Perioperative blood transfusion and cancer recurrence: meta-analysis for explanation

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Authors' objectives
To present a quantitative synthesis of the results from observational studies, and to explain disagreements across studies in regard to the relationship between perioperative transfusion and cancer recurrence.

Searching
MEDLINE was searched from 1982 to 30 June 1994 for English language studies. Bibliographies of retrieved articles were also examined.

Study selection
Study designs of evaluations included in the review
Observational studies were included. Experimental clinical studies were excluded. To be included in the review, studies had to have a hypothesis relating the deleterious effect of blood (red cell) transfusion on cancer recurrence and contain information on the number of patients, both untransfused and transfused, who experienced or did not experience the adverse outcome.

Specific interventions included in the review
Perioperative transfusion.

Participants included in the review
Patients undergoing surgery for cancer of the colorectum, breast, head and neck, lung, prostate and stomach. For a tumour site to be included in the review at least five articles had to be identified.

Outcomes assessed in the review
The outcomes assessed were cancer recurrence, death due to cancer recurrence or death due to any cause.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The random-effects model was used to estimate the average adverse transfusion effect across studies. The transfusion effect was measured using the relative risk (RR) of cancer recurrence in the transfused patients versus that measured in the untransfused patients.

How were differences between studies investigated?
Heterogeneity across the studies was tested using the chi-squared test. If studies were not homogeneous, then the following factors were examined as potential explanations: sample size, study design, negative outcome, year of
publication, percentage of patients transfused, percentage with negative outcome and type of statistical analysis.

**Results of the review**

Sixty studies involving 19,387 patients were included:

- colorectal cancer, 28 studies with 8,374 patients;
- breast cancer, 8 studies with 3,814 patients;
- head and neck cancer, 7 studies with 766 patients;
- lung cancer, 6 studies with 1,362 patients;
- prostate cancer, 6 studies with 2,829 patients;
- stomach cancer, 5 studies with 2,242 patients.

Twenty-eight (46.7%) of the 60 reports concluded that perioperative transfusion was associated with an adverse clinical outcome. The 'average' adverse transfusion effect was significant (P<0.05) at all sites except for breast cancer. The 'average' transfusion effect ranged from a 6% increase in the risk of a negative outcome in cases of breast cancer to a 262% increase in risk for patients undergoing resection of head and neck cancer. Calculated RRs and 95% confidence intervals were:

- colorectal: 1.49 (95% CI: 1.23, 1.79);
- breast: 1.06 (95% CI: 0.90, 1.24);
- head and neck: 3.62 (95% CI: 2.15, 6.08);
- lung: 1.30 (95% CI: 1.02, 1.66);
- prostate: 1.51 (95% CI: 1.13, 2.01);
- gastric: 2.44 (95% CI: 1.60, 3.71).

When studies of colorectal cancer were separated into two design groups (retrospective and prospective), the RR was 1.60 (95% CI: 1.27, 2.02) and 1.18 (95% CI: 0.93, 1.51) respectively.

**Authors' conclusions**

'Average' adverse transfusion effects were calculated from observational studies prior to any adjustment for the effect of confounding factors. The crude increase in the risk of an adverse outcome ranged from 6% in breast cancer to 262% in head and neck carcinomas, and was significant in all cancer sites except for breast. However, this study is not able to attribute this effect to either the transfusion effect or effect(s) of uncontrolled confounders. A number of the original studies found that by controlling for confounding they decreased the effect size of the transfusion. Further randomised controlled trials are needed to address this issue.

**CRD commentary**

The results of this review should be viewed with great caution as no attempt was made to control for confounding factors, which could be related to cancer recurrence. Therefore, crude (or unadjusted) increases in the risk of an adverse outcome could be attributable to the transfusion or to confounding factors.

It is important to note that the association between transfusion and negative outcome was only found significant by retrospective studies, and not by prospective ones.
The author specifically excluded 3 RCTs investigating blood transfusion and prognosis in cancer patients.

**Bibliographic details**
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**Other publications of related interest**
Vamvakas EC. Transfusion-associated cancer recurrence and postoperative infection. Transfusion 1996;36:175-86.

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