Yasuda et al. Renal Replacement Therapy (2018) 4:6
DOI 10.1186/s41100-018-0148-9

Renal Replacement Therapy

RESEARCH Open Access

Comparison of two polysulfone membranes for continuous renal replacement therapy for sepsis: a prospective cross-over study

Hideto Yasuda[1,2,3*], Kosuke Sekine[4], Takayuki Abe[3,5], Shinichiro Suzaki[2], Atsushi Katsumi[2], Naoshige Harada[2], Hidenori Higashi[2], Yuki Kishihara[2], Hidetaka Suzuki[2] and Toru Takebayashi[3]

Abstract

Background: In Japan, the most commonly used hemofilters for patients with acute kidney injury (AKI) treated with continuous renal replacement therapy (CRRT) are made of polysulfone membranes. The aim of this study was to compare the efficacy of two commercially available polysulfone membranes for the removal of solutes.

Methods: This single-institution, prospective cross-over study was conducted between December 2010 and January 2012. Two polysulfone membranes, Hemofeel SHG (Toray) and Excelflo AEF (Asahi Kasei Medical), were compared in eight intensive care unit patients (median age, 80 years; seven men) who had severe sepsis that required CRRT and who required vasopressor treatment to maintain their mean blood pressure above 65 mmHg. The primary outcome measure was the efficacy of solute removal, evaluated for high-mobility group protein 1 (HMGB-1) and myoglobin.

Results: The main cause of sepsis was abdominal infection (50%); the mortality was 62.5%. Blood clearance of myoglobin in 1 h was significantly greater with SHG ($p = 0.02$), particularly at 24 h ($p = 0.17$). Blood creatinine clearance did not differ significantly between the two membranes after 1 h, but SHG demonstrated slightly greater appearance at 24 h. There were no significant differences between the two membranes in the clearance of other solutes including HMGB-1.

Conclusions: This preliminary study compared the use of two polysulfone membranes in patients with sepsis requiring CRRT and showed that the polysulfone membrane SHG was capable of removing myoglobin with greater efficacy.

Keywords: Acute kidney injury, Membranes, Myoglobin, Renal replacement therapy, Sepsis, Shock

Background

In Japan, the most commonly used hemofilters for patients with acute kidney injury (AKI) who are undergoing treatment for continuous renal replacement therapy (CRRT) are made of polysulfone membranes [1]. Sepsis is a life-threatening condition with a prevalence of 288 hospital-treated sepsis cases per 100,00 person years; in-hospital mortality has been reported as 17% for sepsis and 26% for severe sepsis [2]. The progression of AKI stage and newly developed AKI after hospital admission in patients with severe sepsis and septic shock increased 28-day mortality [3]. CRRT is used not only for hemodynamically unstable patients with AKI and chronic kidney disease (CKD), such as for correcting electrolyte and acid–base balance abnormalities or removing solutes and extra fluid, but also for patients suffering from severe sepsis and septic shock, to remove various inflammatory cytokines [4, 5]. However, CRRT is often performed under more limited treatment conditions than those for intermittent renal replacement therapy (IRRT) in critically ill patients [4, 6–8]. Unlike IRRT, there are restrictions on blood and dialysate flow rates in CRRT, and its efficiency is often influenced by the dialysis membrane used.

The solute removal efficacy during renal replacement therapy depends not only on blood flow rate, dialysate flow rate, and solute concentration, but also on the dialysis membrane used [9]. Several types of CRRT dialysis membranes have been developed over the history of hemodialysis therapy, and these differ in their ability to

* Correspondence: yasudahideto@me.com
[1]Department of Intensive Care Unit, Kameda Medical Center, 929 Higashi-chou, Kamogawa-shi, Chiba 296-8602, Japan
[2]Intensive Care Unit, Department of Emergency and Critical Care Medicine, Japanese Red Cross Musashino Hospital, Tokyo, Japan
Full list of author information is available at the end of the article

remove solutes [10–16]. This depends on the membrane's composition and morphology, such as its inner diameter, the pore size (either radius or diameter), thickness of the skin layer, and the surface porosity of membrane. These differences may affect the blood concentrations of several drugs, including antibiotics, and so clinical outcome can be influenced by both the type of dialysis and the dialysis membrane used [17, 18]. There is one study on the removal of solutes by membranes such as high flux membranes [19], but, as yet, differences in dialysis efficacy between different polysulfone membranes have not been reported. The aim of this study was to compare the efficacy of solute removal of two commercially available polysulfone membranes mostly used in Japan.

Methods

Study design and setting

This prospective cross-over study was conducted in an eight-bed intensive care unit (ICU) at a single center of the Advanced Emergency Medical Center in Japan (Japanese Red Cross Musashino Hospital, Tokyo, Japan) between December 2010 and January 2012. This study protocol was approved by the local ethics committee, and the study was conducted in accordance with the principles of the Helsinki Declaration. Informed consent was obtained from all the participants or their surrogate decisionmakers. This study is described according to the Strengthening the Reporting of Observational Studies (STROBE) guidelines.

Subjects

Patients were eligible for inclusion in this study if they were in severe sepsis or septic shock, in need of CRRT, admitted to ICU, and needing a vasopressor to maintain their mean blood pressure at over 65 mmHg (within a suitable range). The definitions of sepsis, severe sepsis, and septic shock followed those of the American College of Chest Physicians and the Society of Critical Care Medicine [20]. The criteria for the initiation of CRRT were the following: (1) uncontrolled acidosis, (2) uremia, (3) uncontrolled hyperkalemia, and (4) volume overload. Patients were excluded from this study if they were younger than 15 years, pregnant, their physician decided they should be excluded, or they did not agree to participate.

During the study period, eight patients who met these criteria were included in the study. Seven were men and the median age was 80 years (interquartile range (IQR) 76–81 years).

Operational conditions for CRRT

Two polysulfone membranes, Hemofeel SHG 1.3 m^2 (SHG; Toray, Tokyo, Japan) and Excelflo AEF 1.3 m^2 (AEF; Asahi Kasei Medical, Tokyo, Japan) were used for CRRT in this study (Table 1). To create the vascular access, ICU physicians inserted a 12-Fr flexible triple-lumen catheter (GamCath Catheter, Baxter, Japan) into the internal jugular or the femoral vein, if the patient did not have shunt for hemodialysis. The operation of the hemodiafiltration system was monitored with a personal bedside console (ACH-10 Asahi Kasei Medical, Tokyo, Japan). The CRRT mode used was continuous veno-venous hemodiafiltration as follows: blood flow, 100 mL/min; dialysate, substitution solution and filtrate flow rates, all 400 mL/h. We used nafamostat mesilate for anticoagulation, with a protocol that maintained the activated partial thromboplastin time (APTT) at 60–80 s. The decision about whether to remove water by CRRT was left to the discretion of the individual physicians.

Study protocol and data collection

The study protocol is shown in Fig. 1. In this cross-over protocol, the patients underwent CRRT with either the SHG or the AEF hemofilter for 24 h, and this was then replaced with the other type for a further 24 h. Blood and effluent samples were drawn from the inlet and outlet of the hemofilter at the start of CRRT and after 1, 24, 25, and 48 h. The following data were recorded for each time point: vital signs (Glasgow Coma Scale score, mean arterial pressure, heart rate, respiratory rate, body temperature, and urine volume), the vasopressor dose (dopamine, dobutamine, noradrenaline, adrenaline, and vasopressin), blood sample results (white and red blood cell counts, hematocrit, platelet count, sodium, potassium, bilirubin, urea, creatinine, creatine kinase, myoglobin, and HMGB-1), and arterial blood gas analysis results (fraction of inspiratory oxygen, pH, PaO_2, HCO_3, and lactate). The following data were obtained for each subject: age, sex, comorbidity, date of hospital admission, date of ICU admission, acute physiology, and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score on the day of ICU admission, and primary diagnosis at the time they were included in this study. In addition, the date of ICU discharge and the patient's outcome (discharge alive or death in hospital) were recorded.

Table 1 Comparison of SHG and AEF

	SHG	AEF
Membrane manufacturer	Toray Medical Co. Ltd., Tokyo, Japan	Asahi Kasei Medical, Tokyo, Japan
Hemofilter	Polysulfone membrane	Polysulfone membrane
Membrane surface area, m^2	1.3	1.3
Inside diameter, μm	200	225
Thickness of membrane, μm	40	45

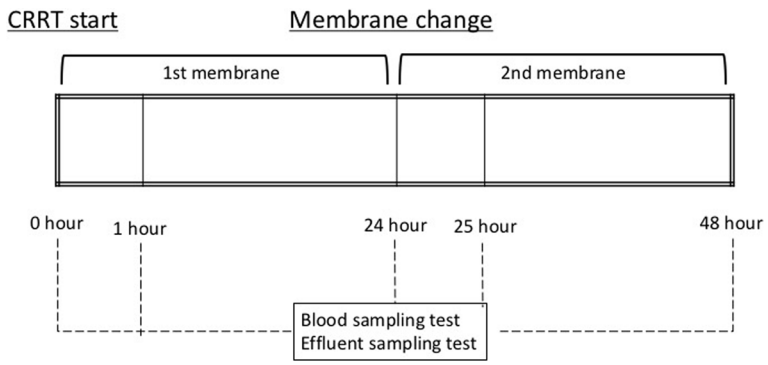

Fig. 1 Study protocol

Calculations

Blood clearance (Kb) and effluent clearance (KE) were calculated for each solute using the following formulas:

$$\mathrm{Kb} = \{(\mathrm{QBin} \times \mathrm{CBin}) - (\mathrm{QBin} - \mathrm{QF}) \times \mathrm{CBout}\}/\mathrm{CBin}$$

$$\mathrm{KE} = (\mathrm{CE}/\mathrm{CBin}) \times (\mathrm{QDin} + \mathrm{QF})$$

where QBin, QDin, and QF are the inlet blood flow rate, inlet dialysate flow rate, and filtration rate of the hemofilter, respectively, CBin and CBout are the plasma concentrations of the solute in inlet and outlet blood of the hemofilter, and CE is the concentration of the effluent dialysate of the hemofilter.

Outcome measures

The primary outcome measure was the removal efficacy for the medium-sized solute molecules myoglobin and HMGB-1 between two membrane types. The secondary outcome was its efficacy for removing small and other medium-sized solute molecules.

Statistical analysis

The data are presented as mean and standard deviation (SD) or median with interquartile range (IQR) for continuous variables and as number and percentages for categorical variables. Paired t tests and the mixed-effect model were used for comparisons between the membranes for the clearance of solutes and to investigate the possible carry-over effect of the hemofilter, using Holm's procedure. Mean differences with 95% confidence intervals were also calculated. No missing data were imputed; if any cases were lost to follow-up, they were to be excluded. The significance level for all tests was two-sided 5%. All statistical analyses except for the mixed-effect model were performed using JMP software, version 11 (SAS Inc., Cary, NC); the mixed-effect model was performed using SAS (SAS Inc., Cary, NC).

Results

The demographic characteristics of the eight patients are shown in Tables 2 and 3. In four patients (50%), the cause of sepsis was abdominal infection; five of the patients (63%) died. There was no case of loss to follow-up.

Figures 2 and 3 show the results for each of the two membranes for blood clearance and effluent clearance of each solute at 1 and 24 h after the start of CRRT using the SHG and AEF membranes. There were no significant differences in the blood clearance of blood urea, creatine kinase, and HMGB-1 in 1 or 24 h. However, the blood clearance of myoglobin in 1 h was significantly higher when using the SHG membrane (mean difference, 8.0 ml/min; 95% CI 1.8 to 14.1 ml/min; $p = 0.02$). Over 24 h, blood clearance with the SHG membrane tended to be higher, but the difference did not achieve statistical significance (mean difference, 7.4 ml/min; 95% CI − 4.1 to 18.7 ml/min; $p = 0.17$). The blood clearance of creatinine showed the opposite tendency, with no significant difference in 1 h (mean difference, − 2.0 ml/min; 95% CI − 6.2 to 2.2 ml/min; $p = 0.29$) but slightly higher clearance with SHG in 24 h (mean difference 3.6 ml/min; 95% CI 0.6 to 6.6 ml/min; $p = 0.02$). Effluent clearance showed similar results to blood clearance: the effluent clearance of myoglobin in 1 h was significantly higher with SHG than that with AEF (mean difference, 1.0 ml/min; 95% CI 0.60 to 1.41 ml/min; $p < 0.01$).

No significant difference was found between the SHG and AEF membranes in the change of clearance between 1 and 24 h after the start of CRRT, except for the blood clearance of creatinine (mean difference, 5.6 ml/min; 95% CI 1.7 to 9.5 ml/min, $p = 0.01$) (Table 4). However, although there was a significant difference in the change of blood clearance for creatinine from 1 to 24 h after the start of CRRT between the two types of membrane, the difference was negligible.

There was no carry-over effect due to the difference in membrane in any solute, except for the effluent clearance of creatinine in 24 h (Table 5).

Table 2 Patient characteristics

	Total ($n = 8$)	SHG → AEF ($n = 4$)	AEF → SHG ($n = 4$)
Age, median (IQR), years	80 (76–81)	80 (78–83)	78 (74–81)
Gender, male (number, %)	7 (87.5%)	3 (75%)	4 (100%)
Height, median (IQR), cm	167 (153–170)	167 (149–172)	166 (153–170)
Weight, median (IQR), kg	56 (46–71)	51 (44–58)	65 (48–82)
Body mass index, median (IQR), kg/m^2	20.5 (15.1–25.6)	17.1 (14.4–20.9)	25.2 (19.1–28.5)
Source of sepsis, *n*, (%)			
Intrathoracic	2 (25%)	1 (25%)	1 (25%)
Intraabdominal	4 (50%)	3 (75%)	1 (25%)
Urogenital	1 (25%)	0 (0%)	1 (25%)
Skin/soft tissue/bone/joint	1 (25%)	0 (0%)	1 (25%)
APACHE II score, median (IQR)	21 (16–26)	23 (14–28)	19 (16–25)
SOFA score, median (IQR)	11 (9–13)	12 (10–14)	10 (8–13)
ICU stay, median (IQR), day	4.5 (4.0–27.8)	7 (4.3–30.8)	4.0 (4.0–26.5)
Hospital mortality, *n*, (%)	5 (62.5%)	3 (75%)	2 (50%)
Acute kidney injury, *n*, (%)	3 (37.5%)	1 (25%)	2 (50%)
Lactate, median (IQR), mg/dL	34.7 (19.0–65.7)	45.7 (27.3–65.7)	22.0 (15.0–181.1)
Procalcitonin, median (IQR), ng/mL	5.2 (3.8–17.2)	12.8 (4.8–46.7)	4.2 (1.5–8.3)
Glasgow Coma Scale, median (IQR)	13 (6–15)	10 (4–15)	14 (8–15)
Noradrenaline, median (IQR), μg/kg/min	0.3 (0.2–0.35)	0.28 (0.20–0.47)	0.30 (0.11–0.4)

Data are presented as median (IQR) or *n* (%)
APACHE acute physiology and chronic health evaluation, *SOFA* sequential organ failure assessment, *ICU* intensive care unit, *IQR* interquartile range

Discussion

The results of this study showed that the use of the SHG membrane resulted in higher blood clearance of myoglobin and creatinine than using the AEF membrane. There was no difference between the two types of membrane in the clearance of other solutes, and no carry-over effect was observed for any solute.

Few such studies involving CRRT have been reported. One study in critically ill patients with acute renal failure treated with CRRT investigated solute clearance and compared different kinds of membranes [11]. It reported that some dialysis membranes produced high creatinine and bicarbonate clearance, but it did not statistically verify the differences in clearance. In general, though,

Table 3 Baseline serum parameters in each homofilter

Serum parameters	Total ($n = 8$)	SHG → AEF ($n = 4$)	AEF → SHG ($n = 4$)
PaO_2/FiO_2 ratio, Torr	260 (180–375)	260 (191–273)	309 (171–456)
pH	7.38 (7.26–7.44)	7.40 (7.31–7.50)	7.32 (7.22–7.43)
Bicarbonate	18.9 (16.7–23.7)	18.7 (16.7–21.3)	21.0 (12.1–35.9)
Bilirubin, mmol/L	0.8 (0.2–1.6)	1.1 (0.3–1.6)	0.5 (0.2–2.7)
Creatinine, mg/dL (μmol/L)	2.3 (1.3–3.3)	1.8 (0.9–2.5)	2.9 (1.5–4.8)
Urea, mg/dL	66 (33–76)	51 (23–79)	70 (41–76)
Sodium, mEq/L	142 (136–147)	142 (137–142)	143 (136–150)
Potassium, mEq/L	4.0 (3.1–4.6)	3.5 (3.1–4.4)	4.3 (3.3–5.6)
Creatine kinase, IU/L	618 (117–1319)	871 (203–3717)	512 (100–974)
Myoglobin, ng/ml	3059 (478–6528)	3609 (1242–11,901)	1745 (389–6253)
HMGB-1, ng/ml	6.9 (5.6–13.0)	9.2 (6.4–13.0)	5.7 (4.8–85.4)
Hematocrit, %	30.8 (25.1–36.4)	34.0 (26.5–37.6)	28.0 (25.1–33.3)
Plate count, 10^3/μL	9.8 (7.6–16.3)	9.2 (6.9–14.5)	13.2 (7.8–21.0)

Data are presented as median (IQR) or n (%)
HMGB-1 high mobility group box-1, *IQR* interquartile rang

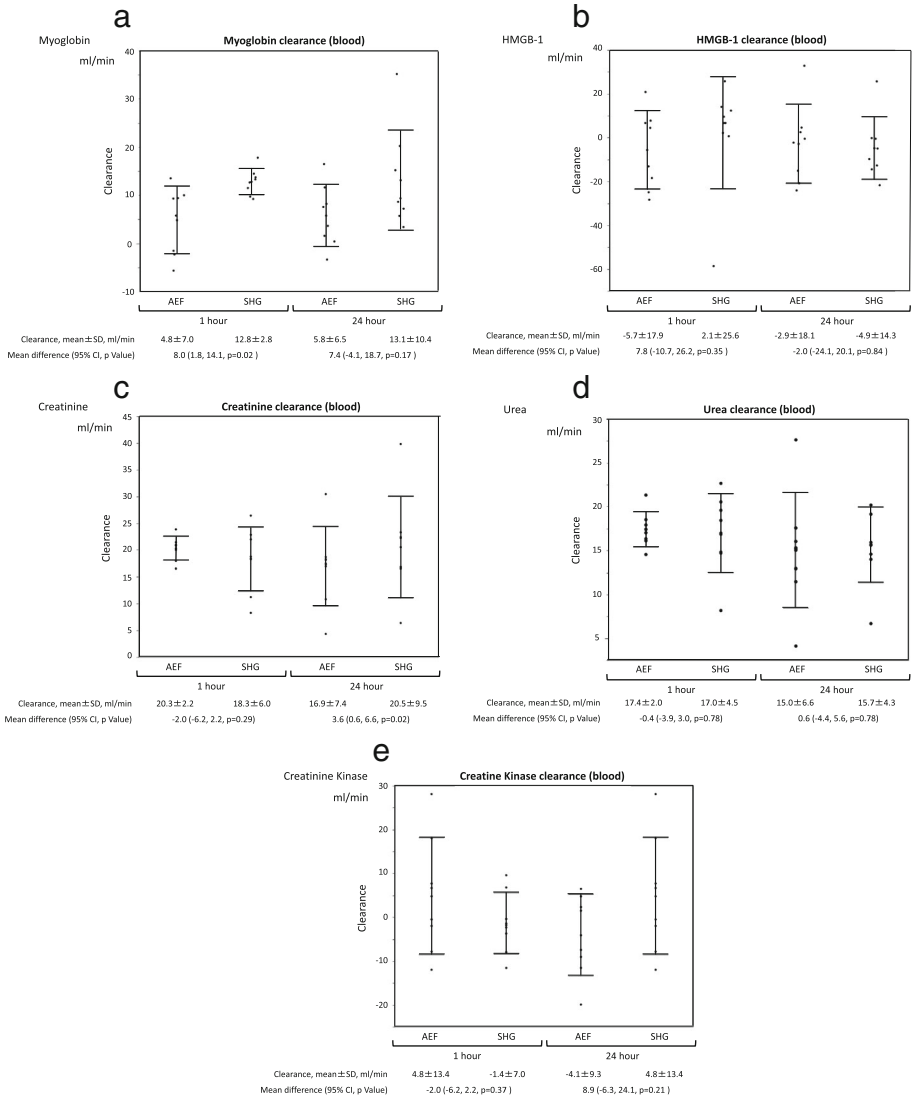

Fig. 2 Comparison between the two membranes (SHG and AEF) of the blood clearance of various solutes. **a** Myoglobin, **b** HMGB-1, **c** creatinine, **d** urea, and **e** creatine kinase

most studies of dialysis membranes so far have reported results obtained during IRRT with maintenance dialysis patients. The results of such studies cannot be applied to the membranes used during CRRT for patients in the acute phase. Unlike CRRT, the solute removal during IRRT depends not only on the dialysis membrane but also on the blood and dialysate flow rates. However, in Japan, the dialysate flow rate during CRRT is less than 5% of that during IRRT [21], and so the dialysis membrane makes a greater difference to dialysis efficiency with CRRT. Thus, the results of comparisons of dialysis membranes made during IRRT cannot be directly applied to membranes used in CRRT.

However, there have not previously been any studies that compared the solute removal efficacy of dialysis membranes, particularly polysulfone membranes, during CRRT. The present study, for the first time, compared the use of two dialysis membranes with patients and showed that SHG had a significantly higher ability than AEF to remove myoglobin and creatinine. However, because there has been no other study that compared polysulfone membranes in patients, these differences cannot yet be concluded. Nor is it possible to clarify the mechanism underlying the differences between the two membranes from the results of this study. All commercial polysulfone membranes include different amounts of and different kinds of polyvinylpyrrolidon as a hydrophilic agent. One possible explanation is structural differences between the two types of membrane, such as inside diameters of the hollow fiber, effective length of

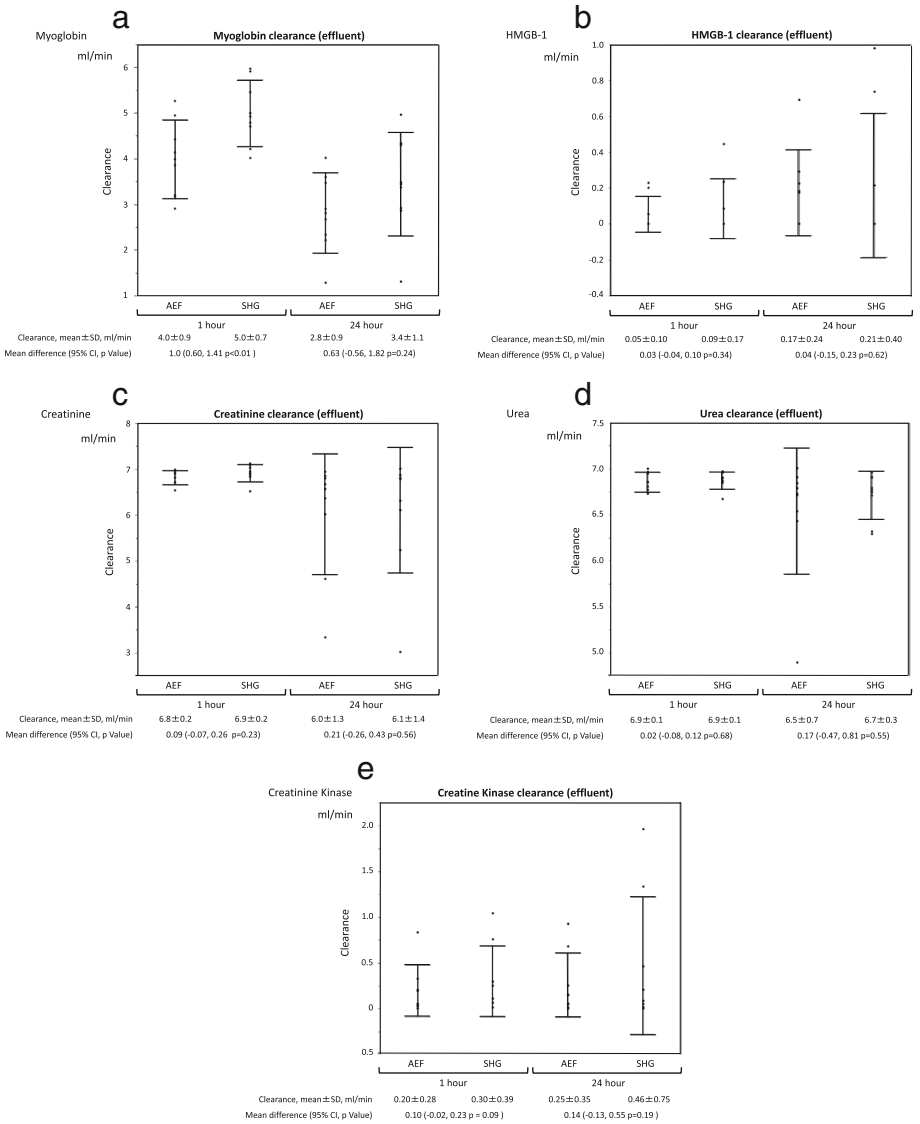

Fig. 3 Comparison between the two membranes (SHG and AEF) of the effluent clearances of various solutes. **a** Myoglobin, **b** HMGB-1, **c** creatinine, **d** urea, and **e** creatine kinase

the module, thickness of the skin layer, the pore size (either radius or diameter), and the surface porosity of the membrane, as well as the difference in chemical composition between them [22, 23]. The physicochemical heterogeneity provided by the hydrophilic–hydrophobic microdomains present at the surface of the SHG membrane impedes the formation of stable hydrophobic interactions between the various solutes and the membrane surface. Medium-sized molecules may be more susceptible than small molecules to this physicochemical heterogeneity, which may explain why there were no differences between the two membranes in this study in the clearance of small-molecule solutes. However, this is no more than a hypothesis, and a future study is needed to confirm it.

According to the results of the present study, SHG may provide better dialysis efficiency for the removal of medium-sized molecules, which may result in a decrease in the number of dialyzers needed and the dialysis time; this in turn may lead to a reduction in dialysis costs. This may be advantageous not only for health care workers but also for patients and stakeholders.

This study had several limitations. First, it included only eight patients and 16 dialysis membranes and was conducted in single center; the sample size was therefore not optimal for comparing solute clearance between two membranes. It is possible that a large difference in solute removal could not be recognized between the two dialysis membranes. Second, in this study, statistically significant differences in myoglobin clearance were observed

Table 4 Change of clearance in 24 h

	SHG	AEF	Mean difference	95% CI	*p* value
Blood clearance					
Myoglobin, median (IQR), ml/min	0.3 (− 9.0, 9.6)	1.0 (− 5.1, 7.0)	− 0.63	− 12.8, 11.6	0.91
HMGB-1, median (IQR), ml/min	− 7.0 (−27.0, 13.1)	2.8 (− 18.3, 23,9)	− 9.7	− 38.7, 19.3	0.45
Creatinine, median (IQR), ml/min	2.2 (− 4.6, 9.0)	− 3.4 (− 9.8, 3.1)	5.6	1.7, 9.5	0.012
Urea, median (IQR), ml/min	− 1.3 (− 2.5, − 0.2)	− 2.4 (− 7.9, 3.2)	1.1	− 4.5, 6.6	0.67
Creatine kinase, median (IQR), ml/min	6.2 (− 7.7, 20.1)	− 8.9 (− 24.1, 6.3)	15.1	− 13.4, 43.6	0.25
Effluent clearance					
Myoglobin, median (IQR), ml/min	− 1.55 (− 2.59, − 0.52)	− 1.18 (− 1.63, − 0.73)	− 0.38	− 1.65, 0.90	0.51
HMGB-1, median (IQR), ml/min	0.13 (− 0.07, 0.33)	0.12 (− 0.03, 0,27)	0.01	− 1.57, 0.18	0.90
Creatinine, median (IQR), ml/min	− 0.81 (− 1.96, 0.35)	− 0.80 (− 1.06, 0.35)	− 0.01	− 0.29, 0.28	0.97
Urea, median (IQR), ml/min	− 0.16 (− 0.42, 0.10)	− 0.31 (− 0.86, 0.24)	0.15	− 0.44, 0.74	0.56
Creatine kinase, median (IQR), ml/min	0.17 (− 0.14, 0.48)	− 0.06 (− 0.05, 0.17)	0.11	− 0.15, 0.36	0.36

HMGB-1 high mobility group box-1, *IQR* interquartile range, *CI* confidence interval

between the two membranes, but it is unclear whether this difference was clinically important. It may be possible to evaluate the effectiveness of the membrane by verifying how much the solute concentration has decreased after a certain time has elapsed. However, rather than basing the evaluation on the change in solute concentration before and after using the membrane, one problem with this method is that the solute concentration may be influenced by the patient's residual renal function and underlying disease. It would therefore not be possible to estimate the performance of the dialysis membrane unconditionally. Finally, the types of solute examined in this study may not have been sufficient to verify the difference in clearance between the two membranes. For example, we did not consider solutes such as β2 microglobulin or inflammatory cytokines, which have been well validated in recent years [24–26]. However, we examined the difference in the clearance of HMGB-1, which has been the focus of attention in recent years, and reported a difference between the two polysulfone membranes in its clearance. There has been no previous report on the clearance of HMGB-1 in polysulfone membranes, and so the usefulness of HMGB-1 is not known. Because the clearance of this solute is also influenced by the protein binding rate, its clearance is not necessarily constant. Thus, there is a possibility that the differences between the membranes may be underestimated.

Table 5 Carry-over effect

		p value
Blood clearance		
Clearance 1 h	Myoglobin	0.56
	HMGB-1	0.30
	Creatinine	0.60
	Urea	0.99
	Creatine kinase	0.54
Clearance 24 h	Myoglobin	0.56
	HMGB-1	0.81
	Creatinine	0.61
	Urea	0.69
	Creatine kinase	0.71
Effluent clearance		
Clearance 1 h	Myoglobin	0.67
	HMGB-1	0.72
	Creatinine	0.84
	Urea	0.07
	Creatine kinase	0.23
Clearance 24 h	Myoglobin	0.77
	HMGB-1	0.99
	Creatinine	0.01
	Urea	0.26
	Creatine kinase	0.23

HMGB-1 high mobility group box-1

Conclusions

In conclusion, this preliminary study comparing the use of two polysulfone membranes in patients with sepsis requiring CRRT and showed that the SHG membrane was capable of removing myoglobin with greater efficacy then the AEF membrane. However, it remains unclear whether the differences were clinically meaningful, and further study is needed.

Abbreviations

AKI: Acute kidney injury; APACHE: Acute physiology, and chronic health evaluation; APTT: Activated partial thromboplastin time; CI: Confidence interval; CKD: Chronic kidney disease; CRRT: Continuous renal replacement therapy; HMGB-1: High-mobility group protein 1; ICU: Intensive care unit; IQR: Interquartile range; IRRT: Intermittent renal replacement therapy;

SD: Standard deviation; SOFA: Sequential organ failure assessment; STROBE: Strengthening the Reporting of Observational Studies

Acknowledgements
The authors would like to thank all study participants.
The authors would like to thank Enago (www.enago.jp) for the English language review.

Funding
This study was supported by Toray Medical.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
HY is the guarantor of the content of the manuscript, including the data and analysis. He had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including especially the adverse effects. SS contributed substantially to the study concept and design, data analysis and interpretation, and critical revision of the manuscript for important intellectual content. TA contributed to the accuracy of the data analysis. KS, AK, NH, HH, YK, and HS contributed to the study design, the acquisition and the interpretation of data, and drafting of the manuscript. TT contributed to the study design and drafting of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
This study protocol was approved by the local ethics committee at Japanese Red Cross Musashino Hospital named Clinical Research Judging Committee.

Consent for publication
Informed consent was obtained from all the participants or their surrogate decisionmakers.

Competing interests
The authors declare that they have no competing interests.

Publisher's Note

Author details
[1]Department of Intensive Care Unit, Kameda Medical Center, 929 Higashi-chou, Kamogawa-shi, Chiba 296-8602, Japan. [2]Intensive Care Unit, Department of Emergency and Critical Care Medicine, Japanese Red Cross Musashino Hospital, Tokyo, Japan. [3]Department of Preventive Medicine and Public Health, Keio University School of Medicine, Tokyo, Japan. [4]Department of Medical Engineer, Kameda Medical Center, Chiba, Japan. [5]Biostatistics Unit at Clinical and Translational Research Center, Keio University Hospital, Tokyo, Japan.

Received: 10 September 2017 Accepted: 16 January 2018
Published online: 21 February 2018

References

1. Japanese Society of Education for Physicians and Trainees in Intensive Care (JSEPTIC): Available at<http://www.jseptic.com/rinsho/pdf/questionnaire_120325.pdf>. Accessed 25 Nov 2017.
2. Fleischmann C, Scherag A, Adhikari NK, et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. Am J Respir Crit Care Med. 2016;193:259–72.
3. Kim WY, Huh JW, Lim CM, Koh Y, Hong SB. Analysis of progression in risk, injury, failure, loss, and end-stage renal disease classification on outcome in patients with severe sepsis and septic shock. J Crit Care. 2012;27:104. e101-107
4. Ronco C. Continuous renal replacement therapies for the treatment of acute renal failure in intensive care patients. Clin Nephrol. 1993;40:187–98.
5. Hoffmann JN, Hartl WH, Deppisch R, Faist E, Jochum M, Inthorn D. Hemofiltration in human sepsis: evidence for elimination of immunomodulatory substances. Kidney Int. 1995;48:1563–70.
6. Forni LG, Hilton PJ. Continuous hemofiltration in the treatment of acute renal failure. N Engl J Med. 1997;336:1303–9.
7. Vinsonneau C, Camus C, Combes A, et al. Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. Lancet. 2006;368:379–85.
8. Schefold JC, von Haehling S, Pschowski R, et al. The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): a prospective randomized controlled trial. Crit Care. 2014;18:R11.
9. Keshaviah P. Technology and clinical application of hemodialysis. In: Striker GE, Klahr S, Decker BC, editors. The principles and practice of nephrology. Philadelphia: 2nd edition Mosby. 1991. p. 740. ISBN-10:1556641494. ISBN-13: 978-1556641497
10. Palmer SC, Rabindranath KS, Craig JC, Roderick PJ, Locatelli F, Strippoli GF. High-flux versus low-flux membranes for end-stage kidney disease. Cochrane Database Syst Rev. 2012:CD005016. https://doi.org/10.1002/14651858.CD005016.pub2.
11. Ifediora OC, Teehan BP, Sigler MH. Solute clearance in continuous venovenous hemodialysis. A comparison of cuprophane, polyacrylonitrile, and polysulfone membranes. ASAIO J. 1992;38:M697–701.
12. Ingram AJ, Parbtani A, Churchill DN. Effects of two low-flux cellulose acetate dialysers on plasma lipids and lipoproteins—a cross-over trial. Nephrol Dial Transplant. 1998;13:1452–7.
13. Krieter DH, Lemke HD. Polyethersulfone as a high-performance membrane. Contrib Nephrol. 2011;173:130–6.
14. Mudge DW, Rogers R, Hollett P, et al. Randomized trial of FX high flux vs standard high flux dialysis for homocysteine clearance. Nephrol Dial Transplant. 2005;20:2178–85.
15. Ouseph R, Hutchison CA, Ward RA. Differences in solute removal by two high-flux membranes of nominally similar synthetic polymers. Nephrol Dial Transplant. 2008;23:1704–12.
16. Lee D, Haase M, Haase-Fielitz A, Paizis K, Goehl H, Bellomo R. A pilot, randomized, double-blind, cross-over study of high cut-off versus high-flux dialysis membranes. Blood Purif. 2009;28:365–72.
17. Jamal JA, Mueller BA, Choi GY, Lipman J, Roberts JA. How can we ensure effective antibiotic dosing in critically ill patients receiving different types of renal replacement therapy? Diagn Microbiol Infect Dis. 2015;82:92–103.
18. Philip KNL, Tian Q, Ip M, Gomersall CD. In vitro adsorption of gentamicin and netilmicin by polyacrylonitrile and polyamide hemofiltration filters. Antimicrob Agents Chemother. 2010;54:963–5.
19. Villa G, Zaragoza JJ, Sharma A, Neri M, De Gaudio AR, Ronco C. Cytokine removal with high cut-off membrane: review of literature. Blood Purif. 2014;38:167–73.
20. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992;20:864–74.
21. Uchino S, Toki N, Takeda K, et al. Validity of low-intensity continuous renal replacement therapy. Crit Care Med. 2013;41:2584–91.
22. Excelflo AEFAEF: Available at<http://www.asahi-kasei.co.jp/medical/pdf/apheresis/excelflo-aef_document.pdf>. Accessed 22 Apr 2017.
23. Hemofeel SHG: Available athttp://www.info.pmda.go.jp/downfiles/md/PDF/480220/480220_22100BZX01046000_A_01_03.pdf. Accessed 19 Jan 2018.
24. Ahrenholz PG, Winkler RE, Michelsen A, Lang DA, Bowry SK. Dialysis membrane-dependent removal of middle molecules during hemodiafiltration: the beta2-microglobulin/albumin relationship. Clin Nephrol. 2004;62:21–8.
25. Lian JD, Cheng CH, Chang YL, Hsiong CH, Lee CJ. Clinical experience and model analysis on beta-2-microglobulin kinetics in high-flux hemodialysis. Artif Organs. 1993;17:758–63.
26. Pellicano R, Polkinghorne KR, Kerr PG. Reduction in beta2-microglobulin with super-flux versus high-flux dialysis membranes: results of a 6-week, randomized, double-blind, crossover trial. Am J Kidney Dis. 2008;52:93–1.