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Anticoagulation, Delivered Dose and Outcomes in CRRT: the Program to Improve Care in Acute Renal Disease (PICARD)

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Abstract

Background—Delivered dialysis dose by CRRT depends on circuit efficacy, which is influenced in part by the anticoagulation strategy. We evaluated the association of anticoagulation strategy used on solute clearance efficacy, circuit longevity, bleeding complications, and mortality.

Methods—We analyzed data from 1740 sessions 24 hours in length among 244 critically-ill patients, with at least 48 hours on CRRT. Regional citrate, heparin or saline flushes was variably used to prevent or attenuate filter clotting. We calculated delivered dose using the standardized Kt/V_{urea} . We monitored filter efficacy by calculating FUN/BUN ratios.

Results—Filter longevity was significantly higher with citrate (median 48, IQR 20.3–75.0 hours) than with heparin (5.9, IQR 8.5–27.0 hours) or no anticoagulation (17.5, IQR 9.5–32 hours, $p < 0.0001$). Delivered dose was highest in treatments where citrate was employed. Bleeding complications were similar across the three groups ($p = 0.25$). Compared to no anticoagulation, odds of death was higher with the heparin use (OR 1.82, 95% CI 1.02–3.32; $p = 0.033$) but not with citrate (OR 1.02 95% CI 0.54–1.96; $p = 0.53$).

Conclusions—Relative to heparin or no anticoagulation, the use of regional citrate for anticoagulation in CRRT was associated with significantly prolonged filter life and increased filter efficacy with respect to delivered dialysis dose. Rates of bleeding complications, transfusions, and mortality were similar across the three groups. While these and other data suggest that citrate anticoagulation may offer superior technical performance than heparin or no anticoagulation,

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adequately powered clinical trials comparing alternative anticoagulation strategies should be performed to evaluate overall safety and efficacy.

Keywords

Anticoagulation; Citrate; Continuous Renal Replacement Therapy

INTRODUCTION

Continuous renal replacement therapies (CRRT) require anticoagulation to prevent clotting in the extracorporeal circuit. Systemic unfractionated heparin and regional citrate are the two most commonly employed methods to prevent circuit clotting (1, 2). Systemic unfractionated heparin has traditionally been the most common form of anticoagulation in CRRT. Heparin has several advantages including relatively low cost, ease of administration, and wide availability. Monitoring of partial thromboplastin time (PTT) is familiar to most physicians and nurses in ICU and dialysis practice; moreover, heparin can be relatively easily reversed (with protamine) if required (3). However, systemic use of unfractionated heparin has several drawbacks including most importantly bleeding complications, which if significant, requires transfusions. Relatively rare conditions, including heparin-induced thrombocytopenia (and arterial thrombosis), and heparin resistance (4–8) can also complicate its use. Regional citrate anticoagulation constitutes an alternative to systemic unfractionated heparin and has some advantages; however, regional citrate anticoagulation is more cumbersome to deliver, and requires more extensive monitoring to prevent or attenuate metabolic consequences such as hypocalcemia, metabolic alkalosis and, in some patients with advanced chronic liver disease, an anion gap metabolic acidosis (9).

The efficacy of CRRT depends on circuit longevity, which is influenced by anticoagulation and several operational characteristics of the modality. Maintaining the patency of the extracorporeal circuit could reduce the difference between prescribed and delivered dialysis dose, mainly due to circuit downtime as shown by previous studies (10–13). In this study, we evaluated the association of three alternative anticoagulation strategies (regional citrate, systemic unfractionated heparin and no anticoagulation (saline flushes alone) on CRRT safety and efficacy. We hypothesized that regional citrate anticoagulation would be associated with enhanced filter longevity and efficiency of solute clearance compared with unfractionated heparin or no anticoagulation. In addition, we hypothesized that after adjusting for co-morbid conditions and severity of illness, in-hospital mortality rates would be lower in patients managed with citrate anticoagulation.

MATERIAL AND METHODS

Patients and Data

The Program to Improve Care in Acute Renal Disease (PICARD) group included five academic medical centers in the United States: University of California San Diego, Cleveland Clinic Foundation, Maine Medical Center, Vanderbilt University, and University of California San Francisco. Over a 31-month period (February 1999 to August 2001), all patients consulted for acute kidney injury (AKI) in the intensive care unit (ICU) were

evaluated by PICARD study personnel for potential study participation. Informed consent was obtained from all study participants or their proxies.

We analyzed data from 1740 sessions 24 hours in length among 244 critically ill patients with at least 48 hours on CRRT (continuous venovenous hemofiltration, hemodialysis or hemodiafiltration (CVVH, CVVHD or CVVHDF)) [Figure 1]. A detailed description of PICARD inclusion and exclusion criteria, data elements, data collection and management strategies has been described elsewhere (14). Acute kidney injury (AKI) was defined as an increase in serum creatinine (sCr) ≥ 0.5 mg/dL with baseline sCr < 1.5 mg/dL, or an increase in sCr ≥ 1.0 mg/dL with baseline sCr ≥ 1.5 mg/dL and < 5.0 mg/dL. Patients with a baseline sCr ≥ 5.0 mg/dL were not considered for study inclusion. Patients who were contacted by study personnel and who signed informed consent were enrolled in the study cohort. The Committees on Human Research at each participating clinical site approved the study protocol and informed consent.

We applied conventional definitions and reviewed medical records to define the presence or absence of chronic conditions. All interventions were determined by the treating physicians and not influenced by the study personnel including the timing, modality, and intensity of dialysis, and the type of anticoagulation if provided. The distribution of type of CRRT treatment and type of anticoagulation provided is shown in Figure 1.

Dialysis Technique

Three types of CRRT were employed: pre-dilution CVVH, CVVHD, and pre-dilution CVVHDF. These modalities were performed with five different CRRT machines; almost half (48%) of treatments were performed using a Gambro PRISMA (Lakewood, CO) CRRT machine, with a 0.7 to 1.8 m² AN69 membrane (MF-100 filter set for Prisma); 26% of the treatments were performed using an Aquarius Baxter system; 20% of the treatments were performed using a HOSPAL Gambro PRISMA machine and 5% were performed with a B. Braun Diapact machine, with a polysulfone synthetic high-flux filter (Fresenius NR60); and other types of CRRT machines were employed in fewer than 1% of treatments.

By study protocol, the type of anticoagulation was determined by each center and each team of treating physicians. Patients generally received regional citrate anticoagulation, systemic heparin anticoagulation or no anticoagulation; with the latter, saline flushes were employed to prevent or ameliorate filter clotting.

The mean 24 hours heparin dose employed was 9681 ± 7102 IU. The 4% trisodium citrate (TSC) mean infusion rate was 180 ml/h and the mean TSC dose was 445 ± 161 mmol. TSC was added at the arterial catheter port and ionized calcium levels were sampled post filter. Citrate flow rates were subsequently adjusted based on post-filter ionized calcium values to be maintained within a range of 0.25 to 0.4 mmol/L."

Quantification of dose

Dose assessment was performed using $StdKt/V_{urea}$ since it allows comparing treatment efficacy among different renal replacement modalities and treatment schedules. Delivered $StdKt/V_{urea}$ were computed using the following equations:(15)

$$StdKt/V_{CVVH} = [(Q_r + Q_{uf\ net}) \times (Q_p / (Q_p + Q_r))] \times 10.080 / (W \times 0.55) \times S$$

$$StdKt/V_{CVVHD} = (Q_d + Q_{uf\ net}) \times [10.080 / (W \times 0.55)] \times S$$

$$StdKt/V_{CVVHDF} = [(Q_d + Q_r + Q_{uf\ net}) \times (Q_p / (Q_p + Q_r))] \times 10.080 / (W \times 0.55) \times S$$

Where W is patient weight; S is sieving coefficient; Q_d is dialysate flow rate (mL/hr); Q_r is replacement flow rate; Q_{uf net} is net ultrafiltration rate; and Q_p is plasma flow rate at the blood pump and is calculated by this formula:

$$Q_p = (1 - \text{hematocrit}) \times Q_b$$

For prescribed *StdKt/V* a total of 24 hour prescribed treatment time was considered; Q_d, Q_r, and Q_{uf net} were derived from original prescription and W was pre-dialysis body weight. For calculating delivered *StdKt/V* observed Q_d, Q_r, and Q_{uf net} were used, these flow rates are adjusted for effective time of treatment (in a 24 hour treatment period); W was post-dialysis body weight.

Filter monitoring

In 590 sessions in which effluent urea nitrogen (FUN) was available, we assessed filter efficiency by measuring FUN and blood urea nitrogen (BUN) levels every 12 hours and calculating FUN/BUN ratios for each 12-hour period of filter use.

Bleeding complications

We defined bleeding complications as follows: 1) a decrease in hemoglobin of ≥ 1.5 g/dL below the level of hemoglobin at initiation of CRRT; and 2) transfusion of one or more units of packed red blood cells.

Statistical Analysis

Results are presented as means, medians, and interquartile ranges as appropriate. Baseline characteristics and outcome measures were compared using the t test or the Wilcoxon rank sum test for quantitative variables, and the Pearson χ^2 test or Fisher exact test for proportions. Filter life hours was compared using Kruskal-Wallis Test. $P < 0.05$ was considered statistically significant. Multivariable adjustment for variables including age, gender, etiology of acute kidney injury, and SOFA score was performed using a Poisson regression model. IBM SPSS statistical (19.0, SPSS Inc., USA) was used for all analyses.

RESULTS

The mean age was 54.6 years; 60% were men; 43% were white; and 19% had chronic kidney disease. The mean serum creatinine (sCr) at CRRT initiation was 4.0 ± 2.1 mg/dL, median (IQR) daily urine output was 407 (150 to 1030) mL, and mean SOFA and APACHE 3 scores were 8.2 ± 3.9 and 101.1 ± 24.7 , respectively (Table 1). In 94% of the patients, the reason for starting dialysis was a combination of volume problems (oliguria <400 cc/24 hours or signs of volume overload) and solute problems (e.g. BUN ≥ 80 mg/dL and/or sCr ≥ 6 mg/dL, electrolyte disturbances, and pH). In 6% of the cases, the indication for dialysis was exclusively volume related.

Compared to systemic unfractionated heparin, regional citrate was used more frequently in patients with liver disease (44% vs. 16%; $p=0.004$). We found no significant differences between the use of unfractionated heparin or citrate with respect to baseline hemoglobin concentrations (10.1 g/dL vs. 10.6 g/dL; $p=0.58$), platelet count (165,000/mcL vs. 118,000/mcL; $p=0.08$), pH 7.34 vs. 7.34; $p=0.90$), and bicarbonate concentration (21.3 mEq/L vs. 20.3 mEq/L; $p=0.37$).

CVVHDF, CVVHD, and CVVH were employed in 60%, 28%, and 12% of the treatments respectively. The mean blood flows among the three different types of CRRT were: CVVHDF 110 ± 25 ml/min; CVVHD 160 ± 20 ml/min; and CVVH 151 ± 9 ml/min ($p < 0.001$). The mean dialysate fluid flow rate was higher in patients treated with CVVHD as compared with patients treated with CVVHDF (1566 ± 707 mL/h vs. 1084 ± 288 mL/h; $p < 0.001$). The mean replacement fluid flow rate was higher in patients treated with CVVH as compared with patients treated with CVVHDF (937 ± 244 mL/h vs. 582 ± 278 mL/h; $p < 0.001$). The mean ultrafiltration flow rate was different among the three types of CRRT (CVVHDF 941 ± 282 mL/h, CVVHD 175 ± 71 mL/h, and CVVH 115 ± 51 ; $p < 0.001$). The median (IQR) of prescribed and delivered dose (expressed as mL/kg/h) was significantly different among the three different types of CRRT employed: *prescribed* 25 mL/Kg/h (20 to 25) and *delivered* 21.1 mL/kg/h (12.3 to 21.6) for CVVH; *prescribed* 22 mL/Kg/h (20 to 25) and *delivered* 19.3 mL/kg/h (15.0 to 24.2) for CVVHD; and *prescribed* 30 mL/Kg/h (25 to 35) and *delivered* 27.5 mL/kg/h (20.1 to 28.3) for CVVHDF. Expressed as $StdKt/V_{urea}$ the median (IQR) of delivered dose was also higher in patients who were treated with CVVHDF 9.1 (7.1 to 11.5) as compared to patients who were treated with either CVVH 6.5 (3.9 to 8.1) or CVVHD 5.8 (4.6 to 7.4) [$p < 0.001$ for both comparisons)].

As shown in Figure 2, delivered $StdKt/V$ was highest in treatments where citrate was employed as an anticoagulant. Notably, the delivered $StdKt/V$ was significantly lower in treatments where systemic unfractionated heparin was used than in treatments in which filter was managed with saline flushes.

Table 2 shows filter life and delivered $StdKt/V$ by type of CRRT and anticoagulation. Among modalities CVVHDF had the highest delivered dose when regional citrate was used as the anticoagulant. Filter longevity was significantly lower with unfractionated heparin and among filters where no anticoagulant was used.

Finally, in those treatments where effluent urea nitrogen was available, higher filter efficiency (FUN/BUN ratio) was found in treatments where regional citrate was used to prevent filter clotting (Figure 3). As shown with delivered $StdKt/V$, the FUN/BUN ratio was higher (more efficient clearance) when using saline flushes than with unfractionated heparin (Figure 3).

Seventy (28.6%) patients had a decline in hemoglobin concentration > 1.5 g/dL below the level of hemoglobin at CRRT initiation. Rates of declines in hemoglobin concentration > 1.5 g/dL were observed in 43%, 39%, and 19% in the systemic unfractionated heparin, regional citrate, and no anticoagulation groups, respectively ($p=0.0009$). There was no difference in the variation of daily hemoglobin levels in the systemic unfractionated heparin, regional

citrate, and no anticoagulation groups, respectively (delta hemoglobin of -0.03 ± 1.9 , -0.07 ± 1.9 , and $+0.05 \pm 2.2$; $p = 0.262$). Packed red blood cell transfusions were required in 44%, 25%, 31% in the systemic unfractionated heparin, regional citrate, and no anticoagulation groups, respectively ($p = 0.06$). No difference in in-hospital mortality was found between the use of systemic unfractionated heparin and regional citrate (48% vs. 58%; $p = 0.21$). After adjusting for age, gender, etiology of acute kidney injury and SOFA score, compared to no anticoagulation, the odd of death was higher with the use of UFH (OR 1.82, 95% CI 1.02 to 3.32; $p=0.033$) but not with citrate (OR 1.02 95% CI 0.54 to 1.96; $p = 0.53$).

DISCUSSION

Maintaining circuit patency during CRRT is a key factor for providing adequate volume control and solute clearance in patients with severe, dialysis-requiring acute kidney injury (AKI). The impact of filter clotting on the delivered dose of CRRT is greater than the impact of filter clotting in intermittent hemodialysis (IHD) since the lower solute clearance of CRRT requires a continuous or nearly continuous treatment without interruptions to achieve a prescribed dialysis dose (16). Several studies have shown that one of the major barriers for delivering a prescribed dose is filter clotting or fouling (10, 17–20). Recently, we showed that filter function affects the likelihood of delivering a prescribed dose; we assessed filter efficiency by calculating effluent urea nitrogen to blood urea nitrogen ratios (FUN/BUN ratio) for each 12 hour period of filter use. The median FUN/BUN ratio at the time of filter change was 0.96 (0.94 to 0.98) in non-clotted filters compared with 0.87 (0.77 to 0.95) in low sieving or clotted filters (21). We further demonstrated that the mean prescribed/delivered dose ratio was higher in treatments where the FUN/BUN ratio was greater than 0.9 (0.84 ± 0.12 vs. 0.79 ± 0.11) (21).

In the analyses presented here, we evaluated the use of two alternative anticoagulation strategies on delivered dialysis dose of CRRT in critically ill patients with AKI. We assessed delivered dose by computing $StdKt/V$, since it allows us to compare the relative efficiency of alternative CRRT modalities and treatment schedules. Previous studies that have compared systemic unfractionated heparin and regional citrate focused on the effects of these two anticoagulants on filter patency but failed to explore how these distinct anticoagulation strategies affect filter efficiency and consequently the delivered dialysis dose, bleeding complications and transfusions. However, a more recent study that evaluate, in critically ill patients with severe acute kidney injury following cardiac surgery, the efficacy and safety of regional citrate anticoagulation using a low concentration citrate solution have also shown that delta of prescribed vs. delivered dose was $4.7 \pm 12.1\%$ when citrate was used as compared with $13 \pm 20.5\%$ when heparin was used (22).

Our finding of the superiority of regional citrate over systemic unfractionated heparin in terms of filter life is consistent with some previous studies. In our study, the mean filter life in treatments where regional citrate was used (54.5 hours) was longer than some previous reported studies. In the study of Palsson and Niles who used a simplified citrate system for delivering regional citrate anticoagulation during CVVH, the reported mean filter life span was 29.5 ± 17.9 hours in 85 filters that were used, of which 64 were lost because of clotting (23). Bagshaw et al. reported a median filter life span with regional citrate anticoagulation of

40 hours (IQR 14 to 72 hours) in a prospective cohort study in which the effects of regional citrate with CVVHDF and of systemic unfractionated heparin with CVVH were compared (2). In a more recent study, Betjes et al. randomized 48 critically-ill patients at low risk for bleeding to either CVVH with regional citrate or systemic unfractionated heparin anticoagulation and reported a median circuit survival time in the citrate group of 36 hours (24). Moreover, two recent studies have supported the notion that citrate is superior to heparin, however filter life span in circuits where citrate was used was longer than what we have reported. In the first study, Monchi et al. (25) analyzed data from 20 patients, and using a crossover design patients were randomized to either systemic unfractionated heparin or regional citrate. In total, 49 circuits were analyzed (heparin=23 and citrate=26). The authors found a significantly longer filter life in circuits where citrate was used (70 hours [IQR 44 – 140] vs. 40 hours [IQR 17 to 48]; $p=0.0007$). They also found a reduced risk of bleeding with regional citrate anticoagulation; 0.2 units of packed red blood cells were transfused per day vs. 1-unit circuits where anticoagulation was managed with systemic unfractionated heparin (25). In the second study, Kutsogiannis et al. reported a median citrate circuit survival time of 124.5 hours (95% CI 95.3 – 157.4) and a median heparin circuit survival time of 38.3 hours (95% CI 24.8 – 61.9) (26). In addition, after adjustment for antithrombin-III levels and illness severity score, the relative risk of hemorrhage with regional citrate anticoagulation was significantly lower than with systemic unfractionated heparin, although the confidence limits were wide owing to the small sample size (RR 0.14; 95% CI 0.02 to 0.96, $p=0.005$) (26). Our study confirms and extends these findings in a larger critically ill cohort using a diverse array of modalities and devices.

If we look to the treatments where CVVHDF was used, no significant difference was found in terms of delivered $StdKt/V$ comparing regional citrate, systemic unfractionated heparin or saline flushes. However, the number of filters used to achieve that delivered dose was lower in the regional citrate group (Table 2). We have also provided evidence that $StdKt/V$ could be used as a unified dose expression to assess and compare treatment efficacy of different CRRT modalities and among different treatment frequencies, and could be used as standard method to monitor dose delivered. This is an unresolved issue since there are no established metrics for monitoring the dose delivered or ensuring the quality of renal replacement therapy we are providing to critically-ill patients with AKI (27). Kleger and Fassler recently explored the concept of using circuit longevity as quality indicator in CRRT. These authors showed that in addition to monitoring the complication rates of alternative anticoagulation strategies, the evaluation of circuit longevity using survival analysis (i.e., time to access or system failure) is a simple feasible means of assessing the quality of CRRT in the intensive care unit (28). Our findings confirm those of Uchino et al., who analyzed data from 48 critically-ill patients treated with CVVH using two hundred and sixty-six filters. The authors reported a significant inverse correlation between down time and percentage of delta creatinine and urea over each 24 hour cycle; the most common reason for down time was filter clotting (10).

In addition to improving circuit longevity, reducing the incidence of bleeding complications, and enhancing the delivered dialysis dose, regional citrate may offer additional advantages over heparin or no anticoagulation strategies. Citrate may improve membrane biocompatibility; compared to heparin, citrate anticoagulation attenuates the release of

myeloperoxidase, elastase, interleukin 1 β , and platelet factor 4 (29–32). Citrate also down regulates the inflammation induced by foreign material by causing deep hypocalcemia in the filter modulating intracellular calcium signaling. These beneficial effects could possibly be linked to increased rates of the recovery of kidney function and decrease in mortality rates as shown by Oudemans van Straaten et al. in a randomized controlled trial comparing regional citrate to low-molecular weight systemic anticoagulation for CVVH (33).

Data from PICARD do not show significant differences in terms of a large decline in hemoglobin, transfusion or mortality. However, compared to patients on no anticoagulation, the odd of death associated with systemic unfractionated heparin was significantly higher as compared with the use of regional citrate anticoagulation.

Our study has several strengths. We included patients from five tertiary care academic medical centers across the USA with different demographics and clinical conditions, increasing the generalizability of our results. In contrast to many other studies where information was collected upon initial review or around the time of initiation of dialysis, data from patients enrolled in PICARD were collected from three days preceding the day of AKI diagnosis throughout their ICU course. PICARD affords us with extraordinarily detailed clinical data on a relatively large cohort whose population is reasonably representative of critically ill patients with AKI. Our multicenter prospective study also provides important information on efficacy of the filter and delivered dialysis dose that were not addressed by previous studies; the effect of the type of anticoagulation being used on delivered dose and filter patency highlights the importance of continuously monitoring filter patency in order to ensure that the prescribed dose, or something close to it, is delivered. We have detailed data regarding the rates of bleeding complications and transfusions among different anticoagulation strategies.

The main limitations of the study, as an observational study, is that groups were not randomized for anticoagulation strategy, and since the physicians determined the modality and the intensity of dialysis, according to the patients' clinical condition and local habits and facilities, there would be unavoidable bias in the inclusion of study participants and the treating prescriptions, so we cannot assume a causal relation between the use of regional citrate and outcomes.

In conclusion, the use of regional citrate as an anticoagulant strategy in CRRT is associated with prolonged filter life compared with the use of systemic unfractionated heparin. Regional citrate improves filter patency and the efficiency of solute clearance, which translates into a higher delivered dialysis dose, as defined using *StdKt/V*. While randomized trials conducted to date have shown no difference in the effect of higher versus standard dialysis dose, the type of anticoagulation should be considered and accounted for in future studies, as we aim to refine and improve CRRT for all treated patients.

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Disclosure:

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Figure 1.

Distribution of type of CRRT and different anticoagulation strategies used.

CRRT, continuous renal replacement therapies; CVVH, continuous veno-venous hemofiltration; CVVHD, continuous veno-venous hemodialysis; CVVHDF, continuous veno-venous hemodiafiltration.

Figure 2.

Delivered dose of dialysis measured as Standard Kt/V_{urea} in CRRT sessions using unfractionated heparin, regional citrate and no anticoagulation. A higher proportion of regional citrate was employed on CVVHDF treated patients, as compared with other modalities (CVVHD and CVVH).

CRRT, continuous renal replacement therapies; CVVH, continuous veno-venous hemofiltration; CVVHD, continuous veno-venous hemodialysis; CVVHDF, continuous veno-venous hemodiafiltration.

Figure 3.

Shows filter efficiency measure as FUN/BUN ratio and type of anticoagulation used (systemic unfractionated heparin and regional citrate). Filters in which regional citrate was used showed a higher FUN/BUN ratio.

FUN, effluent urea nitrogen; BUN, blood urea nitrogen.

Table 1

Baseline characteristics at continuous renal replacement initiation

Variable	All (n=244)	None (n=116)	Heparin (n=71)	Citrate (n=57)	P value
Mean age (years)	54.6	52.6	58.9	49.0	Sal/none vs. hep p=0.02 Hep vs. cit p=0.02
Male (%)	59.4	59.7	66.7	45.6	Hep vs. cit p=0.03
Race/ethnicity: Caucasian (%)	78.1	74.6	90.5	57.9	Sal/none vs. hep p=0.03 Hep vs. cit p<0.0001
Etiology of AKI:					
Acute Tubular Necrosis	76.1	81.5	76.0	70.2	ns
Infection	7.5	10.8	4.8	8.8	ns
Hepatic failure	17.7	24.6	13.5	17.5	ns
Congestive heart failure	8.8	13.8	9.6	1.8	Sal/none vs. cit p=0.05
Nephrotoxicity	25.7	27.7	28.8	17.5	ns
Obstruction	0.4	0	1.0	0	ns
Volume depletion	17.3	26.1	11.5	17.5	Sal/none vs. hep p=0.04
Vascular	17.7	13.8	27.9	3.5	Sal/none vs. hep p=0.04 Hep vs. cit p=0.03
Mean SOFA score	11.3	11.3	10.4	13.0	Sal/none vs. cit p=0.05 Hep vs. cit p=0.03
Mean Apache 3 score	100.2	100.3	95.6	108.6	Hep vs. cit p=0.03
Mean AM weight (kg)	93.5	91.1	98.8	80.5	Hep vs. cit p=0.01
Median UO (mL)	400	490	515	226	Sal/none vs. cit p=0.01
Mean creatinine (mg/dL)	4.0	3.8	4.2	3.8	ns
Mean BUN (mg/dL)	79.3	75.2	80.2	82.3	ns

Variable	All (n=244)	None (n=116)	Heparin (n=71)	Citrate (n=57)	P value
Mean platelets (1000/mm ³)	135.6	106.8	164.8	117.6	Sal/none vs. hep p=0.02 Hep vs. cit p=0.02
Mean hemoglobin (g/dL)	10.1	9.6	10.1	10.6	Sal/none vs. cit p=0.05

Table 2

Comparisons of the delivered dose with use of heparin, citrate or no anti-coagulation among different types of CRRT

Type of anticoagulant	Median (IQR) delivered Standard Kt/V by type of therapy			
	Mean Filter Life Hrs (number of filters)	CVVH [Number of sessions]	CVVHD [Number of sessions]	CVVHDF [Number of sessions]
Citrate	54.5 (173)	1.7 (0.59–2.9) [n = 2]	[n = 0]	8.2 (5.9–10.4) [n = 467]
Heparin	21.1 (824)	2.85 (1.8–4.1) [n = 84]	5.6 (4.6–7.4) [n = 288]	8.31 (5.8–10.8) [n = 196]
No anticoagulant	23.1 (403)	7.3 (5.3–9.0) [n = 105]	5.9 (4.5 – 7.3) [n = 189]	8.5 (6.3–11.2) [n = 399]
<i>p</i> value	< 0.001	< 0.001	0.584	0.062