

Continuous-Flow Cell Saver Reduces Cognitive Decline in Elderly Patients After Coronary Bypass Surgery

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Background—Cerebral microembolization during cardiopulmonary bypass may lead to cognitive decline after cardiac surgery. Transfusion of the unprocessed shed blood (major source of lipid microparticulates) into the patient during cardiopulmonary bypass is common practice to reduce blood loss and blood transfusion. Processing of shed blood with cell saver before transfusion may limit cerebral microembolization and reduce cognitive decline after surgery.

Methods and Results—A total of 226 elderly patients were randomly allocated to either cell saver or control groups. Anesthesia and surgical management were standardized. Epi-aortic scanning of the proximal thoracic aorta was performed in all patients. Transcranial Doppler was used to measure cerebral embolic rates. Standardized neuropsychological testing was conducted 1 week before and 6 weeks after surgery. The raw scores for each test were converted to Z scores, and then a combined Z score of 10 main variables was calculated for both study groups. The primary analysis was based on dichotomous composite cognitive outcome with a 1-SD rule. Cognitive dysfunction was present in 6% (95% confidence interval, 1.3% to 10.7%) of patients in the cell saver group and 15% (95% confidence interval, 8% to 22%) of patients in the control group 6 weeks after surgery ($P=0.038$). The severity of aortic atheroma and cerebral embolic count were similar between the 2 groups.

Conclusions—The present report demonstrates that processing of shed blood with cell saver results in clinically significant reduction in postoperative cognitive dysfunction after cardiac surgery. These findings emphasize the clinical importance of lipid embolization in contributing to postoperative cognitive decline in patients exposed to cardiopulmonary bypass. (*Circulation*. 2007;116:1888-1895.)

Key Words: brain ■ cardiopulmonary bypass ■ cognitive symptoms ■ surgical blood loss

Recently, cardiopulmonary bypass (CPB) has celebrated its 50th anniversary demonstrating its vital role in the cardiac surgery setting. Although the practice of running CPB has changed over the years, some of the mainstay components of the CPB circuit have remained the same. One of these components is a cardiotomy suction reservoir that is used to return “suctioned” blood from the wound, sternum, and thorax back to the patient to reduce blood loss and blood transfusion. However, the blood collected in cardiotomy suction contains high levels of cellular debris and lipid microparticulates,^{1,2} which have been shown to cause microembolization to the brain blood vessels.³ One pathology study examined tissue blocks from the brains of patients who died after cardiac surgery from nonneurological causes. The pathological and chemical features of the multiple cerebral microemboli closely resembled the brain microemboli that originated from cardiotomy suction blood in experimental animal studies.⁴ Cerebral microembolization is considered one of the most

likely causal factors leading to cognitive decline after cardiac surgery, which occurs in a considerable number of patients and may result in reduced quality of life during otherwise successful surgery.^{5,6}

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Previous investigators have shown that when shed blood from the cardiotomy reservoir was processed with a cell saver device, it considerably reduced cerebral lipid microembolization.⁷ Cell savers are commonly used in noncardiac surgery when excessive blood loss is a concern (eg, abdominal aortic aneurysm surgery). Cell savers clean and process shed blood, making it suitable for retransfusion into the patient. In addition to effective removal of fat particles, cell savers appear to be efficient in removing cytokines, S-100 β protein, platelet and fibrin aggregates, and complement and coagulation activation products from shed blood.⁸⁻¹¹

Received February 21, 2007; accepted August 13, 2007.

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Clinical trial registration information—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00296985.

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Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.107.698001

Removal of these factors from shed blood may reduce the incidence of cognitive decline after cardiac surgery by decreasing the risk of microembolization and/or decreasing the amount of inflammatory activation. However, there have been no human studies investigating a direct link between fat emboli and cognitive dysfunction after cardiac surgery. Consequently, the link between lipid emboli and postoperative cognitive decline is inferential and not definitive because the data are from either animal or human autopsy studies.¹² A recent evidence-based review assigned a class IIb, level B evidence for blood cell processing and secondary filtration in decreasing the deleterious effects of reinfused shed blood.¹³ More studies are required to build up level I clinical evidence.

The objective of this study was to determine whether the replacement of cardiomy suction with a continuous-flow cell saver device would improve neuroprotection by minimizing cerebral microembolization and reduce cognitive decline in elderly patients after coronary artery bypass graft (CABG) surgery. We therefore performed a randomized, double-blinded trial of cell saver versus cardiomy suction (ie, control) to test our hypothesis.

Methods

Study Population

After approval by the University Health Network Research Ethics Board, informed consent was obtained from 233 patients older than 60 years who were scheduled for elective CABG surgery. We focused on patients older than 60 years because of their increased risk of postoperative cognitive decline, thereby increasing our ability to detect a clinically significant reduction in cognitive impairment. Patients were excluded if they required redo CABG surgery, emergent surgery, or a surgical procedure in addition to CABG, as well as if they had severe kidney or liver disease (creatinine >133 mg/dL and bilirubin >2 mg/dL), symptomatic cerebrovascular disease, history of stroke, transient ischemic attacks, or atrial fibrillation. We also excluded patients who were unable to complete a preoperative assessment and those who could not speak English. Patients were randomly allocated to either cell saver or control (ie, cardiomy suction) groups according to a computer-generated randomization code in predetermined size blocks. Patients were unaware of their group assignment.

Anesthetic Management

All patients received premedication with lorazepam 2 mg 1 to 2 hours before surgery. Anesthetic technique was standardized to include fentanyl 10 to 20 μ g/kg, midazolam 0.1 mg/kg, pancuronium 0.15 to 0.20 mg/kg, and isoflurane 0.5% to 1.5%. All patients received tranexamic acid 50 mg/kg intravenously after induction of anesthesia. After surgery, patients were transferred to the intensive care unit for postoperative ventilation. Sedation was achieved with propofol infusion 0.5 to 4 mg/kg per hour and morphine boluses. Patients were extubated according to standard criteria.

Operative Technique and Management of CPB

After median sternotomy, patients underwent harvesting of saphenous veins and internal thoracic arteries as conduits. Heparin was given to maintain activated clotting time >400 seconds. Management of CPB included systemic temperature drift to 33°C to 34°C (nasopharyngeal), alpha-stat pH management, mean perfusion pressure between 60 and 80 mm Hg, pump flow rates of 2.0 to 2.4 L/min per square meter, and hematocrit >20%. A single aortic cross-clamp technique was used in all patients. Myocardial protection was achieved with intermittent antegrade and occasionally retrograde cold blood cardioplegia. A 32- μ m filter (Avecor Affinity, Minneap-

olis, Minn) was used in the arterial perfusion line. Before separation from CPB, patients were rewarmed to 36°C to 37°C. During rewarming, the maximal inflow temperature was limited to 37°C. After separation from CPB, heparin was neutralized with protamine.

The continuous-flow cell saver (Fresenius Corporation, Concord, Calif) was used to process shed blood before returning it back to the patient. In control patients, cardiomy suction was used in a standard closed venous reservoir where cardiomy blood was collected and reinfused through the arterial circuit back to the patient. Both the cell saver and cardiomy suction were used during the same time periods, from full heparinization (activated clotting time >400 seconds) to immediately after the initial dose of protamine was given.

Echocardiographic Assessment

A comprehensive transesophageal echocardiography examination with the use of multiplane 4- to 7-MHz probe and Hewlett-Packard Sonos 5500 echocardiograph (Philips Medical Systems, Andover, Mass) was performed after induction of anesthesia to rule out an intracardiac or valvular source of potential emboli. In addition to transesophageal echocardiography, epiaortic scanning was used by the surgeon to scan the ascending aorta from aortic valve to mid-aortic arch in transverse and longitudinal planes. A 6- to 15-MHz epiaortic probe (Philips Medical Systems, Andover, Mass) covered with ultrasound gel and wrapped in sterile Surgi-Tip transducer cover (CIVCO Medical Instruments, Kalona, Iowa) was utilized. Aortic atheroma was graded on a 4-point scale as previously described.¹⁴ The real-time echocardiographic findings were communicated to the operating surgeons who were free to modify the operating technique and apply ultrasound guidance for any intended aortic manipulation to minimize potential embolization.

Transcranial Doppler Measurements

As a secondary outcome, we chose a subset of patients in each group with adequate transcranial Doppler (TCD) signal to determine whether the use of cardiomy suction reduces the amount of TCD-detected emboli. Difficulty in obtaining an adequate acoustic window for TCD measurements in elderly patients is well recognized and limited the number of patients available for secondary outcome analysis.

TCD monitoring (MultiDop X4, DWL Electronic Systems, Sipplingen, Germany) of the middle cerebral artery was performed continuously from 2 minutes before cannulation of the aorta to 2 minutes after aortic decannulation. The technique of detection and analysis of embolic hits was used, as previously described.¹⁵ We calculated a total number of emboli during CPB using a sum from both middle cerebral arteries.

Neuropsychological Testing

The neuropsychological testing was conducted 1 week before (baseline) and 6 weeks after surgery by a trained psychometrist blinded to the treatment arm assignment. The prehospital discharge testing was not conducted because such data are confounded by a variety of factors including medication, fatigue, pain, sleep deprivation, and the traumatic effects of surgery.¹⁶ Moreover, the predischarge testing can be frustrating and difficult for some patients, which could compromise compliance on the 6-week follow-up tests.

The proposed battery of tests complied with the international consensus on assessing neuropsychological outcome¹⁶ and included tests for learning and memory, attention, concentration, and psychomotor speed, as well as language and higher intellectual functioning. Of the battery of 12 tests, 10 main variables were chosen a priori to be used in the analyses: (1) Rey Auditory Verbal Learning Test, (2) Rey Visual Design Learning Test, (3) Halstead-Reitan Trail-Making Tests Parts A and B (Trails B–Trails A) time, (4) Grooved Pegboard Test time, (5) Wechsler Memory Scale Digit Span Forward, (6) Wechsler Memory Scale Digit Span Backward, (7) Wechsler Memory Scale Spatial Span Forward, (8) Wechsler Memory Scale Spatial Span Backward, (9) Choice and Simple

Reaction Time Tests (Choice Reaction Time—Simple Reaction Time), and (10) Verbal Fluency Test.

Parallel versions of the tests were used when available to minimize learning effects between the baseline and 6-week follow-up assessments. If improved performance was reflected by a lower score (Trails A and B, Grooved Pegboard, Simple and Choice Reaction Times tests), the directional data were reversed so that all improvements gave positive change scores. Tests not completed were treated as omissions and not as failures.

To estimate the change in performance from baseline to 6 weeks after surgery, the raw scores for each test were converted to Z scores. A Z score was calculated for each main variable in each patient by subtracting the preoperative score from the postoperative score and dividing the difference by the preoperative SD of that variable.^{17,18} This standardized score allowed the classification of patients on the basis of the 1-SD rule. Patients with a positive score of $>+1$ were considered improved, and patients with a negative score of <-1 were considered deteriorated. The primary outcome was the dichotomous cognitive deterioration variable based on the combined cognitive score.

Sample Size Justification and Statistical Analysis

Given that the prevalence of postoperative cognitive dysfunction at 6 weeks after CABG surgery is 36%,⁵ to see a 50% reduction in cognitive dysfunction from 36% to 18% in patients receiving cell saver management strategy, with $\alpha=0.05$ and power $1-\beta=0.8$, a group of 95 patients in each arm of the study is required, for a total of 190 patients in the randomization schedule. We estimated an attrition rate of 10%. The final sample size for randomization purposes therefore was increased to a total of 209 patients.

Comparability of both groups with respect to demographic data and surgical characteristics was tested with the use of χ^2 statistics on qualitative variables and the *t* test on quantitative variables. For the primary analysis of composite dichotomous cognitive outcome, the 2 groups were compared with the χ^2 test for differences in probabilities of a 2×2 contingency table. Confidence intervals (CIs) for proportions were calculated at 95%. Paired *t* tests were used for the raw cognitive score comparisons between baseline and 6-week follow-up. A 2-tailed *t* test was used to compare the hematologic and coagulation laboratory parameters between the 2 groups at predetermined time points. The emboli count, extubation time, and hospital length of stay were analyzed with the Mann-Whitney *U* test. All analyses were performed on an intention-to-treat basis. A probability value <0.05 was considered significant. Statistical analysis was conducted with the use of SPSS computer software.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Randomization Schematic

Given the planned length of the study, it was decided to add additional test subjects to help ensure that a sufficient sample size was collected to determine a significant difference in cognitive decline if one existed. As a result, a total of 226 patients were randomized to compensate for potentially higher than expected dropout rates. The decision to add subjects was made without breaking the study blind. All randomized patients completed baseline cognitive testing (112 patients in the cell saver group and 114 in the control group). Patients who were not randomized included 5 patients who refused to participate in the study before surgery, 1 patient who sustained cardiac arrest before surgery, and 1 patient whose surgery was cancelled. Cognitive outcome could not be determined at 6-week follow-up in 13 and 15 patients in the cell saver and control groups, respectively ($P=0.72$). In the cell saver group, the follow-up cognitive

testing was not performed in 3 patients because of a change in planned surgical management (1, exploration of the ascending aorta; 1, mitral valve repair; 1, off-pump surgery), and 10 patients refused to participate in the follow-up cognitive testing. In the control group, the follow-up cognitive testing was not performed in 2 patients because of a change in planned surgical management (1, exploration of the ascending aorta; 1, off-pump surgery), 1 patient died, and 12 patients refused to participate in the follow-up cognitive testing.

Demographic Data and Surgical Characteristics

No differences were detected with respect to the baseline demographic data, preoperative variables, and surgical characteristics between the 2 groups (Table 1).

Neuropsychological Outcomes

Baseline neuropsychological test scores were similar between the 2 groups. The raw neuropsychological test scores are reflected in Table 2.

On the basis of the primary composite outcome, cognitive dysfunction was present in 6% (95% CI, 1.3% to 10.7%) of patients in the cell saver group and 15% (95% CI, 8% to 22%) of patients in the control group ($P=0.038$). The rates of cognitive improvement were similar between the 2 groups: 19% (95% CI, 11.4% to 26.6%) in the cell saver group versus 17% (95% CI, 9.8% to 24.2%) in the control group ($P=0.712$) (Figure 1).

Aortic Atheroma Characteristics

The severity and distribution of atheroma were similar between the 2 groups. A total of 40 (36%) and 42 patients (37%) had atheroma >2 mm present in either the ascending aorta or aortic arch in the cell saver and control groups, respectively ($P=0.860$).

TCD Findings

Adequate TCD signal was acquired in 43 patients (38%) in the cell saver group and 41 patients (36%) in the control group. Median emboli count was 90 (range, 5 to 1531) in the cell saver and 133 (range, 18 to 1811) in the control group ($P=0.31$).

Hematologic Parameters and Postoperative Morbidity

The median amount of shed blood recycled via cardiomy reservoir was 800 mL (range, 175 to 3840 mL). The median amount of red cell concentrate transfused after processing via cell saver was 401 mL (range, 188 to 980 mL).

Patients in the cell saver group had higher hemoglobin levels during the first 24-hour postoperative period. Patients in the control group had higher platelet count and lower international normalized ratio and partial thromboplastin time values at intensive care unit admission. No differences were detected in the discharge hematologic laboratory test values between the 2 groups (Table 3).

A total of 28 patients (25%) in the cell saver group and 14 patients (12%) in the control group received fresh frozen plasma (FFP) transfusion at any time during the perioperative

Table 1. Demographic Variables and Surgical Characteristics

	Cell Saver Group (n=112)	Controls (n=114)
Baseline demographics		
Age, y	67.5±6.0	67.0±6.1
Male, n (%)	100 (89)	103 (90)
Height, cm	169.4±9.8	170.1±8.4
Weight, kg	83.1±17.6	82.5±13.5
Left ventricular ejection fraction <40%	9 (8)	10 (8.8)
Coexisting illness, n (%)		
Diabetes mellitus	43 (38)	40 (35)
Hypertension	80 (71)	76 (67)
Peripheral vascular disease	10 (9)	9 (8)
Myocardial infarction	46 (41)	40 (35)
Preoperative medication, n (%)		
β-Blockers	85 (76)	88 (77)
Angiotensin-converting enzyme inhibitors	56 (50)	69 (60)
Nitrates	108 (96)	112 (98)
Calcium channel blockers	42 (37)	34 (30)
Aspirin	98 (88)	104 (91)
Statins	93 (83)	91 (80)
Preoperative laboratory variables		
PTT, s	36.9±5.7	37.0±5.0
INR, U	1.03±0.14	1.02±0.07
Hemoglobin, g/dL	137±12	139±11
Platelet count, 10 ³ /mm ³	234±62	223±56
Creatinine, mg/dL	93.1±16.8	92.4±19.7
Intraoperative variables		
CPB time, min	86±18	89±19
Cross-clamp time, min	64±14	66±13
Minimum temperature on CPB, °C	33.8±1.5	33.9±1.2
Minimum hematocrit on CPB, %	22.9±3.1	23.4±2.9
No. of distal anastomoses	3.7±0.85	3.6±0.90
Total heparin, U	51 644±22 024	49 090±15 489
Total protamine, mg	453±130	472±92

Data are expressed as mean±SD or number of patients (%). PTT indicates partial thromboplastin time; INR, international normalized ratio.

period ($P=0.018$). The FFP transfused group received significantly more cell saver blood than the FFP not transfused group ($P<0.0001$) (Figure 2). Blood use and postoperative morbidity and mortality are reflected in Table 4.

Discussion

Replacement of cardiomy suction with the continuous-flow cell saver is a novel approach to improve neuroprotection and enhance recovery of cognitive function in patients undergoing cardiac surgery. The cell saver separates red cells from plasma and debris by washing and differential centrifugation, providing a high concentration of red blood cells and no or little contaminants.¹⁹ The present study demonstrates that “cleansing” of the unprocessed shed blood reduces cognitive

Table 2. Raw Scores of Neuropsychological Tests at Baseline and 6-Week Follow-Up

Tests (by Group)	Timing of Tests		P
	Baseline	6-Week Follow-Up	
VF			
Cell saver (n=99)	35.83±14.04	37.60±16.35	0.109
Control (n=99)	34.22±11.50	36.03±10.60	0.034
SSF			
Cell saver (n=96)	7.20±1.69	7.54±1.66	0.047
Control (n=94)	7.29±1.45	7.23±1.44	0.709
GPB			
Cell saver (n=95)	90.81±21.79	87.43±20.38	0.024
Control (n=96)	91.49±24.28	87.51±33.11	0.091
RVDLT			
Cell saver (n=99)	4.91±2.02	5.17±2.06	0.161
Control (n=99)	5.05±2.14	5.27±2.01	0.268
DSB			
Cell saver (n=96)	6.09±2.19	6.37±2.23	0.059
Control (n=94)	6.04±2.28	6.29±2.42	0.060
RAVLT			
Cell saver (n=99)	7.23±2.98	7.94±2.85	0.005
Control (n=99)	7.41±2.82	7.45±3.19	0.856
Trails B–A			
Cell saver (n=96)	54.25±35.17	51.83±36.23	0.548
Control (n=97)	53.86±33.91	56.00±44.78	0.559
SSB			
Cell saver (n=96)	6.78±1.69	7.31±1.96	0.003
Control (n=95)	6.83±1.76	6.90±1.61	0.666
DSF			
Cell saver (n=96)	10.16±2.39	10.28±2.54	0.529
Control (n=96)	10.08±2.20	10.29±2.05	0.243
CRT–SRT			
Cell saver (n=98)	409.87±120.09	373.09±148.07	0.023
Control (n=96)	432.73±115.20	413.78±87.80	0.121

Data are expressed as mean±SD. VF indicates Verbal Fluency; SSF, Spatial Span Forward; GPB, Grooved Pegboard; RVDLT, Rey Visual Design Learning Test; DSB, Digit Span Backward; RAVLT, Rey Auditory Verbal Learning Test; SSB, Spatial Span Backward; DSF, Digit Span Forward; CRT, Choice Reaction Time; and SRT, Simple Reaction Time.

decline in elderly patients after CABG surgery. The overall incidence of cognitive dysfunction 6 weeks after surgery was 6% in the cell saver group versus 15% in the cardiomy suction (control) group. Although our observed rates of cognitive dysfunction are considerably lower than expected at the inception of this study, they are consistent with the recent evidence of cognitive decline after cardiac surgery, ranging from 7.4% to 13.9%.^{20–22}

Cerebral embolization is likely a primary mechanism of central nervous system injury after cardiac surgery.^{14,23,24} However, the contribution of each type of embolic material (gaseous, solid, or lipid) to the perioperative brain injury is currently unknown. In the present study, the severity and

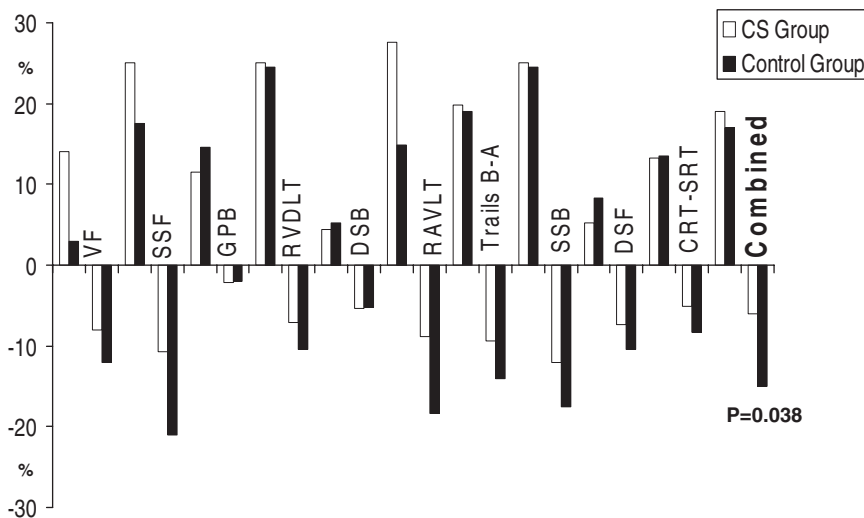


Figure 1. Rates of improvement (positive bars) and deterioration (negative bars) in neuropsychological test scores 6 weeks after CABG surgery. Values shown are expressed as a percentage of patients outside 1 SD on Z score for each test. CS indicates cell saver group; VF, Verbal Fluency; SSF, Spatial Span Forward; GPB, Grooved Pegboard; RVDLT, Rey Visual Design Learning Test; DSB, Digit Span Backward; RAVLT, Rey Auditory Verbal Learning Test; SSB, Spatial Span Backward; DSF, Digit Span Forward; CRT, Choice Reaction Time; and SRT, Simple Reaction Time. The *P* value refers to the χ^2 test for the combined score of the cognitive deterioration variable.

distribution of atheroma (a major contributor to solid particle embolization) were similar between the 2 groups. In addition, no difference existed in the TCD-detected embolic count, predominantly representing larger emboli. Consequently, it is likely that the better cognitive scores in the cell saver group were primarily attributed to the lower lipid cerebral embolic load. This hypothesis is supported by a recent report from Kaza et al,²⁵ who showed that fat particles as small as 10 to 50 μm are effectively removed by the cell saver compared with the cardiomy suction management strategy. Such microscopic particles of fat would travel through the middle cerebral artery undetected by the TCD devices.

Interestingly, an experimental animal study was performed to determine the brain tolerance to cerebral microemboli, comparing the size versus quantity of the embolic load. The investigators noted that embolic material originating from human carotid atheromatous plaques was composed of various sizes of particles, the smaller particles (20 to 60 μm) being 90 times more common than larger ones (60 to 100 μm). Furthermore, smaller particles were more likely to

cause neuronal ischemia and subtle neurological dysfunction, whereas larger particles were more likely to cause brain infarction.^{26,27} If the same relationship exists during CPB in patients undergoing cardiac surgery, the amount of embolic load to the brain is many-fold greater for smaller emboli. Consequently, one would expect that subtle and diffuse neurological dysfunction would be more common than clinically apparent focal neurological sequelae (ie, stroke). Indeed, this observation has been confirmed by numerous clinical studies.

Recent clinical studies have also emphasized the existence of an association between the cerebral embolic load and the task-orientated reduction in cerebral blood flow in the affected areas of the brain, as identified by functional magnetic resonance imaging.^{24,28} Furthermore, it is possible that any inflammatory processes that follow an initial embolic insult can considerably modulate the extent of injury resulting in deleterious systemic hemodynamic effects,²⁹ as well as cognitive dysfunction.^{30,31} In fact, the inflammatory mediators are decreased in cell saver blood,⁸ and decreased systemic

Table 3. Perioperative Hematologic and Coagulation Laboratory Tests

Laboratory Test and Study Group	T1	T2	T3	T4
Hemoglobin, g/dL				
Cell saver	137±12	98±15*	97±11†	102±11
Control	139±11	94±14	95±9	102±10
Platelet count, 10 ³ /mm ³				
Cell saver	234±62	120±37†	136±36	294±123
Control	223±56	130±43	143±37	277±94
INR, U				
Cell saver	1.03±0.14	1.59±0.30*	1.32±0.17	1.62±0.53
Control	1.02±0.07	1.47±0.20	1.28±0.13	1.66±0.60
PTT, s				
Cell saver	36.9±5.7	41.4±8.3*	43.2±7.1	45.1±7.2
Control	37.0±5.0	38.1±5.9	42.6±7.3	45.0±8.9

T1 indicates preoperatively; T2, arrival in intensive care unit; T3, 24 hours postoperatively; T4, hospital discharge; INR, international normalized ratio; and PTT, partial thromboplastin time.

**P*=0.01, †*P*=0.04.

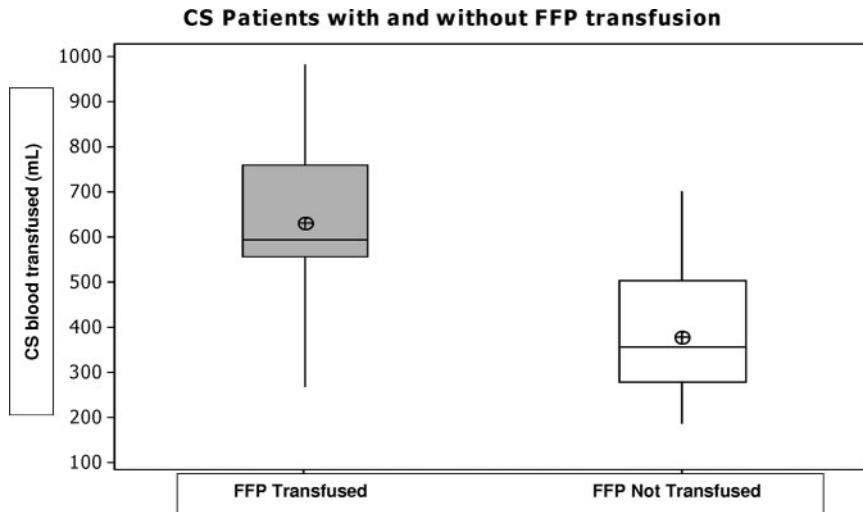


Figure 2. Association between the FFP transfusion rates and the amount of processed cell saver (CS) blood transfusion. The box plot displays the interquartile range representing the 25th (Q1) and 75th (Q3) percentiles. A line across the box is the median. The whiskers represent the lowest and highest observations inside the region. Symbol of plus sign within a circle indicates mean value. The mean amount of the cell saver blood transfused was 632 mL (95% CI, 604 to 660 mL) in the FFP Transfused group and 379 mL (95% CI, 357 to 399 mL) in the FFP Not Transfused group; $P=0.0001$.

inflammatory response has been observed in patients without cardiomy suction.³² Therefore, the reduced cognitive decline observed in the cell saver group may also be due to modified systemic inflammatory response with the application of cell saver. However, this hypothesis was not tested directly in our study.

Although the transfusion outcomes were not the primary objective of our study, they deserve some commentary and possibly further prospective evaluation. First, patients in the cell saver group had higher hemoglobin levels during the first 24 hours after surgery; however, the perioperative packed red cell transfusion rates were similar between the 2 groups. Second, patients in the cell saver group had higher international normalized ratio and lower platelet count at the time of

intensive care unit admission. These findings are likely a reflection of the principle of the cell saver methodology. Although the cell saver is efficient in removing the detrimental debris from shed blood, it “cleans” the blood from plasma and platelets. The result of this process is a red cell mass with a high hematocrit, which may result in a dilutional coagulopathy if transfused in large quantities. A post hoc analysis showed that the group of patients that received a FFP transfusion had a significant increase in the amount of transfused cell saver blood (Figure 2).

A recent small randomized study by Jewell et al⁹ showed that postoperative blood loss, hemoglobin concentration, platelet count, and blood product transfusion were similar between the patients managed with either cell saver or

Table 4. Comparison of Blood Utilization, Postoperative Complications, and Length of Stay

	Cell Saver Group (n=112)	Control Group (n=114)	P
Blood utilization			
24-h postoperative blood loss	787±373	733±342	0.256
Packed red cells, n (%)	59 (52)	57 (50)	0.687
Total No. of units transfused	125	115	
FFP, n (%)	28 (25)	14 (12)	0.018
Total No. of units transfused	68	44	
Platelets, n (%)	13 (11)	14 (12)	0.876
Total No. of units transfused	70	80	
Postoperative morbidity			
Atrial fibrillation, n (%)	41 (36)	40 (35)	0.812
Myocardial infarction, n (%)	4 (3.5)	3 (2.6)	0.683
Renal failure, n (%)	3 (2.6)	4 (3.5)	0.719
Stroke, n (%)	0 (0)	1 (0.8)	NA
Death, n (%)	0 (0)	1 (0.8)	NA
Extubation time, h	6 (2–56)	5 (2–41)	0.694
Hospital length of stay, d	6 (4–18)	6 (4–14)	0.107

Data are expressed as mean±SD, number of patients (%), or median (range). NA indicates not applicable. Blood product transfusion is reflected as the number of patients transfused at any time during the hospital stay.

cardiotomy suction. Two other studies reported that employment of cell saver was not associated with any adverse impact on coagulation parameters or increased blood product transfusion rates.^{33,34} However, the extensive use of cell salvage systems to process cardiomy blood may lead to a critical loss of coagulation factors and platelets, resulting in a bleeding diathesis.³⁵ The findings of our study are in agreement with the latter statement. Recent clinical practice guidelines of perioperative blood transfusion and blood conservation in cardiac surgery prepared by the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists task forces suggest that on the basis of available evidence, only a weak recommendation for autotransfusion during CPB with a cell-saving device can be made. The authors agreed that most of the studies were too heterogeneous and underpowered to draw firm conclusions.³⁶ A large, prospective, randomized controlled trial with the primary objective concentrating on transfusion outcomes would be required to provide further evidence.

In conclusion, the present report is, to the best of our knowledge, the first randomized controlled trial demonstrating that processing of shed blood with a continuous-flow cell saver results in clinically significant reduction in postoperative cognitive dysfunction after CABG surgery. These findings emphasize the clinical importance of lipid embolization in contributing to postoperative cognitive dysfunction in patients exposed to CPB.

Acknowledgments

We would like to thank the Fresenius Corporation for making the cell saver device available for the purpose of the study. The authors would like to thank Bobbi Jo Anderson for her assistance in coordinating this project. We would like to acknowledge the support of the Department of Anesthesia, the Division of Cardiac Surgery, and the Perfusionists at Toronto General Hospital, University Health Network and Department of Anesthesia, University of Toronto.

Source of Funding

This study was funded by the Heart and Stroke Foundation of Ontario.

Disclosures

None.

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CLINICAL PERSPECTIVE

Cerebral microembolization as well as inflammatory response during cardiopulmonary bypass may lead to cognitive decline after cardiac surgery. Currently, transfusion of the unprocessed shed blood (major source of lipid microparticulates and inflammatory mediators) into the patient during cardiopulmonary bypass is common practice to reduce blood loss and blood transfusion. However, processing of shed blood with cell saver before transfusion may reduce the risk of microembolization and/or limit the amount of inflammatory activation. The objective of this study was to determine whether the replacement of cardiomy suction with a continuous-flow cell saver device would reduce cognitive decline in elderly patients after coronary artery bypass graft surgery. A total of 226 patients were randomly allocated to either cell saver or control groups. Cognitive dysfunction was present in 6% (95% confidence interval, 1.3% to 10.7%) of patients in the cell saver group and 15% (95% confidence interval, 8% to 22%) of patients in the control group 6 weeks after surgery ($P=0.038$). Whereas the packed red cell and platelet transfusion rates were similar between the 2 groups, the fresh frozen plasma transfusion rates were 25% versus 12% of patients in the cell saver and control groups, respectively ($P=0.018$). The present report demonstrates that processing of shed blood with a continuous-flow cell saver results in statistically significant reduction in postoperative cognitive dysfunction after coronary artery bypass graft surgery. An association between the fresh frozen plasma transfusion rates and the amount of processed cell saver blood transfusion requires further investigation.