Is it the best practice to throw away clotting factors and plasma proteins?

Achieving the maximum patient benefit from residual ECC blood based on evidence.

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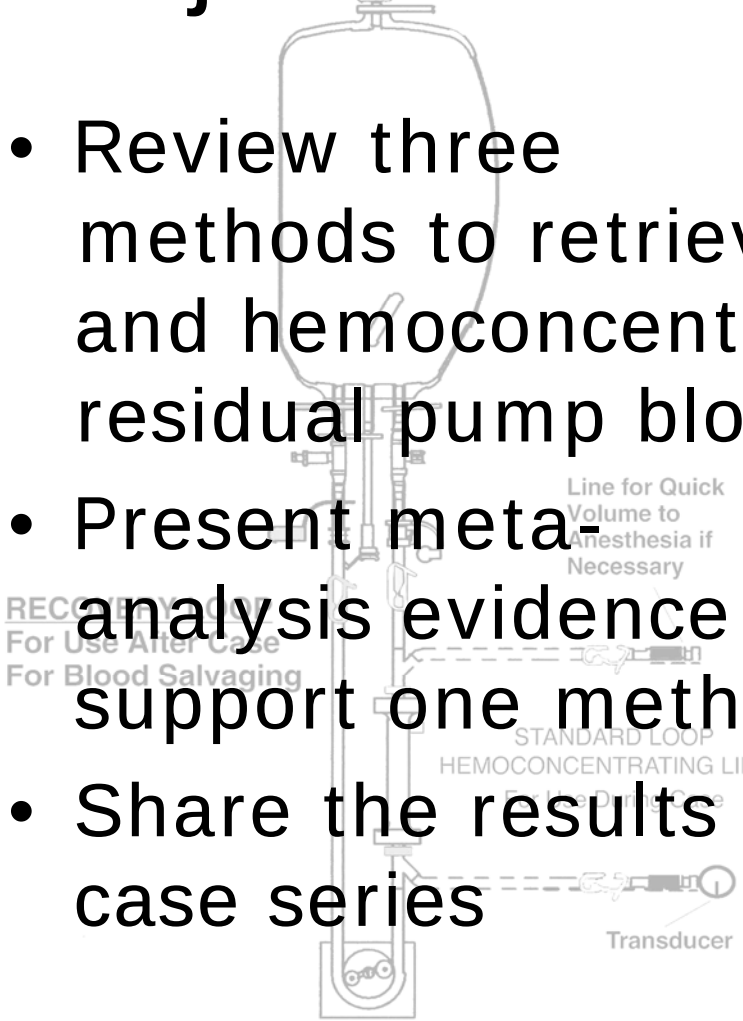
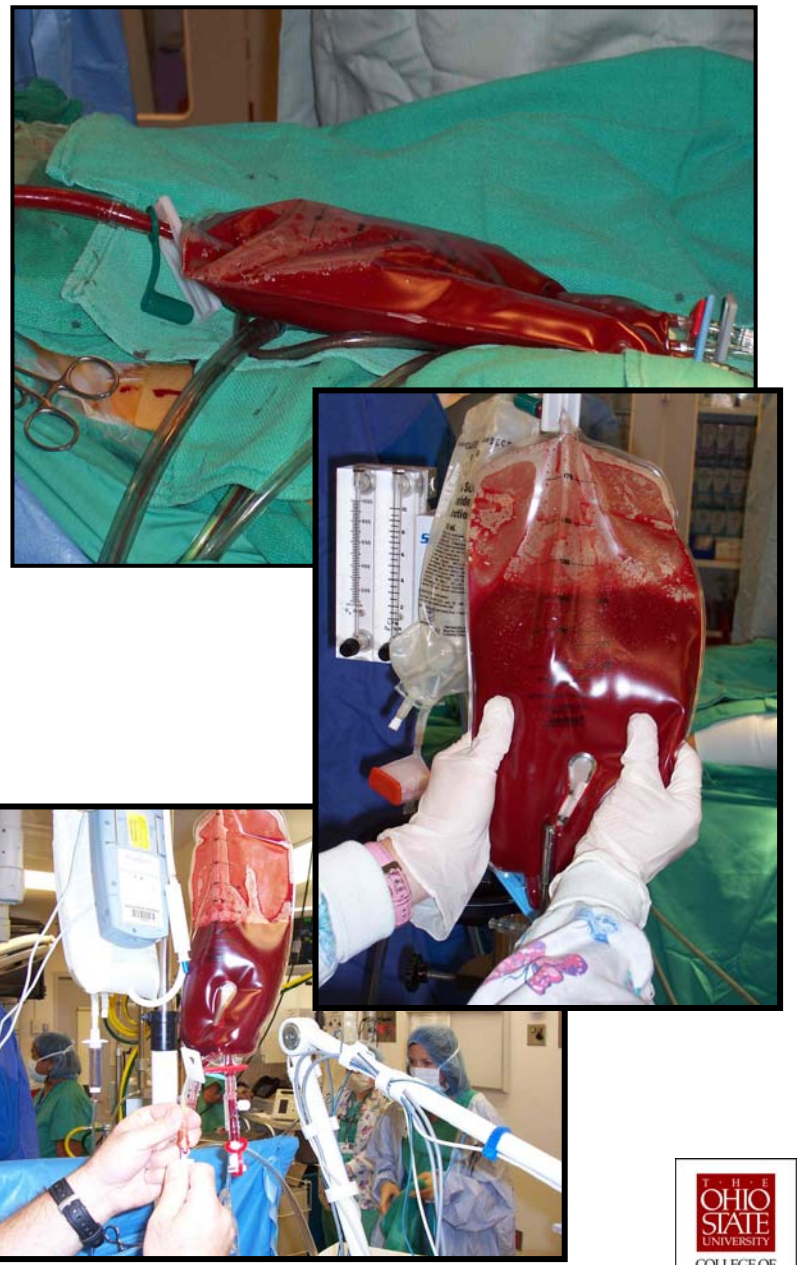
Acknowledge Scott Beckmann CCP, & Salem Hospital Cardiac Surgery Team, Salem OR, and FMC-EA, San Diego, CA

Objectives

- Review three methods to retrieve and hemoconcentrate residual pump blood
- Present meta-analysis evidence to support one method
- Share the results of a case series





Problem

Perfusion 2005; **20**: 237–241

Are we doing everything we can to conserve blood during bypass? A national survey

D Belway[1], FD Rubens[2], D Wozny[3], B Henley[1] and HJ Nathan[3]

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Introduction: Despite major advances in biomaterial research and blood conservation, bleeding is still a common complication after cardiopulmonary bypass and cardiac surgery remains a major consumer of blood products. Although the underlying mechanisms for these effects are not fully established, two proposed major etiologies are the hemodilution associated with the use of the heart–lung machine and the impact of reinfusion of shed cardiotomy blood. Therapeutic strategies that primarily encompass the use of devices or technologies to overcome these effects may result in improved clinical outcomes. ***Objective:*** To determine the extent to which 1) lipid/leukocyte filtration and centrifugal processing of cardiotomy blood, and 2) modified ultrafiltration (MUF) are currently applied in adult cardiac surgery in Canada. Canada, addressing details regarding the frequency of use of cardiotomy blood processing and MUF. ***Results:*** All questionnaires (36, 100%) were completed and returned. With regards to cardiotomy blood management, in 21 centers (58%), no specific processing steps were utilized exclusive of the integrated cardiotomy reservoir filter. Of the remaining centers, two (6%) reported using lipid/leukocyte filtration and 15 (42%) reported washing their cardiotomy blood. Three centers (8%) reported using MUF at the end of CPB. ***Conclusions:*** Despite growing concern about the potential detrimental effects of cardiotomy blood, few centers in Canada routinely manage this blood with additional filtration and/or centrifugal processing prior to reinfusion. Similarly, MUF, demonstrated to be effective in the pediatric

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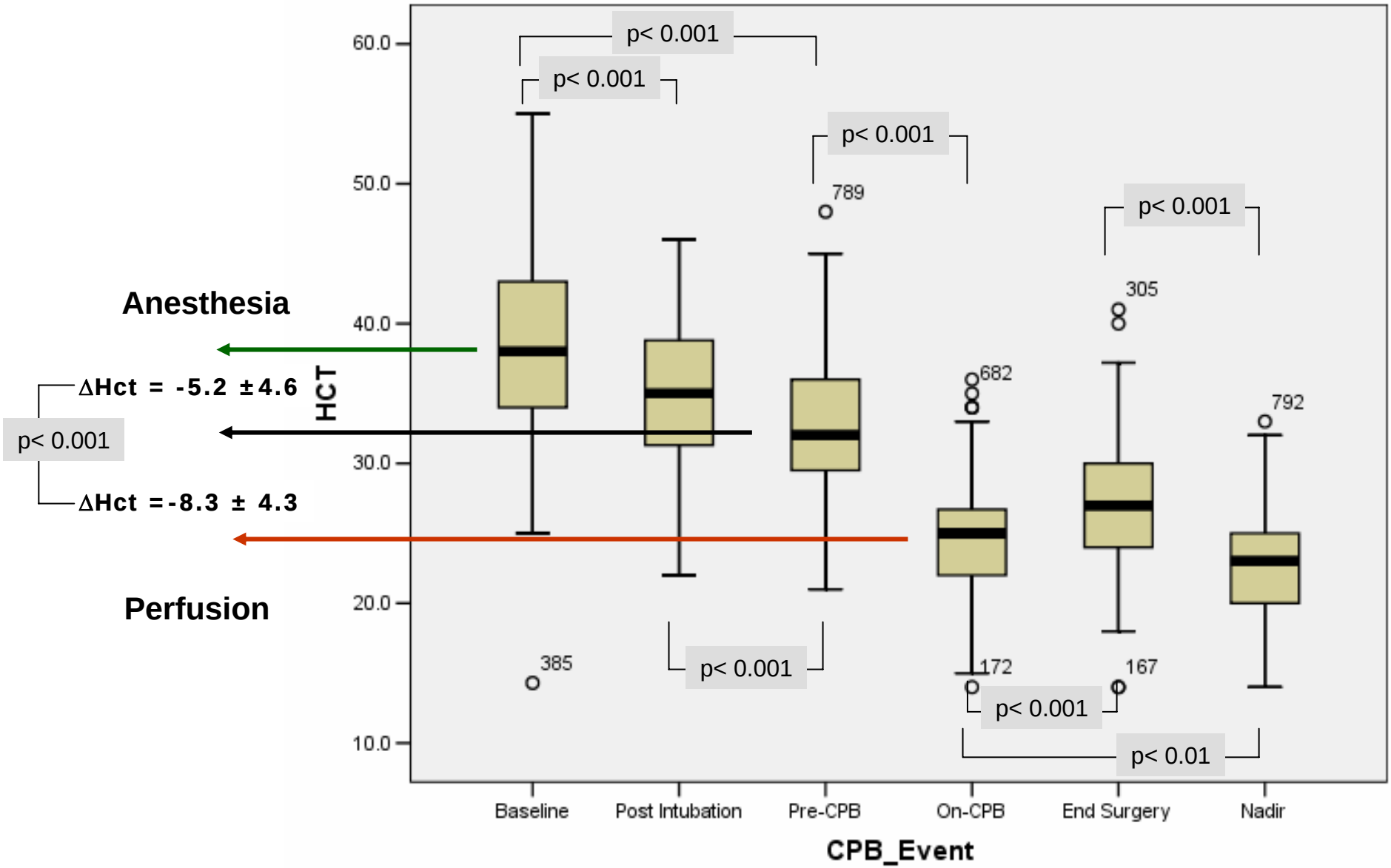
Problem: Drop in Hct with Anesthesia Versus CPB Hct Drop



n = 125 -145 adult cardiac surgery patients in September 2005 @ perfusion.com

Cardiopulmonary Support and Physiology

JTCVS. 2002; 124:20-7.
33,000 articles
225 articles met criteria

Cardiopulmonary bypass: Evidence or experience based?

Claus Bartels, MD, Anja Gerdes, MD, Jörg Babin-Ebell, MD, Friedhelm Beyersdorf, MD, Udo Boeken, MD, Torsten Doenst, MD, Peter Feindt, MD, Michael Heiermann, MD, Christian Schlensak, MD, and Hans-Hinrich Sievers, MD

Objective: Evidence-based medicine is emerging as a new paradigm for medical practice. The purpose of this study was to evaluate the amount and quality of scientific evidence supporting principles that are currently applied for cardiopulmonary bypass performance.

Comparison of Three Blood-Processing Techniques During and After Cardiopulmonary Bypass

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Ann Thor Surg. 1993;56:938-43.

See related editorial on page 11.

investigated cardiopulmonary bypass principles did not prove to be of a high enough level to allow general recommendations to be made.

Conclusions: The scientific data concerning the effectiveness and safety of key principles of cardiopulmonary bypass are insufficient in both amount and quality of scientific evidence to serve as a basis for practical, evidence-based guidelines.

Written on behalf of the Working Group on Extracorporeal Circulation and Mechanical Ventricular Assist Devices of the German

Ultrafiltration benefits

- Selective, rapid removal of plasma water & dissolved solutes, (<50K Daltons) including drugs. e.g. Integrilin, ReoPro, Aggrestat
- Conservation cellular blood components & proteins
  - Hct
  - platelets & clotting factors
  - albumin & plasma proteins
- Removes anaphylatoxins
  - C3a, C4a, C5a
  - IL-1, IL-2, IL-6, IL-8,
  - TNFα, TNFβ
  - MDF, bradykinins
- Improves organ fx
  - myocardial fx
  - cerebral oxygenation
  - pulmonary compliance
- Reduces post-op blood loss & transfusions
- Reduces perioperative morbidity
- Adjunctive to diuretics for the treatment of fluid retention

1. **Naik, 1991, Hospital for the Sick, Great Ormond St. UK.**
2. **Luciani, 2001, MUF reduces morbidity after adult cardiac operations. A prospective, randomized clinical trial.**

Evidence: Techniques to scavenge residual ECC blood

Method	Description	References
Direct infusion (DI)	transfer bag and infusion	Boldt, et al., 1989; Sutton, et al., 1993
	pump directly to patient	Smigla, et al., 2004
Hemoconcentration and infusion (HC)	bag, recirculate, concentrate and infuse [Hemobag®]	Hopeck, et al., 1981; Sanford, et al., 1982; Tamari, et al., 1984; Boldt, et al., 1989; Roeder, et al., 2004; Samolyk, et al., 2005
	modified ultrafiltration with hemoconcentrator	Nakamura, et al., 1990; Groom et al., 1994; Darling et al., 1998; Kiziltepe, et al., 2001; Darling et al., 1998, 2002
Cell washing and infusion (CW)	pump to cell processor, centrifuge and wash	Moran, et al., 1978
Combined methods	pump through hemoconcentrator to patient	Smigla, et al., 2004
	hemoconcentrate cell processing waste	Johnson, et al., 1994; Stammers, et al., 1996

See references for citations

Evidence: Clinical comparisons of methods to salvage residual ECC blood - random patient assignment

Authors	Methods	Measured parameters
Moran, et al., 1978	CW v. DI	CTD, UO, HCT, homologous blood
Luckenbach, et al., 1980	CW v. DI	UO, HCT, homologous blood,
Brickley, et al. 1982	CW v. HC	HCT, platelet count, COP, ACT
Solem, et al., 1987	CW v. HC	PP, COAG, fibrinolytic activation
Boldt, et al., 1989	CW v. HC	FIB, antithrombin III, platelet count, process time, CTD, PFH, elastase, organ function
Nakamura, et al., 1990	CW v. HC	HCT, platelet count, PFH, PP, immunoglobulin
Sutton, et al., 1993	CW v. HC v. DI	HCT, platelet count, PFH, [heparin], CTD, COP, COAG
Johnson, et al., 1994	CW v. HC	FIB, platelet count, PP, leukocytes, CTD
Solem, et al., 1987	CW v. HC	Final product concentrations, PP, activation of the COAG and fibrinolytic system
Eichert, et al., 2001	CW v. HC v. DI	Cost, HCT, COAG, ACT
Nitescu, et al., 2002	CW v. HC	HCT, hemoglobin, PFH, leucocytes, platelets, PP, potassium
Samolyk, et al., 2005*	CW v. HC	Homologous blood, cost, HCT, platelet count, CTD, time on ventilator, ICU time, hospital days

Techniques: DI = direct infusion, HC = hemoconcentration and infusion, and CW = cell washing and infusion; PFH = plasma free hemoglobin; COAG = coagulation profile; HCT = hematocrit; CTD = chest tube drainage; FIB = fibrinogen concentration; COP = colloidal osmotic pressure; PP = plasma proteins; ACT = activated clotting time; Causal comparative study - matched control group

Evidence: Therapeutic and safety issues associated with three methods to process residual pump blood

Issues (outcomes)	Authors
preserving renal and other organ function	Boldt, et al., 1989; Samolyk, et al., 2005
pump blood processing speed	Nakamura, et al., 1990; Samolyk, et al., 2005
preserving platelets and platelet function	Nakamura, et al., 1990; Sutton, et al., 1993; Johnson, et al., 1994; Eichert, et al., 2001; Nitescu, et al., 2002
preserving plasma proteins and colloidal osmotic pressure	Brickley, et al. 1982; Sutton, et al., 1993; Johnson, et al., 1994; Nitescu, et al., 2002;
plasma free hemoglobin	Boldt, et al., 1989; Nakamura, et al., 1990; Sutton, et al., 1993;
pump blood infusion rate	Smigla, et al., 2004; Samolyk, et al., 2005
removal of free water	Boldt, et al., 1989
activation and removal of leukocytes, elastase, cytokines and SIRS mediators	Heerdt, et al., 2004; Hoffmann & Faist, 2001; Journois, 1999; Nakamura, et al., 1990; Boldt, et al., 1989;
heparin and aprotinin concentration	Clar & Larson, 1995; Sutton, et al., 1993; Boldt, et al., 1989
chest tube drainage	Boldt, et al., 1989; Nakamura, et al., 1990; Sutton, et al., 1993; Solem, et al., 1997
allogeneic blood use and cost	Eichert, et al., 2001; Samolyk, et al., 2005;
activation of fibrinolysis	Solem, et al., 1987

See references for citations

Meta-Analysis: Patient (1 hr) post infusion % Hematocrit

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Moran, 1978 (25)	37 ± 0.6				37 ± 0.9
Luckenbach, 1980 (19)	22.5 ± 1.9	4.22 (<0.05)	29.2 ± 1.2		
Brickley, 1982 (8)			23.7 ± 4.6	0.30 (ns)	22.6 ± 2.5
Solem, 1987 (15)			33.5 ± 4.2	-0.62 (<0.05)	36.0 ± 3.7
Boldt, 1989 (20)			33.4 ± 2.7	-0.91 (ns)	36.0 ± 3.0
Nakanura, 1990 (6)			27.0 ± 1.2	1.74 (<0.05)	29.0 ± 1.1
Boldt, 1991 (10)			28.0 ± 2.0	0.60 (ns)	26.0 ± 3.8
Sutton, 1993 (20) ± SEM	25.5 ± 1.0	2.10 (ns)	27.5 ± 0.9	1.89 (ns)	25.6 ± 1.1
Johnson, 1994 (14)			27.5 ± 8.5	-0.90 (ns)	33.8 ± 5.0
Eichert, 2001 (10) [Hb]	10.2 ± 1.0	-0.54 (ns)	10.1 ± 1.1	-0.10 (ns)	10.2 ± 1.0
Sirvinaskas, 2005 (42)	30.5 ± 0.6				33.0 ± 0.8
mean values					

n = sample size; ± 1 Stdev; DI = direct infusion; HC = hemoconcentrate and infuse; CW = cell wash and infuse; d (p) is Cohen d and study p value; ns = not significant; Cohen d: <0.20 is small effect, 0.2 - 0.6 is medium effect, and >0.6 is large effect

$$Cohen\ d = \frac{\left(\overline{X}_{HC} - \overline{X}_{CW}\right)}{\sigma_{pooled}}$$ Cohen...*Psych Bull.* 1992;112:135-9.

Meta-Analysis: Patient (1 hr) post infusion platelet count

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Boldt, 1989 (20)			228 ± 26	2.42 (<0.05)	139 ± 45
Nakanura, 1990 (6) [% platelet recovery]			69	1.06 (ns)	48
Boldt, 1991 (10)			215 ± 38	1.35 (<0.05)	170 ± 28
Sutton, 1993 (20) ± SEM	152 ± 11	2.73 (ns)	197 ± 23	3.33 (ns)	137 ± 11
Johnson, 1994 (14)			180 ± 74	0.23 (ns)	166 ± 52
Eichert, 2001 (10) [Hb]	144 ± 50	0.16 (ns)	152 ± 47	0.19 (ns)	144 ± 39
mean values					

n = sample size; ± 1 Stdev; DI = direct infusion; HC = hemoconcentrate and infuse; CW = cell wash and infuse; d (p) is Cohen d and study p value; ns = not significant; Cohen d: <0.20 is small effect, 0.2 - 0.6 is medium effect, and >0.6 is large effect

$$Cohen\ d = \frac{\left(\overline{X}_{HC} - \overline{X}_{CW}\right)}{\sigma_{pooled}}$$

Meta-Analysis: Patient (1 hr) post infusion [total protein]

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Brickley, 1982 (8)			7.1 ± 0.45	0.20 (ns)	7.0 ± 0.54
Boldt, 1989 (20)			5.43 ± 0.6	2.73 (<0.05)	3.91 ± 0.5
Nakanura, 1990 (6) [% TP recovery]			5.9 ± 0.4	4.09 (<0.05)	4.1 ± 0.5
Johnson, 1994 (14)			4.5 ± 0.6	0.96 (ns)	3.9 ± 0.7
mean values					

Meta-Analysis: Patient (1 hr) post infusion COP

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Brickley, 1982 (8)			11.7 ± 1.7	0.06 (ns)	11.6 ± 1.8
Boldt, 1989 (20)			19.3 ± 2.1	2.68 (<0.05)	14.3 ± 1.6
Sutton, 1993 (20) ± SEM	11.8 ± 0.4	0.88 (ns)	12.2 ± 0.5	3.53 (<0.05)	10.6 ± 0.4
mean values					

Meta-Analysis: Patient (1 hr) post infusion [fibrinogen]

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Solem, 1987 (15)			280 ± 40	-2.90 (ns)	320 ± 110
Boldt, 1989 (20)			208 ± 53	1.03 (ns)	150 ± 59
Nakanura, 1990 (6) [% recovery]			77 ± 12	2.10 (<0.01)	50 ± 146
Sutton, 1993 (20) ± SEM	196 ± 16	2.79 (ns)	248 ± 21	3.05 (ns)	191 ± 16
mean values					

Meta-Analysis: Patient (1 hr) post infusion free $[Hb]_p$

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Brickley, 1982 (8)			27 ± 20	0.43 (ns)	33 ± 06
Boldt, 1989 (20)			34 ± 17	0.55 (ns)	26 ± 11
Nakanura, 1990 (6) [% free Hb removal]			48 ± 18	-1.23 (<0.05)	72 ± 21
Sutton, 1993 (20) ± SEM	40 ± 03	1.41 (ns)	45 ± 04	1.99 (ns)	36 ± 05
mean values					

Meta-Analysis: Patient (1 hr) post infusion - miscellaneous

Source (n)	DI Group	Cohen d (p): HC v. DI	HC Group	Cohen d (p): HC v. CW	CW Group
Solem, 1987 (15): F VIII-C			328 ± 150	0.94 (ns)	195 ± 133
Moran, et al., 1978 (25): cc homologous blood	2,175 ± 175				1,642 ± 195
Luckenbach, 1980 (19): cc homogous blood			0 ± 0	2.38 (<0.05)	79 ± 47
Sirvinaskas, 2005 (42): % patients receiving donor blood	37.8				28.6
Boldt, 1989 (20): [heparin]			1.55 ± 0.6	0.46 (ns)	1.33 ± 0.3
Boldt, 1989 (20): TEG ma			52 ± 11	0.96 (<0.05)	44 ± 07
Moran, et al., 1978 (25): cc / kg urine output	79				75
Luckenbach, 1980 (19): cc urine output			494 ± 64	-2.39 (<0.05)	681 ± 90
Nakanura, 1990 (6): [BUN]			14.0 ± 7.8	-0.74 (ns)	20.5 ± 9.6

n = sample size; ± 1 Stdev; DI = direct infusion; HC = hemoconcentrate and infuse; CW = cell wash and infuse; d (p) is Cohen d and study p value; ns = not significant; Cohen d: <0.20 is small effect, 0.2 - 0.6 is medium effect, and >0.6 is large effect

The Hemobag® Technique

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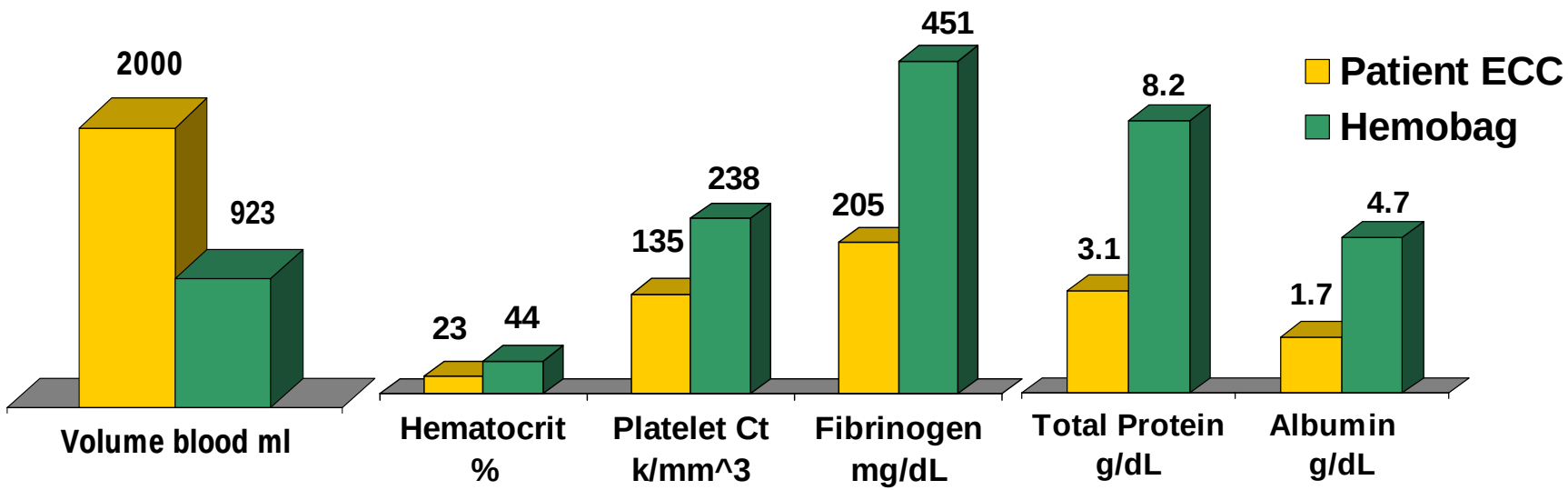
Demographics

Parameter	Control Group	Hemobag® Group	p Value
Patient group size	102	102	NS
Percent male	75	76	NS
Age in years	65 +/- 11	64 +/- 13	NS
BSA m^2	2.0 +/- 0.24	2.0 +/- 0.22	NS
Pre-op weight kg	86 +/- 17	89 +/- 18	NS
% CABG surgery patients	63	61	NS
% Valve surgery patients	18	19	NS
% Valve + CABG patients	19	20	NS
National Bayes risk score	5.2 +/- 7.4	5.0 +/- 6.4	NS
CPB time min	138 +/- 55	137 +/- 52	NS
Ischemic min	94 +/- 34	93 +/- 38	NS

Mean +/- 1 stdev. Nominal data evaluated by chi-square analysis; Other data analyzed by independent sample t-test.

Control Group: ANH. CW, HC, CW ECC vs.
HB Group: ANH. CW, HC, Hemobag®

Average change in blood parameters with Hemobag®



- **2000 ml of autologous residual ECC blood is concentrated to about 923 ml**
- **The total protein and albumin concentration increased significantly ($p < 0.05$)**
- **Hematocrit, platelet count and fibrinogen concentration increased significantly ($p < 0.05$) with hemoconcentration**
- **Factors VII, IX & X > 260 %**

Equivalent FFP Volume & Concentration

- Average Hemobag® volume reinfused: 810 ml
  - Average Hemobag® [fib] concentration: 410 mg/dL
  - Total Hemobag® fibrinogen: 3,321 mg
  - 975 mg fibrinogen in one unit FFP
- Hemobag® equivalent to 3.4 units of FFP regarding [fib]
- Current FFP usage nationwide:
  - In 2003: 2.7 M units
  - In 2004: 3.3 M units

Parameter	Control Group	Hemobag® Group	p Value
Pre-op HCT %	39.7 +/- 5.0	39.9 +/- 5.0	NS
Hemobag® content platelet K/mm³	NM	238 +/- 73	NM
Post-op platelet K/mm³	100 +/- 39	109 +/- 39	NS
Hemobag® content fibrinogen mg/dl	NA	451 +/- 174	NA
Hemobag® total protein gm/dl	NA	8.2 +/- 1.9	NA
Hemobag® albumin	NA	4.7 +/- 1.1	NA
Pre-CPB autologous blood draw (ANH) ml/kg	5.0 +/- 3.3	5.5 +/- 2.8	NS
Hemobag® content HCT %	NA	44 +/- 6	NA
Low operative HCT %	23.1 +/- 3.5	23.9 +/- 2.6	NS
Hemobag® F VII, IX, X	NA	> 260%	NA

Mean +/- 1 stdev. Nominal data evaluated by chi-square analysis; Other data analyzed by independent sample t-test. [ ] and NS are not significant at $p < 0.05$, NM is not measured, NR is not recorded and NA is not applicable.

Parameter	Control Group	Hemobag® Group	p Value
FFP units per patient	1.2 +/- 2.3	1.03 +/- 1.0	[0.191]
Platelet pheresis packs per patient	0.6 +/- 1.0	0.5 +/- 0.8	[0.124]
% Patients transfusion-free	27 %	47 %	0.008
RBC transfusions per patient	1.6 +/- 1.8	1.2 +/- 1.8	NS
Post-op bleeding cc/kg	9.0 +/- 5.9	7.6 +/- 6.3	NS
Donor exposures per patient	3.7 +/- 4.9	2.9 +/- 3.9	NS
Cost blood products $ per patient	$1,157 +/- 1,317	$898 +/- 1189	[0.074]
Total blood product $ per group	$112,233	$87,143	NA
Discharge HCT	31.5 +/- 3.5	31.8 +/- 3.6	NS
% Patients with pulmonary complications	46 +/- 50	37 +/- 48	NS
Total hospital days	13.6 +/- 7.8	8.7 +/- 4.6	0.039

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Case Series Conclusions

- Significantly more Hemobag® patients received no blood products
- HB patients received about 20% less total donor exposures compared to control group, and had fewer average exposures to FFP, platelet packs, cryoprecipitate and RBC transfusions
- HB patients experienced no differences in pulmonary or renal complications, and had shorter average hospital lengths of stay
- HB patients had significantly higher post-operative platelet counts and tended to have higher hematocrit nadirs
- HB techique retrieved and concentrated blood proteins including fibrinogen and clotting Factors VII, IX and X
- The Hemobag® is useful in the treatment of Jehovah Witness patients
- Use of the Hemobag® is safe and effective, even when employed in conjunction with multiple blood conservation techniques

Hemobag Video

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