Association of blood transfusion with increased mortality in myocardial infarction: a meta-analysis and diversity-adjusted study sequential analysis
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CRD summary
The authors concluded that blood transfusion or a liberal blood transfusion strategy compared with no blood transfusion or a restricted blood transfusion strategy was associated with higher all-cause mortality. The authors’ conclusions reflect the evidence presented and seem reliable.

Authors’ objectives
To evaluate the potential risk-benefit of blood transfusion in patients with myocardial infarction.

Searching
MEDLINE, EMBASE, CINAHL, Scopus, Web of Science and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from January 1966 to March 2012 for relevant studies published in English. Search terms were reported. References of included studies and reviews articles were scanned. ClinicalTrials.gov and proceedings from major international cardiology meetings were searched for relevant trials.

Study selection
Studies that compared blood transfusion with no blood transfusion or a liberal versus restricted blood transfusion strategy in patients with myocardial infarction were eligible for inclusion. Eligible studies had to report on mortality and had to report mean haemoglobin level for both groups. Confounding factors had to be adjusted between the groups. Studies that assessed the effect of transfusion of components other than whole blood or red blood cells were excluded.

Most studies included patients who presented with ST-segment and non-ST-segment elevation myocardial infarction. Patient mean age ranged from 67 to 77.8 years. From 45.9% to 99% of patients were men. Baseline haemoglobin level ranged from 8.91g/dL to 13.9g/dL.

Two reviewers independently selected studies for the review; disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed using the Newcastle-Ottawa Scale which covered adequacy of selection, comparability of groups and outcomes assessment.

Two reviewers independently evaluated study quality; disagreements were resolved by consensus.

Data extraction
Data were extracted to calculate hazard ratios (HR), relative risks (RR) and their 95% confidence intervals (CI).

Two reviewers independently extracted data; disagreements were resolved by consensus.

Methods of synthesis
Pooled hazard ratios and risk ratios and their 95% confidence intervals were calculated using a random-effects model (DerSimonian-Laird method). Heterogeneity was assessed using I² (<25% indicated low heterogeneity and >75% indicated high heterogeneity). Publication bias was assessed with a funnel plot, the Egger test and the trim-and-fill method. The number needed to harm (NNH) was calculated.

Subgroup analyses were planned for patients with ST-segment elevation myocardial infarction and for patients with haematocrit of less than 30%. The study sequential analysis of diversity-adjusted information size for the outcome of all-cause mortality was calculated.

Sensitivity analysis excluded one study at a time. Multivariate meta-regression was used to assess the influence of the variables: follow-up period, history of bleeding, baseline creatinine level, baseline haemoglobin level, nadir of
haemoglobin level, change in haemoglobin level during the hospital stay and use of glycoprotein IIb or IIIa, thrombolytics or antiplatelets.

**Results of the review**

Ten studies (one randomised trial and nine observational studies) were included in the review (203,757 patients; reporting differences were noted between tables and text). The authors stated that most studies were considered to have intermediate risk of bias. Follow-up ranged from one month to 12 months, where reported. There was no evidence of publication bias.

Meta-analyses showed that blood transfusion/liberal blood transfusion increased all-cause mortality compared to no blood transfusion/restricted blood transfusion in anaemic patients with myocardial infarction (RR 2.91, 95% CI 2.46 to 3.44; \( I^2 = 92\% \); NNH=8; 10 studies). Similar results were found when using adjusted mortality instead of the actual number of events (HR 2.25, 95% CI 1.68 to 3.02; \( I^2 = 98\% \); nine studies). Blood transfusion/liberal blood transfusion was also associated with a higher risk of subsequent myocardial infarction (RR 2.04, 95% CI 1.06 to 3.93; \( I^2 = 98\% \); seven studies).

Subgroups of patients with ST-segment elevation myocardial infarction and patients with haematocrit of less than 30% showed no significant difference in mortality between blood transfusion and comparator.

Meta-regression showed that blood transfusion was associated with higher mortality after adjustment of different variables. Sensitivity analysis confirmed that no single study was the source of heterogeneity. Study sequential analysis of observational studies on all-cause mortality suggested firm evidence for a 20% relative risk increase with blood transfusion or a liberal blood transfusion strategy compared with no blood transfusion or a restricted blood transfusion strategy.

**Authors’ conclusions**

Blood transfusion or a liberal blood transfusion strategy compared with no blood transfusion or a restricted blood transfusion strategy was associated with higher all-cause mortality rates in patients with myocardial infarction.

**CRD commentary**

The review addressed a clear question and was supported by appropriate inclusion criteria. Several relevant data sources were searched. The search was restricted to studies in English so language bias could not be ruled out. Suitable methods were employed to reduce the risks of reviewer error and bias throughout the review process. Study quality was assessed using appropriate criteria. A reasonable level of information about individual studies was provided. Appropriate methods were used to pool data and assess heterogeneity. The authors acknowledged some limitations due to observational study designs, diverse patients’ characteristics and the restriction to studies in English.

Despite significant heterogeneity (which the authors tried to explore by using sensitivity analysis and multivariate meta-regression) the forest plot consistently showed significantly less harmful effect with no blood transfusion. The authors’ conclusion reflects the evidence presented and appears to be reliable.

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

**Practice:** The authors stated that a practice of routine or liberal blood transfusion in myocardial infarction should not be encouraged.

**Research:** The authors stated that randomised controlled trials with adequate sample size and with low risk for bias were needed for more definitive conclusions. A less harmful effect was found with blood transfusion in subgroup of patients with ST-segment elevation myocardial infarction and with haematocrit of less than 30% so future research should identify specific subgroups that may benefit from blood transfusion.

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