Toin University of Yokohama
Research Bulletin, No.46, June 2022

Articles

Experimental study on blood coagulation inhibitory effect of venous air-trap chamber of hemodialysis circuit

Ishigaki Hideki*, Makita Hiroki[1], Shimazaki Naoya[2], Oku Tomoko[3], Motohashi Yuka[3], Yamauchi Shinobu[4] and Sato Toshio[4]

(Received Date: March 10, 2022)

I. Introduction

Clots of coagulated blood are formed in the venous air-trap chamber of the hemodialysis circuit when blood comes into contact with air or blood flow stagnates within the chamber. These clots of coagulated blood are trapped by a trapping filter placed at the bottom of the chamber to prevent them from flowing into the body of the hemodialysis patient. However, as the amount of trapped coagulated blood increases, more blood flow tends to stagnate within the chamber, which promotes coagulation. All the blood within the chamber eventually coagulates, after which all the blood in the hemodialysis circuit also coagulates, preventing further hemodialysis. Efforts to prevent the occurrence of intracircuit coagulation in recent years have included decreasing contact with air within the chamber and reducing the amount of blood used for initial filling of the hemodialysis circuit (priming volume), with different hemodialysis circuit companies developing and marketing individual solutions to this issue. However, a multi-institution questionnaire survey asking about intracircuit coagulation found that 94% of institutions had experienced excessive intracircuit coagulation despite implementation of various preventive measures. This problem thus remains unresolved. According to a report on the standardization of hemodialysis circuit published by the Japan Association for Clinical Engineering Technologists, the standard specifications for the chamber are length 110–150 mm and internal diameter 16–20 mm, and the design should prevent retrograde blood flow to the pressure monitor line when pressure changes. However, that report did not discuss the effect on the blood coagulation system of the design parameters of the chambers used in different institutions. Resolution of this issue will require clarification of the effects on the blood coagulation system of the chamber design parameters shown in ***Figure 1***, comprising the chamber length (L), blood inflow angle (θ), and trapping filter shape.

The first step toward this is to create a faithful reproduction in the laboratory of the intracircuit coagulation that occurs in clinical settings. Bovine

* Ishigaki Hideki: Graduate student of Engineering, Department of Biomedical Engineering, Toin University of Yokohama, 1614, Kurogane-cho, Aoba-ku, Yokohama 225-8503, Japan
[1] Makita Hiroki: Graduate School of Engineering, Toin University of Yokohama
[2] Shimazaki Naoya: Lecturer, Faculty of Medical Technology, Gunma Paz University, 1-7-1 Tonyamachi, Takasaki-shi, Gunma 370-0006, Japan
[3] Oku Tomoko and Motohashi Yuka: Lecturer, Faculty of Biomedical Engineering, Toin University of Yokohama
[4] Yamauchi Shinobu: Associate Professor, Graduate School of Engineering, Faculty of Biomedical Engineering, Toin University of Yokohama
[4] Sato Toshio: Professor, Faculty of Biomedical Engineering, Toin University of Yokohama

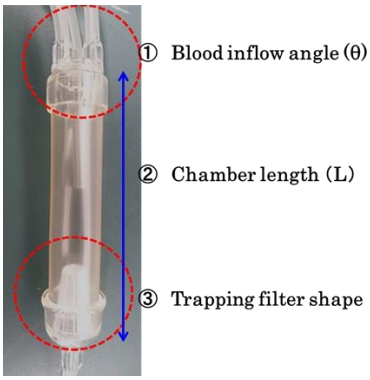

Fig.1 Design parameters affecting blood coagulation in venous air-trap chamber

blood mixed with calcium chloride is generally used for intracircuit clotting simulations, but individual differences in bovine blood mean that the time taken for blood to finish clotting frequently varies even in experiments conducted under identical conditions, making the anticoagulation performance of chambers difficult to evaluate with a high degree of reproducibility. The present study first investigated a highly reproducible method of simulating intracircuit clotting using bovine blood. We then used this simulation method to investigate the effect of differences in chamber length (L) on blood clotting within the chamber. We also attempted to ascertain differences in flows within the chamber due to different chamber lengths using particle image velocimetry (PIV) to visualize flows inside the chamber. We further used a three-dimensional (3D) printer to produce prototypes of chambers with different blood inflow angles (θ) at the top to investigate the effects of differences in blood inflow angle (θ) on blood clotting within the chamber.

II. Experimental Methods

1. Blood coagulation simulation methods using bovine blood

We filled a hemodialysis circuit (NK-Y030PV, Nikkiso Co., Ltd.) with bovine blood, and formed a closed circuit using a connector to join the tips of the blood removal and blood return circuits. The bovine blood was then circulated by roller pump at a set flow rate of 200 ml/min, and a solution of 0.2 g of calcium chloride dissolved in 10 ml of physiological saline was injected into the chamber via the level-adjustment line to serve as a coagulation-promoting agent. At the same time, changes over time in intracircuit pressure were measured using a digital manometer (EM-160W, Hodaka Co., Ltd.). Because the bovine blood was being circulated in a closed circuit, the injection of 10 ml of solution into the circuit would increase the intracircuit pressure. To prevent this, 10 ml of circulating bovine blood was aspirated from a venous access port at the same time as the 10 ml of solution was injected, returning the elevated intracircuit pressure to its original level. This experiment was repeated three times under the same conditions, and the coagulation completion time (T_{COAG}) was measured. In this study, T_{COAG} was defined as the time between injection of the coagulation-promoting agent and the time at which intracircuit pressure exceeded 200 mmHg. The closed circuit ran through a constant-temperature water bath with the water temperature maintained at 37°C to keep the temperature of the bovine blood in the circuit at 37°C.

2. Production of prototype chambers of different chamber length (L) and blood inflow angle (θ), and measurement of coagulation time (T_{COAG})

The venous air trap chamber [L = 14 cm, θ = 0° (side inflow), mesh-type trapping filter] of a commercially available hemodialysis circuit (NK-Y030PV, Nikkiso Co., Ltd.) was taken as the standard chamber. A prototype chamber with L = 10 cm was produced from this by cutting out a 4-cm-long cylindrical portion and reattaching the cut surfaces. Another prototype chamber with L = 18 cm was produced by cutting a standard chamber

into two, inserting the 4-cm-long cylindrical portion, and reattaching the cut ends. ***Figure 2*** shows the three prototype chambers of different lengths. In preliminary experiments prior to the circulation of bovine blood, water was circulated and the tube downstream from the chamber was clamped shut to confirm that no leakage occurred even when pressure within the chamber increased. T_{COAG} was then measured for the three chambers of different lengths following the method described in Section 2-1 above.

Next, to investigate the effect on blood coagulation of the inflow of blood at different angles into the top of the chamber, we prepared five different types of chambers with different values of $\theta = 0°$ (commercial product, side inflow), 30°, 45°, 60°, and 90° (commercial product, vertical inflow). The upper parts of the chambers with $\theta = 30°$, 45°, and 60° were designed using computer-aided design (CAD) software (Fusion360, Autodesk Co., Ltd.). Chambers were made from heat-resistant acrylic resin using a 3D printer (M3DS-200, MITS Electronics Co., Ltd.), after which the top parts of 14-cm-long commercially available chambers with cone-shaped trapping filters were cut off and replaced with the specially formed upper parts. ***Figure 3*** shows the series of tasks from CAD data preparation to attachment of the upper parts of the chambers. T_{COAG} was then measured by the same method described above.

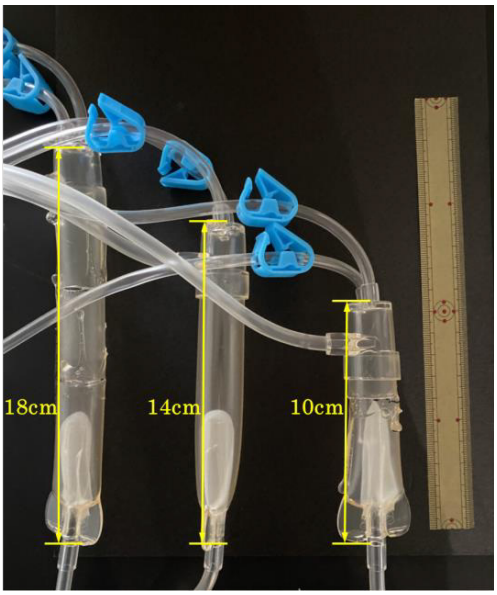

Fig.2 Three prototype chambers of different lengths

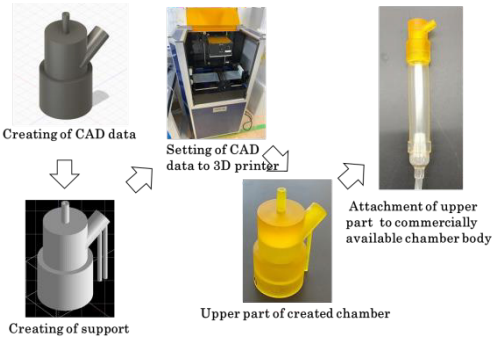

Fig.3 Series of tasks from CAD data preparation to attachment of the upper parts of the chambers

3. Visualization of flow inside chamber by PIV

After the chambers that we produced had been fixed in the water-filled water bath, water containing tracer particles (ferrite) was circulated using a roller pump at the set flow rate of 200 mL/min (***Figure 4***). Chambers were then illuminated from the side with a laser sheet, and the behavior of tracer particles was photographed with a high-speed camera. The images thus obtained were used to generate flow line maps using dedicated flow analysis software (FlowExpert2D, Katoken Co., Ltd.) in an attempt to visualize flows within the chambers.

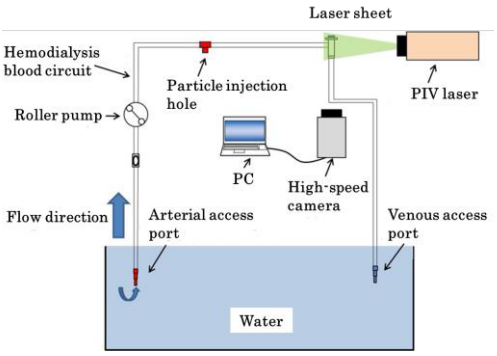

Fig.4 Visualization of flows within the chambers by PIV

III. Experimental Results

1. Results of blood coagulation simulation using bovine blood

Figure 5 shows the results of intracircuit pressure measurements from the injection of the coagulation-promoting agent until coagulation was complete. In all three experiments, intracircuit pressure began to increase rapidly after approximately 900 s and Tcoag was approximately 970 s, confirming their high reproducibility. This indicated that using the blood coagulation simulation method described in this paper may enable the anticoagulation performance of different chambers to be compared and evaluated without the effect of individual differences in bovine blood.

2. Experimental results from chambers of different lengths

Figure 6 shows the results of Tcoag measurements using chambers of length 10 cm, 14 cm, and 18 cm (θ = 0°, mesh-type trapping filter). For L = 18 cm, Tcoag was approximately 840 s; for L = 14 cm, Tcoag was approximately 970 s; and for L = 10 cm, Tcoag was approximately 1080 s, indicating that shorter length was associated with longer coagulation time.

Figure 7 shows the results of PIV visualization of flows within the chambers of different lengths. For L = 10 cm, rapid inflow from the inlet formed a rotational flow along the chamber inner wall, while flowing toward the trapping filter downstream. For L = 14 cm and L = 18 cm, vortices and flow stagnation occurred near the area upstream from the center of the chamber.

3. Flow visualization results from chambers with different values of θ

Figure 8 shows the results of PIV visualization of the flows within the chambers with different values of θ. For θ = 0°, the flow stagnated in the upper part of the chamber, and vortices were generated near the center. For θ = 30°, a rotational flow was generated throughout the chamber. For θ = 45°, multiple vortices were generated near the

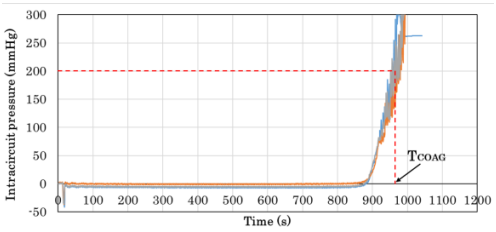

Fig.5 Measurement results of coagulation completion time Tcoag

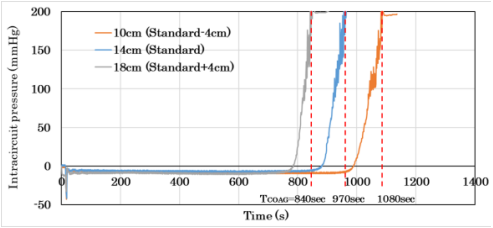

Fig.6 Measurement results of Tcoag for different chamber lengths

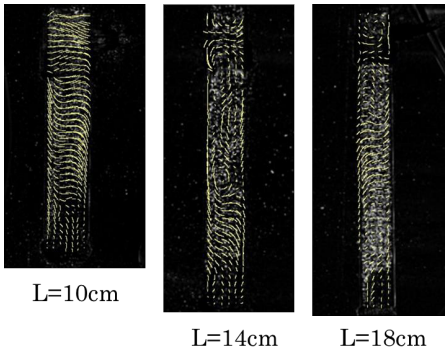

Fig.7 Flow visualization results by PIV for different chamber lengths

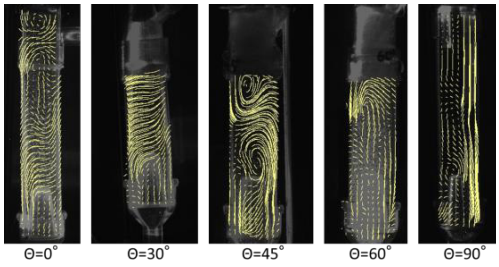

Fig.8 Flow visualization results by PIV for different blood inflow angles

inlet. For θ = 60°, the flow stagnated near the center. For θ = 90°, a flow heading straight from the inlet toward the trapping filter along the chamber wall was observed, but stagnation of the flow near the chamber wall on the opposite site to this flow and above the trapping filter was also evident.

IV. Discussion

To quantitatively evaluate the effects of the chamber design parameters of chamber length (L), blood inflow angle (θ), and trapping filter shape on chamber anticoagulation performance, the establishment of a highly-reproducible method for simulating blood coagulation using bovine blood is essential. In our previous experimental method, we had kept bovine blood in beakers, into which the blood removal and blood return tips were placed to circulate the bovine blood within the circuit. However, with that method the bovine blood also came into contact with air while in the beakers, and blood flow was also stagnant within the beakers, resulting in the formation of coagulum in the beakers. This may have been one reason for the different T_{COAG} values obtained from experiments conducted under the same conditions. The method used in the present study was improved by circulating bovine blood within a closed circuit, thereby reproducing the clinical situation in which the blood circulating within the circuit only comes into contact with air in the top of the chamber. As a result, when the experimental conditions were the same, values of T_{COAG} were consistent with high reproducibility, indicating that this method can be used for quantitative comparisons and evaluations of the effect on anticoagulant performance by measuring the T_{COAG} of chambers with varying values of different design parameters.

The results of T_{COAG} measurements in chambers of different lengths showed that a shorter chamber extends the time until coagulation, meaning that coagulation was less likely to occur. As can also be seen from the results of PIV flow visualization (Figure 7), when L = 10 cm, the bovine blood flowed smoothly through the entire chamber in a rotational flow from the inlet to the trapping filter, without the generation of vortices or flow stagnation. When L = 14 cm or 18 cm, however, vortices were generated or the flow stagnated within the chamber, resulting in the formation of clots of coagulated blood, and trapping of these by the filter promoted further blood coagulation.

The results of flow visualization in chambers with varying values of θ showed that when θ = 30°, a rotational flow through the entire chamber was generated, and no vortices or flow stagnation was observed, suggesting that this value may give the best anticoagulant performance. There are currently only two designs of commercially available chambers, with θ = 0° (horizontal inflow) or θ = 90° (vertical inflow), with most having θ = 0°. Given that intracircuit coagulation is reported from clinical settings using chambers with θ = 0°, improved chambers with θ = 30° might greatly reduce the risk of intracircuit coagulation.

V. Conclusion

Based on the blood coagulation simulation method using the closed circuit proposed in this paper, we conducted a quantitative evaluation of the effects of various chamber design parameters on anticoagulant performance. We found that a chamber with a length (L) of 10 cm and a blood inflow angle (θ) of 30° may provide the best anticoagulant performance. As a topic for further research, we intend to measure the T_{COAG} of bovine blood using a chamber with θ = 30°, and to verify the results by PIV flow visualization. We also intend to conduct further investigations into the effects of differences in trapping filter shape on anticoagulant performance, produce an actual

prototype of a chamber with the combination of length, inflow angle, and trapping filter shape that provides optimum anticoagulant performance, and compare this with commercially available chambers to ascertain the ideal chamber shape.

[Notes]

1) Gotow A, Fukunaga S: Effects of hemodialytic maerials on the blood coagulation, Material and coagulation 2012; 10(2): 80–85.
2) Tsukamoto I, Murasugi H, Tsuchiya Y, Yamashita Y, Takane H and Suzuki H: Evaluation of extracorporeal circuit systems in premature clotting in continuous renal replacement therapy, J Jpn Soc Blood Purif Crit Care 2012; 3(1): 8–13.
3) Donald FB, Daniel EC, Bassem MM, Jingmei S, Erika JM, Jessica LB and Todd WB: Differences in coagulation between hemodialysis and peritoneal dialysis, Perit Dial Int 2014; 34(1): 33–40.
4) Karlien F, Christelle O, Kristin J, Wilfried C, Vicky DM, Christian T and Karl MW: Hemodialysis does not induce detectable activation of the contact system of coagulation, Kidney Int 2020; 5(6): 831–838.
5) Marianne S: Activation of platelets and coagulation during haemodialysis, Ned Tijdschr Klin Chem Labgeneesk 2016; 41: 17–27.
6) Krzysztof D, Radoslaw D, Anastassis S and Andreas G: Continuous monitoring of blood clotting during hemodialysis, and cardiopulmonary bypass, Forum Nefrologiczne 2014, 7(4): 269–273.