Effect of Dynamic Circuit Pressures Monitoring on the Lifespan of Extracorporeal Circuit and the Efficiency of Solute Removal During Continuous Renal Replacement Therapy

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Research

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Abstract

Objective: To observe the effects of dynamic pressure monitoring on the lifespan of the extracorporeal circuit and the efficiency of solute removal during continuous renal replacement therapy (CRRT).

Materials and Methods: A prospective observational study was performed at the West China Hospital of Sichuan University in the intensive care unit. Analyses of the downloaded pressure data recorded by CRRT machines and the solute removal efficiencies, calculated by 2*Ce/(Cpre+Cpost), where Ce, Cpre and Cpost are the concentrations of the effluent, pre-filter blood, and post-filter blood, respectively, were performed. Samples were collected at 0, 2, 6, 12, 24 h after the initiation of CRRT. We measured the concentrations of creatinine, blood urea nitrogen (BUN) and β2-microglobulin in the plasma and effluent.

Results: Extracorporeal circuits characterized by moderate-severe (M-S) access outflow dysfunction (AOD) events, defined as access outflow pressure less than or equal to -200 mm Hg more than 5mins, had shorter lifespans with no anticoagulation (17.6±11.2 h vs. 35.1±17.1 h, P=0.001) or with regional citrate anticoagulation (RCA) (40.3±22.2 h vs. 55.9±21.7 h, P=0.016). Moreover, Cox regression analysis revealed that the lack of moderate-severe AOD events, RCA, or continuous veno-venous hemodiafiltration (CVVHDF) independently prolonged the circuit lifespan. All tested solutes removal efficiencies started to decline at 12h. Furthermore, efficiencies of all solutes removal dropped obviously at 24h when TMP≥ 150mmHg.

Conclusion: RCA and CVVHDF predicted a longer circuit lifespan. Moderate-severe AOD events were associated with a shorter circuit lifespan when RCA or no anticoagulation was used. Replacement of extracorporeal circuit might be considered if TMP≥ 150mmHg at 24h.

Introduction

Continuous renal replacement therapy (CRRT) slowly and effectively removes water and solutes from critically ill patients [1]. Prolonging the lifespan of CRRT circuits is fundamental for better therapeutic effects. The extracorporeal circuit, which is the key part of CRRT, consists of a vascular access outflow lumen, prefilter tubing, a filter, post-filter tubing, an air-trap chamber, pre-vascular inflow tubing and a vascular access inflow lumen. Frequent clotting in the extracorporeal circuit may lead to massive blood loss, shorter effective treatment times, and increased medical costs [2]. Many factors might influence circuit survival, including anticoagulation, vascular access, CRRT treatment parameters (e.g, modality, filter membrane, blood flow rate), hematocrit and blood coagulation [3–9]. However, the mechanisms of extracorporeal circuit failure are still not clear.

In the past, pressure data were obtained by manual recording every hour. With developments in science and technology, mainstream CRRT machines can continuously record changes in pressure, such as access outflow pressure (AOP), pre-filter pressure (PFP), effluent pressure (EP), and return inflow pressure (RIP), every minute during therapy and store the data on internal storage. A few trials have investigated the pressure changes during CRRT [10, 11], stored pressures data can be downloaded into an Excel

spreadsheet to obtain detailed pressure data and the precise circuit lifespan [12]. CRRT removes waste and maintains the electrolyte and acid-base balance via various techniques, such as dispersion, convection, ultrafiltration and adsorption. It is logical to believe that the removal efficiencies of diverse sizes of solutes are different due to their distinct characteristics and removal methods. Previous studies that focused on solute removal predominantly focused on modality and pre/post-dilution. Many influencing factors remain unknown. In addition, no trials have investigated the relationship between dynamic pressure monitoring and solute removal efficiency hindered by the extraction method. We hypothesized that continuous pressure changes during CRRT affect the extracorporeal circuit lifespan and solute removal efficiency.

Materials And Methods

Study design

This prospective, observational, cohort study was performed in the ICU of West China Hospital of Sichuan University, Chengdu China. The data were recorded from October 2018 to December 2019. The study was approved by Institutional Review Board of West China Hospital, Sichuan University (2017-06). Informed consent was obtained from the patient or responsible surrogate.

Study population

A total of 395 episodes of CRRT in 131 patients were included. These episodes represented 16,244.1 h of treatment. The study cohort included all patients who received at least one complete episode of CRRT. All therapies used a Prismaflex machine (Baxter, USA). Patients were excluded if (1) CRRT was performed using a non-Prismaflex machine, (2) the modality was not in continuous veno-venous hemofiltration (CVVH) or continuous veno-venous hemodiafiltration (CVVHDF), such as plasma exchange (PE), and (3) patients was pregnant, aged under 18 years, breastfeeding or patients had other special conditions. The severity of the illness in each patient was assessed by the sequential organ failure assessment (SOFA) score.

CRRT protocol

The CRRT equipment was Prismaflex (Baxter, USA) with the AN69 ST150 filter (Baxter, USA). All the patients used double-lumen venous catheters for vascular access. All femoral vascular access was achieved via 13F dual-lumen catheters (Baxter, USA), and jugular access was achieved via 11.5Fr catheters (Baxter, USA). The blood rate was maintained at 150 to 200 mL/min. CVVH was performed in the pre-dilution mode. CVVHDF was performed in the post-dilution mode, and the ratio of dialysate to replacement fluid was 1:1. The replacement fluid used was the standard bicarbonate-based solution (QINGSHAN LIKANG, China). RCA was the first choice in all circuits, with low-molecular-weight heparin (LMWH) or no anticoagulation as the alternative. Extracorporeal circuit cessation occurred when the circuit clotted or the circuit reached the maximum recommended use. The effective treatment period for each extracorporeal circuit was a maximum of 72 h.

Measurement of pressure dynamics in the extracorporeal circuit

The methods used to extract, store, and analyze the continuous pressure data were similar to those described in a previous publication [12]. The pressure variables included minute AOP, effluent pressure (EP), prefilter pressure (PFP), and return inflow pressure (RIP) from relevant circuit points. TMP was calculated from these data using the equation: TMP= (PFP + RIP)/2−EP.

Access outflow dysfunction (AOD) was defined as an AOP − 200 mmHg according to a previous study[10]. We defined three types of AOD events on the basis of total minutes of AOD: mild (≤ 5 min), moderate (5 min < timing ≤ 60 min) and severe (time > 60 min).

Sample collection in the extracorporeal circuit during CRRT and measurement

Samples (blood and effluent) were obtained at 2, 6, 12, and 24 h when CRRT was used in the post-dilution CVVHDF modality. The concentrations of blood urea nitrogen (BUN), creatinine(Cr) and β2-microglobulin in the plasma and effluent were measured in the clinical laboratory of West China Hospital of Sichuan University. Solute removal efficiency = 2*Ce/(Cpre + Cpost), where Ce, Cpre and Cpost are the concentrations of the effluent, blood prefilter, and postfilter, respectively. The data of solute removal efficiency were matched with the accurate pressures data at the same timepoint.

Collection of patient characteristics

For each circuit evaluated, demographics, including sex, age, diagnosis, weight, height, and SOFA score, were collected. Laboratory tests before the initiation of CRRT were conducted, including assessments of hemoglobin, platelets, indexed normalized ratio (INR), and activated partial thromboplastin time (APTT). We obtained the following CRRT parameters: anticoagulation, modality, dose, vascular access site and the reason for extracorporeal circuit failure.

Statistical Methods

Variables are reported as the medians with standard deviation. Variability of pressures was defined as the standard deviation for all pressure. Comparisons between groups were performed using one-way analysis of variance or the chi-squared test. Variables associated with extracorporeal circuit lifespan were analyzed using the Cox regression model. A *p* value less than 0.05 was considered statistically significant. Data were analyzed using SPSS version 19.0 (SPSS Inc., Chicago, Ill., USA).

Results

Patients and extracorporeal circuits

A total of 395 episodes (Fig. 1) in 131 patients, accounting for 16,244.1 h of effective treatment time, were included in the study. Over the course of our study, 96 cases (24.3%) were electively ended (i.e., the circuit had been used for 72 h). Clotting of the filter or air-trap chamber occurred in 299 cases (75.7%). The average lifespan of the extracorporeal circuit was 41.1 ± 24.8 h. For anticoagulation, RAC was the primary choice (48.6%), followed by no anticoagulation (31.1%), and LMWH (20.3%). In the cluster of modality, the proportion of CVVHDF was 81.3%, and CVVH was 18.7%. The average prescribed dose of CRRT was 31.3 ± 3.2 ml/kg/h. The femoral vein accounted for 93.2% of vascular access. Right side femoral vein access was used in 61.6% of the cases, and the left side was used in 38.4% of the cases. Alternative vascular accesses included the jugular vein (6.8%), of which 88.2% of the cases were accessed on the right side. The details are reported in **Table 1**.

Dynamic pressure changes during CRRT with different extracorporeal circuit failures (ECF)

For further analysis, we defined three types of extracorporeal circuit failures [10] according to circuit lifespan, including early (≤ 12 h), intermediate (> 12 h, ≤ 24 h) and late (> 24 h). A total of 134 circuits (33.9%) experience early-intermediate failure, and 261 circuits (66.1%) experienced late failure. The mean changes in the AOP, PFP, EP, RIP and TMP data were completely distinct in the different groups. The Dynamic mean pressure curve graphs are shown in Fig. 2.

The negative value of AOP was smallest in the early group (-62.87 ± 2.31 mmHg), which was 23.5 and 4.87 mmHg lower than that in the late and intermediate groups, respectively. The overall changes in the PFP were also varied among the different types of ECF: the mean value in the early, intermediate and late groups were 133.43 ± 21.95 mmHg, 150.47 ± 28.09 mmHg and 104.92 ± 3.89 mmHg, respectively. About EPs, intermediate group had the smallest value of mean extracorporeal circuit data, followed by the late and early groups. In data of RIPs, the lowest and highest mean values were 46.38 ± 1.11 mmHg and 61.22 ± 7.74 mmHg in the late group and intermediate group, respectively. In cure graph of TMP, the line in the early and intermediate groups increased rapidly, with mean data of 98.12 ± 34.48 mmHg and 120.15 ± 38.891 mmHg, respectively. Moreover, the variability of late groups was statistically smaller than that compared to the other groups (P□0.05) in all totally different extracorporeal circuit pressure cluster (AOP, PFP, EP, RIP, TMP). The detail variability data are shown in **Table 2**.

Access outflow dysfunction (AOD) events under different anticoagulants

A total of 143 circuits experienced at least one AOD episode, and no significant difference was found (41.0 ± 25.7 vs. 41.3 ± 23.6 h, P = 0.91) in the lifespan of the circuits in which no AOD event occurred. However, the circuits without moderate-severe AOD events were significantly prolonged compared to those with moderate-severe AOD events during CRRT (43.0 ± 24.4 vs. 28.6 ± 24.2 h, P = 0.003) (Fig. 3).

In our study, RCA was associated with longer circuits survival (31.3 ± 20.0 h vs. 23.9 ± 19.1 h vs. 54.6 ± 22.2 h, P < .0.05). Moreover, different anticoagulation strategies had distinct effects on moderate-severe

AOD events in the circuit lifespan. When no anticoagulation was used, the lifespan of circuits without moderate-severe AOD events was significantly prolonged (17.6 ± 11.2 h vs. 35.1 ± 17.1 h, P = 0.001). The same effect existed when RCA was used (40.3 ± 22.2 h vs. 55.9 ± 21.7 h, P = 0.016). However, the effect of moderate-severe AOD events on circuit survival disappeared with the use of LMWH (24.4 ± 15.5 h vs. 24.9 ± 16.3 h, P = 0.96; Fig. 4**)**.

Analysis of risk factors of extracorporeal circuit survival

Comparison between the early-intermediate and late groups revealed that circuits in the chronic group had a lower occurrence of moderate-severe AOD episodes (22.4% vs. 8.0%, P < 0.001), lower platelet count (102.67 ± 90.11 vs. 133.46 ± 84.86 $*10^9$/l, P = 0.011) and higher use of the CVVHDF modality (90.4% vs. 63.4%, P < 0.001). However, mild AOD events, hemoglobin, PT, INR, APTT and vascular access (P > 0.05) were not significantly different between these two groups (**Table 3**). Variables associated with a shorter lifespan of the extracorporeal circuit are shown in **Table 4**. According to the Cox regression model, moderate-severe AOD events (HR 1.893, 95CI% 1.300 to 2.756, P = 0.001) were risk factors for circuit survival during CRRT. RCA (HR 0.391, 95CI% 0.293 to 0.521, P < 0.001) and CVVHDF (HR 0.546, 95CI% 0.376 to 0.793, P = 0.001) were independently associated with a longer lifespan of the extracorporeal circuit.

Solute removal efficiency and dynamic pressure changes

The removal efficiency of medium-macro molecular solutes (β_2-microglobulin) was significantly lower than that of BUN and creatinine at different time during CRRT. All efficiencies of tested solutes removal (BUN, creatinine and β2-microglobulin) dropped gradually with operation time prolonged (Fig. 5). The details of solute removal efficiency in different anticoagulation modalities were presented in *Supplementary Appendix File*. According to the precise TMP data which was matched with sample collection time,two groups were formed: TMP < 150 mmHg and TMP ≥ 150 mmHg. The solute removal efficiency in the lower TMP group showed greater clearance ability than that in the higher TMP group. Moreover, this phenomenon significantly occurred between the TMP < 150 mmHg and TMP ≥ 150 mmHg group for BUN (0.92 ± 0.10 vs. 0.83 ± 0.16, P = 0.001), creatinine (0.77 ± 0.20 vs. 0.63 ± 0.23, P = 0.007), and β2-microglobulin (0.46 ± 0.11vs. 0.29 ± 0.08, P < 0.001) at 24 h (Fig. 6).

Discussion

Main findings

We analyzed continuous pressure data from CRRT and found that, after classifying the different types of circuits failure, moderate-severe access outflow dysfunction was associated with a shorter lifespan of extracorporeal circuit compared to mild dysfunction. Moreover, when anticoagulation was performed with citrate or when anticoagulation was not performed, M-S was associated with shorter circuit survival compared to that observed when LMWH was used. We found that the use of CVVHDF and citrate and the absence of moderate-severe AOD events prolonged the lifespan of extracorporeal circuit. Our study

demonstrated distinct downtrend in small-molecule and macro-molecular solutes in removal efficiency under different anticoagulation modalities. Solutes removal efficiency declined significantly at 24 h or TMP ≥ 150 mmHg. Meanwhile, removal efficiency declined when circuit survival up to 24 h while TMP ≥ 150 mmHg compared with those in TMP < 150 mmHg at 24 h.

Relationship to Previous Studies

Lifespan of extracorporeal circuit

Recent published studies [3, 4] suggested that citrate was superior to heparin for circuit survival and anticoagulation-related bleeding risk. However, the lifespan of extracorporeal circuit still varied greatly in studies despite whatever anticoagulant applied. A multicenter, randomized controlled study [13] of 174 patients compared circuit survival when different anticoagulants used, namely, citrate and heparin, during CRRT. The lifespans of the two groups were 37.5 ± 23 h and 26.1 ± 19 h, respectively. The standard deviation confirmed the variability in circuit survival. Matthew Brain [9] reported a meta-analysis about non-anticoagulant factors (such as vascular access, dialysis membrane, and modality) on the lifespan of extracorporeal circuit, but the value of this article decreased due to the biased problem. Factors influencing the lifespan of extracorporeal circuit are not exactly definite so further studies are needed. AOP is a major concern in circuit pressures monitoring on the lifespan of extracorporeal circuit. Access outflow pressure is measured between the catheter and the blood pump. Since the inner blood is sucked by extracorporeal circuit, the AOP is generally negative and less than − 50 mmHg [14]. A recently published observational study [10] was the first study to acquire continuous pressure data accurately during CRRT, and these pressures accurately reflect the real state of each part of the extracorporeal circuit. This study suggested that an AOP less than or equal to -200 mmHg could be considered a dysfunction, and AOD events can shorten the survival of the extracorporeal circuit. The study still had some limitations, such as the inclusion of a narrow population (most were postoperative patients) and the lack of RCA data. A recent retrospective study [11] suggested that the occurrence of an AOD event within 4 h after the initiation of CRRT significantly reduced the lifespan of extracorporeal circuit by 12.9 h compared to the absence of an AOD event. COX analysis of two studies [10, 11] suggested that AOD events were independent risk factors for circuit survival, which indicates that AOP status warrants concern.

AOD events are quite common in the clinic, and these events are an indirect indicator of the quality and function of the vascular access. Several causes of AOD were proposed: 1.The patient's body position may change frequently due to the needs of nursing or other therapy. The catheter may be suddenly bent or folded, which results in a sharp decrease in AOP and an extremely negative value. This interference is the most common reason for an AOD event in the clinic [15, 16]. 2. The formation of thrombus or fibrous sheath in the lumen of catheter or the collapse or thrombosis of the central vein where catheter was placed may cause an AOD event. 3. Blood flow exceeding the maximum allowable range of the double-lumen catheter (> 350 or 400 ml/min) may also cause an AOD event. The occurrence of moderate-severe AOD events should be avoided as much as possible. The results of our study suggested that short-term

access outflow dysfunction (AOD) is not enough to affect the lifespan of the extracorporeal circuit. Only AOD that lasted a sustainable time (≥ 5 min), such as a moderate-severe AOD event, affected the extracorporeal circuit, especially circuits with citrate and no anticoagulation. Notably, this phenomenon did not indicate heparin were superior to RCA and no anticoagulation but only indicated that moderate-severe AOD events should be a concern. The possible explanation for this result is that different anticoagulants play distinct roles. Citrate prevents coagulation by complexing ionized calcium in the extracorporeal circuit. The part entering the human body is metabolized from one molecule of citrate into three molecules of bicarbonate in the mitochondria of the liver, skeletal muscle, and kidney [17]. Notably, complexed calcium is released, and lost calcium is supplemented in postfilter. Therefore, citrate, is an ideal regional anticoagulant that effectively maintains an anticoagulation effect in the extracorporeal circuit and avoids bleeding in the body. LMWH exerts systemic anticoagulant effects by enhancing antithrombin III activity and inhibiting thrombin (factor IIa) and factor Xa. The pharmacokinetics are complex. Therefore, the variability in the high risk of bleeding individuals is a disadvantage. In addition, COX analysis showed that moderate-severe AOD events were a risk factor for circuit survival.

Solute removal efficiency

Using of RCA has been verified to prolong the circuit survival and avoid a system "shutdown" because of the early clotting of the circuit. Nevertheless, a decrease in solute clearance occurs even if extracorporeal circuit functioning properly. From now no when should we replace the extracorporeal circuit accurately is a mystery and Even the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines do not have a suggestion about that point, and how and when does solute removal efficiency decay are still indeterminate. Therefore, it is very valuable to find an indicator to determine whether to replace extracorporeal circuit. Clogging of hemofilter membranes and clotting of the circuit are associated with the rise in TMP [14]. Compared with other pressures data, TMP is particularly important in the study of solute removal efficiency. The relationship between TMPs and solute removal efficiency has not been investigated. Previous trials have studied the effects of diverse filter membranes and dilution methods on removal efficiency [18, 19]. A large multicenter randomized controlled (RENAL) study [20] of 1508 patients investigated the effect of high-dose (40 ml/kg *ml) and low-dose (25 ml/kg* ml) on 90-day survival rate during CRRT and suggested no difference. A uniform CRRT dose was used in our study to exclude its effect on solute removal efficiency. A study [18] focused on the effect of membrane materials (Sureflux150E vs AV-400) on solute clearance; however, the results showed no difference between cellulose triacetate membranes and synthetic membranes on the removal of solutes (urea nitrogen and creatinine). Our study only used ST150 membrane (polyacrylonitrile material) to decrease an interference of materials. A small multicenter randomized controlled study [21] recently focused on effects of different modalities (CVVH vs. CVVHD), convection and diffusion, on solute clearance using similar doses. The results showed no significant difference at 0 h and 4 h ($P > 0.05$) for small solutes (urea nitrogen and creatinine) and medium-macro molecules (inflammatory mediators, such as IL-6). No study has analyzed the solute removal efficiency and continuous pressure in extracorporeal circuit because of the prior lack of effective data extracting methods. Therefore, our study is innovative.

Solutes have distinct removal efficiencies due to unique characteristics. The kidney is the only excretory organ of β2-microglobulin (11.8 kD). A previous study[22] showed that the risk of death increased 11% when the concentration of β2-microglobulin increased by 10 mg/L in blood. Therefore, our study selected it as a representative medium-macro-molecular solute. It has been thought that small molecules, such as urea nitrogen, freely pass through the dialysis membrane for 100% removal. However, a randomized controlled study conducted by William D. LyndonD [23] revealed that the measured clearance rates of urea nitrogen and creatinine in a high-dose group during CRRT were significantly different from the achieved clearance rates of 7.1% and 13.9% ($P < 0.001$), respectively. The results showed that the clearance of urea nitrogen and creatinine was not 100%, and the ability to removing creatinine was significantly overestimated compared to urea nitrogen. However, this study had some limitations, such as the lack of a downward trend in the removal effects for diverse solutes. A recent prospective cohort study [24] investigated the effect of high-flux filters (surface area 1.8 m^2) on the clearance of various solutes during CRRT. The results showed that the clearance of small molecule solutes (Cr and BUN) was not different at 72 h (0.99 ± 0.03 vs. 0.91 ± 0.16, P = 0.074; 1 ± 0 vs. 0.95 ± 0.17, P = 0.5), but β2-microglobulin changed substantially (0.61 ± 0.09 vs. 0.48 ± 0.13, P = 0.002). The results of this study are higher than our results at every sample collection time. The explanation for this phenomenon may be that the removal efficiency of the high-flux filter was higher than an ordinary filter. In addition, the lifespan of all the circuits were extreme (72 h), and no filter coagulation occurred with the use of citrate as the anticoagulation. Therefore, solute removal may decrease more slowly when the extracorporeal circuit is running well.

Strengths And Limitations

Our study has important clinical significance because continuous pressures data are still not completely utilized. In our study, we collected various modalities of anticoagulation and multiple RCA data (48.6%) compare to other trails [10, 11]. Moreover, we creatively combined the dynamic pressure monitoring with the solute removal efficiency during CRRT and offered a new idea for circuit replacement.

Our study also has several limitations. First, it was a single-center observational study, and the findings require verification by multicenter studies. In addition, our study used data from a single type of machine, modality, dose, dialyzer membrane so risk factors of circuit survival and the results of access outflow dysfunction need more various data to confirm the results.

Conclusion

RCA and CVVHDF prolonged circuit survival during CRRT. Moderate-severe AOD events should be concerned, especially when RCA or no anticoagulation used. With the prolonged using of extracorporeal circuit, all tested solutes removal efficiency started to significantly declined at 12 h. Besides with the increase of TMP, solute removal efficiency descended dramatically. Moreover, extracorporeal circuit might be replaced when lifespan up to 24 h if TMP ≥ 150 mmHg because of the decrease in solute removal efficiency.

Abbreviations

CRRT
continuous renal replacement therapy; AOD:access outflow dysfunction; BUN:blood urea nitrogen; RCA:regional citrate anticoagulation; LMWH:low-molecular-weight heparin; CVVHDF:continuous veno-venous hemodiafiltration; CVVH:continuous veno-venous hemofiltration; AOP:access outflow pressure; PFP:pre-filter pressure; EP:effluent pressure; RIP:return inflow pressure; SOFA:sequential organ failure assessment score; ECF:extracorporeal circuit failure; KDIGO:Kidney Disease:Improving Global Outcomes

Declarations

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Authors' contributions

All of the authors agree to the submission of this paper. L.Z., as the corresponding author of this paper, was mainly responsible for program design and modification. P.L., L.L., X.T., M.G., T.W., L.C., were involved in this clinical trial and vouch for the adherence of the trial to the protocol, for the accuracy of the data. P.L conducted the statistical analysis and wrote the first draft. All of the authors reviewed, revised, and approved the final version of the manuscript.

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Availability of data and materials

The data that support the findings of this study are not available due to the clinical study report being finalized. However, the data will be available from the authors upon reasonable requests at a later time.

Ethics approval and consent to participate

The trial was approved by Institutional Review Board of West China Hospital, Sichuan University(2017-06). Informed consent was obtained from either the patient or from the patient's legally authorized representative if the patient was unable to provide consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1. Demographic and laboratory features of patients and the extracorporeal circuit

Age (years)	56.7±14.0
Sex (male/female)	86/45
SOFA score	14±2
Diagnosis	
Respiratory disease	33
Cardiovascular disease	30
Digestive diseases	43
Neurological disorders	5
Sepsis	20
Episodes of CRRT	395
Extracorporeal circuit lifespan	41.1±24.8 h
Use of anticoagulation	(%)
LMWH/unfractionated heparin	80 (20.3%)
Regional citrate anticoagulation	192 (48.6%)
No anticoagulation	123 (31.1%)
Reason for changing extracorporeal circuit	
Clotting of air-trap chamber	38 (9.6%)
Programmed change	96 (24.3%)
Vascular access	
Right femoral veins	227 (57.4%)
Left femoral veins	141(35.8%)
Internal jugular vein	27 (6.8%)
CVVH	74 (18.7%)
CVVHDF	321 (81.3%)
Dose of CRRT (ml/kg/h)	31.4±3.1
Hemoglobin (g/L)	85.0±19.0
Platelet (*10^9/L)	113.0±89.4
INR	1.5±0.6
APTT, s	45.1±21.7

Table 2 Pressure Data of different extracorporeal circuit failures

	Early ECF	Intermediate ECF	Late ECF
AOP, mmHg	-86.37±13.03	-67.69±8.20	-62.87±2.31
AOP variability, mmHg	37.73±23.28	20.31±14.33	13.79±10.21
PFP, mmHg	133.43±21.95	150.47±28.09	104.91±3.89
PFP variability, mmHg	32.86±12.33	37.89±15.20	12.67±8.12
EP, mmHg	-3.52±26.07	-13.49±25.03	-4.30±6.44
EP variability, mmHg	26.05±13.73	37.04±15.60	15.91±9.81
RIP, mmHg	55.82±7.25	61.22±7.74	46.37±1.11
RIP variability, mmHg	14.88±8.39	15.53±9.14	9.97±5.99
TMP, mmHg	98.12±34.48	120.15±38.89	80.79±8.11
TMP variability, mmHg	32.40±16.12	46.40±20.75	14.38±11.64

Table 3 Comparisons between the Intermediate and Late groups

	Early-intermediate ECF N =134	Late ECF N =261	P value
Lifespan of extracorporeal circuit (h)	14.02±5.73	55.42±16.24	<0.001
With AOD	83 (61.9%)	142 (54.4%)	0.22
With mild AOD	54 (40.3%)	121 (46.4%)	0.34
With M-S AOD	30 (22.4%)	21 (8.0%)	<0.001
Hemoglobin	82.67±18.04	86.23± 19.40	0.17
Platelet (*10^9/L)	133.46±84.86	102.67±90.11	0.011
PT, s	16.93±6.07	17.85±14.42	0.58
INR	1.54±0.54	1.51±0.74	0.73
APTT, s	41.48±19.26	45.55±24.40	0.20
Modality (CVVHDF)	85 (63.4%)	236 (90.4%)	<0.001
Vascular access (femoral)	129 (96.3%)	239 (91.6%)	0.14
Location of femoral vein (right)	79 (61.2%)	132 (55.4%)	0.38

Table 4 Cox regression analysis of variables associated with shorter circuit survival

Variables	HR (95%CI)	P value
Regional citrate anticoagulation	0.391 (0.293 0.521)	<0.001
Moderate-severe AOD	1.893 (1.300 2.756)	0.001
Hemoglobin>85 g/L	0.819 (0.631 1.063)	0.134
Platelet>110*10^9/L	1.168 (0.902 1.513)	0.239
CVVHDF	0.546 (0.376 0.793)	0.001

Figures

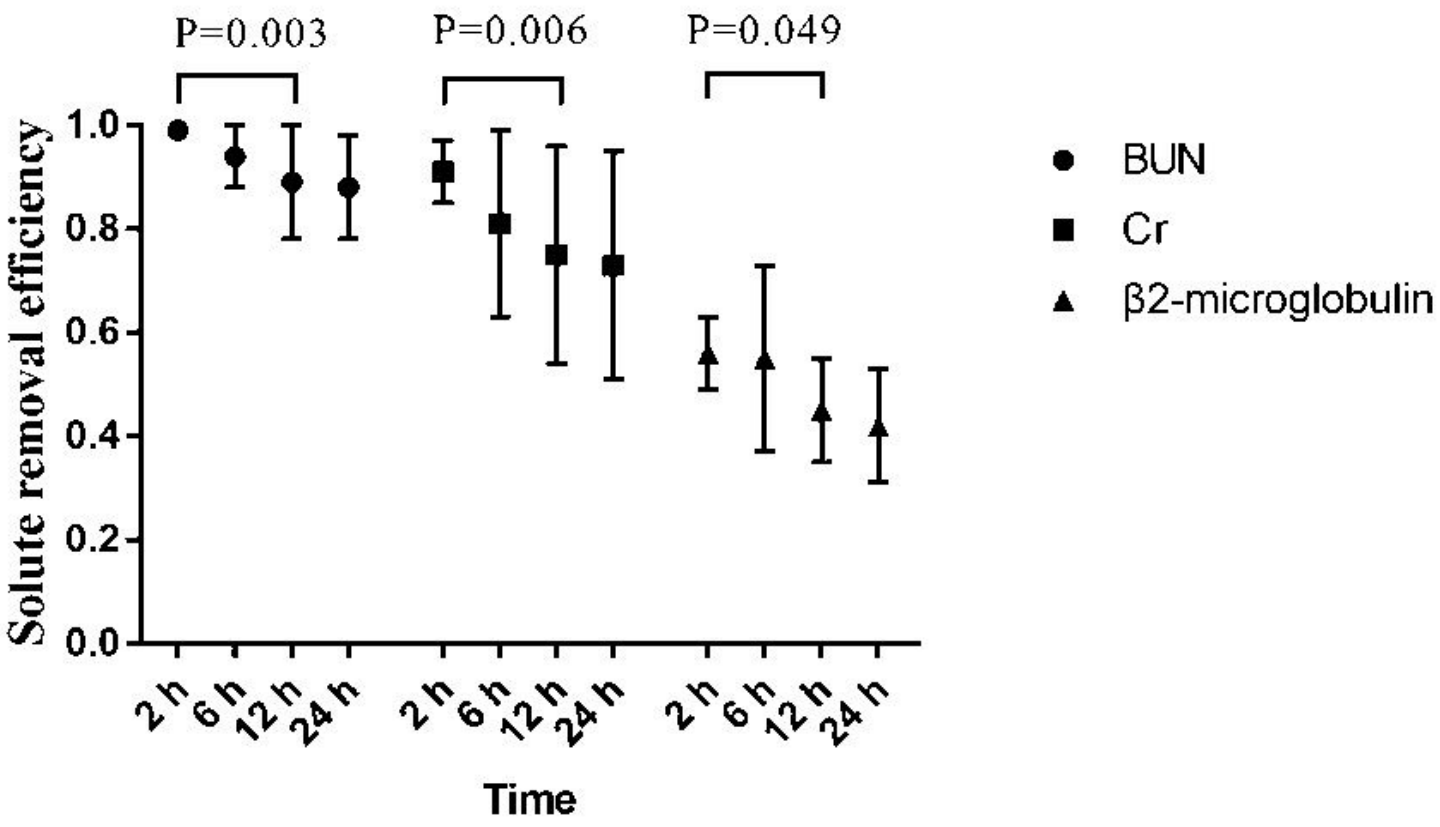

Figure 1

Numbers of CRRT Episodes Enrolled in the Study, Assigned to different extracorporeal circuit failures Group, and Included in the Analysis

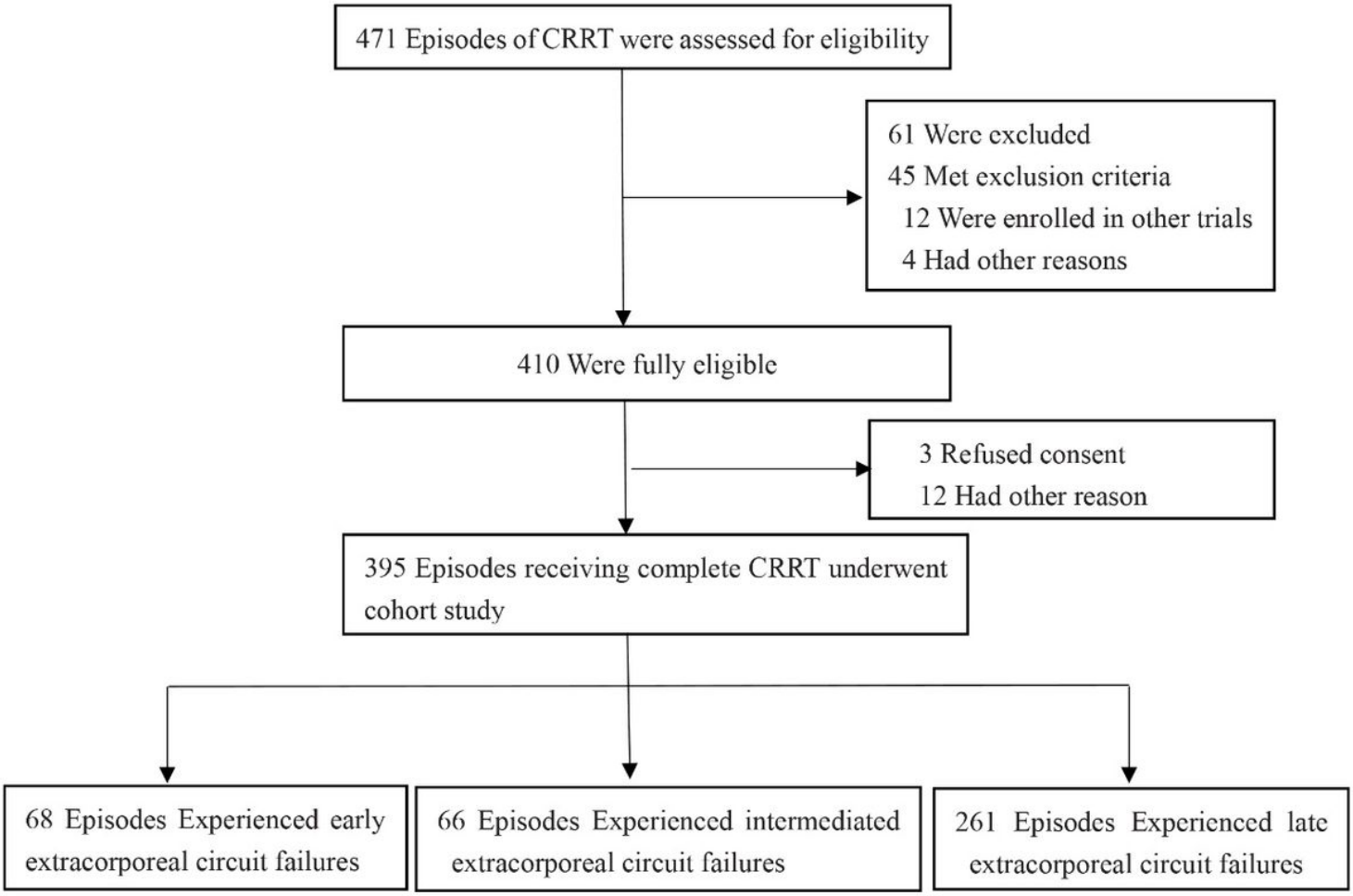

Figure 2

Dynamic mean pressure curve of every minute over time by early, intermediate and late extracorporeal circuit failures. Shaded areas = 95% confidence of the mean. Lifespan of the early group ended at 11 h, the intermediate group ended at 23 h, and the late group ended at 24 h. AOP, PFP, EP, RIP and TMP are the average values of each pressure minute.

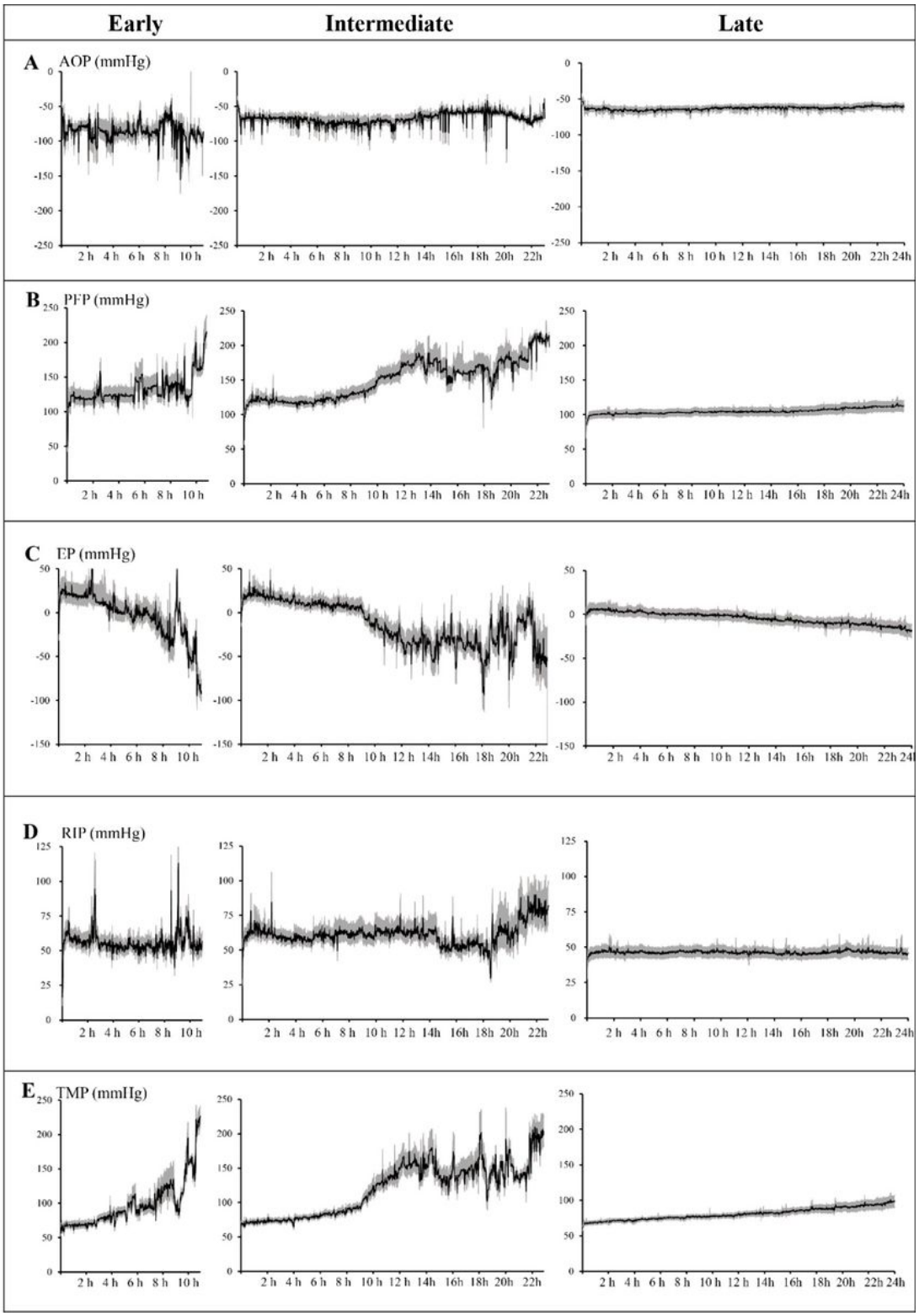

Figure 3

Circuit lifespans with different patterns of AOD events

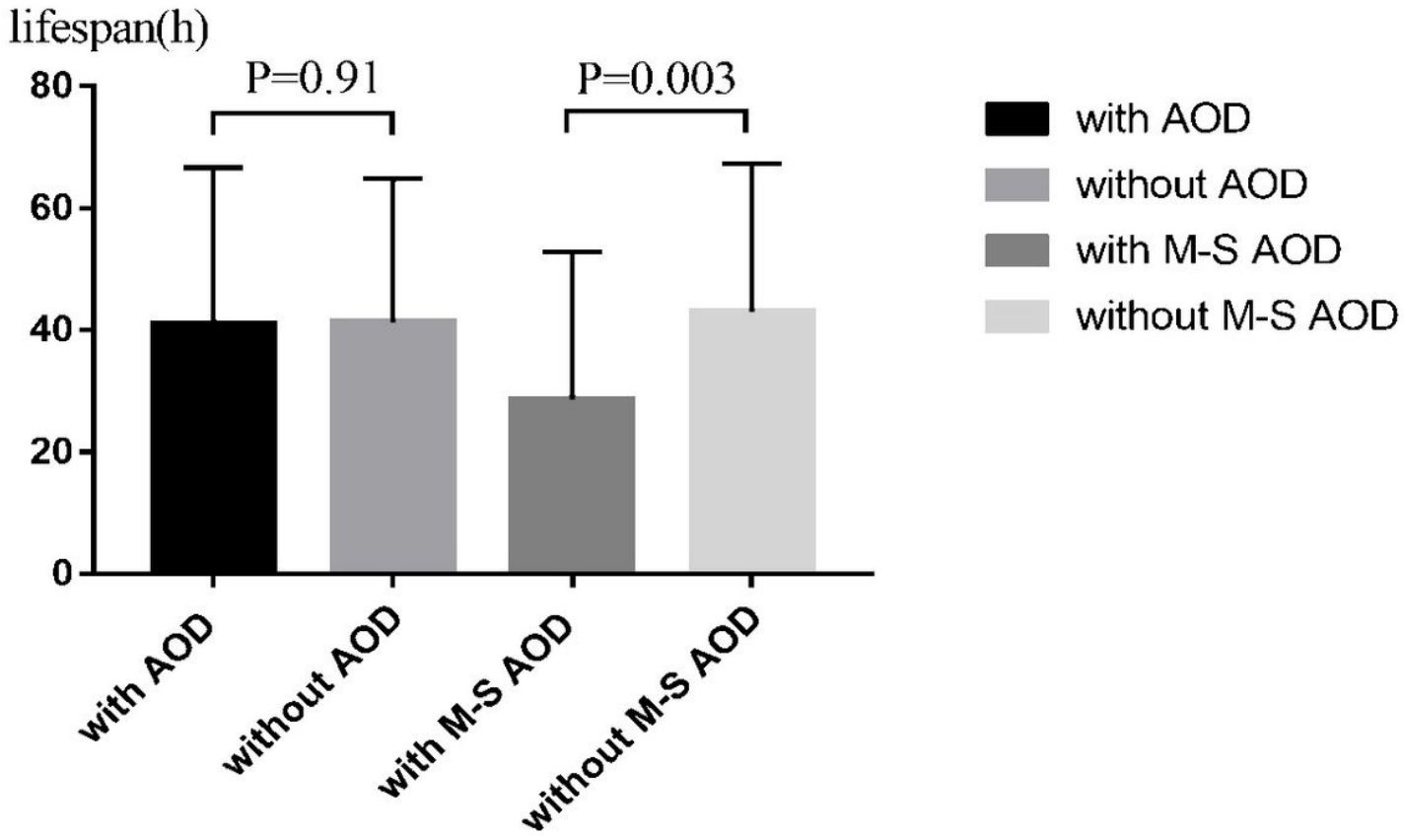

Figure 4

Lifespan of extracorporeal circuits that experienced M-S AOD events in various anticoagulation conditions

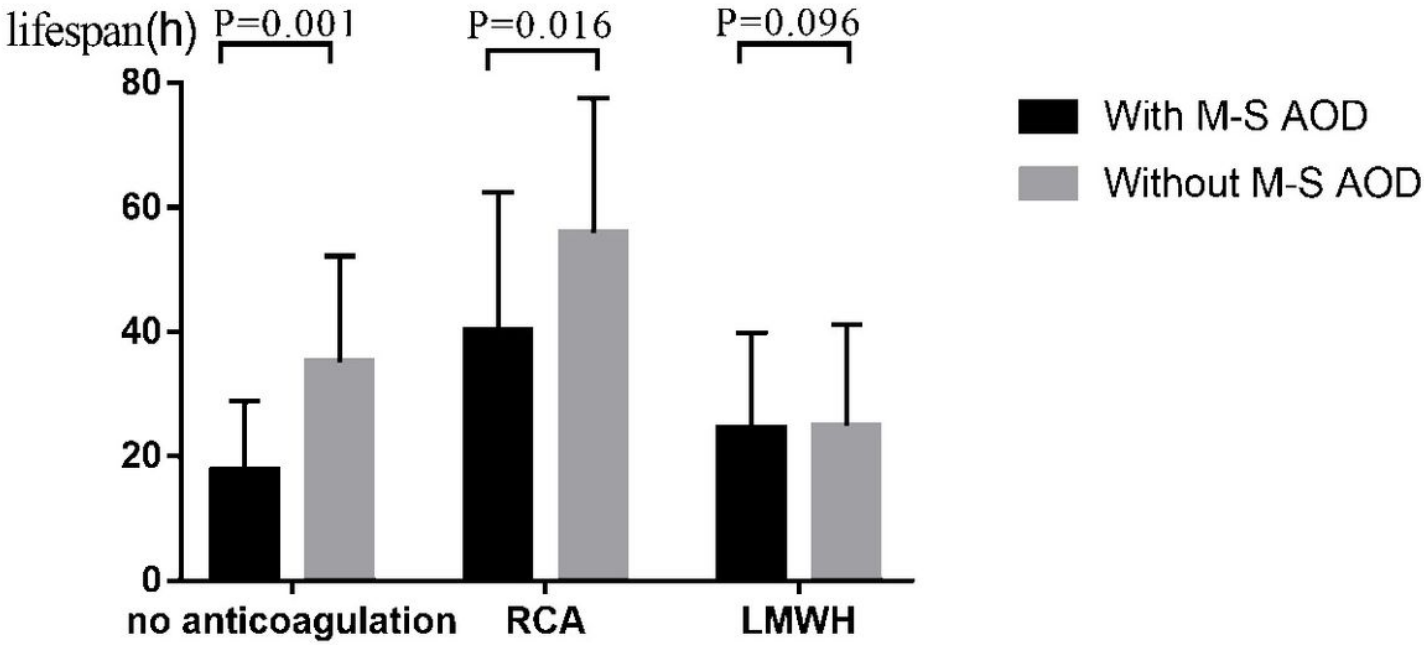

Figure 5

Solute removal efficiency at different time

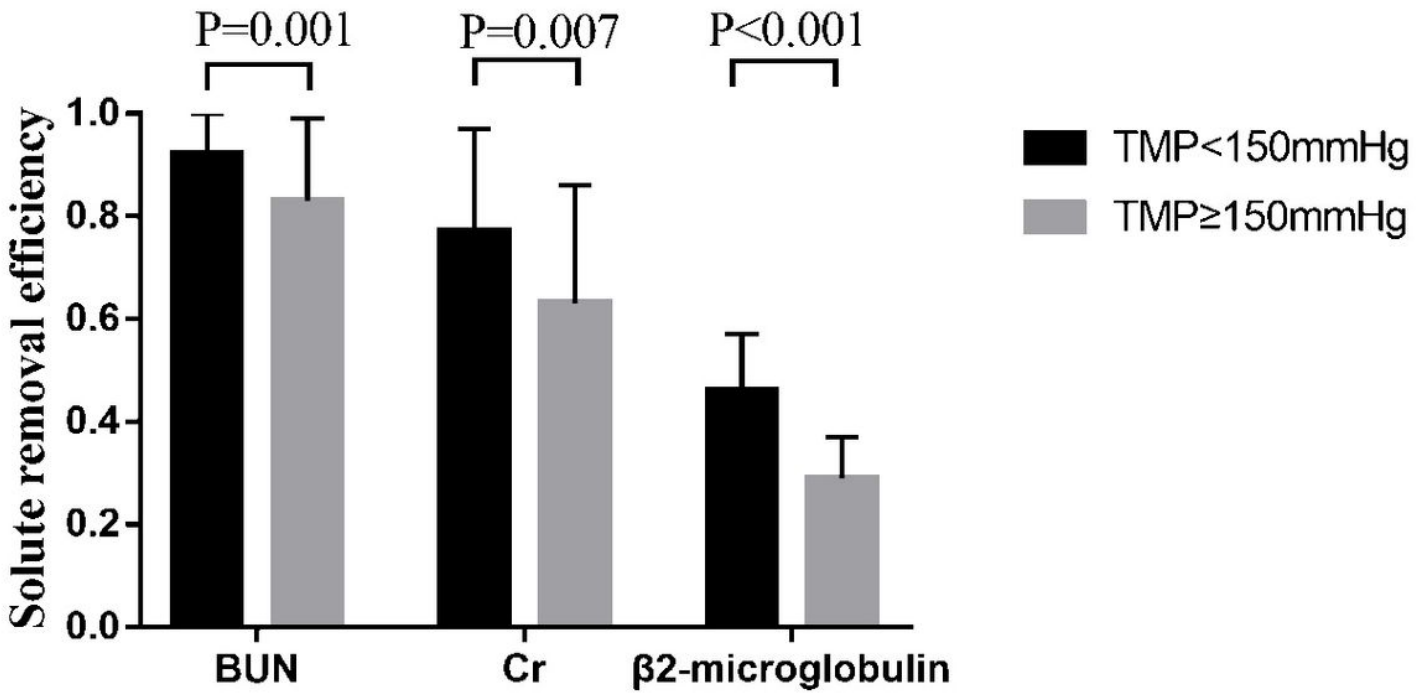

Figure 6

Solute removal efficiency in different TMPs groups at 24h