

# Intraoperative Cell Saving: Is the Solution the Actual Problem?

Krishnan Pillay, MHSc, Perfusion;\*† Shobashini Perumal, BHSc, Medical Laboratory Science\*‡

\*Department of Biomedical and Clinical Technology, Faculty of Health Sciences, Durban University of Technology, Durban, South Africa; †Department of Cardiovascular Perfusion, Division of Cardiothoracic Surgery, Inkosi Albert Luthuli Central Hospital, Durban, South Africa; and ‡National Health Laboratory Services, Inkosi Albert Luthuli Central Hospital, Durban, South Africa

**Abstract:** Allogenic blood is a scarce, precious, and expensive resource that is not always available on demand. After termination of cardiopulmonary bypass, a large amount of residual pump blood remains in the extracorporeal circuit. The cell saver washes and concentrates this blood with .9% normal saline (NS), making autologous blood available and reducing the demand for allogenic blood. To quantify the quality of residual pump blood it was washed with either NS or a bicarbonate-buffered solution (Balsol). A qualitative in vitro analysis was conducted. Residual cardiopulmonary bypass blood from forty bypass circuits was processed with a cell saver device, using NS or Balsol solution. Measurements

made compared the pH, electrolytes, metabolites, hematocrit, hemoglobin, osmolality, albumin, total protein, and strong ion difference. There were significant differences between the NS and Balsol groups. In the Balsol group, osmolality, electrolytes, and strong ion difference were similar to the constitution of Balsol solution after washing, but not with the normal saline group. Washing residual cardiopulmonary bypass pump blood with Balsol solution results in a resuspended red cell concentrate with a superior electrolyte profile and a strong ion difference similar to that of residual pump blood. *J Extra Corpor Technol. 2021;53:62-7*

The development of cardiac surgery assisted with cardiopulmonary bypass (CPB) would not have been possible without the prescription of allogenic blood. However, the deleterious effects of allogenic blood transfusions have been well documented, these include hemolytic and allergic transfusion reactions, transfusion-related acute lung injury, and graft versus host disease (1,2). In addition, there is also the rare risk of viral and bacterial transmitted infections. Public concern about transfusion-transmitted diseases, in particular, human immunodeficiency virus, challenged the value of allogenic blood transfusions, with patients demanding treatment without allogenic blood (3). Stored blood also undergoes time-dependent biochemical and morphologic changes that are collectively known as “storage lesions” that can contribute toward patient pathology (4).

Religious beliefs such as those of Jehovah’s Witness have also imposed restrictions on clinicians regarding the use of blood products. Furthermore, blood banks in developing countries may lack the resources and infrastructure needed to supply the demand for blood and blood products.

The introduction of the intraoperative cell saving (ICS) machine was an attractive alternative and alleviated many of the problems stemming from allogenic blood. It collects, anticoagulates, filters, centrifuges, and washes blood from the surgical field or residual pump blood remaining in the CPB circuit. The result of which is a resuspended red cell concentrate (RCC) equivalent that reduces or completely eliminates the demand for allogenic bank blood. The washing process has also reported to ameliorate levels of micro-aggregates (5), pro-inflammatory cytokines (6), and plasma-free hemoglobin (Hb) (7), which may result in undesirable post transfusion complications. However, ICS almost completely washes out platelets and coagulation factors, and large volume reinfusion can result in dilutional coagulopathy which increases fresh frozen plasma use (8). This dilutional coagulopathy can also increase bleeding and result in a paradoxical increase in allogenic RCC transfusions (9).

Received for publication August 29, 2020; accepted January 28, 2021.  
Address correspondence to: Krishnan Pillay, MHSc, Department of Cardiovascular Perfusion, Division of Cardiothoracic Surgery, Inkosi Albert Luthuli Central Hospital, 800 Vusi Mzimela Road, Cato Manor, Durban 4091, South Africa. E-mail: krishnanpil@gmail.com  
The senior author has stated that the 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.

Little attention has however been given to the manufacturer’s recommendation of NS as a wash solution. Evidence suggests that NS is in no way “normal” or “physiologic” and how it was brought into in vivo clinical practice as an intravenous fluid remains obscure (10). In vivo animal studies reported that NS as a wash solution resulted in a progressive metabolic acidosis (11), and washing with a balanced multi-electrolyte crystalloid solution was associated with fewer acid–base and electrolyte derangements (12). The ubiquitous use of NS as a wash solution for ICS warrants further investigation.

The objective of the investigation was to compare the measured variables when washing residual CPB pump blood with either NS or Balsol solution. It is hypothesized that washing residual pump blood with Balsol as opposed to NS will improve the quality of the processed blood.

**MATERIALS AND METHODS**

The residual pump blood from 40 patients requiring cardiac surgery with CPB was equally divided into the NS group or Balsol group for processing with intraoperative cell saver. The first 20 consecutive patients investigated were the NS group and the second 20 consecutive patients were the Balsol group. The variables measured were hematocrit (HCT), Hb, protein levels, strong ion difference (SID), pH, electrolytes, metabolites, and osmolality of residual pump blood, when washed with either NS or Balsol solution. Written and informed consent was obtained from all patients older than 18 years, where ICS was used. Ethics approval was granted by the Durban University of Technology (ethical clearance number: IREC 021/15). The study was conducted at Inkosi Albert Luthuli Central Hospital, Kwazulu Natal, South Africa.

The CPB circuit was primed with 1.5 liters of Balsol, and eight thousand international units of heparin was added to this. CPB was performed with standard nonpulsatile flow with a standard flow index of 2.4 L/min/m<sup>2</sup>. Hypothermia during CPB was maintained between 28 and 32°C (core) and HCT between 20% and 30%. Cardio protection consisted of cold blood cardioplegia (Buckberg 4:1 ratio) or cold St Thomas II cardioplegia. Maintenance fluid during CPB for both the Balsol and NS groups was Balsol. Calcium, potassium, and sodium bicarbonate were administered as required during CPB to correct deficits for both groups. Weaning off CPB was performed after rewarming to a rectal temperature of at least 35°C, for both groups.

The Medtronic autolog cell saver machine (Medtronic, Minneapolis, MN) was used for both study groups. It operates at a speed of 10,000 revolutions per minute (RPM) with a bowl volume of 135 mL and a wash volume of 250 mL. The blood collection reservoir was primed with either 100 mL of NS or Balsol with 25,000 international

**Table 1.** Constituents of NS and Balsol solutions.

Constituents	Normal Saline*	Balsol†
pH	5.5	7.4
Sodium (mmol/L)	154	130
Potassium (mmol/L)	0	4
Magnesium (mmol/L)	0	1.5
Chloride (mmol/L)	154	110
Bicarbonate (mmol/L)	0	27
Osmolarity (mOsmol/L)	308	273
Strong ion difference (mEq/L)‡	0	27

\*Sabax sodium chloride .9% (Adcock Ingram).

†Balsol, bicarbonate buffered solution (Fresenius Kabi).

‡Strong ion difference is calculated and expressed in mEq/L.

units of heparin added per liter, for both Balsol and NS groups, respectively. Suction was regulated between –100 and –150 mmHg for both groups. Immediately upon termination of CPB, a pre-wash blood sample was collected from the CPB circuit. Residual pump blood was flushed out of the CPB circuit into the cell saver reservoir with 1 liter of Balsol and was processed with either NS or Balsol, respectively (Table 1). All blood collected in the cell saver reservoir from the onset of the procedure was processed together with the residual pump blood.

Immediately after processing of all blood, a post-wash blood sample was taken. Both pre- and post-wash blood sample analyses included pH, sodium, potassium, chloride, ionized calcium, pO<sub>2</sub>, pCO<sub>2</sub>, glucose, lactate, Total CO<sub>2</sub> (TCO<sub>2</sub>), actual bicarbonate (HCO<sub>3</sub><sup>-</sup>), HCT, and Hb analyzed with the GEM 4000® premier™ blood gas analyzer (Werfen, Barcelona, Spain). Laboratory blood sample analysis included total magnesium, inorganic phosphate, albumin, and total protein analyzed with the Siemens Advia 1800 blood gas analyzer (Siemens Healthcare, Erlangen, Germany), and osmolality with the Gonotec osmometer (Gonotec, Berlin, Germany). Laboratory blood samples were centrifuged at 1400 RPM and were frozen at –20°C in a bio-freezer. It was analyzed at the end of the study in a batch to negate the occurrence of errors and artifact.

SID was calculated with the following equation:

$$SID = [\text{SUM OF STRONG CATIONS} - \text{SUM OF STRONG ANIONS}].$$

$$SID = [\text{SODIUM} + \text{POTASSIUM} + \text{CALCIUM}] - [\text{CHLORIDE} + \text{LACTATE}].$$

Ionized magnesium was not available and was therefore excluded from the equation (13), and SID is expressed in mEq/L. Monovalent ion concentrations remain the same, and divalent ions require a conversion factor of two from mmol/L to mEq/L.

## STATISTICAL ANALYSIS

Statistical analyses were performed using STATA v. 13 (StataCorp, College Station, TX). The values presented in Table 2 are means (SD). Two sets of analyses were performed, the changes *within* the groups, before (pre wash) and after (post wash) washing, and the changes *between* the NS and Balsol groups, where  $change = post-wash - pre-wash$  values. The within group differences were analyzed using the paired Student's *t* test after the Shapiro–Wilks normality test demonstrated normal distributions. Wilcoxon's matched pairs signed rank test was used to examine within group differences when normal distributions were not demonstrated. Comparison of the differences between groups (NS vs. Balsol) was performed using Student's *t* test for two independent groups or Wilcoxon's rank sum test for unmatched data as appropriate. All *p* values < .05 were considered statistically significant.

## Summary of Results

Forty adult patients requiring elective cardiac surgery were recruited, and all samples were successfully collected and analyzed, with the data summarized in Table 2. As anticipated for both the NS and Balsol groups, HCT and Hb levels increased significantly ( $p < .05$ ). Pre- and post-wash blood volumes were similarly significant ( $p < .05$ ) for both groups ([NS:  $2,620 \pm 935.2$  mL versus  $476.4 \pm 222.1$ ] and [Balsol:  $2,612 \pm 859.7$  vs.  $447.4 \pm 153.9$ ]). Total protein and albumin were both washed out below the analytical range of instruments for both groups.

In the NS group, post-wash levels for pH, sodium, chloride, and osmolality increased significantly ( $p < .05$ ). Post-wash levels of  $pCO_2$  and total magnesium in the NS group fell below the analytical range of instruments. Post-wash values for  $TCO_2$  and actual bicarbonate were incalculable by the blood gas analyzer in the NS group. All other post-wash levels in the NS group decreased significantly ( $p < .05$ ).

In the Balsol group, post-wash levels for pH,  $TCO_2$ , and actual bicarbonate increased significantly ( $p < .05$ ). Post-wash potassium, total magnesium, and SID levels were similar to pre-wash levels. All other post-wash levels in the Balsol group decreased significantly ( $p < .05$ ).

Significant differences ( $p < .05$ ) were also observed in the change between the NS and Balsol groups with  $pCO_2$ , potassium, sodium, chloride, total magnesium, ionized calcium, osmolality, and SID.

## DISCUSSION

Early studies investigating the quality of intraoperative cell saver blood usually used expired (5), or long stored (14), allogenic RCC with NS as a wash solution. Recent studies continue to use expired RCC (15), or RCC older than 5 days (16), but with different wash solutions. The choice of wash solutions may also vary in composition and differ in availability across countries. Solutions such as Isolyte-S, Normosol-R, and Plasma-Lyte A are not available in South Africa and contain acetate that requires

**Table 2.** Effect of washing residual pump blood with NS versus Balsol wash solution.

Variable	Pre-Wash Saline	Post-Wash Saline	Pre-Wash Balsol	Post-Wash Balsol	Change in Saline	Change in Balsol
pH	7.5 ± 0.1	7.7 ± .1*	7.5 ± 0.1	7.7 ± .1†	.2 ± 0.1	.2 ± 0.1
$pCO_2$ (mmHg)	28.3 ± 2.9	<6.0*‡	30.15 ± 6.0	18.9 ± 4.9†	-22.25 ± 2.9	-11.25 ± 6.4§
$pO_2$ (mmHg)	607.3 ± 72.0	220.6 ± 19.4*	582.9 ± 69.5	226 ± 10.8†	-386.7 ± 68.7	-356.9 ± 65.1
Potassium (mmol/L)	4.5 ± 0.5	1.0 ± .7*	4.2 ± 0.4	4.6 ± 0.3	-3.5 ± 0.8	.4 ± .4§
Sodium (mmol/L)	132.9 ± 3.2	146.3 ± 1.9*	134.7 ± 2.2	125.6 ± 1.0†	13.4 ± 3.8	-9.15 ± 2.1§
Chloride (mmol/L)	107.8 ± 3.1	127.4 ± 2.1*	108.8 ± 2.7	100.2 ± 1.4†	19.7 ± 3.0	-8.6 ± 3.0§
Total magnesium (mmol/L)	1.7 ± 0.7	<.29*‡	1.4 ± 0.4	1.4 ± .03	-1.4 ± 0.7	.0065 ± .4§
Ionized calcium (mmol/L)	1.0 ± .09	.1 ± .03*	.9 ± 0.1	.02 ± .04†	-.9 ± 0.1	-.92 ± .1§
Inorganic phosphate (mmol/L)	.9 ± .40	.09 ± .04*	.8 ± 0.2	.1 ± .024†	-.8 ± 0.3	-.73 ± .19
Lactate (mmol/L)	4.5 ± 1.8	1.7 ± .6*	4.3 ± 1.8	1.6 ± .4†	-2.9 ± 1.6	-2.77 ± 1.4
Glucose (mmol/L)	13.4 ± 3.10	1.55 ± .7*	12.1 ± 3.2	1.6 ± .7†	-11.9 ± 2.8	-10.44 ± 2.7
Osmolality (mOsm/kg)	256.9 ± 38.4	296.2 ± 57.5*	288.8 ± 20.6	272.8 ± 19.9†	39.3 ± 65.4	-15.95 ± 29.0§
Albumin (g/L)	22.2 ± 4.1	<10*‡	23.2 ± 3.3	<10†‡	-12.2 ± 4.1	-13.2 ± 3.3
Total protein (g/L)	40.6 ± 9.3	<20*‡	40.6 ± 6.4	<20†‡	-20.6 ± 9.3	-20.65 ± 6.4
Hematocrit (%)	27.05 ± 2.2	62.3 ± 6.1*	27.4 ± 2.2	62.6 ± 3.8†	35.3 ± 5.6	35.25 ± 4.7
Hemoglobin (g/dL)	9.0 ± 0.7	20.7 ± 2.0*	9.2 ± 0.9	20.9 ± 1.3†	11.7 ± 1.9	11.66 ± 1.7
$TCO_2$ (mmol/L)	22.4 ± 2.9	X	22.9 ± 2.8	24.3 ± .5†	X	1.33 ± 2.7
Actual bicarbonate (mmol/L)	21.51 ± 2.8	X	22.0 ± 2.7	23.7 ± .6†	X	1.68 ± 2.6
Strong ion difference (mEq/L)	27.1 ± 2.1	18.4 ± 2.2*	27.6 ± 3.0	28.44 ± 1.5	-8.7 ± 3.1	.84 ± 3.3§

\**p* value < .05 is significant prewash vs. post-wash NS.

†*p* value < .05 is significant prewash vs. post-wash Balsol.

‡ $pCO_2$ , total magnesium, albumin, and total protein values all fell below the analytical range post-wash; therefore, the lower limit of the electrode reference range was used for statistical analysis.

§*p* value < .05 is significant change in NS vs. change in Balsol.

X,  $TCO_2$  and actual bicarbonate were incalculable by blood gas analyzer.

metabolization in the liver to convert it to bicarbonate. Ringer's lactate solution was available, but contained lactate as a bicarbonate precursor. This investigation is different as it used residual pump blood post CPB that was washed with either NS or Balsol. Hb and HCT recovery are standard parameters used to assess the quality of washed blood. But, potassium and albumin elimination is often also used as guide to the quality of washed blood (17). However, albumin is not readily available for point of care testing, and potassium elimination may not always be desired. Therefore, this investigation also sought to quantify the quality of processed blood using Peter Stewart's SID formula.

The results revealed that Hb and HCT yield increased significantly in both groups with a similar post-wash volume recovery. The resultant yield was similar to that observed by other investigators (17,18). Total protein and albumin were both significantly washed out below the analytical range, which represents a washout of approximately 50% in both study arms. Halpern and coworkers (11,12) also observed a similar 50% washout at the end of the processing compared with baseline. Naumenko and coworkers (7) observed a washout of plasma protein exceeding 70%; this was found to be independent of wash rates and significantly greater at a higher centrifuge speed. Lindau and coworkers (19) recently observed a removal ratio for albumin of 97.9% with the latest continuous auto transfusion technology, the CATsmart<sup>®</sup> (Fresenius Kabi, Homburg, Germany).

The prewash SID on termination of CPB was similar for both groups at approximately 27 mEq/L. This similarity was attributed to Balsol having a calculated SID of 27 mEq/L. Balsol was used to prime the bypass circuit and was used as a maintenance solution during CPB. Post-wash SID significantly decreased in the NS group, but there was no significant change in the Balsol group, the change between groups was significant. In vitro and in vivo research by Morgan and colleagues (20–22) demonstrated that a solution with an SID of approximately 24 mEq/L is balanced, and when infused, will maintain a neutral acid–base status (standard base excess = 0) at standard physiologic state with pH = 7.4 and pCO<sub>2</sub> = 40 mmHg. These demonstrations were later confirmed in a physicochemical simulation model, where the SID of a hypothetical fluid was equal to the Henderson–Hasselbalch actual bicarbonate of 24.5 mEq/L (23). In the Balsol group, post-wash pCO<sub>2</sub> decreased significantly, whereas post-wash TCO<sub>2</sub> and actual bicarbonate increased significantly to approximately 24 mmol/L. This is in contrast to observations of Huber and coworkers (16), where pCO<sub>2</sub> increased and bicarbonate decreased significantly after washing allogenic RCC with a bicarbonate-buffered hemofiltration solution (BB-HS). Post-wash pCO<sub>2</sub> levels in the NS group fell below the analytical range, therefore TCO<sub>2</sub> and bicarbonate were incalculable. Other investigators washing blood with NS also observed similar reductions in pCO<sub>2</sub> (11,12,14,16). In

this study, the SID of the resuspended RCC immediately after processing all the residual pump blood was approximately 18 mEq/L and 28 mEq/L for the NS and Balsol groups, respectively. Post-wash Balsol group SID was similar to SID of blood on termination of CPB.

There was a similar significant reduction in post-wash pO<sub>2</sub> levels in both study arms, which can be explained by simple diffusion into the atmosphere during the collection phase. However, pO<sub>2</sub> was still above 200 mmHg in the post-wash blood for both groups. Other investigators washing stored allogenic RCC with NS (14) and BB-HS (16) observed a significant increase in pO<sub>2</sub> levels. Glucose and lactate were significantly reduced in the post-wash blood recovered in both groups with no differences between groups. These results are similar to observations by previous investigators (5,14,16).

There was a similar significant increase in post-wash pH levels for both NS and Basol groups. Halpern and coworkers (12) observed similar in vivo results in the averaged wash cycles when investigating high-volume cell saver washing with NS and Isolyte-S. When washing long stored allogenic RCC with NS, de Vroege and coworkers (14) observed no change in pre- and post-wash pH levels that remained persistently low. However, Huber and coworkers (16) observed a significant decrease and a significant increase in post-wash pH levels after washing stored allogenic RCC with NS and BB-HS, respectively.

Balsol and NS have an osmolality of 273 mOsmol/L and 308 mOsmol/L, respectively. Post-wash osmolality for the Balsol group decreased significantly to a level similar to that of the Balsol wash solution. Post-wash osmolality for the NS group increased significantly, and the change between groups was also significant. By contrast, Varghese and investigators (5) observed a significant decrease in osmolality after washing outdated RCC with NS using two different cell saver machines. In this study, post-wash inorganic phosphate levels decreased significantly in both groups, with the change between groups being similar, this was because of both wash solutions being void of this constituent. Previous investigations also observed significant reductions in phosphate when washing blood with NS (5,11). Ratliff and coworkers (15) found no significant difference in final phosphate levels after washing with three solutions. However, their results also reveal a reduction in phosphate greater than 50% from the first pre-wash to the last post-wash cycle. Huber and coworkers (16) observed a significant increase in adenosine triphosphate (ATP) after washing allogenic RCC with BB-HS, but no change when washed with NS. Although ATP was not measured in the present study, it highlights the importance of phosphate as a constituent in the development of future tailored wash solutions for ICS.

The present study revealed post-wash calcium significantly decreased in both groups, because of it being void in

both wash solutions. Halpern and coworkers (11) also observed a significant reduction in post-wash calcium when washing with NS. However, Huber and coworkers (16) observed a significant increase in calcium after washing allogenic RCC with NS and a BB-HS solution. The increase was greater in the BB-HS group as that solution contained calcium. Varghese and coworkers (5) observed no change in pre- and post-wash calcium levels when washing allogenic RCC with NS. The present study revealed total magnesium was significantly washed out below the analytical range in the NS group. Other investigators also observed decrease in magnesium when washing with NS (11,15). However, pre- and post-wash total magnesium levels were similar in the Balsol group. Ratliff and coworkers (15) observed minor elevated magnesium levels when washing allogenic RCC with Normosol-R and Plasma-Lyte A. These elevated magnesium levels are a result of Normosol-R, Plasma-Lyte A, and Balsol all containing 3 mEq/L magnesium.

Post-wash potassium levels significantly decreased in the NS group; by contrast, pre- and post-wash potassium levels were similar in the Balsol group. The change between groups was also significant. A cohort of previous investigations using NS as a wash solution revealed a significant washout of potassium (5,11,14,15–17). However, when alternate wash solutions were investigated, potassium levels were either reflective of the wash solution (15) or significantly reduced because of it being void in the wash solution (16). Washing long-stored allogenic RCC with NS is justified to prevent transfusion related hyperkalemia (24), and hyperkalemic cardiac arrest (25). By contrast, washing large quantities of homologous blood with NS for rapid reinfusion can result in a dilution-induced hypokalemic dysrhythmia (26). Swindell and coworkers (27) demonstrated that washing irradiated allogenic RCC with NS significantly decreased potassium levels, and ameliorated hyperkalemia in neonates and infants requiring CPB. However, there was a significant concomitant increase in sodium levels.

Post-wash chloride levels increased significantly in the NS group and decreased significantly in the Balsol group, and the change between groups was also significant. Other investigators washing allogenic RCC with NS also observed similar significant increases in chloride (11,15,16), and when alternate wash solutions were used, similar significant reductions were observed (15,16). Post-wash sodium levels increased significantly in the NS group and decreased significantly in the Balsol group, and the change between groups was also significant. Other investigators washing allogenic RCC with NS also observed similar significant increases in sodium (5,11,14–16). However, when alternate solutions were used, sodium levels were more reflective of that solution (15). Although not in the scope of this investigation but clinically relevant is that NS infusion has been shown to reduce renal blood flow velocities and

renal cortical tissue perfusion in healthy volunteers (28), this may have implications for critically ill patients who require CPB where ICS is used. Furthermore, patients requiring cardiac surgery with CPB are at high risk for electrolyte depletion (29) therefore careful consideration in the choice of wash solution for ICS is needed.

In conclusion, the data from this study has corroborated many of the observations of previous investigations using NS as a wash solution for ICS. The use of NS as a wash solution is justified in attenuating potassium levels when massive infusion of long stored allogenic or irradiated RCC is required. But, there is a concomitant and disproportionate elevation in sodium and chloride levels and a depletion in magnesium and phosphate levels in the electrolyte profile. The clinical complications with regard to these electrolyte imbalances have been reported to be deleterious. However, the data in this study demonstrates that in the clinical setting, washing residual CPB blood with Balsol results in a resuspended RCC concentrate with an osmolality and electrolyte profile that is superior than washing blood with NS. Furthermore, the calculation of SID aids in quantifying the quality of the washed product, and may prove useful in designing wash solutions for future use. It is recommended that *in vivo* research is conducted to assess clinical implications of infusing resuspended RCC washed with alternative solutions.

## ACKNOWLEDGMENTS

We would like to thank the perfusion staff at Inkosi Albert Luthuli Central Hospital who assisted with sample collection.

## REFERENCES

1. Mahdy AM, Webster NR. Perioperative systemic haemostatic agents. *Br J Anaesth.* 2004;93:842–58.
2. Madjdpour C, Spahn DR. Allogenic red blood cell transfusions: Efficacy, risks, alternatives and indications. *Br J Anaesth.* 2005;95:33–42.
3. Spahn DR, Casutt M. Eliminating blood transfusions: New aspects and perspectives. *Anesthesiology.* 2000;93:242–55.
4. Offner PJ. Age of blood: Does it make a difference. *Crit Care.* 2004;8: S24–S26.
5. Varghese BW, Erren M, Westphal M, et al. Processing of stored packed red blood cells using autotransfusion devices decreases potassium and microaggregates: A prospective, randomized, single blinded *in vitro* study. *Transfus Med.* 2007;17:89–95.
6. Amand T, Pincemail J, Blaffart F, et al. Levels of inflammatory markers in the blood processed by autotransfusion devices during cardiac surgery associated with cardiopulmonary bypass circuit. *Perfusion.* 2002;17:117–23.
7. Naumenko KS, Kim SF, Cherkanova MS, et al. The Haemonetics® cell saver 5 washing properties: Effect of different washing pump and centrifuge speeds. *Interact Cardiovasc Thorac Surg.* 2008;7:759–63.
8. Djaiani G, Fedorko L, Borger MA, et al. Continuous flow cell saver reduces cognitive decline in elderly patients after coronary bypass surgery. *Circulation.* 2007;116:1888–95.
9. Rubens FD, Boodhwani M, Mesana T, et al. The cardiotomy trial: A randomized double-blind study to assess the effect of processing of

- shed blood during cardiopulmonary bypass on transfusion and neurocognitive function. *Circulation*. 2007;116:189–97.
10. Awad S, Allison SP, Lobo DN. The history of 0.9% saline. *Clin Nutr*. 2008;27:179–88.
  11. Halpern NA, Alicea M, Seabrook B, et al. Cell saver autologous transfusion: Metabolic consequences of washing blood with normal saline. *J Trauma*. 1996;41:407–15.
  12. Halpern NA, Alicea M, Seabrook B, et al. Isolyte S, a physiologic multi electrolyte solution, is preferable to normal saline to wash cell saver salvaged blood: Conclusions from a prospective, randomized study in a canine model. *Crit Care Med*. 1997;25:2031–8.
  13. Morgan TJ, Power G, Venkatesh B, et al. Acid-base effects of a bicarbonate-balanced priming fluid during cardiopulmonary bypass: Comparison with plasma-lyte 148. A randomised single blinded study. *Anaesth Intensive Care*. 2008;36:822–9.
  14. De Vroeghe R, Wildevuur WR, Muradin JAG, et al. Washing of stored red blood cells by an autotransfusion device before transfusion. *Vox Sang*. 2007;92:130–5.
  15. Ratliff TM, Burnside JL, Hodge AB, et al. The impact of three different wash solutions on autotransfusion products. *J Extra Corpor Technol*. 2018;50:113–6.
  16. Huber D, Witt L, Sumpelmann R, et al. Comparison of bicarbonate-buffered fluid and isotonic saline as cell saver washing fluids for packed red blood cells. *Paediatr Anesth*. 2013;23:1021–6.
  17. Serrick CJ, Scholz M, Melo A, et al. Quality of red blood cells using autotransfusion devices: A comparative analysis. *J Extra Corpor Technol*. 2003;35:28–34.
  18. Damgaard S, Nielsen CH, Andersen LW, et al. Cell saver for on-pump coronary operations reduces systemic inflammatory markers: A randomized trial. *Ann Thorac Surg*. 2010;89:1511–7.
  19. Lindau S, Kohlhaas M, Nosch M, et al. Cell salvage using the continuous autotransfusion device CATSmart - an observational bicenter technical evaluation. *BMC Anesthesiol*. 2018;18:189.
  20. Morgan TJ, Venkatesh B, Hall J. Crystalloid strong ion difference determines metabolic acid-base change during *in vitro* hemodilution. *Crit Care Med*. 2002;30:157–60.
  21. Morgan TJ, Venkatesh B. Designing ‘balanced’ crystalloids. *Crit Care and Resusc*. 2003;5:284–91.
  22. Morgan TJ, Venkatesh B, Hall J. Crystalloid strong ion difference determines metabolic acid-base change during acute normovolaemic haemodilution. *Intensive Care Med*. 2004;30:1432–7.
  23. Omron EM, Omron RM. A physicochemical model of crystalloid infusion on acid-base status. *J Intensive Care Med*. 2010;25:271–80.
  24. Knichwitz G, Zahl M, Van Aken H, et al. Intraoperative washing of long stored packed red blood cells by using an autotransfusion device prevents hyperkalemia. *J Anesth Analg*. 2002;95:324–5.
  25. Sohn HM, Park YH, Byon HJ, et al. Application of the continuous autotransfusion system (CATS) to prevent transfusion-related hyperkalemia following hyperkalemic cardiac arrest in an infant -A case report-. *Korean J Anesthesiol*. 2012;62:281–4.
  26. Peng YG, Janelle GM, Perschau ER, et al. Dilutional hypokalaemia-induced arrhythmias associated with intraoperative cell salvage and reinfusion. *J Cardiothorac Vasc Anesth*. 2006;20:568–9.
  27. Swindell CG, Barker TA, McGuirk SP, et al. Washing of irradiated red blood cells prevents hyperkalaemia during cardiopulmonary bypass in neonates and infants undergoing surgery for complex congenital heart disease. *Eur J Cardio Thorac Surg*. 2007;31:659–64.
  28. Chowdhury AH, Cox EF, Francis ST, et al. A randomized, controlled, double-blind crossover study on the effects of 2-L infusion of 0.9 % saline and plasma-lyte® 148 on renal blood flow velocity and renal cortical tissue perfusion in healthy volunteers. *Ann Surg*. 2012;256:18–24.
  29. Polderman KH, Girbes ARJ. Severe electrolyte disorders following cardiac surgery: A prospective controlled observational study. *Crit Care*. 2004;8:R459–66.