

Table 1. Study characteristics for anticoagulation

Study	Population	Comparison	Number of patients (citrate / heparin)	Severity (citrate / heparin)	Modality/replacement dialysate fluid flow	Filter	Exclusion criteria
Betjes, 2007	Need for RRT; combined medical and surgical ICU, the Netherlands	Regional citrate (2.7 mmol/L blood flow, Srisawat ion Ca ²⁺ 0.25–0.35 mmol/L) vs. systemic heparin (bolus of 3000–5000 IU, maintained APTT at 50–70 s)	21 / 27	SAPS 51.4 / 51.0	CVVH; postdilution; Blood flow 150 ml/h; Fixed hemofiltration 1500 ml/h	High-flux triacetate hemofilter (UF-205; Nipro Corporation, Osaka, Japan)	Patients after cardiothoracic surgery; contraindication to heparin or citrate
Brain, 2014	AKI; ICU, Austria	Regional citrate (adjusted according to arterial ion Ca ²⁺ , serum ion Ca ²⁺ 1.0–1.35 mmol/L) vs. systemic heparin (bolus of 5000 IU, APTT maintained at 50 s)	19 / 11	APACHE 80 / 61	CVVHDF; predilution; Blood flow 191 ml/h (citrate)/217 ml/h (heparin)	ST-100; ST-150; M100	Contraindication to citrate or heparin, pregnancy, or lactation
Fealy, 2007	AKI; tertiary hospital ICU, Austria	Regional citrate (3.1 mmol/L of blood flow, serum ionized calcium 1.1–1.3 mmol/L) vs. regional heparinization (1500 IU/h and protamine postfilter (15 mg/h))	10 / 10	SAPS 41 / 41	CVVH; predilution; Blood flow 150 ml/h; Fluid replacement 2000 ml/h	1.3 m ² APS650 polysulfone hollow fiber membrane (Asahi Medical, Tokyo, Japan)	Liver failure; hepatitis; contraindication to citrate or heparin
Gattas, 2015	AKI; ICU, Austria	regional citrate (2.5–3.3 mmol/L blood flow, serum ion Ca ²⁺ 1.0–1.2 or 0.91–1.1 mmol/L) vs. regional heparin (1000 or 1500 IU/h, protamine [15 or 10 mg/h])	105 / 107	APACHE 25.6 / 25.0	CVVHDF/CVVH; Predilution; Blood flow 150/200 ml/h	Aquarius or Prismaflex	Stay in ICU less than 24 h; age <18 years; pregnant or breastfeeding; ischemic hepatitis or liver failure; allergy to heparin or protamine; HIT; chronic kidney disease requiring dialysis prior to ICU admission.
Hetzel, 2011	AKI; university hospital ICU, Germany	Regional citrate (HF-citrate solution flow based on 42 ml/kg/h in predilution; Equivalent to ca. 4 mmol citrate per 1 L blood) vs. systemic Heparin (HFsolution flow based on 42 ml/kg/h in predilution)	87 / 83	SOFA 9.95 / 9.95 APACHE 21.8 / 22.04	CVVH; predilution; Blood/HF-solution flow 3:1	AV600S high-flux membrane, surface area 1.4 m ² , Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany	Contraindications to either intervention, metabolic alkalosis, pregnancy or lactation, chronic dialysis, other therapeutic anticoagulation, HIT
Kutsogiannis, 2005	AKI; Tertiary and community hospital ICU, Canada	Regional citrate (maintain posthemofilter ion Ca ²⁺ 0.25 and 0.35 mmol/L) vs. systemic heparin (initial bolus of 50 U/kg, maintain APTT at 45–65 s)	16 / 14	LODC 7.75 / 9.42	CVVHDF; predilution; Blood flow 125 ml/min; Dialysate flow rates 1000 ml/hr; hemofiltration rates 1000 ml/h.	PRISMA M-100 AN69 (polyacrylonitrile) hemofilter	Liver failure; contraindication to citrate or heparin
Monchi, 2004	AKI; medical and surgical ICU, Belgium	Regional citrate (starting rate of 4.3 mmol/1 of blood flow, maintain the serum ionized calcium concentration below 0.3 mmol/1 in the circuit) vs. systemic heparin (infusion of heparin was commenced at an initial rate of 1000 U/h, and adjusted	8 / 12	SAPS 40 / 42	CVVH; postdilution; Blood flow 175 ml/min	1.6 m ² highly permeable polysulfone membrane	Cirrhosis, severe coagulopathy, high risk of bleeding

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		between 500 and 2000 U/h to maintain APTT at 60–80 s)					
Oudemans-Van Straaten, 2009	AKI; teaching hospital ICU, the Netherlands	Regional citrate (3 mmol/L blood flow, serum ionized calcium 0.9–1.0 mmol/L) vs. systemic nadroparin (bolus of 2850 IU/h; maintenance of 380 IU/h, BW > 100 kg:3800 IU at initial, followed by 456 IU/h)	97 / 103	SAPS 59 / 61 APACHE 28 / 28	CVVH; postdilution; Blood flow 220 ml/h; Filtrate flow of 4000 ml/h	1.9 m ² cellulose triacetate hollow fiber membrane (UF 205, Nipro, Osaka, Japan)	Cirrhosis, bleeding, HIT, chronic dialysis, contraindication to citrate or heparin; therapeutic anticoagulation
Schilder, 2014	AKI, uraemia, multiorgan failure; ICU, the Netherlands	Regional citrate (3 mmol/L blood flow, targeting systemic ionized calcium levels of 1.0–1.35 mmol/L) vs. systemic heparin (a heparin bolus of 5000 IU at the start of CVVH a separate heparin pump (20 000 IU/48 ml) (2.0 ml/h); APTT maintained at 50 s)	66 / 73	SOFA 10 / 11 APACHE 23 / 25	CVVH; predilution; Blood flow 180 ml/min	Not reported	High bleeding risk; other therapeutic anticoagulation; HIT
Stucker, 2015	AKI; University hospital ICU, Switzerland	regional citrate (adjust the citrate solution flow rate to the patients' blood flow rate to target a blood citrate concentration of 3 mmol/L, postfilter ion Ca ²⁺ 0.25– 0.30 mmol/L) H: Systemic heparin (a minimal dose of 500 UI/h)	54 / 49	SOFA 63 / 65 APACHE 28 / 29	CVVHDF; 2/3 predilution and; Dialysate flow 10 ml/kg/h; Blood flow 100–200 ml/min	Biocompatible high-flux membrane measuring 1.5 m ² (ST-150; Gambro)	Hemorrhagic disorders; severe thrombocytopenia; heparin-induced thrombocytopenia; liver failure; liver transplantation
Wu, 2015	AKI; hospital ICU, China	Regional citrate (dose of 4 L/h with a fixed citrate infusion rate of 28 mmol/h) vs. systemic heparin (loading dose, 40 IU/kg; maintenance dose, 4 IU/kg per h)	15 / 19	APACHE 16.2 / 17.0	CVVH; Blood flow 180–200 ml/min	high flux AV600S (polysulfone, 1.4 m ² , Fresenius Medical Care)	INR >1.8; PT >50% above the upper limit of normal values; PLT <50 x 10 ⁹ /L; liver failure; other therapeutic anticoagulation
Zarbock, 2020	AKI, sepsis, septic shock; 26 centers, Germany	Regional citrate (30 ml/kg/ h, delivered dose: 20– 25 ml/kg/h; target ion Ca ²⁺ 0.25–0.35 mmol/L) vs. systemic heparin (target APTT: 45–60 s)	300 / 296	SOFA 11.5 / 11.5 APACHE 28.4 / 28.5	CVVH/CVVHDF; postdilution; Blood flow 10 ml/h (citrate)/110 ml/h (heparin); Dialysate flow 1593.1 ml/h (citrate)/1603.2 ml/h (heparin)	Not reported	Bleeding risk or an active bleeding; disease or organ damage related to hemorrhagic diathesis; dialysis-dependent chronic kidney insufficiency; lactate acidosis; kidney transplant within the last 12 months; pregnant or breastfeeding; Abortus imminens