JECT. 2007;39:103–108
The Journal of The American Society of Extra-Corporeal Technology

Case Series

Improved Coagulation and Blood Conservation in the Golden Hours After Cardiopulmonary Bypass

Scott R. Beckmann, BS, CCP;*† Dee Carlile, CCP;*† Randall C. Bissinger, MD;* M. Burrell, MD;* Thomas Winkler, MD;‡ William W. Shely, MD‡

**Salem Hospital, Salem, Oregon; †Fresenius Medical Care Extracorporeal Alliance, San Diego, California; and ‡Northwest Surgical Associates Division of*
The Oregon Clinic, Salem, Oregon

Presented at AmSECT 44th International Conference, Las Vagas, Nevada, April 19–22, 2006.

Abstract: The Hemobag (HB) technique allows the open-heart team to safely concentrate the residual cardiopulmonary bypass (CPB) circuit contents and return a high volume of concentrated clotting factors and blood cells back to the patient as autotransfusion. Hematocrit, platelet count, fibrinogen concentration ([Fib]), prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR) were compared between two prospective convenience groups of cardiac surgical patients whose residual circuit blood was processed by the HB ($n = 10$) or by the Cell Saver (CS; $n = 10$) at two times after CPB: (a) after acute normovolemic hemodilution (ANH) infusion and protamine administration and (b) after admission to the intensive care unit (ICU), ~1 hour after CPB and HB content infusion. Minimal cell processing was also used in the HB patients to conserve blood. "Golden hours" is defined as the first few hours after CPB and protamine sulfate administration and extend into the ICU, when maintaining hemostasis is vital during cardiac surgery and is the most susceptible period for blood product administration and the opportunity to improve patient outcome. Except for PTT, all parameters changed significantly from the ANH infusion and protamine administration to ~1 hour after HB blood infusion and arrival in the ICU. Fibrinogen ($p = .048$) and hematocrit ($p = .046$) were significantly higher in the HB group compared with the CS group at the end of the golden hour despite infusion of significantly more allogeneic blood products ($p = .070$) and more washed red blood cells (RBCs; $p = .001$) in the CS group. All but one of the HB patients did not receive any allogeneic blood products during the golden hours. Use of the HB technique for salvaging blood is associated with significant increases in the patient's protein and cellular concentrations and lowered coagulation times in the important, first few golden hours after CPB, and except for one patient, without the addition of expensive and precarious allogeneic blood products. **Keywords:** case series, Hemobag, ultrafiltration, hematocrit, residual circuit blood, blood salvaging, blood conservation, blood management, cost savings, ethics. *JECT. 2007;39:103–108*

The Hemobag (HB; Global Blood Resources, Somers, CT) technique of autotransfusion allows the open-heart team to safely concentrate the residual cardiopulmonary bypass (CPB) circuit contents and return a high volume of concentrated clotting factors and blood cells back to the patient (1) (See Figure 1).

The HB technique seems to have many of the benefits of modified ultrafiltration (MUF) after CPB in regard to rapidly concentrating the patient's autologous blood and plasma without the surgical time delay associated with the traditional MUF techniques (2,3).

The purpose of this study was to present the changes in red blood cell and fibrinogen concentration and clotting tests in the first hour after protamine administration for two series of patients. One series of 10 patients had the CPB circuit residual blood processed by the HB technique, and in the other 10 patient series, the residual circuit blood was washed by a cell processor.

Address correspondence to: Scott Beckmann, 875 Oak Street, Suite 5020, Salem, OR 97301. E-mail: srbeckmann@comcast.net.
The senior author has stated that authors have reported no material, financial or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

MATERIALS AND METHODS

A two prospective cohort case-series observational design was constructed and approved by the hospital research review committee. The surgical team alternately

selected 20 patients between November 2005 and February 2006 to obtain two well-matched observation groups. The residual circuit blood from each patient was processed by the HB technique or washed by the Cell Saver (Cell Saver 5; Haemonetics Corp., Braintree, MA).

Central hospital laboratory hematocrit, platelet count, fibrinogen concentration ([Fib]), prothrombin time (PT), partial thromboplastin time (PTT), and international normalization ratio (INR) values were compared in convenient sample groups of patients. Surgical patients were judged against each other at two times after CPB: (a) after acute normovolemic hemodilution (ANH) infusion and protamine administration and (b) after admission to ICU, ~1 hour after CPB and HB and ANH content infusion.

An ANH volume (~4 mL/kg) was withdrawn from each patient after heparinization, sequestered, and returned immediately after protamine administration in both the HB and CS patients. Minimal cell processing was also used in both groups of patients to conserve blood. Immediately after bypass, the residual CPB circuit blood was processed by the Cell Saver 5 in the CS patients and the Hemobag technique was used in the HB patients. Residual heparin in the HB contents was neutralized with an additional 50 mg of protamine sulfate after the HB content was infused. The decision to transfuse allogeneic blood bank products was made by the same physicians using the same algorithms for both treatment groups of patients during the time periods in this study.

Process indicators and central hospital laboratory results were statistically compared by independent group *t* test or ANOVA between the CS and HB patients before and after the first hours immediately after protamine administration and the reinfusion of ATS, ANH, and HB blood. Specific factor comparisons were made using Bonferroni adjustments. The α level was set at 0.05 or 0.10 depending on the factors. Statistical analysis was performed using SPSS software (SPSS 14.0; SPSS, Chicago, IL).

RESULTS

Table 1 presents the demographics for the two convenience groups. There was no significant difference between the two groups in age, sex, body surface area, weight, time on CPB, or the distribution of the types of procedures or the surgeons.

Table 2 lists the treatment and laboratory-dependent variables for each patient in the two groups at two time periods in the study. Table 3 lists the patient-by-patient allogeneic, ANH, ATS, and HB volumes used in the few hours immediately after protamine sulfate infusion.

Table 4 presents the results of the statistical analysis of the differences between groups. Except for PTT, all parameters changed significantly from the post-protamine and HB, ATS, and ANH blood infusion to ~1 hour after arrival in the ICU.

Fibrinogen and Hct were significantly higher in the HB group at the end of the golden hours. Significant reductions in PT and INR were also observed after HB content infusion; however, there was only a strong trend in decreased average PTT. CS patients needed significantly

Table 1. Patient descriptive statistics.

Group	Patient	Procedure	Sex	Age (years)	Weight (kg)	BSA (m^2)	CPB (min)
Cell saver patients	1	CABG	Female	81	75	1.81	100
	2	Reop Valve	Female	74	87	1.96	206
	3	Valve	Female	71	76	1.81	88
	4	Valve	Male	76	87	2.09	116
	5	CABG	Male	65	109	2.4	103
	6	CABG	Male	57	74	1.87	95
	7	CABG	Female	64	77	1.78	113
	8	Valve, CABG	Female	78	69	1.66	155
	9	CABG	Male	55	62	1.72	71
	10	CABG	Male	73	76	1.81	152
	Mean SD	70% CABG	50% Male	69	79	1.89	120
				9	13	0.22	40
Hemobag patients	1	CABG	Male	77	78	1.83	99
	2	Valve	Male	62	118	2.38	73
	3	CABG	Male	48	94	2.05	161
	4	Valve, CABG, Maze	Male	81	75	1.93	140
	5	CABG	Female	77	69	1.58	83
	6	Valve, CABG	Female	72	83	1.8	134
	7	CABG	Male	36	126	2.42	117
	8	CABG	Female	79	64	1.76	143
	9	Reop Valve	Female	83	67	2.41	92
	10	Valve	Female	68	62	1.6	115
	Mean SD	70% CABG	50% Male	68	84	1.98	116
				15	22	0.33	29

The descriptive statistics for the two patient groups. There was no significant difference ($p = .05$) between groups in any of the descriptive parameters.

Table 2. Laboratory results by patient series and event.

Group	Event	Patient	Hct	Plt	Fib	PT	PTT	INR
Cell saver patients	Before	1	27	69	249	18.2	38	1.5
		2	26	58	176	18.5	34	1.5
		3	26	126	180	20	32	1.7
		4	26	131	136	19.8	40	1.7
		5	24	90	183	19.5	31	1.7
		6	25	115	226	18.2	39	1.5
		7	25	64	172	19.7	39	1.7
		8	22	82	212	21.2	30	1.8
		9	23	81	151	18.4	31	1.5
		10	23	85	262	22	37	1.9
	After	1	33	92	287	17.5	34	1.4
		2	30	94	248	16	30	1.3
		3	32	140	181	17.9	33	1.5
		4	38	100	160	20.2	41	1.7
		5	26	121	227	17.5	32	1.5
		6	32	111	220	16.8	37	1.4
		7	32	161	225	17.5	33	1.4
		8	34	92	239	18.5	30	1.5
		9	29	123	174	16.2	31	1.3
		10	30	138	426	15	32	1.2
Hemobag patients	Before	1	24	46	173	23.1	27	1.8
		2	28	63	198	25.7	52	2.1
		3	24	92	290	20	36	1.7
		4	24	49	184	20	37	1.7
		5	22	87	138	22	36	1.6
		6	24	114	118	19	41	1.5
		7	24	178	262	17	28	1.4
		8	28	82	240	17.8	31	1.5
		9	22	34	160	22.6	55	1
		10	23	72	226	19	35	1.6
	After	1	33	111	289	18.2	24	1.4
		2	36	115	312	19.2	36	1.5
		3	36	112	423	16	30	1.4
		4	31	89	216	18	31	1.5
		5	35	176	219	19	34	1.4
		6	36	146	326	17	35	1.3
		7	36	222	324	15	24	1.3
		8	36	140	301	15.5	28	1.2
		9	30	100	224	19	47	1.6
		10	36	129	315	15.2	30	1.2

The two events are before = immediately after protamine infusion and after = 1 hour after ANH, ATS, and Hemobag blood infusion; Plt is platelet count (K/mm^3); Fib is fibrinogen concentration (mg/dL); Prothrombin time (PT) and partial thromboplastin time (PTT) are seconds; The International Normalization Ratio (INR) is unitless.

more donor blood products than the HB patients, where 9 of the 10 HB patients needed no allogeneic blood during their hospital stay.

All coagulation test results improved significantly in both patient groups, but CS patients were exposed to substantially more fresh frozen plasma (5 of 10 CS patients) than the 1 of 10 patients in the HB group. Significantly more CS patients received allogeneic blood products than the HB group ($p = 0.025$). Figure 2 shows the financial ramifiations, which were substantial, with the CS group blood charges at $12,563 exceeding the HB group costs of $1722.

DISCUSSION

The data presented in this observational case study of two prospective convenient groups of patients focuses on the first few or golden hours after CPB and protamine sulfate infusion when gaining hemostasis is most important during cardiac surgery. Historically, the first hours after CPB represents the vast majority of operative delay and re-exploration bring backs for bleeding. Most allogeneic blood products are transfused in the golden hours, and the decision to do so is often based on arbitrary clinical observations without adequate documentation for the real need for the bank blood components (4–6).

Use of the HB technique for salvaging residual circuit blood has been associated with overall increases in the patient's protein and cellular concentrations. The purpose of this study was to quantify the effects of infusing concentrated residual bypass circuit blood compared with washed CPB blood during the golden hour after terminating CPB. If the salvage of fibrinogen and other clotting factors with the HB technique is clinically significant, we hypothesize that clotting parameters and allogeneic blood use would be lower in the golden hours after CPB.

The design of this case series has several limitations that are associated with most other case studies. The generalization of our results is limited because the patients were not randomized to two groups. The chance of a type 2 statistic error (failing to reject the null hypothesis when it is actually false) is greater in this method because of the lower group size and absence of randomization.

Despite the limitations of this case series design to reach higher levels of evidence, there are several observations from these data for our two well-matched groups that are remarkable when the residual extracorporeal circuit blood is concentrated compared with washed. We observed that the HB patients realized significantly higher hematocrits and fibrinogen concentrations at the end of the golden hour than the CS group, despite the fact that significantly more allogeneic red blood cells (RBCs) were infused in the CS patients. The platelet counts increased significantly in both treatment groups to similar values by the end of the golden hour, but 4 of 10 CS patients needed platelet packs compared with only 1 of 10 HB patients that needed allogeneic platelets.

The potentially deleterious effects of the transfusion of allogeneic blood products are well studied (7–9). The results of this case series observation strongly suggest that cardiac surgery patients may be spared donor exposures when the residual bypass circuit blood is concentrated to preserve platelets, fibrinogen, and clotting factors compared with washing the circuit contents, even when blood products are indicated by many established transfusion protocols.

Despite concerns that residual CPB circuit blood contains vasoactive and immunologic-active chemicals, and the paradigms about unwashed, salvaged blood, the infusion of the bypass circuit contents after processing with a hemoconcentrator does not seem to be associated with increased patient complications or morbidity (10–17).

Table 3. ANH, ATS, Hemobag, and allogeneic blood use by patient series.

Group	Patient	Plt Pkg	RBC	FFP	Cryo	ANH	HB Vol	ATS	Dnr Exp
Cell saver	1	0	0	0	0	450	0	730	0
patients	2	2	3	3	0	360	0	1215	8
	3	0	2	0	0	500	0	750	2
	4	3	6	8	10	400	0	2500	27
	5	10	0	2	0	450	0	750	12
	6	0	0	0	0	0	0	900	0
	7	2	0	2	0	350	0	750	4
	8	0	2	0	0	400	0	720	2
	9	0	0	0	0	400	0	700	0
	10	0	0	2	0	480	0	720	2
Hemobag	1	0	0	0	0	900	1000	225	0
patients	2	0	0	0	0	600	900	0	0
	3	0	0	0	0	800	900	450	0
	4	2	0	4	2	400	800	225	8
	5	0	0	0	0	350	600	225	0
	6	0	0	0	0	0	800	450	0
	7	0	0	0	0	800	1000	225	0
	8	0	0	0	0	500	2150	0	0
	9	0	0	0	0	350	550	225	0
	10	0	0	0	0	480	1250	450	0

The number of platelet packs (Plt Pkg), units of red blood cells (RBC), fresh frozen plasma (FFP) and cryoprecipitate (Cryo) transfused in the first hours after protamine infusion. ANH is acute normovolemic hemodilution and ATS is autotransfusion washed RBCs. Donor exposures (Dnr Exp) are the total number of allogeneic donor exposures observed.

Table 4. Mean parameter values and comparisons.

Parameter	Treatment	Post CPB and Prot	After 1-Hour ICU	Pairwise *p*	Hemobag Effect	Event Effect	Interaction
Hct	CS	24.7 ± 1.6	31.6 ± 3.2	.010	0.106	<0.001	0.035
	HB	24.3 ± 2.1	34.5 ± 2.3				
Donor exposures	CS	*	2.7 ± 7.4	*	0.107	*	*
	HB	*	0.8 ± 2.5				
Allogeneic RBCs	CS	*	1.3 ± 2.0	*	0.070	*	*
	HB	*	0				
Platelet packs	CS	*	1.7 ± 3.1	*	0.169	*	*
	HB	*	0.2 ± 0.6				
FFP transfusions	CS	*	1.7 ± 2.5	*	0.159	*	*
	HB	*	0.4 ± 1.3				
Cryo units infused	CS	*	1.0 ± 3.2	*	NS	*	
	HB	*	0.2 ± 0.6				
ATS vol RBCs	CS	*	1039 ± 613	*	0.001	*	*
	HB	*	248 ± 166				
HB vol processed	CS	0	*	*	<0.001	*	*
	HB	995 ± 453	*	*			
INR	CS	1.6 ± 0.1	1.5 ± 0.1	NS	NS	0.021	NS
	HB	1.6 ± 0.3	1.4 ± 0.1				
PT	CS	19.2 ± 0.8	17.7 ± 1.4	NS	NS	0.002	NS
	HB	20.6 ± 2.7	17.2 ± 1.7				
PTT	CS	35 ± 4	34 ± 4	NS	NS	NS	NS
	HB	38 ± 9	32 ± 7				
[Fib]	CS	195 ± 42	239 ± 76	.044	0.122	0.001	NS
	HB	199 ± 55	295 ± 63				
Plt Cnt	CS	90 ± 26	117 ± 24	NS	NS	0.001	NS
	HB	82 ± 42	134 ± 40				

Values are mean ± SD. Hct is percent hematocrit. [Fib] is fibrinogen concentration in mg/dL. Plt Cnt is platelet count in K/mm^3. PT is prothrombin time in sec and PTT is partial thromboplastin time in seconds. INR is the unitless international normalization ratio. Pairwise *p* is Bonferroni comparison between HB and non-HB values after 1-hour ICU period. Hemobag effect is between the Hemobag (HB) and Cell Saver (CS) groups. Event is between post CPB and post 1 hour. 2 × 2 ANOVA or an independent study *t* test was used for statistical comparison of HB effect.

We consider the native whole blood that was sufficient to circulate through the patient just moments before while on CPB, to be more than viable to return to the patient at the separation of CPB, only now highly concentrated.

The HB does not totally remove potentially harmful contaminants that may be washed away by most RBC washers; however, the contaminants seem to be transient and reversible in vivo, with the patient blood levels re-

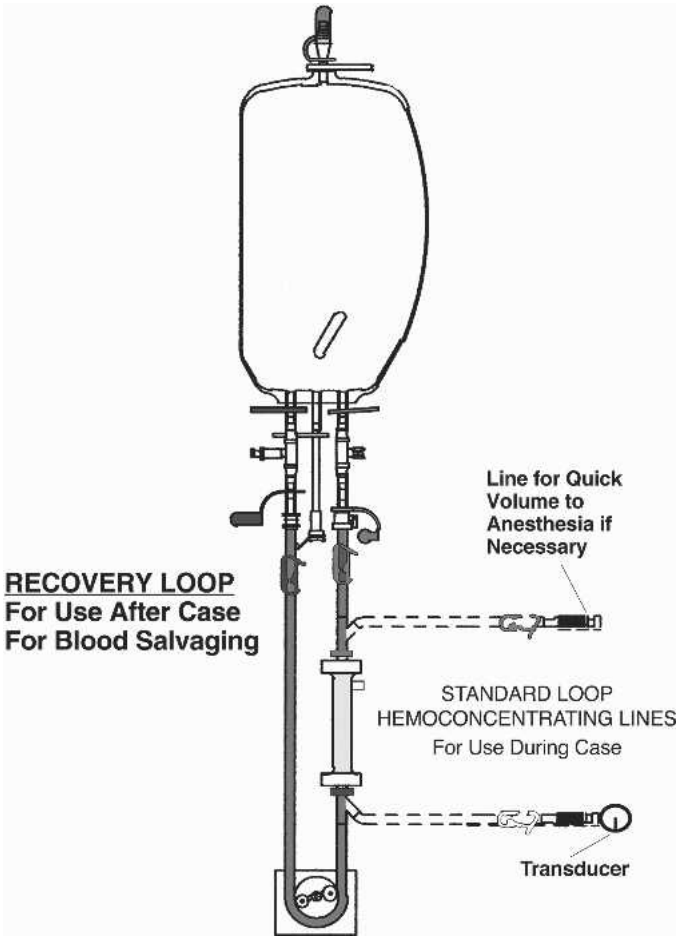

Figure 1. The hemoconcentrator is configured in a standard ECC loop for use during CPB. The Hemobag contents are recirculated and concentrated in a multipass fashion after blood is displaced from the ECC into the Hemobag and its recovery loop.

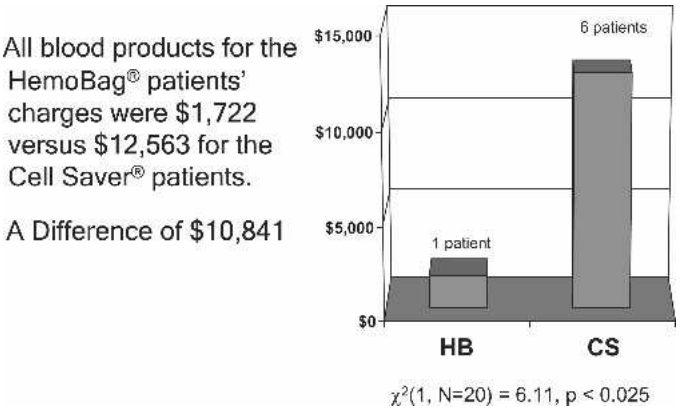

Figure 2. The total cost of allogeneic blood products for the two groups: CS is the Cell Saver group ($n = 10$) and HB is the Hemobag group ($n = 10$). Significantly ($p = .025$) fewer HB patients needed donor exposures.

turning to baselines within hours (18–22). Coagulation and homeostasis seem to be immediately improved with the infusion of concentrated autologous whole blood.

The patient changes associated with the HB off-line MUF seem to provide the same physiologic benefits in adults that are well known and reported with traditional MUF procedures (23,24).

Globally, cardiac surgery programs are searching for new ways to reduce hemodilution and maintain viscosity with higher colloid osmotic pressures. Higher protein levels help to lessen the crystalloid volume requirements that result in dilutional anemia, organ edema, and the concomitant morbidity. The technique with the HB offers a unique cost-effective method to reduce the complications and organ dysfunction associated with hemodilution, while simultaneously reducing the need for allogeneic blood product exposure and the need to change from familiar CPB circuitry (2).

Ethically, in the face of a growing global blood shortage and demand for blood products, discarding any viable native cell concentrates and fractions is not in the patient's best interest, especially when those same patients are exposed to allogeneic blood product replacements with their inherit problems, morbidity, and mortality.

The HB technique offers perfusionists a new tool for autotransfusion and a new role in helping to optimize coagulation and homeostasis in the important first few "golden hours" after the termination of CPB. In accordance with our hospital's established and published goal, ". . . that our patients will receive the best quality care they expect and deserve . . . ," the use of the HB in our program clearly helps achieve this patient service goal and adheres to ethical principals with regard to blood management and conservation. The positive results from our case series observation hopefully will lead readers to design a prospective randomized trial to test the two treatments in a more comprehensive study, but these scientific results should not be overshadowed because they shed light on a new form of autotransfusion for blood salvaging at a critical time when autologous blood is jugular to homeostasis and both short- and long-term survival.

ACKNOWLEDGMENTS

The authors thank the entire Salem Hospital cardiac surgical team, critical care nursing staff, the Directors of blood bank and laboratory services, their staff, and administrative assistant.

REFERENCES

1. Roeder B, Graham S, Searles B, Darling E. Evaluation of the Hemobag: A novel ultrafiltration system for circuit salvage. J Extra Corpor Technol. 2004;36:162–5.
2. Samolyk KA, Beckmann SR, Bissinger RC. A new practical technique to reduce allogeneic blood exposure and hospital costs while preserving clotting factors after cardiopulmonary bypass: The Hemobag. Perfusion. 2005;20:343–9.
3. Moskowitz DM, Klein JJ, Shander A, et al. Use of the Hemobag® for modified ultrafiltration in a Jehovah Witness patient undergoing cardiac surgery. J Extra Corpor Technol. 2006;38:265–70.

4. Friedman MT, Ebrahim A. Adequacy of physician documentation of red blood cell transfusion and correlation with assessment of transfusion appropriateness. Arch Pathol Lab Med. 2006;130:474–9.
5. Spiess BD, Royston D, Levy JH, et al. Platelet transfusions during coronary artery bypass graft surgery are associated with serious adverse outcomes. Transfusion. 2004;44:1143–8.
6. Shander A, Moskowitz D, Tijhwani TS. The safety and efficacy of "bloodless" cardiac surgery. Semin Cardiothorac Vasc Anesth. 2005; 9:53–63.
7. Koch CG, Li L, Duncan AI, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med. 2006;4: 1608–16.
8. Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA. 2004;292:1555–62.
9. Spiess BD. Transfusion of blood products affects outcome in cardiac surgery. Semin Cardiothorac Vasc Anesth. 2004;8:267–81.
10. Solem JO, Olin C, Tengborn L, et al. Postoperative autotransfusion of concentrated drainage blood in cardiac surgery. Experience with a new autotransfusion system. Scand J Thorac Cardiovasc Surg. 1987; 21:153–7.
11. Tassani P, Richter JA, Eising GP, et al. Influence of combined zero-balanced and modified ultrafiltration on the systemic inflammatory response during coronary artery bypass grafting. J Cardiothorac Vasc Anesth. 1999;13:285–91.
12. Das S, Dunning J. Is prophylactic haemofiltration during cardiopulmonary bypass of benefit during cardiac surgery? Interactive Cardiovasc Thorac Surg. 2003;2:420–23.
13. Berdat PA, Eichenberger JE, Pfammatter J-P, et al. Elimination of proinflammatory cytokines in pediatric cardiac surgery: Analysis of ultrafiltration method and filter type. J Thorac Cardiovasc Surg. 2004;127:1688–96.
14. Munoz M, Cobos A, Campos A, et al. Post-operative unwashed shed blood transfusion does not modify the cellular immune response to surgery for total knee replacement. Acta Anaesthesiol Scand. 2006; 50:443–50.
15. Svenmarker S, Engstrom KG, Karlsson T, et al. Influence of pericardial suction blood retransfusion on memory function and release of protein S100B. Perfusion. 2004;19:337–43.
16. Salas MJ, de Vega N, Carmona Aurioles J, et al. Autotransfusion after cardiac surgery. Hematological, biochemical and immunological properties of shed mediastinal blood. Rev Esp Anestesiol Reanim. 2001;48:122–30.
17. Axford TC, Dearami JA, Tagno G, MacGregor H, Valeri CR, Khuri SF. Safety and therapeutic effectiveness of reinfused shed blood after open heart surgery. Ann Thorac Surg. 1994;57:615–22.
18. Luciani G, Menon T, Vecchi B, Auriemma S, Mazzucco A. Modified ultrafiltration reduces morbidity after adult cardiac operations: A Prospective, randomized clinical trial. Circulation. 2001;104:I–253.
19. Raman JS, Hata M, Bellomo R, et al. Hemofiltration during cardiopulmonary bypass for high risk adult cardiac surgery. Int J Artif Organs. 2003;26:753–7.
20. Long GW, Glover JL, Bendick PH, et al. Cell washing versus immediate reinfusion of intraoperatively shed blood during abdominal aortic aneurysm repair. Am J Surg. 1993;166:97–102.
21. Flom-Halvorsen JI, Ovruum E, Tangen G, et al. Autotransfusion in coronary artery bypass grafting: disparity in laboratory tests and clinical performance. J Thorac Cardiovasc Surg. 1999;118:610–7.
22. Wilcox T, Chase G, Charlier J-L, et al. Pericardial suction blood—what are we doing about it? Proc Inaugural Perfusion Downunder. J Extra Corpor Technol. 2006;38:49–50.
23. Onoe M, Magara T, Yamamoto Y, Nojima T. Modified ultrafiltration removes serum interleukin-8 in adult cardiac surgery. Perfusion. 2001;16:37–42.
24. Leyh RG, Bartels C, Joubert-Hubner E, Bechtel JF, Sievers HH. Influence of modified ultrafiltration on coagulation, fibrinolysis and blood loss in adult cardiac surgery. Eur J Cardiothorac Surg. 2001; 19:145–51.