# Intraoperative Hydroxyethyl Starch 70/0.5 Administration May Increase Postoperative Bleeding - A retrospective Cohort Study

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**Abstract**

PURPOSE: There are few studies in the literature that evaluated the safety of hydroxyethyl starch with a molecular weight of 70 kDa and a molar substitution ratio of 0.5 (HES 70/0.5). In this study, we investigated the relationship between intraoperative HES 70/0.5 administration and postoperative bleeding.

METHODS: This is a single-center, retrospective cohort study. Subjects were postoperative adult patients who stayed in the intensive care unit (ICU) for more than 24 hours during the period January 1, 2010 and December 31, 2012. We compared postoperative adult patients with and without intraoperative HES 70/0.5 administration. The primary outcome was the drainage volume from surgical sites during the first 24 hours after ICU admission. We conducted propensity score matching between the control group and the HES group.

RESULTS: We analyzed data for 869 patients who met our inclusion criteria. By propensity score matching, we successfully created 190 matched pairs of the HES group and control group, with no significant differences in patient characteristics. The drainage volume during the first 24 hours after ICU admission was greater in the HES group than in the control group (400 ± 479mL vs. 260 ± 357mL, P=0.003).

CONCLUSION: Our retrospective cohort study suggested that intraoperative HES 70/0.5 administration was associated with increase in postoperative bleeding.

## INTRODUCTION

Hydroxyethyl starch (HES), an artificial colloid produced with potato or waxy maze, has been used for fluid resuscitation all over the world [1-3]. HES is classified according to its molecular weight (MW; high, ◘400 kDa; medium; 200 – 400 kDa; low, <200 kDa), number of hydroxyethyl residues per 10 glucose subunits (molar substitute ratio [MSR]) and C2/C6 ratio (C2/C6 ratio; >8, high, <8, low). Until recently, it has been thought that HES of smaller MW and MSR may be associated with fewer complications (nephrotoxicity and coagulopathy), and that third-generation HES (MW 130, MSR 0.4) is associated with adverse events less frequently than first- and second-generation HES (MW ◘200kDa, MSR ◘0.5) [2, 3]. However, recent studies have shown that HES 130/0.4 is associated with a high incidence of required renal replacement therapy and blood products transfusion [4, 5].

In Japan, HES of MW 70 kDa and MSR of 0.5 (HES 70/0.5) has been commonly used for decades. However, there are few studies reporting on the safety of HES 70/0.5 [6-9]. We previously reported that, although intraoperative HES 70/0.5 administration was not associated with postoperative acute kidney injury, HES 70/0.5 was associated with more intraoperative blood products transfusion in this study [6]. Since patients with more intraoperative bleeding might have been treated with more fluid resuscitation including HES, we could not evaluate whether HES 70/0.5 administration was the cause or the result of intraoperative bleeding. Therefore, in the present study, we evaluated the impact of intraoperative HES 70/0.5 administration on postoperative bleeding using the propensity score matching technique.

## METHODS

Our Institutional Review Board approved the study design (registration number: 26-068 7573; principal investigator: Toko Fukushima, date of registration: July 7, 2014) and approved to waive the need for informed consent because this study did not require any intervention and the data for each patient were anonymous. This was a retrospective cohort study conducted at the intensive care unit (ICU) in Tokyo Jikei University Hospital. All adult (18 years of age or older) postoperative patients admitted to the ICU between January 1, 2010 and December 31, 2012 and who stayed in the hospital for more than 24 hours were included. If patients had more than two operations after admission, the first operation was only included. Obstetrics and liver transplantation cases were excluded because such patients often have a very high volume of intraoperative bleeding, that could significantly affect our study findings. Patients who were treated with HES in the ICU were also excluded.

Patient characteristics and intraoperative data were retrieved from the operating room database (ORSYS, Philips Electronics Japan, Tokyo, Japan) and including age; gender; height; body weight; days from hospital admission to surgical operation; end-stage kidney disease; type of surgery (elective or emergent); type of anesthesia (general or regional); medical department or department of surgery; with or without cardiopulmonary bypass (CPB) on cardiac surgery; duration of surgery; volume of bleeding; urine output; tranexamic acid use; American Society of Anesthesiologists Physical Status (ASA-PS) and administration volume of crystalloid, HES 70/0.5 (Hespander, Fresenius Kabi Japan Inc, Tokyo, Japan), albumin, concentrated red cell (CRC), fresh frozen plasma (FFP), and concentrated platelets (PL). The following data were retrieved from the ICU database and patient information system (PIMS, Philips

Electronics Japan, Tokyo, Japan): Acute Physiology And Chronic Health Evaluation II score (APACHE II) on the day of ICU admission [10], body temperature, activated partial thromboplastin time (APTT), prothrombin time international normalized ratio (PT-INR), platelet count, hemoglobin and fibrinogen at ICU admission, ionized calcium, pH, ratio of arterial oxygen partial pressure to fractional inspired oxygen ($PaO_2/F_IO_2$), administration volume of HES, CRC, PL and FFP, duration of mechanical ventilation and drainage volume from surgical sites during the first 24 hours after ICU admission, reoperation for bleeding, and ICU and hospital mortality.

*Statistical methods*

Baseline characteristics for the full cohort were summarized in numbers and percentages for categorical variables, and means and standard deviations for continuous variables. All patients were divided into two groups according to intraoperative HES administration. We constructed a logistic model for calculating the propensity score (PS) for each subject to be administered HES during surgical operation based on the following preoperative variables: age, sex, body mass index, end-stage kidney disease, days from hospital admission to surgical operation, types of surgery, emergency of the surgery, ASA-PS, and type of anaesthesia. PS matching was performed in a one-to-one fashion between the treatment group and the non-treatment group using calipers of width equal to 0.2 of the standard deviation of the logit of the PS [11]. Covariate balances before and after matching were checked by comparing standardized differences [12]. We obtained standardized differences (SD) within 10% in all variables to indicate successful balancing. Postoperative variables before and after PS matching were analyzed for differences between groups by the Mann-Whitney U test for

continuous variables and Fisher's exact test for categorical variables [13]. Two-tailed $P<0.05$ was considered to have statistical significance for all analyses. All statistical analyses were performed using JMP® Pro 11.2.0 (SAS Institute Inc., Cary, NC, USA).

**RESULTS**

From January 1, 2010 to December 31, 2012, a total of 5259 patients aged 18 years or older underwent operation. Among these patients, we analyzed 869 patients who met the inclusion criteria. A total of 653 patients (75.1%) received HES intraoperatively. Patient demographic and intraoperative characteristics are summarized in Tables 1 and 2. Patients in the HES group less frequently had a history of end-stage kidney disease (6.4% vs. 23.2%) and emergency surgery (23.4% vs. 35.7%) than the control group (Table 1). Intraoperative HES administration was used more often for the Cardiac surgery, neurosurgery and vascular surgery. The duration of surgery was longer for the HES group than for the control group (315minutes vs. 262minutes, $P$=0.002). Patients in the HES group also had a larger intraoperative volume of bleeding (1345mL vs. 623mL, $P$<0.001) and urine output (946mL vs. 619mL, $P$<0.001) than the control group. The intraoperative administration volumes of crystalloid (2622mL vs. 1600mL, $P$<0.001) and CRC (1113mL vs. 752 mL, $P$<0.001) were greater in the HES group compared with the control group (Table 2).

Variables at ICU admission and patient outcomes are summarized in Table 3. The APACHE II score was not different between the two groups. Regarding bleeding tendency, platelet count and fibrinogen level at ICU admission were less (fibrinogen; 2.29g/L, vs. 2.72g/L $P$<0.001, platelet count: $120x10^3$ μ/L vs. $150x10^3$ μ/L, $P$<0.001), and PT-INR (1.4 vs. 1.2, $P$<0.001) was greater in the HES group compared with the control group. The drainage volume from surgical sites during the first 24 hours after ICU admission was greater in the HES group compared with the control group (454mL vs. 277mL, $P$<0.001, Figure 1). ICU mortality and hospital mortality were not different between the two groups.

Characteristics, intraoperative and postoperative data of propensity score-matched patients are shown in Tables 4, 5 and 6. After propensity matching, 463 patients in the HES group and 26 patients in the control group were rejected and a total of 190 matched-paired patients between the two groups were created. The C-index for the propensity-score model was 0.77, indicating acceptable discrimination ability. On matched-patient characteristics in the operating room, volume of bleeding was greater in the HES group than in the control. However, other variables were not different between the two groups (Table 5). At ICU admission, patients in the HES group had lower fibrinogen and platelet count (fibrinogen; 2.46g/L, vs. 2.77g/L $P<0.001$, platelet count: $132x10^3$ μ/L vs. $156x10^3$ μ/L, $P=0.001$). Hemoglobin was also significantly lower (102g/L vs. 108g/L, $P<0.001$) in the HES group despite similar requirements for intraoperative CRC transfusion (Table 6). The drainage volume during the first 24 hours after ICU admission was greater in the HES group than in the control group (400mL vs. 260mL, $P=0.003$, Figure 1). ICU and hospital mortality were not different between the two groups (Table 6).

## Discussion

### *Key Findings*

In this retrospective, single-center study, we evaluated the impact of intraoperative HES 70/0.5 administration on postoperative bleeding. To reduce imbalances between the study groups, we conducted propensity score matching and found that patients who received HES 70/0.5 intraoperatively had a lower fibrinogen level and platelet count at ICU admission and higher drainage volume postoperatively during the first 24 hours after ICU admission. In the present study, we could not conclude whether HES 70/0.5 was the cause or the result of postoperative bleeding. However, these findings suggest that intraoperative HES 70/0.5 administration, despite its small MW, might cause postoperative bleeding.

### *Comparison to Previous Studies*

HES has been reported to cause bleeding tendency, due to hemodilution, decrease in coagulation factors and von Willebrand factor (vWF), and inhibition of platelet function [14-20]. Platelet adhesion and aggregation occur after membrane glycoprotein (GP) IIb-IIIa complex binding to coagulation factor VIII and vWF, which is reduced by HES administration. In addition, HES reduces the availability of activated GP IIb-IIIa by covering the platelet surface [2, 3, 21,22].

We previously reported that intraoperative HES 70/0.5 administration was not associated with postoperative acute kidney injury in patients with major intraoperative blood loss (□1000mL) [6]. We also reported that propensity score-matched patients with HES 70/0.5 administration had more intraoperative blood loss and received more intraoperative CRC transfusion than the control group. The design of our previous study

could not determine whether increased intraoperative blood loss was related to HES administration or not. To further study the impact of intraoperative HES administration on bleeding tendency, in the present study, we evaluated postoperative bleeding by comparing the intraoperative HES 70/0.5 group with the control group. Although a few previous studies reported that HES 70/0.5 was associated with a low risk of bleeding, they were small in size, and the primary outcome was not postoperative bleeding [7-9]. The present study specifically evaluated postoperative bleeding and found that patients in the HES 70/0.5 group were associated with a slight but statistically significant increase in bleeding after surgery compared with the matched control group.

HES 70/0.5 administration has been reported to more effectively maintain the peripheral circulation, colloid osmotic pressure, and hemodynamics than Ringer's solution [15,16]. However, Jamnicki et al. reported that HES 70/0.5 administration is associated with a decrease in the level of coagulation factor VIII and vWF [14]. Franz et al. also reported that HES 70/0.5 inhibits platelet function by reducing the availability of the functional receptor for fibrinogen on the platelet surface [22]. Although we did not evaluate the level of coagulation factors or platelet function in the present study, these side effects might have occurred in the HES group, which could be the reason for increased postoperative blood loss.

*Significance and Implications*

Given that the magnitude of side-effects of HES is related to its MW and MSR [2, 3, 22,23], HES 130/0.4 has been considered to be associated with fewer adverse events than other forms of HES. However, recent studies suggest that HES 130/0.4 is also associated with nephrotoxicity and coagulopathy [4, 5, 24]. For example, large

multicenter randomized controlled trials (the Crystalloid versus Hydroxyethyl Starch Trial [CHEST] study [4] and the Scandinavian Starch Severe Sepsis/Septic Shock [6S] study [5]) showed that the number of CRC transfusions was greater with HES 130/0.4 administration than the control group. A post hoc analysis of 6S also showed that the HES 130/0.4 group had more bleeding tendency [24]. HES 130/0.42/7 in the 6S study, however, is a potato based starch and have different side effects from waxy maize based HES 130/0.4/9[2].

Whereas HES 70/0.5 has been commonly used for decades in Japan, HES 130/0.4 is used globally. Some authorities suggest that HES 130/0.4 could be used safely if the amount of HES administration is restricted [25,26]. However, others suggest that HES 130/0.4 should not be used because of issues regarding patient safety [27-29]. HES 130/0.4 has a larger MW and lower MSR than HES 70/0.5. Although MSR is more dominant for reducing side effects than MW[2] and HES 130/0.4 was reported to have more beneficial effect on coagulation than HES 70/0.5[22], the present study showed that any types of HES should be administered with a great caution, even if indicated.

*Strengths and Limitations*

To the best of our knowledge, this is the largest observational study investigating associations between HES 70/0.5 administration and bleeding tendency. However, this was a single-center, retrospective, observational study and also involves several limitations. First, we could not collect indications for intraoperative HES administration, and selection bias may have affected our results. To reduce the possibility of selection bias, we conducted propensity score matching, which showed increased postoperative bleeding in the HES group. Second, we also could not collect information on

preoperative antiplatelet and anticoagulant administration. For example, aspirin administration before surgery has been reported to increase risks of postoperative bleeding [30]. In the present study, approximately 80% of the patients underwent cardiac, vascular, or neurosurgical endovascular procedures, and they were likely to have received antiplatelet or anticoagulant drugs. However, in the propensity score-matched pairs, the percentage of patients from these respective parent units was similar (82.6% vs. 78.0%). Third, we used drainage volume from surgical sites as a marker for postoperative bleeding, which was not the true bleeding volume. However, drainage volume has been used as a marker for bleeding in several previous studies [31-33]. For example, Dixon et al. showed that chest drainage bleeding was associated with volume of transfusion and mortality [32]. Using propensity score matching, we also found that the incidence of reoperation for bleeding was more than double in the HES group compared with the matched control group (4.7% vs. 1.6%), although this difference was not statistically significant ($P$=0.140).

## Conclusions

We investigated the impact of intraoperative HES 70/0.5 administration on postoperative bleeding tendency. Our results showed that patients receiving intraoperative HES 70/0.5 had greater drainage volume from surgical sites (a marker for postoperative bleeding) during the first 24 hours after surgery.

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**Table 1. Characteristics for Study Patients With and Without HES Administration**

| | HES N=653 | | Control N=216 | | SD |
|---|---|---|---|---|---|
| **Age, years** | 66.8 | [13] | 61.5 | [16.5] | 0.083 |
| **Parent unit** | | | | | |
| **Cardiac Surgery, n** | | | | | |
| **With CPB** | 164 | (25.1) | 66 | (30.6) | 0.123 |
| **Without CPB** | 83 | (12.7) | 7 | (3.2) | 0.357 |
| **Major abdominal surgery** | 118 | (18.1) | 37 | (17.1) | 0.026 |
| **Neurosurgery, n** | 99 | (15.2) | 68 | (31.5) | 0.393 |
| **Vascular Surgery, n** | 151 | (23.1) | 23 | (10.7 | 0.336 |
| **Others** | 38 | (5.8) | 15 | (6.9) | 0.045 |
| **Male, n** | 442 | (67.7) | 141 | (65.3) | 0.051 |
| **Body mass index, kg/m$^2$** | 22.6 | [3.7] | 22.7 | [4.1] | 0.004 |
| **Admission to surgery, days*** | 6.2 | [9.6] | 9 | [26.4] | 0.362 |
| **End-stage kidney disease, n** | 42 | [6.4] | 50 | [23.2] | 0.487 |
| **Emergency surgery, n** | 153 | [23.4] | 77 | [35.7] | 0.272 |
| ASA-PS | | | | | |
| **1** | 33 | (5.1) | 11 | (5.1) | <0.001 |
| **2** | 292 | (44.7) | 74 | (34.3) | 0.214 |
| **3** | 290 | (44.4) | 111 | (51.4) | 0.14 |
| **4** | 34 | (5.2) | 18 | (8.3) | 0.124 |
| **5** | 4 | (0.6) | 2 | (0.9) | 0.035 |
| **General anesthesia, n** | 629 | (96.3) | 200 | (92.6) | 0.162 |

Data are expressed as average [Standard deviation] or (percentages).

* Duration between hospital admission to having surgery

HES = hydroxyethyl starch; SD = Standardized differences, CPB = Cardiopulmonary bypass, ASA-PS = American Society of Anesthesiologists physical status

**Table 2. Intraoperative Variables for Patients With and Without HES Administration**

| | HES N=653 | | Control N=216 | | p-value |
|---|---|---|---|---|---|
| **Duration of surgery, minutes** | 315 | [204] | 262 | [164] | 0.002 |
| **Volume of bleeding, mL** | 1345 | [3516] | 623 | [1281] | <0.001 |
| **Urine output, mL** | 946 | [1089] | 619 | [604] | <0.001 |
| **Administration volume** | | | | | |
| **Crystalloid, mL** | 2622 | [2098] | 1600 | [937] | <0.001 |
| **HES, mL** | 1069 | [850] | - | - | |
| **CRC, mL** | 1113 | [1699] | 752 | [1184] | <0.001 |
| **FFP, mL** | 419 | [889] | 371 | [628] | 0.391 |
| **PL, mL** | 88 | [197] | 90 | [176] | 0.571 |
| **Albumin, mL** | 287 | [590] | 269 | [587] | 0.103 |
| **Tranexamic acid, n** | 131 | (20.1) | 53 | (25.0) | 0.179 |

Data are expressed as average [Standard Deviation] or (percentages).

HES = hydroxyethyl starch; CRC = concentrated red cell; FFP = fresh frozen plasma;

PL = concentrated platelet.

**Table 3. Postoperative Variables for Patients With and Without HES Administration**

| | HES N=653 | | Control N=216 | | p-value |
|---|---|---|---|---|---|
| **APACHE II** | 15.5 | [5.3] | 16.1 | [6.6] | 0.461 |
| **Body temperature, °C** | 36.7 | [0.8] | 36.8 | [0.8] | 0.101 |
| **APTT, seconds** | 40.8 | [17.6] | 44.6 | [23.4] | 0.555 |
| **PT-INR** | 1.4 | [0.5] | 1.2 | [0.3] | <0.001 |
| **Fibrinogen, g /L** | 2.29 | [1.24] | 2.72 | [1.26] | <0.001 |
| **Platelet count, $10^3$ µ/L** | 120 | [59] | 155 | [80] | <0.001 |
| **Hemoglobin, g /L** | 102 | [16] | 107 | [22] | <0.001 |
| **Ionized calcium, mmol/L** | 1.13 | [0.06] | 1.13 | [0.07] | 0.629 |
| **pH** | 7.37 | [0.06] | 7.36 | [0.06] | 0.265 |
| **$PaO_2/FiO_2$ ratio** | 393.7 | [221] | 386 | [179] | 0.990 |
| **CRC, mL** | 176 | [381] | 167 | [322] | 0.571 |
| **FFP, mL** | 126 | [315] | 69 | [182] | 0.037 |
| **PL, mL** | 33 | [98] | 19 | [73] | 0.035 |
| **Reoperation for bleeding, n** | 19 | (2.9) | 3 | (1.4) | 0.317 |
| **Length of ICU stay, days** | 4 | [4.8] | 4.1 | [4.3] | 0.264 |
| **ICU mortality, n** | 13 | (2.0) | 5 | (2.3) | 0.784 |
| **Length of hospital stay, days** | 42.8 | [41.8] | 47.1 | [57.4] | 0.876 |
| **Hospital mortality, n** | 39 | (6.0) | 15 | (6.9) | 0.626 |

Data are expressed as average [Standard Deviation] or (percentages).

HES = hydroxyethyl starch; APACHE II = acute physiology and chronic health

evaluation II score; APTT = activated partial thromboplastin time; PT-INR = prothrombin time - international normalized ratio; CRC = concentrated red cell; FFP = fresh frozen plasma; PL = concentrated platelet; MV = mechanical ventilation.

**Table 4. Characteristics for Propensity Score-matched Patients With and Without HES Administration**

| | HES N=190 | | Control N=190 | | SD |
|---|---|---|---|---|---|
| **Age, years** | 63 | [16] | 63 | [16] | 0.005 |
| **Parent unit** | | | | | |
| **Cardiac Surgery, n** | | | | | |
| **With CPB** | 62 | (32.6) | 60 | (31.6) | 0.021 |
| **Without CPB** | 7 | (3.7) | 7 | (3.7) | <0.001 |
| **Major abdominal surgery** | 22 | (11.6) | 28 | (14.7) | 0.092 |
| **Neurosurgery, n** | 67 | (35.3) | 59 | (31.1) | 0.089 |
| **Vascular Surgery, n** | 21 | (11.0) | 22 | (11.6) | 0.019 |
| **Others** | 11 | (5.8) | 14 | (7.4) | 0.064 |
| **Male, n** | 116 | (61.1) | 123 | (64.7) | 0.075 |
| **Body mass index, kg/m$^2$** | 22.7 | [3.9] | 22.7 | [4.2] | 0.003 |
| **Admission to surgery, days*** | 6.4 | [13.9] | 6.7 | [12.1] | 0.046 |
| **End-stage kidney disease, n** | 30 | (15.8) | 32 | (16.8) | 0.027 |
| **Emergency surgery, n** | 72 | (37.9) | 68 | (35.8) | 0.044 |
| **ASA-PS** | | | | | |
| **1** | 13 | (6.8) | 11 | (5.8) | 0.041 |
| **2** | 73 | (38.4) | 70 | (36.8) | 0.033 |
| **3** | 92 | (48.4) | 94 | (49.5) | 0.022 |
| **4** | 11 | (85.8) | 14 | (7.4) | 0.064 |
| **5** | 1 | (0.5) | 1 | (0.5) | 0 |
| **General anesthesia, n** | 177 | (93.2) | 176 | (92.6) | 0.023 |

Data are expressed as average [Standard deviation] or (percentages).

* Duration between hospital admission to having surgery

HES = hydroxyethyl starch; SD = Standardized differences; CPB = Cardiopulmonary bypass, ASA-PS = American Society of Anesthesiologists physical status

**Table 5. Intraoperative Variables for Propensity Score-matched Patients With and Without HES Administration**

| | HES N=190 | | Control N=190 | | p-value |
|---|---|---|---|---|---|
| **Duration of surgery, minutes** | 264 | [178] | 264 | [162] | 0.837 |
| **Volume of bleeding, mL** | 1022 | [2876] | 642 | [1349] | 0.007 |
| **Urine output, mL** | 744 | [854] | 619 | [581] | 0.367 |
| **Administration volume** | | | | | |
| **Crystalloid, mL** | 2047 | [1687] | 1647 | [927] | 0.114 |
| **HES, mL** | 819 | [599] | - | - | <0.001 |
| **CRC, mL** | 937 | [1381] | 781 | [1231] | 0.081 |
| **FFP, mL** | 408 | [969] | 372 | [643] | 0.913 |
| **PL, mL** | 98 | [193] | 89 | [176] | 0.751 |
| **Albumin, mL** | 228 | [456] | 220 | [528] | 0.205 |
| **Tranexamic acid, n** | 47 | (24.7) | 48 | (25.3) | >0.999 |

Data are expressed as average [Standard Deviation] or (percentages).

HES = hydroxyethyl starch; CRC = concentrated red cell; FFP = fresh frozen plasma; PL = concentrated platelet.

**Table 6. Postoperative Variables for Propensity Score-matched Patients With and Without HES Administration**

| | HES N=190 | | Control N=190 | | p-value |
|---|---|---|---|---|---|
| **APACHE II** | 15.9 | [5.5] | 15.8 | [6.3] | 0.641 |
| **Body temperature, °C** | 36.7 | [0.7] | 36.8 | [0.7] | 0.873 |
| **APTT, seconds** | 42.7 | [20.6] | 44.6 | [23.2] | 0.804 |
| **PT-INR** | 1.3 | [0.3] | 1.2 | [0.2] | <0.001 |
| **Fibrinogen, g /L** | 2.46 | [1.51] | 2.77 | [1.30] | <0.001 |
| **Platelet count, $10^3$ µ/L** | 132 | [66] | 156 | [82] | 0.014 |
| **Hemoglobin, g /L** | 102 | [17] | 108 | [22] | <0.001 |
| **Ionized calcium, mmol/L** | 1.13 | [0.061] | 1.13 | [0.063] | 0.931 |
| **pH** | 7.37 | [0.062] | 7.364 | [0.061] | 0.264 |
| **$PaO_2/FiO_2$ ratio** | 414.7 | [229.] | 386 | [187] | 0.173 |
| **CRC, mL** | 196 | [406] | 166 | [329] | 0.885 |
| **PL, mL** | 35 | [103] | 19 | [72] | 0.087 |
| **FFP, mL** | 104 | [250] | 76 | [190] | 0.328 |
| **Reoperation for bleeding, n** | 9 | (4.7) | 3 | (1.6) | 0.140 |
| **Length of ICU stay, days** | 4.6 | [4.9] | 4 | [4.0] | 0.446 |
| **ICU mortality, n** | 4 | (2.1) | 3 | (1.6) | >0.999 |
| **Length of hospital stay, days** | 44.9 | [37.3] | 42.6 | [43.7] | 0.133 |
| **Hospital mortality, n** | 13 | (6.8) | 11 | (5.8) | 0.834 |

Data are expressed as average [Standard Deviation] or (percentages).

HES = hydroxyethyl starch; APACHE II = acute physiology and chronic health

evaluation II score; APTT = activated partial thromboplastin time; PT-INR = prothrombin time - international normalized ratio; CRC = concentrated red cell; FFP = fresh frozen plasma; PL = concentrated platelet; MV = mechanical ventilation.

Figure 1. The drainage volume during the first 24 hours after ICU admission. Data are expressed as average. HES = hydroxyethyl starch.