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Abstract

Objective: The choice of the prime solution for cardiopulmonary bypass can play an important role in limiting the effect on blood coagulation, but it is still unclear what the effect of colloids on blood coagulation is. The aim of this study was to investigate the effect of synthetic colloids on blood loss and blood coagulation in patients after on-pump coronary artery bypass graft (CABG) procedures.

Methods: Sixty elective, on-pump CABG patients were randomly assigned to receive the prime solutions lactated Ringer's solution combined with hydroxyethyl starch 130/0.4 (HES, 6% Volulyte, Fresenius Kabi Nederland BV, Zeist, the Netherlands) (HES group) or gelatin (Gelofusin®, B Braun Melsung AG, Melsungen, Germany) (Gelo group). Blood loss was assessed using post-operative chest tube output; secondary endpoints were number of blood component transfusions, routine coagulation test values and rotation thromboelastometry values (Rotem® delta, Pentapharm GmbH, Munich, Germany).

Results: Total post-operative chest tube output was 500 ± 420 ml in the HES group versus 465 ± 390 ml in the Gelo group (p = 0.48). No significant differences were observed in any of the routine coagulation tests values, thromboelastometry parameters or number of blood component transfusions between the groups.

Conclusions: In this randomized, controlled trial of adults after on-pump CABG procedures, there was no significant difference in blood loss or blood coagulation between the HES group and the Gelo group.

Keywords

colloids; coagulation; gelatin; hetastarch; thromboelastography

Introduction

Different prime solutions are used for cardiopulmonary bypass (CPB) and can be divided into crystalloids and colloids. CPB causes the activation of blood coagulation, with an increased risk of post-operative bleeding.[1] The choice of the prime solution for CPB can play an important role in limiting the effect on blood coagulation. Colloids are often combined with a crystalloid as the prime solution for CPB during cardiac surgery, since colloids are more effective in maintaining hemodynamic stability and regional tissue perfusion than crystalloids.[2-4] However, the infusion of colloid solutions causes a dilutional coagulopathy, regardless of the kind of colloid used.[5,6] Fibrinogen deficiency seems to play an essential role in the cause of dilutional coagulopathy.[7] In addition, fibrinogen may be one of the first plasma factors which becomes critical by the dilution of the patient's plasma by colloids, since colloids affect the reticular fibrin network.[8-11]

Combinations of lactated Ringer's solution with gelatin and lactated Ringer's solution with Hydroxyethyl Starch (HES) 130/0.4 impair *in vitro* the coagulation system to a significantly lesser extent than each colloid administered in solitary (gelatin or HES 130/0.4).[5]

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Which of these colloids is superior compared to the other remains unclear.

Previous *in vivo* studies have shown that, when HES 130/0.4 or gelatin is used as CPB priming solution, it results in the same extent of blood loss.[12-14] However, these studies have not assessed *ex vivo* coagulation variables, such as thromboelastometry, to get more insight into the impairment of colloids on fibrin polymerization. When colloids are used only after cardiac surgery, HES 130/0.4 and gelatin impaired coagulation to the same extent, resulting in a similar extent of blood loss and *ex vivo* coagulation variables.[15,16]

The aim of this study was to compare the effect of HES 130/0.4 or gelatin, both in combination with lactated Ringer's solution as CPB priming, on blood loss and blood coagulation in on-pump CABG patients.

Materials and Methods

Patients

Sixty on-pump CABG patients, of both sexes, were included in this prospective, randomized, controlled trial. All the patients were hospitalized in the Amphia Hospital (Breda, the Netherlands). The study was approved by the appropriate Ethics authority (St Elisabeth Hospital Ethics Committee, Tilburg, the Netherlands, Ref: NL35250.008.11) and registered with EudraCT (ref: 2011-000156-42) and written informed consent was obtained from all subjects. The study was executed in the time period from July 2011 until July 2012. Criteria for inclusion were: body surface area (BSA) ≥1.60, pre-operative haemoglobin (Hb) ≥7.5 mmol/l and pre-operative number of platelets ≥150 x 10^9/l. Exclusion criteria were: emergency cardiac interventions, re-operations, coagulation impairments as a result of thrombolytica <48 hours pre-operatively, abnormal coagulation profile (PT >17 seconds or aPTT >50 seconds)(prothrombin time and activated prothromboplastin time, respectively), use of platelet aggregation inhibitors (carbasalate or clopidogrel <3 days pre-operative), kidney function impairments (creatinin >140 mmol/l), liver function impairments (ASAT >50^E/l or ALAT >60^E/l)(aspartate aminotransferase and alanine aminotransferase, respectively), fibrinogen level ≤2.5 g/l - ≥7.0 g/l and surgical interventions other than planned.

Study groups

Patients were randomly assigned by a computer-generated randomization table to receive one of the following prime solutions during CPB:

I. 550 – 650 ml HES 130.04 (HES, 6% Volulyte), 550 – 650 ml lactated Ringer's solution, 100 ml mannitol (Mannitol 20%, 200 g/l, Baxter Healthcare,® Uden, the Netherlands), 7500 IU heparin (Heparin LEO, 5000 IU/ml, LEO Pharma, Amsterdam, the Netherlands) (the HES group)
II. 550 – 650 ml gelatin, 550 – 650 ml lactated Ringer's solution, 100 ml mannitol, 7500 IU heparin (the Gelo group)

Fluid administration

The maximum dose of HES 130/0.4 was calculated for the patients enrolled in the HES group at 50 ml per kg bodyweight/24 h (the manufacturer's recommended maximum dose).[17] At reaching the maximum dose of HES 130/0.4, sodium chloride (Sodium Chloride 0.9%, Baxter Healthcare,®) or lactated Ringer's solution was administered. Both the Gelo group and the HES group had CPB prime volumes between 1200 and 1400 ml. During CPB, in the case of suspected hypovolemia, additional group-specific fluid was administered. During the surgical procedure, allogeneic packed red blood cell transfusions were administrated when the haematocrit was <24%. Blood components were transfused according to the anesthetic protocol. After CPB, the remaining volume was processed with a cellsaver (Xtra, Sorin® Group, Mirandola, Italy). At arrival at the intensive care unit (ICU), patients received gelatin (Gelo group) or HES 130/0.4 (HES group), according to the ICU protocol.

Cardiopulmonary bypass

Arterial cannulation (DLP® arterial cannula straight or curved, Medtronic Inc®, Minneapolis, MN, USA) was inserted in the aorta ascendens. Venous cannulation (Dual-stage venous drainage cannula 36/51 fr, Medtronic Inc® MC2) was inserted in the right atrium up to the inferior vena cava. During CPB, the system used was a custom-made closed circuit (Maquet Cardiopulmonary AG®, Herrlingen, Germany or Medtronic Inc®). The components of the system used were a cardiotomy reservoir (40μ filter, Medtronic Inc®), a venous reservoir (CMBVR-800, Medtronic Inc®/ BO-JVR 1900, Maquet Cardiopulmonary AG®), an oxygenator (Affinity®, Medtronic Inc®/ Quadrox-I adult®, Maquet Cardiopulmonary AG®) and an arterial filter (Affinity®, Medtronic Inc®/ Quart®, Maquet Cardiopulmonary AG®). Saturation, hematocrit (SAT/HCT® monitor, Cobe, Sorin Group, Italy), pH, PO_2, PCO_2 and potassium were measured during CPB by the inline monitor system (CDI 500, Terumo, Cardiovascular Systems Corporation®, Tokyo, Japan). The values of the inline monitoring system were calibrated using the laboratory blood gas sample. The cardiac index was 2–2.4 l/min/m^2 during

CPB. The operation was performed under mild hypothermia or normothermia (34–37ºC) and warm blood cardioplegia was used as the myocardial preservation method. Heparin was administered according to standard hospital procedure (350 IU/kg heparin) and adjusted during CPB after monitoring by the activating clotting time (ACT) measurements, using the Hemochron Jr. Signature® (International Technodyne Corporation, Edison, NJ, USA). After measuring the baseline ACT (before surgery), a heparin titration curve was used. By means of the heparin titration curve (ACT <450 seconds), extra heparin units were administrated. After the CABG procedure, the ACT was measured. By means of the heparin titration curve, protamine (5000 IU/ml MPH, Protamine hydrochloride, Meda Pharma BV, Amstelveen, the Netherlands) was administrated at the end phase of the surgery to antagonise the heparin (ratio heparin: protamine 1:1). Post-operative chest tube output was examined 1, 3, 6 and 12 hour(s) after the CPB procedure. Furthermore, standard laboratory tests were analyzed, which included hematocrit, colloid osmotic pressure (COP) and troponin. Also, the number of blood component transfusions was assessed.

Anesthesia

Premedication consisted of 3.75 mg midazolam, orally. Before the induction of anesthesia, all patients were monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement and pulse oximetry and a catheter was placed in the radial artery for blood sampling and continuous monitoring of the mean arterial pressure (MAP). Anesthesia was induced with midazolam 5 mg, propofol 100 mg, sufentanil 50 µg and pancuronium 0.1 mg/kg. Patients were intubated and mechanically ventilated. Anesthesia was maintained with remifentanyl 0.1 µg/kg/min and sevoflurane 1%; an internal jugular central venous catheter, a Foley bladder catheter, a rectal temperature probe and a transesophageal echocardiography probe were routinely inserted. During CPB, remifentanyl 0.1 µg/kg/min and sevoflurane 1%, via a vaporizer inserted into the oxygenator's gas supply line, were continued.

Thromboelastometry and laboratory analyses

Rotation thromboelastometry, (Rotem® delta, Pentapharm GmbH, Munich, Germany) a methodology based on thromboelastography originally described by Hartert more than 50 years ago, is a whole blood viscoelastic method that allows the rapid assessment of coagulation in both laboratory and near patient settings.[18,19] Rotem® is characterized by specific variables which describe the interaction of platelets with the coagulation factors from initial platelet-fibrin interaction, through platelet aggregation, clot strengthening and fibrin cross-linking, to eventual clot lysis.[18] The impairment of fibrin polymerization induced by intravascular volume replacement with colloids or crystalloids perioperatively was detected by thromboelastometry.[5,19]

Rotrol® control tests for the Rotem system were performed weekly in accordance with the guidelines of the manufacturer. Blood samples for thromboelastometry were collected in 2.7 ml blood collection tubes containing 0.14 ml citrate solution (Sarstedt, Nuembrecht, Germany) at 37°C. Blood samples for Rotem® analyses were collected before the administration of colloids and induction of anesthesia, after the on-pump CABG procedure (after administration of protamine) and one and three hours post-operatively in the ICU. Maximum clot firmness (MCF), clotting time (CT) and clotting formation time (CFT) of InTEM®, HepTEM®, ExTEM® and FibTEM® were examined with Rotem®.

The routine coagulation tests included the international normalized ratio (INR), activated partial thromboplastin time (aPTT), number of platelets and fibrinogen levels (method of Clauss). Blood samples for routine coagulation tests were collected in 2.7 ml blood collection tubes containing 0.14 ml citrate solution (Sarstedt). Blood samples for routine coagulation tests were collected one day before the on-pump CABG procedure and post-operatively (upon arrival at the ICU and one day after the on-pump CABG procedure).

Statistical analysis

Sample size was based on the study of Schramko et al., showing that the standard deviation for 24-h post-operative blood loss indicated by the chest tube output was 420 ml.[16] A difference of 450 ml in total chest tube output was considered clinically relevant, power was calculated by means of Altman's nomogram (power of 0.8 (1 – β) and a statistical significance level (α) of 0.05) and each treatment arm required 30 patients. Statistical tests were performed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL) version 20. The Shapiro-Wilk Test was used to analyse distribution of continuous variables.

Results are expressed as mean ± standard deviation (SD) for normally distributed data and median ± interquartile range (IQR) for not normally distributed data. In the case of a normal distribution, comparison of continuous variables was done, using the independent samples-T test, otherwise the Mann-Whitney U test was used. Results were corrected, based on the Bonferroni method. A statistical difference was reached when *p* values were 0.05 or less.

Table 1. Patient demographics and surgical data. Values are mean ± SD.

	HES group	Gelo group
Gender (m/f)	24/6	25/5
Age (yr)	65.1 ± 9.6	65.3 ± 7.8
BSA (m^2)	2.00 ± 0.23	1.99 ± 0.19
DM (yes/no)	7/23	6/24
EuroSCORE I (%)	3.1 ± 1.6	3.4 ± 1.8
Pre-operative hematocrit (l/l)	0.42 ± 0.03	0.42 ± 0.03
CPB time (min)	89 ± 21	85 ± 23
AoX (min)	58 ± 16	55 ± 18
Number of anastomoses	3.7 ± 0.9	3.8 ± 0.9
Amount of heparin (mg)	370 ± 82	360 ± 96
Amount of protamine (mg)	306 ± 67	307 ± 63
Temperature (°C)	35 ± 1.0	35 ± 1.0

AoX: aortic cross-clamp time; BSA: body surface area; CPB: cardiopulmonary bypass; DM: diabetes mellitus; SD: standard deviation.

Table 2. Cumulative chest tube output (ml). Values are median ± IQR. Significant difference when $p<0.05$ (Mann-Whitney U test).

	HES group	Gelo group	*p*-value
Post-operative 1 hour (ml)	200 ± 165	150 ± 165	0.25
Post-operative 3 hours (ml)	300 ± 150	225 ± 205	0.33
Post-operative 6 hours (ml)	325 ± 250	300 ± 230	0.38
Post-operative 12 hours (ml)	425 ± 300	375 ± 255	0.56
Total (before removing drains) (ml)	500 ± 420	465 ± 390	0.48
Duration drains (hours)	18 ± 4	18 ± 5	0.93

IQR: interquartile range.

Results

Patient demographics and surgical data were similar in the Gelo group and the HES group (Table 1). Total chest tube output was 500 ± 420 ml in the HES group versus 465 ± 390 ml in the Gelo group ($p = 0.48$) (Table 2).

The maximum calculated dose of HES 130/0.4 was not reached in the patients in the HES group. Intra-operatively, 850 ± 500 ml of colloids were administrated in the HES group and 800 ± 555 ml of colloids in the Gelo group ($p = 0.64$). The administration of infusion solutions was maintained during the presence of the chest tube drains (18 ± 5 hours). In the ICU, 500 ± 950 ml (HES group) and 500 ±1000 ml (Gelo group) of colloids were administrated ($p = 0.47$). Intra-operatively, crystalloid administration was 1780 ± 275 ml in the HES group and 1780 ± 325 ml in the Gelo group ($p = 1.00$). In the ICU, 3145 ± 1265 ml (HES group) and 3050 ± 960 ml (Gelo group) of crystalloids were administered ($p = 0.74$). During the study, no anaphylactic reactions occurred.

There were no significant differences in any of the thromboelastometry variables at baseline. A significant difference in MCF InTEM® between the HES and the Gelo groups was observed only after the administration of protamine ($p = 0.022$, CI -7.41 to -0.60) (Table 3). There was a significant difference in CFT HepTEM® after the administration of protamine ($p = 0.032$, CI 1.88 to 41.26) and 3 hours post-operatively ($p = 0.042$, CI -4.12 to 43.12) Table 4). There were no significant differences in any of the thromboelastometry variables CT (Intem®, HepTEM® and Extem®) between the groups (Table 4). After Bonferroni correction, no variables were significant.

There were no significant differences in any of the routine coagulation tests values (fibrinogen level, number of platelets, aPTT, INR) between the groups (Table 5).

During the study period, seven patients received packed red blood cells, four in the HES group and three in the Gelo group. From the patients who received packed red blood cells, the median cumulative units of red blood cells transfused was 1 ± 2 in the HES group and 1 ± 0 in the Gelo group ($p = 0.22$). In the Gelo group, no patients received fresh frozen plasma (FFP) transfusions, however, in the HES group, two patients received two units of FFP ($p = 0.15$). Of the 60 on-pump CABG patients, one patient received one unit of platelets (HES group) ($p = 0.31$). From the patients who received fibrinogen concentrate, the median requirement for fibrinogen concentrate transfusion was 2 ± 3 in the HES group compared to 2 ± 1 in the Gelo group ($p = 0.38$).

No significant differences were determined in the standard laboratory test values (hematocrit, colloid

Table 3. Maximum Clot Firmness (Rotem®).Values are mean ± SD unless stated otherwise. Significant difference when $p<0.05$ (Independent samples T-test for normally distributed data and Mann-Whitney U test for not normally distributed data).

	HES group	Gelo group	*p*-value
MCF InTEM® (mm)			
Baseline (median ± IQR)	65 ± 5	65 ± 10	0.71
After administration of protamine	60 ± 4	56 ± 6	0.022
Post-operative 1 hour	61 ± 4	60 ± 5	0.47
Post-operative 3 hours	62 ± 4	59 ± 7	0.094
MCF HepTEM® (mm)			
Baseline	62 ± 4	62 ± 5	0.97
After administration of protamine	57 ± 5	54 ± 7	0.074
Post-operative 1 hour	58 ± 5	57 ± 6	0.57
Post-operative 3 hours	60 ± 5	57 ± 7	0.14
MCF ExTEM® (mm)			
Baseline	66 ± 4	65 ± 4	0.82
After administration of protamine	62 ± 4	59 ± 6	0.15
Post-operative 1 hour	61 ± 5	61 ± 6	0.93
Post-operative 3 hours	62 ± 5	61 ± 6	0.44
MCF FibTEM® (mm)			
Baseline	19 ± 5	17 ± 4	0.092
After administration of protamine	12 ± 4	11 ± 4	0.87
Post-operative 1 hour (median ± IQR)	12 ± 5	11 ± 3	0.90
Post-operative 3 hours	12 ± 5	12 ± 3	0.98

IQR: interquartile range; MCF: maximum clot firmness; SD: standard deviation.

osmotic pressure and troponin) between the Gelo group and the HES group. In both groups, the hematocrit decreased after CPB (HES group: 29 ± 3%; Gelo group: 29 ± 3%, but, on arrival at the ICU, the hematocrit was increased towards the baseline values (HES group: 34 ± 3 %; Gelo group: 35 ± 4 %). The preoperative COP was 20.4 ± 2.5 mmHg in the HES group and 19.1 ± 1.8 mmHg in the Gelo group. The post-operative COP was 19.2 ± 2.3 mmHg in the HES group and 18.7 ± 2.6 mmHg in the Gelo group ($p = 0.45$). The post-operative troponin level was 0.21 ± 0.14 µg/l in the HES group and 0.18 ± 0.12 µg/l in the Gelo group ($p = 0.11$).

Discussion

This prospective study has shown a similar effect on blood loss and blood coagulation after on-pump CABG procedure when the colloids HES 130/0.4 and gelatin were compared, both combined with crystalloids. This randomized, controlled trial has not show any difference in post-operative chest tube output between the two groups. Of the 60 on-pump CABG patients, one patient (Gelo group) had a re-thoracotomy because of surgical bleeding, caused by leakage of a venous graft.

In accordance with previous studies, there was no difference in post-operative chest tube output, hematocrit or number of platelet and blood component transfusions.[12-14] Boks et al. showed a significant post-operative reduction in COP in their HES 130/0.4 group compared to the gelatin group.[12] In our study, we could not find such a difference. This could be explained by the facts that we used less colloids and because of the combination with crystalloids as CPB priming solution.

It is of critical importance to choose the optimal fluid replacement therapy for limiting the effect on blood coagulation.[16] In addition, Schramko et al.[16] assessed *ex vivo* coagulation variables, using thromboelastometry, to detect the impairment of fibrin polymerization induced by intravascular volume replacement with HES 130/0.4 and gelatin. They found no difference in the impairment of fibrin polymerization between HES 130/0.4 and gelatin, however, they used colloids only after cardiac surgery; during CPB a crystalloid was administered. In addition to the study of Schramko et al.,[16] no statistical difference was found on the impairment of fibrin polymerization between HES 130/0.4 and gelatin, when they were used as CPB prime solutions.

There are limitations in this study. First, it was not blinded, because of logistical reasons. However, there was no difference observed in the infusion volumes between the groups. The power was calculated on chest tube output as the primary endpoint. This relatively small sample size may limit the outcome of the secondary endpoints, such as routine coagulation tests values, Rotem® values and number of blood component transfusions, although post-operative chest tube output is a clinically valuable parameter. Furthermore, all the patients have undergone on-pump CABG, with a normal

Table 4. Clotting time (Rotem®) and Clotting formation time (Rotem®). Values are mean ± SD unless stated otherwise. Significant difference when $p<0.05$ (Independent samples T-test for normally distributed data and Mann-Whitney U test for not normally distributed data).

	HES group	Gelo group	*p*-value
CT InTEM® (s)			
Baseline (median ± IQR)	187 ± 38	162 ± 34	0.11
After administration of protamine	249 ± 61	259 ± 72	0.59
Post-operative 1 hour	185 ± 25	192 ± 26	0.28
Post-operative 3 hours (median ± IQR)	176 ± 23	175 ± 49	0.99
CT HepTEM® (s)			
Baseline (median ± IQR)	192 ± 44	185 ± 48	0.57
After administration of protamine	256 ± 60	258 ± 52	0.88
Post-operative 1 hour	193 ± 27	199 ± 36	0.50
Post-operative 3 hours (median ± IQR)	180 ± 32	181 ± 36	0.63
CT ExTEM® (s)			
Baseline	49 ± 7	48 ± 6	0.59
After administration of protamine (median ± IQR)	74 ± 15	75 ±11	0.96
Post-operative 1 hour (median ±IQR)	58 ± 11	58 ± 8	0.51
Post-operative 3 hours (median ± IQR)	56 ± 7	53 ± 14	0.37
CFT InTEM® (s)			
Baseline (median ± IQR)	67 ± 25	66 ± 16	0.70
After administration of protamine (median ± IQR)	99 ± 36	102 ± 53	0.13
Post-operative 1 hour (median ± IQR)	82 ± 20	89 ± 39	0.35
Post-operative 3 hours (median ± IQR)	77 ± 19	88 ± 36	0.22
CFT HepTEM® (s)			
Baseline	71 ± 16	72 ± 16	0.82
After administration of protamine	111 ± 28	132 ± 45	0.032
Post-operative 1 hour (median ± IQR)	87 ± 34	93 ± 33	0.54
Post-operative 3 hours (median ± IQR)	83 ± 21	100 ± 34	0.042
CFT ExTEM® (s)			
Baseline	83 ± 15	86 ± 18	0.50
After administration of protamine (median ± IQR)	111 ± 54	114 ± 49	0.94
Post-operative 1 hour	115 ± 30	112 ± 27	0.69
Post-operative 3 hours	115 ± 29	116 ± 30	0.90

CFT: clotting formation time; CT: clotting time; IQR: interquartile range; SD: standard deviation.

baseline coagulation profile. A larger effect in blood loss or on impairment of fibrin polymerization could possibly occur in more prolonged and complex procedures with a higher risk of bleeding. The results may have been different in patients with depleted counts and lower hematocrit. Thereby, a difference in platelet function could possibly have been found directly after CPB. Unfortunately, in this study, that was not measured. In the future, clinical studies to assess the effect of HES 130/0.4 and gelatin on platelet function are required.

Besides the fact that HES 130/0.4 and gelatin seem to have the same effect on blood loss and blood coagulation, there are also other factors which determine the choice of colloid. HES 130/0.4 causes less allergic reactions compared to gelatin, with a frequency of 0.058% for HES and 0.345% with gelatin.[20]

Furthermore, HES 130/0.4 and gelatin have different intra-vascular volume effects. HES 130/0.4 has a volume effect from six to eight hours and gelatin from two to three hours. The prolonged volume effect of HES 130/0.4 could be interesting to maintain normovolemia.

HES 130/0.4 is derived from waxy maize starch in contrast to gelatin which is made of bovine collagen. The administration of infusion fluid of animal origin could entail a risk of infection.

On the other hand, patients with severe sepsis who receive fluid resuscitation with HES 130/0.4 have a higher risk for renal-replacement therapy compared to those who receive Ringer's acetate.[21] With patients in the ICU, Myburgh et al. also showed increased renal-replacement therapy in patients resuscitated with HES 130/0.4 compared to those resuscitated with saline.[22] However, pathophysiological disorders of coagualation in these patients are of a different order from our population group. Recently, a review has shown that, when HES 130/0.4 was used during cardiac surgery, it has not led to increased adverse renal effects compared with other

Table 5. Routine coagulation tests: fibrinogen level, number of platelets, aPTT and INR. Values are mean ± SD unless stated otherwise. Significant difference when $p < 0.05$ (Independent samples T-test for normally distributed data and Mann-Whitney U test for not normally distributed data).

	HES group	Gelo group	*p*-value
Fibrinogen level (g/l)			
Baseline (mean ± IQR)	3.8 ± 1.1	3.5 ± 1.2	0.12
After arrival in ICU (mean ± IQR)	2.4 ± 1.2	2.3 ± 1.2	0.51
Post-operative 1 day	3.6 ± 0.9	3.3 ± 0.9	0.26
Number of platelets (10^9/l)			
Baseline (mean ± IQR)	254 ± 114	258 ± 82	0.92
After arrival in ICU	200 ± 51	191 ± 49	0.46
Post-operative 1 day	209 ± 4.8	194 ± 41	0.19
aPTT (s)			
Baseline	31.6 ± 3.2	31.5 ± 3.6	0.97
After arrival in ICU	27.4 ± 2.5	28.8 ± 4.7	0.17
Post-operative 1 day	27.5 ± 2.6	26.7 ± 2.5	0.27
INR (s)			
Baseline (mean ± IQR)	1.0 ± 0.1	1.0 ± 0.1	0.75
After arrival in ICU (mean ± IQR)	1.2 ± 0.1	1.2 ± 0.2	0.24
Post-operative 1 day (mean ± IQR)	1.1 ± 0.2	1.1 ± 0.1	0.25

aPTT: activated partial thromboplastin time; ICU: intensive care unit; INR: international normalized ratio; IQR: interquartile range; SD: standard deviation.

colloids.[23] Further investigation is needed to clarify those issues.

In our study, the focus was on blood loss and blood coagulation, particularly on post-operative chest tube output and secondly on the difference in fibrin polymerization.

In conclusion, this randomized, controlled trial of adults after on-pump CABG procedures showed no significant difference in blood loss and blood coagulation between HES 130/0.4 and gelatin when they were combined with lactated Ringer's solution.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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