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Differences in chamber structure contribute to the incidence of venous air trap chamber coagulation during AN69ST-CHF: clinical and in vitro evaluation

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Abstract

Background During continuous kidney replacement therapy (CKRT) in patients with sepsis and critical conditions, circuit coagulation can occur, often for unclear reasons. In this study, we investigate how the structure of the venous air trap chamber may contribute to venous air trap chamber coagulation. Clinical data were evaluated and experiments were performed.

Methods The clinical evaluation involved patients who underwent continuous hemofiltration (CHF) using an acrylonitrile-co-methallyl sulfonate surface-treated (AN69ST) hemofilter (AN69ST-CHF) and either an ACH-Σ or Prismaflex CKRT machine in our ICU from April to July 2019. The patient data were divided into two groups based on CKRT machine and the percentage of CHF procedures that could continuously be performed for 22 h (CHF target achievement rate), and coagulation sites were evaluated. Statistical analysis was performed by the Mann–Whitney *U* test and Pearson's chi-square test. For in vitro experiments, a system was constructed to circulate a 33% glycerol solution at a flow rate of 150 ml/min. In a venous air trap chamber, fluid dye disappearance times and fluid movements were visually evaluated.

Results The clinical evaluation included 22 procedures (8 patients) in the ACH-Σ group and 22 procedures (11 patients) in the Prismaflex group, without significant differences in patient backgrounds between the groups. The CHF target achievement rate was 72.7% (16/22) in the ACH-Σ group and 77.3% (17/22) in the Prismaflex group, revealing no significant difference ($p = 0.73$). However, significantly fewer venous air trap chamber coagulations were observed in the Prismaflex group (1/5) than in the ACH-Σ group (5/6) ($p < 0.01$). In vitro evaluation found that the dye disappearance time was significantly shorter when using the Prismaflex device ($17.5 \text{ s} \pm 0.7 \text{ s}$) than the ACH-Σ device ($51.2 \text{ s} \pm 0.7 \text{ s}$; $p < 0.05$). Visual evaluation revealed that in the ACH-Σ venous air trap chamber the upper layer of the accumulated fluid was quite stagnant, whereas fluid flowed with uniform agitation through the Prismaflex venous air trap chamber. Hence, differences were observed in fluid flow and retention in the vein air trap chambers, depending on the chamber structure.

Conclusion Chamber structure may contribute to the occurrence of venous air trap chamber coagulation during CKRT.

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Keywords AN69ST, ACH- Σ , Prismaflex, Blood circuit coagulation, Venous air trap chamber, Horizontal inflow chamber, Vertical inflow chamber, Vortex flow

Introduction

In Japan, 40% of patients requiring blood purification are complicated by sepsis [1], and the mortality rate of patients with septic acute kidney injury (AKI) requiring continuous kidney replacement therapy (CKRT) is as high as 50% [2]. In particular, during CKRT, patients with sepsis and critical illnesses can experience hypercoagulability and unexpected circuit coagulation. CKRT circuit coagulation can lead not only to downtime and insufficient purification volume [3, 4] but also to loss of the patient's blood [5]. Furthermore, the frequent replacement of CKRT circuits and hemofilters is a significant burden for healthcare professionals, so it is essential to find ways to reduce the incidence of CKRT circuit coagulation. Although studies have been analyzing the management of anticoagulants [6, 7], choice of hemofilter [8, 9] and choice of vascular access [10, 11], there have not been clear conclusions yet on how to prevent CKRT circuit coagulation.

In Japan, various blood purification machines are used, and the structure of blood circuits differs among the different models. In particular, the structure of the venous air trap chamber, which plays a role in removing air bubbles and blood clots, varies greatly among blood circuits. To the best of our knowledge, with the note that we already published part of the here presented data in the Japanese language [12], there have not been reports on CKRT circuit coagulation [13] that focused on the chamber structure [14, 15] from both clinical and in vitro perspectives. Therefore, we set out to test the hypothesis that "differences in chamber structure contribute to the incidence of venous air trap chamber coagulation."

The purpose of this study is to retrospectively evaluate the incidence of blood circuit coagulation during continuous hemofiltration with acrylonitrile-co-methallyl sulfonate surface-treated (AN69ST-CHF) using the ACH- Σ and Prismaflex CKRT machines available in Japan and to compare the fluid flows in the venous air trap chambers in these two machines in an in vitro study.

Methods

Clinical evaluation

The study period was from April to July 2019. Among the patients who underwent CHF with an AN69ST hemofilter (Baxter Inc) in our ICU, those who used ACH- Σ (Asahi Kasei Medical Inc) or Prismaflex (Baxter Inc) as the CKRT machine were included in the

study. The study was approved by the ethics committee of Fujita Health University. The need for informed consent was waived for this study because it was a retrospective observational study (trial registration: HM23-289). In total, 13 patients were included. Due to the limited number of CKRT machines owned by our ICU, the CKRT machines available at the start of each treatment were used, and if treated multiple times, the same patient might be treated with a different machine.

Patients were anticoagulated with nafamostat mesylate (NM) as the sole anticoagulant at a dose rate of 30 mg/h. Since the CKRT circuit was changed daily at our institution, CHF was terminated at 22 h, and then CHF could be resumed with the next new CKRT circuit within 2 h. Therefore, we defined a CHF that could be performed for more than 22 h with one AN69ST hemofilter as having achieved the goal. We divided the CHF procedure results into two groups, based on whether ACH- Σ or Prismaflex was used, and compared the CHF target achievement rates and coagulation sites between them. The blood circuits used were CHDF-FSA for the ACH- Σ machine and Prismaflex sepXiris Set 150 for the Prismaflex machine. The venous air trap chamber of the CHDF-FSA circuit has a vertical inflow and built-in filter, and the chamber volume is 18 ml (Fig. 1). The venous air trap chamber of the Prismaflex sepXiris Set 150 has of filterless structure with horizontal inflow, and the chamber volume is 10 ml (Fig. 1). The conditions for CHF in both groups were a blood flow rate (QB) of 150 ml/min, a filtration flow rate (QF) of 1000 ml/h, and a total NM dosage rate of 30 mg/h. When water removal was performed, the rate of replacement fluid was adjusted accordingly to maintain a constant QF. The route of NM administration was 20 mg/h of NM before hemofilter and 10 mg/h of NM after hemofilter in the ACH- Σ group using the aliquot administration method and 30 mg/h of NM only before hemofilter in the Prismaflex group. The target achievement rate when CHF was performed and the coagulation site when the target was not achieved were analyzed by comprehensively determining the inlet pressure, venous pressure, transmembrane pressure difference, filtration pressure trend, and coagulation site from the logs of each CKRT machine. Patient background data, including age, gender, inflammation, severity score, and coagulation system, were extracted from the electronic medical record. Various laboratory parameters and severity scores were calculated from

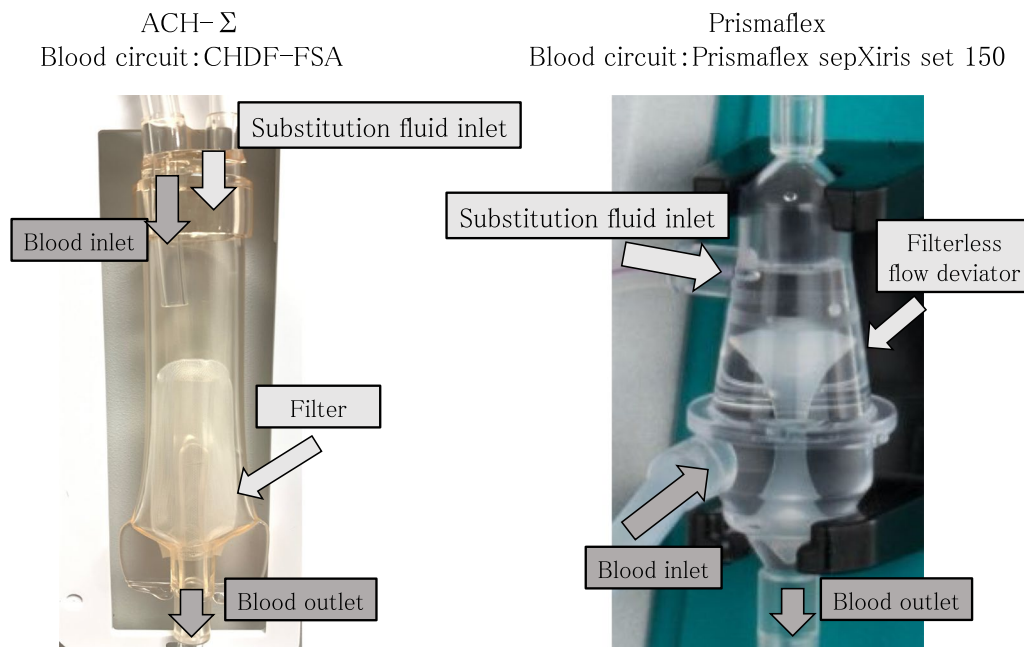


Fig. 1 Different structures of venous air trap chambers. The venous air trap chamber of the CHDF-FSA circuit has a vertical inflow and a built-in filter. The venous air trap chamber of the Prismaflex sepXiris Set 150 has a horizontal inflow and filterless structure

data for blood samples collected at 6:00 AM on the day of CHF. Data were expressed as median and interquartile range, and statistical analysis was performed by the Pearson's chi-square test for gender and also for sepsis and by the Mann–Whitney *U* test for the other data.

In vitro evaluation

The CKRT machines and blood circuits used were ACH-Σ: CHDF-FSA circuit and Prismaflex: Prismaflex sepXiris Set 150. Visual evaluation of dye disappearance time and fluid flow in the venous air trap chamber were performed using venous air trap chambers of different structures as described below for experiments 1 and 2.

Investigation of the dye disappearance time in a venous air trap chamber

An experimental system was constructed in which a reservoir was filled with 1.5 liters of 33% glycerin solution (Fujifilm Wako Pure Chemicals Corporation) and circulated at a flow rate of 150 ml/min by a blood pump. The arterial circuit was connected to a water reservoir, and the vein circuit was connected to a tank for waste blood (Fig. 2A). The time from the injection of 1 ml of stock solution for simulated blood (Sakamoto Model Co.) into the venous air trap chamber until the dye disappeared was measured visually three times using either CKRT machine, and the average values were compared. Data are expressed as mean \pm standard deviation, and the Mann–Whitney *U* test was used for statistical analysis. The dye

loss time was measured in the presence of three clinical engineers.

Visual evaluation of fluid flow in a venous air trap chamber

The reservoir was filled with 1.5 liters of 33% glycerin solution and mixed with 10 ml of silver paint (Pentel Corporation) for visualization of flow in the venous air trap chamber. A recirculation experimental system was constructed in which both the arterial circuit and the vein circuit were connected to a water reservoir and circulated by a blood pump at a flow rate of 150 ml/min. The fluid flow in the venous air trap chamber was visually evaluated (Fig. 2B).

Results

Clinical evaluation

During the observation period, 22 procedures (for 8 patients) were performed in the ACH-Σ group and 22 procedures (for 11 patients) in the Prismaflex group. The rates of sepsis were 6/8 (75%) in the ACH-Σ group and 9/11 (72.7%) in the Prismaflex group. No significant differences were found between patients in the two groups in regard to blood collection test parameters related to inflammation, severity scores, and the coagulation system (Table 1).

The percentage of CHF procedures that were uninterrupted for 22 h, defined as “the target achievement rates”, were 72.7% (16/22) for the ACH-Σ-vertical inflow group (dispensing method: NM 20 mg/h before

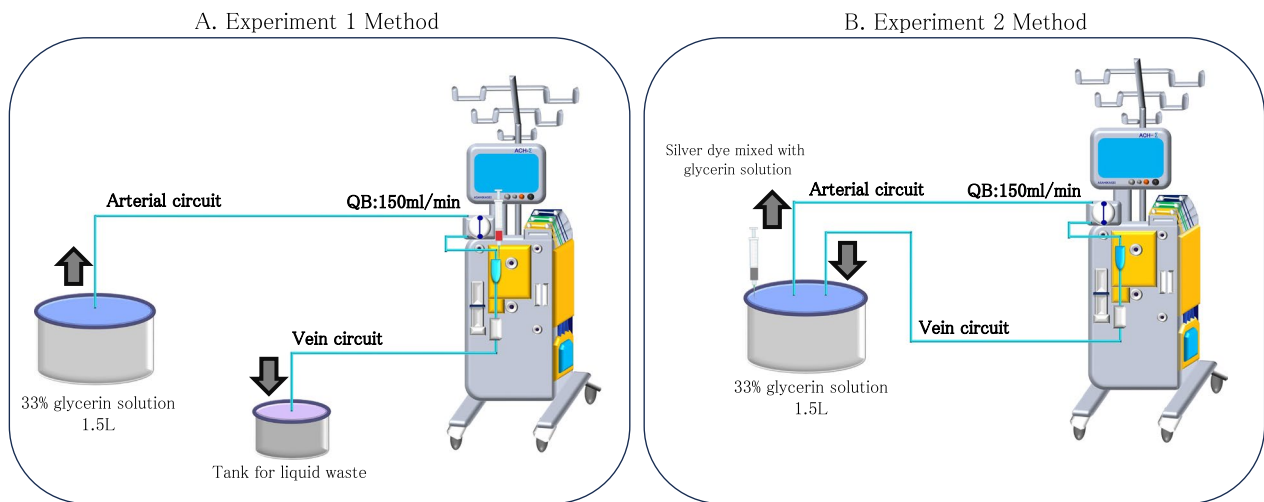


Fig. 2 In vitro evaluation methods. **A** Experiment 1 method. The arterial circuit was connected to a water reservoir, and the vein circuit was connected to a tank for waste fluid, creating a system with a flow rate of 150 ml/min. For visualization of the flow, 1 ml of dye was injected into the venous air trap chamber. The time period of dye disappearance from within the venous air trap chamber was measured after dye injection, using visual evaluation. **B** Experiment 2 method. An experimental system was constructed in which both the arterial circuit and vein circuit were connected to a water reservoir, with a recirculating flow at a rate of 150 ml/min. The circulating fluid was a glycerin solution mixed with silver dye, and the fluid movement in the chamber was visually monitored

Table 1 Background of patients

	ACH-Σ group (8 patients/22 procedures)	Prismaflex group (11 patients/22 procedures)	p value
Age	63 (39, 77)	72 (63, 77)	0.41
Male/female	5/3	6/5	0.29
Sepsis% (patients)	75% (6)	81% (9)	0.72
APACHE II score	19 (10, 23)	19 (11.8, 23)	0.77
DIC score	4 (2, 6.3)	3 (1, 5)	0.31
White blood cell (10 ³ /μl)	12.3 (7.3, 18.3)	12.6 (7.5, 15)	0.73
CRP (mg/dl)	16.1 (9.4, 20.0)	14.1 (5.3, 19.1)	0.50
PCT (ng/ml)	3.4 (1.4, 7.5)	3.6 (0.7, 12.6)	0.87
blood platelet (10 ⁴ /uL)	7.4 (4.3, 13.4)	8 (6.3, 15.0)	0.23
PT (s)	14.4 (13.3, 15.7)	14.6 (13.6, 17.1)	0.20
APTT (s)	43 (35.3, 50.5)	46.2 (37.7, 51.0)	0.57
Fibrinogen (mg/dL)	325 (275, 455.8)	396 (274.8, 512)	0.34
FDP (ug/ml)	17.9 (11.8, 42.5)	14.6 (10.0, 25.9)	0.26
D-dimer (ug/ml)	12.9 (10.1, 24.9)	12.7 (6.4, 24.5)	0.35
TAT (ng/ml)	13.2 (6.0, 24.8)	6.4 (4.8, 19.4)	0.30

Presented data are based on electronic records and include the test results of blood samples drawn at 6:00 a.m. on the morning of the day CHF was performed. Data are expressed as median and interquartile range, and statistical analysis was performed by the Pearson's chi-square test for gender, and also for sepsis, and by the Mann-Whitney U test for the other data

APACHE II score acute physiology and chronic health evaluation II score, DIC score disseminated intravascular coagulation score, CRP c-reactive protein, PCT procalcitonin, PT prothrombin time, APTT activated partial thromboplastin time, FDP fibrin degradation product, TAT thrombin-antithrombin complex

hemofilter and NM 10 mg/h after hemofilter) and 77.3% (17/22) for the Prismaflex-horizontal inflow group (NM 30 mg/h before hemofilter only), concluding no significant difference between the two groups ($p = 0.73$) (Table 2). The number of procedures for which the

target was not met was six in the ACH-Σ group and five in the Prismaflex group.

As for the coagulation sites, the following observations were made. In the ACH-Σ-vertical inflow group (six coagulations), one hemofilter coagulation and five venous

Table 2 The target achievement rates and coagulation sites in the CKRT circuit

	ACH-Σ group (22 procedures)	Prismaflex group (22 procedures)	<i>p</i> value
Achievement procedures (%)/unachieved procedures (%)	16 (72.7%)/6 (27.3%)	17 (77.3%)/5 (22.7%)	0.73
Venous air trap chamber coagulation	5	1	<0.01
Arterial circuit coagulation	0	1	0.19
Hemofilter coagulation	1	3	0.14
Vascular access catheter coagulation	0	0	

The percentage of CHF procedures that were fully uninterrupted for 22 h, defined as “the target achievement rates,” were 72.7% (16/22) for the ACH-Σ group (dispensing method: NM 20 mg/h before hemofilter and NM 10 mg/h after hemofilter) and 77.3% (17/22) for the Prismaflex group (NM 30 mg/h before hemofilter only), concluding no significant difference between the two groups ($p=0.73$)

The number of procedures for which the target was not met was six in the ACH-Σ group and five in the Prismaflex group

In the ACH-Σ group (6 coagulations), one hemofilter coagulation and five venous air trap chamber coagulations were observed, and in the Prismaflex group (five coagulations), one arterial circuit coagulation, three hemofilter coagulations, and one venous air trap chamber coagulation were observed. Venous air trap chamber coagulation occurred significantly less frequently in the Prismaflex group (5/6 in the ACH-Σ versus 1/5 in the Prismaflex group; $p < 0.01$). Statistical analysis was performed by Pearson's chi-square test

air trap chamber coagulations were observed. In the Prismaflex-horizontal inflow group (five coagulations), one arterial circuit coagulation, three hemofilter coagulations, and one venous air trap chamber coagulation were observed. This concluded that venous air trap chamber coagulation occurred significantly less frequently in the Prismaflex group ($p < 0.01$; Table 2).

Unachieved procedures were selected and backgrounds of patient were compared between the ACH-Σ and Prismaflex groups; blood platelets and fibrinogen were significantly higher in the Prismaflex group, but no factors contributing to circuit coagulation were found (Table 3).

Filters in the target unachieved group could not let blood through due to blood circuit coagulation and hemofilter coagulation, and therefore, it was difficult to determine coagulation sites at a more detailed level.

In vitro evaluation

Experiment 1: investigation of the dye disappearance time in a venous air trap chamber

In the in vitro circuits, the dye disappearance time in the venous air trap chamber was significantly shorter when using the Prismaflex-horizontal inflow group

Table 3 Background patients of unachieved procedures

	ACH-Σ group (3 patients/6 procedures)	Prismaflex group (4 patients/5 procedures)	<i>p</i> value
Age	60 (39, 77)	63 (30, 74.5)	0.70
Male/female	2/1	3/1	0.88
Sepsis% (patients)	33% (1)	40% (2)	0.39
APACHE II score	23 (10, 23.5)	19 (10, 25.5)	0.85
DIC score	4 (2.5, 6.3)	3 (1, 3.5)	0.16
White blood cell (10^3 /ul)	8.8 (5.5, 19.1)	15 (14.2, 20.7)	0.17
CRP (mg/dl)	10.7 (5.9, 19.0)	4.9 (1.2, 16.7)	0.52
PCT (ng/ml)	1.3 (1.0, 4.0)	0.52 (0.3, 8.8)	0.41
blood platelet (10^4 /ul)	5.6 (3.6, 12.4)	21.8 (11.8, 32.4)	0.03
PT (s)	13.9 (12.7, 14.5)	13.2 (12.7, 16.4)	1.0
APTT (s)	41.3 (37.8, 60.6)	39 (31.1, 51)	0.41
Fibrinogen (mg/dl)	277 (209, 299)	431 (325, 566)	0.04
FDP (ug/ml)	20.9 (11.6, 44.5)	14.7 (9.3, 25.9)	0.41
D-dimer (ug/ml)	18.4 (7.9, 23.6)	14 (7.1, 25.3)	0.93
TAT (ng/ml)	14.8 (3.7, 34.0)	10.2 (7.7, 156)	0.41

Presented data are based on electronic records and include the test results of blood samples drawn at 6:00 a.m. on the morning of the day CHF was performed. Data are expressed as median and interquartile range, and statistical analysis was performed by the Pearson's chi-square test for gender and also for sepsis, and by the Mann-Whitney *U* test for the other data

APACHE II score acute physiology and chronic health evaluation II score, DIC score disseminated intravascular coagulation score, CRP c-reactive protein, PCT procalcitonin, PT prothrombin time, APTT activated partial thromboplastin time, FDP fibrin degradation product, TAT thrombin-antithrombin complex

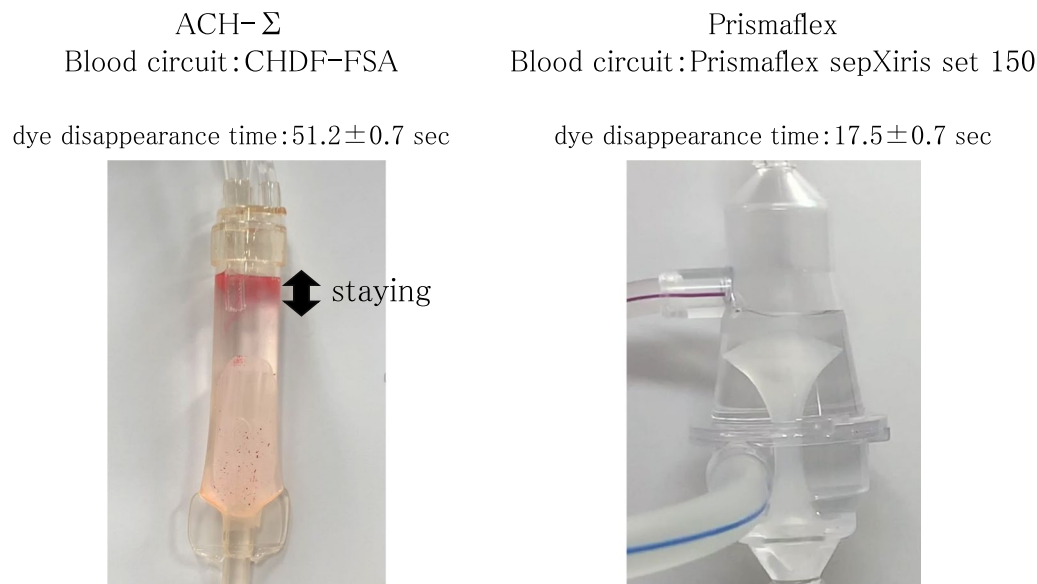


Fig. 3 Experiment 1: investigation of the dye disappearance time in a venous air trap chamber. The dye disappearance time in the venous air trap chamber was significantly shorter when using Prismaflex (17.5 ± 0.7) than when using ACH- Σ (51.2 ± 0.7 ; $p < 0.05$). In the Prismaflex group, fluid throughout the entire chamber was mixed and no retention was observed, but in the ACH- Σ group, retention in the absence of fluid flow was observed in the upper layer of the accumulated liquid

(17.5 ± 0.7 ; $n = 3$) than the ACH- Σ -vertical inflow group (51.2 ± 0.7 ; $n = 3$) ($p < 0.05$) (Fig. 3).

Experiment 2: visual evaluation of fluid flow in a venous air trap chamber

Visual evaluation of the fluid flow in the venous air trap chamber revealed that in the ACH- Σ -vertical inflow circuit the fluid flowed vertically from the top of the chamber to the lower part and displayed a nonuniform motion, pulsately “rolling” upward from the bottom of the chamber. Notably, in the upper layer of the accumulated fluid no fluidity was observed except for the thin top-to-bottom flow from the incoming fluid, and stagnation occurred (Fig 4).

When using the Prismaflex-horizontal inflow circuit, fluid was observed to flow into the lower side of the chamber and form a swirling flow. Fluid flowed uniformly throughout the venous air trap chamber, and no stagnation was observed (Fig 4).

Discussion

Although there have been scattered reports on blood circuit coagulation occurring during CKRT (e.g., [13]), the present study is, to the best of our knowledge, the first to evaluate this from both clinical and in vitro perspectives. In this study, we evaluated the occurrence of circuit coagulation during AN69ST-CHF, comparing between using ACH- Σ or Prismaflex.

Since our institution performs CHF using cytokine-adsorbing hemofilter (CAH) [16] with cytokine

adsorption capacity for the purpose of controlling mediators from the early stage of sepsis, AN69ST was selected as the hemofilter [17, 18].

Clinical evaluation showed no significant difference between the use of ACH- Σ versus Prismaflex in the rate of target achievement during AN69ST-CHF, but an examination of the site of coagulation during target nonachievement showed that venous air trap chamber coagulation occurred significantly less frequently in the Prismaflex group.

In this study, the route of administration of the anti-coagulant NM differed between the ACH- Σ and Prismaflex groups. AN69ST is a copolymer of acrylonitrile and sodium metharylsulfonate and is thought to adsorb cytokines through ionic bonding of the sulfonate group (negative charge) of sodium metharylsulfonate with the amino groups (positive charge) of cytokines [19]. The reason why there were more cases of filter coagulation in the Prismaflex group is not clear. NM has been reported to adsorb strongly to the AN69ST hemofilter due to its positive charge [20]. As a countermeasure, at our institution, when AN69ST-CHF is performed using ACH- Σ , NM is administered by a dispensing method, in which NM is administered before and after the hemofilter. In contrast, Prismaflex has only one route to administer anticoagulant, namely before the hemofilter [21], so that is how we administered NM in those cases. Although the route of NM administration was different between ACH- Σ and Prismaflex groups, the total NM dosing was the same at

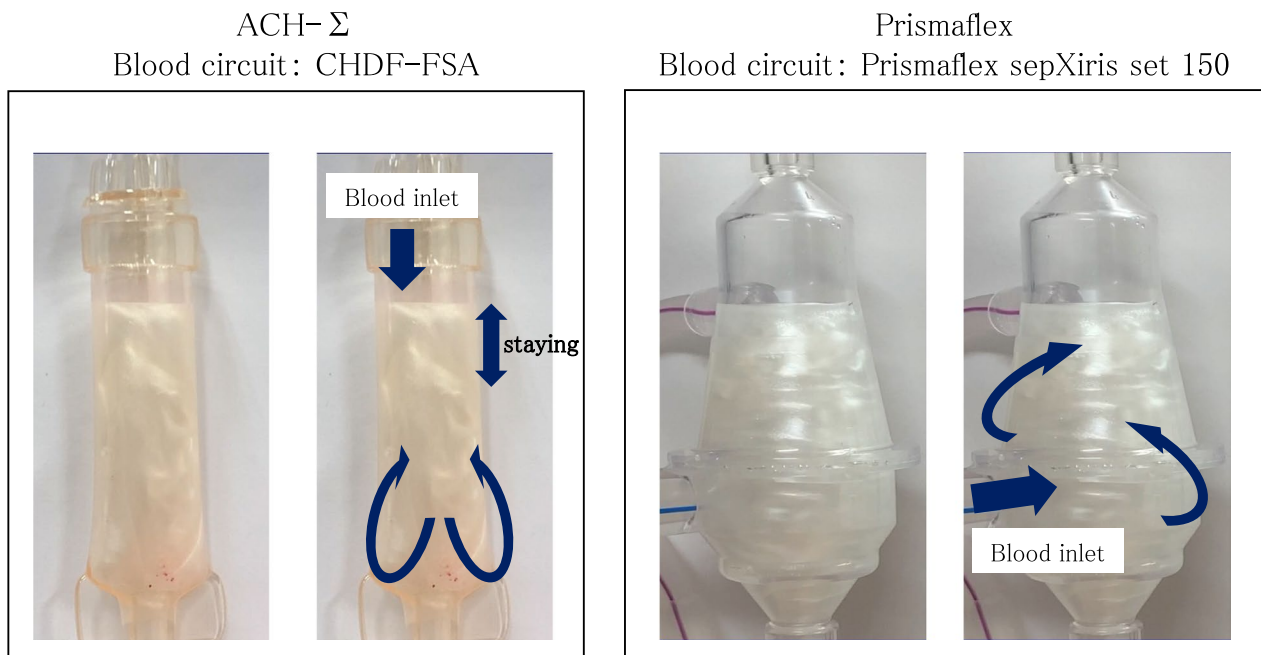


Fig. 4 Experiment 2: visual evaluation of fluid in a venous air trap chamber. In ACH- Σ , we observed a nonuniform motion of fluid winding pulsatilely upward from the bottom of the chamber. In addition, there was no fluidity in the upper layer of the liquid surface, and stagnation occurred. In Prismaflex, the fluid was observed to flow uniformly in a swirling movement through the chamber

30 mg/h. The ACH- Σ group showed a significantly higher incidence of venous air trap chamber coagulation, despite the 10 mg/h of NM administered after hemofilter. Since there are significant differences between the ACH- Σ and Prismaflex venous air trap chamber structures used in this study, we suspect that the difference in chamber structure may contribute to the occurrence of venous air trap chamber coagulation. In agreement with this idea, our in vitro experiments showed that differences in chamber structure affect the flow of fluid in the venous air trap chamber.

In the in vitro studies, using experimental circuits, the use of Prismaflex-horizontal inflow resulted in a much faster disappearance of added dye than when using ACH- Σ -vertical inflow. Furthermore, when using Prismaflex-horizontal inflow, the dye flowed without stagnation throughout the entire vein air trap chamber, whereas in ACH- Σ -vertical inflow a dye flow was only observed at the bottom of the chamber and there was no dye flow in the, seemingly stagnant, upper layer of the accumulated liquid. While venous air trap chambers play a role in removing clots and bubbles [15], thrombus formation in venous air trap chambers can also occur [22]. Various factors have been postulated to cause the coagulation in the venous air trap chamber, one of which is the retention of blood. This is because blood retention in the venous air trap chamber increases the extracorporeal circulation

time and the likelihood of blood coagulation in the chamber.

In ACH- Σ -vertical inflow, the fluid flows vertically from the inlet pipe at the top of the chamber to the bottom, and shows a nonuniform motion at the bottom of the chamber, including an upward pulsatile rolling. The pulsatile motion is attributed to the effect of the pulsatile flow caused by the roller pump. The fluid is subjected to a vertical force toward the bottom of the chamber, creating a flow that winds upward from the bottom of the chamber but disappears before reaching the upper layer of the accumulated liquid, probably explaining the stagnation of that upper layer.

In contrast, when using Prismaflex-horizontal inflow, the fluid flowed uniformly throughout the venous air trap chamber without stagnation as a swirling flow, and the dye disappeared quickly. In the venous air trap chamber of Prismaflex-horizontal inflow, the fluid flows along the sides of the chamber because that is where the blood inlet pipes are connected to and deliver their flow (Fig. 4). As a result, we found that, in the Prismaflex venous air trap chamber, the fluid flowed in a swirling motion and agitated the entire chamber.

The ACH- Σ and Prismaflex venous air trap chambers used in this study differ not only in the inflow method but also in the presence or absence of filters. The ACH- Σ venous air trap chamber has a built-in filter,

whereas the Prismaflex venous air trap chamber is filterless. It is possible that the presence or absence of a filter affected the fluid flow in the venous air trap chamber. The volume of the venous air trap chamber in Prismaflex is 10 ml, while the volume of the venous air trap chamber in ACH- Σ is 18 ml. The difference in chamber volume may have affected the dye disappearance time.

We believe that our combination of clinical and in vitro evaluation of the occurrence of circuit coagulation during AN69ST-CHF using ACH- Σ or Prismaflex has confirmed the hypothesis that “differences in construction, such as chamber shape and volume, contribute to the occurrence of venous air trap chamber coagulation.”

There are several limitations to this study. First of all, in the clinical treatments using ACH- Σ versus Prismaflex, NM dosing was different before and after hemofilter. Since we did not measure activated coagulation time (ACT) before and after hemofilter in this study, we were not able to evaluate the effect of the difference in NM dosage before and after hemofilter on anticoagulation in the respective CKRT circuits; therefore, we believe that a future study should address the possible effects of differences in NM administration.

Second, because the coagulation site could not be identified visually for the target unachieved circuits, a clinical engineer identified the coagulation site based on a comprehensive analysis of the logs of each CKRT machine. Because the coagulation site was deduced from the pressure pattern in the circuit, it is possible that the coagulation site was not precisely identified. In the future, we will need to wash the circuits that did not achieve the target with saline solution, etc. and examine the coagulation site more closely.

Third, the ACH- Σ and Prismaflex venous air trap chambers used in this study differed not only in chamber shape and inflow methods but also in the presence versus absence of filters. Therefore, it was not possible to conclude which of the individual factors contributed to venous air trap chamber coagulation. In the future, it will be necessary to investigate the contribution of isolated factors to venous air trap chamber coagulation, for example, by using the same chamber geometry and focusing on the inflow method or the presence versus absence of a filter.

Fourth, the in vitro evaluation was conducted in the presence of three clinical engineers, but the fluid flows in the venous air trap chamber were not quantitatively evaluated. Since our hospital does not have a system to quantitatively evaluate fluid flows, we conducted the in vitro evaluation from a human observation perspective. In the future, it will be necessary to construct a system to quantitatively evaluate fluid flows in venous air trap chambers

and to study the effects of different chamber structures on fluid flows in more detail.

Conclusions

We evaluated whether differences in chamber construction contribute to the occurrence of venous air trap chamber coagulation by clinical and in vitro evaluation. Prismaflex has a structure that minimizes the occurrence of venous air trap chamber coagulation, and the fluid flows without stagnation throughout the venous air trap chamber as a swirling flow. Our data suggest that construction differences, such as the shape and volume of the venous air trap chamber, contribute to the coagulation of the venous air trap chamber.

Abbreviations

CKRT	Continuous kidney replacement therapy
ICU	Intensive care unit
AKI	Acute kidney injury
CHF	Continuous hemofiltration
QB	Blood flow rate
QF	Filtration flow rate
NM	Nafamostat mesylate
AN69ST	Acrylonitrile-co-methallyl sulfonate surface-treated
AN69ST-CHF	CHF with AN69ST
APACHE II score	Acute physiology and chronic health evaluation II score
DIC score	Disseminated intravascular coagulation score
CRP	C-reactive protein
PCT	Procalcitonin
PT	Prothrombin time
APTT	Activated partial thromboplastin time
FDP	Fibrin degradation product
PIC	Plasmin- α 2 plasmin inhibitor complex
TAT	Thrombin-antithrombin complex

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Author contributions

K.S. wrote the manuscript and analyzed the data. K.M. designed the study and revised the manuscript. N.K., T.N., T.K., and S.K. contributed to data collection. K.M., N.K., and O.N. discussed the results and contributed to the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data used in this article are available from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Fujita Health University. The need for informed consent was waived for this study because it was a retrospective observational study. Trial registration: HM23-289. Registered 5 December 2023-Retrospectively registered, https://fujita.bvits.com/esct/publicsh_document.aspx?ID=8350.

Consent for publication

Since this is a retrospective observational study and noninvasive to the patients, we believe that the informed consent procedure can be omitted. Notification of the study to patients is posted on the website of the

Department of Anesthesiology and Critical Care Medicine, Fujita Health University School of Medicine, as an opt out.

Competing interests

Kazuhiro Moriyama has consulting contracts with Baxter Limited and Asahi Kasei Medical Co., Ltd.. The other authors declare that they have no competing interest.

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References

- Abe M, Shiga H, Tatsumi H, et al. Results of the 2018 Japan Society for Blood Purification in Critical Care survey: current status and outcomes. *Ren Replace Ther*. 2022;8:58.
- Miyamoto Y, Iwagami M, Aso S, et al. Temporal change in characteristics and outcomes of acute kidney injury on renal replacement therapy in intensive care units: analysis of a nationwide administrative database in Japan, 2007–2016. *Crit Care*. 2019;23:1–11.
- Shin J, Song HC, Hwang JH, et al. Impact of downtime on clinical outcomes in critically ill patients with acute kidney injury receiving continuous renal replacement therapy. *ASAIO J*. 2021;68:744–52.
- Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R. Continuous is not continuous: the incidence and impact of circuit “down-time” on uraemic control during continuous veno-venous haemofiltration. *Intensive Care Med*. 2003;29:575–8.
- Cutts MW, Thomas AN, Kishen R. Transfusion requirements during continuous veno-venous haemofiltration: the importance of filter life. *Intensive Care Med*. 2000;26:1694–7.
- Zarbock A, Küllmar M, Kindgen-Milles D, et al. Effect of regional citrate anticoagulation vs systemic heparin anticoagulation during continuous kidney replacement therapy on dialysis filter life span and mortality among critically ill patients with acute kidney injury: a randomized clinical trial. *JAMA*. 2020;27(324):1629–39.
- Zhou Z, Liu C, Yang Y, et al. Anticoagulation options for continuous renal replacement therapy in critically ill patients: a systematic review and network meta-analysis of randomized controlled trials. *Crit Care*. 2023;27:222.
- Schetz M, Van Cromphaut S, Dubois J, Van den Berghe G. Does the surface-treated AN69 membrane prolong filter survival in CRRT without anticoagulation? *Intensive Care Med*. 2012;38:1818–25.
- Wong ET, Ong V, Remani D, et al. Filter life and safety of heparin-grafted membrane for continuous renal replacement therapy—a randomized controlled trial. *Semin Dial*. 2021;34:300–8.
- Parietti JJ, Megarbane B, Fischer MO, et al. Catheter dysfunction and dialysis performance according to vascular access among 736 critically ill adults requiring renal replacement therapy: a randomized controlled study. *Crit Care Med*. 2010;38:1118–25.
- Karkar A, Ronco C. Prescription of CRRT: a pathway to optimize therapy. *Ann Intensive Care*. 2020;10:32.
- Shimizu K, Kuriyama N, Moriyama K, et al. Evaluation of circuit coagulation during AN69ST-CHF using ACH-Σ and Prismaflex. *J Jpn Soc Blood Purif Crit Care*. 2022;13:121–5. https://doi.org/10.34325/jsbpcc.13.2_121.
- Baldwin I. Factors affecting circuit patency and filter “life.” *Contrib Nephrol*. 2007;156:178–84.
- Baldwin I, Fealy N, Carty P, et al. Bubble chamber clotting during continuous renal replacement therapy: vertical versus horizontal blood flow entry. *Blood Purif*. 2012;34:213–8.
- Jonsson P, Stegmayr C, Stegmayr B, et al. Venous chambers in clinical use for hemodialysis have limited capacity to eliminate microbubbles from entering the return bloodline: an in vitro study. *Artif Organs*. 2023;47:961–70.
- Hirasawa H, Oda S, Nakamura M, et al. Continuous hemodiafiltration with a cytokine-adsorbing hemofilter for sepsis. *Blood Purif*. 2012;34:164–70.
- Shiga H, Hirasawa H, Nishida O, et al. Continuous hemodiafiltration with a cytokine-adsorbing hemofilter in patients with septic shock: a preliminary report. *Blood Purif*. 2014;38:211–8.
- Moriyama K, Nishida O. Targeting cytokines, pathogen-associated molecular patterns and damage associated molecular patterns in sepsis via blood purification. *Int J Mol Sci*. 2021;22:8882.
- Moriyama K, Kato Y, Hasegawa D, et al. Involvement of ionic interactions in cytokine adsorption of polyethyleneimine-coated polyacrylonitrile and polymethyl methacrylate membranes in vitro. *J Artif Organs*. 2020;23:240–6.
- Nakamura Y, Hara S, Hatamoto H, et al. Adsorption of nafamostat mesilate on AN69ST membranes: a single-center retrospective and in vitro study. *Ther Apher Dial*. 2017;21:620–7.
- Salvatori G, Ricci Z, Bonello M, et al. First clinical trial for a new CRRT machine: the Prismaflex. *Int J Artif Organs*. 2004;27:404–9.
- Baldwin I, Tan HK, Bridge N, et al. Possible strategies to prolong circuit life during hemofiltration: three controlled studies. *Ren Fail*. 2002;24:839–48.

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