

Original Article
Laboratory Medicine



OPEN ACCESS

Received: Jan 17, 2025
Accepted: Apr 7, 2025
Published online: Sep 27, 2025

Address for Correspondence:

Tae-Yop Kim, MD, PhD

Department of Anesthesiology and Pain Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, 120-1 Neungdong-ro, Gwangjin-gu, Seoul 05030, Korea.

Email: taeyop@gmail.com

© 2025 The Korean Academy of Medical Sciences.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Chung-Sik Oh <https://orcid.org/0000-0001-8874-5186>
Ju Deok Kim <https://orcid.org/0000-0002-9236-5183>
Won-Kyoung Kwon <https://orcid.org/0000-0001-5753-2479>
Sookyung Lee <https://orcid.org/0009-0003-2105-2539>
Hyun Kang <https://orcid.org/0000-0003-2844-5880>
Tae-Yop Kim <https://orcid.org/0000-0003-0806-8969>

Trial Registration

ClinicalTrials.gov Identifier: [NCT02700607](https://clinicaltrials.gov/ct2/show/study/NCT02700607)

Impact of Intravascular Fluid Resuscitation on Whole Blood Viscosity During Endovascular Detachable Coiling Procedure for Unruptured Intracranial Aneurysm: A Prospective Randomized Controlled Trial

Chung-Sik Oh ^{1,2}, Ju Deok Kim ³, Won-Kyoung Kwon ¹, Sookyung Lee ¹, Hyun Kang ⁴, and Tae-Yop Kim ^{1,2}

¹Department of Anesthesiology and Pain Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea

²Research Institute of Medical Science, Konkuk University School of Medicine, Seoul, Korea

³Department of Anesthesiology and Pain Medicine, Kosin University College of Medicine, Busan, Korea

⁴Department of Anesthesiology and Pain Medicine, Chung-Ang University College of Medicine, Seoul, Korea

ABSTRACT

Background: Whole blood viscosity (WBV) determines wall shear stress, representing dynamic force and contributing to aneurysmal remodeling. We hypothesized that administering balanced crystalloid (Group-C) or hydroxyethyl starch (HES) 130/0.4 (Group-HES) for IV fluid management would have a different impact on high-shear WBV during the endovascular detachable coiling (EDC).

Methods: Thirty EDC patients randomly got HES (Group-HES, n = 15) or crystalloid (Group-C, n = 15) as the main IV fluid resuscitation during the procedure. The WBV at a shear rate of 300 sec⁻¹ of arterial blood samples (WBV₃₀₀), which depict WBV at a larger-sized artery, were determined and analyzed before and after the EDC procedure (Pre and Post). The changes in hematocrit (Hct) and arterial-to-inspired-fraction oxygen ratio (P/F-O₂ ratio) were determined as indices of the degrees of hemodilution and extravascular fluid shift, respectively.

Results: The median (25–75%) volume of infused crystalloid was 800 (700, 1,200) mL in Group-C and those of HES and crystalloid were 400 (150, 750) and of 500 (400, 600) mL in Group-HES, respectively. Pre-WBV₃₀₀ showed no significant inter-group difference. However, Post-WBV₃₀₀ in Group-HES was significantly lower than in Group-C (3.40 ± 0.33 vs. 3.95 ± 0.79 centipoise, P = 0.023). The Hct and P/F-O₂ ratios were comparable between the two groups.

Conclusion: Our study showed that HES infusion provided significantly lower WBV than crystalloid infusion during the EDC procedure. Further study is warranted to determine whether the lower WBV after HES infusion would enhance clinical outcomes.

Trial Registration: ClinicalTrials.gov Identifier: [NCT02700607](https://clinicaltrials.gov/ct2/show/study/NCT02700607)

Keywords: Blood Viscosity; Crystalloid; Colloid; Hemodilution; Intracranial Aneurysm; Endovascular Procedure

Funding

This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI22C1952).

Disclosure

The authors have no potential conflicts of interest to disclose.

Data Sharing Statement

Data sharing statement is provided in

Supplementary Material 1.**Author Contributions**

Conceptualization: Oh CS, Kim TY. Data curation: Kwon WK, Lee S, Kim JD. Formal analysis: Kang H. Funding acquisition: Kim TY. Investigation: Oh CS, Kim TY. Methodology: Oh CS, Kim TY, Kim JD. Writing - original draft: Oh CS, Kim TY, Kang H.

INTRODUCTION

Aneurysm rupture is the most serious consequence of cerebral aneurysms, and it is caused by complex mechanisms involving various rheological and hemodynamic factors and their interaction with the aneurysm zone of the cerebral arteries.¹⁻⁵

Wall shear stress (WSS) is a dynamic friction force generated by blood movement across the vascular surface. It is considered to play a critical role in the formation and remodeling of aneurysms.¹⁻³ Whole blood viscosity (WBV) is a viscous force of the blood. As a determinant of WSS,^{6,7} it influences the kinetic energy of the blood flow against the vascular wall of cerebral arteries in the aneurysmal zone.^{1,2,4,5}

The endovascular detachable coiling (EDC) procedure locates detachable coils within the cerebral aneurysmal sac via the peripheral vessel in patients with a cerebral aneurysm or subarachnoid hemorrhage. During the procedure, IV fluid management with crystalloids or colloids should focus on maintaining euolemia,⁸ but the varying physicochemical characteristics of IV fluids can have different impacts on WBV in both macro- and micro-circulation.

The HES-induced hemodilution affects blood coagulation and blood viscosity,^{9,10} and the high molecular weight of HES enables a long-lasting volume effect.¹¹ Previous studies showed that HES has a more profound impact on reducing WBV compared to crystalloid infusion in IV fluid management for preventing hypotension during epidural analgesia.¹² Given the significance of WBV's impact on WSS in narrow vascular areas like cerebral aneurysms treated with endovascular coils, it is crucial to investigate the comparative effects of crystalloid and colloid on WBV during the EDC procedure. However, few studies have evaluated the impact of crystalloid and HES on WBV during neurointerventional procedures.

Therefore, we hypothesized that HES would be more effective in reducing blood viscosity than balanced crystalloid for IV fluid management. This study was designed to compare the effects of balanced crystalloid and HES on high-shear WBV during the EDC procedure.

METHODS**Study population**

All patients scheduled for an elective EDC procedure for unruptured cerebral aneurysms were enrolled. Patients were excluded based on the following criteria: 1) preoperative hematocrit (Hct) < 30%, 2) preoperative left ventricular ejection fraction < 50%, 3) hemolysis indicated during laboratory tests, 4) ischemic heart disease, chronic renal disease, and chronic liver disease, 5) current use of antiplatelet or anticoagulant medications, 6) acute respiratory insufficiency with impaired oxygenation, defined as preoperative oxygen saturation < 90%, 7) acute or chronic infection, and 8) being underweight or overweight (body mass index < 20 or > 30 kg.m⁻²).

Before anesthesia induction, patients were randomly assigned to receive either a balanced crystalloid solution (Group-C) or a HES solution (Group-HES) by opening a sequentially numbered envelope that contained the randomization assignment. The anesthesia team and care providers, including the intervention and nursing teams, were instructed to follow the protocol. A research assistant responsible for determining eligibility and enrolling

patients obtained informed consent. A data collector, responsible for gathering data, including blood samples, was blinded to the allocation. Both the research assistant and data collector did not engage in patient care. Throughout the perioperative period and until the completion of statistical analysis, the research team members remained blinded to the study.

Anesthesia

The anesthesia for the EDC procedure was standardized, as described below. Anesthesia was induced after establishing routine non-invasive monitoring, including electrocardiography, non-invasive arterial blood pressure (BP), pulse oximetry, temperature, oxygen (O₂) saturation, and bispectral index (BIS). Train-of-four (TOF) monitoring was performed by attaching two electrodes to stimulate the ulnar nerve and a sensor between the thumb and index finger. Propofol 1.2–2.0 mg/kg and then rocuronium 0.6 mg/kg were administered intravenously for anesthesia induction. A target-controlled intravenous infusion of remifentanyl at 7–12 ng/mL was performed and maintained until the end of surgery. Assisted ventilation of air and O₂ mixture was followed in the inspired fraction of oxygen to an air (FiO₂ of 0.8). After tracheal intubation at the time of loss of TOF response, controlled ventilation with FiO₂ of 0.3–0.4 with tidal volume (TV) of 6 mL/kg and positive end-expiratory pressure of 6 cmH₂O was applied. After tracheal intubation, sevoflurane was started for anesthesia, which was adjusted to maintain the values of the BIS from 40 to 60. The respiratory rate was adjusted to maintain an end-tidal carbon dioxide of 40 mmHg.

Cannulation of the left radial artery was performed using a 22-gauge catheter immediately after anesthesia induction for monitoring invasive systemic arterial BP and stroke volume variation (SVV, FloTrac™ sensor on EV1000™ monitor; Edwards Lifesciences, Irvine, CA, USA). After achieving stable hemodynamics and an adequate depth of anesthesia, the EDC procedure commenced.

Fluid administration during the procedure

The same technique of infusing crystalloid (Plasma Solution-A™; HK inno.N Co, Seoul, Korea) was employed in both groups, from patient monitoring to initiating the EDC procedure. However, fluid administration was split into two groups after starting the EDC procedure. The crystalloid in Group-C and HES 130/0.4 (Volulyte™; Fresenius Kabi Ltd, Seoul, Korea) for Group-HES were administered respectively to maintain the SVV < 15 at the instantaneous application of TV 6 mL/kg during the EDC procedure.

Blood samples

Arterial blood samples (3 mL) were obtained from radial artery immediately after induction of anesthesia (Pre), and at the end of the EDC procedure (Post). The blood samples for WBV were collected in ethylenediaminetetraacetic acid (EDTA) tubes and analyzed. Arterial blood gas analysis (ABGA) was also performed at the same time points.

Analysis of WBV

The arterial blood samples were analyzed immediately after obtaining blood by an in vitro WBV test using a scan-capillary tube (SCT) viscometer (Hemovister™; Ubiosus, Inc., Seongnam, Korea). The arterial blood in each EDTA tube was attached to a U-shaped vertical capillary tube, and the blood was sucked into the tube to form two vertical blood columns with different heights on both ends of the U-shaped tube (Fig. 1). As the stopcock in the middle of the tube was opened, the pressure gap (gravity) from the different heights

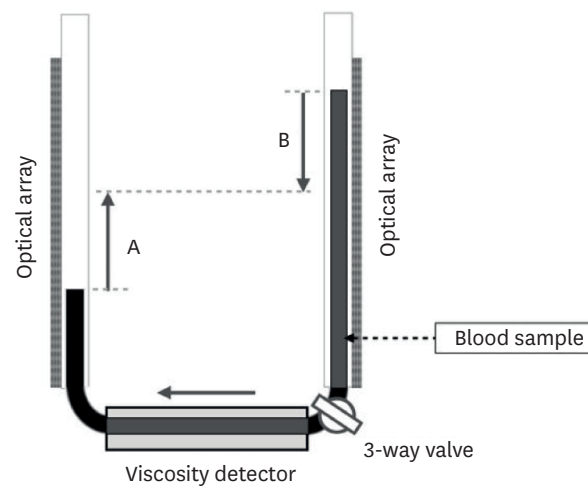


Fig. 1. Schema for analyzing WBV at various SRs with the scanning capillary tube viscometer. The blood sample was introduced into a single-use U-shaped tube. When the computer-controlled 3-way valve in the tube was opened, gravity allowed blood at a higher position in the column to fall (**A**) and blood at a lower position to rise (**B**). The optical array of the viscometer detected the elevation and depression of the blood levels (arrows A and B), and the viscosity was automatically determined by the pressure drop and flow rate change, compensating for the effect of surface tension inside the tubes. The initial blood flow rate was determined by the height difference of blood columns in both arms of the U-shaped tube and the diameter of the horizontal part of the tube in the viscosity detector. Throughout a viscosity test, the flow rate inside the capillary tube varied from an initial maximum speed down to zero when the two fluid levels in the columns reached the same elevation. From a single automated scan of this sweeping and decelerating motion of the blood column, the viscometer captured WBV data at the varying SRs (1–1,000 sec^{-1}). WBV = whole blood viscosity, SR = share rate.

of the blood columns moved the blood columns to one side to achieve equilibrium in height. Throughout the blood movement, the blood flow inside the tube varied from an initial maximum speed to zero when two fluid levels in the columns reached the same elevation. During the blood movement, the WSS (the ratio of the blood velocity to the tube diameter) and wall share rate (SR) were generated in the tube and detected by an optical array of the viscometer. WBV at a particular wall SR (WBV_{SR}) was mathematically calculated using the following equation:

$$\text{WBV}_{\text{SR}} = \text{WSS}/\text{wall SR}$$

The SCT viscometer captured WBV data at SRs ranging from 1 to 1,000 sec^{-1} , and it provided two representative WBVs: WBV at SR of 300 sec^{-1} (WBV_{300}) as the high-shear WBV and WBV at SR of 5 sec^{-1} (WBV_5) as low-shear WBV, respectively.⁶ For the present study, WBV_{300} change was employed to analyze the WBV changes in the large-sized cerebral arteries.

Clinical measurements

The total volume of intravenous fluids, urine output, and ABGA results during the EDC procedure were measured at the beginning (Pre) and end of the procedure (Post). We also compared the changes in Hct as an index of hemodilution and the arterial oxygen partial pressure ratio to fractional inspired oxygen (P/F-O_2 ratio) as an index of extravascular fluid shift.

Statistical analysis

The primary endpoint of the present study was to determine the inter-group difference in WBV_{300} at the end of the EDC procedure. A pilot study was conducted to estimate the required group size to measure WBV_{300} at the end of the EDC procedure in patients who

received crystalloid. The mean and standard deviation of WBV_{300} in these patients were 3.90 centipoise (cP) and 0.83 cP, respectively. We assumed WBV_{300} to be lower after administration of HES rather than crystalloid, and we set a 25% mean difference in WBV_{300} at the end of the EDC procedure between the two groups. With $\alpha = 0.05$, two-tailed, and a power of 80%, 13 patients in each group were required. Considering a drop-out rate of 10%, the number of patients was calculated to be 15 per group.

For inter-group comparisons, the data distribution was initially assessed for normality using the Shapiro–Wilk test and q-q plot. Independent two-tailed *t*-tests were conducted to compare the means of continuous variables with normal distributions. When the data were not normally distributed, the Mann-Whitney *U* test was utilized. For categorical variables, the number of patients (*n*) and percentages (%) were calculated. Normally distributed continuous data are presented as mean $\pm$ standard deviation. Continuous data that are not normally distributed are represented as median (25–75%). For categorical variables, the number of patients (*n*) and their proportion (%) were calculated. Data in the figures are presented as means $\pm$ standard error. All calculations were performed using the Statistical Package for the Social Sciences 20® (IBM Corp., Armonk, NY, USA). A value of $P < 0.05$ was considered indicative of statistical significance.

Ethics statement

The study used a prospective randomized design and was approved by the Institutional Review Board (IRB; approval number KUH1160101 granted by the IRB of Konkuk University Medical Center, Seoul, Korea; Chairperson Prof SH. Lee). Informed consent was submitted by all subjects when they were enrolled. The study was registered at ClinicalTrials.gov (Trial registration number NCT02700607) and conducted at a single tertiary medical center (Konkuk University Medical Center, Seoul, Korea).

RESULTS

In total, 40 patients were eligible for the study, and 10 patients were excluded for the following reasons: 2 had an ischemic heart disease, and 8 had a renal disease. Therefore, 30 patients were included in the final analysis (Group-C, *n* = 15 vs. Group-HES, *n* = 15) (**Fig. 2**).

There were no significant differences in demographic data between Group-C and Group-HES, except for the volume of fluid administered (**Table 1**). The total amounts of IV fluid were comparable in both groups. The volume of IV crystalloid was 800 (700–1,200) mL in Group-C and 500 (400–600) mL in Group-HES, while the volume of HES was 400 (150–750) mL in Group-HES (**Table 1**).

The mean value of Pre- WBV_{300} did not show a statistically significant inter-group difference. However, as the primary endpoint of the present study, the mean value of Post- WBV_{300} in Group-HES was significantly lower than that in Group-C (3.40 ± 0.34 cP vs. 3.95 ± 0.79 cP, respectively; $P = 0.023$) (**Fig. 3**). Although Pre- WBV_5 did not show a statistically significant inter-group difference, the mean value of Post- WBV_5 in Group-HES was significantly lower than that in Group-C (9.76 ± 1.76 cP vs. 12.50 ± 3.39 cP, respectively; $P = 0.011$) (**Fig. 4**).

The Hct and the P/F- O_2 ratio at the preoperative and postoperative stages did not show statistically significant intergroup differences (**Table 2**). All ABGA values, including pH,

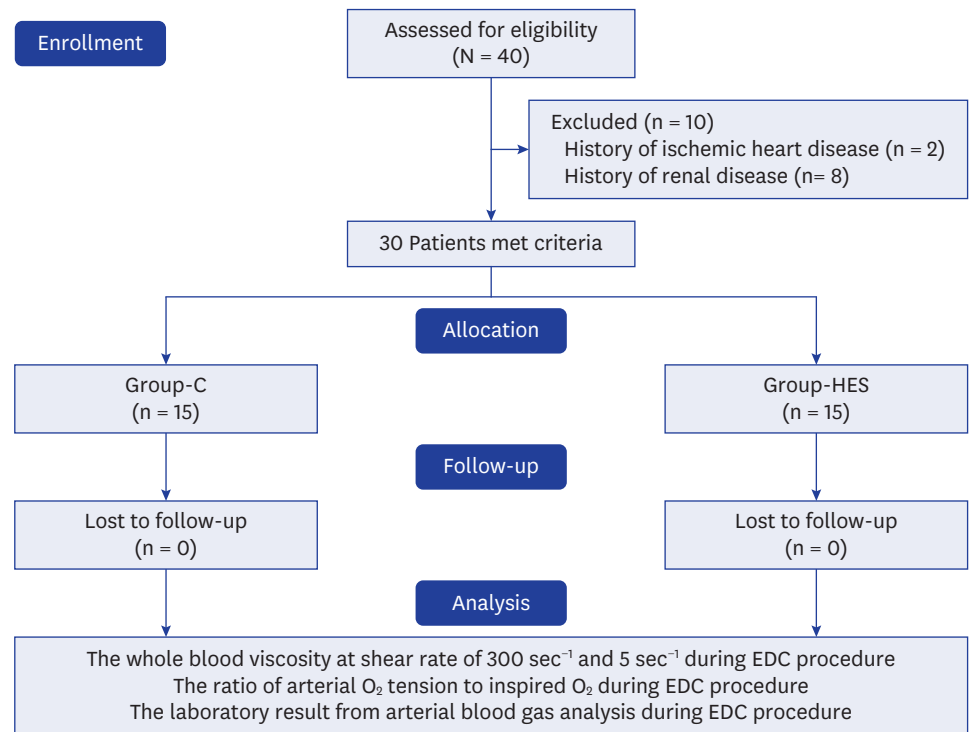


Fig. 2. Consolidated Standards of Reporting Trials flow diagram.

Group-C = patients with balanced crystalloid infusion, Group-HES = patients with hydroxyethyl starch (130/0.4) infusion, EDC procedure = endovascular detachable coiling procedure, O₂ = oxygen.

Table 1. Demographic profiles between the crystalloid and colloid groups

Variables	Group-C (n = 15)	Group-HES (n = 15)
Age, yr	53.3 ± 15.2	57.2 ± 12.0
Sex, male/female	6/9	5/10
Height, cm	162 ± 10	161 ± 9
Weight, kg	64 (60, 77)	61 (56, 70)
Underlying disease		
Hypertension	7	5
Diabetes mellitus	3	1
Anesthesia duration, min	175 (150, 215)	180 (145, 228)
Total amount of fluid, mL	800 (700, 1,200)	1,000 (650, 1,260)
Crystalloid, mL	800 (700, 1,200)	500 (400, 600)
HES, mL	0	400 (150, 750)
Urine output, mL	640 (455, 925)	800 (385, 1,050)

Data are presented as mean ± standard deviation, numbers, or median (25–75%).

Group-C = patients with balanced crystalloid infusion, Group-HES = patients with hydroxyethyl starch (130/0.4) infusion, HES = hydroxyethyl starch solution (130/0.4).

serum electrolytes, calcium, magnesium, lactate, and glucose, were also comparable between the two groups (Table 2).

DISCUSSION

The present study demonstrated that intraprocedural HES infusion significantly reduces WBV and is associated with significantly lower WBV than crystalloid infusion during the EDC procedure.

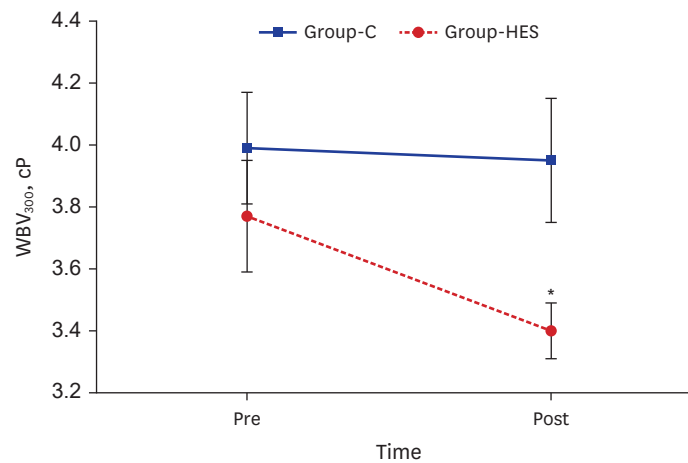


Fig. 3. The changes in WBV₃₀₀ before and after the EDC procedure. Data are presented as mean $\pm$ standard error. WBV₃₀₀ = whole blood viscosity at share rate of 300 sec⁻¹, EDC procedure = endovascular detachable coiling procedure, Group-C = patients with balanced crystalloid infusion, Group-HES = patients with hydroxyethyl starch (130/0.4) infusion, cP = centipoise, Pre = preoperative, Post = postoperative. **P* = 0.023 compared to Group-C.

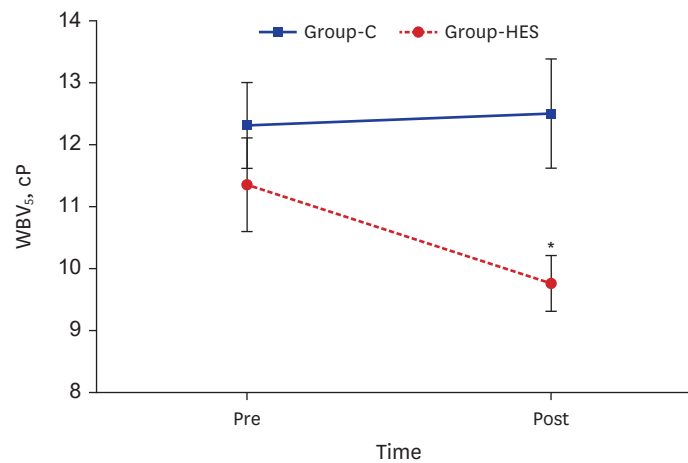


Fig. 4. The changes in WBV₅ before and after the EDC procedure. Data are presented as mean $\pm$ standard error. WBV₅ = whole blood viscosity at share rate of 5 sec⁻¹, EDC procedure = endovascular detachable coiling procedure, Group-C = patients with balanced crystalloid infusion, Group-HES = patients with hydroxyethyl starch (130/0.4) infusion, cP = centipoise, Pre = preoperative, Post = postoperative. **P* = 0.011 compared to Group-C.

Hemodilution with IV crystalloid or colloid infusion was widely adopted in the past to prevent vascular spasms and aneurysmal rupture as part of “Triple-H prophylaxis,” which consists of hypervolemia and hypertension.¹³⁻¹⁷ The strategy has shifted from pursuing hypervolemia to euvolemia. Currently, the primary aim of IV fluid management during the EDC is to prevent both hypovolemia and hypervolemia during the EDC procedure.⁸ In the present study, HES infusion of less than 400 mL reduced WBV at SR of 300 sec⁻¹ without affecting Hct, a reliable indicator of the hemodilution effect. This result supports that HES may be superior to crystalloids in reducing WBV in hemodilution, even without affecting Hct values.

Previous studies inconsistently reported the impact of HES infusion on blood viscosity. Haass et al. showed that HES reduces blood viscosity in patients with ischemic attacks,¹⁸ and this finding aligns with our results. The physiology of reduced blood flow in ischemic conditions

Table 2. Comparison of values from arterial blood gas analysis in both groups

Variables	Group-C (n = 15)	Group-HES (n = 15)	Differences	P value
Hct, %				
Pre	34.6 ± 3.8	34.7 ± 4.5	-1.30 (-3.25, 2.98)	0.931
Post	34.0 ± 3.8	32.0 ± 5.6	1.91 (-1.67, 5.48)	0.284
pH				
Pre	7.41 ± 0.04	7.40 ± 0.02	0.01 (-0.01, 0.03)	0.284
Post	7.40 ± 0.02	7.40 ± 0.03	0.00 (-0.02, 0.02)	0.868
PaO ₂ , mmHg				
Pre	283.1 ± 70.3	281.0 ± 101.5	2.16 (-63.2, 67.5)	0.946
Post	253.5 ± 76.6	262.1 ± 104.0	-8.51 (-76.8, 59.8)	0.800
P/F-O ₂				
Pre	416.9 ± 85.6	415.8 ± 83.1	1.13 (-62.00, 64.23)	0.971
Post	357.5 (297.6, 406.0)	390.9 (367.8, 479.5)	-55.20 (-97.30, 9.10)	0.098
PaCO ₂ , mmHg				
Pre	35.2 ± 4.6	36.2 ± 3.4	-1.00 (-4.00, 2.00)	0.500
Post	35.2 ± 2.8	34.8 ± 3.3	0.43 (-1.86, 2.71)	0.705
BE, mmol/L				
Pre	-1.35 ± 1.48	-1.01 ± 1.32	-0.34 (-1.43, 0.75)	0.524
Post	-1.59 ± 1.53	-2.05 ± 1.90	0.47 (-0.90, 1.83)	0.486
Na ⁺ , mmol/L				
Pre	139.8 ± 1.8	140.7 ± 1.6	-0.89 (-2.20, 0.44)	0.179
Post	141.8 ± 2.2	142.4 ± 2.8	-0.53 (-2.54, 1.48)	0.592
K ⁺ , mmol/L				
Pre	5.9 ± 8.3	5.9 ± 8.3	0.03 (-6.20, 6.26)	0.993
Post	3.9 (3.7, 4.3)	3.8 (3.7, 4.0)	0.09 (-0.17, 0.34)	0.482
Cl ⁻ , mmol/L				
Pre	108.8 ± 2.0	109.8 ± 1.5	-1.02 (-2.39, 0.34)	0.136
Post	110.5 (109.5, 112.9)	112.1 (110.3, 114.1)	-1.30 (-3.10, 0.80)	0.217
Ca ²⁺ , mmol/L				
Pre	1.17 (1.15, 1.22)	1.19 (1.15, 1.20)	-0.00 (-0.05, 0.41)	0.870
Post	1.69 ± 1.93	2.09 ± 2.34	-0.40 (-2.06, 1.27)	0.629
Mg ²⁺ , mmol/L				
Pre	0.59 ± 0.08	0.58 ± 0.11	0.01 (-0.06, 0.08)	0.783
Post	0.65 (0.62, 0.69)	0.59 (0.54, 0.68)	0.45 (-0.50, 0.13)	0.340
Glucose, mg/dL				
Pre	102.0 (98.0, 111.0)	96.0 (92.5, 105.5)	5.00 (-4.00, 13.00)	0.250
Post	101.7 ± 13.3	102.6 ± 12.1	-0.90 (-11.48, 9.68)	0.862
Lactate, mmol/L				
Pre	1.27 ± 0.31	1.31 ± 0.55	-0.04 (-0.39, 0.31)	0.820
Post	0.96 ± 0.29	1.14 ± 0.43	-0.18 (-0.48, 0.12)	0.224

Data are presented as mean ± standard deviation or median (25–75%).

Group-C = patients with balanced crystalloid infusion, Group-HES = patients with hydroxyethyl starch (130/0.4) infusion, Hct = hematocrit, Pre = preoperative, Post = postoperative, PaO₂ = arterial oxygen tension, P/F-O₂ ratio = the ratio of arterial oxygen tension/inspired oxygen fraction, PaCO₂ = arterial carbon dioxide tension, BE = base excess.

may be similar to that observed after the EDC procedure. Menu et al. also demonstrated that the administration of HES decreases blood viscosity in animal studies, which aligns with our results.¹⁹

In contrast, studies in different clinical settings have postulated contradictory results: HES increased blood viscosity in trauma patients¹⁰ and sepsis.²⁰ However, we may have to account that these findings were demonstrated in in vitro analyses; trauma with severe blood loss itself can increase the blood viscosity, and sepsis itself can also increase the blood viscosity, potentially compromising microcirculation²¹ and aggravating tissue hypoxia and organ dysfunction.^{22,23} Thus, the overall effect of HES on WBV may vary based on the underlying patient condition. HES can have a more profound effect on reducing WBV, particularly under conditions of reduced blood flow, such as cerebral or limb ischemia, or narrowed vasculature diameter.

While our study did not analyze the clinical impacts of HES-induced WBV reduction, Ernst et al.²⁴ revealed that the administration of HES reduced WBV and improved pain-free walking distance and resting blood flow in patients with peripheral artery occlusive disease. Additionally, Hartmann et al.²⁵ revealed enhanced hemispheric and regional blood flow following the administration of HES in patients with acute cerebral ischemia. All these studies indicate that HES reduces blood viscosity and enhances blood flow, which is diminished due to cerebral or limb ischemia or the EDC procedure.

The vascular wall is influenced by two forces: wall pressure and wall tension. Wall pressure refers to the kinetic energy of blood flow and the force that acts perpendicularly to the vascular surface. Wall tension, on the other hand, is the force exerted by the vascular wall in the opposite direction and of equal magnitude to the pressure. WSS is a determinant of wall pressure, and its change predicts the aneurysm rupture.^{4,5} Furthermore, despite the ongoing debate about whether low or high WSS regions contribute to the rupture,^{2,3} WSS is regarded as playing a critical role in the remodeling of intracranial aneurysms: aneurysms arise in the vasculature exposed to abnormally high levels of WSS. Once the aneurysm develops, intra-aneurysmal flow creates areas with lower and higher WSS.¹⁻³

The crystalloid has far less viscosity than HES and blood. Therefore, adding crystalloids into the blood sample would quickly reduce the sample's viscosity. However, while the IV infusion of HES during the EDC procedure significantly reduced WBV, the infused crystalloid did not affect post-procedural WBV in the present study. These results may require consideration of the different pharmacokinetic characteristics of the infused crystalloid and HES solutions: the infused crystalloid, approximately 1,200 mL, exhibits its peak volume effect within an hour, after which most of the infused crystalloid rapidly shifts to extravascular interstitial fluid space.²⁶ Therefore, the infused crystalloid solution may distribute outside the IV space and may not affect WBV. On the contrary, HES may remain longer in the IV space and reduce WBV for an extended period.²⁷

In cerebral arteries with fast blood flow, WSS largely depends on the velocity of the blood flow rather than on the viscous force of the blood, such as WBV. Furthermore, blood is a shear-thinning fluid; it becomes less viscous, and WBV's contribution to WSS becomes less.^{2,6,7} However, WBV is still the major determinant of viscous force, and its variations can affect variable WSS. Furthermore, in the aneurysmal arteries (known as the "aneurysmal zone"), the impact of WBV increases and becomes remarkable.² Therefore, it may be necessary to evaluate the changes in WBV as a rheological factor inducing vasospasm of the cerebral artery and aneurysm rupture. In cerebral arteries with higher blood flow velocity, high-shear WBV primarily depended on Hct and the deformability of red blood cells.²⁸ Practically, it is challenging to determine the changes in WBV specific to the selection of IV fluids for intraoperative or intraprocedural fluid management. While no suitable modalities currently exist to analyze the change of in vivo WBV in cerebral arteries, our study suggests the potential efficacy of the SCT viscometer in monitoring the WBV change during the EDC procedure.

Since blood is a non-Newtonian shear-thinning fluid, WBV varies at different vascular SRs throughout the systemic circulation: WBV becomes lower in large arteries with faster blood flow, where vascular SR can reach up to 300 sec⁻¹. In comparison, WBV increases in microcirculation or vascular systems with slower blood flow, where vascular SR becomes 1–5 sec⁻¹.^{6,29} The low-shear WBV is affected by changes in composition or rheological properties of plasma.³⁰ The successfully placed coils following the EDC procedure obstruct blood flow

in the aneurysmal sac, elevate the low-shear WSS, and promote clot formation and occlusion of the coiled aneurysm sac.^{31,32} The reduced WBV_s in Group-HES suggests a potential negative impact of HES infusion on the post-procedural outcome related to the clot formation and occlusion³¹⁻³³ and recanalization of the coiled aneurysm.³⁴

Our study has the following limitations. First, we only conducted in vitro analyses of WBV changes before and after the IV fluid resuscitation for the EDC procedure. Clinical parameters such as the alterations in cerebral blood flow, vascular diameter, and other hemodynamic factors related to inducing spasm or rupture were not examined and analyzed due to the limited applicability or lack of clinically available monitors. Second, the potential bias from using the contrast dye for radiological imaging during the EDC procedure was not evaluated. Third, the assessment of clinical outcomes, such as the incidences of perioperative vasospasm and aneurysmal rupture, was not considered due to the study design, which employed a small sample size limited to determining WBV changes.

In conclusion, our study demonstrated that HES infusion was superior to crystalloid infusion in reducing high-shear WBV during the EDC procedure. This would be beneficial in preventing increases in WSS and friction force in the blood flow during the procedure. Further studies are warranted to confirm if the reduced WBV can enhance clinical outcomes in these patients.

SUPPLEMENTARY MATERIAL

Supplementary Material 1

Data sharing statement

REFERENCES

1. Meng H, Tutino VM, Xiang J, Siddiqui A. High WSS or low WSS? Complex interactions of hemodynamics with intracranial aneurysm initiation, growth, and rupture: toward a unifying hypothesis. *AJNR Am J Neuroradiol* 2014;35(7):1254-62. [PUBMED](#) | [CROSSREF](#)
2. Munarriz PM, Gómez PA, Paredes I, Castaño-Leon AM, Cepeda S, Lagares A. Basic principles of hemodynamics and cerebral aneurysms. *World Neurosurg* 2016;88:311-9. [PUBMED](#) | [CROSSREF](#)
3. Sforza DM, Kono K, Tateshima S, Viñuela F, Putman C, Cebal JR. Hemodynamics in growing and stable cerebral aneurysms. *J Neurointerv Surg* 2016;8(4):407-12. [PUBMED](#) | [CROSSREF](#)
4. Axier A, Rexiati N, Wang Z, Cheng X, Su R, Aikeremu R, et al. Effect of hemodynamic changes on the risk of intracranial aneurysm rupture: a systematic review and meta-analysis. *Am J Transl Res* 2022;14(7):4638-47. [PUBMED](#)
5. Varble N, Trylesinski G, Xiang J, Snyder K, Meng H. Identification of vortex structures in a cohort of 204 intracranial aneurysms. *J R Soc Interface* 2017;14(130):20170021. [PUBMED](#) | [CROSSREF](#)
6. Kim H, Cho YI, Lee DH, Park CM, Moon HW, Hur M, et al. Analytical performance evaluation of the scanning capillary tube viscometer for measurement of whole blood viscosity. *Clin Biochem* 2013;46(1-2):139-42. [PUBMED](#) | [CROSSREF](#)
7. Cho YI, Cho DJ, Rosenson RS. Endothelial shear stress and blood viscosity in peripheral arterial disease. *Curr Atheroscler Rep* 2014;16(4):404. [PUBMED](#) | [CROSSREF](#)
8. De Sloovere VT. Anesthesia for embolization of cerebral aneurysms. *Curr Opin Anaesthesiol* 2014;27(4):431-6. [PUBMED](#) | [CROSSREF](#)
9. Thyges C, Madjdpour C, Frascarolo P, Buclin T, Bürki M, Fisch A, et al. Effect of high- and low-molecular-weight low-substituted hydroxyethyl starch on blood coagulation during acute normovolemic hemodilution in pigs. *Anesthesiology* 2006;105(6):1228-37. [PUBMED](#) | [CROSSREF](#)

10. Neff TA, Fischler L, Mark M, Stocker R, Reinhart WH. The influence of two different hydroxyethyl starch solutions (6% HES 130/0.4 and 200/0.5) on blood viscosity. *Anesth Analg* 2005;100(6):1773-80. [PUBMED](#) | [CROSSREF](#)
11. Madjdpour C, Dettori N, Frascarolo P, Burki M, Boll M, Fisch A, et al. Molecular weight of hydroxyethyl starch: is there an effect on blood coagulation and pharmacokinetics? *Br J Anaesth* 2005;94(5):569-76. [PUBMED](#) | [CROSSREF](#)
12. Marcinkowska-Gapińska A, Kowal P, Chałupka Z. The changes of low-shear-rate hemorheological properties depending on the fluid used for transfusion. *Clin Hemorheol Microcirc* 2002;27(3-4):171-6. [PUBMED](#)
13. Hoff R, Rinkel G, Verweij B, Algra A, Kalkman C. Blood volume measurement to guide fluid therapy after aneurysmal subarachnoid hemorrhage: a prospective controlled study. *Stroke* 2009;40(7):2575-7. [PUBMED](#) | [CROSSREF](#)
14. Muench E, Horn P, Bauhuf C, Roth H, Philipps M, Hermann P, et al. Effects of hypervolemia and hypertension on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation after subarachnoid hemorrhage. *Crit Care Med* 2007;35(8):1844-51. [PUBMED](#) | [CROSSREF](#)
15. Mori K, Arai H, Nakajima K, Tajima A, Maeda M. Hemorheological and hemodynamic analysis of hypervolemic hemodilution therapy for cerebral vasospasm after aneurysmal subarachnoid hemorrhage. *Stroke* 1995;26(9):1620-6. [PUBMED](#) | [CROSSREF](#)
16. Hoff RG, Rinkel GJ, Verweij BH, Algra A, Kalkman CJ. Nurses' prediction of volume status after aneurysmal subarachnoid haemorrhage: a prospective cohort study. *Crit Care* 2008;12(6):R153. [PUBMED](#) | [CROSSREF](#)
17. Sen J, Belli A, Albon H, Morgan L, Petzold A, Kitchen N. Triple-H therapy in the management of aneurysmal subarachnoid haemorrhage. *Lancet Neurol* 2003;2(10):614-21. [PUBMED](#) | [CROSSREF](#)
18. Haass A, Kroemer H, Jäger H, Müller K, Decker I, Wagner EM, et al. Dextran 40 or HES 200/0.5? Hemorheology of the long-term treatment of ischemic cerebral attacks. *Dtsch Med Wochenschr* 1986;111(44):1681-6. [PUBMED](#)
19. Menu P, Bleeker W, Longrois D, Caron A, Faivre-Fiorina B, Muller S, et al. In vivo effects of Hb solutions on blood viscosity and rheologic behavior of RBCs: comparison with clinically used volume expanders. *Transfusion* 2000;40(9):1095-103. [PUBMED](#) | [CROSSREF](#)
20. Castro VJ, Astiz ME, Rackow EC. Effect of crystalloid and colloid solutions on blood rheology in sepsis. *Shock* 1997;8(2):104-7. [PUBMED](#) | [CROSSREF](#)
21. Alexy T, Detterich J, Connes P, Toth K, Nader E, Kenyeres P, et al. Physical properties of blood and their relationship to clinical conditions. *Front Physiol* 2022;13:906768. [PUBMED](#) | [CROSSREF](#)
22. Piagnerelli M, Boudjeltia KZ, Vanhaeverbeek M, Vincent JL. Red blood cell rheology in sepsis. *Intensive Care Med* 2003;29(7):1052-61. [PUBMED](#) | [CROSSREF](#)
23. Naumann DN, Hazeldine J, Bishop J, Midwinter MJ, Harrison P, Nash G, et al. Impact of plasma viscosity on microcirculatory flow after traumatic haemorrhagic shock: a prospective observational study. *Clin Hemorheol Microcirc* 2019;71(1):71-82. [PUBMED](#) | [CROSSREF](#)
24. Ernst E, Matrai A, Kollar L. Placebo-controlled, double-blind study of haemodilution in peripheral arterial disease. *Lancet* 1987;1(8548):1449-51. [PUBMED](#) | [CROSSREF](#)
25. Hartmann A, Tsuda Y, Lagrèze H. Effect of hypervolaemic haemodilution of regional cerebral blood flow in patients with acute ischaemic stroke: a controlled study with hydroxyethylstarch. *J Neurol* 1987;235(1):34-8. [PUBMED](#) | [CROSSREF](#)
26. Ewaldsson CA, Hahn RG. Kinetics and extravascular retention of acetated ringer's solution during isoflurane or propofol anesthesia for thyroid surgery. *Anesthesiology* 2005;103(3):460-9. [PUBMED](#) | [CROSSREF](#)
27. Hahn RG. Adverse effects of crystalloid and colloid fluids. *Anaesthesiol Intensive Ther* 2017;49(4):303-8. [PUBMED](#)
28. Kim BJ, Lee YS, Zhanov A, Yang S. A viscometer for simultaneous measurement of whole blood viscosity and its determinants: hematocrit and red blood cell deformability. *Analyst (Lond)* 2019;144(9):3144-57. [PUBMED](#) | [CROSSREF](#)
29. Alexy T, Pais E, Armstrong JK, Meiselman HJ, Johnson CS, Fisher TC. Rheologic behavior of sickle and normal red blood cell mixtures in sickle plasma: implications for transfusion therapy. *Transfusion* 2006;46(6):912-8. [PUBMED](#) | [CROSSREF](#)
30. Weiss N. A critical review on the use of lipid apheresis and rheopheresis for treatment of peripheral arterial disease and the diabetic foot syndrome. *Semin Dial* 2012;25(2):220-7. [PUBMED](#) | [CROSSREF](#)
31. Otani T, Ii S, Shigematsu T, Fujinaka T, Hirata M, Ozaki T, et al. Computational study for the effects of coil configuration on blood flow characteristics in coil-embolized cerebral aneurysm. *Med Biol Eng Comput* 2017;55(5):697-710. [PUBMED](#) | [CROSSREF](#)

32. Jeon JP, Cho YD, Rhim JK, Yoo DH, Kang HS, Kim JE, et al. Extended monitoring of coiled aneurysms completely occluded at 6-month follow-up: late recanalization rate and related risk factors. *Eur Radiol* 2016;26(10):3319-26. [PUBMED](#) | [CROSSREF](#)
33. Park W, Song Y, Park KJ, Koo HW, Yang K, Suh DC. Hemodynamic characteristics regarding recanalization of completely coiled aneurysms: computational fluid dynamic analysis using virtual models comparison. *Neurointervention* 2016;11(1):30-6. [PUBMED](#) | [CROSSREF](#)
34. Morga R, Moskała M, Popiela T, Rajzer M, Wilk A, Kłosiński M, et al. Recanalization of embolized endovascular intracranial aneurysms and changes in the blood viscosity: a pilot study. *Med Sci Monit* 2020;26:e919059. [PUBMED](#) | [CROSSREF](#)