Concern about risks associated with allogeneic red blood cell transfusion has led to interest in methods of decreasing patient exposure to perioperative transfusion.

Objective: To perform a meta-analysis to determine the degree to which predonation of autologous blood reduces patients’ exposure to allogeneic blood and all transfusions of red blood cells (allogeneic or autologous).

Methods: We searched MEDLINE, EMBASE, bibliographies, annual reports, press releases, newsletters from organizations with interests in the blood system, and personal files for randomized studies and concurrent control cohort studies in which the control groups were patients excluded for nonmedical reasons.

Results: Patients who predonated autologous blood were less likely to receive allogeneic blood in the 6 randomized studies (n=933) (odds ratio [OR], 0.17; 95% confidence interval [CI], 0.08-0.32) and in the 9 cohort studies (n=2351) (OR, 0.19; 95% CI, 0.14-0.26). However, autologous donors were more likely to undergo transfusion with allogeneic and/or autologous blood (for randomized studies: OR, 3.03; 95% CI, 1.70-5.39 and for cohort studies: OR, 12.32; 95% CI, 5.90-25.40). Studies that reported use of transfusion protocols found less benefit with preoperative autologous donation, although the difference was not statistically significant.

Conclusions: Preoperative autologous donation of blood decreases exposure to allogeneic blood but increases exposure to any transfusion (allogeneic and/or autologous). There is a direct relationship between the transfusion rate in the control group and the benefit derived from preoperative autologous donation. This suggests that other methods of decreasing blood transfusion, such as surgical technique and transfusion protocols, may be as important as preoperative autologous donation of blood.

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METHODS

LOCATING RESEARCH

The entire MEDLINE database from 1966 to April 1996 was searched using the Medical Subject Headings in MEDLARS with the term blood transfusion, autologous. The only restriction was to limit the studies to those using human subjects. Abstracts and letters were included. This strategy produced 2275 articles. Other methods of identifying articles included (1) searching EMBASE using the terms blood transfusion and autologous combined with autotransfusion; (2) hand searching the bibliographies of all the studies included in the final analysis; (3) contacting organizations with interests in the blood system, such as the Red Cross of Canada, for annual reports, press releases, newsletters, and other information; and (4) asking all investigators of the International Study of Perioperative Transfusion Group if they were aware of additional relevant articles.

Preoperative autologous donation of blood was defined as the process by which patients donate blood prior to elective surgery and subsequently receive their own blood in the perioperative period if transfusion is required. Two of us (M.A.F. and P.S.W.) independently reviewed the titles and abstracts of all articles identified by the search strategy to determine which articles were relevant for this meta-analysis. This review yielded 768 articles that evaluated preoperative autologous blood donation, which were then retrieved and reviewed. Sixty-one articles reported patient exposure to allogeneic blood and were either randomized controlled studies or observational studies that compared patients who predonated blood with patients who did not predonate blood.

SELECTING RESEARCH

Three criteria, established a priori, were then applied to the full text of the 61 articles chosen for review. To be included in the primary analysis, randomized controlled studies had to meet the following criteria: (1) patients allocated to donate autologous blood preoperatively were compared with patients who did not donate blood preoperatively; (2) patients underwent elective surgery; and (3) the proportion of patients who underwent transfusion with allogeneic blood was reported (this was the primary outcome). For the secondary analysis, cohort studies were included only if they met these 3 criteria and the clinical characteristics of the control group were likely to be similar to the patients who donated autologous blood. The control group had to undergo surgery during the same period as the group donating autologous blood to remove the bias that may occur because of a change in practice over time.

Examples of an acceptable control group were patients who were excluded from preoperative donation of autologous blood either because of geographic inaccessibility to the blood donation center or because it was a surgeon’s practice not to refer any patients to autologous blood donation programs. If patients in the control group were medically ineligible for predonation or if the method of choosing the control group was not explained, the study was excluded from this analysis. Each article was reviewed in full by 2 observers (M.A.F. and P.S.W.). Interobserver reliability was determined for the first and third inclusion criteria (study type and proportion of patients who underwent transfusion with allogeneic blood). Disagreements were resolved by consensus.

DATA ABSTRACTION

From the 61 studies evaluated for inclusion in the final analysis, we recorded data on the following outcomes: number of patients exposed to allogeneic blood; total number of patients who underwent transfusion with red blood cells (including both allogeneic and autologous units); reported transfusion protocol; hematocrit and/or hemoglobin values prior to preoperative autologous blood donation; preoperative hematocrit and/or hemoglobin values; last reported hematocrit and/or hemoglobin values before discharge; blood loss during surgery; use of iron supplementation in autologous blood donors; number of autologous units of blood requested; number of autologous units of blood collected; total number of units of red blood cells transfused; and postoperative complications (eg, infections, myocardial infarction, angina, prolonged hospital admission, venous thrombosis, or survival). The quality of the randomized studies was assessed using the criteria of Jadad et al,11 and the interobserver agreement on the quality score was determined. The nonrandomized studies were not assessed for methodological quality.

DATA ANALYSIS

The effect of preoperative autologous donation of blood on the proportion of patients who received allogeneic blood was summarized with a pooled estimate of the odds ratio (OR) using a random effects model.12 Analyses were performed using software (Meta-Analyst 0.998, Lau and Chalmers). Study heterogeneity (a measure of the variability of the results among the studies) was tested with the Cochrane Q test for overall heterogeneity, and statistically significant heterogeneity was indicated at P<.05.

The randomized studies and concurrent control cohort studies were analyzed separately. Subgroup analyses were performed according to whether a transfusion protocol was reported (randomized and cohort studies) and the type of surgery (randomized studies only).

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Table 1. Characteristics of Studies Included in the Meta-analysis

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Study Design</th>
<th>Type of Surgery</th>
<th>No. of Patients (Control/Auto)</th>
<th>Mean Age, y (Control/Auto)</th>
<th>Male-Female (Control/Auto)</th>
<th>Iron Supplementation</th>
<th>Transfusion Protocol Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elawad et al, 1991</td>
<td>RCT</td>
<td>Hip arthroplasty</td>
<td>15/45</td>
<td>71/71</td>
<td>9/6/24:21</td>
<td>Yes†</td>
<td>None</td>
</tr>
<tr>
<td>Lorentz et al, 1991</td>
<td>RCT</td>
<td>Hip arthroplasty</td>
<td>15/16</td>
<td>63/58</td>
<td>5:10/8:8</td>
<td>Yes</td>
<td>Hb &lt;90 in intensive care unit, or Hb &lt;100 in ward</td>
</tr>
<tr>
<td>Hoynck van Papendrecht et al, 1992</td>
<td>RCT</td>
<td>Colon resection</td>
<td>137/245</td>
<td>67/65</td>
<td>NA</td>
<td>Yes</td>
<td>Hb &lt;105, &gt;500 mL EBL</td>
</tr>
<tr>
<td>Heiss et al, 1993</td>
<td>RCT</td>
<td>Colon resection</td>
<td>62/58</td>
<td>61/59</td>
<td>31:31/30:28</td>
<td>Yes</td>
<td>Hb &lt;100</td>
</tr>
<tr>
<td>Busch et al, 1993</td>
<td>RCT</td>
<td>Colon resection</td>
<td>236/239</td>
<td>68/66</td>
<td>132:104/141:98</td>
<td>Yes</td>
<td>&gt;500 mL of EBL, Hb &lt;105</td>
</tr>
<tr>
<td>Kajikawa et al, 1994</td>
<td>RCT</td>
<td>Liver resection</td>
<td>21/10</td>
<td>NA/58</td>
<td>NA</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Love et al, 1987</td>
<td>OP</td>
<td>Cardiac surgery</td>
<td>58/58</td>
<td>55/57</td>
<td>44:14/44:14</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Toy and Strauss, 1987</td>
<td>OP</td>
<td>All types of elective surgery</td>
<td>558/33</td>
<td>52/47</td>
<td>NA</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Britton et al, 1989</td>
<td>OP</td>
<td>Cardiac surgery</td>
<td>111/104</td>
<td>64/59</td>
<td>NA</td>
<td>Yes</td>
<td>Control; Hct &lt;0.25; Auto: all auto units regardless of Hct</td>
</tr>
<tr>
<td>O’Hara et al, 1994</td>
<td>OP</td>
<td>Aortic aneurysm resection</td>
<td>72/73</td>
<td>68/68</td>
<td>67:5/64:9</td>
<td>No</td>
<td>Hct &lt;0.30 or Hb &lt;100</td>
</tr>
<tr>
<td>Giurati et al, 1995</td>
<td>OP</td>
<td>Radical hysterectomy</td>
<td>29/28</td>
<td>50/46</td>
<td>0:29/0:28</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Sandrelli et al, 1995</td>
<td>OP</td>
<td>Cardiac surgery</td>
<td>344/348</td>
<td>53/52</td>
<td>291:53/294:54</td>
<td>Yes</td>
<td>Hb &lt;80‡</td>
</tr>
<tr>
<td>Toy et al, 1992</td>
<td>OR</td>
<td>Hip arthroplasty</td>
<td>84/240</td>
<td>63</td>
<td>47/53</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Yamada et al, 1993</td>
<td>OR</td>
<td>Radical prostatectomy</td>
<td>34/37</td>
<td>71/64</td>
<td>34/0:37:0</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Clugston et al, 1995</td>
<td>OR</td>
<td>Mammoplasty</td>
<td>63/81</td>
<td>35/34</td>
<td>0:63/0:81</td>
<td>Yes</td>
<td>None</td>
</tr>
</tbody>
</table>

*Auto indicates autologous predonation; RCT, randomized controlled trial; Hb, hemoglobin value; NA, not available; EBL, expected blood loss; Hct, hematocrit value; OP, observational, prospective study; and OR, observational, retrospective study.
†Patients randomized to 4 groups: control, autologous blood predonation with no iron supplementation, autologous blood predonation with iron supplementation, and autologous blood predonation with iron and folate supplementation.
‡Also used guidelines by Goodnough et al.
§In this study, the mean age is for the entire group and the male-female ratio is a percentage.

STUDY LOCATION, SELECTION, AND EVALUATION

Of the 61 studies, 21 were rejected because there was no control group, which left 6 randomized controlled studies and 34 cohort studies. Of the concurrent control cohort studies, 25 were rejected because the control group was not appropriate (the control group was not described in 12 studies; patients had been excluded from autologous blood donation for medical reasons in 11 studies; and allogeneic blood use in the 2 groups was not described 2 studies). Six randomized controlled studies and 9 concurrent control cohort studies (7 prospective, 2 retrospective) were included in the analysis. A list of the excluded studies is available from the authors upon request. One randomized study was published as 2 separate articles in an overlapping population. The article with the greatest number of patients was used for our analysis. Disagreement among the reviewers occurred on 3 occasions regarding the eligibility of the observational studies only (k=0.86). All 6 randomized studies scored 2 on the quality scale by Jadad et al. Since it is ethically inappropriate to blind autologous blood donors to the treatment they received, the maximum possible score for quality in these studies was 3. There was no disagreement on the quality of the articles.

STUDIES INCLUDED IN THE META-ANALYSIS

Summary data from the 6 randomized and 9 concurrent control cohort studies used in the final analysis are presented in Table 1 and Table 2. The sample size in the randomized studies varied from 31 to 423 with a total of 933 patients included in the meta-analysis. The sample size in the cohort studies varied from 57 to 692 with a total of 2351 patients included in the meta-analysis.

EFFICACY IN RANDOMIZED STUDIES

The 6 randomized studies were conducted in patients who underwent the following types of procedures: colorectal surgery for bowel cancer (3), hip arthroplasty (2), and liver resection (1). All 6 studies demonstrated a statistically significant decrease in exposure to allogeneic blood in patients who predeposited autologous blood compared with those who did not. The OR when all these studies were combined was 0.17 (95% confidence interval [CI], 0.08-0.32), demonstrating that preoperative autologous blood donation decreased the exposure to allogeneic blood. The OR for colorectal surgery was 0.26 (95% CI, 0.19-0.37) compared with 0.20 (95% CI, 0.00-0.28) in patients who underwent hip arthroplasty. The OR in studies in which a transfusion protocol was reported was 0.25 (95% CI, 0.17-0.37) compared with 0.02 (95% CI, 0.00-0.24) in those that...
**Table 2. Outcomes of the Studies in the Meta-analysis**

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Preoperative Hematocrit Values (Control/Auto)</th>
<th>Day 7† Hematocrit Values (Control/Auto)</th>
<th>Estimated Mean Blood Loss, mL (Control/Auto)</th>
<th>Autologous Blood Units Transfused, % (Control/Auto)</th>
<th>Patients Who Underwent Transfusion, % (Control/Auto)‡</th>
<th>Total No. of Units Transfused (Control/Auto)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elavad et al.13 1991</td>
<td>43.0/38.5/</td>
<td>33.6/33.0/</td>
<td>2105/1524/1409/1519§</td>
<td>69</td>
<td>93/96</td>
<td>NA/93</td>
</tr>
<tr>
<td>Lorentz et al.14 1991</td>
<td>NA</td>
<td>NA</td>
<td>1720/1855</td>
<td>71</td>
<td>67/NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hoyncx van Papendrecht et al.15 1992</td>
<td>41.8/37.0</td>
<td>37.6/37.0</td>
<td>775/850 (Median)</td>
<td>NA</td>
<td>61/73</td>
<td>264/283</td>
</tr>
<tr>
<td>Heiss et al.16 1993</td>
<td>42.4/37.3</td>
<td>39.9/39.9</td>
<td>900/1000</td>
<td>NA</td>
<td>60/91</td>
<td>102/148</td>
</tr>
<tr>
<td>Busch et al.17 1993</td>
<td>42.7/37.9</td>
<td>NA</td>
<td>775/750</td>
<td>NA</td>
<td>62/75</td>
<td>NA</td>
</tr>
<tr>
<td>Kajikawa et al.18 1994</td>
<td>38.7/37.5</td>
<td>NA/NA</td>
<td>1193/1086</td>
<td>NA</td>
<td>62/80</td>
<td>NA</td>
</tr>
<tr>
<td>Love et al.19 1987</td>
<td>41.0/38.3</td>
<td>29.6/30.9</td>
<td>NA</td>
<td>NA</td>
<td>52/87</td>
<td>119/160</td>
</tr>
<tr>
<td>Toy and Strauss.20 1997</td>
<td>42.1/38.8</td>
<td>NA</td>
<td>NA</td>
<td>75</td>
<td>36/80</td>
<td>NA/740</td>
</tr>
<tr>
<td>Britton et al.21 1989</td>
<td>39.4/36.6</td>
<td>32.2/34.4</td>
<td>699/611</td>
<td>100</td>
<td>79/100</td>
<td>NA</td>
</tr>
<tr>
<td>O’Hara et al.22 1994</td>
<td>40.3/37.5</td>
<td>NA</td>
<td>2336/2519</td>
<td>NA</td>
<td>64/NA</td>
<td>NA</td>
</tr>
<tr>
<td>Giurati et al.23 1995</td>
<td>NA</td>
<td>NA</td>
<td>640/648</td>
<td>67</td>
<td>38/79</td>
<td>36/41</td>
</tr>
<tr>
<td>Sandrelli et al.24 1995</td>
<td>NA</td>
<td>NA</td>
<td>695/710</td>
<td>NA</td>
<td>46/NA</td>
<td>NA</td>
</tr>
<tr>
<td>Toy et al.24 1992</td>
<td>42.1/42.4,§</td>
<td>33.0/33.3,§</td>
<td>NA</td>
<td>NA</td>
<td>60/93,§</td>
<td>NA</td>
</tr>
<tr>
<td>Clugston et al.25 1995</td>
<td>42.0/38.6</td>
<td>33.1/33.5</td>
<td>575/700</td>
<td>54</td>
<td>21/68</td>
<td>20/41</td>
</tr>
</tbody>
</table>

*Auto indicates autologous predonation; NA, not available. Studies reporting hemoglobin values had these values converted to hematocrit values by dividing by 3.3.
†Day 7 or the value closest to day 7.
‡Any blood transfusion (allogeneic and/or autologous).
§Patients randomized to 4 groups: control, autologous blood predonation with no iron supplementation, autologous blood predonation with iron supplementation, and with iron and folate supplementation.
||Nine percent of patients who donated autologous blood preoperatively had no autologous units of blood transfused.
¶Twenty-six percent of patients who donated autologous blood preoperatively had no autologous units transfused.
§§Primary hip arthroplasty.
**Revision hip arthroplasty.

**Hematocrit Values**

Preoperative hematocrit values were an average of 3.5 units lower in patients who donated autologous blood than in patients in the control group. The last hematocrit values before patient discharge were similar in both patient groups in the 8 studies in which this was recorded, and these values were not affected by the use of a transfusion protocol. They ranged from 0.30 to 0.38 in the 7 studies reporting this outcome.

**Unused Autologous Blood**

Six studies provided data that enabled an accurate assessment of the number of autologous units not used. With the exception of the study that transfused all predonated units regardless of the patients’ hematoglobin...
or hematocrit values,20 25% to 46% of units were not used. In 2 other studies,16,17 9% and 26% of the autologous blood donor patients had none of their units returned, but data about the proportion of autologous units not used were not provided. In one study20 of patients undergoing mammoplasty, the transfusion rate in the control group was only 3%.

CLINICAL COMPlications

Only 1 of the randomized studies17 provided data on the recurrence of cancer and overall survival. It demonstrated a statistically significant increase in 4-year disease-free survival in patients with colorectal cancer who did not undergo transfusion with any blood compared with patients who underwent transfusion with either autologous or allogeneic blood (73% vs 59%, respectively; P < .001). Of the randomized studies in colorectal cancer, 2 studies16,17 provided data on the incidence of postoperative infection. There was no statistically significant increase in the risk of postoperative infection (OR, 1.44; 95% CI, 0.49-4.26). The studies included in our meta-analyses did not provide sufficient information to determine if medical complications, such as myocardial infarction, angina, prolonged hospital admission, and venous thrombosis, differed between the groups who pre-donated blood and those who did not.

This meta-analysis of 6 randomized studies suggests that preoperative donation of autologous blood reduces exposure to allogeneic blood (OR, 0.17; 95% CI, 0.08-0.32). These studies were performed in patients undergoing colorectal resection, hip arthroplasty, and liver resection. Patients undergoing cardiac, urologic, vascular, gynecological, and mammoplasty surgery were assessed in 9 cohort studies that met our inclusion criteria. The OR for the cohort studies was similar to that of the randomized controlled studies (OR, 0.19). Thus, it is likely that preoperative autologous donation of blood reduces exposure to allogeneic red blood cells in most types of surgery with considerable blood loss.

One of the striking results of this meta-analysis is that patients who predonated autologous blood were considerably more likely to receive any blood transfusion (auto-logous and/or allogeneic) than patients in the control group. This may be partly due to the lower mean preoperative hematocrit values in patients undergoing preoperative autologous donation of blood; however, it is almost certainly also due to a more liberal transfusion policy with autologous blood.20 Although some argue that the safety of autologous blood justifies a more liberal transfusion policy in autologous donors, most15 believe that the criteria for transfusion should be the same in those who predonate autologous blood and those who do not.

Autologous blood is associated with a smaller chance of transmitting viral infections than allogeneic blood. However, the likelihood of becoming infected with hepatitis or the human immunodeficiency virus with allogeneic blood is now very low. The most recent published estimate21 from the United States is 1 in 493,000 transfusions for human immunodeficiency virus, 1 in 103,000 for hepatitis C, and 1 in 63,000 for hepatitis B. In addition, an infectious agent that we are currently unaware of may be transmitted by allogeneic blood. However, noninfectious complications, such as transfusion of the wrong unit of blood because of laboratory, clerical, or ward error, bacterial contamination, and fluid overload because of excess transfusion, occur at least as frequently in recipients of autologous blood as in patients who receive allogeneic blood. The reported frequency of these complications varies, but a recent review22 from New York State found a 1 in 33,000 chance of ABO incompatibility and a 1 in 600,000 chance of a fatal acute hemolytic transfusion reaction. Thus, it is possible that autologous blood donors, if they are more likely to receive transfusion of any kind, are ultimately placed at higher risk than nondonors. The donation procedure itself is also not completely free of risk because older patients with cardiac disease are more likely to have a reaction associated with donation than younger, healthier patients.23, in one study, autologous blood donors were 12 times more likely to have a reaction requiring hospitalization than donors of blood intended for allogeneic use (the actual incidence was low in both groups: 1 of 198,000 allogeneic donations and 1 of 17,000 autologous donations). For patients to derive the full benefits of preoperative autologous blood donation, it is important that clinicians recognize that collection and transfusion of autologous blood is not entirely without risk and they should not alter the transfusion threshold.

There are a number of limitations of this meta-analysis. First, there were only 6 randomized studies with a total of 933 patients. The largest study included 475 patients, but 3 studies included fewer than 100 patients. Previous meta-analyses that included a similar number of patients were subsequently shown to have overestimated the benefit of therapy compared with large, definitive, randomized studies. Second, the results of the eligible studies were statistically and clinically heterogeneous. Since all the randomized studies found a decrease in exposure to allogeneic red blood cells with preoperative autologous donation of blood, the heterogeneity concerns the degree of benefit from autologous donation of blood, rather than whether the
Advantages include patients’ sense of control over their care, the decrease in the risk of transmission of known viral infections, the possibility of avoiding unknown infections, avoidance of alloimmunization to donor blood components and other immunomodulatory effects related to allogeneic blood transfusion, and the lack of adverse effects from the use of medications. Disadvantages include the inconvenience of predonation to the patient, medical contraindications to preoperative autologous donation of blood for some patients, a strain on the blood collection system because of the extra organizational requirements of preoperative autologous donation of blood, and difficulties with scheduling surgery. Also, in the manner the technique was used in these studies, patients who predonate autologous blood are more likely to receive any transfusion of blood (allogeneic and/or autologous) than patients who do not donate their own blood preoperatively.

Recently completed meta-analyses of randomized studies[1] (also A.L. and D.F., unpublished data, 1997) of the efficacy of aprotinin, tranexamic acid, and erythropoietin found all to be effective with ORs varying from 0.32 to 0.55. Thus, to determine which blood conservation technology is most appropriate, large direct comparisons of preoperative autologous donation of blood with the other modalities are needed. These studies will require strict transfusion policies and should incorporate economic evaluations to determine the relative advantages and disadvantages of the various options available to decrease perioperative exposure to allogeneic blood.
REFERENCES