Effect of priming solution and ultrafiltration on post-operative bleeding and blood transfusion in cardiac surgery. Randomized controlled trial

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Abstract
Objective: Assess the effectiveness of priming the extracorporeal circulation system with albumin–mannitol combined with ultrafiltration during extracorporeal circulation to reduce post-operative bleeding and transfusion requirements in heart surgery, as well as its impact on the fluid balance, coagulation and hematocrit parameters, re-operation for bleeding, ICU, and hospital length of stay.

Material and methods: A total of 134 patients scheduled for heart surgery were randomised to receive Ringer’s lactate 1500 mL in the priming reservoir (group C), or mannitol 20% 250 mL, albumin 20% 150 mL and Ringer’s lactate 1100 mL combined with ultrafiltration (group T). Bleeding volume, transfusions, fluid balance, coagulation, and haematology parameters were determined until 48 h in the post-operative period.

Results: There was a reduction of postoperative bleeding in group T, 1165 ± 789 mL vs 992 ± 662 mL (p = 0.17), and red blood cell concentrate transfusions, 694 ± 843 mL vs 413 ± 605 mL (p = 0.03). Intra-operative and post-operative fluid balance was significantly less positive in group T, with an overall balance of 2292 ± 2152 mL vs 5388 ± 2834 mL (p < 0.001). There were higher values of haemoglobin and hematocrit, intraoperative (p < 0.001), on admission to ICU (p = 0.001), and at 6 h (p = 0.05) in group T, and lower INR at 6 h (p = 0.01) and 24 h (p = 0.02). Re-operation rate and length of stay in ICU were higher in group C, but not statistically significant.

Keywords
Priming solution; Ultrafiltration; Cardiopulmonary bypass; Bleeding; Blood transfusion; Cardiac surgery

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Conclusions: The priming of extracorporeal reservoir with mannitol, albumin, and Ringer’s lactate, combined with ultrafiltration, significantly improves intra- and post-operative fluid balance, resulting in a reduction in blood transfusions, with no significant decrease in post-operative bleeding, re-operation bleeding rate, and length of stay in the ICU.

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PALABRAS CLAVE
Solución de cebado; Ultrafiltración; Bypass cardíopulmonar; Sangrado; Transfusión sanguínea; Cirugia cardiaca

Repercusión del cebado con coloides y la ultrafiltración sobre el sangrado posoperatorio y la transfusión sanguínea en cirugía cardiaca. Ensayo clínico aleatorizado

Resumen
Objetivo: Valorar la eficacia del cebado del sistema de circulación extracorpórea con albúmina-mannitol asociado a ultrafiltración para reducir el sangrado posoperatorio y las necesidades transfusionales en cirugía cardiaca, así como su repercusión sobre los balances hídricos, los parámetros de coagulación y hematimetría, la reintervención por sangrado y la estancia en UCI y hospitalaria.

Material y métodos: Ciento treinta y cuatro pacientes programados en cirugía cardiaca fueron aleatorizados para recibir en el cebado Ringer lactato 1.500 mL (grupo C), o 250 mL de manitol 20%, 150 mL de albúmina 20% y 1.100 mL de Ringer lactato asociado a ultrafiltración (grupo T). Se determinaron el volumen de sangrado, las transfusiones, los balances hídricos, los parámetros de coagulación y la hematimetría hasta las 48 h del posoperatorio.

Resultados: Encontramos una reducción en el grupo T del sangrado posoperatorio, 1.165 ± 789 mL frente a 992 ± 662 mL (p = 0,17), y de la transfusión de hemáties, 694 ± 843 mL frente a 413 ± 605 mL (p = 0,03). El balance hídrico intraoperatorio y posoperatorio fue significativamente menos positivo en el grupo T, con un balance global de 2.292 ± 2.152 mL frente a 5.388 ± 2.834 mL (p < 0,001). Hubo valores superiores de hemoglobina y hematocrito intraoperatorio (p < 0,001), al ingreso en UCI (p = 0,001) y a las 6 h (p = 0,05) en el grupo T, e inferiores de INR a las 6 h (p = 0,01) y 24 h (p = 0,02). Las tasas de reintervención y estancia en UCI fueron superiores en el grupo C, pero no significativas.

Conclusiones: El cebado del sistema de circulación extracorpórea con manitol, albúmina y Ringer lactato, asociado a ultrafiltración, mejora significativamente los balances hídricos intraoperatorio y posoperatorio y reduce el volumen de transfusión de sangre, con una repercusión no significativa sobre el sangrado posoperatorio, reintervenciones por sangrado y estancia en UCI.

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Introduction

Postoperative haemorrhage is a common complication of cardiac surgery that requires a large amount of blood products. Several studies have shown the association between blood transfusions and morbidity and mortality.1–5 These risks are directly associated with the amount of blood given, although exposure to just 1 or 2 units of RBC is already a major risk factor.1,5 Reducing perioperative blood loss and exposure to blood transfusions should, therefore, be a priority not only for the anaesthesiologist but also for the entire surgical team.

The high rate of intraoperative blood loss and transfusion during cardiac surgery is due to a number of factors such as contact with non-endothelial surfaces, endothelial injury, ischaemia-reperfusion injury, haemodilution and inflammation, which in turn activate coagulation and the kinin–kallikrein, fibrinolytic, and complement systems, affecting platelet clumping and clot stability.6 Haemodilution plays an important role; in vitro studies and observation of procedures involving cardiopulmonary bypass (CPB) have shown that it lowers not only haematocrit levels but also causes haemostatic alternations.7,8

Various strategies for reducing haemodilution and its associated problems have been explored, including changing the composition of the by-pass pump priming solution, reducing the volume of solution used, or inducing a negative balance by the administration of diuretics or use of ultrafiltration techniques. Although the use of non-blood priming solutions in by-pass pumps is now standard practice in adult cardiac surgery, the ideal solution and its effect on blood loss and blood product requirements is the subject of
much debate.9-12 The use of haemofilters, haemoco- 

nity techniques.

Although many studies have analysed the use of di-

ferent priming solutions or ultrafiltration systems, to

the best of our knowledge the combined effect of both

these on blood loss and the need for transfusion has

never been explored. We hypothesise that the combined use of con-

ventional ultrafiltration techniques together with the addition of

mannitol and albumin to the priming solution could limit

haemodilution and improve clinical outcomes. The primary

aim of the study is to evaluate the effect of the forego-

ing on reducing postoperative blood loss, the percentage of

transfused patients, and intra- and postoperative transfu-

sion requirements. The secondary aim is to study the effect

of the foregoing on intra- and postoperative fluid balance,

coaulation and blood count parameters, the need for rein-

tervention due to blood loss, and length of ICU and hospital

stay.

**Patients and methods**

The study was approved by the independent ethics

committees of both our hospital and autonomous commu-

nity (EudraCT number 2008-008009-23), and we obtained

informed consent from all patients. This is a phase IV,

randomised, single centre, placebo controlled, open label,

parallel group study. Patient follow-up continued until dis-

charge from the hospital.

Inclusion criteria were: aged 18 or over, elective car-

diac surgery with CPB, with a minimum stay in the ICU

of 48 h, and patient informed consent. Exclusion criteria

were: patients scheduled for thoracic aortic surgery

cumulative arrest, reintervention, severe liver failure

(cirrhosis, Child-Pugh class B-C), severe kidney failure

(creatinine over 2 mg/dL or glomerular filtration rate

less than 30 mL/min/m²), coagulation dis-

order or platelet count below 150,000/mm³, patient

receiving antiplatelet agents up to 72 h prior to surgery,

patient receiving low-molecular-weight heparin up to

12 h prior to surgery or heparin sodium up to 4 h prior to

surgery, preoperative anaemia (haemoglobin level under

12 g/dL in women and 13 g/dL in men), need for preo-

perative inotropic drugs or intra aortic balloon pump, or allergy

to any of the study drugs.

Study patients were randomised in a computer-generated

1:1 ratio. In patients assigned to the treatment group

(group T), the CPB priming solution was mannitol 20%

250 mL, albumin 20% 150 mL, and lactated Ringer’s solu-

tion 1100 mL. After disconnection from CPB, a further dose

of mannitol 20% 100 mL was administered intravenously

for 10 min. All patients in this group were haemocon-

centrated by means of conventional haemofiltration at a

blood flow rate of 300 mL/min and a circuit pressure of

450 mmHg during CPB using an SH 14 Sorin filter® (Sorin

Group, Milan, Italy). In control group patients (group C),

the CPB priming solution was lactated Ringer’s solution

1500 mL, with a dose of 20 mg furosemide (Seguril®) diluted

in 100 mL of 0.9%, saline solution administered for 10 min

after CPB. Haemofiltration was not performed in these

patients.

All patients received 1.5 mg/kg tranexamic acid

(Amcarlbin®) followed by continuous perfusion of

1 mg/kg/h until surgery was complete. CPB was performed

using a cone centrifugal pump (Bio-Medicus performer

Medtronic: Minneapolis, Minnesota, USA) with a membrane

oxygenator (PrimO2x Sorin®, Milan, Italy), and a blood

flow of 2.5–3 L/min/m², under moderate hypothermia

(34°C). Activated clotting time (ACT) was maintained

at minimum 480 s by means of regular doses of heparin

sodium. At the end of CPB, heparin was reversed using

proteinate sulphate according to blood heparin levels

and ACT. Patients received 3 mL/kg/h intraoperative lac-

tated Ringer’s solution. During the postoperative period,

1500 mL of glucose saline solution was administered over

the first 24 h, and no more than 1500 mL over the follow-

ing 24 h. Blood pressure, central venous pressure and cardiac

output were monitored in all patients using a FloTrac

Vigileo system® (Edwards, Lifesciences, Irvine, Califor-

nia, USA). To maintain haemodynamic stability, patients

were given 6% hydroxyethyl starch (Isohes®) based on

conventional monitoring parameters of up to 50 mL/kg/day,

and vasoactive drugs at the discretion of the attending

anaesthesiologist to maintain mean blood pressure

>60 mmHg, central venous pressure at 8–12 mmHg and

cardiac output at >2L/min/m². Transfusion of packed

red blood cells (pRBC) was carefully defined to maintain

haemoglobin levels above 8 g/dL in the pre-CPB period,

6 g/dL during CPB, 7 g/dL in the post-CPB period, and

8 g/dL in the postoperative period. Plasma and platelets

were administered at the end of CPB at the discretion of

the attending anaesthesiologist in the presence of diffuse

blood loss with little or no clotting, not associated with

active blood loss from vascular, coronary or surgical field

blood vessel anastomoses or abundant, life-threatening

local bleeding. During the postoperative period a stan-

dard protocol based on the results of clotting tests and

blood loss was followed (Fig. 1). During the postope-

rative period, antiplatelet agents and anticoagulants

were not administered until 12 h after the end of surgery.

Patients were discharged from the ICU according to ICU

criteria.

During the study, we recorded: (1) amount of blood

(mL) collected from chest drains 24 h and 48 h post-surgery;

(2) transfusion of pRBC (number of units and mL, con-

sidering each unit to contain 350 mL), fresh frozen plasma (mL)

or platelets (number of units and mL, considering each unit

to contain 150 mL) from the start of CPB until exit from

theatre, and during the first 48 h in the ICU; (3) number of

patients requiring pRBC, plasma or platelets during surgery

and in the first 48 h post-surgery; (4) intraoperative fluid bal-

ance: (fluid volume + priming solution volume + cardioplegia

solution volume + transfusion volume) – (haemofiltrate vol-

ume + diuresis + suction blood + residual blood in the reser-

voir) × 1 mL/kg/h for negligible losses; (5) postoperative

fluid balance (fluid volume + transfusion volume + oral intake

volume) – (diuresis + suction blood + 0.5 mL/kg/h for negligi-

ble losses); (6) blood haemoglobin at disconnection from

CPB and haemoglobin, INR, APTT, platelets and fibrinogen

on admission to the ICU and at 6, 24 and 48 h; (7) number of

patients needing vasoactive or inotrope drugs; (8) number
of patients needing reintervention due to bleeding or blockage during the first 48 h post-surgery, and (9) length of stay in the ICU and hospital.

To calculate the sample size we retrospectively collected the mean ± standard deviations for blood loss in the first 24 h and the number of intraoperative and postoperative blood transfusion from a sample of 200 patients undergoing CPB heart surgery. On the basis of these data, we estimated that a sample size of 67 patients per treatment group would be needed to show a 30% reduction in blood loss, with an estimated 5% loss, a confidence interval of 95% (p < 0.05) in a two-tailed test with a power of 80%. Of the total number of patients, 90% required transfusion of blood products during the first 48 h. To show a 30% reduction in the percentage of patients receiving transfusion in the first 48 h, including time in theatre, using the same statistical criteria, we estimated that 40 patients would be needed in each group. Therefore, 134 patients were included, divided into two groups of 67 patients.

Data were analysed statistically with SPSS® 20.0 on an intention-to-treat basis. All randomised subjects (treated and evaluable) were included. Continuous quantitative variables were expressed as mean and standard deviation; non-continuous quantitative variables were expressed as median and interquartile range; and qualitative variables were expressed as absolute numbers and percentages. All confidence intervals were set at 95%. The student’s t test was used to analyse continuous quantitative variables, and the Chi-squared or Fisher’s test was used for qualitative variables. The Wilcoxon test was used to analyse differences between non-continuous or non-normal quantitative variables.

Results

A total of 134 patients were included, 67 in each group. One patient in group T and 1 in group C died during surgery due to circumstance not related to the protocol or study products. Finally, 132 patients were included in the study, 66 in each group. The study groups were comparable in terms of demographic characteristics, preoperative tests, usual medication, kidney function, type of surgery, additive EuroSCORE I, duration of CPB, aortic clamping and surgery (Table 1).

With regard to the primary aims of the study, blood loss in group T patients fell by 18% at 24 h and by 15% at 48 h, although this reduction was not statistically significant (Table 2). Group T patients receive less volume of pRBC: 6% less intraoperative transfusion, 40% less in the postoperative period, with a total reduction of 28% after 48 h; only the postoperative period volume was statistically significant. The volume of plasma and the units of platelets given were similar in both groups, with no significant differences (Table 2). There were no significant differences in the percentage of patients needing intraoperative or postoperative pRBC transfusion, or overall. Neither did we find difference in the plasma or platelet transfusion rate (Fig. 2). Significantly, fewer pRBC units were needed per T-group patient in the postoperative period (Table 2). Nine C-group patients (13.6%) needed additional protamine during the immediate postoperative period vs 1 (1.5%) patient from the T group (p = 0.009).

With regard to the study’s secondary aims, CPB, intraoperative, postoperative and overall fluid balance was positive and significantly higher in group C (Table 3). We observed a 77% reduction in fluid balance during CPB, 66% in the intraoperative period, 44% in the postoperative period, and 57% overall in group T vs control, although the balance remained positive. Haemofiltrate volume in group T was 1885 ± 691 mL. Group C patients received 68 ± 46 mg furosemide during ICU stay vs 53 ± 39 mg in group T (p = 0.04). In group T, 52% of patients required inotropics or vasoactive drugs vs 58% in group C (p = 0.6). Preoperative haemoglobin levels and clotting test results after CPB disconnection, on admission to the ICU, and a 6, 24 and 48 h are shown in Table 4. We found significantly higher haemoglobin

Figure 1  Postoperative transfusion protocol. APTT: activated partial thromboplastin time; Fbg: fibrinogen; INR: international normalised ratio.
and haematocrit levels in group T during the intraoperative period (p < 0.001), on admission (p = 0.001) and at 6 h (p = 0.05), and lower INR rates at 6 h (p = 0.01) and 24 h (p = 0.02). Group C patients stayed longer in the ICU than those in group T: 2 (2–3) days vs 3 (2–4) days (p = 0.053). Hospital stay did not vary between groups: 15 ± 11 days (group C) vs 14 ± 8 days (group T) (p = 0.52). None of our study patients died in the postoperative period and up to discharge from hospital.

Five (7.6%) group C patients vs 1 (1.5%) group T patient required reintervention for bleeding or blockage (p = 0.095). When patients with reintervention were excluded from the analysis, we found no significant differences in blood loss: 937 ± 490 mL (group T) vs 1017 ± 556 mL (group C) (p = 0.39), or in volume of pRBC given: 745 ± 592 mL (group T) vs 871 ± 836 mL (group C) (p = 0.33). Differences in ICU stay, however, were significant: 2.6 vs 3.1 days (p = 0.026).

### Table 1 Demographic, preoperative and surgical data.

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 66)</th>
<th>Group T (n = 66)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>69 ± 10</td>
<td>66 ± 12</td>
<td>0.10</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>25/41</td>
<td>29/37</td>
<td>0.48</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76 ± 13</td>
<td>73 ± 13</td>
<td>0.12</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164 ± 10</td>
<td>163 ± 10</td>
<td>0.50</td>
</tr>
<tr>
<td>Preoperative data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.2</td>
<td>0.10</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.62 ± 0.12</td>
<td>0.64 ± 0.10</td>
<td>0.72</td>
</tr>
<tr>
<td>Preoperative medication (number of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betablockers</td>
<td>29</td>
<td>28</td>
<td>0.86</td>
</tr>
<tr>
<td>Diuretics</td>
<td>31</td>
<td>27</td>
<td>0.48</td>
</tr>
<tr>
<td>ACEI</td>
<td>27</td>
<td>29</td>
<td>0.73</td>
</tr>
<tr>
<td>LMWH</td>
<td>7</td>
<td>10</td>
<td>0.44</td>
</tr>
<tr>
<td>Surgical data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of surgery (number of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valvular</td>
<td>43</td>
<td>42</td>
<td>0.73</td>
</tr>
<tr>
<td>Coronary</td>
<td>15</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>8</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Duration of CPB (min)</td>
<td>105 ± 36</td>
<td>96 ± 35</td>
<td>0.14</td>
</tr>
<tr>
<td>Clamp time (min)</td>
<td>76 ± 28</td>
<td>72 ± 23</td>
<td>0.36</td>
</tr>
<tr>
<td>Length of surgery (min)</td>
<td>292 ± 45</td>
<td>294 ± 37</td>
<td>0.72</td>
</tr>
<tr>
<td>Additive EuroSCORE I</td>
<td>5.8 ± 3.4</td>
<td>5.1 ± 2.6</td>
<td>0.18</td>
</tr>
</tbody>
</table>

C: control group; CPB: cardiopulmonary bypass; LMWH: low-molecular-weight heparin; ACEI: angiotensin-converting enzyme inhibitors. Data expressed as mean ± standard deviation or absolute numbers.

### Table 2 Postoperative bleeding and transfusion of pRBC and blood products.

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 64)</th>
<th>Group T (n = 64)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding at 24 h post-surgery (mL)</td>
<td>884 ± 650</td>
<td>725 ± 532</td>
<td>0.13</td>
</tr>
<tr>
<td>Bleeding at 48 h post-surgery (mL)</td>
<td>1165 ± 789</td>
<td>992 ± 662</td>
<td>0.17</td>
</tr>
<tr>
<td>Intraoperative pRBC transfusion (mL)</td>
<td>419 ± 540</td>
<td>392 ± 396</td>
<td>0.75</td>
</tr>
<tr>
<td>Postoperative pRBC transfusion (mL)</td>
<td>694 ± 843</td>
<td>413 ± 605</td>
<td>0.03</td>
</tr>
<tr>
<td>Total pRBC transfusion (mL)</td>
<td>1113 ± 1174</td>
<td>805 ± 767</td>
<td>0.08</td>
</tr>
<tr>
<td>Intraoperative pRBC transfusion/patient (units)</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
<td>0.71</td>
</tr>
<tr>
<td>ICU pRBC transfusion/patient (units)</td>
<td>1.5 (0–2)</td>
<td>1 (0–2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total pRBC transfusion/patient (units)</td>
<td>2 (1–4)</td>
<td>2 (1–3)</td>
<td>0.35</td>
</tr>
<tr>
<td>Total plasma transfusion (mL)</td>
<td>613 ± 741</td>
<td>455 ± 446</td>
<td>0.14</td>
</tr>
<tr>
<td>Total platelet transfusion (units)</td>
<td>0.9 (0–1)</td>
<td>0.5 (0–1)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

C: control group; pRBC: packed red blood cells; T: treatment group; ICU: Intensive Care Unit. Data expressed as mean ± standard deviation or median (interquartile range).
Similarly, our studies were designed to compare the effects of different priming solutions on blood loss and fluid balance during CPB. These comparisons were based on prospectively collected data from patients undergoing cardiac surgery.

Discussion

Our results show a significant reduction in the volume of blood given during the postoperative period together with less positive intraoperative and postoperative balances relative to CPB pump priming and the use of ultrafiltration. Blood loss, reintervention for bleeding, and length of stay in the ICU fell in the treatment group, although these values were not significant.

The reduction in blood loss was both clinically and statistically insignificant, showing that combining these treatment strategies is of little value. This result is in line with the findings of earlier meta-analyses comparing different priming solutions.11,12 Similarly, studies in conventional ultrafiltration showed no significant reduction in blood loss.13,14 The synergistic combination of blood loss and fluid administration diminishes substrate quantity and quality, affects the procoagulant-anticoagulant balance, and probably reduces clot stability.15 Studies have reported a decrease in factors II, V, VII, VIII, IX, X, XI, XIII and Von Willebrand factor levels, dilutional thrombocytopenia, transient disruption of platelet clumping and adhesion, and disruption of thromboelastographic parameters in proportion to the

Table 3  Perioperative fluid balance.

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 64)</th>
<th>Group T (n = 64)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative administration of crystalloid solution (mL)</td>
<td>1586 ± 490</td>
<td>1034 ± 399</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intraoperative administration of colloid solution (mL)</td>
<td>531 ± 384</td>
<td>515 ± 503</td>
<td>0.83</td>
</tr>
<tr>
<td>Balance during CPB (mL)</td>
<td>2404 ± 713</td>
<td>552 ± 787</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intraoperative fluid balance (mL)</td>
<td>3328 ± 1165</td>
<td>1132 ± 1111</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intraoperative administration of crystalloid solution (mL)</td>
<td>5445 ± 886</td>
<td>4964 ± 939</td>
<td>0.003</td>
</tr>
<tr>
<td>Postoperative administration of colloid solution (mL)</td>
<td>1039 ± 898</td>
<td>982 ± 831</td>
<td>0.71</td>
</tr>
<tr>
<td>Postoperative diuresis (mL)</td>
<td>3901 ± 1044</td>
<td>4153 ± 1239</td>
<td>0.094</td>
</tr>
<tr>
<td>Postoperative balance (mL)</td>
<td>2074 ± 2294</td>
<td>1161 ± 1832</td>
<td>0.013</td>
</tr>
<tr>
<td>Final balance (mL)</td>
<td>5388 ± 2834</td>
<td>2292 ± 2152</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

C: control group; CPB: cardiopulmonary bypass; T: treatment group.
Data expressed as mean ± standard deviation.

Table 4  Haemoglobin, platelet and clotting levels.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Intraoperative</th>
<th>Admission</th>
<th>6h</th>
<th>24h</th>
<th>48h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>C</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.4 ± 1.3</td>
<td>14.3 ± 1.2</td>
<td>7.4 ± 1.1</td>
<td>8.8 ± 1.2</td>
<td>8.9 ± 1.2</td>
<td>9.7 ± 1.2</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>C</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>42.9 ± 3.6</td>
<td>43.3 ± 3.9</td>
<td>22.1 ± 3.2</td>
<td>26.4 ± 3.5</td>
<td>26.8 ± 3.7</td>
<td>29.1 ± 3.5</td>
</tr>
<tr>
<td>Platelets (10^11/L)</td>
<td>C</td>
<td>T</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>220.5 ± 54.3</td>
<td>211.7 ± 58.0</td>
<td>119.1 ± 33.6</td>
<td>127.2 ± 43.6</td>
<td>134.0 ± 44.7</td>
<td>119.2 ± 41.4</td>
</tr>
<tr>
<td>INR</td>
<td>C</td>
<td>T</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>1.09 ± 0.2</td>
<td>1.1 ± 0.2</td>
<td>1.5 ± 0.2</td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.1</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>APTT (s)</td>
<td>C</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35.1 ± 5.0</td>
<td>34.5 ± 5.3</td>
<td>45.4 ± 15.1</td>
<td>45.3 ± 7.7</td>
<td>38.6 ± 4.9</td>
<td>42.7 ± 6.3</td>
</tr>
<tr>
<td>Fbg (mg/dL)</td>
<td>C</td>
<td>T</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>388.3 ± 83.0</td>
<td>365.8 ± 85.3</td>
<td>208.3 ± 72.7</td>
<td>237.3 ± 78.0</td>
<td>350.8 ± 98.5</td>
<td>515.1 ± 111.1</td>
</tr>
</tbody>
</table>

APTT: activated partial thromboplastin time; C: control group; Fbg: fibrinogen; Hb: haemoglobin; INR: international normalised ratio; T: treatment group.
Data expressed as mean ± standard deviation.

* p < 0.001.
** p < 0.05.
level of haemodilution. In our study, however, plasma, platelet and fibrinogen administration was similar, as were clotting values on admission to the ICU. This suggests that haemostasis was similarly affected over the course of the surgery. Neither have any significant differences been reported by other studies evaluating the effect of priming solutions or ultrafiltration on clotting and platelet function tests. The absence of major changes in clotting and difference in blood loss in our study could be due to the effect of the administration of blood products after CPB disconnection and later in the ICU. Although the rate of rein- tervention for bleeding was higher in the control group, this was found to be caused in all cases by a bleeding vessel, and was not attributed to coagulopathy. When these patients were excluded from the analysis, we found no effect on the amount of blood loss or of pRBC transfusion. Length of stay in the ICU was, however, affected in both groups, but more significantly in group C due to more comparable data.

Despite similar blood loss in both groups, control group patients had higher pRBC requirements, mainly in the postoperative period. Haemodilution could have had an important effect on this. The use of crystalloid cardiopulmonary solution and more flexible perioperative fluid therapy protocols is a predictor of haemodilution and increased transfusion demand. In their meta-analysis, Russell et al. found that demand for blood was not significantly reduced when using albumin prime, although the heterogeneity of the studies included and differences in transfusion criteria could have affected the results. The use of ultrafiltration, however, particularly modified ultrafiltration techniques, succeeds in significantly reducing blood transfusion requirements to nearly 1 unit, similar to the findings of our study. The fact that the number of patients requiring blood transfusion is higher in our study than that reported by other authors suggests that haemodynamic management was based more on the administration of fluids than of vasoactive drugs. This resulted in a highly positive balance that could have undermined the benefits of the treatment strategy.

Plasma volume expansion lowers blood haemoglobin levels and can lead to over-transfusion. A more useful parameter for evaluating real blood loss and assessing transfusion needs could be RBC mass. However, this is difficult to calculate, since the use of standard formulae is subject to bias. There is no simple method for measuring RBC mass in clinical practice, and it is hard to estimate real blood volume due to administration of fluids and leakage into the interstitial space.

A positive intraoperative fluid balance leads to longer length of stay in the ICU and more re-admissions, a trend towards more kidney and pulmonary complications, greater need for inotropic drugs and longer intubation time. Total blood volume and extravascular accumulation of fluid take at least 24 h to normalise when using colloidal priming solution, and even longer when crystalloid solution is used. Onotic pressure remains low for 24 h post-surgery when using crystalloids, a factor that could contribute to continued accumulation of extravascular fluid and morbidity. Although we did not record complications in our study, the longer length of ICU stay in the control group could be linked to a positive fluid balance and its effect on organs such as the lungs, kidneys and heart. Although the reduced demand for blood is not striking in quantitative terms, several studies have shown that reducing blood transfusion by 1 unit reduces the risk of complications and mortality by 15–20%.

The real cost of treatment per patient in group T was €235 (€112 for haemofilter, €22 for mannitol and €121 for albumin). The price of a unit of pRBC, including compatibility testing and administration cost, is €243. The per-patient cost of blood transfusion in group T was €479, and €552 in group C. The cost of a 1-day stay in the ICU, according to current rates applied by health services attached to the Regional Ministry of Health of the Basque Country (http://www.osakidetza.euskadi.net/r85-cp/proc05/es/contenidos/Informacion/libro_tarifas/es/ libro_tarifas.html), is €1603. The per-patient cost of ICU stay in group T was €4202, and €8509 in group C. The total cost per patient in group T was €4934, and €7061 in group C, giving a final overall saving of €2127 per patient.

This study has certain limitations. It is a single-centre study, which restricts extrapolation of our conclusions. We did not establish guidelines for intraoperative administration of plasma and platelets because no point-of-care methods for controlling platelet function and thromboelastographic were available. As a result, various strategies might have been used to manage haemostatic changes, postoperative bleeding and transfusion requirements. Intraoperative and postoperative administration of fluids based on conventional targets (central venous pressure and cardiac output), meanwhile, could have affected haemodynamic management and resulted in difference in fluid administration strategies.

In conclusion, mannitol, albumin and lactated Ringer’s in CPB priming solution, together with haemofiltration during bypass, do not reduce blood loss or the number of patients requiring blood transfusion, although they do help reduce

![Figure 2](http://www.elsevier.es) Percentage of patients requiring transfusion of blood products. Inter-group differences were not significant. pRBC: packed red blood cells.
positive fluid balance, thereby reducing haemodilution, transfusion requirements, and length of ICU stay. Despite its limitations, we believe our results could have a bearing on clinical practice and improve the cost-effectiveness of CPB surgery.

Conflict of interests

The authors declare they have no conflicts of interest.

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