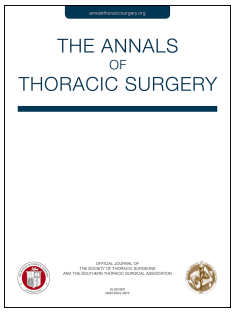

Dextran- versus crystalloid-based prime in cardiac surgery: A prospective randomized pilot study

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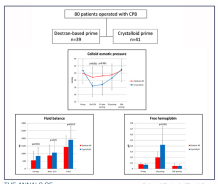

Dextran- versus crystalloid-based prime in cardiac surgery:

A prospective randomized pilot study

Running head: Dextran-based priming solution

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ABSTRACT

Background. The optimum priming fluid for the cardiopulmonary bypass (CPB) circuit is still debated. We compared a new hyperoncotic priming solution containing dextran 40, which has an electrolyte composition that mimics extracellular fluid, with a standard crystalloid-based prime.

Methods. Eighty cardiac surgery patients were included in this double-blind randomized single-centre study. The patients were randomized to either a dextran-based prime or a crystalloid prime containing Ringer acetate and mannitol. The primary endpoint was colloid oncotic pressure (COP) in serum during CPB. Secondary endpoints included fluid balance, bleeding and transfusion requirements, pulmonary function, hemolysis, systemic inflammation, and markers of renal, hepatic, myocardial, and brain injury. Blood samples were collected before, during, and after CPB.

Results. COP was higher in the dextran group than in the crystalloid prime group on CPB (18.8±2.9 vs. 16.4±2.9 mmHg, p<0.001) and 10 min after CPB (19.2±2.7 vs. 16.8±2.9 mmHg, p<0.001). Patients in the dextran group required less intravenous fluid during CPB (1090±499 vs. 1437±543 ml; p=0.003) and net fluid balance was less positive 12h after surgery (+1,431±741 vs. +1,901±922 ml; p=0.014). Plasma free hemoglobin was significantly lower in the dextran group 2h after CPB (0.18±0.11 vs 0.41±0.33, p=0.001). There were no significant differences in bleeding, transfusion requirements, organ function, systemic inflammation, or brain and myocardial injury markers between the groups at any time point.

Conclusions. Our results suggest that a hyperoncotic dextran-based priming solution preserves intraoperative COP compared to crystalloid prime. Larger studies with clinically valid endpoints are necessary to evaluate hyperoncotic prime solutions further.

Word count: 249

Keywords: Cardiopulmonary bypass, colloids, cardiac surgery

The cardiopulmonary bypass (CPB) circuit is primed with a fluid to avoid air bubbles, which would otherwise enter the circulation and cause air emboli, and to compensate for the loss of circulating blood volume at the start of CPB. There is no consensus on the optimum prime fluid. A balanced crystalloid solution, such as Ringer's acetate, is most commonly used for CPB priming (1), with additives (such as mannitol) to maintain homeostasis. However, when a crystalloid is used hemodilution occurs during CPB, with a decrease in oncotic pressure, resulting in a shift of fluid over the capillary bed to the interstitial compartments, which may contribute to interstitial oedema (2).

A hyperoncotic priming solution may increase oncotic pressure and thus reduce the shift of fluid during and after CPB. Overall, this may result in a less positive fluid balance and potentially less effects on organ function. A hyperoncotic priming solution based on dextran 40 has recently been developed (PrimECC®; Xvivo Perfusion, Gothenburg, Sweden). The solution has an electrolyte composition that mimics extracellular fluid to further reduce the fluid shift and maintain homeostasis. We tested the hypothesis that this priming solution maintains oncotic pressure during CPB, resulting in a less positive fluid balance in patients undergoing elective cardiac surgery. Secondary aims of the study were to evaluate aspects of the solution in terms of bleeding, transfusion requirements, hemolysis, organ function, and systemic inflammation.

PATIENTS AND METHODS

Ethics approval

This study was approved by the Regional Research Ethics Committee in Gothenburg (entry number: T847-16) and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects. The study was registered at ClinicalTrials.gov prior to enrolment (identifier: NCT0276154).

Patients

We included 84 elective cardiac surgery patients [mean age 66.7 ± 6.9 years (range 49-77), 71% men] at Sahlgrenska University Hospital from May 2016 to July 2017. Inclusion criteria were age ≥18 years and an expected CPB time >75 min. Exclusion criteria were previous cardiac surgery, coagulation disorder, malignancy, known liver or kidney disease, on-going septicaemia or sepsis, systemic inflammatory disease treated with corticosteroids, on-going antithrombotic medication other than acetylsalicylic acid, and not being able to understand Swedish. The study was ended after full inclusion. A flow chart of patient enrolment is given in Figure 1. Four patients were excluded after randomization, resulting in 80 patients who could be evaluated. Patient characteristics are listed in Table 1.

Study design

This was a prospective, randomized, single-centre, double-blind controlled study. The patients were randomized 1:1 to either CPB with dextran-based solution or Ringer acetate (Fresenius Kabi AB, Uppsala, Sweden) and mannitol (Fresenius Kabi AB) priming. The content of the priming solutions is given in Table 2. Before surgery, a perfusionist not assigned to the case opened an opaque envelope containing the allocation and prepared the heart-lung machine. The patient, surgeons, anesthetists, perfusionist, and intensive care unit personnel were all blind as to the allocation. A research assistant not otherwise involved in the study generated the random allocation sequence. The primary endpoint was oncotic pressure during CPB. Predefined secondary endpoints included perioperative fluid balance, intraoperative and postoperative bleeding volume, transfusion requirements, renal function, hepatic function, pulmonary function, myocardial injury markers, cerebral injury markers, and systemic inflammatory activation. The study protocol is provided as supplemental material.

Blood samples for oncotic pressure measurements were collected from an arterial line at five time points: (1) immediately after induction of anesthesia; (2) during CPB (when the aortic cross-clamp was released); (3) 10 minutes after CPB was weaned; (4) 2h after CPB; and (5) 24h after CPB. Blood samples for the remaining analyses were collected from the arterial line at three time points: (1) immediately after induction of anesthesia; (2) 2h after

CPB; (3) and 24h after CPB. Lung oxygenation capacity was evaluated from the PaO_2/FiO_2 ratio, which was measured twice while the patient was on a mechanical ventilator: (1) immediately before surgery; and (2) 2h after CPB.

Patient data (age, gender, body mass index, presence of diabetes, smoking habits, medications), type of surgery, CPB time, aortic cross-clamp time, total operating time, intraoperative fluid balance (from induction of anesthesia to skin closure), postoperative fluid balance (from skin closure to 12h postoperatively), total fluid balance (intraoperatively+postoperatively), the amount of crystalloids and colloids infused, urine output, intraoperative and postoperative bleeding, transfusions administered during hospital stay, time on mechanical ventilation, time in the intensive care unit, total length of stay, and heparin and protamine doses were registered for all patients. Fluid balance was defined as the sum of infused or ingested fluids minus urine output. The amounts of priming solution, blood cardioplegia, and insensible water losses were not included in the fluid balance calculations. Intraoperative blood loss was estimated based on waste suction volume, cell saver volume, and swabs used. Postoperative bleeding was chest drainage output during the first 12 hours postoperatively. The report of the study follows the CONSORT 2010 statement (3).

Clinical management

Ticagrelor and clopidogrel were discontinued at least three and five days, respectively, before surgery. Preoperative aspirin treatment was not discontinued. The CPB circuit was primed with 1,300 ml solution according to the patient's allocation. Patients were given 350 IU/kg of heparin, additional heparin was used to maintain an activated clotting time of >480 seconds. CPB flow rate was 2.4 $l/min/m^2$ and mean arterial pressure was kept to 50–70 mmHg throughout the procedures by the use of fluid administration and/or vasopressors/vasodilators. Retrograde autologous priming was not applied. Cold-blood cardioplegia was used for cardioprotection. At termination of CPB, Ringer acetate (Fresenius

Kabi AB) was used for “wash-in” of residual blood in the CPB circuit. Heparin effect was reversed with protamine (1 mg/100 units of heparin). Target mean arterial pressure after CPB was 70-80 mmHg. Pulse pressure variation (PPV) was monitored after CPB and in the ICU to guide fluid therapy. A PPV <12% was considered as postoperative hypovolemia. Blood products were transfused according to a predefined transfusion protocol. Red blood cells were transfused if hemoglobin was <70 g/L (<100 g/L in bleeding patients), if hematocrit was <20%, or if patients had on-going bleeding. Plasma was transfused in patients with on-going bleeding (>200 ml/h) and coagulopathy documented by thromboelastography. Platelet concentrate was administered in patients with on-going bleeding (>200 ml/h) and thrombocytopenia (<75×10^9/L). Cell saver was used at the surgeon’s discretion. The final decision regarding transfusion and fluid hemodynamic management was left to the anesthetist in charge**.**

Laboratory tests

Oncotic pressure was analyzed with an Osmomat 050 analyzer (Gonotec, Berlin, Germany). Serum S100B concentration was measured on a Modular E170 instrument (Roche Diagnostics, Penzberg, Germany). S100B and hemolysis index were analyzed in 62 patients only (31 in each group) due to shortage of plasma. Inflammatory activation was assessed by IL-6 plasma concentration (4,5), kidney function by serum creatinine, hepatic function by aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT), myocardial injury by troponin-T and hematology by hemoglobin concentration, hematocrit, and platelet count. All variables were analyzed with clinical standard methods. Hemolysis index was measured on a Cobas c501 instrument (Roche Diagnostics, Penzberg, Germany) by bichromatic spectrophotometry at 570 nm and 600 nm wavelength pair, as previously described (5). The hemolysis index was recalculated to free hemoglobin in g/L using the formula [f-Hb = (0.915×hemolysis index+2.634)/100] (6).

Statistical analysis

A power calculation was performed based on a pilot study. We assumed that the COP in the crystalloid group would be 15 mmHg with a standard deviation of 6 mmHg and that COP in the dextran group would be 30% higher, i.e. 19.5 mmHg, which results in a standardized difference of 0.75 (90% power and a significance level of 0.05). Forty patients in each group were needed. All analyses were performed on the original assigned groups. Normality of distribution was tested with the Shapiro-Wilk test. Results are expressed as mean and standard deviation (SD), median and range or 25th and 75th percentiles (where appropriate), or number and percentage. Statistical significance was defined as $p < 0.05$. Student's t-test, the Mann-Whitney U-test, or the Chi-square test was used to compare groups as appropriate. Variables measured at more than two time points were analyzed with ANOVA for repeated measurements. The influence of CPB time on variables statistically different between groups was tested with ANCOVA with group and CPB time as covariates. Correlations between CPB time and secondary outcome variables were assessed with Pearson's product-moment test. Statistica software (StatSoft, Tulsa, OK, USA) was used for statistical analyses.

RESULTS

General

One patient in the dextran group and two in the crystalloid group died within 30 days of the operation. The remaining patients recovered and were discharged from hospital after median 6 (25th and 75th percentiles 5-8) days. Preoperative and intraoperative variables are presented in Table 1. Mean CPB time was despite randomization longer in the crystalloid group than in the dextran group (107±39 vs 91±25 min, p=0.042), while total operation time did not differ (195±55 vs 187±46 min, p=0.49).

Oncotic pressure

COP was significantly higher in the dextran priming group during CPB (18.8±2.9 vs. 16.4±2.9 mmHg; p<0.001) and 10 min after CPB (19.2±2.7 mmHg vs. 16.8±2.9 mmHg; p<0.001), Figure 2. The differences were caused by a reduction of COP in the crystalloid group while the COP remained stable in the dextran group. There was no significant difference between the groups 2h and 24h after CPB.

Fluid balance

Patients in the dextran-based priming group received significantly less crystalloids in the intraoperative period than the crystalloid group (1,079±501 ml vs. 1,410±535 ml; p=0.006) (Table 3). The amount of intraoperatively administered colloid was comparable in the two groups. Urine output during CPB was significantly higher in the crystalloid prime group (249±186 vs. 105±155 ml; p<0.001). For the total intraoperative+postoperative period, there was no significant difference in urine output between groups (Table 3). The amount of fluid ingested orally during the first 12h after the operation was not significantly different between the groups. The total intravenous fluid balance for the intraoperative period and up to 12h after CPB was significantly less positive in the dextran prime group (+1,431±741 ml vs. +1,901±922 ml; p=0.014). The group differences remained statistically significant also after adjustment for CPB time, Supplementary Table 1.

Postoperative organ function, systemic inflammation, and hemolysis

Biomarkers reflecting renal function, hepatic function, myocardial injury, brain injury, systemic inflammation, and pulmonary function were not significantly different between the groups at any time point (Table 4). Free hemoglobin was significantly lower in the dextran group 2h after CPB (0.18±0.11 vs. 0.41±0.33 g/L, p=0.001, Table 4). The difference remained significant between the groups also after adjustment for the difference in CPB time (p=0.005) and after the 10 patients that received autotransfusion of cell salvaged blood were excluded (p=0.034).

Bleeding and transfusion

Intraoperative, postoperative, and total bleeding volumes were not significantly different in the two groups (Table 5). Three patients, one in the dextran group and two in the crystalloid group, were re-explored because of bleeding. There were no significant differences in the incidence and volumes of transfusions during hospital stay between the groups (Table 5). Serum hemoglobin and hematocrit levels were significantly higher in the crystalloid group two hours after surgery, but they were not significantly different 24h after the operation.

COMMENT

The main findings in this randomized pilot study were as follows: (1) a hyperoncotic prime solution containing dextran 40 maintained a higher oncotic pressure during and immediately after CPB than a crystalloid-based prime; (2) the dextran-based prime was associated with reduced intravenous fluid administration and a less pronounced positive intraoperative fluid balance; (3) the dextran-based prime was associated with reduced hemolysis; and (4) postoperative organ function and bleeding/transfusion variables did not differ significantly between the groups.

The choice of fluid for CPB prime is debated (1, 7). Colloids maintain the intravascular colloid oncotic pressure, leading to a reduced fluid shift from the intravascular space into the interstitial compartments. However, colloids may impair coagulation and cause anaphylactic reactions (8).

Comparison of colloid vs. crystalloid prime and their effect on fluid balance has previously been reported in a few articles (9-15). To our knowledge, there is no study comparing various artificial colloids in this clinical context. In line with our results, most of the previous studies showed higher COP and less positive fluid balance with colloids. Our study differs from the previous ones in several respects. Firstly, most of these studies used hydroxyethyl starch (HES) as a colloid. Only one small study with 20 patients has evaluated

dextran 40 as a priming solution (10). Secondly, none of the previous studies included comprehensive data on postoperative organ function. Finally, the previous randomized studies were mostly markedly smaller than the present one.

Perioperative organ function was assessed in the present study by laboratory tests reflecting renal, hepatic, systemic inflammatory response, and pulmonary function, as well as acute myocardial and brain injury. None of the tests indicated that organ function was jeopardized by using dextran. Furthermore, there were no significant differences in bleeding volumes and transfusions between the groups. This is especially interesting, as artificial colloids, especially when given in large concentrations, are well known to impair hemostasis (16). Dextran has antithrombotic properties, since it affects platelet adhesiveness and aggregation because of a decrease in coagulation factor VIII and von Willebrand factor levels (17). It should be noted that the present study is underpowered for comparisons of clinical endpoints and that the study should in this aspect be regarded as a pilot study. However, the present study provides information about organ function and bleeding, which may give a first indication if the treatment is associated with important side effects. Furthermore, the study provides information about inter-individual and inter-group variations, essential for designing larger studies with clinically relevant endpoints.

One interesting observation was the lower level of hemolysis (−56%) in the dextran group two hours after CPB. The difference between the groups remained significant after adjustment for CPB time. Hemolysis in cardiac surgery is caused by mechanical shear stress during CPB and by retransfusion of suctioned or cell salvaged blood, and results in the release of free hemoglobin (18). Free hemoglobin reduces the bioavailability of nitric oxide and has therefore been suggested to contribute to microcirculatory dysfunction, which may then lead to organ injury. The kidneys appear to be especially sensitive to hemolysis (18). The mechanism behind the lower hemolysis with dextran is not fully understood, but it has been suggested that dextran reduces the effects of shear stress on red blood cells (19,20).

Anaphylactic reaction is a safety concern in the use of all colloids, including albumin. A meta-analysis reported that the incidence of anaphylaxis from dextrans is 21.9 per 100,000 injections (0.0219%) (21). The risk for severe reactions is reduced 35-fold if a hapten is used (22). In the present study, where a hapten (dextran 1) was added to the dextran-based solution, no dextran-related reactions occurred.

This study has important limitations. As discussed earlier, the study was not powered for the clinical endpoints and the results should be interpreted with caution. Despite randomization, the crystalloid prime group had longer CPB time than the dextran prime group. However, all group differences remained significant after adjusting the results for CPB time. Lung function was only evaluated in the immediate postoperative period, since the patients were extubated early after surgery, precluding exact measurements of F_iO_2/PaO_2.

In conclusion, the results of the present study suggest that the use of a hyperoncotic priming solution containing dextran 40 preserves intraoperative COP. Large-scale randomized clinical trials with clinically valid endpoints and/or focused investigations in patients with increased perioperative risk, e.g. renal dysfunction, are needed to evaluate hyperoncotic prime solutions further.

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Table 1. Preoperative and perioperative variables in 80 cardiac surgery patients randomized to dextran-based or crystalloid-based priming solution. Mean and standard deviation or number and proportion (%).

	Dextran-based prime N=39	Crystalloid prime N=41	P-value
Male gender (n, %)	28 (72%)	29 (71%)	0.91
Age (years)	65.8±6.1	67.±7.6	0.25
Body mass index (kg/m^2)	26.8±4.0	27.3±4.0	0.56
Diabetes (n, %)	5 (13%)	5 (12%)	0.93
Operation (n, %)			0.47
CABG	14 (36%)	13 (32%)	
Aortic valve replacement	11 (28%)	7 (17%)	
Mitral valve repair or replacement	4 (10%)	4 (10%)	
Valve+CABG	4 (10%)	10 (24%)	
Other	6 (15%)	7 (17%)	
Euroscore II (%)	1.6±1.1	2.2±2.7	0.20
CPB-time (min)	91±25	107±39	0.042
Aortic clamp time (min)	68±24	77±33	0.16
Total operation time (min)	187±46	195±55	0.49
Total heparin dose (units)	34102±6675	33170±4438	0.46
Total protamine dose (mg)	337±53	336±42	0.99
Mean arterial pressure during CPB (mmHg)	61±8	61±9	0.74
Vasopressor administration during ECC	37 (95%)	36 (88%)	0.26

Temperature during CPB (bladder) (°C)	36.1±0.3	36.1±0.4	0.69
Lowest temperature (bladder) (°C)	35.7±0.4	35.6±0.7	0.47

Key: CABG, Coronary artery bypass surgery; CPB, Cardiopulmonary bypass; mg, milligrams.

Table 2. Composition and colloid osmotic pressure of the priming solutions.

	Dextran-based prime	Ringer-acetate + mannitol
Prime volume (ml)	1300	1100 + 200
Mannitol 150 g/L (g)	-	30
Dextran 40 (g)	45	-
Dextran 1(g)	3 g	-
Sodium chloride (g)	5.84	5.9
Potassium chloride (mg)	298	300
Magnesium chloride (mg)	203	200
Calcium chloride (mg)	294	295
Sodium lactate (g)	3.36	-
Sodium acetate (g)	-	4.1
Water (ml)	1000	1000
Colloid osmotic pressure (mmHg)	61	21

Table 3. Fluid replacement therapy, urinary output and fluid balance intraoperative and 12 hours post-CPB for each intervention. Mean and standard deviation.

	Dextran-based prime N=39	Crystalloid prime N=41	P-value
Crystalloids (ml)			
Intraoperative	1079±501	1410±535	0.006
Postoperative first 12h	2380±519	2412±718	0.82
Colloids (ml)			
Intraoperative	10±50	27±81	0.28
Postoperative first 12h	64±111	110±166	0.15
Oral fluids (ml)			
Postoperative first 12h	345±379	300±259	0.54
Total fluids (ml)			
Intraoperative IV	1090±499	1437±543	0.004
Postoperative first 12h IV	2444±526	2522±739	0.59
Postop first 12h IV including oral	2788±701	2821±825	0.85
Total IV	3534±535	3959±917	0.014
Total IV+oral	3878±664	4258±1022	0.053
Urine production (ml)			
Intraoperative (excluding CPB)	430±303	347±214	0.16
During CPB	105±155	249±186	<0.001
Postoperative first 12h	1568±462	1462±473	0.31
Total intraoperative+postop 12h	2103±584	2057±563	0.72
Fluid balance (ml)			
Intraoperative	555±595	841±574	0.031

Postoperative first 12h excluding oral	876±677	1060±745	0.25
Postoperative first 12h including oral	1221±808	1360±797	0.44
Total intraop+postop excluding oral	1431±741	1901±922	0.014
Total preop+postop including oral	1775±866	2201±1011	0.047

Key: CPB, cardiopulmonary bypass; h, hour; IV=intravenous.

Table 4. Laboratory variables preoperative, 2h and 12h post-CPB for each intervention. Mean and standard deviation.

	Dextran-based prime N=39	Crystalloid prime N=41	P-value
IL-6 (ng/L)			
Preoperative	3.4±3.1	4.7±5.5	
Postoperative 2h	121±97	134±124	0.91
Postoperative 24h	198±140	212±173	
Troponin-T (ng/L)			
Preoperative	26±53	13±10	
Postoperative 2h	756±1088	1384±2787	0.40
Postoperative 24h	581±581	899±1460	
Free hemoglobin (g/L)			
Preoperative	0.08±0.03	0.07±0.02	
Postoperative 2h	0.20±0.10**	0.42±0.32	0.001
Postoperative 24h	0.05±0.04	0.05±0.02	
S100B (µg/L)			
Preoperative	0.05±0.04	0.05±0.02	
Postoperative 2h	0.67±0.46	0.94±0.80	0.078
Postoperative 24h	0.18±0.27	0.15±0.07	
ASAT (IU/L)			
Preoperative	22.9±7.1	24.7±16.5	
Postoperative 2h	49.4±30.0	75.9±90.0	0.092
Postoperative 24h	77.1±42.9	78.2±64.7	

ALAT (IU/L)			
Preoperative	27.7±13.5	31.8±33.5	
Postoperative 2h	27.0±10.6	40.0±48.2	0.27
Postoperative 24h	34.7±24.1	41.2±48.2	
Serum creatinine (µmol/L)			
Preoperative	84±20	83±18	
Postoperative 24h	100±27	102±38	0.35
Postoperative 48h	98±29	106±43	
PaO_2/FiO_2 ratio			
Preoperative	0.43±0.19	0.37±0.18	0.084
Postoperative 2h	0.33±0.10	0.38±0.13	

Key: IL, interleukin; ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; PaO_2, partial pressure of oxygen in arterial blood; FiO_2, fraction of inspired oxygen. **=p<0.01 between the groups at the same time point.

Table 5. Hematologic variables, bleeding volume, and transfusions in the dextran-based group and the crystalloid group. Mean and standard deviation, median and 25^{th}-75^{th} percentile or number and proportion (%).

	Dextran-based prime N=39	Crystalloid prime N=41	P-value
Hemoglobin (g/L)			
Preoperative	125±14	126±14	
Postoperative +2h	107±10**	115±12	0.008
Postoperative +24h	109±11	109±13	
Hematocrit (%)			
Preoperative	0.36±0.05	0.37±0.04	
Postoperative +2h	0.31±0.03**	0.34±0.04	0.030
Postoperative +24h	0.32±0.03	0.32±0.04	
Platelet count (10^9/L)			
Preoperative	206±54	202±52	
Postoperative +2h	162±39	180±58	0.019
Postoperative +24h	169±39	161±70	
Bleeding volume (ml)			
Intraoperative	446±348	562±504	0.27
Postoperative first 12h	500±198	511±216	0.80
Total (preop+postop)	946±434	1056±557	0.32
Red blood cell transfusion (unit)			
Proportion	11 (28.2%)	14 (34.1)	0.57
Mean	1.00±2.11	1.10±1.79	0.82

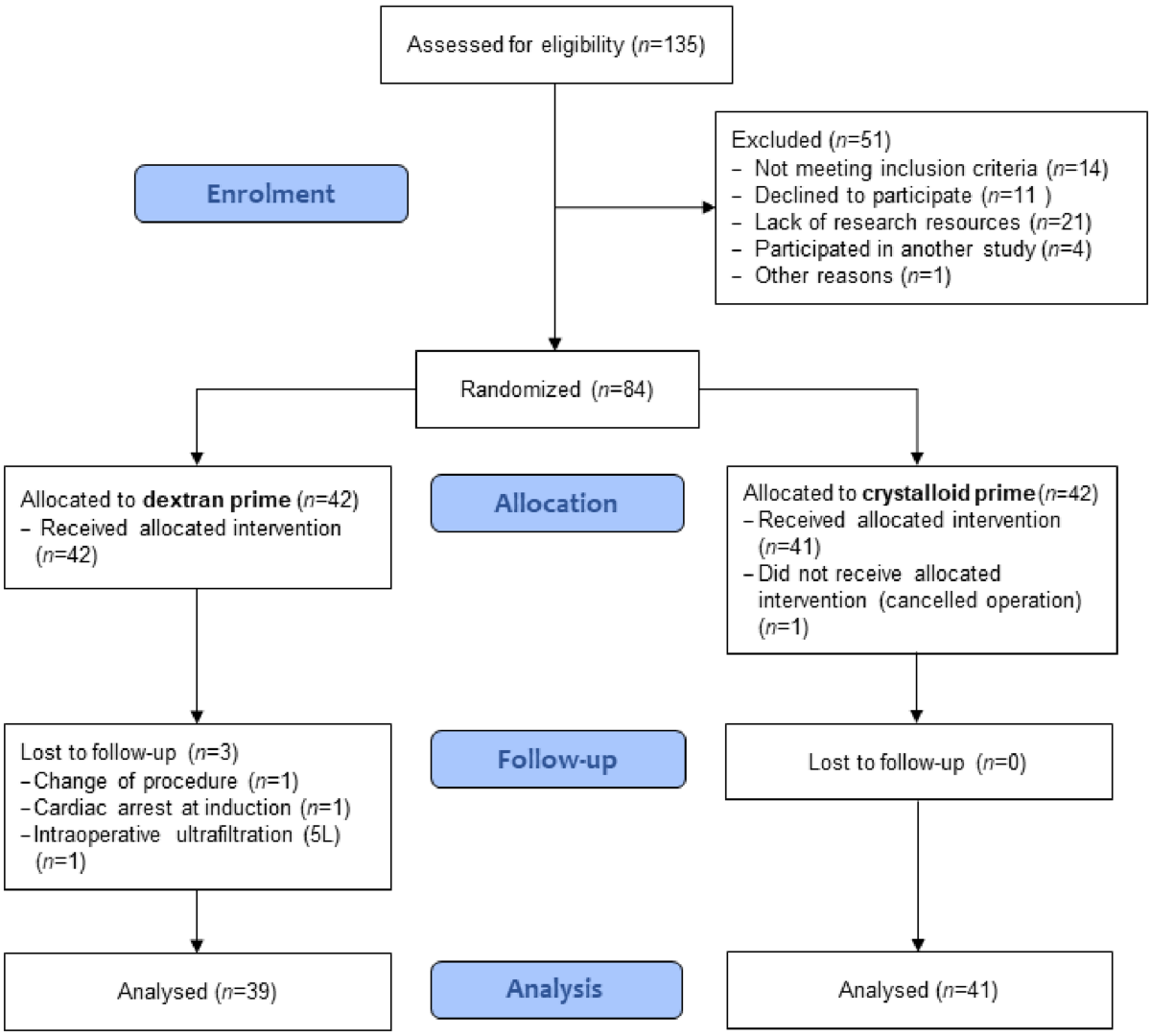
Median	0 (0-2)	0 (0-2)	0.62
Plasma transfusion (unit)			
Proportion	3 (7.7%)	6 (14.6%)	0.33
Mean	0.26±1.04	0.27±0.71	0.95
Median	0 (0-0)	0 (0-0)	0.62
Platelet transfusion (unit)			
Proportion	7 (17.9%)	3 (7.3%)	0.15
Mean	0.28±0.76	0.12±0.78	0.36
Median	0 (0-0)	0 (0-0)	0.44
Red blood cell salvage			
Proportion	2 (17.9%)	8 (7.3%)	0.052
Retransfused volume (ml)			
Mean	625±318	535±272	0.69
Median	625 (400-850)	465 (325-800)	1.00

** = p<0.01 between groups at the same time point.

FIGURE LEGENDS

Figure 1. Number of patients enrolled, allocated, followed-up and analyzed in the study.

Figure 2. Colloid osmotic pressure before, during and after cardiopulmonary bypass (CPB) in the dextran group and in the crystalloid group. Mean and standard deviation. *** = P<0.001.


Assessed for eligibility (n=135)
Enrolment
Excluded (n=51)
- Not meeting inclusion criteria (n=14)
- Declined to participate (n=11)
- Lack of research resources (n=21)
- Participated in another study (n=4)
- Other reasons (n=1)
Randomized (n=84)
Allocated to dextran prime (n=42)
- Received allocated intervention (n=42)
Allocation
Allocated to crystalloid prime (n=42)
- Received allocated intervention (n=41)
- Did not receive allocated intervention (cancelled operation) (n=1)
Lost to follow-up (n=3)
- Change of procedure (n=1)
- Cardiac arrest at induction (n=1)
- Intraoperative ultrafiltration (5L) (n=1)
Follow-up
Lost to follow-up (n=0)
Analysed (n=39)
Analysis
Analysed (n=41)