Beneficial Effects of Leukocyte Depletion of Transfused Blood on Postoperative Complications in Patients Undergoing Cardiac Surgery

A Randomized Clinical Trial

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***Background*—**Leukocytes in transfused blood are associated with several posttransfusion immunomodulatory effects. Although leukocytes play an important role in reperfusion injury, the contribution of leukocytes in transfused blood products has not been investigated. To estimate the role and the timing of leukocyte filtration of red cells in cardiac surgery, we performed a randomized study.

***Methods and Results*—**Patients scheduled for cardiac surgery were randomly allocated to receive either packed cells without buffy coat (PC, n=306), fresh-filtered units (FF, n=305), or stored-filtered units (SF, n=303) when transfusion was indicated. We evaluated the periods of hospitalization and stay at the intensive care unit, and the occurrences of postoperative complications up to 60 days after surgery. The average hospital stay was 10.7 days, of which 3.2 days were in the intensive care unit, without significant differences between the groups. In the PC trial arm, 23.0% of the patients had infections versus 16.9% and 17.9% of the patients in the leukocyte-depleted trial arms (P=.13). Within 60 days, 45 patients had died, 24 patients in the PC trial arm (7.8%), versus 11 (3.6%) and 10 (3.3%) patients in the FF and SF trial arms, respectively (P=.015).

***Conclusions*—**In cardiac surgery patients, especially when more than three blood transfusions are required, leukocyte depletion by filtration results in a significant reduction of the postoperative mortality that can only partially be explained by the higher incidence of postoperative infections in the PC group. **(*Circulation*. 1998;97:562-568.)**

Key Words: leukocytes ■ blood ■ surgery ■ mortality ■ coronary disease

Transfusion of allogenic leukocytes may result in unwanted transfusion sequelae[1,2] such as HLA-antibody formation,[3] transmission of viruses,[4] febrile transfusion reactions, graft versus host disease,[5] and, ex vivo, the depression of lymphocyte transformation tests[6] and natural killer cell functions.[7] Hampered wound healing, increased risk of anastomotic leakage, and postoperative infections are also shown to be related to perioperative blood transfusions,[7-9] and in some studies even a role for transfused leukocytes was observed.[8,10] Filtration of allogenic blood products to remove leukocytes contributes to reduction of alloimmunization[1,2] and cytomegalovirus transmission.[4] Whether the filtration of blood is beneficial with regard to postoperative infections compared with modest leukocyte depletion by buffy coat removal still remains open.[9,10] Moreover, it is not known whether prestorage leukocyte depletion (ie, filtration within 24 hours after donation) or poststorage depletion (ie, filtration shortly before transfusion) is preferred. Poststorage filtration does not remove leukocyte fragments that are formed during storage and it does not prevent cytokine production during storage,[11-14] but it does remove the microaggregates formed by leukocyte fragments and platelets. On the basis of animal experiments evaluating leukocyte antibody formation or growth enhancement of tumors, it is advised to filter the blood within 24 to 36 hours after donation.[14] Because there are no conclusive results concerning this topic in humans,[15] we designed a single-center, randomized, controlled clinical trial in cardiac surgery patients.

Adult patients undergoing cardiac surgery (bypass and/or valve surgery) were selected as eligible subjects because they form a large, rather homogeneous, likely-to-be-transfused, patient group that routinely receives unfiltered blood products. In this trial, two comparisons with regard to transfusion policies are made: first, the use of buffy coat–depleted blood

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products versus by filtration leukocyte depleted blood products, and second, when filtration is applied, the use of prestorage versus poststorage leukocyte depletion. Accordingly, three trial arms are included. The primary end points of the study were postoperative infections and HLA antibody formation. For all study arms the primary and secondary end points in relation to the type and number of transfusions received were evaluated. The large amount of work for the antibody screening is still in progress and will be reported later on. Here we report on the incidence of postoperative infections and on some of the secondary end points, especially the duration of hospitalization and the postoperative mortality within 60 days.

Methods

Study Design

The trial protocol was approved by the ethical committee and informed consent was obtained from the patients. Before cardiac surgery, patients were, by means of a randomization list at the hospital transfusion service, randomly allocated to one of the following three trial arms: (1) the PC trial arm, in which when transfusion was indicated, standard packed cells (PC) without buffy coat were transfused, (2) the prestorage filtration FF trial arm, in which when transfusion was indicated, freshly filtered (ie, <24 hours after donation) units were transfused, and (3) the poststorage filtration SF trial arm, in which when transfusion was indicated, 6- to 20-day stored packed cells without buffy coat were filtered shortly before transfusion.

Because of logistic reasons it was decided beforehand that patients in the SF trial arm would receive FF units if no compatible SF units were in store and when patients in the FF or SF trial arm needed more than 10 units within 48 hours, further transfusions would consist of PC units. In all trial arms the same transfusion indications were used, aiming at a hemoglobin level >6.0 mmol/L. The primary end points of the study were postoperative infections and HLA antibody formation. Mortality, hospitalization period, and other postoperative complications were secondary end points. The study size was based on the requirement to detect a 10% difference in incidence of postoperative infections and a 15% difference in immunization between standard (PC) and filtered (FF/SF) blood.

Patient Population

Adult patients undergoing coronary artery bypass graft (CABG) surgery, cardiac valve surgery, or a combination of both, who had not received blood within the last 6 months, were eligible. Nine hundred forty-four patients were randomized between March 1992 and August 1994. Thirty patients were excluded from analysis: 19 patients because they were shown to have received blood transfusions within the last 6 months before surgery and 11 because cardiac surgery was cancelled for various reasons. The included population therefore consisted of 914 patients. The surgeons and anesthetists were blind to the randomization result. All patients were cooled systemically to 27°C, and the same cardiopulmonary bypass (CPB) circuits with a 40-μm arterial filter were used in all trial arms. Antibiotic prophylaxis was given for 24 hours with CABG and for 48 hours with valve or combined surgery. After termination of the CPB, heparin was neutralized (1 vol/vol) with protamine sulfate. Further adjustments with protamine were guided by the activated clotting time (ACT).

Blood Products

For all trial arms the shelf life of the blood (ie, time between donation and transfusion) had to be between 7 and 21 days. The packed cells were prepared by the standard procedure of spinning whole blood in citrate-phosphate-dextrose (CPD) solution (500±50 mL blood in 73 mL CPD) at 3000*g* for 10 minutes with subsequent extraction of plasma and buffy coat. PC were reconstituted with 100 mL SAG-Mannitol. The average remaining leukocyte content was (mean±SD) $0.8\pm0.5\times10^9$ leukocytes per unit PC as counted by hemocytometry (Sysmex K1000, TOA Medical Electronics Europe). The FF units were prepared by passing a <24-hours-old unit of PC (prepared as described above) through a Cellselect-Optima leukocyte filter (NPBI, Emmer-compascuum, which is also merchandized as Erypur-Optima, Organon Technica), a nonwoven polyester flatbed filter. The SF units were prepared by passing a 6- to 20-day stored unit of PC through a Cellselect-Optima leukocyte filter. The Nageotte counting chamber was used for counting leukocytes in the filtered products; the average leukocyte content (mean±SD) was $1.2\pm1.4\times10^6$ per FF unit and $1.1\pm1.4\times10^6$ per SF unit.

Postoperative Bacterial Infections

For diagnosing postoperative bacterial infections the US CDC (Centers for Disease Control and Prevention) definitions for nosocomial infections were used.[16] Only respiratory tract infections (positive sputum culture and at least two of the following symptoms: fever, pulmonary infiltrate on radiograph, or clinical signs and symptoms), bacteriuria (positive urine culture with $>10^5$ white blood cells/mL with fever and/or clinical symptoms of cystitis), bacteremia (>1 positive blood culture, fever, and septic shock symptoms), and wound infections (positive wound fluid culture and local symptoms or abscess), were found in the study population.

Mortality

Patient survival was registered until day 60. Many patients concluded their postoperative contact with the thrombosis services between day 60 and day 90 and were thereafter controlled only by their local cardiologist.

Analyses and Statistics

Demographic, clinical, blood transfusion, and laboratory data were collected and checked with the patient records and the hospital computer information system. These data were entered into a database and converted to SPSS for statistical analysis.

In the analyses, three trial arms (PC versus FF versus SF) were compared; when indicated, nonfiltered versus leukocyte depleted, filtered transfusions (PC versus LD; LD=FF+SF) were also analyzed. For the infection analyses, 5 patients who had died during (the day of) surgery were excluded.

The first analyses were performed according to randomization (intention to treat), using all 914 patients. Since the postoperative effects of transfused blood were the main subject of the trial, in an additional analysis (according to transfusion) patient groups were made according to the actually received type of blood, and subgroups were defined according to the number of transfusions received. In the analysis according to transfusion, the 10 patients who, because of clerical errors had solely received a type of blood they had not been randomized for (transfusion violations), were crossed over to the group of the actually received type of blood. The 66 patients who had received more than one type of blood, either because of clerical error or because they needed >10 units within 48 hours, remained in their original trial arm.

For comparison of discrete parameters, χ^2 statistics were applied. Comparison of continuous parameters was done with ANOVA or the Kruskal-Wallis test. Mortality within 60 days was analyzed with Kaplan-Meier curves and log-rank analyses. As a yes/no phenomenon, mortality within 60 days was multivariately analyzed with logistic regression to identify risk factors.

Results

Patient Characteristics

The patients in the three trial arms are comparable with respect to patient characteristics and clinical variables (Table 1). As a university hospital, we have a regional function in performing more complex surgery on more high-risk patients. This is reflected by 30% of the patients being older than 70 years, 60% of the patients undergoing CABG

TABLE 1. Patient Characteristics

	PC	FF	SF
Included patients	306	305	303
Age,* y	64.4±9.5	62.9±9.8	63.3±9.1
<55, %	18.3	20.7	18.0
55-65, %	27.5	28.9	29.2
66-75, %	39.9	41.3	43.6
>75, %	14.4	9.2	8.5
Sex			
Male, n	221	225	206
Female, n	85	80	97
History of			
Heart surgery, %	14.7	15.7	14.9
Myocardial infarction, %	50.3	44.6	46.4
Present			
Aortic insufficiency, %	9.2	8.8	10.8
Decomp cordis, %	3.5	3.3	3.6
Preoperative			
Hb*, mmol/L	8.8±0.9	8.9±0.9	8.8±0.9
Ht*, fraction	0.42±0.04	0.43±0.04	0.42±0.04
Platelet count*, $\times 10^9$/L	233±57	236±60	233±60
Peroperative			
Type of surgery			
Bypass, %	76.5	73.8	76.6
Grafts†	2.22	2.26	2.23
IMA‡, %	25.4	25.8	26.8
Valve, %	16.0	19.0	18.5
Both, %	7.5	7.2	5.0
Surgery*, min	127±56	125±51	121±50
Cardiopulmonary bypass*, min	68±28	70±31	66±29
Myocardial infarction, %	5.88	5.90	6.27
Postoperative			
Hb*, mmol/L	6.6±0.7	6.6±0.7	6.5±0.7
Ht*, fraction	0.32±0.03	0.31±0.03	0.31±0.03
Platelet count*, $\times 10^9$/L	125±44	131±48	127±46

Patient characteristics of the 914 included patients in the packed cells (PC), the fresh-filtered (FF), and the stored-filtered (SF) trial arms. No statistically significant differences between the three groups are present.

*Mean±SD.

†Mean number of grafts per patient.

‡% internal mammary artery used as graft.

having a history of myocardial infarction, and 75% of the bypasses being a venous graft. In our group of 914 relatively high-risk patients, 48 did not receive any blood transfusion, 777 received 1 to 10 blood transfusions (mean, 5.5; median, 4), and 89 needed more than 10 transfusions (mean, 16.9; median, 14). These different transfusion categories are equally distributed over the three trial arms. Transfusion violations caused by clerical errors were found three times in the FF and seven times in the SF arm; 23 patients in the FF trial arm and 43 patients in the SF trial arm received, according to protocol, additional blood products from another trial arm (Table 2).

Postoperative Infections

Considering all 909 patients at risk for postoperative infection, 195 bacterial infections occurred in 175 patients (19.3%). Of these, 96 patients were diagnosed with a respiratory tract infection, 65 patients had a period of bacteriuria, 19 patients had bacteremia, and 15 had a wound infection, of which 4 developed a mediastinitis. Bacterial infections were seen more frequently in the PC trial arm: 78 infections in 70 patients (23.0%) versus 58 in 51 (16.9%) and 59 infections in 54 patients (17.9%) in the FF and SF trial arms, respectively. This difference was not statistically significant in the intention-to-treat analysis (P=.13, Table 3).

For the analysis of the postoperative infections according to transfusion specified in Table 4, 861 patients were evaluable. The infection rate was 23.5% in the PC-transfused group versus 17.9% in both the FF- and the SF-transfused groups (8.3% in nontransfused). With the subgroup analysis of patients transfused with >3 units of blood, the infection rates became 31.4% in the PC-transfused group versus 23.8% and 21.3% in the FF- and SF-transfused groups, respectively. When the PC-transfused patients are compared with the LD–transfused patients, it shows a clear and significant lower infection rate in the patient group receiving leukocyte-depleted blood transfusions (P=.04).

Hospitalization

The average hospitalization period was 10.7±7.2 days (mean±SD) for the total population and showed no significant differences between the trial arms (P=.62). The patients in the PC trial arm spent on average 3.5 days in the intensive care unit (ICU) versus 3.2 and 3.0 days for FF and SF patients, respectively (P=.095, Table 3).

The analysis according to transfusion revealed a small (clinically not relevant) difference in time spent in the ICU between the PC-transfused and the leukocyte-depleted–transfused group (3.54 versus 3.19 days, P=.043).

Mortality

The analysis on mortality within 60 days after surgery shows a significant difference among the three trial arms. Twenty-four patients died in the PC group versus 11 in the FF group and 10 in the SF group (7.8% versus 3.6% versus 3.3%, P=.019, Table 3). The number of patients who died of cardiac causes (ie, infarction, congestive heart failure, or arrhythmia) is slightly but not significantly higher in the PC trial arm. A highly significant difference is found in the number of patients who died of noncardiac causes such as multiorgan failure or dehiscence of the aortic bypass anastomosis (P=.001, Table 3).

In the analysis according to transfusion, the mortality within 60 days was significantly lower in the patient groups that had received at least part of the transfusions as leukocyte-depleted blood (FF or SF) compared with the patient group that has received solely PC units (P=.025, Table 5). The number of blood transfusions shows a clear dose-effect relation with the chance on postoperative mortality with all three types of blood. No difference in mortality between the transfusion groups is observed when 1 to 3 units of blood were transfused. In case of four or more transfusions, the difference is statistically significant. When the FF- and the SF-transfused groups

TABLE 2. Transfusion Characteristics

	Total	Randomization PC	FF	SF
Included patients	914	306	305	303
Transfusions				
No. units of blood*	5.43±5.1	5.44±5.5	5.34±4.1	5.52±5.6
Shelf life, d*	13.2±5.7	13.4±6.0	12.7±6.3	13.4±4.5
No. units of plasma*	4.22±4.0	4.31±4.2	3.85±3.1	4.24±4.3
Nontransfused, n	48	12	20	16
Only PC units, n	303	294	3	6
Only FF units, n	260	0	259	1
Only SF units, n	237	0	0	237
PC+FF units, n	23	0	23	0
PC+SF units, n	35	0	0	35
FF+SF units, n	6	0	0	6
PC+FF+SF, n	2	0	0	2
Transfused, n	866	294	285	287
Analysis according to transfusion				
PC-transfused, n	303	294	3	6
FF-transfused, n	283	0	282	1
SF-transfused, n	280	0	0	280

Transfusion characteristics of the 914 included patients in the packed cells (PC), the fresh-filtered (FF), and the stored-filtered (SF) trial arms.

*Mean±SD.

are combined in the LD-transfused group, the postoperative mortality is 12.5% in the PC-transfused group versus 5.1% in the LD–transfused group ($P=.005$).

Analysis of Risk Factors for Mortality

In view of the significant findings with respect to mortality, the analysis of risk factors will be restricted to this outcome measure. In a univariate analysis, the following preoperatively known risk factors for postoperative mortality are revealed: older age ($P<.001$), type of surgery ($P<.001$), previous open heart surgery ($P=.008$), preoperative platelet count ($P=.009$), PC trial arm ($P=.015$), history of myocardial infarction ($P=.037$), and female sex ($P=.039$). No statistically significant association between postoperative mortality and presence of aortic insufficiency ($P=.07$), preoperative hematocrit value, preoperative leukocyte count, weight, height, previous surgery, or presence of cardiac decompensation is found. The most important ($P<.001$) peroperativelyand immediate postoperatively known risk factors found are the number of blood transfusions received, duration of surgery, maximum creatinine phosphokinase–MB (CK-MB) level, and minimum platelet count.

In a multivariate logistic regression analysis with all univariately significant preoperatively known risk factors, type of surgery ($P<.001$), age ($P=.002$), history of myocardial infarction ($P=.002$), previous open heart surgery ($P=.005$), preoperative platelet count ($P=.006$), PC trial arm ($P=.012$), and sex ($P=.043$) are all shown to have independent prognostic value for the postoperative mortality. The number of blood transfusions received and the duration of surgery as postoperatively known risk factors can give extra information if added to this model. When the number of blood transfusions received is added, it becomes the most important risk factor ($P<.001$), whereas age ($P=.004$), history of myocardial infarction ($P=.005$), PC trial arm ($P=.009$), type of surgery ($P=.015$), and preoperative platelet count ($P=.023$) remain as independent risk factors. With also entering the duration of surgery into the model, type of surgery looses its statistical significance ($P=.096$), whereas the other risk factors and their probability values hardly change.

Discussion

As a new and unexpected finding (not previously reported), a significantly lower mortality was observed in the patients transfused with filtered leukocyte-depleted blood compared with those who received transfusions of packed cells without buffy coat (Table 5). The overall mortality after cardiac surgery is reported in literature in The Netherlands varying from 0.8% to 3.8% for simple bypass surgery and from 5% to >10% in complicated surgery in high-risk patients.[17,18] In our study, with >30% of the patients being >70 years old, 60% of the bypass patients having a history of myocardial infarction, 15% of the patients having had prior cardiac surgery, and only ±25% of the bypasses using a internal mammary artery, we found an overall mortality of 4.9%. Most of the identified risk factors for mortality are in agreement with previous published results[19,20] and all were evenly distributed over the three trial arms (Table 2). However, in the unquestionably biased subgroup of deceased patients, this even distribution was not observed. Preoperative myocardial infarction had occurred in only 12.5% of the deceased PC patients, whereas it had occurred in 45.5% and 50.0% of the deceased FF and SF

TABLE 3. Intention-to-Treat Analyses

	Total	PC	FF	SF	*P*
No.	914	306	305	303	
Infections					.13
At risk*	909	305	302	302	
Patients	175	70	51	54	
Percentage	19.3	23.0	16.9	17.9	
Infections	195	78	58	59	
Hospitalization, d					.62
Mean	10.7	10.9	10.6	10.7	
SD	7.2	6.9	7.6	6.9	
Median	8	8	8	8	
Min, max	0, 80	0, 57	0, 71	0, 80	
Intensive care unit period, d					.095
Mean	3.2	3.5	3.2	3.0	
SD	4.9	4.6	4.8	5.2	
Median	2	2	2	2	
Min, max	0, 70	0, 36	0, 43	0, 70	
Mortality					.015
Patients	45	24	11	10	
Percentage	4.9	7.8	3.6	3.3	
Causes of death					
Cardiac	33	14	10	9	.53
Myocardial infarction	11	4	4	3	
Heart failure	13	6	3	4	
Arrhythmia	9	4	3	2	
Noncardiac	12	10	1	1	.001
Multiorgan failure	9	7	1	1	
Anastomotic dehiscence	3	3	0	0	

Intention-to-treat analyses of the 914 included patients in the packed cells (PC), the fresh-filtered (FF), and the stored-filtered (SF) trial arms.

*Peroperative deaths were excluded from the infection analysis.

patients, respectively. Although death for all causes was higher in the PC group, the difference was mainly due to additional patients dying of multiorgan failure or anastomotic dehiscence (Table 3). The observation that patients who underwent a valve operation, especially when combined with CABG surgery, had more benefit from leukocyte-depleted blood transfusions than patients who solely underwent CABG surgery, is probably explained by the number of blood transfusions administered (mean±SD; CABG, 4.5±4.3; valve, 6.5±6.0; combined, 9.4±7.9) and by the duration of surgery (CABG, 121 minutes; valve, 119 minutes; combined, 178 minutes). When the number of blood transfusions received and the duration of surgery were entered in a multivariate analysis, the type of surgery lost its statistical significance as an independent risk factor for mortality.

The difference in duration of hospitalization between the trial arms did not reach statistical significance. The stay in the ICU tended to be longer for the PC-transfused patients ($P=.043$). However, this difference in duration of ICU stay is small (0.35 day) and may not be of clinical significance. Postoperative bacterial infections occurred in 19.1% of the patients and were dose-dependently related to the number of transfusions in all trial arms, as was reported earlier in cardiac surgery patients.[21] Infections were more common in the PC trial arm, and this difference with the leukocyte-depleted arms reached statistical significance in the heavily transfused (>3 blood transfusions) patients (Table 4).

In this study, no posttransfusional differences were found between patients transfused with FF units and those transfused with SF units. Our observations pose some intriguing questions, especially concerning the underlying mechanism(s) of reduced mortality, since several components of the transfused blood may be involved. The production of histamine, serotonin, elastase, and acid phosphatase[22-26] by the remaining granulocytes and of proinflammatory cytokines as interleukin-1β, tumor necrosis factor-α, and interleukin-6 by the mononuclear cells during the initial period of storage cannot be held responsible for the differences in mortality. In all trial arms the buffy coat was removed within 6 hours after donation, and the average shelf life of the transfused products was the same (Table 2). In the SF units the same amounts of such "metabolites" will have been produced as in the PC units, whereas the filtration procedure does not lower the concentrations of these soluble factors.[24] The same argument applies to leukocyte cell fragments. Such fragments are equally formed in PC units and SF units, less in FF units, and they pass the polyester fiber filter used for leukocyte depletion.[27].

Microaggregates composed of disintegrated leukocytes, platelets, and fibrinogen formed in the PC and SF units during storage do not pass a polyester fiber filter[28] and are therefore only transfused with PC units. They may cause nonspecific immunosuppression by impairment of the mononuclear phagocytosis functions, leading to decrease of clearance of bacteria introduced during surgery.[29] A role of microaggregates in the increased infection rates after PC transfusions therefore cannot be excluded, but the higher mortality was not solely explained by the increase in infections.

A further explanation for the beneficial effect of filtration that must be considered are the remaining leukocytes that are actually transfused.[30] In a recent study, Jensen et al[10] found a significant increase in postoperative infections in patients transfused with more than 2 PC units (which contained an equal amount of leukocytes as 3 PC units in our study) compared with patients transfused with filtered red cells. In a prior study in colorectal carcinoma patients (n=871), we observed no difference in survival or in postoperative infections between patients transfused with PC (also buffy coat–depleted) or filtered red cells.[9] However, only 254 patients (22.9%) in the colorectal carcinoma study received more than three blood transfusions compared with 512 patients (56.0%) in the present study. This may partly explain the results in the three studies. Moreover, in both studies that we performed there is a deleterious role of blood transfusions that was also present in receivers of filtered red cells.[9] Apart from receiving more blood transfusions compared with colorectal carcinoma patients are the patients in the present study exposed to artificial surfaces during CPB. This results in activation of platelets, leukocytes, coagulation, and the complement system.[31,32] Blood transfusions were mostly given at the end of surgery, after which transfused leukocytes, activated during storage, are introduced to already activated inflammatory

TABLE 4. Types of Bacterial Infections, Analysis According to Transfusion

	Total, n (%)	PC-t, n (%)	FF-t, n (%)	SF-t, n (%)	P*	
					3 Arms	2 Arms
Transfused patients	866	303	283	280		
Peroperative death	5	1	3	1		
At risk	861	302	280	279		
Patients with infection	171 (19.9)	71 (23.5)	50 (17.9)	50 (17.9)	.15	.06
No. infections	190	79	57	54		
Respiratory tract	94 (10.9)	36 (11.9)	30 (10.7)	28 (10.0)		
Bacteruria	64 (7.4)	25 (8.3)	18 (6.4)	21 (7.5)		
Bacteremia	18 (2.1)	10 (3.3)	5 (1.8)	3 (1.1)		
Wound infection	14 (1.6)	8 (2.6)	4 (1.4)	2 (0.7)		
Patients receiving >3 blood transfusions						
At risk	508	175	164	169		
Patients with infection	130 (25.6)	55 (31.4)	39 (23.8)	36 (21.3)	.08	.04
No. infections	147	63	45	39		
Respiratory tract	69 (13.6)	29 (16.6)	21 (12.8)	19 (11.2)		
Bacteruria	52 (10.2)	18 (10.3)	17 (10.4)	17 (10.1)		
Bacteremia	15 (3.0)	9 (5.1)	4 (2.4)	2 (1.2)		
Wound infection	11 (2.2)	7 (4.0)	3 (1.8)	1 (0.6)		

PC-t indicates PC-transfused patients; FF-t, FF-transfused patients; and SF-t, SF-transfused patients. See Table 2.
Analysis according to transfusion on the postoperative bacterial infections in the PC-transfused, the FF-transfused, and the SF-transfused patients.
*P: 3 arms=PC-t vs FF-t vs SF-t; 2 arms=PC-t vs FF-t/SF-t.

response systems,[33-35] thus aggravating tissue damage through cytokines and oxygen radical release.[36,37] Transfusion may not only enhance the systemic inflammatory response but also spread an otherwise localized phenomenon. However, because only a small group develops multiorgan failure, there must be additional unknown factors making patients susceptible to multiorgan failure.[30,38]

Because the difference in mortality concerns a small percentage of patients, this difference in mortality could only be revealed by analyzing a large number of patients who received large numbers of blood transfusions. The decrease in mortality by using leukocyte-depleted blood is an absolute 4% of the operated population. Considering the large numbers of cardiac surgery performed, this is a substantial decrease in absolute numbers of death.

From this study we conclude that when, in cardiac surgery, more than 3 units of blood are transfused, leukocyte depletion of blood transfusions results in a significantly decreased mortality. Nevertheless, since our observation is new and associated with increased costs for transfusion, it is urgent to confirm our results and investigate the clinical risk factors and the underlying mechanism(s) before changing transfusion guidelines.

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TABLE 5. Mortality Rate at Day 60, Analysis According to Transfusion

	PC-t		FF-t		SF-t		P*	
	n	% †	n	% †	n	% †	3 Arms	2 Arms
Transfused	303	7.9	283	3.5	280	3.6	.025	.009
No. of transfusions								
1-3	127	1.6	117	0.9	111	1.8	.82	
4-6	105	4.8	97	1.0	99	2.0		
7-10	39	10.3	39	2.6	43	4.7	.014	.005
>10	32	40.6	30	23.3	27	14.8		

Mortality rate at day 60 for the 866 transfused patients, grouped according to transfusions received, in packed cells (PC-t), fresh-filtered (FF-t), and stored-filtered (SF-t) transfused patients. n=number of patients at risk.
% †Percentage of patients who died within 60 days after surgery.
*P: 3 arms=PC-t vs FF-t vs SF-t; 2 arms=PC-t vs FF-t/SF-t.

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