Risk Factors for Artificial Kidney Failure During Continuous Renal Replacement Therapy

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Abstract: **Objective** To explore the influencing factors of artificial kidney failure (AKF) during continuous renal replacement therapy (CRRT). **Methods** We conducted a retrospective observational study on 70 patients undergoing 199740 minutes of CRRT comprising 143 circuits at the Department of Intensive Care Medicine of First Affiliated Hospital of Chongqing Medical University from August 2021 to August 2022. **Results** The occurrence rate and total time of access outflow dysfunction (AOD) in AKF group increased significantly than those in nAKF group. Receiver Operating Characteristic (ROC) Curve analysis showed the optimal cutoff value of AOD total time (AODTT) was 7 minutes. Logistic regression analysis further showed that AODTT≥7 min was an independent predictor of AKF. **Conclusion** The presence of AOD was related to AKF. AODTT≥7 min during CRRT was an independent risk factor for AKF.

Keywords: Continuous Renal Replacement Therapy; Artificial Kidney Failure; Access Outflow Dysfunction

Introduction

Continuous renal replacement therapy (CRRT), which can continuously and slowly remove extra water and solutes retained, has become an effective multiple organ support therapy, widely used to manage renal and extra-renal problems such as fluid overload or severe acidosis in intensive care unit (ICU)[1]. However, CRRT prescription is not always fully delivered. Many factors could hinder CRRT delivery generating a gap between prescription and delivery. Maintaining extracorporeal circuit (ECC) function is important for safe and effective CRRT delivery[2]. ECC includes a double-lumen catheter, its vascular access outflow and inflow lumen, filter, pre-filter and post-filter tubing, air-trap chamber and pre-vascular inflow tubing. When dysfunction occurs at any part of the ECC, it can cause the failure of the entire artificial kidney (AKF)[3], leading to unexpected treatment interruptions, inefficient blood purification, blood loss, more waste and cost[4].

CRRT modality, dilution type, anticoagulation mode and catheter function highly influence ECC life[5,6]. Modern CRRT equipment can automatically monitor circuit pressure at intervals of 1 minute, including access outflow pressure (AOP), pre-filter pressure (PFP), effluent pressure (EP) and return inflow pressure (RIP)[7]. The transmembrane pressure (TMP) can be estimated by the following formula: TMP=(PFP+RP)/2-EP[8]. Automated monitoring circuit pressure at different points during CRRT may contribute to early identify where and how ECC dysfunction occurs, prompt to modify the settings, avoid unplanned CRRT interruptions or avoidable downtime[9]. The current study aims to explore the influencing factors of AKF during CRRT.

1. Materials and methods

1.1 Study subjects

We conducted a retrospective observational study of patients who underwent CRRT in the Department of Intensive Care Medicine of the First Affiliated Hospital of Chongqing Medical University from August 2021 to August 2022. The exclusion criteria were as follows: CRRT connected to an ECMO circuit, pressure data could not be obtained and incomplete data. Due to its retrospective observational nature, written informed consent was not required.

1.2 Data collection

General information including age and sex, and CRRT-related parameters were collected. Pressure of extracorporeal circulation circuit during CRRT was downloaded, decompressed and extracted.

1.3 Definition

AKF was defined by the following criteria: 1)TMP ≥ 450mmHg, blood does not return due to complete clotting of filter; 2)TMP ≥ 250mmHg in hour prior to circuit cessation; 3)AP and RP extremes (AP≤-250mmHg or RP≥+350mmHg in hour preceding circuit cessation)[10]; 4) unscheduled CRRT cessation due to dysfunctional ECC. Access outflow dysfunction (AOD) was defined as AOP<-200mmHg[3].

1.4 Statistical analysis

Statistical analysis was performed using SPSS 26.0 statistical software. All numeric data with a normal distribution were presented as means±SD and analyzed using Student's t-test. Numeric variables with skew distribution were expressed as median (interquartile range) and compared using Mann-Whitney U test. Categorical variables were expressed as percentages and analyzed using chi-square test. Receiver-operating characteristic (ROC) curve analysis and binary logistic regression analysis were conducted to predict risk factors for AKF. $P<0.05$ was considered statistically significant.

2. Results

2.1 Changes of CRRT-related parameters

In total, 70 patients including 98 males and 45 females aged 14–90 years, undergoing 199740 min of CRRT comprising 143 CRRT circuits were enrolled in this study. According to whether AKF occurs, CRRT circuits were divided into AKF group and nAKF group. We explored the risk factors for AKF and found significantly increased AOD occurrence and AOD total time (AODTT) in the AKF group compared with the non-AKF group ($p<0.05$). No differences in CRRT modalities, anticoagulation mode, vascular access and dilution mode were noted between the two groups (Table 1).

Table 1 Comparison of CRRT-related parameters in AKF group and nAKF group

	nAKF (n=94)	AKF (n=49)	*P*
Modality			
CVVHDF	84(89.36)	41(83.67)	0.33
CVVH	10(10.64)	8(16.33)	
Anticoagulation			
Citric acid	75(79.79)	44(89.80)	0.07
Low molecular weight heparin	16(17.02)	2(4.08)	

Non-anticoagulant	3(3.19)	3(6.12)	
Dilution			
Post-dilution (CVVHDF)	84(89.36)	41(83.67)	0.33
Pre- and post-dilution (CVVH)	10(10.64)	8(16.33)	
Vascular access			
Internal jugular vein	5(5.32)	1(2.04)	0.35
femoral vein	89(94.68)	48(97.96)	
AOD	51(54.26)	39(79.59)	0.00
AOD total time	1(0,7)	17(1,55)	0.00

2.2 Risk factors for AKF during CRRT

Because longer AODTT was found to be associated with AKF, we performed ROC analysis to assess the predictive value of this variable for AKF. The area (95% CI) under ROC of AODTT to predict AKF was 0.69 (0.57~0.80). The optimal cutoff value, sensitivity and specificity of AODTT were 7 min, 65% and 77%, respectively. Logistic regression analysis further showed that AODTT≥7 min was an independent predictor of AKF (P<0.05).

Table 2 Independent risk factors for AKF during CRRT

	P	OR	95% CI
Presence of AOD (versus absence)	0.91	1.07	0.35 ~ 3.28
AODTT≥7min (versus<7min)	0.00	5.44	1.78~ 16.65

3. Discussion

Today, CRRT has been widely used in critically ill patients to optimize fluid and solutes management[11]. Maintaining ECC patency and filter performance is crucial to ensure CRRT delivery in a safe and high-quality manner[3]. In fact, dysfunctional vascular access and ECC clotting remain the main reasons for unscheduled treatment cessation and circuit replacement, which may reduce CRRT efficacy, increase blood loss, workload and costs[9]. Early identifying risk factors for AKF might help to adjust settings, increase circuit life and efficiency.

Vascular access plays a significant role in determining ECC life. Catheter bending, collapse of a central vein around the catheter, and sudden catheter position changes usually leading to intermittent occlusion, and progressive thrombus or fibrous sheath in the lumen of a catheter, inducing circuit blood flow rapid decrease or even flow cessation were reported to be related to shortened circuit life[12]. Baldwin et al. used ultrasound to monitor circuit blood flow and found that blood flow reductions occurred frequently without machine alarms alerting the operator, and then no corrective responses were made, eventually inducing stasis and circuit failure[13]. Automated electronic monitoring ECC pressure at different points is helpful for early identifying vascular access dysfunction, making corrective response, and then preventing AKF. We found 62.94% circuits experienced AOD similar to 56.96% reported by Zhang et al.[9]. It is reported AOD events could shorten circuit life[3], our study also showed the occurrence of AOD in circuits with AKF (79.59%) was higher than circuits without AKF (54.26%). We further found total time of AOD in AKF group increased significantly than those in nAKF group, and AODTT≥7 min was an independent risk factor for AKF, suggested an alarming level of AODTT≥7 min could be set to alert the operator, then make corrective response to prevent circuit failure. However, this is a single center, retrospective observational study, further multicenter prospective randomized controlled studies are needed to corroborate our findings.

CRRT-related parameters including treatment modality, dilution and anticoagulation modes, and vascular access sites are also related to circuit life. It is reported CVVHDF/CVVHD provided longer filter life compared to CVVH[14,15]; the filter life in Pre-dilution CVVH might be longer than post-dilution CVVH because the blood is diluted prior to entry into the

filter[12]; citrate anticoagulation (RCA) might improve filter life compared with systemic heparin anticoagulation[16]. Whereas, our study included 87.41% circuits in CVVHDF with post-dilution group, only 18 (12.59%) circuits in CVVH with pre-dilution and post-dilution group, no circuit in CVVH with post-dilution group; 83.22% circuits in RCA group, only 18(12.59%) and 6 (4.2%) circuits in low molecular weight heparin group and non-anticoagulant group, respectively, we didn't find significant differences between AKF group and nAKF group in CRRT treatment modality, anticoagulation and dilution mode. A study showed better filter life with femoral vein access compared with internal jugular vein and subclavian vein catheterization; no difference was detected between internal jugular and subclavian vein catheterization[17]. However, no difference in catheter dysfunction rates was found between femoral and internal jugular sites[18].This study included 95.81% circuits in femoral vein group, only 6 circuits in internal jugular vein group and no circuits in subclavian vein group, showed no significant difference between AKF group and nAKF in vascular access sites. We need to enlarge sample size to further explore risk factors for AKF.

In summary, this retrospective observational study showed that the presence of AOD was related to AKF, and AODTT≥7 min was an independent risk factor for AKF.

Funding

This study was supported by grant from Clinical Medicine Postgraduate Joint Training Base of Chongqing Medical University-the First Affiliated Hospital of Chongqing Medical University (lpjd202001).

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