PÉCSI TUDOMÁNYEGYETEM
UNIVERSITY OF PÉCS

aiti

CRRT - alvadásgátlás

Csontos Csaba
PTE KK AITI

Alvadás – kőr és patron

- Körhöz köthető faktorok
- Filtrációs frakció
- De-aeration chamber
- Vénas út
- Elégtelen véralvadás gátlás

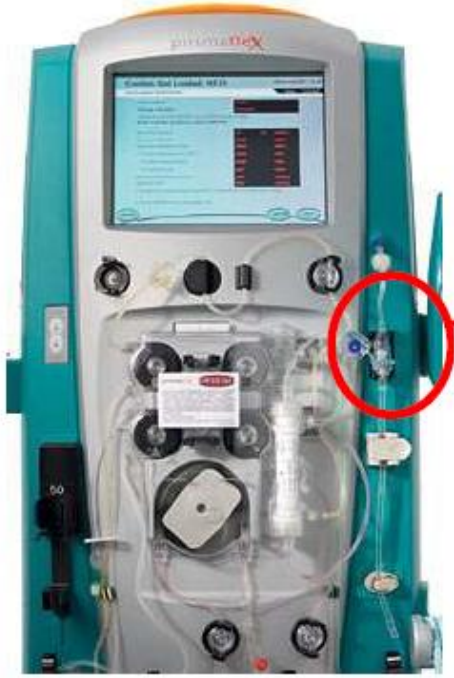
Alvadás - kör

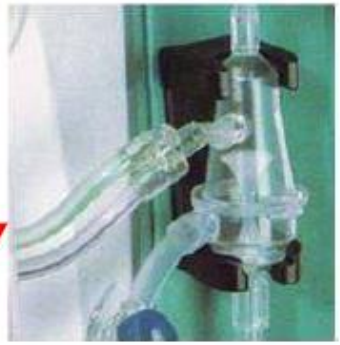
- A csöveket heparinnal „bortjuk be” a feltöltés során
  - Feltöltés során 5000 E UH
  - Kínai Cytosorb esetén 12500 E UH

Filtrációs Frakció (QUF/QP)

- Magas UF Rata & alacsony véráramlás = alvadás
- Példa:
  - 100 kg ffi
  - post-dilúciós CVVH,
  - BFR 150 mL/min,
  - CVVH dose 25 ml/kg/h
  - hct 30%
- Total UF Ráta = 2500 mL/h
- FF= UF/1-HTCxBFR
- FF = 2500/(0.7 X 150 X 60) = 40% !!!

Circuit Considerations





DEAERATION CHAMBER

Postdilutio szerepe

A vér fölött legyen folyadék!!!!!

Vénás út

- Nagy átmérő/ rövid, de megfelelő hosszúságú
  - Jobb IJ = 12–15 cm
  - Bal IJ = 15–20 cm
  - Femorális = 19–24 cm
- Beszúrás helye
  - Jobb IJ preferált
  - Subclavia – legkevésbé ajánlott
- A kanülvég megfelelő helye:
  - IJs & SCs → VCS a Cava – Pitvar határon
  - Femorális → VCI = 24 cm Katéter
- Ne csökkentsük a lument csapokkal vagy egyéb eszközökkel.
- Speciális e célra gyártott kanülök használata javasolt.

Filter alvadása

- Következmények
  - Terápia megszakítások
  - Csökken a dózis
  - Csökken a filter hatékonysága.
- A megfelelő antikoagulálás célja
  - A filter maximális élettartamának biztosítása
  - A kezelés hatékonyságának fokozása
- Jele
  - TMP emelkedik
  - Kifolyónyomás csökken

Antikoagulálás lehetőségei

- Citrát
- Nem frakcionált heparin
- Regionális heparin és protamin
- LMWH
- Thrombin antagonisták
- Prostaglandinok - PGI2, PGE1

Heparin

- A tüdőembólia protokollt kell alkalmazni
  - A gép nem tud 0,1 ml-t adagolni
  - A javasolt hígítás 100 E/ml
  - Adható a géptől független perfúzorral is.

Na Heparin adagolása aPTI alapján
(célérték: 50-70 sec, Na Heparin higítása: 500NE/ml)

aPTI (másodperc)	Bólus dózis (E)	Perfuzor leállítás (percek)	Dózis módosítás (ml/óra)	aPTI ismétlése (óra)
<40	3000	0	+0,2	6
40-49	0	0	+0,1	6
50-70	0	0	0 (nincs változtatás)	12-24
71-85	0	0	-0,1	6
86-100	0	30	-0,2	6
101-150	0	60	-0,3	6
151-200	0	60	-0,6	6
>200	0	60	-0,8	6

Citrát antikoaguláció

- A CRRT alkalmazása nem jelenti feltétlenül a szisztémás antikoaguláció alkalmazását. Vérzésveszély illetve posztoperatív betegeknél is biztonságosan alkalmazható.
- A helyi citrát antioagulálás relális alternatíva valamennyi CRRT modalítás esetében.
- Nem alkalmazható Novalung kezelés esetén (túl magas a citrát terhelés) – már ez is kérdéses.

Miért citrát ?

- Kritikus állapotú betegekben a heparin:
  - Fokozza a vérzésveszélyt
  - Heparin-indukálta thrombocytopenia (HIT)
  - Antithrombin mediált pro-inflammatorikus hatások
- A heparin kontraindikációi:
  - Aktív vérzés
  - Sebészi beavatkozás
  - Thrombocytopénia
- Óvatosan adható:
  - Vese és májbeteg
  - Magas vérzésveszély

Observed bleeding events with heparin anticoagulation during CRRT

A number of studies have compared bleeding events observed during CRRT using heparin or citrate anticoagulation, with four studies showing a trend toward less bleeding using citrate.[1]

References[2–7]	Patients	Modality	Incidence of bleeding events		*P* value
			Heparin group	Citrate group	
Monchi M, *et al. Intensive Care Med.* 2004; 30:260–265[2]	n = 12 (heparin) n = 8 (citrate)	CVVH with heparin or citrate	n = 1	n = 0	–
Kutsogiannis DJ, *et al. Kidney Int.* 2005; 67:2361–2367[3]	n = 14 (heparin) n = 16 (citrate)	CRRT with heparin or citrate	–	RR 0.17[a] (0.03–1.04)	*P* = 0.06
Betjes MG, *et al. J Nephrol.* 2007; 20:602–608[4]	n = 27 (heparin) n = 21 (citrate)	CVVH with heparin or citrate	n = 10	n = 0	*P* <0.01
Oudemans-van Straaten HM, *et al. Crit Care Med.* 2009; 37:545–552[5]	n = 103 (nadroparin)[b] n = 97 (citrate)	CVVH with **nadroparin** or citrate	16%	6%	*P* = 0.08
Hetzel GR, *et al. Nephrol Dial Transplant.* 2011; 26:232–239[6]	n = 83 (heparin) n = 87 (citrate)	CVVH with heparin or citrate[c]	14.5%[d]	5.7%[d]	–
Stucker F, *et al. Crit Care.* 2015; 19:91[7]	n = 49 (heparin) n = 54 (citrate)	CVVHDF with heparin or citrate	n = 0	n = 4	–

Miért citrát?

- 5 citrát és heparin antioagulálást összehasonlító tanulmányt publikáltak eddig.
- 3 esetében a filter hosszabb élettartamát találták citrát mellett
- 2 esetben kevesebb vvt. Igényeltek a citrátos betegek.

Kidney Disease Improving Global Outcomes

- **Chapter 5.3: Anticoagulation for CRRT:**
  - For anticoagulation in CRRT, we suggest using regional citrate anticoagulation rather than heparin in patients who do not have contraindications for citrate'.

Alacsony vs magas konc citrát oldat

- A magas citrát koncentrációjú oldatok sok Na-t tartalamaznak.
- A sokkal nagyobb ezen oldatok esetében
  - A hypernatrémia
  - A metabolikus alkalózis veszélye
- Az ACD-A oldat magas koncentrációban tartalmaz dextrózt.

Citrát oldatok

Composition (mmol/L)				
	ACD-A[1]	4% Trisodium citrate[1]	Low concentration citrate[2]	Plasma[3]
Citrate	74.8	136	18	–
Citric acid	38	–	–	–
Chloride	–	–	86	98–106
Sodium	224	420	140	136–145
Dextrose	124	–	–	4.2–6.4[a]

Alternative protocols using dilute citrate solutions with physiological sodium levels have been developed since 1999.[4–7]

Citrate in CRRT – Advantages & Disadvantages

Advantages:[1,2]

- ✓ Anticoagulation restricted to extracorporeal circuit
- ✓ Decreased risk of bleeding vs. systemic heparin
- ✓ Less circuit downtime vs. heparin – higher dose of therapy
- ✓ Can be used in heparin contraindications, e.g. HIT.

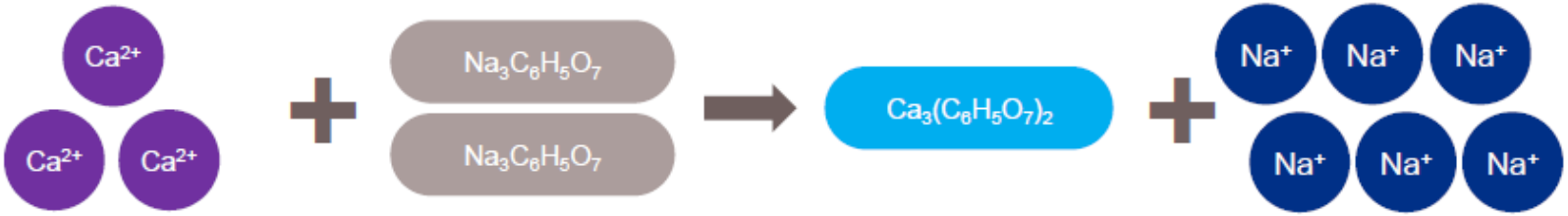
Disadvantages:[1]

- ✓ Initial educational work
- ✓ Requires monitoring of calcium level and pH
- ✓ Potential risk of metabolic complications
- ✓ Citrate accumulation if citrate not adequately metabolized – see later for detail.

1. Oudemans-van Straaten HM, *et al. Crit Care.* 2011; 15: 202;
2. Bagshaw SM, *et al. Crit Care.* 2005; 20:155–161.

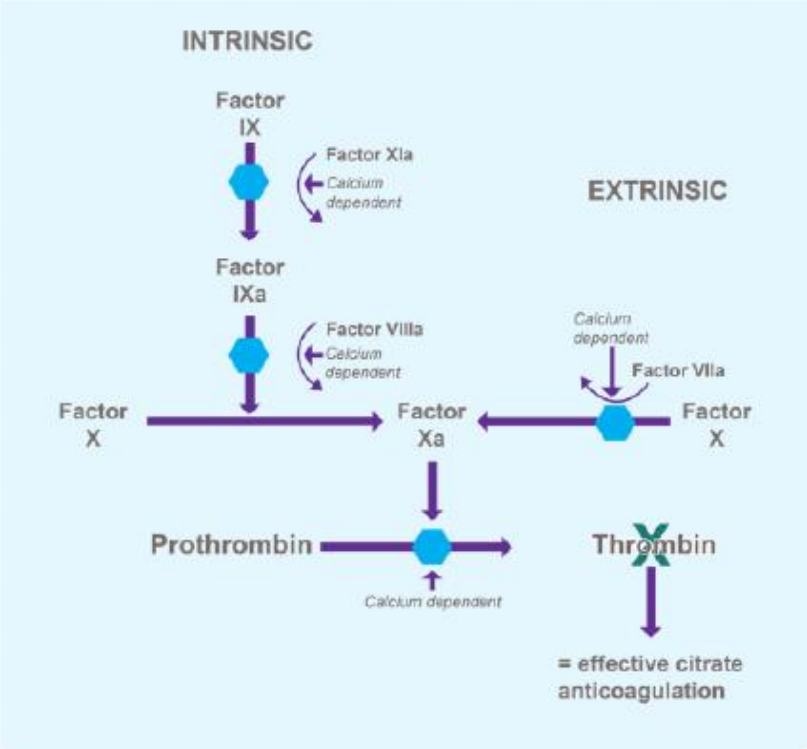
How does citrate work?

1. Citrate chelates ionized calcium and magnesium[1]



3 Calcium ions + 2 Sodium Citrate molecules = 1 Sodium Citrate molecules + 6 Sodium ions

Citrát



- A citrát az ionizált Ca megkötése útján gátolja az alvadást.
  - Számos ponton blokkolja az alvadási folyamatot – végeredmény a trombin képződés gátlása.

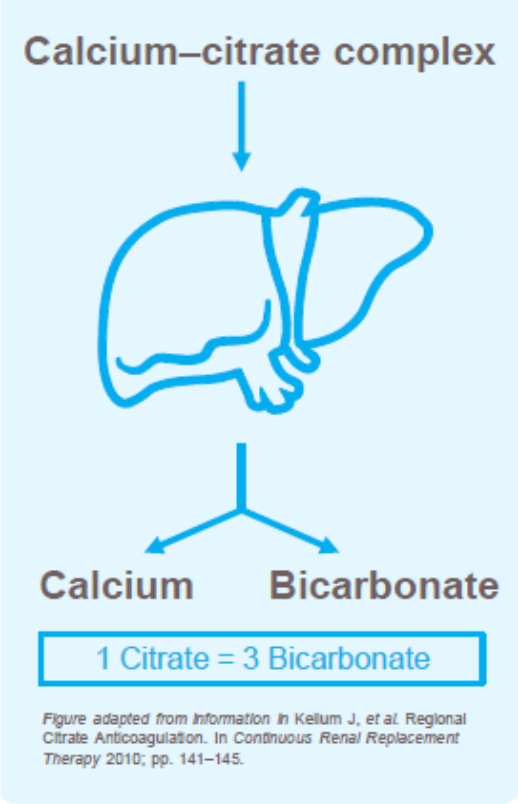


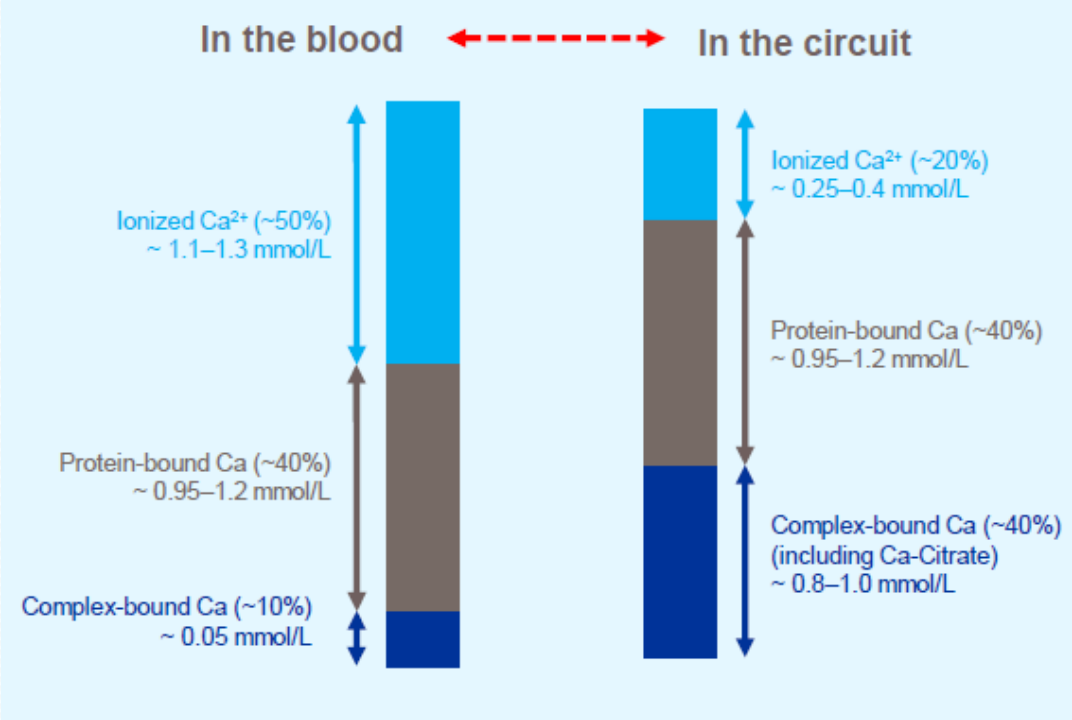
Figure adapted from information in Kellum J, *et al.* Regional Citrate Anticoagulation. In *Continuous Renal Replacement Therapy* 2010; pp. 141–145.

- A trisodiumcitrát a leggyakrabban használt vegyület, melyet a kör artériás szárába infundálunk.
- A normál se Ca szint fenntartásához a kör után Ca pótlás szükséges vagy a körbe vagy egy külön vezetéken keresztül a megfelelő ionizált Ca szint fenntartásához.
- A citrát a májban, izomban, vesében Bikarbonáttá metabolizálódik, miközben Kálcium szabadul fel.
- Az oldatokat úgy adagoljuk, hogy a körben az ionizált Ca szint 0.25 és 0.4 mmol/l között, a szisztémás ionizált Ca szint 1.1 és 1.3 mmol/l között legyen.

Citrát antikoaguláció

A citrátból ionizált CA mellett CA-citrát komplex jön létre, így csökken a körben az ionizált CA szintje, ami megakadályozza az alvadást.

A cél ionizált Ca szint a körben 0.25 - 0.40 mmol/l



Schneider et al. Critical Care (2017) 21:281
DOI 10.1186/s13054-017-1880-1

Critical Care

VIEWPOINT Open Access

Complications of regional citrate anticoagulation: accumulation or overload?

Antoine G. Schneider[1,2*], Didier Journois[3] and Thomas Rimmelé[4,5]

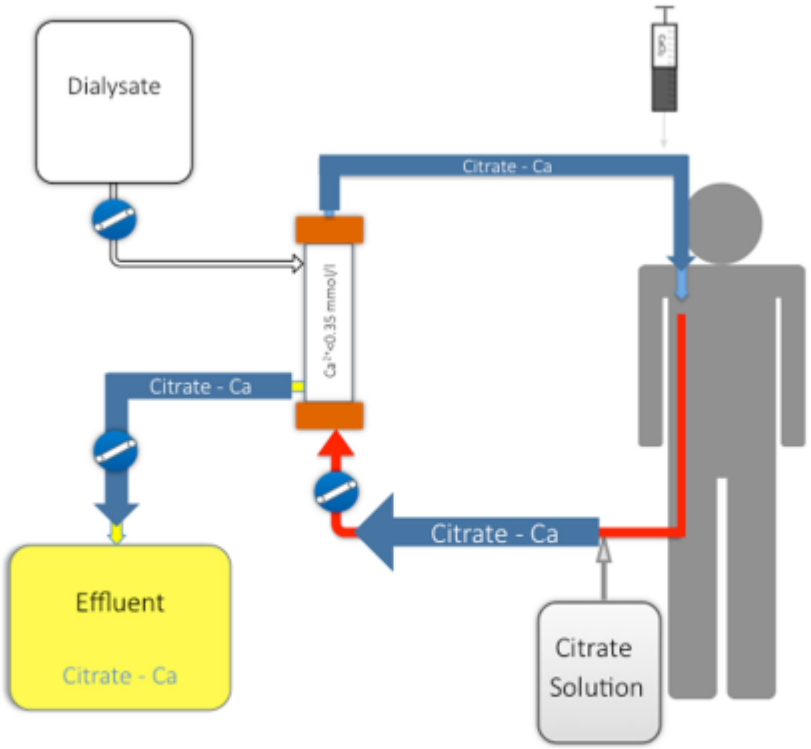


Fig. 2 Schematic view of a CRRT circuit with regional citrate administration in CVVHD mode. Alternative modes can be used (postdilution CVVH, combined pre- and postdilution CVVH, CVVHDF, etc.) according to the protocol used. Citrate solution is administered at the beginning of the CRRT circuit. It forms citrate–calcium complexes, which are largely removed from the blood at the level of the filter. Only complexes which are not removed through the hemofilter return to the patient's blood and need to be metabolized

Practical management of regional citrate anticoagulation in CRRT[1,2,a]

1. Measure serum electrolytes before initiation
   - ✓ At 1 hour, measure post-filter ionized calcium to check circuit calcium
2. Measure patient ionized calcium to check systemic calcium
3. Adjust citrate dose or calcium compensation according to table
4. Make adjustments as required and repeat measurement after 1 hour
5. Once ideal values/steady state reached, measure 4 hourly for first 24 hours, then 6 hourly
6. Measure total calcium once a day to check calcium ratio

Image source: Baxter_Renal_Foundations_Media_Asset_Library_v1.0

* The below is a commonly used monitoring plan and is not intended as a definitive guide to management of patients undergoing CRRT with citrate. Responsibility remains with the clinical team managing the patient

1. Davenport A & Tolwani A. *NDT Plus.* 2009; 2:439–447;
2. Collin, adapted by Gambro, CVVH protocol for regional citrate anticoagulation on Prismaflex system. Protocol 2013; 1-2. HCEN15816_1.

Veszélyek

- Azon állapotok esetén amikor a citrát metabolizmusa zavart szenved felszaporodhat a szervezetben.
  - Súlyos májelégtelenség/cirrhosis
  - Csökkent máj vérátáramlás
  - Az izom keringés nagymértékű csökkenése (súlyos sokk)
  - Nagy kiterjedésű izom sérülés/károsodás

Veszélyek

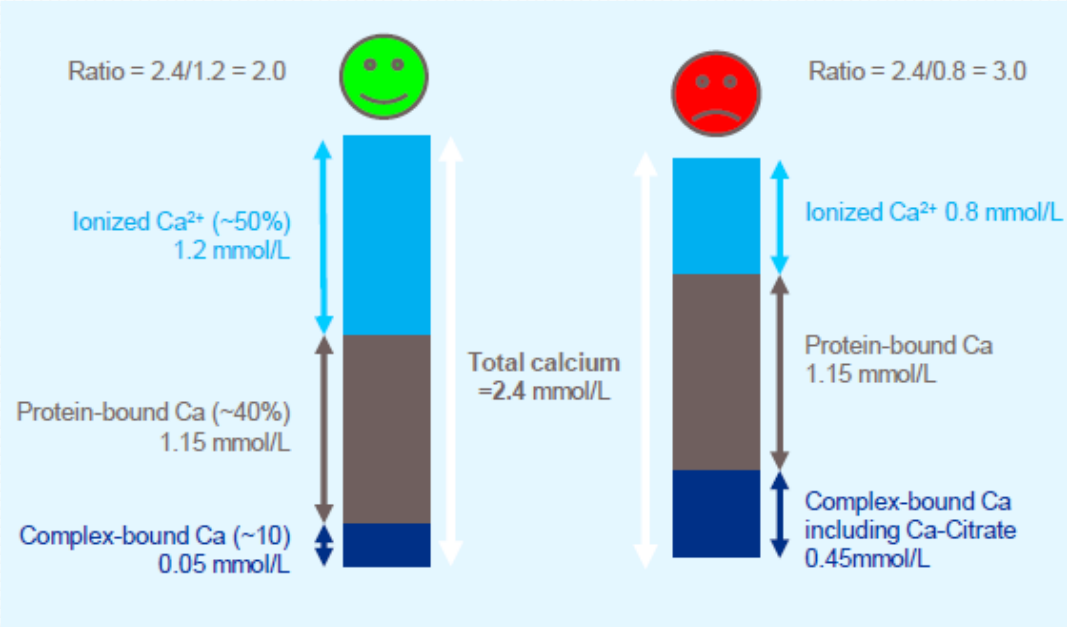
- Ha több citrátot infundálunk, mint amit a metabolizmus és dializis eltávolít a kalcium-citrát komplex a beteg keringésében marad.
- A citrát alvadásgátlás fő limitációja a mitokondriális citrát metabolizmus csökkenése következtében fellépő citrát felhalmozódás.

Veszélyek

- A citrát nem toxikus a tünetek a másodlagos hypokalcémia és acidózis következményei.
- A beteg ionizált Ca szintjének monitorozása ezért kötelező.
- Az ionizált Ca szint csökkenése a citrát felhalmozódás szenzitív indikátora.
- A citrát accumulátio emeli az össz Ca szintet, hisz megnő a citráthoz kötött Ca menyisége.

Veszélyek

Ca/ionCa < 2,3



Citrate CRRT in liver failure[1]

The liver citrate anticoagulation threshold study (L-CAT)[1]

- ✓ Ratio of total/ionized calcium ≥2.5: n = 3 (2%).[1]
- ✓ Estimated 72-hour filter survival was 96%, after censoring for discontinuation due to non-clotting causes (e.g. renal recovery, death).[1]

	Normal liver	Mild impairment	Severe impairment	*P* value
Severe alkalosis	2%	0%	5%	0.41
Severe acidosis	13%	16%	14%	0.95
Severe Hypocalcemia	8%	14%	12%	0.7
Severe Hypercalcemia	0%	0%	0%	n.s.

Regional citrate anticoagulation (RCA) for continuous renal replacement therapy is widely used in intensive care units (ICUs).[1]

However, concern exists about the safety of citrate in patients with liver failure (LF).[1]

The aim of this study was to evaluate safety and efficacy of RCA in ICU patients with varying degrees of impaired liver function.[1]

CONCLUSIONS:
RCA-CVVHD can be safely used in patients with LF.[1]

The technique yields excellent filter patency and thus can be recommended as first-line anticoagulation for the majority of ICU patients.[1]

1. Slowinski T, *et al. Crit Care.* 2015; 19: 19:349. Dol 10.1186/s13054-015-1066-7

Regional Citrate Versus Heparin Anticoagulation for Continuous Renal Replacement Therapy: A Meta-Analysis of Randomized Controlled Trials

Mei-Yi Wu, MD,[1] Yung-Ho Hsu, MD,[1] Chyi-Huey Bai, PhD,[2] Yuh-Feng Lin, MD,[1] Chih-Hsiung Wu, MD, PhD,[3] and Ka-Wai Tam, MD, MS[4]

Am J Kidney Dis. 59(6):810-818.

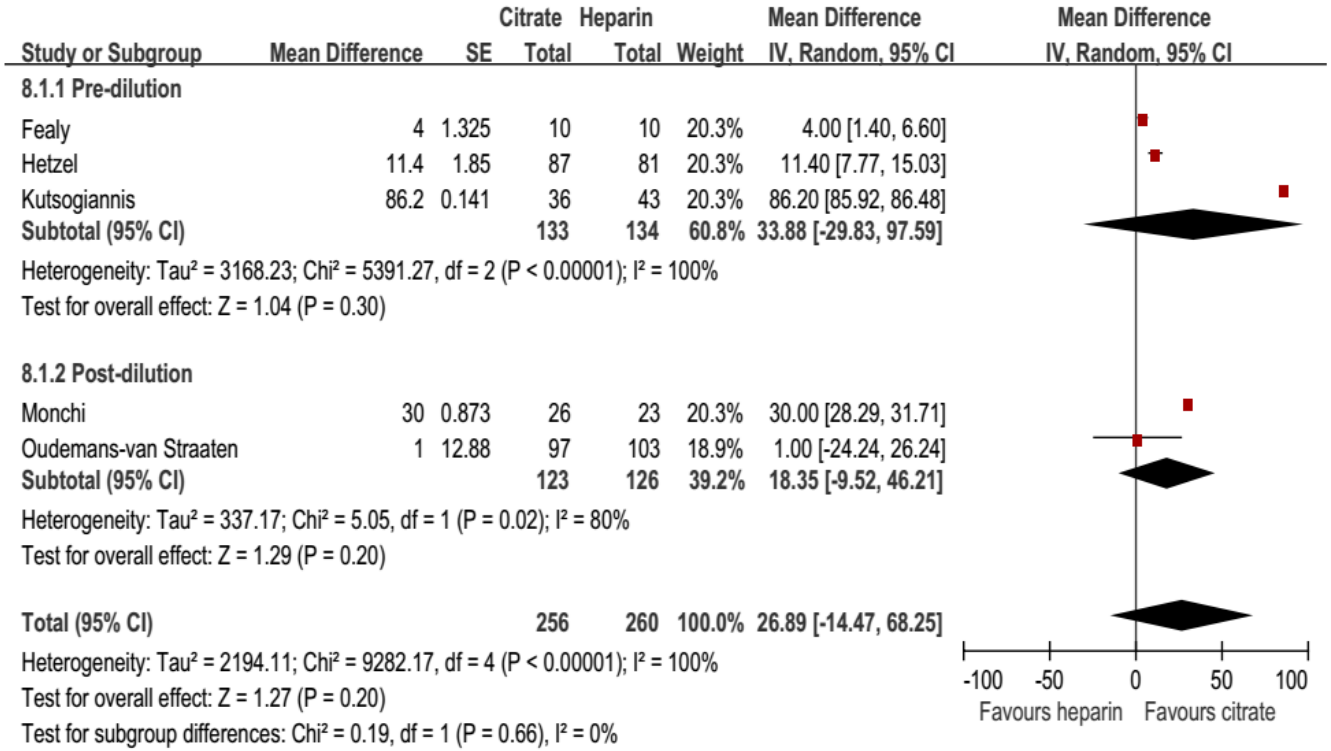


Figure 2. Forest plot of comparison: citrate versus heparin. Outcome: circuit survival time. Abbreviations: CI, confidence interval; SE, standard error.

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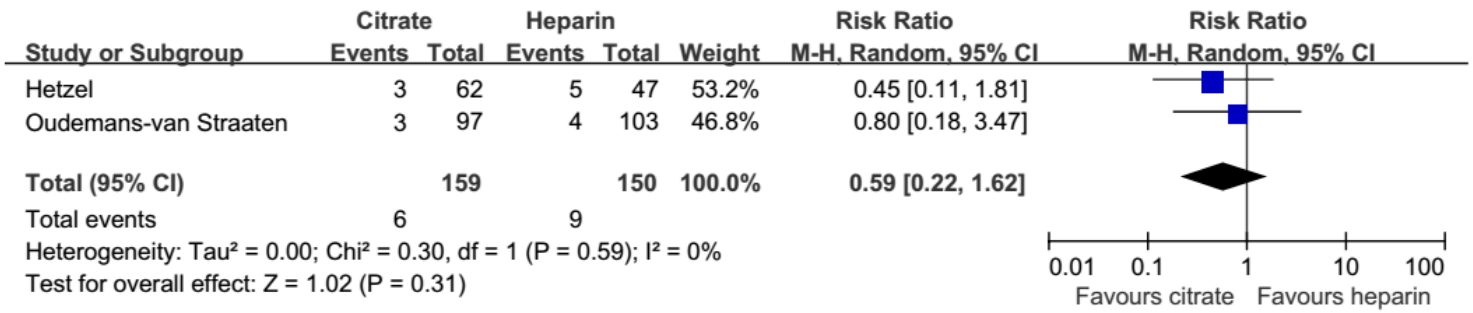

Figure 6. Forest plot of comparison: citrate versus heparin. Outcome: incidence of heparin-induced thrombocytopenia. Abbreviation: CI, confidence interval.

A Randomized Controlled Trial of Regional Citrate Versus Regional Heparin Anticoagulation for Continuous Renal Replacement Therapy in Critically Ill Adults*

David J. Gattas, MD, MMed (ClinEpi), FCICM, FRACP[1,2];
Dorrilyn Rajbhandari, RN Post Grad Dip (Clinical Nursing)[1,2]; Celia Bradford, MD, FCICM[3];
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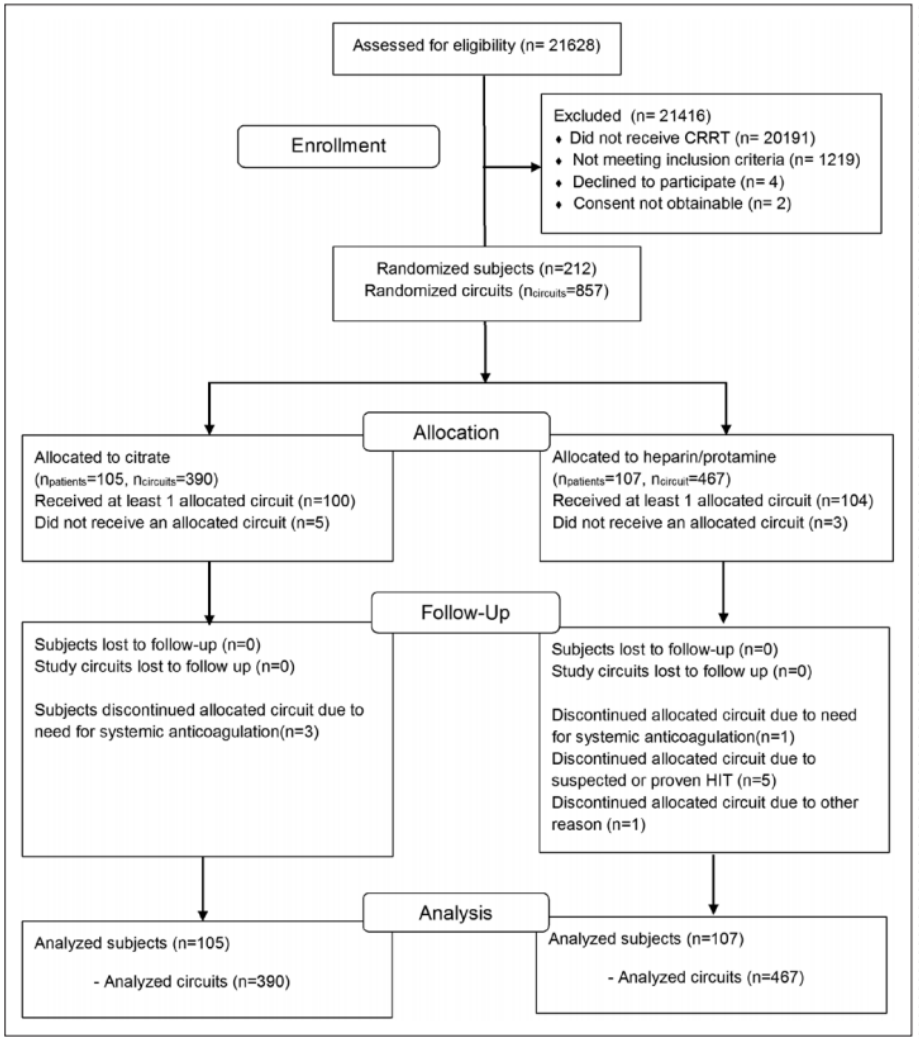

Figure 1. Flow diagram of participants showing assessment of eligibility, enrollment, treatment allocation and follow-up in the trial. CRRT = continuous renal replacement therapy, HIT = heparin-induced thrombocytopenia.

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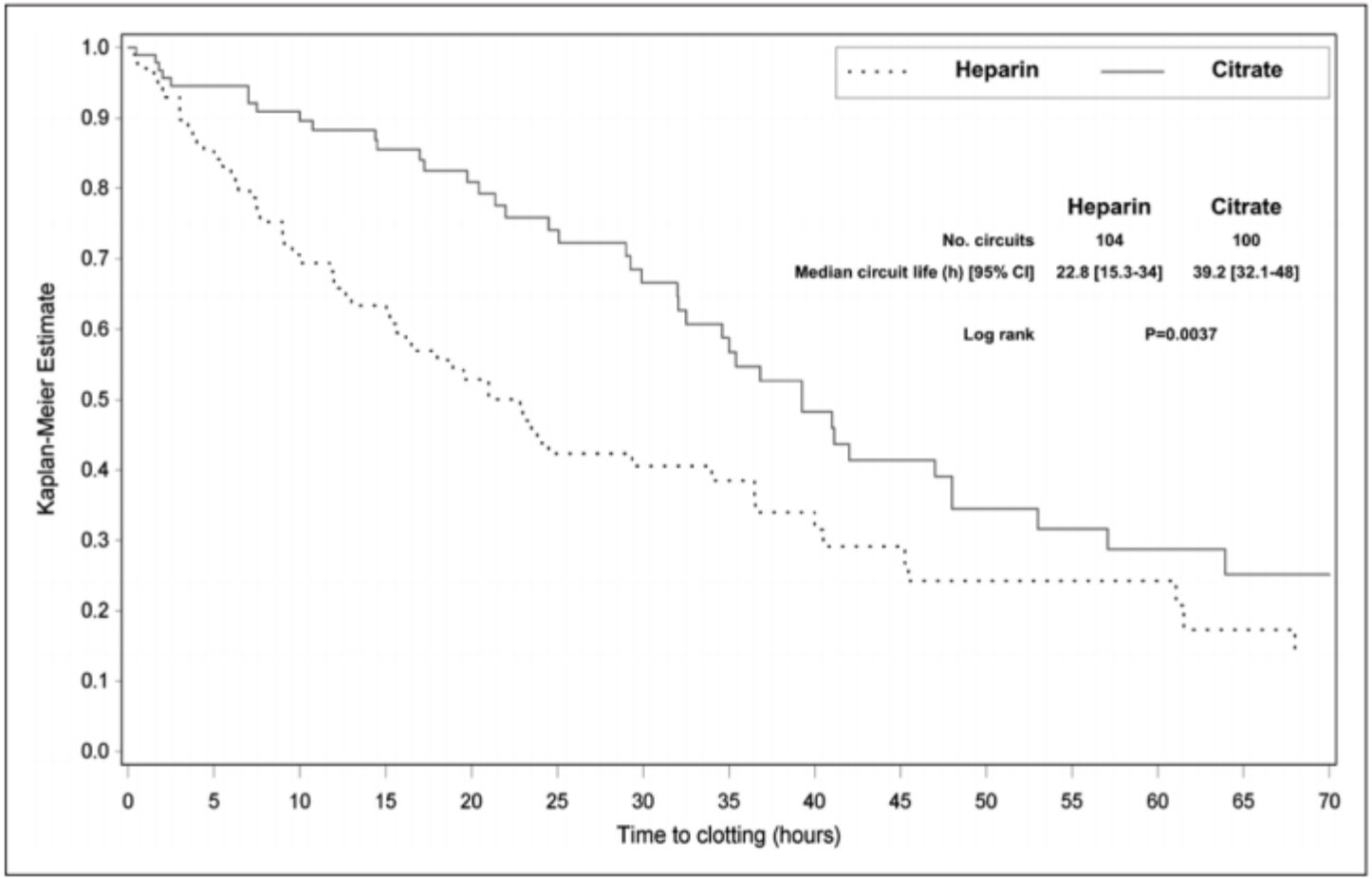

Figure 2. Kaplan-Meier estimate of the probability of continuous renal replacement therapy circuit survival for the first circuit.

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TABLE 2. Change in Interleukin-6, Interleukin-8, and Interleukin-10 Levels Between 0 and 48–72 Hr Following Commencement of Continuous Renal Replacement Therapy

	Citrate[a]			Heparin[b]			
Variable	*t* = 0 Hr	*t* = 48–72 Hr	Change Score	*t* = 0 Hr	*t* = 48–72 Hr	Change Score	*p*[c]
IL-6, median, pg/mL (IQR)	102.7 (214.0)	48.3 (58.1)	−29.3 (171.5)	141.7 (285.6)	53.8 (99.0)	−66.5 (262.1)	0.4
IL-8, median, pg/mL (IQR)	108.0 (114.0)	54.7 (42.6)	−26.2 (127.4)	115.8 (132.4)	53.8 (48.8)	−25.8 (131.0)	0.86
IL-10, median, pg/mL (IQR)	40.3 (63.3)	36.7 (44.9)	−0.7 (39.6)	37.7 (143.0)	36.2 (53.2)	−6.9 (111.1)	0.76

TABLE 3. Clinical Outcomes and Continuous Renal Replacement Therapy Process Measures

Variable	Citrate (*n* = 105)	Heparin (*n* = 107)	Total	*p*
Clinical				
ICU mortality, *n*/total (%)	28/105 (26.7)	25/107 (23.4)		0.58
ICU length of stay, median (IQR), d	9.0 (12)	9.0 (13)		0.79
Hospital mortality, *n*/total (%)	33/105 (31.4)	31/107 (29.0)		0.7
Red cells transfused				
Patients transfused, *n*/total (%)	52/101 (52)	48/103 (47)		0.58
Volume of red cells, mean (SD)	908 (770)	872 (917)		0.83

Pediatr Nephrol (2017) 32:1971–1978
DOI 10.1007/s00467-017-3694-4

ORIGINAL ARTICLE

Citrate versus heparin anticoagulation in continuous renal replacement therapy in small children

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Fig. 2 Kaplan–Meier survival curve indicating circuit survival time in the subgroup where only clotted filters were included

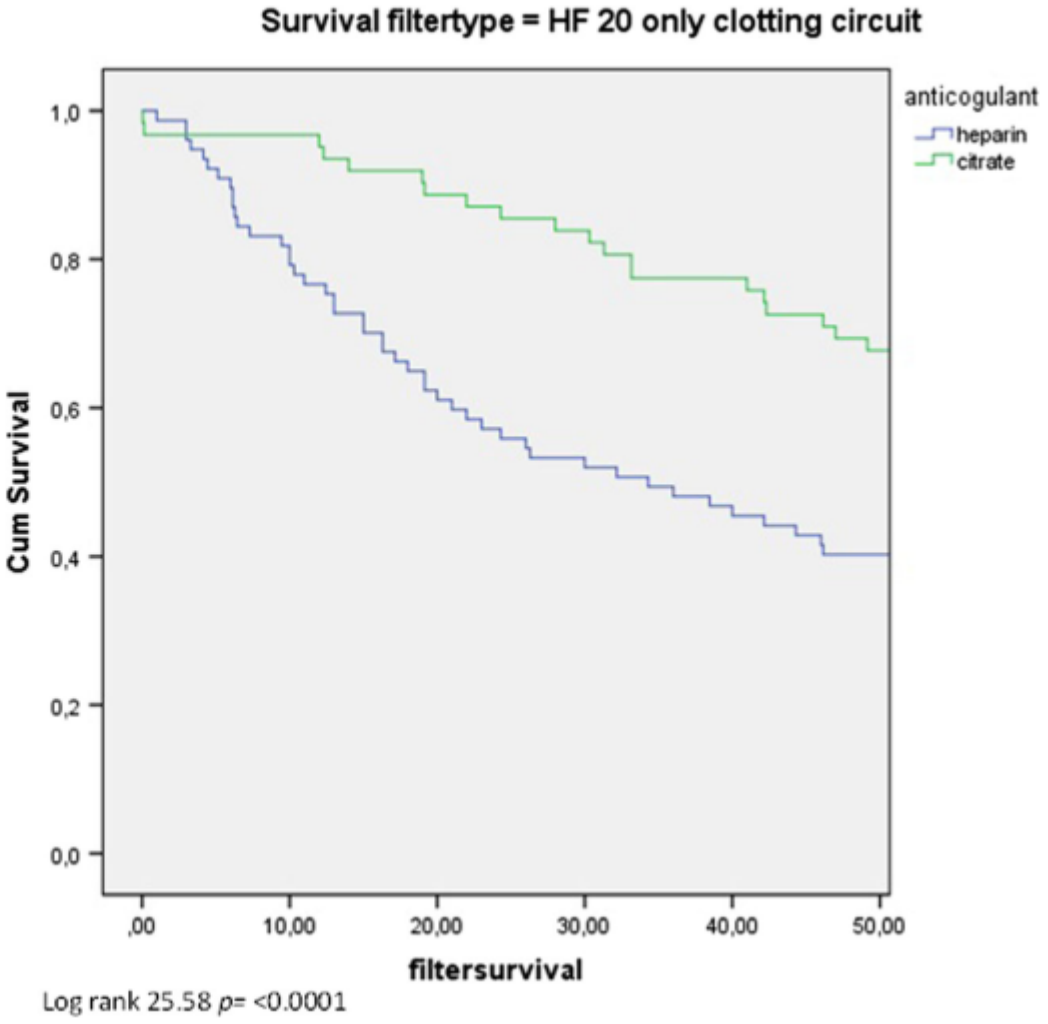

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Table 3 Reasons for circuit failure in the heparin and citrate group

	Heparin (n = 121)	Citrate (n = 105)	p value
Circuit clotting	51 (42%)	18 (17.1%)	<0.001*
Vascular access malfunction	12 (10%)	9 (8.6%)	0.82
Transport to radiology/operating room	8 (6.6%)	7 (6.7%)	0.98
Switch to other substitution fluid	0	5 (4.8%)	0.02*
Scheduled filter replacement after 72 h**	26 (21.4%)	42 (40%)	0.004*
Technical issues/alarms***	13 (10.8%)	9 (8.6%)	0.66
End of CRRT treatment	6 (5%)	14 (13.3%)	0.03*
Other reasons	5 (4.2%)	1 (0.9%)	0.22

*Significant

**Advised maximum duration of HF20 filter use according to Baxter international, Deerfield, IL, USA

***Incorrect scale balance caused blood pump stop and shutdown of the circuit

JAMA | Original Investigation

Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury

A Randomized Clinical Trial

JAMA. 2020;324(16):1629-1639. doi:10.1001/jama.2020.18618
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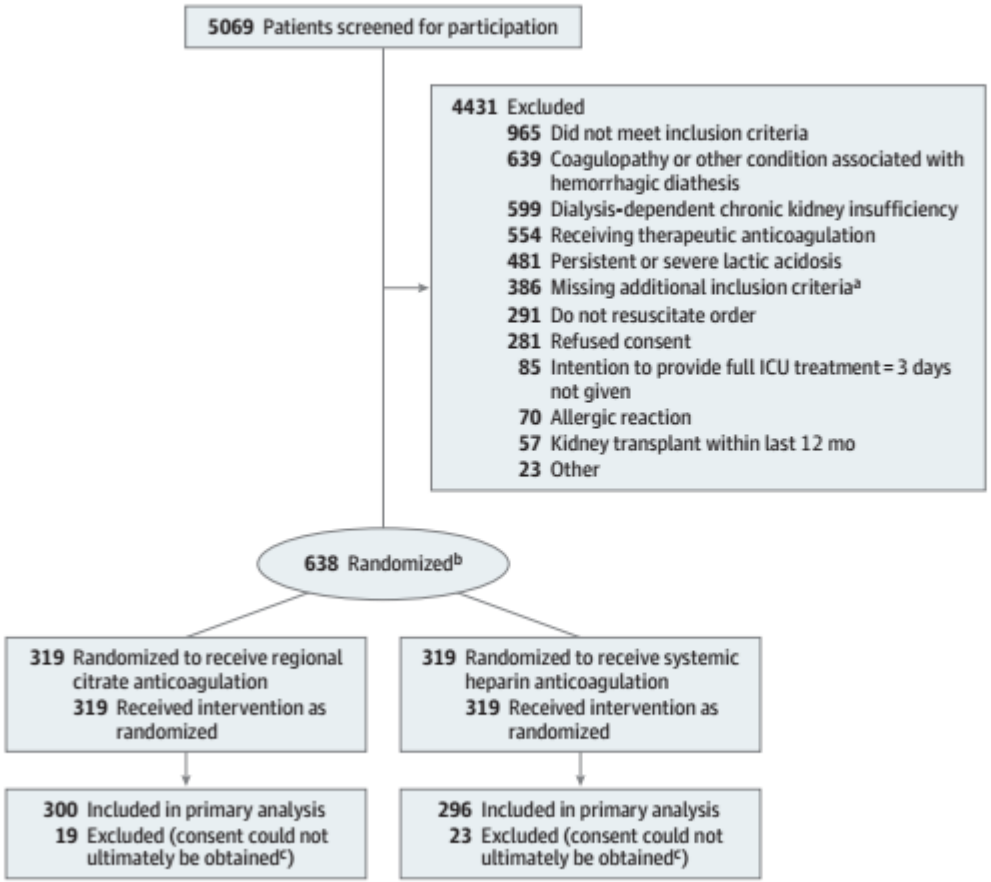
Figure 1. Participant Flow in the RICH Trial



Abbreviations: ICU, intensive care unit; RICH, Regional Citrate vs Systemic Heparin Anticoagulation for Continuous Kidney Replacement Therapy in Critically Ill Patients with Acute Kidney Injury.

[a] Severe sepsis or septic shock, use of vasopressor, refractory fluid overload.

[b] Randomization was performed centrally in a 1:1 proportion using the Pocock minimization method of stratified randomization, accounting for the factors study center, sex, cardiovascular Sequential Organ Failure Assessment (SOFA) score (0-2 vs 3-4), and presence or absence of oliguria.[9,14]

[c] Reasons for including but not analyzing patients were refusal of the guardianship procedure by the local court, no written consent of guardian prior to the death of the patient, no written consent of the guardian at all, or timeline issues (details reported in Supplement 3)

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Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury

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Table 2. Clinical Outcomes in the RICH Trial

	Regional citrate anticoagulation (n = 300)	Systemic heparin anticoagulation (n = 296)	Absolute difference (95% CI)	OR or HR (95% CI)	*P* value
Primary outcome					
Filter life span, h					
Mean (SD)	44.9 (26.9)	33.3 (25.1)	11.2 (8.2 to 14.3) [adjusted][a]		<.001
Median (IQR)	46.5 (18.8-70.3)	26.0 (12.0-50.6)	15.4 (11.3 to 19.5)[b]		
90-d all-cause mortality					
Unadjusted, No. (%)	150 (51.2)[c]	156 (53.6)[c]	−2.4 (−10.5 to 5.8)[d]	HR, 0.91 (0.72 to 1.13)	.38
				1.004)	.054
					.011
				1.09)	.24
				0.49)	<.001
Received RBC transfusion	197/293 (67.2)	184/290 (63.4)	3.8 (−3.9 to 11.5)[d]	OR, 1.18 (0.84 to 1.66)	.34
RBC transfusion volume, median (IQR), mL	500 (0-1085) [n = 293]	560 (0-1200) [n = 290]	0 (0 to 0)[b]		.85
Infection, No. (%)					
New culture-proven infection since start of dialysis	204 (68.0)	164 (55.4)	12.6 (4.9 to 20.3)[d]	OR, 1.71 (1.23 to 2.39)	.002
Length of stay, median (IQR), d					
ICU (primary)					
Naive[h]	16.0 (8.0-29.0)	13.5 (7.0-25.0)	1.0 (−1.0 to 3.0)[b]		.19
Censored[f]	25.0 (13.0-43.0)	25.0 (12.0-52.0)	−1.0 (−7.0 to 7.0)	HR, 0.97 (0.78 to 1.21)	.80
Hospital					
Naive[h]	27.0 (13.0-51.0)	27.0 (14.0-49.5)	0.0 (−3.0 to 4.0)[b]		.83
Censored[f]	46.0 (28.0-99.0)	55.0 (32.0-95.0)	−9.0 (−18.0 to 5.0)	HR, 1.04 (0.83 to 1.30)	.75
All-cause mortality, No. (%)[i]					
28 d	114 (38.7)	128 (43.8)	−5.1 (−13.0 to 2.9)[d]	HR, 0.84 (0.66 to 1.09)	.19
60 d	137 (46.7)	147 (50.4)	−3.7 (−11.9 to 4.4)[d]	HR, 0.88 (0.70 to 1.11)	.27
365 d	175 (60.1)	174 (60.0)	0.1 (−7.9 to 8.1)[d]	HR, 0.95 (0.77 to 1.17)	.63

Conclusions

Among critically ill patients with acute kidney injury receiving continuous kidney replacement therapy, anticoagulation with regional citrate, compared with systemic heparin anticoagulation, resulted in significantly longer filter life span. The trial was terminated early and was therefore underpowered to reach conclusions about the effect of anticoagulation strategy on mortality.

Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury

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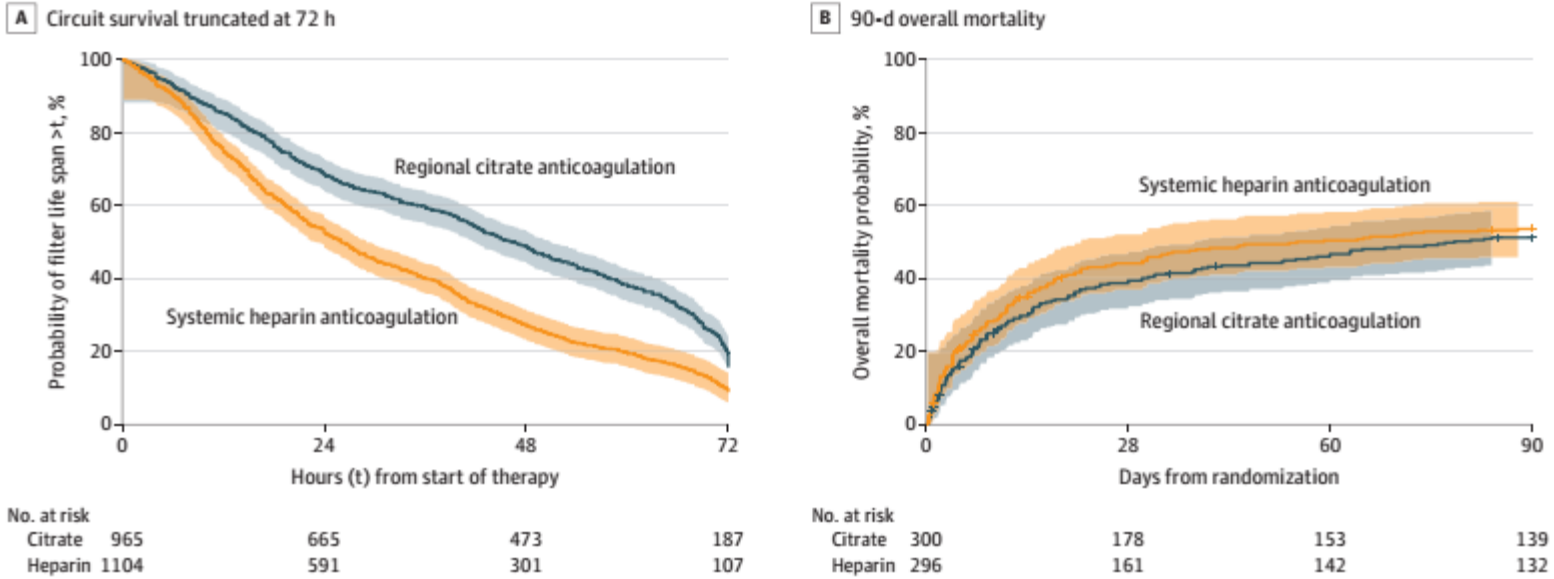
Figure 2. Kaplan-Meier Curves With Hall-Wellner Confidence Bands



A, Time (hours) from start of kidney replacement therapy to filter replacement. All circuits were observed to failure or 72 hours. B, 90-day overall mortality, with median (interquartile range) observation time 90 days. Ticks perpendicular to curves indicate censored patients (n = 19).

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Table 3. Adverse Events

	No. (%)	
	Regional citrate anticoagulation (n = 300)	Systemic heparin anticoagulation (n = 296)
Hypophosphatemia[a]	45 (15.4)	18 (6.2)
Severe cardiac rhythm disorders	10 (3.4)	9 (3.1)
Heparin-induced thrombocytopenia[b]	8 (2.7)	9 (3.1)
Severe alkalosis[c]	7 (2.4)	1 (0.3)
Neurologic complications[d]	4 (1.4)	4 (1.4)
Severe hypocalcemia[e]	4 (1.4)	1 (0.3)
Respiratory complications[f]	3 (1.0)	6 (2.1)
Citrate accumulation[g]	2 (0.7)	0
Gastrointestinal complications[h]	2 (0.7)	10 (3.4)
Other cardiovascular complications[i]	2 (0.7)	5 (1.7)
Metabolic acidosis[j]	1 (0.3)	2 (0.7)
Hyperkalemia	0	4 (1.4)
Thrombotic, thromboembolic complications	0	3 (1.0)

[a] Phosphate level less than 0.5 mmol/L.

[b] Positive antibody test result.

[c] pH greater than 7.50 and bicarbonate concentration greater than 30 mmol/L.

[d] Includes complications such as seizures, delirium, and hypoxic brain damage.

[e] Ionized calcium level less than 0.9 mmol/L.

[f] Includes complications such as pneumonia, acute respiratory distress syndrome, Horowitz index less than 200 for at least 1 hour, and respiratory complications with the need of reintubation or recannulation.

[g] Ratio of Ca^{2+} total to Ca^{2+} ion, 2.5 or greater.

[h] Includes all gastrointestinal bleeding events requiring at least 1 unit of packed red blood cells.

Includes complications such as ischemia, cardiogenic shock, cardiac decompensation.

pH less than 7.2 and bicarbonate concentration less than 20 mmol/L (excluding lactic acidosis).

Stucker et al. Critical Care (2015) 19:91
DOI 10.1186/s13054-015-0822-z

CRITICAL CARE

RESEARCH Open Access

Efficacy and safety of citrate-based anticoagulation compared to heparin in patients with acute kidney injury requiring continuous renal replacement therapy: a randomized controlled trial

Fabien Stucker[1†], Belen Ponte[1†], James Tataw[1], Pierre-Yves Martin[1], Hannah Wozniak[2], Jérome Pugin[2] and Patrick Saudan[1*]

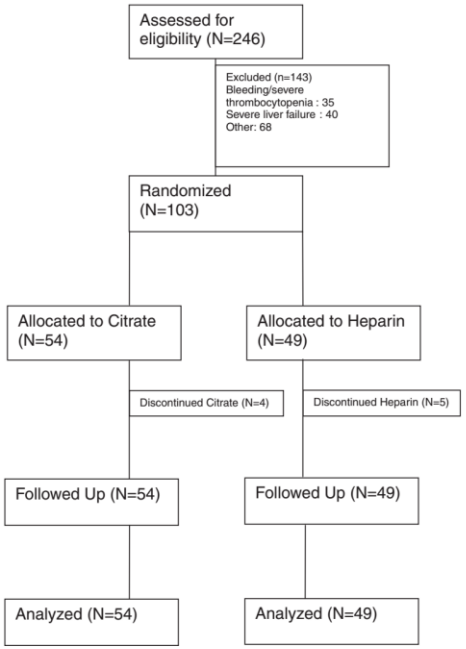

Figure 1 Flow chart of the trial.

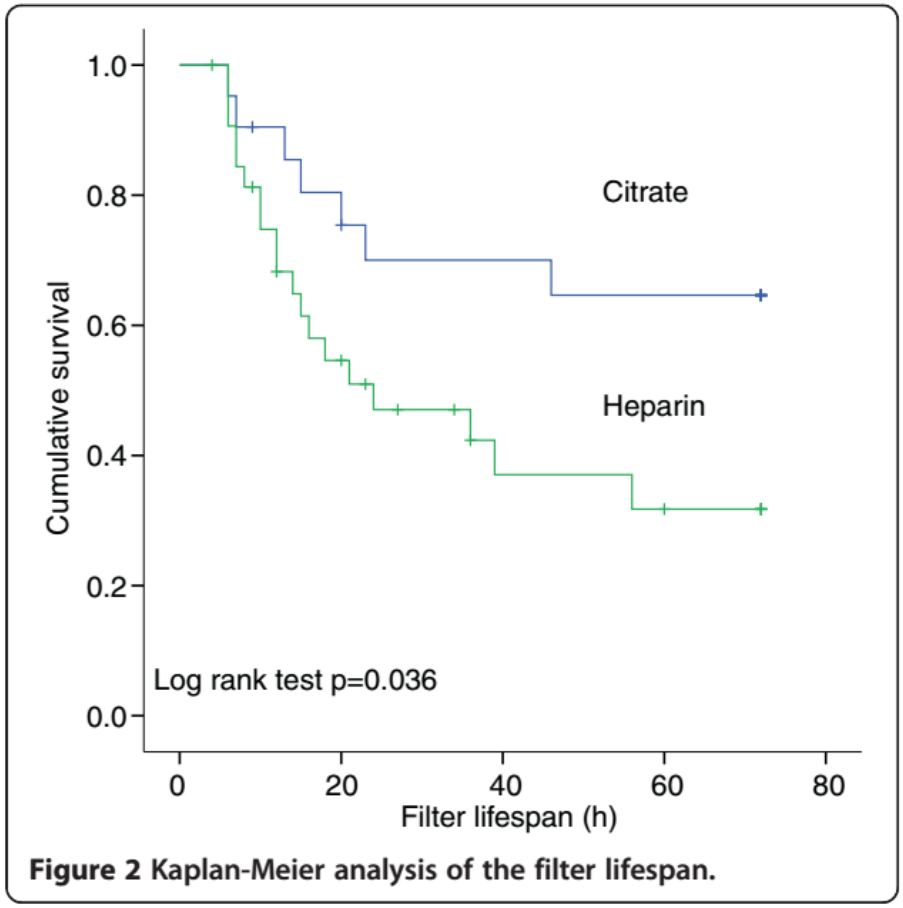

Figure 2 Kaplan-Meier analysis of the filter lifespan.

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Side effects	32	27	0.17
Bleeding	0	4 (8)	
HIT	1 (2)	2 (4)	
Filter clotting	3 (6)	18 (37)	
Metabolic disorders:	14	3	
Metabolic alcalosis	3	0	
Respiratory alkalosis	0	1	
Metabolic acidosis	3	1	
Severe hypocalcemia	6	1	
Ca total/calcium ion ratio >2.5	1	0	
CRRT, days	3 (2 to 6)	3 (2 to 5)	0.30
ICU, days	7 (4 to 15)	7 (4 to 12)	0.79
Hospital, days	22 (6 to 35)	16 (9 to 30)	0.45
Survival at 28 days	43 (80)	36 (74)	0.46
Survival at 90 days	40 (74)	35 (73)	0.90

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Regional citrate versus systemic heparin anticoagulation for continuous renal replacement therapy in critically ill patients with acute kidney injury (RICH) trial: study protocol for a multicentre, randomised controlled trial

Melanie Meersch,[1] Mira Küllmar,[1] Carola Wempe,[1] Detlef Kindgen-Milles,[2] Stefan Kluge,[3] Torsten Slowinski,[4] Gernot Marx,[5] Joachim Gerss,[6] Alexander Zarbock,[1] SepNet Critical Care Trials Group

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