 days to six months.

Relevant studies were selected by two independent reviewers, and disagreements were resolved by discussion.

Assessment of study quality
The quality of trials was assessed on aspects of randomisation, blinding, reporting of withdrawals, generation of random numbers, and allocation concealment. The attainable score ranged from 0 to 5 (highest quality).

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted on the outcomes listed above, in order to calculate risk ratios (RR) and 95% confidence intervals (CI). In addition, missing patient data, non-intention-to-treat analysis, and details of loss to follow-up were sought.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Risk ratios and 95% confidence intervals were synthesised in a meta-analysis using a fixed-effect model. Statistical heterogeneity was assessed using the Cochran's test and the $I^2$ statistic. ($I^2$ over 50% indicating significant heterogeneity).

Results of the review
Two RCTs (n=153 and n=774 patients) were included in the review. Individual quality scores were not presented, but both trials were reported to be double-blind, with adequate details of withdrawals.

Despite an overall 7% reduction in mortality in patients receiving L-arginine, the difference between groups was not
statistically significant. There was no statistically significant heterogeneity. No other results were reported.

**Authors' conclusions**

Oral L-arginine supplementation had no effect on the clinical outcomes of patients with acute myocardial infarction.

**CRD commentary**

The review question was clear and inclusion criteria appeared to be reproducible for all aspects except for outcomes. Although many outcomes were proposed for the evaluation, the results focused only on mortality. The search strategy addressed some relevant sources. The selection of studies was conducted with sufficient attempts to minimise reviewer error and bias, but the process was unclear for quality assessment and data extraction.

Criteria for a formal quality assessment were presented, but the full results were not reported. Although statistical heterogeneity was not present, the authors refer to the lack of power due to the inclusion of only two trials (one of which provided disproportionate weighting). This, together with reported clinical heterogeneity, meant that the chosen method of synthesis may not have been appropriate.

The authors' conclusion reflected the evidence presented in terms of mortality, but is unlikely to be reliability due to the potential methodological concerns identified above, the small number of trials identified, and the omission of other clinical outcome results.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that a larger number of adequately powered and sufficient quality randomised controlled trials are needed to assess the effectiveness of oral L-arginine supplementation in patients with unstable coronary artery disease and other cardiovascular conditions.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.