THE EFFECT OF LEUKOCYTE-DEPLETED BLOOD CARDIOPLEGIA IN PATIENTS WITH SEVERE LEFT VENTRICULAR DYSFUNCTION: A RANDOMIZED, DOUBLE-BLIND STUDY

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Background: The propensity for leukocytes to cause reperfusion injury in patients undergoing heart surgery is widely accepted. Reperfusion injury may result in myocardial damage and unfavorable operative outcome, especially in patients with severely reduced ejection fractions. This study was performed to evaluate the impact of leukocyte filtration on the postoperative course of patients undergoing coronary bypass surgery.

Methods: Thirty-two patients with coronary artery disease and left ventricular ejection fraction less than 35% were included in this double-blind, randomized study. Two serial leukocyte removal filters (Pall BC1B filter [Pall Biomedical, Portsmouth, England], group F, 15 patients) or two dummy filters (group C, 17 patients) were connected to the blood cardioplegia line. Leukocyte count, hemodynamic measurement, and transesophageal echocardiography were performed before and after cardiopulmonary bypass. Cardiac-specific enzymes were analyzed from arterial blood during the first 72 hours and from coronary sinus blood 30 and 60 minutes after aortic unclamping.

Results: Patient characteristics were similar in the two groups (ejection fraction $20.9\% \pm 4.3\%$ in group C and $21.1\% \pm 4.8\%$ in group F; $P = .773$). No early death or perioperative myocardial infarction occurred. Leukocyte count, hemodynamic parameters, cardiac troponin T, cardiac troponin I, and creatine kinase MB mass levels in arterial blood were similar in the two groups. Group F showed lower release of cardiac troponin T from the coronary sinus 30 minutes after unclamping of the aorta (group F, 0.263 ± 0.12 ng/mL; group C, 0.6 ± 0.32 ng/mL; $P = .005$). Lower doses of dopamine were necessary after cardiopulmonary bypass (group F, 0.36 ± 0.11 mg $\cdot$ kg⁻¹ $\cdot$ min⁻¹; group C, 0.49 ± 0.14 mg $\cdot$ kg⁻¹ $\cdot$ min⁻¹; $P = .003$). A moderate increase in ejection fraction was observed at 30 minutes in both groups (group F, $30.3\% \pm 6.2\%$; group C, $28.0\% \pm 6.3\%$; $P = .239$) and a significant increase at 60 minutes in group F (group F, $32.5\% \pm 6.0\%$; group C, $27.4\% \pm 7.5\%$; $P = .012$).

Conclusions: These results indicate that serial leukocyte filters connected to the blood cardioplegia line decrease myocardial cell injury and may therefore help to improve outcome of patients with severely depressed ejection fractions undergoing coronary artery bypass grafting. (J Thorac Cardiovasc Surg 2000;120:642-50)

Leukocyte depletion during cardiopulmonary bypass (CPB) and its effect on reperfusion injury and postoperative lung dysfunction have been thoroughly inves-

tigated over the past several years.¹⁻⁶ Leukocyte depletion has been shown to prevent myocardial edema, to decrease the incidence of ventricular arrhythmias, and

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0022-5223/2000 \$12.00 + 0 12/1/109707

doi:10.1067/mtc.2000.109707

Received for publication March 27, 2000; revisions requested May 18, 2000; revisions received June 13, 2000; accepted for publication June 26, 2000.

to reduce free radical-mediated lung injury⁷ and cardiac reperfusion injury in animal models. Neutrophil granulocytes may cause myocardial stunning due to production of oxygen-derived free radicals,^{8,9} which may damage cell membranes, sarcoplasmic reticulum, and different enzymes. Furthermore, granulocytes can plug capillaries during ischemia; after their degranulation, cell membranes may be damaged by different cell enzymes.¹⁰⁻¹⁵ Temporary reduction of circulating activated neutrophils by leukocyte-depleting filters during the early period of reperfusion after ischemia may decrease release of free oxygen radicals and therefore reduce endothelial injury (eg, endothelial adherence, capillary plugging, no-reflow phenomenon).^{10,13}

Several reports describe leukocyte depletion in human beings. A broad spectrum of indications for leukocyte depletion in cardiac surgery is reported, such as myocardial ischemia,^{16,17} heart transplantation,^{18,19} depressed left ventricular function,²⁰ left ventricular hypertrophy,²¹ cyanotic heart disease, and different elective cardiac procedures.²²⁻²⁵

This study was performed in patients undergoing coronary artery bypass grafting (CABG) with severely depressed left ventricular function. The blood cardioplegic solution and initial reperfusion blood volume were depleted of leukocytes only. This management combines the advantages of leukocyte depletion during the initial period of CPB and ischemia and the early period of reperfusion.²⁶ On the other hand, the technical problems of filtration of the total arterial blood volume could be avoided.

Methods

Patients. The study includes 32 male patients undergoing CABG during a 5-month period. The inclusion criteria were left ventricular ejection fraction (LVEF) less than 35%, age younger than 75 years, and elective or urgent CABG. Patients with anemia, immunodeficiency, leukocytopenia, or thrombocytopenia and reoperations were excluded from the study. The patients were divided into two groups: group C (15 control patients, who did not receive leukocyte-depleted blood cardioplegic solution) and group F (17 patients, who did receive leukocyte-depleted blood cardioplegic solution [Pall BC1B filter; Pall Biomedical, Portsmouth, England]). In group C, two "dummy filters" were placed within the cardioplegia line, and in group F, two leukocyte removal filters were inserted. The study design was randomized and double blind. The perfusionist incorporated two Pall BC1B leukocyte removal filters or two empty dummy filters within the blood cardioplegia line according to the random list. Neither the surgeon nor the anesthesiologist was informed of the type of leukocyte removal filter. All operations were performed by one surgeon and one anesthesiologist, who handled transesophageal echocardiography and hemodynamic measurements.

Surgical protocol. Patients were premedicated with flunitrazepam by mouth (1 mg for those weighing < 70 kg or 2 mg for those weighing > 70 kg) the evening before the operation. Before the operation, patients received their usual morning dose of antianginal medication and 2 mg of flunitrazepam. Total intravenous anesthesia with sufentanil citrate (250-500 µg), pancuronium bromide (12-16 mg), and propofol (500-1000 mg) was used. The first dose of cefazolin (2 g) was given intravenously for infection prophylaxis during introduction of anesthesia and the second dose (1 g) was given after completion of CPB. After endotracheal intubation, patients received mechanical ventilation with an oxygen (FiO₂: 0.5) and air mixture. Radial artery and thermodilution pulmonary artery catheters (7F True Size thermodilution catheter; Baxter Healthcare Corp, Irvine, Calif) were placed for hemodynamic measurements. CPB was administered with the use of a hollow-fiber membrane oxygenator (Bard HF 5701, Bard, Inc, Haverhill, Mass) with a venous cardiectomy reservoir. A roller pump (Multiflow, Stöckert, Munich, Germany) was used with a standard nonpulsatile flow rate of 2.4 L · min⁻¹ · m⁻². A 40-µm heparin-coated arterial filter (Bentley, Irvine, Calif) was placed within the arterial line. Standard cannulation technique was used with cannulas placed in the ascending aorta and right atrium (2-stage venous cannula). After systemic heparinization (500 units/kg), CPB was initiated. Additional heparin was added during CPB to maintain the activated clotting time over 400 seconds. The left ventricle was vented via the aortic root. A 14F retrograde cannula (RC-014; Research Medical, Midvale, Utah) was placed into the coronary sinus. Distal anastomoses of the grafts were performed during aortic crossclamping, and proximal anastomoses were made after unclamping. Patients were weaned from CPB as usual. When necessary, dopamine (Dopamin; Giuliani, Hannover, Germany) was given to maintain the arterial blood pressure over 80 mm Hg. If additional cardiac support was necessary, enoximone (Perfan I.V.; Myogen, Westminster, Colo) was administered. The consumption of inotropic drugs after aortic unclamping up to the end of the operation was expressed in milligrams per kilogram per minute. After completion of CPB, heparin was neutralized by administration of protamine sulfate (1 mg/100 units of heparin) to achieve an activated clotting time of ±10% of baseline value.

A prime solution comprising 1600 mL of Ringer solution (Braun Schiwa B. GmbH & Co KG, Glandorf, Germany), 100 mL of mannitol 20%, 100 mL of sodium bicarbonate 8.4%, and 5000 units of heparin was used. Acid-base balance was managed according to the alpha-stat concept. Two million units of aprotinin (Trasylol; Bayer AG, Leverkusen, Germany) was added in the priming solution and an additional dose of 1 million units after initiation of rewarming. For myocardial preservation, two cold blood cardioplegic solutions (4°C; 1:4 ratio of blood to cardioplegic solution) were administered at a rate of 250 mL · min⁻¹ for 4 minutes. The composition of the two solutions was as follows: solution I contained sodium chloride, 1.006 g; sodium hydroxide, 0.290 g; citric acid in water, 0.690 g; potassium chloride, 2.631 g; and glucose, 16.832 g; solution II contained sodium

chloride, 1.043 g; sodium hydroxide, 0.298 g; citric acid in water, 0.723 g; potassium chloride, 0.909 g; and glucose, 17.45 g (BC-Card I and BC-Card II; Planer, Graz, Austria). Solution I was used initially until cardiac arrest and solution II thereafter. Repeated doses ($50 \text{ mL} \cdot \text{min}^{-1}$) were given every 20 minutes. Solution II was then infused as the final cardioplegic solution ("hot shot," $\geq 34.5^\circ\text{C}$) for 4 minutes immediately before aortic unclamping. For the next 6 minutes, either leukocyte-depleted or non-leukocyte-depleted blood ($50 \text{ mL} \cdot \text{min}^{-1}$) was administered. All patients received a combination of antegrade and retrograde infusion of cardioplegic solution. Fifty percent of the cardioplegic solution was given antegradely and 50% retrogradely. A heat exchanger for blood cardioplegia (Eurosets Vision; HMT, Fürstentfeldbrück, Germany) was incorporated in the cardioplegia line. Patients were not actively cooled, but their systemic temperature was allowed to drop to $33^\circ\text{C} \pm 1^\circ\text{C}$. Rewarming was started 10 minutes before release of the aortic clamp.

Sample collection. Blood samples were collected proximal and distal to the filters 2 minutes after the first doses of cardioplegic solution were begun and 2 minutes after the terminal dose of cardioplegic solution was started. For hematologic testing, blood samples were taken from the radial artery before initiation of CPB, 30 minutes after aortic crossclamping, and 1, 30, and 60 minutes and 6, 12, 24, and 48 hours after completion of CPB. Samples for cardiac troponin T (cTnT), troponin I (cTnI), and creatine kinase MB (CK-MB) mass were taken from the coronary sinus before initiation of CPB, 30 minutes after aortic crossclamping, and 1, 30, and 60 minutes after completion of CPB. Samples for cTnT, cTnI and CK-MB mass were taken from the radial artery before initiation of CPB, 30 minutes after aortic crossclamping, and 1, 30, and 60 minutes and 6, 12, 24, 48, and 72 hours after completion of CPB.

Leukocyte count. Blood cell counts were immediately determined with the use of a counter (K-1000; Sysmex Corporation of America, Long Grove, Ill) and differential cell counting for neutrophils in Nageotte chambers with a dilution of 1:100.

Biochemical assays. Blood samples were taken for biochemical assays after defined time intervals. The blood samples were centrifuged for 10 minutes at 2000g. The serum was frozen in aliquots and stored at -80°C until subsequent analysis. cTnT was measured by means of the Troponin T STAT immunoassay Elecsys 2010 Analyser (Roche Diagnostics GmbH, Mannheim, Germany). cTnI was quantified by means of the AxSYM Troponin I System (Abbott, Wiesbaden, Germany). CK activity (CK-NAC; Boehringer Mannheim, Division of Roche), CK-MB activity (Boehringer Mannheim, Division of Roche), and CK-MB mass (Sandwich immunoassay test) were calculated. Analysis was done at one laboratory and without knowledge of the patients' outcomes.

Hemodynamic measurements. Heart rate, mean arterial blood pressure, and pulmonary capillary wedge pressure were measured. Cardiac output was measured with the thermodilution technique. Cardiac index, stroke index, and left

ventricular stroke work index were measured before initiation of CPB (I), 30 minutes after completion of CPB (II), 60 minutes after completion of CPB (III), and 12 hours after admission to the intensive care unit (IV).

Echocardiography. Intraoperative transesophageal echocardiography was performed with a Hewlett-Packard Sonos 2500 system and a 3.7/5.0-MHz phased-array omniplane transducer (Hewlett-Packard Company, Andover, Mass). Left ventricular ejection fraction (LVEF) was calculated as follows: $(\text{End-diastolic volume} - \text{End-systolic volume}) / \text{End-diastolic volume}$. Left ventricular end-diastolic and end-systolic volumes were estimated by acoustic quantification (echocardiographic automatic border detection) in the transverse 4-chamber view by means of the method of discs (according to Simpson's rule).

These echocardiographic data were measured before initiation of CPB (I) and 30 minutes (II) and 60 minutes after completion of CPB (III).

Data analysis. Patients were randomized by means of a computer-generated series of random numbers. The patients were assigned to either leukocyte-depleted blood cardioplegia or non-leukocyte-depleted blood cardioplegia. The results were reported as the mean $\pm$ the standard deviation of the mean. The Mann-Whitney *U* test or Wilcoxon rank-sum test for difference in medians was used for comparisons of nominal data.

Ethics. All patients gave written informed consent, and the study was performed according to the guidelines of the institutional ethical committee.

Results

Clinical results. Preoperative LVEF measured by transthoracic echocardiography was $21.5\% \pm 4.2\%$ in group C and $21.1\% \pm 4.8\%$ in group F ($P = .773$). There were no significant differences regarding preoperative data and risk factors, surgical data, and patient outcomes between group C and group F (Table I). All patients survived and one patient with preoperative and postoperative ventricular fibrillation received a defibrillator. Intensive care unit stay in group F was shorter, but not significantly so (group C, 67.3 ± 102 hours; group F, 40.6 ± 38.6 hours; $P = .081$).

Leukocyte count. There was no effective leukocyte depletion (neutrophil granulocytes) in group C, but there was significant leukocyte depletion in group F. Filtration rate was 96.0% during the first dose and 96.3% during terminal dose of cardioplegia (Fig 1). Filtration of platelets was lower than 5% and no significant changes in systemic leukocyte count during the first 72 hours was observed in either group.

Measurement of cardiac enzymes. No significant differences regarding systemic release of cTnT, cTnI, and CK-MB mass during the first 72 hours was observed in either group. In group C the peak value of

Fig 1. Leukocyte count proximal and distal to two Pall BC1B filters (group F) and proximal and distal to the dummy filters (during first and terminal dose of blood cardioplegia).

Table I. Patients' characteristics, risk factors, and surgical data

	Group C (n = 15)		Group F (n = 17)		P value
	No.*	%	No.*	%	
Patient characteristics					
Male/female	15/0		17/0		
Age (y)	64.6 ± 8.0		63.6 ± 7.7		.793
BSA (m ²)	1.95 ± 0.17		1.90 ± 0.15		.498
Weight (kg)	82.1 ± 10.4		78.1 ± 10.4		.326
EF (%)	20.9 ± 4.3		21.1 ± 4.8		.773
Previous MI	10/15	66.7	11/17	64.7	
LVEDP (mm Hg)	26.1 ± 7.1		26.0 ± 9.1		.693
Risk factors					
Smoking	5/15	33	7/17	41.2	
Hypertension	8/15	55.3	7/17	41.2	
Hyperlipidemia	5/15	33	6/17	35.3	
Diabetes	4/15	26.7	7/17	41.2	
COLD	5/15	33	3/17	17.7	
Renal insufficiency	2/15	13.3	3/17	17.7	
Carotid disease	1/15	6.7	3/17	17.7	
Peripheral vascular disease	4/15	26.7	5/17	29.4	
Surgical data					
Operation time (min)	224.9 ± 30.3		221.1 ± 39.8		.895
CPB time (min)	116.8 ± 19.0		110.9 ± 23.7		.678
Crossclamp time (min)	72.1 ± 15.1		77.1 ± 22.4		.305
Distal anastomosis	4.1 ± 1.2		4.0 ± 1.1		.910
Blood loss (mL/24 h)	390 ± 180		410 ± 220		.823
Intubation time (min)	341 ± 117		377 ± 189		.895
ICU stay (h)	67.3 ± 102		40.6 ± 38.6		.081
PO ₂ /FIO ₂ 1.0 (mm Hg)	333 ± 116		363.9 ± 92		.295
Death	0/15		0/17		
MI	0/15		0/17		
LCOS	0/15		0/17		
IABP	0/15		0/17		
Stroke	0/15		0/17		
Infections	0/15		0/17		
VF	1/15	6.7	0/17		

The internal thoracic artery was used in 7 patients of group C and in 10 patients of group F. BSA, Body surface area; EF, left ventricular ejection fraction; MI, myocardial infarction; LVEDP, left ventricular end-diastolic pressure; COLD, chronic obstructive lung disease; CPB time, duration of cardiopulmonary bypass; crossclamp time, duration of aortic crossclamping; ICU, intensive care unit; Po₂/Fio₂ 1.0, first oxygen partial pressure after CPB with Fio₂ 1.0; LCOS, low cardiac output syndrome; IABP, intra-aortic balloon pump assistance; VF, ventricular fibrillation.

*Unless otherwise indicated, the figures in these columns indicate the number of patients.

Fig 2. Measurement of cardiac enzymes (cTnT, cTnI, CK mass) preoperatively and during the first 72 hours after the operation. *Peak level; cTnT, cardiac troponin T, $P = .371$; cTnI, cardiac troponin I, $P = .178$; CK mass, creatinine mass, $P = .562$; 1 to 11, time points 1 to 11 (see "Sample collection" in the "Methods" section).

cTnT (cTnI; CK-MB mass) was 4.91 ± 2.2 ng/mL (165.7 ± 45.9 ng/mL; 9.05 ± 2.6 U/L) ($P = .371$; $P = .178$; $P = .562$) and in group F, 3.52 ± 1.2 ng/mL (111.8 ± 57.8 ng/mL; 8.1 ± 2.0 U/L) (Fig 2). Group F showed significantly lower cTnT release from the coronary sinus 30 minutes after aortic unclamping (group F, 0.263 ± 0.12 ng/mL; group C, 0.6 ± 0.32 ng/mL; $P = .005$) and a moderate decrease after 60 minutes (group F, 1.64 ± 1.35 ng/mL; group C, 2.09 ± 2.02 ng/mL; $P = .282$) (Fig 3).

Hemodynamic measurements. Hemodynamic variables (heart rate, mean arterial pressure, cardiac index, stroke index, and left ventricular stroke work index) were similar in the two groups before initiation of CPB. These parameters were then evaluated 30 and 60 minutes after completion of CPB and 12 hours after admission to the intensive care unit. No significant changes in hemodynamic parameters were seen in either group (Table II).

Requirement for dopamine and enoximone. Significant lower doses of dopamine for weaning from CPB were required in group F (group F, 0.36 ± 0.11 mg $\cdot$ kg $^{-1}$ $\cdot$ min $^{-1}$; group C, 0.49 ± 0.14 mg $\cdot$ kg $^{-1}$ $\cdot$ min $^{-1}$; $P = .003$) (Fig 4). No additional enoximone was given in group F (0/17), whereas 5 of 15 patients in group C received additional doses of enoximone. All patients (17/17) in group F had spontaneous sinus rhythm after release of the aortic crossclamp, but 4 of 15 patients in group C required electrical defibrillation.

Estimation of LVEF. The LVEF calculated by computerized transesophageal echocardiography before initiation of CPB (I) was similar in the two groups (group F, $24.9\% \pm 4.5\%$; group C, $24.3\% \pm 4.1\%$; $P = .834$). There was a moderate increase 30 minutes after CPB (II) in both groups (group F, $30.3\% \pm 6.2\%$; group C, $28.0\% \pm 6.3\%$; $P = .239$) and a significant increase 60 minutes after CPB (III) (group F, $32.5\% \pm 6.0\%$; group C, $27.4\% \pm 7.5\%$; $P = .024$). The differences in increase between LVEF I to LVEF III in group F ($24.9\% \pm 4.4\%$ to $32.5\% \pm 5.9\%$; $P = .0005$) were significantly higher than those in group C ($24.3\% \pm 4.1\%$ to $27.4\% \pm 7.5\%$; $P = .357$) (Fig 5).

Discussion

Most animal experiments using leukocyte depletion show positive effects regarding left ventricular recovery and lung function after ischemia and reperfusion. Some controversies exist concerning indication, the best time frame, and the best method for leukocyte depletion. Different filtration methods have been described in the literature, such as filtration of total arterial or venous blood, filtration during the controlled

Fig 3. Troponin T (cTnT) release from coronary sinus 30 and 60 minutes after unclamping of the aorta.

Table II. Hemodynamic measurements

	I	P value	II	P value	III	P value	IV	P value
LVSWI ($\text{gm} \cdot \text{m}^{-1} \cdot \text{m}^{-2}$)								
Group C	36.1 ± 9.3		24.9 ± 7.3		29.8 ± 5.5		29.3 ± 8.4	
Group F	27.6 ± 6.7	.103	23.1 ± 4.5	.656	20.7 ± 6.7	.0139	26.5 ± 6.45	.876
PCWP (mm Hg)								
Group C	13.0 ± 2.7		13.9 ± 5.2		10.9 ± 1.9		14.6 ± 4.4	
Group F	13.4 ± 5.4	.921	11.8 ± 4.4	.299	12.0 ± 2.1	.256	9.50 ± 2.8	.065
MAP (mm Hg)								
Group C	73.4 ± 11.5		64.6 ± 13.4		74.5 ± 11.0		79.9 ± 17.8	
Group F	77.7 ± 14.0	.440	64.7 ± 9.20	.894	70.7 ± 12.9	.486	84.2 ± 13.5	.878
CI ($\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$)								
Group C	2.26 ± 0.39		3.32 ± 0.75		3.15 ± 0.80		3.00 ± 0.66	
Group F	2.18 ± 0.50	.634	3.02 ± 0.38	.351	2.37 ± 0.43	.055	2.25 ± 0.17	.057

I, Before cardiopulmonary bypass; II, 30 minutes after the end of cardiopulmonary bypass; III, 60 minutes after the end of cardiopulmonary bypass; IV, 12 hours after admission to the intensive care unit; LVSWI, left ventricular stroke work index; PCWP, pulmonary capillary wedge pressure; MAP, mean arterial pressure; CI, cardiac index.

reperfusion period, filtration of the blood cardioplegic solution, and filtration of blood components of CPB. Despite laboratory evidence of leukocyte involvement in reperfusion injury, most clinical trials do not show any hemodynamic effect of leukocyte filtration. Data from Pala and colleagues²⁰ showed that leukocyte depletion failed to be effective in patients with a normal ejection fraction. Mihaljevic and colleagues²⁴ stated that leukocyte depletion of total arterial blood did not improve postoperative lung function. However, other studies demonstrate a beneficial outcome after leukocyte filtration. De Vecchi and associates¹⁶ found that leukocyte depletion improved the surgical results in patients with moderate or severe left ventricular dysfunction. Cardiac index showed a trend to greater improvement in the group with leukocyte depletion. Baksaas and coworkers²² demonstrated that leukocyte depletion during the reperfusion period reduced the

number of circulating leukocytes in patients undergoing elective CABG. However, no effect was seen for myeloperoxidase release, complement activation, or interleukin 6 and interleukin 8 release. Suzuki and coworkers²⁵ found that leukocyte depletion of blood cardioplegic solutions significantly decreased the release of CK-MB and cTnT.

These results are consistent with our observations. We found a significant decrease of cTnT levels in coronary sinus blood 30 minutes after unclamping the aorta when using leukocyte filters. Only a moderate decrease of cTnT levels in coronary sinus blood could be seen after 60 minutes. When looking at the peak levels of cTnT, cTnI, and CK-MB mass in the systemic circulation during the first 72 hours, we saw no significant differences between the groups. Sawa and associates^{17,21} demonstrated a better outcome in patients with acute myocardial ischemia or left ventricular hypertrophy treated with

Fig 4. Requirement for dopamine for weaning from CPB.

Fig 5. Ejection fractions (EF) estimated by transesophageal echocardiography in group F and group C. *I*, Before initiation of CPB; *II*, 30 minutes after completion of CPB; *III*, 60 minutes after completion of CPB.

leukocyte-depleted terminal blood cardioplegia; they measured a lower release of malondialdehyde as a marker of lipid peroxidation, lower release of CK-MB, significantly lower postoperative inotropic support and, in patients with left ventricular hypertrophy, lower myocyte damage and endothelial cell damage of capillaries. In patients with cardiogenic shock,¹⁷ the same group observed a significantly lower requirement for dopamine

for weaning from CPB in patients treated with leukocyte-depleted blood cardioplegic solutions, as observed by our group. Mihaljevic and coworkers²⁴ stated that the use of a leukocyte-depleting filter in the arterial line (Leuko-Guard-6; Pall Biomedical, Portsmouth, England) during CPB did not reduce the number of circulating leukocytes at any time during or after filtration (flow $1.8 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$). Mair and coworkers²⁷ could not achieve effective leukocyte depletion using an arterial line filter (LG6). However, Sawa and associates^{17,21} showed more than 95% leukocyte depletion in the coronary circulation during terminal blood cardioplegia reperfusion (Cellsorba-80P, Asahi Medical, Tokyo, Japan) ($300 \text{ mL} \cdot \text{min}^{-1}$ for 10 minutes).

In our study we used two leukocyte filters during blood cardioplegia and terminal reperfusion and achieved more than 96% reduction of leukocytes in the coronary circulation. This is consistent with the results published by Suzuki and colleagues,²⁵ who used the same filter system (98.1% total leukocyte reduction through the filter). Pala and coworkers²⁰ tested leukocyte-depleted blood cardioplegia in patients with an LVEF lower than 35% or greater than 45%. They could not observe an effect in patients with an LVEF greater than 45%, but they found better myocardial protection measured by glutathione redox ratio in patients with an LVEF lower than 35%. We found a significant increase of LVEF in the group with leukocyte depletion 60 minutes after CPB ($P = .012$).

There were several hints that leukocyte depletion with leukocyte filters effectively reduced myocardial

cell damage in our patients. First, the level of cTnT was reduced in group F. As we know, this enzyme is a sensitive marker for myocardial tissue damage, which is up-regulated shortly after ischemia. We assume that cTnI, another specific marker for myocardial damage, was not up-regulated significantly due to the small number of patients enrolled in this study. Second, the requirement for dopamine and enoximone was lower in these patients. Obviously, these leukocyte filters even have a positive hemodynamic effect on left ventricular function. Transesophageal echocardiography objectively confirmed these data. We are unable to explain whether leukocyte filters may decrease early mortality in patients with poor LVEF, since mortality was zero in both groups.

Study limitations

The two groups were identical concerning preoperative infarction rate. However, viability testing by either positron emission tomography or stress echocardiography was not carried out. This, in theory, could show differences regarding extent of viable myocardium that could influence the results. Yet, since the groups were properly randomized, we can assume that myocardial viability of infarcted areas was nearly identical. Endothelial markers were not investigated. However, such markers could influence expression of free oxygen radicals and therefore influence the results.

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