

Comparison of citrate anticoagulation strategies in hemodialysis patients at high risk of bleeding: a multicenter prospective observational cohort study

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Abstract

Background

To explore the effect of different citrate anticoagulation strategies and provide reference for prospective large sample RCT, we collected RCA strategies from different centers systematically and prospectively to compare the effectiveness and safety of different RCA strategies in hemodialysis (HD) patients.

Methods

A prospective observational cohort study was conducted in eight centers in Sichuan, China. RCA strategies were divided into three groups: RCA-one (Prefilter trisodium citrate infusion only); RCA-two (pre and post filter trisodium citrate infusion); RCA + saline (Prefilter trisodium citrate and post filter normal saline infusion). The blood flow ranged from 150–260 ml/min and citrate was infused at a rate of 180–260 mL/h.

Results

Totally 195 patients with 481 sessions of RCA were enrolled, including 141 patients, 337 sessions in the RCA-one group, 51 patients, 133 sessions in the RCA-two group and 3 patients, 11 sessions in the RCA + saline group. The proportion of complete scheduled dialysis time was 97, 99.7 and 97.7% ($p = 0.037$) in three groups respectively, the majority of the adverse events were hypotension (5.5%), muscle cramps (0.8%), and access dysfunction (2.0%), most of which were mild in intensity. Blood coagulation score < 3 in venous expansion chamber were 83.1, 94.6 and 70%, respectively ($p < 0.001$). Blood coagulation score < 3 in dialyzer were 95.3, 96.1 and 90%, respectively ($p = 0.83$). Serum calcium levels before the venous line in RCA-two was significantly decreased at 2 h after treatment ($p = 0.03$). The serious clotting score (= 3) in venous expansion chamber in the RCA-two group was significantly lower than the RCA-one and saline group ($p < 0.001$). RCA-two had the lowest percentage of adverse events including hypotension ($p = 0.023$) and muscle cramps ($p = 0.001$) than other groups.

Conclusion

Citrate anticoagulation is safe and effective in general hemodialysis. Our study shows no significant difference in the circuit survival time among the three administrative strategies of citrates. Administration of citrate to both arterial and venous line appeared to provide better anticoagulation of intravenous jug and had the lowest percentage of adverse events.

Background

In recent years, regional citrate anticoagulation (RCA) has become an appealing alternative since it provides excellent anticoagulation without increasing the risk of bleeding and significantly reduced the occurrence of coagulation in the system and filter during therapy. The advantages of citrate anticoagulation have been reported in continuous renal replacement therapy,[1–5] including longer circuit survival, reduced bleeding risk, improvements in the biocompatibility of the hemodialysis procedure by reducing leukocyte[4, 6], platelet[6] and complement activation[7] in addition to the better inhibition of coagulation cascade, and possible improvement of patient mortality[8, 9]. A meta-analysis conducted in adult critically ill patients with acute kidney injury receiving CRRT found out that RCA is more efficacious in prolonging circuit life span and reducing the risk of bleeding as compared with heparin anticoagulation[10].

Citrate inhibits coagulation and reduces platelet deposition on the dialyzer membrane by depletion of Ca^{++} - factor IV, its anticoagulant effects is safe, immediate, complete, and limits to the dialysis circuit. The dose of citrate is calculated based on the percentage of blood flow and adjusted according to post-dialyzer ionized calcium, with the target range of 0.2–0.4 mmol/l[11].

Usually an adequate amount of Ca^{2+} should be supplemented back to the systemic circulation according to the amount of imported trisodium citrate (TSC). A number of reported RCA protocols lack standardization and can hardly be performed in other dialysis centers because they largely depend on local policies and procedures[12]. Several studies have shown the effectiveness of RCA during intermittent HD procedures. RCA using Ca-free dialysate revealed no serious clotting events, however, serum calcium level needs to be closely monitored as hypocalcemia can occur and Ca^{2+} supplementation is required, resulting in limiting its clinical application[13–15].

Many centers have reported that the calcium infusion rate needs to be adjusted based on repeated measurements of ionized calcium concentrations both in vivo and in an extracorporeal circuit, which increases the complexity and workload of the practice of RCA. It is critical to further explore a superior and simplified anticoagulation approach to achieve both effectiveness and feasibility. The objective of this multicenter study was to compare the efficacy and safety of different administrative strategies of RCA in HD patients with a high bleeding risk.

Methods

Study Design and Patients

A multicenter prospective observational cohort study was conducted at the Center of Sichuan Provincial People's Hospital, Shenzhen Hospital, Peking University, Chengdu Third People's Hospital, Dechang County People's Hospital, the First Affiliated Hospital of Chengdu Medical College, Guanghan People's Hospital, Chengdu First People's Hospital and the First Hospital of Peking University. This study was approved by the Ethics Committee of each hospital. All study components were performed according to

the ethical standards established in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all subjects prior to enrollment and participation.

Based on different anticoagulation protocols patients were divided into the following three groups: RCA-one group (Only arterial line was administered with 4% trisodium citrate, including 141 patients, 337 sessions), RCA-two group (one-quarter of the TSC was transferred from the prefiltered to the post filter based on RCA-one, including 51 patients, 133 sessions), RCA+saline group (arterial line was administered with 4% trisodium citrate, and venous line was administered with saline at a speed of 50 ml/h, including 3 patients, 11 sessions)(Fig 1). The blood flow ranged from 150–260 ml/min and citrate was infused at a rate of 180-260mL/h, without regular calcium gluconate supplement in the venous segment. In addition, one-quarter of the total TSC was imported from the artery line to the venous bubble trap in RCA-two group, RCA+saline group received an extra of 0.9% saline supplement at a speed of 50 mL/h in the venous segment.

Inclusion and excluded criteria

Eligible patients were (1) patients aged 18–70 years and (2) patients who could not receive systemic anticoagulation due to high risk of bleeding [16]. Excluded criteria were patients contraindicated for RCA including those with severe liver failure, hypoxemia, shock, and lactic acid poisoning.

Hemodialysis parameters and coagulation score

Blood gas analysis including Na^+ , K^+ , Ca^{2+} , pH, bicarbonate levels for monitoring HD with RCA was analyzed every 2h in point A, B, C (Fig 1). The pre-dialyzer iCa concentration was measured to assess individual situation, with a desired target range from 0.2 - 0.5 mmol/l. Calcium infusion was adjusted in a timely manner based on repeated measurements of calcium concentration.

The hypercoagulable state of plasma separator and vein ampulla coagulation after treatment were divided into 4 classes based on previous reports [16, 17]: Class I (score=0), Class II (score=1), Class III (score=2), and Class IV (score=3). Citrate dose and calcium gluconate infusion during treatment were adjusted based on iCa level measured at point A and B (Table 1).

Outcomes definition

The primary outcome was circuit survival time (the lifetime of the circuit survival was limited to 240 min). The secondary outcomes included clotting scores. We set up the observation queue database of RCA, adopted a unified coagulation evaluation standard, and carried out on-site and remote training to ensure the reliability and consistence of the protocol and data.

Data collection, sample processing

On-site and remote RCA dialysis technique trainings, including nursing performance, blood gas analysis, coagulation evaluation and database recording were carried out in all participating centers to ensure the

reliability and consistency of the data. Clotting score, dialysis time, adverse events were recorded in the RED Cap database with unified coagulation evaluation standards as required by the attending nurse. At the end of the dialysis session, arterial and venous drip chambers and the filter were inspected by the nurse for visible signs of coagulation. Determination of iCa^{2+} and blood gas analysis at all time points were drawn into heparinized syringes and processed at the bedside.

Statistical analysis

Continuous variables were expressed as the mean \pm SD and categorical variables as absolute and relative frequencies. The student t test was performed to calculate the differences between continuous data of normal distribution, and the Wilcoxon rank sum test or Kruskal-Wallis H test was performed to calculate differences between quantitative data of non-normal distribution. The chi-square test or Fisher's exact test was performed to calculate differences between qualitative data. Kaplan-Meier curves and the log-rank test were used to analyze and compare length of circuit survival time. Cox hazard regression model was used to evaluate the influencing factors of time to clot in three strategies. A p value <0.05 was considered to indicate statistical significance. All statistical analyses were done with SPSS version 19.0.

Results

Patients and baseline characteristics

Between Sep 10, 2017 and June 6, 2018, a total of 195 patients (114 male and 81 female) aged 58.7 ± 16.5 years (range 18–70 years) were included from eight centers. Baseline characteristics and baseline laboratory analyses were generally similar among the groups (Table 2). Patients in RCA+saline group were much older, had more male patients, high amount of diabetes, hypertension, coronary heart disease, cerebrovascular disease, connective tissue disease and Vascular calcification, however, there were very few patients in this group than those in RCA-one and two group. Anemia and thrombocytopenia were most serious/or more common in RCA-one group. No significant differences existed about the reasons for dialysis without heparin including surgery, bleeding, trauma, laboratory abnormalities had between RCA-one and two group, while saline group patients were all contradicted for systemic heparin anticoagulation due to active bleeding or high risk of bleeding.

Efficacy of RCA

Total clotting scores and Circuit survival time

RCA-two group had the highest dose of 4% trisodium citrate in arterial expansion chamber than RCA-one and saline group, while no significant differences in the total dose of trisodium citrate among three groups. The complete scheduled dialysis rate was 99.7% in the RCA-two group, which was significantly higher than the RCA-one and saline group ($p=0.037$) (Fig.2). Estimation of the degree of clotting by calculating the clotting score at the end of dialysis were shown in Table 3. The serious clotting score ($= 3$) in any position (dialyzer, venous expansion chamber) in the RCA-two group were lower than the RCA-one

and saline group. Blood coagulation score <3 in venous expansion chamber were 83.1, 94.6 and 70%, respectively ($p < 0.001$). Blood coagulation score <3 in dialyzer were 95.3, 96.1 and 90%, respectively ($p = 0.83$). These findings indicated that RCA-two could effectively maintain the patency of system and filter during extracorporeal circulation and anticoagulant effect was especially remarkable in venous expansion chamber. Kaplan-Meier analysis showed that there were no significant differences in the circuit survival time among the three groups (Fig.2).

Comparison of Blood Gas Analysis, PH, Ca²⁺, Na⁺ at Different Time Points

As shown in Fig 3, there was no statistically significant change in PH, Ca²⁺, Na⁺ level before and after treatment ($p > 0.05$). Compared with pretreatment, PH and Na⁺ level was increased at 2 and 4 h after treatment, Ca²⁺ level before the venous line in RCA-two was significantly decreased at 2 h after treatment ($p = 0.03$). No serious acid-base imbalance, electrolyte disorder and citrate accumulation were observed.

Cox proportional hazard analysis

Univariable Cox proportional hazard analysis showed that anticoagulation choice (HR 1.038, $P = 0.001$), vascular calcification (HR 0.156, $P = 0.068$), dialysis access (HR 1.704, $P = 0.094$), blood flow (HR 0.985, $P = 0.014$), total dose of 4% trisodium citrate (HR 0.998, $P < 0.001$), haemoglobin (HR 1.018, $P = 0.003$), hematocrit (Hct) (HR 1.031, $P = 0.011$) and cholesterol (HR 1.334, $P = 0.038$) were associated with circuit survival time. According to the univariate analysis we included the above eight potential variables that might affect extracorporeal circuit survival time into the multivariate analysis and found that anticoagulation choice (HR 6.773, $P = 0.014$), total dose of 4% trisodium citrate (HR 0.995, $P < 0.001$) and cholesterol level (HR 1.704, $P = 0.007$) significantly affected circuit survival time (Table 4).

Safety outcomes

Adverse events (AEs) are summarized in Table 5. During the course of this study, the majority of the AEs were hypotension (5.5 %), muscle cramps (0.8%), and access dysfunction (2.0%), most of which were mild in intensity. No serious acid-base imbalance and electrolyte disorder were observed. RCA-two had the lowest percentage of adverse events than other groups ($p = 0.001$).

Discussion

The basic principle of RCA is to reduce the level of ionized calcium in the extracorporeal circuit via infusion of citrate. This way, effective anticoagulation restricted to the extracorporeal circuit is achieved. RCA has been reported significantly prolonged filter lifetime, reduced bleeding complications and provided excellent control of uremia and acid-base status[18]. The 2012 Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for AKI suggest RCA as the preferred anticoagulation approach for CRRT in patients without contraindications for citrate. There is a growing body of evidence that RCA compared to heparin may reduce bleeding complications and transfusion requirements while

prolonging filter lifetime. However, there are limited reports on the effect, safety, and unified operation about RCA in HD with small samples in single center[19]. To explore the effect of different strategies and provide reference for prospective large sample RCT, this study collected RCA strategies from different centers systematically and prospectively to compare the effectiveness and safety of different RCA strategies in HD anticoagulation.

There are a number of different protocols in administration of citrates[3, 4, 11, 15, 18–25]. In most cases, citrate and calcium are administered separately, with citrate being infused prefilter, and calcium being infused postfilter. Some protocols suggest a fixed citrate-to-blood flow ratio, which to some extent simplifies RCA management[25]. To simplify calcium delivery during HD, we unified RCA strategy with calcium-containing dialysate from eight centers. Both RCA-one and two appeared safe and effective, however, serious clotting in the venous expansion chamber usually occur in 40% of RCA in one arm[13, 14, 21], the concentration of iCa^{2+} is particularly high in the venous bubble trap, which would be the key point of clotting[22], this is consistent with previous studies that only administration of citrate to arterial line during HD resulted in significant clotting (up to 40%) in the venous bubble trap[26, 27]. Therefore, we have transferred one quarter of the TSC from the prefiltered to the post filter based on RCA-one with calcium-containing dialysate, which is called RCA-two in this trial.

In this multicenter, prospective, observational clinical study, we found that I–II clotting class accounted for 83.1, 94.6 and 70% in venous line of the three strategies, respectively, and I–II clotting class accounted for 95.3, 96.1 and 90% in dialyzer of the three strategies, respectively. This suggested that RCA could effectively maintain the patency of extracorporeal circulation filter system, and anticoagulant effect was remarkable. Besides, Ca^{2+} levels before the venous line in RCA-two was significantly decreased at 2 h after treatment($p = 0.03$), demonstrating that RCA-two protocol in a Ca^{2+} -containing dialysate, was superior to either traditional RCA-one or RCA + saline in HD patients with a high bleeding risk, and has become increasingly used in patients in whom systemic anticoagulation is contraindicated.

In our study, the observed longer filter life and lower rates of circuit clotting associated with RCA are consistent with previously reported data[3, 24, 28–31]. Implementation of an RCA in a hemodialysis warrants compliance with protocol and intensive education of dialysis staff to minimize therapy-associated complications.

Citrate has little effect on systemic coagulation, and few bleeding complications have been reported[32]. However, use of citrate requires close monitoring for metabolic complications, mainly acid-base and electrolyte disturbance[20, 23]. In this study, all patients successfully completed the dialysis treatment. They maintained hemodynamically stable before and after treatment and no bleeding related complications were observed. No statistically significant changes regarding pH, Ca^{2+} , Na^+ levels before and after treatment were seen. No serious acid-base imbalance and electrolyte disorder were observed especially in RCA-two group, indicating the advantage of citrate anticoagulation.

This study has several strengths. First, our data are based on a large number of observations, close to 481 circuits from 8 centers have been evaluated, up to now this is the largest research to evaluate different RCA strategies in HD. Second, our center is ideal for evaluating RCA complications in real life since it is a large CRRT practice (> 100 patients treated per year) and a rich experience with RCA and a large number of nursing staff with an important turnover. Hence, our findings might apply to many similar-sized units and perhaps even to smaller ICUs. Thirdly, we uniformly applied the RCA protocol with an initial dose of 180–260 mL/h citrate solution in all patients in all included centers. The RCA protocol has strict algorithms for adaptations of citrate- and calcium dose and adherence to the protocol is put into practice by regular rounds of dialysis nurses and nephrologists to all patients several times a day in all included 8 centers.

Several limitations of our study need to be addressed. First, as an observational study, the results need to be validated in a large RCT. Secondly, in the current study, we have not collected long term data on effects of citrate use in hemodialysis patients. We would aim for following up the included patients for another 12 months to explore long term efficacy and safety of RCA anticoagulation protocol. Third, there is significant different number of patients involved among the three groups. For example, RCA + saline group included only 3 patients with 11 sessions, no blood gas analysis of pH, Ca²⁺, Na⁺ levels at different time points were recorded and there we were unable to compare these results with the other two groups. However, the cohort collected comprehensive information in a uniform method from real-world practice of RCA, which could be important for clinical trial designing.

Conclusion

In conclusion, our findings suggest regional citrate anticoagulation appears to be safe and effective mode of anticoagulation and should be considered as the first line anticoagulation method in heparin-free hemodialysis. Administration of citrate to both arterial and venous line (RCA-two) protocol appears to provide superior anticoagulation effect of intravenous jug and have the lowest percentage of adverse events. However, studies with larger sample sizes, and long term follow up duration are needed to assess the effects of citrate in hemodialysis patients and to assist in setting up a protocol for standardization of its use in dialysis units nationally and internationally.

Declarations

Ethics approval and consent to participate

Ethical approval of the study protocol was obtained from the institutional review boards of each participating hospital, including the Sichuan provincial people's Hospital, Shenzhen Hospital, Peking University, Chengdu Third People's Hospital, Dechang County People's Hospital, the First Affiliated Hospital of Chengdu Medical College, Guanghan people's Hospital, Chengdu first people's Hospital and the first hospital of Peking University. Informed written consent for the treatment they received will be obtained from all of the identified patients.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

The trial is conceived and designed by DQH, WHX, AL, BY, YX, SQW, XYZ, ZL, XHZ, DMW, ML, YL and LL collect all the data and manage the trial, SSC and MJX analyze the data and advise on statistical issues at the time of the trial write up. SSC and MJX take overall responsibility for communications during the trial and write the first draft of the report. DQH, AYW and QH monitor data and correct English writing and revise the protocol of this trial. JWZ and AYW contributed to critical review of the manuscript. All authors critical revise of the manuscript for important intellectual content. All authors read and approve the final manuscript.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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Tables

Table 1. Adjustment of citrate dose and calcium gluconate infusion during treatment based on iCa level measurements

At beginning:	
Blood flow	150–260 ml/min
4% Citrate dose	180-260mL/h
iCa level measurements:	iCa pre- and post-filter at baseline, end of treatment, 2 h after treatment,
Target iCa levels:	Dialysis access: >1.0 mmol/L, Pre-filter: 0.2–0.5 mmol/L
Dose adjustment	
iCa pre-filter (point B)	
⊗0.20mmol/L	decrease of effective citrate dose by 5ml/h
0.20-0.40mmol/L	Remain unchanged
0.41-0.50mmol/L	increase of effective citrate dose by 5ml/h
⊗0.50mmol/L	increase of effective citrate dose by 10ml/h
iCa dialysis access (point A)	
1.00-1.20mmol/L	Remain unchanged
0.90-1.00mmol/L	Administration of a 10 mL calcium gluconate base on symptoms of hypocalcemia
⊗0.90mmol/L	Administration of a 10 mL calcium gluconate

Table 2. Baseline demographic and kidney manifestations of patients with

	RCA- one(n=337)	RCA- two(n=133)	RCA+ saline(n=11)	p
Age – yr.	57.8±16.6	59.6±15.9	78.2±3.4	<0.001
n, % for male	57.4	68.2	81.9	0.030
Diabetes%	33.2	37.5	100	0.045
Hypertension%	72.6	89.7	100	<0.001
Coronary heart disease %	30.8	23.5	100	0.001
Cerebrovascular disease%	21.9	7.3	17.3	0.001
Connective tissue disease%	1.9	6.3	3.4	0.043
Vascular calcification%	15.5	21.6	17.6	0.17
Tumor%	6.1	16.4	9.6	0.003
Hemoglobin(g/L)	84.9±23.7	92.1±25.1	94.3±5.8	0.011
Hct%	26.9±7.8	26.7±12.2	29.8±3.4	0.556
Platelet(×10 ⁹ /L)	129.6±71.7	154.9±70.9	210.8±80.7	<0.001
PT(s)	14.5±12.7	13.8±9.5	10.2±0.1	0.736
APTT(s)	33.4±19.2	33.3±7.8	28.6±0.1	0.878
Triglycerides (mmol/L)	1.5±0.8	1.4±0.8	1.5±0.4	0.791
Cholesterol (mmol/L)	3.6±1.1	3.5±1.1	3.8±0.5	0.593
Access type-AV fistula, n/catheter, n ^{bc}	169/160	53/78	11/0	<0.001
Blood flow rate, median (IQR), ml/min ^{abc}	212.2±34.4	200.3±15.7	227.3±16.2	<0.001
The reason for dialysis without heparin				0.001
-surgery%	16.0	33.0	0	
-bleeding%	63.4	58.0	100	
-trauma%	11.6	5.0	0	
-laboratory abnormalities%	9.0	4.0	0	

^ap<0.05 between RCA-one and RCA-two; ^bp<0.05 between RCA-one and RCA+saline; ^cp<0.05 between RCA-two vs RCA+saline

Table 3. Comparison of efficacy of different methods of anticoagulation

	RCA-one(n=337)	RCA-two(n=133)	RCA+saline(n=11)	p
Dialysis time(h)	3.8±0.5	3.8±0.4	3.9±0.3	0.691
successfully completed rate%	97.0	99.7	97.7	0.037
4%trisodium citrate in arterial expansion chamber (ml/h)	223.4±46.3	172.2±43.8	213.6±15.0	<0.001
4%trisodium citrate in venous expansion chamber (ml/h)	-	54.2±19.7	-	
Total 4%trisodium citrate	833.3±199.5	826.4±274.5	733.0±262.4	0.376
Venous expansion chamber clotting score (%)				<0.001
0	19.0	60.8	0	
1	28.5	24.6	20.0	
2	35.6	9.2	50.0	
3	16.9	5.4	30.0	
Efficiency%	83.1	94.6	70.0	
Dialyzer clotting score (%)				0.83
0	51.5	57.4	40	
1	32.2	27.1	30.0	
2	11.5	11.6	20.0	
3	4.7	3.9	10.0	
Efficiency%	95.3	96.1	90.0	

^ap<0.05 between RCA-one and RCA-two; ^bp<0.05 between RCA-one and RCA+saline; ^cp<0.05 between RCA-two vs RCA+saline

Table 4. Influencing factors of time to clot in Cox proportional-hazards models

	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Anticoagulation choice	0.462(0.212-1.006)	0.052	6.773(1.480-30.997)	0.014
Sex	1.367(0.740-2.528)	0.318	-	-
Age	1.003(0.984-1.022)	0.765	-	-
Hypertension	1.811(0.706-4.647)	0.217	-	-
Diabetes mellitus	0.598(0.280-1.276)	0.184	-	-
Vascular calcification	0.156(0.021-1.145)	0.068		
Dialysis access	1.704(0.914-3.177)	0.094	-	-
Blood flow (ml/min)	0.985(0.972-0.997)	0.014	-	-
Total 4%trisodium citrate	0.998(0.997-0.999)	<0.001	0.995(0.993-0.997)	<0.001
Blood platelets($\times 10^9/L$)	1.001(0.997-1.005)	0.522	-	-
Hemoglobin(g/L)	1.018(1.006-1.029)	0.003	-	-
Hct%	1.031(1.007-1.056)	0.011		
PT(s)	0.982(0.929-1.038)	0.406	-	-
APTT(s)	1.005(0.987-1.023)	0.612	-	-
Triglycerides (mmol/L)	1.215(0.810-1.823)	0.347		
Cholesterol (mmol/L)	1.334(1.016-1.752)	0.038	1.704(0.993-0.997)	0.007

HR=Hazard ratio; 95% CI= 95% confidence interval;

Table 5. Secondary outcomes of different methods of anticoagulation

	RCA-one(n=337)	RCA-two(n=133)	RCA+ saline(n=11)	p
Adverse events, n (%)	10.8	1.8	11.1	0.001
Hypotension, n (%) ^a	7.6	0.9	2.0	0.023
Muscle cramps, n (%) ^b	0.7	0	11.1	0.001
acid-base imbalance, n (%)	0	0	0	-
electrolyte disorder, n (%)	0	0	0	-
allergy, n (%)	0	0	0	-
hemolysis, n (%)	0	0	-	-
Access dysfunction, n (%)	2.5	0.9	0	0.51

^ap<0.05 between RCA-one and RCA-two; ^bp<0.05 between RCA-one and RCA+saline; ^cp<0.05 between RCA-two vs RCA+saline

Figures

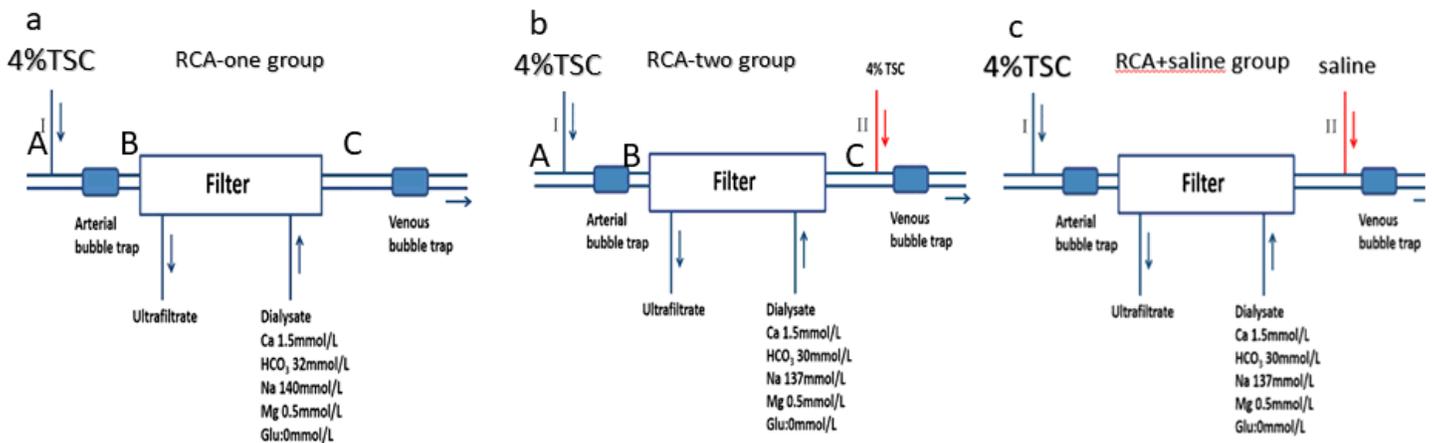
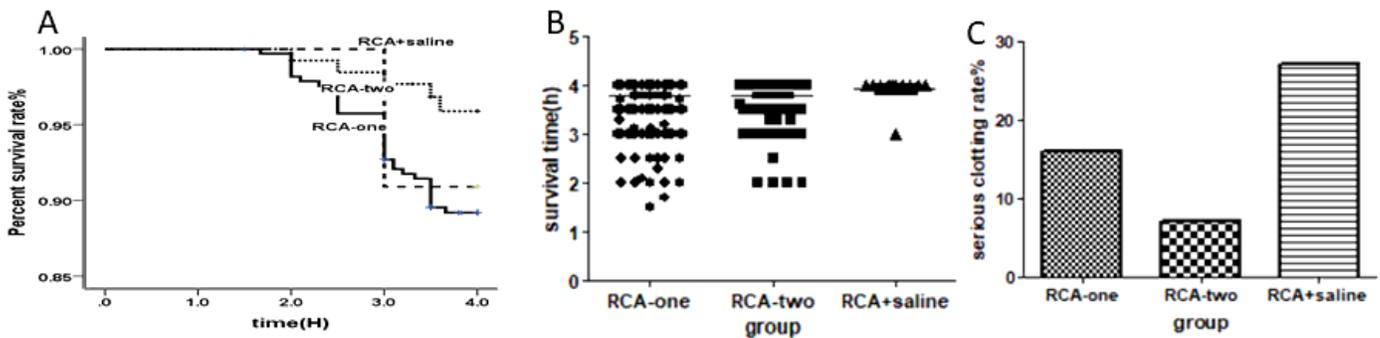


Figure 1

Schematized extracorporeal circuit and dialysate parameters for three anticoagulation strategies. a. RCA-one: 4% TSC was only continuously infused in position I; b. RCA-two: 4% TSC was infused in position I and II, simultaneously. c. RCA+saline: 4% TSC was continuously infused in position I, saline was continuously infused in position II. Abbreviations: RCA, regional citrate anticoagulation; TSC, trisodium citrate. Blood gas analysis Point A: dialysis access, B: pre-filter, C: post-filter.



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Figure 2

Efficacy endpoints and cumulative probability of survival for the circuit. A The Kaplan–Meier curves for uncensored circuit survival among three groups. B The circuit survival time in each group. C Serious clotting rate (the primary outcome) in three groups. The survival analyses were based on the log-rank test.

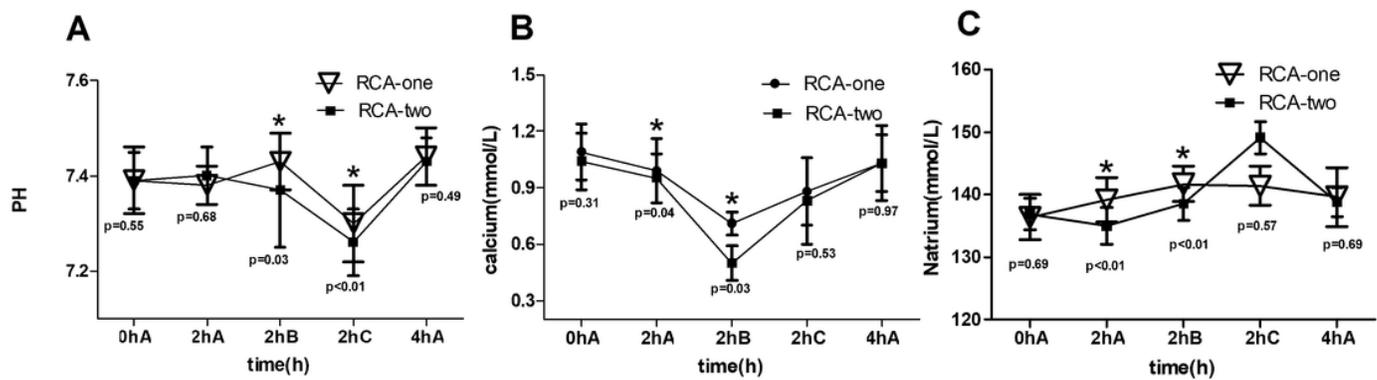


Figure 3

The comparison of values of the internal environmental parameters throughout hemodialysis procedures. PH values among three groups (A)PH values among three groups; (B) Serum calcium values among three groups; (C)Serum sodium values among three groups. Data are expressed as the mean \pm SD. *p<0.05