

The Effect of Universal Leukodepletion of Packed Red Blood Cells on Postoperative Infections in High-Risk Patients Undergoing Abdominal Aortic Surgery

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We evaluated, by using a before-and-after study, the influence of leukoreduction by filtration on postoperative infections and adverse outcomes in patients undergoing elective major aortic surgery. From January 1995 to October 2000, all patients who underwent elective abdominal aortic surgery were included in the analysis. Before the introduction of systematic leukodepletion of packed red blood cells (RBCs), on April 1, 1998, 192 patients received standard or buffy-coat-depleted packed RBCs. Then, 195 patients were transfused with exclusively filtered leukodepleted packed RBCs. No major significant difference was observed between the groups of patients with regard to preoperative cardiac and pulmonary status, anesthetic and surgical techniques, or

transfusion policy. No significant difference in mortality was observed between the two groups. The incidence of postoperative infections was 31% (95% confidence interval, 25%–38%) in the Control group versus 27% (95% confidence interval, 21%–33%) in the Leukodepleted group; severe infectious complications and pneumonia were not significantly different between the two groups of patients. Cardiovascular and respiratory outcomes were not significantly different between the groups. Data from this study suggest that the effect of using leukodepleted RBC on postoperative infections is not of obvious importance.

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The presence of leukocytes in cellular blood components is thought to be associated with a number of significant adverse effects in recipients. Leukocyte reduction reduces the frequency of human leukocyte antigen alloimmunization (1). Cytomegalovirus virus and human T-cell leukemia virus infections (2) and febrile nonhemolytic transfusion reactions may also be significantly reduced (3). Also, leukoreduction might reduce the risk of the transfusion transmission of new-variant Creutzfeldt-Jakob disease (4–6), because transmission of this disease might occur through blood transfusion (7).

The immunosuppressive effects of allogeneic transfusion and the effects of leukodepletion on postoperative infections are still controversial subjects. There have been observational studies evaluating the association between allogeneic transfusion and bacterial

infection (8,9). With rare exceptions (10), these studies demonstrated an increased risk of postoperative bacteria in patients receiving allogeneic transfusions. However, most of the studies did not adequately control for other risk factors associated with infection (11). The risk of serious bacterial infection is associated with the number of units of blood received (12). We identified six clinical trials evaluating the effect of leukoreduction on postoperative bacterial infection (13–18). Four trials reported a decrease in morbidity or mortality, and two did not observe positive effects of deleukocytation. A metaanalysis did not detect clinically important decreases in mortality or postoperative infections (19). There was significant variability among the studies. However, the results of this metaanalysis are very controversial (20,21). Large clinical trials focusing on clinically important infections are still needed to provide definitive evidence of an association of infection and allogeneic blood transfusion and to document the efficacy of leukoreduction. However, it is unlikely that definitive randomized controlled clinical trials will be performed, given the decision for universal leukodepletion of the blood supply in many European countries and in Canada.

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The implementation of universal prestorage leukoreduction of all red blood cell (RBC) units in France provided an ideal opportunity to evaluate, in a high-risk group of patients undergoing major aortic surgery, the influence of leukoreduction in a before-and-after study examining the effects on postoperative infections.

Methods

Since January 1985, a database including all patients undergoing elective abdominal aortic surgery has been constructed by the Department of Anesthesiology. Patients have been included prospectively in the database by submission of a case report form including preoperative evaluation, anesthetic and surgical data, and postoperative outcome. From January 1995 to October 2000, meaning 2.5 yr before and after systematic deleukocytation in France, all patients who underwent elective abdominal aortic surgery were included in the analysis. The trial protocol's being retrospective, the submission to the ethical committee was waived, and informed consent was not required.

Patients were classified into three groups: patients not transfused (Group 1), patients transfused exclusively with autologous blood products (Group 2), and patients transfused with allogeneic blood (Group 3). Patients who received autologous and allogeneic blood products were classified in Group 3. Universal leukodepletion was applied on April 1, 1998. Accordingly, Group 3 patients were further classified as patients who received either standard or buffy-coat-poor packed RBCs (Control group) or patients transfused with filtered, leukodepleted packed RBCs (Leukodepleted group). The database was cross-checked with the Blood Bank database to verify the quality and quantity of blood products transfused. In 37 patients a discrepancy was observed between the two databases, and these patients were eliminated from the final analysis.

Patients could be included in an autologous predonation program. Patients older than 80 yr or who had severe cardiac disease, severe respiratory disease, or relative surgical emergency were excluded. Eligible patients were not systematically included in the predonation program, depending on anesthesiologist evaluation and surgical scheduling. Patients included were required to donate blood three times. The collected blood was separated into packed RBCs and fresh-frozen plasma.

Intraoperative cell saving (Cell Saver IV or Cell Saver V; Haemonetics, Braintree, MA) was used according to the standby procedure. The reservoir and the suction line were systematically mounted at the beginning of the procedure. The centrifugation kit was mounted only if at least 800 mL of blood loss was

collected. After centrifugation and washing, treated units were systematically reinfused into the patient.

Different types of allogeneic blood products were used during the study period. From January 1995 to April 1998, standard or buffy-coat-poor packed RBCs were used. Packed RBCs were prepared by the standard procedure of spinning whole blood in citrate-phosphate-dextrose solution (500 ± 50 mL blood in 73 mL citrate-phosphate-dextrose) at 3000g for 10 min with subsequent extraction of plasma. Standard packed RBCs were reconstituted with 100 mL of SAG-mannitol. Buffy coat removal after centrifugation and plasma extraction reduces the leukocyte count by 75%, to approximately 10^8 leukocytes per unit. From April 1, 1998, universal leukodepletion by filtration was systematically applied. Patients who received either standard or buffy-coat-depleted blood in the control were identified. Leukocyte-depleted packed RBCs were prepared by passing a unit of packed RBCs, prepared as described previously, through a flatbed leukocyte filter. RBC filters are composed of polyester or polyurethane fibers coated with proprietary chemicals and contained in polycarbonate housing. The nature of these proprietary chemicals varies between manufacturers, and the polyester fibers contain a net surface charge that promotes the surface adhesion of white cells. Because blood donations in Paris do not cover transfusion needs, filtered leukocyte-free packed RBCs could have been issued from different blood banks using different leukodepletion protocols with various filters. The French specification is 1×10^6 remaining white cells per unit. Most filters in current use consistently meet or exceed these standards. Prestorage filtration was generally performed during the 24 h after donation. No bedside filtration was performed.

Transfusion of autologous or allogeneic blood products was indicated according to standard rules following the recommendations of the French consensus conference (22): hemoglobin concentration was maintained between 7 and 10 g/dL, depending on the patient's cardiac and respiratory status. In patients included in the autologous predonation program, if the desired hemoglobin concentration was not achieved after transfusion of autologous units, an additional allogeneic transfusion was made.

Preoperative evaluation included clinical evaluation and complementary examinations, according to protocols of the Department of Vascular Surgery. Different protocols for preoperative cardiac evaluation were used during the study period. The main variation was the systematic preoperative coronary angiography performed during the years 1995 and 1996 in patients older than 65 yr scheduled for abdominal aortic aneurysm repair. This strategy then was abandoned because of the frequent rate of normal angiograms. Coronary artery disease was defined as a clinical history

of angina, a previous myocardial infarction, coronary stenosis >70% demonstrated by coronary angiography when indicated, or a combination of these. Chronic obstructive pulmonary artery disease was defined according to standard clinical criteria. A serum creatinine concentration >120 $\mu\text{mol/L}$ for more than 6 mo was used to define chronic renal failure.

Intraoperatively, patients were monitored with five-lead electrocardiogram (ECG) with continuous ST-T segment analysis, invasive arterial blood pressure (Solar 7000; Marquette Electronics Inc., Milwaukee, WI), pulse oxygen saturation, end-tidal CO_2 , and inspiratory and end-tidal anesthetic concentrations. In most patients, surgery was performed under general anesthesia. In some patients, by the decision of the anesthesiologist in charge, general anesthesia was associated with intrathecal analgesia with a combination of sufentanil and morphine. The antibiotic prophylaxis (cefamandole 1.5 g before incision and 0.75 g every 4 h) was modified during the study period.

Patients were operated on with the standard open surgery procedure via a median laparotomy or a lumbotomy. An abdominal aortic graft was inserted and could have been associated with the reimplantation of one or several visceral arteries. In 1997, a new surgical technique was developed in the Department of Vascular Surgery that is based on a custom-made endovascular prosthesis (23-25). Patients eligible for an endovascular prosthesis were excluded from the study because the rate of pulmonary complications is significantly less than that of conventional surgery (25).

If needed, postoperative sedation was accomplished by a propofol infusion until body temperature reached 36°C . Then extubation was performed after clinical assessment. All patients were admitted postoperatively in a postoperative acute care unit for at least 24 h after the induction of anesthesia. Postoperative care included pain treatment with different techniques (subcutaneous morphine, intrathecal morphine, and patient-controlled analgesia), respiratory physical care, plasma volume expansion, and cardiovascular care, when required. During the postoperative period, standard biochemical assays, chest radiographs, 12-lead ECG recordings, and troponin Ic measurements were performed daily on Postoperative Days 1, 2, 3, 5, and 7. The measurements of troponin Ic were repeated when any abnormal value was found (normal value $\leq 0.5 \text{ ng/mL}$).

The major clinical outcome variables prospectively analyzed were mortality and morbidity. Mortality was defined as death occurring during the 30-day period after surgery. Definitions for postoperative complications were prospectively defined when the database was started (January 1985) and have been regularly updated.

The main study outcome was bacterial infections that occurred during the postoperative period until discharge from the hospital. A patient was defined as having infection if one of the following postoperative infections was diagnosed: generalized sepsis, bacteremia, pneumonia, vascular prosthesis infection, or wound infections. A patient was defined as having severe infection if one of the following postoperative infections was diagnosed: generalized sepsis, bacteremia, or vascular prosthesis infection. Generalized sepsis was defined as the presence of localized infection with clinical evidence of bacteremia, with chills, rigor, fever, increased white blood cell count, and two positive blood cultures. Bacteremia was defined by a positive blood culture with an organism that was not a contaminant. Pneumonia was defined as the new appearance on chest radiographs of an infiltrate associated with purulent sputum, a temperature $\geq 38.5^\circ\text{C}$, an abnormal increase in white blood cell count, and a favorable outcome after antibiotic treatment. The criteria for vascular prosthesis infection were generalized sepsis and positive local bacteriology during reoperation. The criterion for wound infections was clinical local aspect compatible with infection associated with positive bacteriology.

Postoperative myocardial infarction was defined as a troponin Ic level $>1.5 \text{ ng/mL}$ (14,15) on two successive measurements, with or without associated ECG changes (new Q waves lasting $\geq 0.04 \text{ s}$ and 1 mm deep or persistent ST-T depression $>1 \text{ mm}$). Congestive heart failure was defined as the postoperative need of sympathomimetic support associated with classic chest radiogram changes and an impairment in left ventricular function on postoperative echography. Arrhythmias were defined as the appearance of ventricular tachycardia or supraventricular tachyarrhythmias requiring treatment. Acute respiratory failure was defined as the presence of atelectasis or pneumonia, as the postoperative need of mechanical ventilation for more than 24 h, or as the clinical need for tracheal reintubation and mechanical ventilation occurring after the first postoperative day. Renal failure was defined as an increase of more than 50% of the preoperative serum creatinine level or a postoperative absolute value $\geq 200 \mu\text{M/L}$.

Gastric hemorrhage was defined as the appearance of nasogastric or rectal bleeding associated with a decrease in hemoglobin level of at least 2 g/dL in the absence of any other source of continuing bleeding. Criteria for hepatic dysfunction were a serum bilirubin $>100 \mu\text{mol/L}$, alkaline phosphatase >3 times normal, or both (16). Major surgical complications were defined as peripheral vascular occlusion or postoperative hemorrhage in relation to the surgical site or any complication requiring immediate redo surgery (acute cholecystitis, intestinal ischemia, or occlusion).

The number of patients to be included was determined with the Casagrande and Pike (26) formula. Assuming that 30% of patients had at least one infection after aortic surgery and there was an expected 50% reduction of this percentage with leukodepleted packed RBCs, 170 patients in each group (340 in total) were needed to demonstrate a possible benefit of this technique with an α risk of 0.05 and a β risk of 0.10. On the basis of our previous prospective studies indicating that 40% of abdominal aortic patients received allogeneic blood transfusions, we were able to estimate that 2.5 yr before-and-after systematic deleukocytation would allow gathering the adequate number of patients.

Data were expressed as mean and SD (Gaussian variables); median $\pm$ interquartile range (non-Gaussian variables); or number, percentage, and 95% confidence intervals (CI) when appropriate. The Kolmogorov-Smirnov test was used to assess the Gaussian distribution of variables. Comparison of two measures was performed with Student's *t*-tests. Comparison of several means was performed with repeated-measures analysis of variance. Comparison of two medians was performed with the Mann-Whitney *U*-test. Comparison of two percentages was performed with Fisher's exact method.

All *P* values are two tailed, and a *P* value of <0.05 was required to reject the null hypothesis. Statistical analysis was performed on a computer using SPSS® Base 10.0 for Windows (SPSS Inc., Chicago, IL).

Results

From January 1995 to December 2000, 925 patients who underwent elective abdominal aortic surgery were included in the database. Patients who underwent an endovascular prosthesis procedure ($n = 182$) were excluded from the analysis. Among the 743 remaining patients, 144 patients were not transfused, 212 received only autologous blood products, and 387 were transfused with allogeneic blood (Fig. 1). Preoperative clinical evaluation of patients transfused with allogeneic blood was significantly different from that of patients exclusively transfused with autologous blood with regard to mean age, prevalence of symptoms of clinical coronary disease, left ventricular heart failure, and severe renal insufficiency (Table 1). Patients transfused with allogeneic blood also developed more postoperative complications when compared with patients who were not transfused or who were transfused exclusively with autologous blood (Table 2).

Patients transfused with allogeneic blood were analyzed according to the type of allogeneic blood that they received. Before the introduction of systematic leukodepletion of packed RBCs, on April 1, 1998, 192 patients received standard ($n = 148$) or exclusively

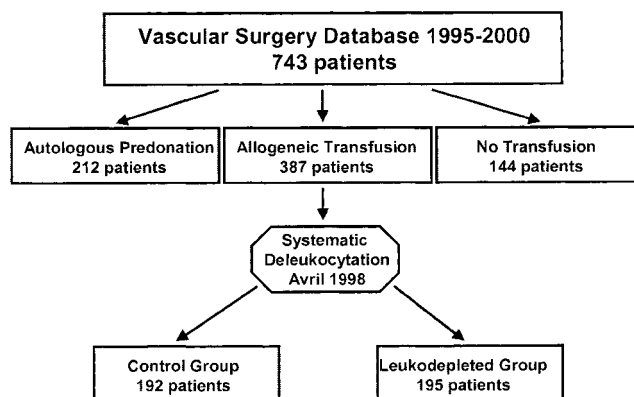


Figure 1. Protocol design: the implementation of universal prestorage leukoreduction of all RBC units in France provided an ideal opportunity to evaluate, in a high-risk group of patients undergoing major aortic surgery, the influence of leukoreduction on a before-and-after study examining the effects on postoperative infections.

buffy-coat-depleted packed RBCs ($n = 44$). Then, 195 patients were transfused exclusively with filtered leukocyte-free packed RBCs. On preoperative evaluation, these two subgroups of patients differed only in incidence of hypertension, treatment with diuretics, and prevalence of chronic respiratory insufficiency. In relation to the different preoperative strategies for preoperative evaluation, several statistically significant differences of the number of performed preoperative coronarographies, the frequency of significant coronary stenosis, and the number of patients with preoperative myocardial revascularization were observed between the two groups (Table 3). No significant difference related to the surgical procedure was observed between the two groups (Table 4). No significant difference was observed in the transfusion policy between the two periods of the study (Table 5). Patients received 3 ± 4 U (mean $\pm$ interquartile range) of packed RBCs in the Control group and 4 ± 4 U in the Leukodepleted group. No significant difference in morbidity or mortality was observed between the two groups (Table 6). Cardiovascular and respiratory outcomes were not significantly different between the Control and Leukodepleted groups. The incidence of postoperative infections, severe infectious complications, and multiple organ failure was not significantly different between the two groups of patients.

During the same study period, in nontransfused patients, the mortality rate (1.5% [95% CI, -1.5% – 4.6%] vs 1.5% [95% CI, -1.5% – 4.6%]), the incidence of infections (17% [95% CI, 8% – 26%] vs 12% [95% CI, 4% – 20%]), and the incidence of severe infections (1.5% [95% CI, -1.5% – 4.5%] vs 3% [95% CI, -1.1% – 7.2%]) were not significantly different between the two epochs before and after deleukocytation, indicating that no other change in the management of these patients had an effect on postoperative mortality and infection rates.

Table 1. Preoperative Evaluation of Patients Transfused with Allogeneic Blood or Autologous Blood or Not Transfused

Variable	Transfused with allogeneic blood	Transfused with autologous blood	Not transfused
No. patients	387	212	144
Age, yr (mean $\pm$ SD)	68 $\pm$ 10*†	62 $\pm$ 9	61 $\pm$ 11
Previous CABG or PTCA, <i>n</i> (%)	70 (18.1%)‡§	18 (8.5%)	12 (8.3%)
Clinical coronary heart disease, <i>n</i> (%)	173 (44.7%)§	52 (24.5%)	39 (27.1%)
Left ventricular insufficiency, <i>n</i> (%)	30 (7.8%)¶	6 (2.8%)	10 (6.9%)
COPD, <i>n</i> (%)	154 (39.8%)	80 (37.7%)	54 (37.5%)
Respiratory insufficiency, <i>n</i> (%)	26 (6.7%)†	11 (5.2%)	8 (5.6%)
Severe renal insufficiency, <i>n</i> (%)	50 (12.9%)§	5 (2.4%)	4 (2.8%)
Diabetes mellitus, <i>n</i> (%)	32 (8.3%)	16 (7.5%)	15 (10.4%)

CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty; COPD = chronic obstructive respiratory disease.

* $P < 0.05$; ‡ $P < 0.01$; || $P < 0.001$, transfused with allogeneic blood versus not transfused.† $P < 0.05$; ¶ $P < 0.01$; § $P < 0.001$, transfused with allogeneic blood versus transfused with autologous blood.**Table 2.** Main Postoperative Complications in Patients Transfused with Allogeneic Blood or Autologous Blood or Not Transfused

Variable	Transfused with allogeneic blood	Transfused with autologous blood	Not transfused
Cardiac complications	67 (17.3%)*†	20 (9.5%)	12 (8.3%)
Severe cardiac complications	45 (11.6%)*†	8 (3.8%)	6 (4.2%)
Pneumonia	79 (20.4%)‡§	30 (14.2%)	13 (9.0%)
Severe respiratory complications	56 (14.5%)†‡	7 (3.3%)	3 (2.1%)
Local infections	27 (7.0%)§	6 (2.8%)	6 (4.2%)
Infections	112 (28.9%)†‡	36 (17.0%)	19 (13.2%)
Severe infections	42 (10.9%)†‡	7 (3.3%)	3 (2.1%)
Prolonged stay in the ICU	67 (17.3%)†‡	8 (3.8%)	3 (2.1%)
Multiple organ failure	33 (8.5%)†‡	0 (0%)	1 (0.7%)
Death	28 (7.2%)*†	0 (0%)	2 (1.4%)

ICU = intensive care unit.

* $P < 0.01$; ‡ $P < 0.001$, transfused with allogeneic blood versus not transfused.§ $P < 0.05$; † $P < 0.001$, transfused with allogeneic blood versus transfused with autologous blood.

Discussion

The major finding of this study was the absence of a significant effect of universal leukodepletion on postoperative infections in high-risk patients undergoing elective abdominal aortic surgery. Although all of the benefits of leukoreduction are important to recipients, it is likely that the most significant potential benefit is a decrease in transfusion-related immune suppression. Kaplan et al. (27) found a moderate decrease in T4/T8 lymphocyte ratios and decreased natural killer activity after repeated allogeneic transfusions. Leukocyte-associated alterations may explain the decrease in the number of rejection episodes (28–30) and improved renal allograft survival observed after allogeneic blood transfusions (31,32). Opelz et al. (33) confirmed their original data in a multicenter clinical trial in which all renal allograft recipients received modern immunosuppressive regimens. A large number of studies have also suggested that allogeneic transfusions accelerate cancer growth (17,34–43), perhaps because of altered immune surveillance. These data suggest that there are long-term immuno-

suppressive effects after nonleukoreduced allogeneic RBC transfusions.

These altered immune responses after allogeneic RBC transfusions may also predispose transfusion recipients to nosocomial infections (15,17,38,44–48). One study demonstrated a dose-response relationship between the number of transfusions and postoperative infections after colorectal surgery (49). A second retrospective study, by Carson et al. (12), observed a similar dose-dependent increase in postoperative infections in 9598 consecutive hip fractures. In summary, there is convincing laboratory and some weaker clinical evidence that allogeneic transfusions induce immune suppression in recipients.

Many authors have suggested that RBC filtration could be used to decrease immunomodulation consequences of allogeneic transfusion (19,21,50,51). Several randomized controlled clinical trials evaluated the immune consequences of RBC transfusions, contrasting rates of cancer recurrence, postoperative infections, or both. Investigators compared either leukocyte-depleted (13–18) or autologous transfusions (38,52) with allogeneic RBCs. Contradictory conclusions have

Table 3. Preoperative Evaluation of Patients Transfused with Standard or Buffy-Coat-Depleted Allogeneic Blood (Control Group) or with Leukodepleted Blood (Leukodepleted Group)

Variable	Control group	Leukodepleted group
No. patients	192	195
Age, yr (mean $\pm$ SD)	68 $\pm$ 9	68 $\pm$ 11
Sex (M/F)	166/26	171/24
Previous myocardial infarction	37 (19.3%)	38 (19.5%)
Previous CABG or PTCA	36 (18.8%)	34 (17.4%)
Clinical coronary heart disease	87 (45.3%)	86 (44.1%)
Left ventricular insufficiency	11 (5.7%)	19 (9.7%)
Hypertension	97 (50.5%)*	134 (68.7%)
Nitrates	42 (21.9%)	31 (15.9%)
β -Blockers	57 (29.7%)	63 (32.3%)
ACE inhibitors	45 (23.4%)	51 (26.2%)
Calcium blockers	75 (39.1%)	79 (40.5%)
Diuretics	24 (12.5%)+	42 (21.5%)
Preoperative coronary angiography	89 (46.6%)*	47 (24.1%)
Coronary stenosis	59 (30.7%)+	37 (19.0%)
Triple vessel disease	15 (7.8%)	13 (6.7%)
Preoperative PTCA or CABG	30 (15.6%)‡	18 (9.2%)
COPD	77 (40.1%)	77 (39.5%)
Respiratory insufficiency	18 (9.2%)‡	8 (4.2%)
Moderate renal insufficiency	19 (9.9%)	18 (9.2%)
Severe renal insufficiency	23 (12.0%)	27 (13.8%)
Diabetes mellitus	16 (8.3%)	16 (8.2%)

Data are presented as *n* (%) unless otherwise noted.

CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty; COPD = chronic obstructive pulmonary disease; ACE = angiotensin-converting enzyme.

* $P < 0.001$; + $P < 0.01$; ‡ $P < 0.05$, transfused with nonleukodepleted blood versus transfused with leukodepleted blood.

Table 4. Surgical Procedure, Surgery Duration, Stay in the Postoperative Acute Care Unit (PACU), and Hospital Stay in Patients Transfused with Standard or Buffy-Coat-Depleted Allogeneic Blood (Control Group) or with Leukodepleted Blood (Leukodepleted Group)

Variable	Control group	Leukodepleted group
Abdominal aortic aneurysm, <i>n</i> (%)	135 (70.3%)	135 (69.2%)
Aortoiliac occlusive disease, <i>n</i> (%)	57 (29.7%)	60 (30.8%)
Associated surgery, <i>n</i> (%)	81 (42.4%)	92 (47.2%)
Surgery duration (h) ^a	3.7 $\pm$ 2.2	3.5 $\pm$ 2.3
Artificial ventilation duration (h) ^a	3.0 $\pm$ 4.0	2.0 $\pm$ 4.0
PACU stay (h) ^a	29 $\pm$ 27	40 $\pm$ 24
Hospital stay (days) ^a	12 $\pm$ 6	12 $\pm$ 8

^a Median $\pm$ interquartile range.

been drawn from the trials examining postoperative infections. Houbiers et al. (14) found an increased rate of postoperative infections in patients receiving leukodepleted as opposed to allogeneic RBCs (42% vs 36%, $P < 0.05$). However, other studies (15–17,38,52) documented clinically important decreases in postoperative infections in patients receiving leukodepleted allogeneic RBCs as compared with standard allogeneic RBC products. The most recent study by van de Watering et al. (13) observed a decrease in 30-day mortality from 7.8% in patients receiving buffy-coat-depleted RBCs compared with 3.6% and 3.3% ($P = 0.015$) in cardiovascular surgical patients receiving either fresh-filtered or stored-filtered RBCs, respectively. However, the number of events was small,

suggesting that the mortality estimates might be quite unstable. In addition, the number of patients with infections was not significantly different between patients treated with filtered blood or with buffy-coat-depleted RBCs. A metaanalysis was performed to evaluate whether allogeneic transfusion was associated with infection (19). This analysis included leukoreduction and autologous transfusion trials, except for the three most recent studies (13,17,18), which had not been published. The summary risk ratios were 0.95 (95% CI, 0.79–1.15) for all-cause mortality and 1.06 (95% CI, 0.88–1.28) for cancer recurrence. There was significant heterogeneity in the postoperative infection data. Trials published by one group (15,16) had a much higher risk than the other trials. The summary

Table 5. Transfusion Variables in Patients Transfused with Standard or Buffy-Coat-Depleted Allogeneic Blood (Control Group) or with Leukodepleted Blood (Leukodepleted Group)

Variable	Control group	Leukodepleted group
Preoperative hemoglobin (g/dL) ^a	12.0 ± 2.6	12.1 ± 2.1
Postoperative hemoglobin (g/dL) ^a	9.4 ± 1.5	9.7 ± 1.3
Intraoperative blood loss (mL) ^a	1500 ± 1500	1500 ± 1500
Postoperative blood loss (mL) ^a	500 ± 550	450 ± 760
ANH (patients)	5 (2.6%)	3 (1.5%)
Cell Saver (patients)	105 (54.7%)	126 (64.6%)
Cell Saver cycles (U) ^a	1 ± 3	2 ± 3
Allogeneic packed RBCs (U) ^a	3 ± 4	4 ± 4
Allogeneic FFP (U) ^a	0 ± 0	0 ± 0
Allogeneic blood products (U) ^a	3 ± 4	4 ± 4

ANH = acute normovolemic hemodilution; RBC = red blood cells; FFP = fresh-frozen plasma.

^a Median ± interquartile range.**Table 6.** Postoperative Complication Rate (95% Confidence Interval) in Patients Transfused with Standard or Buffy-Coat-Depleted Allogeneic Blood (Control Group) or with Leukodepleted Blood (Leukodepleted Group)

Variable	Control group	Leukodepleted group
Pneumonia	22.4% (16.5%–28.3%)	18.5% (13.0%–23.9%)
Local infections	7.3% (3.6%–11.0%)	6.7% (3.2%–10.2%)
Infections	31.3% (24.7%–37.8%)	26.7% (20.5%–32.9%)
Severe infections	12.0% (7.4%–16.6%)	9.7% (5.6%–13.9%)
Postoperative myocardial infarction	6.3% (2.8%–9.7%)	8.2% (4.4%–12.1%)
Postoperative left ventricular failure	5.2% (2.1%–8.4%)	6.2% (2.8%–9.5%)
Supraventricular arrhythmias	5.7% (2.4%–9.0%)	8.2% (4.4%–12.1%)
Ventricular arrhythmias	1.0% (–0.4%–2.5%)	0%
Cardiac complications	16.1% (10.9%–21.4%)	18.5% (13.0%–23.9%)
Cardiac death	3.1% (0.7%–5.6%)	1.0% (–0.4%–2.4%)
Severe cardiac complications	10.9% (6.5%–15.4%)	12.3% (7.7%–16.9%)
Severe respiratory complications	16.1% (10.9%–21.4%)	12.8% (8.1%–17.5%)
Acute renal failure	16.1% (10.9%–21.4%)	14.4% (9.4%–19.3%)
Gastric hemorrhage	6.3% (2.8%–9.7%)	5.1% (2.0%–8.2%)
Surgical reexploration	16.7% (11.4%–21.9%)	12.3% (7.7%–16.9%)
Prolonged stay in the ICU	16.7% (11.4%–21.9%)	17.9% (12.6%–23.3%)
Multiple organ failure	9.4% (5.3%–13.5%)	7.7% (4.0%–11.4%)
Death	8.9% (4.8%–12.9%)	5.6% (2.4%–8.9%)

ICU = intensive care unit.

risk ratio was 1.00 (95% CI, 0.76–1.32) for the four studies that were appropriate to subject to metaanalysis. McAlister et al. (19) concluded that more studies are required before a definitive statement can be made and that at this time there is no evidence that allogeneic blood transfusion increases the risk of clinically important adverse sequelae in patients with cancer who are undergoing surgery. This metaanalysis is very controversial (20,21).

In the Control group, 23% received exclusively buffy-coat-depleted packed RBCs. Buffy-coat removal after centrifugation and plasma extraction reduces the leukocyte blood by 75%, to approximately 10⁸ leukocytes per unit. Buffy-coat depletion should not have influenced our data, because most studies investigating the effect of deleukocytation on postoperative infections have compared buffy-coat-depleted blood

with filtered blood (13,14,16,17). Two trials found a positive effect of leukodepletion on postoperative infections (16,17), and two others did not (13,14). Because patients included in our study were transfused partially or completely with standard packed RBCs, the effect of leukocyte filtration on postoperative infections was more likely to be demonstrated.

The number of packed RBCs transfused to the patients is relatively high in our study, because they received a median of 4 U of packed RBCs. Indeed, several authors have demonstrated a dose-response relationship between the number of transfusions and postoperative infections after colorectal surgery (49) or hip fractures (12). Accordingly, it could be suggested that the influence of leukodepletion on the rate of postoperative infections may decrease with the number of units transfused to the patient. Among randomized studies on

leukodepletion, the number of transfused units is available only for four studies (13-16). Only the study from van de Watering et al. (13) reported a number of transfused units that was comparable to ours. Although this study observed a significant decrease in postoperative mortality in the group of patients transfused with leukodepleted blood, the rate of postoperative infections was not significantly different between the two groups.

Although data were entered prospectively into the database, this study is in essence a retrospective before-and-after study. However, no major significant difference was observed between the groups of patients transfused with leukodepleted and nonleukodepleted packed RBCs with regard to preoperative status, anesthetic and surgical techniques, and transfusion policy. A frequent rate of coronary stenosis was observed during the first epoch of the study. However, during the years 1995-1996, a systematic coronary angiography was performed in patients older than 65 years scheduled for abdominal aortic aneurysm repair. This strategy was abandoned because of the frequent rate of normal examinations. Indications for coronary angiography were then based on clinical symptoms of coronary artery disease. In conclusion, we believe that the observed differences were due to a difference of strategy and not to a difference in the severity of preoperative cardiac status.

Because there was a small trend toward a smaller number of patients with postoperative infections, the power of the study to demonstrate a significant difference could be discussed. The number of patients to be included was determined assuming that 30% of patients would have at least one infection after aortic surgery and expecting a 50% reduction of this percentage with leukodepleted packed RBCs. A total of 340 patients was needed to demonstrate a possible benefit of this technique with an α risk of 0.05 and a β risk of 0.10. This hypothesis was rejected by our analysis. According to the rate of complications observed in this study, more than 5400 patients would be needed to demonstrate a significant difference between the two groups. This calculation demonstrates that the effect of deleukocytation on postoperative infections is really minor.

In conclusion, there are conflicting clinical trials supporting the use of prestorage leukoreduction in patients at risk of adverse consequences from immune suppression induced by allogeneic RBC transfusions. The implementation of universal prestorage leukoreduction of all RBC units in France provided an ideal opportunity to evaluate, in a high-risk group of patients undergoing major aortic surgery, the process of leukoreduction on a before-and-after study examining the effects on postoperative infections. Data from this study suggest that the effect of deleukocytation on postoperative infections seems to be of minor importance.

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