



## Clinical trial results:

**Oxidative stress and Circulating Nuclear DNA (cfDNA) in critically ill patients with acute kidney failure treated with continuous renal replacement therapies.**

**Effect of two anticoagulation strategies of the extracorporeal purification system in renal function recovery.**

### Summary

EudraCT number	2016-004361-12
Trial protocol	ES
Global end of trial date	30 May 2022

### Results information

Result version number	v1 (current)
This version publication date	06 November 2024
First version publication date	06 November 2024

### Trial information

#### Trial identification

Sponsor protocol code	FER-CIT-2016-01
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT06646328
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Fernando Sánchez
Sponsor organisation address	Carrer de Sanz de Bremond, 8, 1, Castelló de la Plana, Spain, 12004
Public contact	Fernando Sánchez, Fernando Sánchez, 34 625978412, sanchez_fermor@gva.es
Scientific contact	Fernando Sánchez, Fernando Sánchez, 34 625978412, sanchez_fermor@gva.es

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2022
Global end of trial reached?	Yes
Global end of trial date	30 May 2022
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

1. To compare the effect on bio-incompatibility induced oxidative stress and systemic oxidative stress in critically ill patients with ARF using two anticoagulation strategies of the extracorporeal system in continuous renal replacement therapies (CRRT) (heparin vs citrate).
2. To compare the effect on extracellular levels of circulating nucleosomes in critically ill patients with ARF employing two anticoagulation strategies of the extracorporeal system CRRT (heparin vs citrate).
3. To evaluate the clinical impact in terms of recovery of renal function in critically ill patients with ARF when two anticoagulation strategies of the extracorporeal system CRRT (heparin vs citrate) are used.

Protection of trial subjects:

Patients who are able to provide consent can participate in the study by signing the Informed Consent (IC) form.

If a patient is unable to provide consent, we will seek consent from their family.

If there is no family available, we will consider the opinion of the person the patient trusts or their designated decision-maker.

If none of these options are available, deferred consent will not be considered and the patient will not be included in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	8
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Inclusion criteria:

Adult patients in the intensive care unit with acute kidney injury requiring continuous renal replacement therapy.

Patients or their families must sign the Informed Consent (IC) form before randomization to participate in the study.

Randomization by sealed envelopes.

### Pre-assignment

Screening details:

Exclusion Criteria:

< 18 years old.

Pregnancy or lactation.

Terminal disease or life expectancy < 48 hours.

Increased risk of bleeding.

Systemic anticoagulation therapy.

Contraindication for heparin.

Heparin-induced thrombocytopenia.

Dialysis before inclusion.

Hypercalcemia.

Severe Hepatitis.

Cirrhosis.

Inclusion in another protocol.

### Period 1

Period 1 title	T0
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Heparin

Arm description:

Anticoagulation with heparin during continuous renal replacement therapies

Arm type	Active comparator
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Unfractionated heparin
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Initial dose of 500–1000 IU/hour with adaptation of the infusion to the patient and the clotting time.

<b>Arm title</b>	Citrate
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Arm description:

Citrate anticoagulation during continuous renal replacement therapies

Arm type	Experimental
Investigational medicinal product name	Trisodium citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

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**Dosage and administration details:**

Regional citrate anticoagulation was used at an initial dose of 4 mmol/L and with a calcium reinfusion solution at an initial dose of 1.7 mmol/L, with adaptation of both infusions to the patient ionic calcium levels.

<b>Number of subjects in period 1</b>	Heparin	Citrate
Started	10	10
Completed	10	10

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**Period 2**

Period 2 title	T1 prefilter (60 minutes)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

**Arms**

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Heparin

## Arm description:

Anticoagulation with heparin during continuous renal replacement therapies

Arm type	Active comparator
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Unfractionated heparin
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

## Dosage and administration details:

Initial dose of 500–1000 IU/hour with adaptation of the infusion to the patient and the clotting time.

<b>Arm title</b>	Citrate
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## Arm description:

Citrate anticoagulation during continuous renal replacement therapies

Arm type	Experimental
Investigational medicinal product name	Trisodium citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

## Dosage and administration details:

Regional citrate anticoagulation was used at an initial dose of 4 mmol/L and with a calcium reinfusion

solution at an initial dose of 1.7 mmol/L, with adaptation of both infusions to the patient ionic calcium levels.

Number of subjects in period 2	Heparin	Citrate
Started	10	10
Completed	10	10

### Period 3

Period 3 title	T1 postfilter (60 minutes)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
Arm title	Heparin

Arm description:

Anticoagulation with heparin during continuous renal replacement therapies

Arm type	Active comparator
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Unfractionated heparin
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Initial dose of 500–1000 IU/hour with adaptation of the infusion to the patient and the clotting time.

Arm title	Citrate
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Arm description:

Citrate anticoagulation during continuous renal replacement therapies

Arm type	Experimental
Investigational medicinal product name	Trisodium citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Regional citrate anticoagulation was used at an initial dose of 4 mmol/L and with a calcium reinfusion

solution at an initial dose of 1.7 mmol/L, with adaptation of both infusions to the patient ionic calcium levels.

Number of subjects in period 3	Heparin	Citrate
Started	10	10
Completed	10	10

#### Period 4

Period 4 title	T2 prefilter (24 hours)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

#### Arms

Are arms mutually exclusive?	Yes
Arm title	Heparin

Arm description:

Anticoagulation with heparin during continuous renal replacement therapies

Arm type	Active comparator
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Unfractionated heparin
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Initial dose of 500–1000 IU/hour with adaptation of the infusion to the patient and the clotting time.

Arm title	Citrate
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Arm description:

Citrate anticoagulation during continuous renal replacement therapies

Arm type	Experimental
Investigational medicinal product name	Trisodium citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Regional citrate anticoagulation was used at an initial dose of 4 mmol/L and with a calcium reinfusion

solution at an initial dose of 1.7 mmol/L, with adaptation of both infusions to the patient ionic calcium levels.

<b>Number of subjects in period 4<sup>[1]</sup></b>	Heparin	Citrate
Started	9	8
Completed	9	8

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One patient in the heparin arm and two in the citrate arm died between periods 3 and 4.

### Period 5

Period 5 title	T2 postfilter (24 hours)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Heparin

Arm description:

Anticoagulation with heparin during continuous renal replacement therapies

Arm type	Active comparator
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Unfractionated heparin
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Initial dose of 500–1000 IU/hour with adaptation of the infusion to the patient and the clotting time.

<b>Arm title</b>	Citrate
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Arm description:

Citrate anticoagulation during continuous renal replacement therapies

Arm type	Experimental
Investigational medicinal product name	Trisodium citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for haemodialysis
Routes of administration	Extracorporeal use

Dosage and administration details:

Regional citrate anticoagulation was used at an initial dose of 4 mmol/L and with a calcium reinfusion



solution at an initial dose of 1.7 mmol/L, with adaptation of both infusions to the patient ionic calcium levels.

<b>Number of subjects in period 5</b>	Heparin	Citrate
Started	9	8
Completed	9	8

## Baseline characteristics

### Reporting groups

Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	

Reporting group values	Heparin	Citrate	Total
Number of subjects	10	10	20
Age categorical			
Units: Subjects			
Adults (18-64 years)	3	7	10
From 65-84 years	7	3	10
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	60.87	68.55	
standard deviation	± 11.11	± 7.32	-
Gender categorical			
Units: Subjects			
Female	3	0	3
Male	7	10	17
Mechanical ventilation			
Units: Subjects			
Yes	5	5	10
No	5	5	10
Vasoactive support			
Units: Subjects			
Yes	8	9	17
No	2	1	3
Personal history: ischemic heart disease			
Units: Subjects			
Yes	1	2	3
No	9	8	17
Personal history: dyslipidemia			
Units: Subjects			
Yes	5	5	10
No	5	5	10
Personal history: diabete mellitus			
Units: Subjects			
Yes	3	2	5
No	7	8	15
Personal history: hypertension			
Units: Subjects			
Yes	6	7	13

No	4	3	7
Personal history: obesity Units: Subjects			
Yes	4	2	6
No	6	8	14
Personal history: CPOD Units: Subjects			
Yes	1	2	3
No	9	8	17
Personal history: chronic kidney disease without dialysis treatment Units: Subjects			
Yes	2	1	3
No	8	9	17
APACHE II score Units: Points arithmetic mean standard deviation	18.40 ± 7.63	19.40 ± 3.72	-
SAPS 3 score Units: Points arithmetic mean standard deviation	62.30 ± 16.25	66.00 ± 13.24	-
SOFA score Units: Points median inter-quartile range (Q1-Q3)	8.00 6.75 to 12.25	9.00 7.00 to 9.00	-
Noradrenaline Units: microgram(s)/kilogram/minute arithmetic mean standard deviation	0.30 ± 0.32	0.44 ± 0.25	-
Lactate Units: mmol/L median inter-quartile range (Q1-Q3)	2.30 1.35 to 4.10	1.90 1.20 to 6.90	-
Urea Units: mg/dl arithmetic mean standard deviation	122.33 ± 91.92	127.90 ± 98.41	-
Creatinine Units: mg/dl arithmetic mean standard deviation	3.70 ± 2.14	3.48 ± 2.38	-
Bilirrubine Units: mg/dl median inter-quartile range (Q1-Q3)	1.33 0.92 to 2.48	0.54 0.34 to 2.54	-
Leukocytes Units: *10 <sup>3</sup> /microL median inter-quartile range (Q1-Q3)	12.80 8.25 to 14.78	11.69 7.88 to 28.18	-
Platelets Units: *10 <sup>3</sup> /mm <sup>3</sup>			

median	179.00	228.50	
inter-quartile range (Q1-Q3)	134.50 to 221.25	160.50 to 332.50	-
Baseline creatinine			
Units: mg/dl			
median	1.16	1.36	
standard deviation	± 0.95	± 1.16	-

## End points

### End points reporting groups

Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	
Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	
Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	
Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	
Reporting group title	Heparin
Reporting group description:	
Anticoagulation with heparin during continuous renal replacement therapies	
Reporting group title	Citrate
Reporting group description:	
Citrate anticoagulation during continuous renal replacement therapies	

### Primary: Recovery of renal function

End point title	Recovery of renal function
End point description:	
Duration of RRT	
End point type	Primary
End point timeframe:	
Through study completion, an average of 20 days	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Days				
median (inter-quartile range (Q1-Q3))	3.50 (2.00 to 8.00)	2.00 (1.00 to 3.50)		

## Statistical analyses

Statistical analysis title	Duration of renal replacement therapy
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[1]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - 0.114

## Primary: Recovery of renal function

End point title	Recovery of renal function
End point description:	Recovery of renal function and dialysis dependency at ICU discharge
End point type	Primary
End point timeframe:	Through study completion, an average of 20 days

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Total				
Creatinine recovered up to previous values	2	5		
Creatinine values >50% from baseline	3	2		
Dialysis dependent	1	0		

## Statistical analyses

Statistical analysis title	Recovery of renal function
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[2]</sup>
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	2.333
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.635
upper limit	8.569

Notes:

[2] - 0.286

### Primary: Recovery of renal function

End point title	Recovery of renal function
End point description:	
Recovery of renal function and dialysis dependency at hospital discharge	
End point type	Primary
End point timeframe:	
Through study completion, an average of 20 days	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Total				
Creatinine recovered up to previous values	5	6		
Creatinine values >50% from baseline	0	0		
Dialysis dependent	1	0		

### Statistical analyses

Statistical analysis title	Recovery of renal function
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[3]</sup>
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	0.833

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.583
upper limit	1.192

Notes:

[3] - 1.00

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description: GSH at the beginning of RRT	
End point type	Secondary
End point timeframe: At the beginning of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.102 (± 0.045)	0.120 (± 0.036)		

### Statistical analyses

Statistical analysis title	GSH at the beginning of RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [4]
Method	t-test, 2-sided

Notes:

[4] - 0.322

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description: GSH prefilter 60 minutes after initiation of RRT	
End point type	Secondary
End point timeframe: 60 minutes after initiation of RRT	



End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
median (standard deviation)	0.125 ( $\pm$ 0.029)	0.135 ( $\pm$ 0.026)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH prefilter 60 minutes after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[5]</sup>
Method	t-test, 2-sided

Notes:

[5] - 0.409

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSH postfilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.102 ( $\pm$ 0.043)	0.149 ( $\pm$ 0.050)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH postfilter 60 minutes after initiation
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[6]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	-0.986
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.907
upper limit	-0.041

Notes:

[6] - 0.041

## Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	
Change in GSH prefilter/postfilter 60 minutes after initiation RRT heparin	
End point type	Secondary
End point timeframe:	
60 minutes after initiation RRT	

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.125 (± 0.029)	0.102 (± 0.043)		

## Statistical analyses

<b>Statistical analysis title</b>	GSH prefilter/postfilter 60 minutes heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[7]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	0.903
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.142
upper limit	1.63

Notes:

[7] - 0.019

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
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End point description:

Change in GSH prefilter/postfilter 60 minutes after initiation RRT citrate

End point type	Secondary
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End point timeframe:

60 minutes after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.135 (± 0.026)	0.149 (± 0.050)		

### Statistical analyses

Statistical analysis title	GSH prefilter/postfilter 60 minutes citrate
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Comparison groups	Citrate v Citrate
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Number of subjects included in analysis	20
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	< 0.05 <sup>[8]</sup>
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Method	t-test, 2-sided
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Notes:

[8] - 0.193

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
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End point description:

GSH prefilter 24 hours after initiation RRT

End point type	Secondary
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End point timeframe:

24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.109 (± 0.055)	0.151 (± 0.044)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH 24 hours after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [9]
Method	t-test, 2-sided

Notes:

[9] - 0.109

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSH postfilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.105 (± 0.056)	0.150 (± 0.038)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH postfilter 24 hours after initiation RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[10]</sup>
Method	t-test, 2-sided

Notes:

[10] - 0.072

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSH prefilter/postfilter 24 hours after initiation RRT heparin
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.109 (± 0.055)	0.105 (± 0.056)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH prefilter/postfilter 24 hours heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[11]</sup>
Method	t-test, 2-sided

Notes:

[11] - 0.582

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSH prefilter/postfilter 24 hours after initiation RRT citrate
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: micromole(s)/millilitre				
arithmetic mean (standard deviation)	0.151 ( $\pm$ 0.044)	0.150 ( $\pm$ 0.038)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH prefilter/postfilter 24 hours citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[12]</sup>
Method	t-test, 2-sided

Notes:

[12] - 0.872

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG at the beginning of RRT
End point type	Secondary
End point timeframe:	At the beginning of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.289 (0.184 to 0.410)	0.290 (0.192 to 0.592)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG at the beginning of RRT
Comparison groups	Citrate v Heparin

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[13]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[13] - 1.00

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG prefilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.370 (0.191 to 0.407)	0.247 (0.215 to 0.338)		

### Statistical analyses

Statistical analysis title	GSSG prefilter 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[14]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[14] - 0.315

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG postfilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.370 (0.176 to 0.543)	0.335 (0.240 to 0.388)		

### Statistical analyses

Statistical analysis title	GSSG postfilter 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[15]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[15] - 0.720

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	
Change in GSSG prefilter/postfilter 60 minutes after initiation RRT heparin	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.370 (0.191 to 0.407)	0.370 (0.176 to 0.543)		

### Statistical analyses

Statistical analysis title	GSSG prefilter/postfilter 60 minutes heparin
Comparison groups	Heparin v Heparin



Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[16]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[16] - 0.678

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG prefilter/postfilter 60 minutes citrate
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.247 (0.215 to 0.338)	0.335 (0.240 to 0.388)		

### Statistical analyses

Statistical analysis title	GSSG prefilter/postfilter 60 minutes citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[17]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[17] - 0.515

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG prefilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.349 (0.223 to 0.676)	0.211 (0.170 to 0.270)		

### Statistical analyses

Statistical analysis title	GSSG 24 hours after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[18]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[18] - 0.105

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG postfilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: micromole(s)/millilitre				
arithmetic mean (standard error)	0.410 (± 0.269)	0.238 (± 0.067)		

### Statistical analyses

Statistical analysis title	GSSG postfilter 24 hours after initiation RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[19]</sup>
Method	t-test, 2-sided

Notes:

[19] - 0.118

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG prefilter/postfilter 24 hours after initiation RRT heparin
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: microcurie(s)/microlitre				
median (inter-quartile range (Q1-Q3))	0.349 (0.223 to 0.676)	0.335 (0.206 to 0.535)		

### Statistical analyses

Statistical analysis title	GSSG prefilter/postfilter 24 hours heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[20]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[20] - 0.674

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG prefilter/postfilter 24 hours after initiation RRT citrate
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: micromole(s)/millilitre				
median (inter-quartile range (Q1-Q3))	0.211 (0.170 to 0.270)	0.271 (0.181 to 0.282)		

### Statistical analyses

Statistical analysis title	GSSG prefilter/postfilter 24 hours citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[21]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[21] - 0.401

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG/GSH at the beginning of RRT
End point type	Secondary
End point timeframe:	At the beginning of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non unit				
median (inter-quartile range (Q1-Q3))	2.288 (1.965 to 3.909)	2.379 (1.834 to 4.855)		

### Statistical analyses

Statistical analysis title	GSSG/GSH at the beginning of RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05 <sup>[22]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[22] - 0.796

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG/GSH prefilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: non unit				
median (inter-quartile range (Q1-Q3))	2.514 (1.941 to 3.973)	2.056 (1.531 to 3.043)		

### Statistical analyses

Statistical analysis title	GSSG/GSH prefilter 60 minutes after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[23]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[23] - 0.278

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG/GSH postfilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: non unit				
median (inter-quartile range (Q1-Q3))	3.988 (2.359 to 8.000)	2.474 (1.302 to 4.282)		

### Statistical analyses

Statistical analysis title	GSSG/GSH postfilter 60 minutes after initiation
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[24]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[24] - 0.278

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG/GSH prefilter/postfilter 60 minutes after initiation RRT heparin
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non unit				
median (inter-quartile range (Q1-Q3))	2.514 (1.941 to 3.973)	3.988 (2.359 to 8.000)		

### Statistical analyses

Statistical analysis title	GSSG/GSH prefilter/postfilter 60 minutes heparin
Comparison groups	Heparin v Heparin

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[25]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[25] - 0.086

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG/GSH prefilter/postfilter 60 minutes after initiation RRT citrate
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non unit				
median (inter-quartile range (Q1-Q3))	2.056 (1.531 to 3.043)	2.474 (1.302 to 4.282)		

### Statistical analyses

Statistical analysis title	GSSG/GSH prefilter/postfilter 60 minutes citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[26]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[26] - 0.441

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG/GSH GSSG prefilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: Non unit				
arithmetic mean (standard deviation)	3.069 ( $\pm$ 1.320)	1.495 ( $\pm$ 0.421)		

### Statistical analyses

Statistical analysis title	GSSG/GSH prefilter 24 hours after initiation
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[27]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	1.659
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.484
upper limit	2.835

Notes:

[27] - 0.007

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	GSSG/GSH postfilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: Non unit				
arithmetic mean (standard deviation)	3.125 ( $\pm$ 1.487)	1.667 ( $\pm$ 0.699)		



### Statistical analyses

<b>Statistical analysis title</b>	GSSG/GSH postfilter 24 hours after initiation
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [28]
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	-1.278
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.391
upper limit	-0.165

Notes:

[28] - 0.028

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	
Change in GSSG/GSH prefilter/postfilter 24 hours after initiation RRT heparin	
End point type	Secondary
End point timeframe:	
24 hours after initiation RRT	

<b>End point values</b>	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Non unit				
arithmetic mean (standard deviation)	2.738 (± 1.081)	2.860 (± 1.436)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG/GSH prefilter/postfilter 24 hours heparin
Comparison groups	Heparin v Heparin

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[29]</sup>
Method	t-test, 2-sided

Notes:

[29] - 0.543

### Secondary: Activation and elimination of free radicals

End point title	Activation and elimination of free radicals
End point description:	Change in GSSG/GSH prefilter/postfilter 24 hours after initiation RRT citrate
End point type	Secondary
End point timeframe:	24 hours citrate

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: Non unit				
arithmetic mean (standard deviation)	1.495 (± 0.421)	1.677 (± 0.699)		

### Statistical analyses

Statistical analysis title	GSSG/GSH prefilter/postfilter 24 hours after
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[30]</sup>
Method	t-test, 2-sided

Notes:

[30] - 0.409

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	MPO at the beginning of RRT
End point type	Secondary
End point timeframe:	At the beginning of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: mU/ml				
median (inter-quartile range (Q1-Q3))	125.673 (95.176 to 147.835)	63.386 (52.239 to 112.167)		

## Statistical analyses

<b>Statistical analysis title</b>	MPO at the beginning of RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[31]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[31] - 0.010

## Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	
MPO prefilter 60 minutes after initiation of RRT	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: mU/ml				
arithmetic mean (standard deviation)	96.691 (± 24.051)	83.726 (± 36.693)		

## Statistical analyses

<b>Statistical analysis title</b>	MPO prefilter 60 minutes
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[32]</sup>
Method	t-test, 2-sided

Notes:

[32] - 0.370

## Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description: MPO postfilter 60 minutes after initiation of RRT	
End point type	Secondary
End point timeframe: 60 minutes after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: mU/ml				
arithmetic mean (standard deviation)	121.892 (± 30.815)	87.577 (± 28.093)		

## Statistical analyses

Statistical analysis title	MPO postfilter 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[33]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	-1.161
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	-0.192

Notes:

[33] - 0.022

## Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
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End point description:	
Change in MPO prefilter/postfilter 60 minutes after initiation RRT heparin	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mU/ml				
arithmetic mean (standard deviation)	96.691 ( $\pm$ 24.051)	121.892 ( $\pm$ 30.815)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO prefilter/postfilter 60 minutes heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[34]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	1.122
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.032
upper limit	2.02

Notes:

[34] - 0.014

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	
MPO prefilter/postfilter 60 minutes citrate	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mU/ml				
arithmetic mean (standard deviation)	83.726 ( $\pm$ 36.693)	87.577 ( $\pm$ 28.093)		

### Statistical analyses

Statistical analysis title	MPO prefilter/postfilter 60 minutes citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[35]</sup>
Method	t-test, 2-sided

Notes:

[35] - 0.680

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	MPO prefilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: mU/ml				
median (inter-quartile range (Q1-Q3))	88.925 (78.249 to 127.644)	87.323 (69.137 to 111.738)		

### Statistical analyses

Statistical analysis title	GSSG 24 hours after initiation RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[36]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[36] - 0.743

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	
MPO postfilter 24 hours after initiation RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: mU/ml				
arithmetic mean (standard deviation)	119.323 (± 45.117)	86.616 (± 22.675)		

### Statistical analyses

Statistical analysis title	MPO postfilter 24 hours after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[37]</sup>
Method	t-test, 2-sided

Notes:

[37] - 0.084

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	
Change in MPO prefilter/postfilter 24 hours after initiation RRT heparin	
End point type	Secondary
End point timeframe:	
24 hours after initiation RRT	

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mU/ml				
median (standard deviation)	103.144 ( $\pm$ 35.376)	119.323 ( $\pm$ 45.117)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO prefilter/postfilter 24 hours heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[38]</sup>
Method	t-test, 2-sided

Notes:

[38] - 0.216

### Secondary: Activation and elimination of biomarkers of inflammation

End point title	Activation and elimination of biomarkers of inflammation
End point description:	Change in MPO prefilter/postfilter 24 hours after initiation RRT citrate
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: mU/ml				
median (inter-quartile range (Q1-Q3))	87.323 (69.137 to 111.738)	84.620 (69.136 to 104.009)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO prefilter/postfilter 24 hours citrate
Comparison groups	Citrate v Citrate



Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[39]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[39] - 0.263

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	Circulating cell-free DNA (cfDNA) at the beginning of RRT
End point type	Secondary
End point timeframe:	At the beginning of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1247.467 (± 732.377)	853.569 (± 526.755)		

### Statistical analyses

Statistical analysis title	cfDNA at the beginning of RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[40]</sup>
Method	t-test, 2-sided

Notes:

[40] - 0.184

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	cfDNA prefilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1416.767 ( $\pm$ 813.978)	894.022 ( $\pm$ 551.939)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA prefilter 60 minutes after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[41]</sup>
Method	t-test, 2-sided

Notes:

[41] - 0.110

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	cfDNA postfilter 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1299.040 ( $\pm$ 643.126)	941.419 ( $\pm$ 603.344)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA postfilter 60 minutes after initiation RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[42]</sup>
Method	t-test, 2-sided

Notes:

[42] - 0.216

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	Change in cfDNA prefilter/postfilter 60 minutes after initiation RRT heparin
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1416.767 (± 813.978)	1299.040 (± 643.126)		

### Statistical analyses

Statistical analysis title	cfDNA prefilter/postfilter 60 minutes heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[43]</sup>
Method	t-test, 2-sided

Notes:

[43] - 0.524

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	Change in cfDNA prefilter/postfilter 60 minutes after initiation RRT citrate
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	894.022 ( $\pm$ 551.939)	941.419 ( $\pm$ 603.344)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA prefilter/postfilter 60 minutes citrate
Comparison groups	Citrate v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[44]</sup>
Method	t-test, 2-sided

Notes:

[44] - 0.448

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	cfDNA prefilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1675.836 ( $\pm$ 882.759)	1234.318 ( $\pm$ 508.296)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA prefilter 24 hours after initiation RRT
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[45]</sup>
Method	t-test, 2-sided

Notes:

[45] - 0.240

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	cfDNA postfilter 24 hours after initiation RRT
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1921.533 (± 779.795)	1184.161 (± 670.064)		

### Statistical analyses

Statistical analysis title	cfDNA postfilter 24 hours after initiation RRT
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[46]</sup>
Method	t-test, 2-sided

Notes:

[46] - 0.062

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	Change in cfDNA prefilter/postfilter 24 hours after initiation RRT heparin
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Heparin	Heparin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1675.836 ( $\pm$ 882.759)	1921.533 ( $\pm$ 779.795)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA prefilter/postfilter 24 hours heparin
Comparison groups	Heparin v Heparin
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[47]</sup>
Method	t-test, 2-sided

Notes:

[47] - 0.075

### Secondary: Activation and elimination of biomarkers of cell damage

End point title	Activation and elimination of biomarkers of cell damage
End point description:	Change in cfDNA prefilter/postfilter 24 hours after initiation RRT citrate
End point type	Secondary
End point timeframe:	24 hours after initiation RRT

End point values	Citrate	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1234.318 ( $\pm$ 508.296)	1184.161 ( $\pm$ 670.064)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA prefilter/postfilter 24 hours citrate
Comparison groups	Citrate v Citrate

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[48]</sup>
Method	t-test, 2-sided

Notes:

[48] - 0.805

## Secondary: Mass transfer of free radicals

End point title	Mass transfer of free radicals
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End point description:

Median levels of total amount of GSH mass removed expressed as a percentage of the filter inlet GSH mass

End point type	Secondary
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End point timeframe:

60 minutes after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: percent				
arithmetic mean (standard deviation)	20.903 (± 21.998)	-1.829 (± 21.074)		

## Statistical analyses

<b>Statistical analysis title</b>	GSH mass transfer 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[49]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	1.055
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.102
upper limit	1.984

Notes:

[49] - 0.030

## Secondary: Mass transfer of free radicals

End point title	Mass transfer of free radicals
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End point description:	
Median levels of total amount of GSH mass removed expressed as a percentage of the filter inlet GSH mass	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: percent				
arithmetic mean (standard error)	-4.798 ( $\pm$ 33.667)	4.765 ( $\pm$ 12.786)		

### Statistical analyses

Statistical analysis title	GSH mass transfer 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[50]</sup>
Method	t-test, 2-sided

Notes:

[50] - 0.462

### Secondary: Mass transfer of free radicals

End point title	Mass transfer of free radicals
End point description:	
Median levels of total amount of GSSG mass removed expressed as a percentage of the filter inlet GSSG mass	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: percent				
arithmetic mean (standard deviation)	-8.903 ( $\pm$ 33.062)	-15.543 ( $\pm$ 39.779)		



### Statistical analyses

<b>Statistical analysis title</b>	GSSG mass transfer 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[51]</sup>
Method	t-test, 2-sided

Notes:

[51] - 0.705

### Secondary: Mass transfer of free radicals

End point title	Mass transfer of free radicals
End point description: Median levels of total amount of GSSG mass removed expressed as a percentage of the filter inlet GSSG mass	
End point type	Secondary
End point timeframe: 24 hours after initiation of RRT	

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: percent				
arithmetic mean (standard deviation)	2.198 (± 33.644)	-6.713 (± 32.103)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG mass transfer 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[52]</sup>
Method	t-test, 2-sided

Notes:

[52] - 0.591

### Secondary: Mass transfer of biomarkers of inflammation

End point title	Mass transfer of biomarkers of inflammation
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End point description:

Median levels of total amount of MPO mass removed expressed as a percentage of the filter inlet MPO mass

End point type	Secondary
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End point timeframe:

60 minutes after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: percent				
arithmetic mean (standard deviation)	-28.197 (± 31.545)	5.483 (± 18.628)		

### Statistical analyses

Statistical analysis title	MPO mass transfer 60 minutes
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Comparison groups	Heparin v Citrate
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Number of subjects included in analysis	18
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	< 0.05 [53]
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Method	t-test, 2-sided
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Parameter estimate	d Cohen
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Point estimate	-1.263
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-2.272
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upper limit	-0.221
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Notes:

[53] - 0.017

### Secondary: Mass transfer of biomarkers of inflammation

End point title	Mass transfer of biomarkers of inflammation
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End point description:

Median levels of total amount of MPO mass removed expressed as a percentage of the filter inlet MPO mass

End point type	Secondary
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End point timeframe:

24 hours after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: percent				
arithmetic mean (standard deviation)	-16.824 ( $\pm$ 40.049)	11.725 ( $\pm$ 19.926)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO mass transfer 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[54]</sup>
Method	t-test, 2-sided

Notes:

[54] - 0.089

### Secondary: Mass transfer of biomarkers of inflammation

End point title	Mass transfer of biomarkers of inflammation
End point description:	Median levels of total amount of CRP mass removed expressed as a percentage of the filter inlet CRP mass
End point type	Secondary
End point timeframe:	60 minutes after initiation RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: percent				
median (inter-quartile range (Q1-Q3))	-3.095 (-5.260 to 0.275)	1.790 (-0.658 to 3.420)		

### Statistical analyses

<b>Statistical analysis title</b>	CRP mass transfer 60 minutes
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[55]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-0.964
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.848
upper limit	-0.056

Notes:

[55] - 0.023

## Secondary: Mass transfer of biomarkers of inflammation

End point title	Mass transfer of biomarkers of inflammation
End point description:	
Median levels of total amount of CRP mass removed expressed as a percentage of the filter inlet CRP mass	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: percent				
arithmetic mean (standard deviation)	-1.206 (± 2.622)	3.131 (± 2.735)		

## Statistical analyses

Statistical analysis title	CRP mass transfer 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[56]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-1.521

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.616
upper limit	-0.383

Notes:

[56] - 0.021

### Secondary: Mass transfer of biomarkers of cell damage

End point title	Mass transfer of biomarkers of cell damage
End point description:	
Median levels of total amount of cfDNA mass removed expressed as a percentage of the filter inlet cfDNA mass	
End point type	Secondary
End point timeframe:	
60 minutes after initiation RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: percent				
arithmetic mean (standard deviation)	-3.310 ( $\pm$ 37.482)	-5.094 ( $\pm$ 40.809)		

### Statistical analyses

Statistical analysis title	DNA mass transfer 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[57]</sup>
Method	t-test, 2-sided

Notes:

[57] - 0.920

### Secondary: Mass transfer of biomarkers of cell damage

End point title	Mass transfer of biomarkers of cell damage
End point description:	
Median levels of total amount of cfDNA mass removed expressed as a percentage of the filter inlet cfDNA mass	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: percent				
median (inter-quartile range (Q1-Q3))	-3.115 (-56.169 to 0.285)	8.240 (-10.390 to 19.463)		

## Statistical analyses

Statistical analysis title	cfDNA mass transfer 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	0.196

## Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description:	
GSH clearance rate 60 minutes after initiation RRT	
End point type	Secondary
End point timeframe:	
60 minutes after initiation RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: millilitre(s)/minute				
arithmetic mean (standard deviation)	17.286 (± 17.332)	-2.792 (± 16.303)		

## Statistical analyses

<b>Statistical analysis title</b>	GSH clearance rate 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[58]</sup>
Method	t-test, 2-sided
Parameter estimate	d Cohen
Point estimate	1.193
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.221
upper limit	2.138

Notes:

[58] - 0.016

## Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description:	
GSH clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: millilitre(s)/minute				
arithmetic mean (standard error)	-3.108 (± 23.930)	5.630 (± 9.530)		

## Statistical analyses

<b>Statistical analysis title</b>	GSH clearance rate 24 hours
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[59]</sup>
Method	t-test, 2-sided

Notes:

[59] - 0.350

### Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description:	
GSH mean clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: millilitre(s)/minute				
arithmetic mean (standard error)	8.741 (± 9.256)	2.626 (± 9.492)		

### Statistical analyses

<b>Statistical analysis title</b>	GSH mean clearance rate
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[60]</sup>
Method	t-test, 2-sided

Notes:

[60] - 0.230

### Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description:	
GSSG clearance 60 minutes after initiation of RRT	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	



End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: millilitre(s)/minute				
arithmetic mean (standard deviation)	-2.164 ( $\pm$ 30.707)	5.630 ( $\pm$ 9.530)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG clearance rate 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[61]</sup>
Method	t-test, 2-sided

Notes:

[61] - 0.554

### Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description:	GSSG clearance 24 hours after initiation of RRT
End point type	Secondary
End point timeframe:	24 hours after initiation of RRT

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: millilitre(s)/minute				
arithmetic mean (standard deviation)	4.449 ( $\pm$ 27.735)	-1.705 ( $\pm$ 26.713)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG clearance rate 24 hours
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[62]</sup>
Method	t-test, 2-sided

Notes:

[62] - 0.658

### Secondary: Clearance rate of free radicals

End point title	Clearance rate of free radicals
End point description: GSSG mean clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe: 24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: millilitre(s)/minuyte				
arithmetic mean (standard deviation)	2.360 (± 25.713)	-9.245 (± 17.104)		

### Statistical analyses

<b>Statistical analysis title</b>	GSSG mean clearance rate
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[63]</sup>
Method	t-test, 2-sided

Notes:

[63] - 0.297

### Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
End point description: MPO clearance 60 minutes after initiation RRT	
End point type	Secondary
End point timeframe: 60 minutes after initiation RRT	

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-12.635 (-47.103 to -3.178)	-4.810 (-9.915 to 14.200)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO clearance rate 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[64]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[64] - 0.133

### Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
End point description:	
MPO clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: millilitre(s)/min				
arithmetic mean (standard deviation)	-8.833 (± 34.858)	6.516 (± 12.095)		

### Statistical analyses

<b>Statistical analysis title</b>	MPO clearance rate 24 hours
Comparison groups	Heparin v Citrate

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[65]</sup>
Method	t-test, 2-sided

Notes:

[65] - 0.256

### Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
End point description:	
MPO mean clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: millilitre(s)/min				
median (inter-quartile range (Q1-Q3))	-16.110 (-29.760 to -10.355)	1.415 (-9.678 to 12.645)		

### Statistical analyses

Statistical analysis title	MPO mean clearance rate
Comparison groups	Citrate v Heparin
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[66]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-0.685
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.611
upper limit	0.261

Notes:

[66] - 0.046

### Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
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End point description:	
CRP clearance 60 minutes after initiation of RRT	
End point type	Secondary
End point timeframe:	
60 minutes after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-2.185 (-4.863 to 0.225)	1.670 (-0.410 to 2.375)		

### Statistical analyses

Statistical analysis title	CRP clearance rate 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[67]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-0.692
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.552
upper limit	0.186

Notes:

[67] - 0.019

### Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
End point description:	
CRP clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-2.120 (-2.623 to -0.113)	2.060 (1.543 to 4.580)		

## Statistical analyses

Statistical analysis title	CRP clearance rate 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[68]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-1.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.998
upper limit	-0.001

Notes:

[68] - 0.010

## Secondary: Clearance of biomarkers of inflammation

End point title	Clearance of biomarkers of inflammation
End point description:	
CRP mean clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe:	
24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-0.058 (-6.064 to 0.837)	0.224 (-3.085 to 1.183)		

## Statistical analyses

<b>Statistical analysis title</b>	CRP mean clearance rate
Comparison groups	Citrate v Heparin
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[69]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	g Hedges
Point estimate	-1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.265
upper limit	-0.198

Notes:

[69] - 0.015

### Secondary: Clearance of biomarkers of cell damage

End point title	Clearance of biomarkers of cell damage
End point description:	cfDNA clearance 60 minutes after initiation of RRT
End point type	Secondary
End point timeframe:	60 minutes after initiation of RRT

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	2.120 (-24.108 to 10.485)	3.525 (-13.073 to 17.500)		

### Statistical analyses

<b>Statistical analysis title</b>	cfDNA clearance rate 60 minutes
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[70]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[70] - 0.853

### Secondary: Clearance of biomarkers of cell damage

End point title	Clearance of biomarkers of cell damage
End point description: cfDNA clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe: 24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-2.230 (-57.878 to -0.440)	8.495 (-9.388 to 13.783)		

### Statistical analyses

Statistical analysis title	cfDNA clearance rate 24 hours
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[71]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[71] - 0.050

### Secondary: Clearance of biomarkers of cell damage

End point title	Clearance of biomarkers of cell damage
End point description: cfDNA mean clearance 24 hours after initiation of RRT	
End point type	Secondary
End point timeframe: 24 hours after initiation of RRT	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: millilitre(s)/minute				
median (inter-quartile range (Q1-Q3))	-0.390 (-10.760 to 0.000)	9.895 (-5.728 to 19.633)		



### Statistical analyses

<b>Statistical analysis title</b>	cfDNA mean clearance rate
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[72]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[72] - 0.054

### Secondary: Length of stay

End point title	Length of stay
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End point description:

ICU length of stay from ICU admission until the date of ICU discharge or date of death from any cause, whichever came first, assessed up to 90 days

End point type	Secondary
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End point timeframe:

From ICU admission until the date of ICU discharge or date of death from any cause, whichever came first, assessed up to 90 days

<b>End point values</b>	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: day				
median (inter-quartile range (Q1-Q3))	8.50 (3.75 to 12.25)	4.50 (1.75 to 7.75)		

### Statistical analyses

<b>Statistical analysis title</b>	ICU length of stay
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[73]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[73] - 0.165

### Secondary: Length of stay

End point title	Length of stay
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End point description:

Hospital length of stay

End point type	Secondary
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End point timeframe:

From hospital admission until the date of documented hospital discharge or date of death from any cause, whichever came first, assessed up to 90 days

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: day				
median (inter-quartile range (Q1-Q3))	18.50 (12.00 to 48.75)	19.50 (12.75 to 30.75)		

### Statistical analyses

Statistical analysis title	Hospital length of stay
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Comparison groups	Heparin v Citrate
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Number of subjects included in analysis	20
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	< 0.05 <sup>[74]</sup>
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Method	Wilcoxon (Mann-Whitney)
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Notes:

[74] - 0.853

### Secondary: Mortality

End point title	Mortality
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End point description:

ICU mortality

End point type	Secondary
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End point timeframe:

Through study completion, an average of 20 days

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: percent				
number (not applicable)	40	30		

### Statistical analyses

Statistical analysis title	ICU mortality
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[75]</sup>
Method	Chi-squared corrected

Notes:

[75] - 1.000

### Secondary: Mortality

End point title	Mortality
End point description:	
Hospital mortality	
End point type	Secondary
End point timeframe:	
Day 90 after ICU admission	

End point values	Heparin	Citrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: percent				
number (not applicable)	40	40		

### Statistical analyses

Statistical analysis title	Hospital mortality
Comparison groups	Heparin v Citrate
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 <sup>[76]</sup>
Method	Chi-squared corrected

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Notes:

[76] - 1.000

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

24 hours

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	5.0
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### Reporting groups

Reporting group title	Active Comparator : Heparin
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Reporting group description: -

Reporting group title	Experimental : Citrate
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Reporting group description: -

Serious adverse events	Active Comparator : Heparin	Experimental : Citrate	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	4	4	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Active Comparator : Heparin	Experimental : Citrate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	1 / 10 (10.00%)	
Investigations			
Platelet count decreased			
subjects affected / exposed	5 / 10 (50.00%)	1 / 10 (10.00%)	
occurrences (all)	5	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2019	Addition of research center and designated researcher

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 March 2020	COVID pandemic.	11 January 2021

Notes:

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early termination leading to a small number of subjects analysed
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Notes: