Intraoperative Autotransfusion in Abdominal Aortic Aneurysm Surgery

Meta-analysis of Randomized Controlled Trials

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Objective: To determine whether intraoperative autotransfusion reduces the percentage of patients undergoing allogeneic blood transfusion.

Data Sources and Study Selection: Using a public domain database (MEDLINE) and a Web-based search engine (PubMed), all intraoperative autotransfusion vs control prospective randomized controlled trials that enrolled patients undergoing elective infrarenal abdominal aortic aneurysm surgery, published between January 1, 1966, and November 30, 2005, were searched. Relevant studies were identified through a manual search of secondary sources including references of initially identified articles.

Data Extraction: Data on detailed inclusion criteria, autotransfusion system type, and incidence of allogeneic blood transfusion were abstracted from each study. Sensitivity analyses were performed by excluding individual trials one at a time and recalculating the pooled risk ratio estimates for the remaining studies.

Data Synthesis: Our search identified 4 randomized controlled trials including data for 292 patients. Pooled analysis demonstrated a statistically significant 37% reduction in risk of allogeneic blood transfusion with intraoperative autotransfusion compared with control (risk ratio, 0.63; 95% confidence interval, 0.41-0.95; \( P = .03 \)) in a random-effects model. There was statistically significant trial heterogeneity of results (\( P = .02 \)) but no evidence of statistically significant publication bias (\( P = .497 \)). Two of 4 sensitivity analyses demonstrated statistically nonsignificant results favoring intraoperative autotransfusion.

Conclusion: Based on a meta-analysis of available randomized controlled trials, intraoperative autotransfusion reduces risk of allogeneic blood transfusion in elective infrarenal abdominal aortic aneurysm surgery.

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METHODS

SEARCH STRATEGY

All prospective randomized controlled trials of IAT vs control (no IAT) that enrolled patients undergoing elective infrarenal AAA surgery were identified using a 2-level search strategy. First, a public domain database (MEDLINE) was searched using a Web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles. The MEDLINE database was searched from January 1, 1966, to November 30, 2005. Keywords included transfusion, abdominal aortic aneurysm, and randomized controlled trials.

STUDY SELECTION, QUALITY ASSESSMENT, AND DATA ABSTRACTION

Studies considered for inclusion met the following criteria: the design was a prospective randomized controlled clinical trial, the study popu-
lution included patients undergoing elective infrarenal AAA surgery, patients were randomly assigned to IAT vs control groups, and main outcomes included incidence of ABT. All qualifying studies were assessed for adequate blinding of randomization and the intervention (IAT) and objectivity of the outcome assessment. Data on detailed inclusion criteria, autotransfusion system type, and incidence of ABT were abstracted, as available, from each study.

STATISTICAL ANALYSIS
For each study, data about the incidence of ABT in both the IAT and control groups were used to generate risk ratios (RRs) (RR <1, favors IAT; RR >1, favors control) and 95% confidence intervals (CIs). Between-study heterogeneity was analyzed using standard χ² tests. P <.05 was deemed statistically significant. Where significant statistical heterogeneity was identified, a random-effects model (method of DerSimonian and Laird) was used preferentially as the summary measure. Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual trials one at a time and recalculating the pooled RR estimates for the remaining studies. Publication bias was assessed graphically using a funnel plot and mathematically using an adjusted rank correlation test (method of Begg and Mazumdar).

RESULTS
SEARCH RESULTS
Our search identified 5 prospective randomized controlled clinical trials of IAT vs control that enrolled patients undergoing elective infrarenal AAA surgery. Three of 4 trials demonstrated a statistically significant benefit of IAT over control for risk of ABT (Figure). Only the trial by Clagett et al demonstrated a statistically nonsignificant ABT risk reduction with IAT over control.

QUALITATIVE FINDINGS
The 4 trials analyzed were by Mercer et al,2 Spark et al,3 Clagett et al,4 and Wong et al.6 There was substantial qualitative heterogeneity in trial design. Only patients in the IAT group of the study by Wong et al underwent acute normovolemic hemodilution to reduce a hemoglobin concentration of 11 g/dL (to convert to grams per liter, multiply by 0.01); in the trial by Clagett et al,4 all patients were given ABT according to the guidelines advocated by Nelson et al,9 which include intraoperative transfusion for hemodynamic instability; hemoglobin concentration less than 10 g/dL (hematocrit <30%); to convert to grams per liter, multiply by 0.01); and postoperative transfusion because of hemoglobin concentration less than 8 g/dL (hematocrit <25%) or 8 to 10 g/dL (hematocrit, 25%-30%) in those with compromised cardiopulmonary status. Patients with hemoglobin concentration of 10 g/dL or greater (hematocrit >30%) did not receive transfusions. In the trial by Mercer et al,2 patients received blood products to maintain a hemoglobin concentration of 8 g/dL during and after surgery. In the trial by Spark et al,3 patients received transfusions of allogeneic blood if the hematocrit value decreased to less than 25%. In the trial by Wong et al,6 allogeneic blood was transfused when the hemoglobin concentration decreased to less than 8 g/dL or when ischemic electrocardiographic changes persisted after correction of hypovolemia. Patients were younger in the trial by Clagett et al6 (mean age, 63 years in the IAT group and 65 years in the control group) than in the other 3 trials.

Among the 4 trials that were used for the present meta-analysis, those by Spark et al and Mercer et al included only patients undergoing AAA surgery. Although 100 patients undergoing AAA repair (n=50) or aortofemoral bypass because of occlusive disease (n=50) were randomized to IAT and control groups in the trial by Clagett et al,3 only data for those undergoing AAA repair were analyzed. The trial by Wong et al included 34 patients who underwent elective infrarenal aortic surgery because of occlusive disease of 145 randomized participants, but we were able to obtain data for the other 111 patients (F. Torella, FRCS, written communication, September 13, 2005). In total, our meta-analysis included data for 292 patients undergoing elective infrarenal AAA surgery randomized to the IAT vs control groups (Table).

Blinding of randomization and the intervention and objectivity of the outcome assessment were not stated in the trial by Spark et al.3 The trial by Clagett et al6 was unblinded. In the trial by Mercer et al,2 patients were blinded to transfusion group allocation. Members of the operating surgical team were responsible for the continuing care of patients, decision to use blood transfusion, and investigation of postoperative complications, and they were independent of the research team but were not blinded to the use of IAT. The trial of Wong et al6 was single-blinded, but the decision to give ABT was made using a rigid protocol and by a physician independent from the research team.

QUANTITATIVE FINDINGS
Three of 4 trials demonstrated a statistically significant benefit of IAT over control for risk of ABT (Figure). Only the trial by Clagett et al demonstrated a statistically nonsignificant ABT risk reduction with IAT over control.

Pooled analysis of the 4 trials, representing 292 patients, demonstrated a statistically significant 37% reduction in risk of ABT with IAT compared with control (RR, 0.63; 95% CI, 0.41-0.95; P = .03) in the random-effects model (Figure). There was statistically significant trial heterogeneity of results (P = .02). To assess the effect of qualitative heterogeneity in trial design and patient selection on the pooled effect estimate, we performed several sensitivity analyses. First, we excluded the trial by Spark et al with the lowest RR (0.14); combining the remaining 3 trials generated an attenuated but still statistically significant result favoring IAT (RR, 0.76; 95% CI, 0.62-0.92; P = .006). Second, we excluded the trial by Clagett et al with the highest RR (0.89). Without the trial by Clagett and colleagues, there was still a statistically significant benefit for IAT in pooled analysis of the remaining 3 trials (RR, 0.51; 95% CI, 0.29-0.92; P = .02). Third, we excluded the trial by Wong et al,6 which enrolled the most patients (n = 111); combining the remaining 3 trials generated statistically nonsignificant results favoring IAT (RR, 0.55; 95% CI, 0.29-1.05; P = .07). Fourth, we excluded the trial...
by Mercer et al.\textsuperscript{2} Without the trial by Mercer and colleagues, there was a statistically nonsignificant benefit for IAT in pooled analysis of the remaining 3 trials (RR, 0.55; 95% CI, 0.28-1.06; \(P = .07\)).

**PUBLICATION BIAS**

To assess publication bias, we generated a funnel plot of the logarithm of effect size vs the standard error for each trial. There was no evidence of statistically significant publication bias (\(P = .497\)).

**Table. Characteristics of Trials**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Spark et al\textsuperscript{3}</th>
<th>Clagett et al\textsuperscript{4}</th>
<th>Wong et al\textsuperscript{6}</th>
<th>Mercer et al\textsuperscript{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autotransfusion group</td>
<td>23</td>
<td>25</td>
<td>59</td>
<td>40</td>
</tr>
<tr>
<td>Control group</td>
<td>27</td>
<td>25</td>
<td>52</td>
<td>41</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autotransfusion group</td>
<td>71 (54-78)\textsuperscript{c}</td>
<td>63 ± 4\textsuperscript{d,e}</td>
<td>73 ± 7.2\textsuperscript{d,f}</td>
<td>72 (69-76)\textsuperscript{c,f}</td>
</tr>
<tr>
<td>Control group</td>
<td>68 (54-82)\textsuperscript{c}</td>
<td>65 ± 6\textsuperscript{d,e}</td>
<td>71 ± 6.5\textsuperscript{d,f}</td>
<td>73 (67-78)\textsuperscript{c,f}</td>
</tr>
<tr>
<td>Preoperative hemoglobin concentration, g/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autotransfusion group</td>
<td>13.5 (12.7-14.5)\textsuperscript{c,f}</td>
<td>≥10\textsuperscript{g}</td>
<td>13.5 ± 1.3\textsuperscript{d,f}</td>
<td>&gt;12\textsuperscript{h}</td>
</tr>
<tr>
<td>Control group</td>
<td>12.8 (10.5-15.2)\textsuperscript{c,f}</td>
<td>≥10\textsuperscript{g}</td>
<td>13.9 ± 1.5\textsuperscript{d,f}</td>
<td>&gt;12\textsuperscript{h}</td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autotransfusion group</td>
<td>1800 (500-2800)\textsuperscript{c,f}</td>
<td>1418 ± 1192\textsuperscript{d}</td>
<td>1050 (691-1500)\textsuperscript{c,f}</td>
<td>1950 (775-2850)\textsuperscript{c,f}</td>
</tr>
<tr>
<td>Control group</td>
<td>1500 (500-3045)\textsuperscript{c,f}</td>
<td>1346 ± 920\textsuperscript{d}</td>
<td>1165 (808-1939)\textsuperscript{c,f}</td>
<td>1270 (775-2850)\textsuperscript{c,f}</td>
</tr>
<tr>
<td>Autotransfusion system</td>
<td>BRAT</td>
<td>Cell Saver</td>
<td>Cell Saver/BRAT2/CATS</td>
<td>Cell Saver</td>
</tr>
</tbody>
</table>

Abbreviations: BRAT, Baylor Rapid Autotransfusion Device (Cobe Cardiovascular Inc, Arvada, Colorado); CATS, Continuous Autologous Transfusion System (Fresenius Kabi AG, Bad Homburg, Germany); Cell Saver Autologous Blood Recovery System (Haemonetics Corp, Braintree, Massachusetts).

\textsuperscript{a}Values excluding data for 50 patients who underwent aortoemoral bypass grafting because of occlusive disease.

\textsuperscript{b}Values excluding data for 34 patients who underwent elective infrarenal aortic surgery because of occlusive disease from the original data (F. Torella, FRCS, written communication, September 13, 2005).

\textsuperscript{c}Values are given as median (range).

\textsuperscript{d}Values are given as mean ± SD.

\textsuperscript{e}Age for total patients including simultaneously studied patients undergoing aortoemoral bypass grafting because of occlusive disease.

\textsuperscript{f}No significant difference between the intraoperative autotransfusion and control groups.

\textsuperscript{g}Inclusion criteria.

\textsuperscript{h}Value shown in the Figure.

**Figure.** Pooled analysis of the outcome. *Mean based on a random-effects model (method of DerSimonian and Laird\textsuperscript{7}); relative risk (RR) less than 1 favors intraoperative autotransfusion, whereas RR greater than 1 favors control. Solid diamonds indicate risk ratio of the individual study; open diamond, the pooled risk ratio; 1, equals equal risk.

Alvarez et al\textsuperscript{5} conducted a systematic review of published studies to determine whether IAT reduced the exposure of ABT in abdominal vascular surgery. To our knowledge, their study is only a meta-analysis of randomized controlled trials. In the subgroup of 100 patients who underwent infrarenal AAA surgery in 2 small randomized controlled trials,\textsuperscript{3,4} the pooled RR for IAT was 0.37 (95% CI, 0.06-2.36). The present meta-analysis of
4 randomized controlled trials including 292 patients, however, demonstrated a statistically significant 37% reduction in risk of ABT with IAT compared with control. The trial by Wong et al is the largest (n=111) of the trials included in the present meta-analysis; the other 3 trials included fewer than 100 patients each.

The present analysis must be viewed in the context of its limitations. First, only data from randomized controlled trials were used, but patients enrolled in randomized trials may not be representative of those typically seen in clinical practice. Second, the oldest trial (published in 1990 by Thompson et al) among those retrieved was excluded because the appropriate information, not included in the article, was sought by the authors without success. Third, the present results may be influenced by a publication bias favoring IAT. Although the statistical tests did not indicate publication bias, there is clearly limited power to detect such bias, given the small number of studies examined. Fourth, 2 of 4 sensitivity analyses, without the trials by Mercer et al or Wong et al, demonstrated statistically nonsignificant results favoring IAT. In conclusion, based on a meta-analysis of available randomized controlled trials, IAT reduces risk of ABT in elective infrarenal AAA surgery.

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REFERENCES