

Regionale antistolling met citraat voor CVVH

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Citrate



- *waarom citraat?*
- *hoe werkt het?*
- *hoe doe ik het?*
- *beperkingen?*
- *voordelen?*

Waarom citraat?

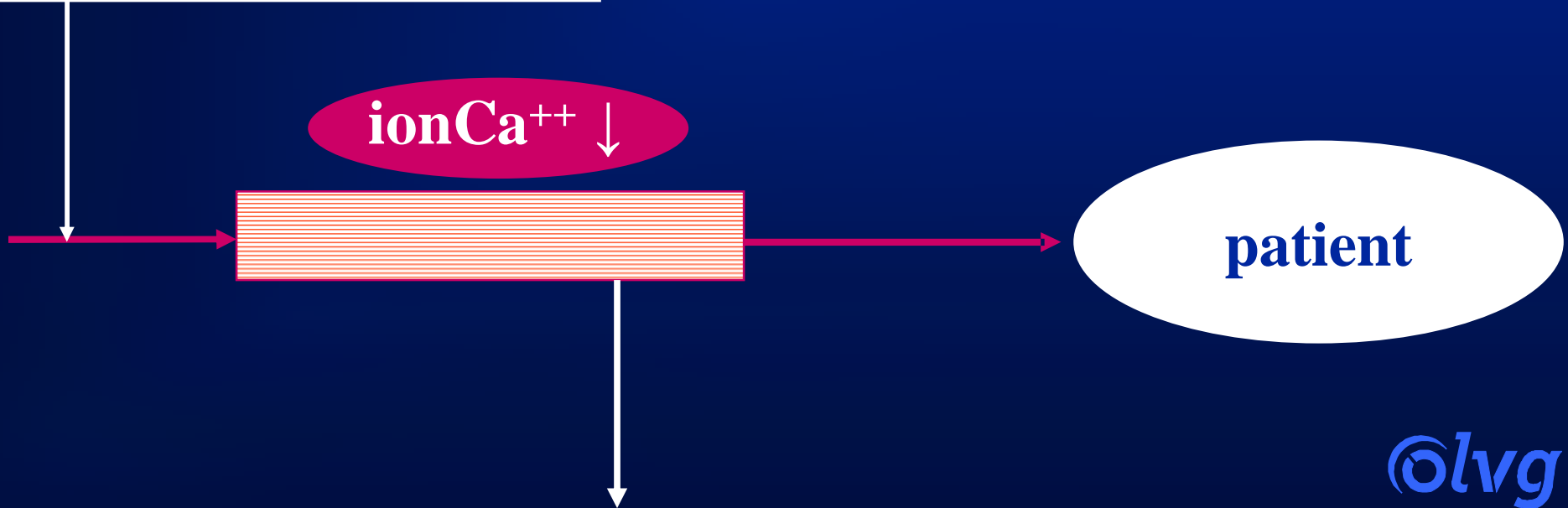
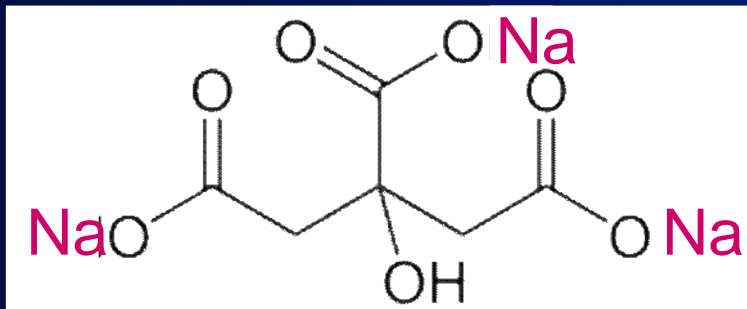
CVVH(DF)

zonder systemische antistolling

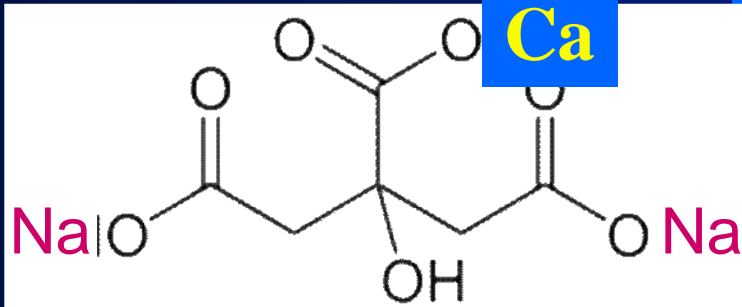
Hoe werkt citraat?

Citraat: anticoagulans

Na₃citraat



Na₃citraat



ionCa

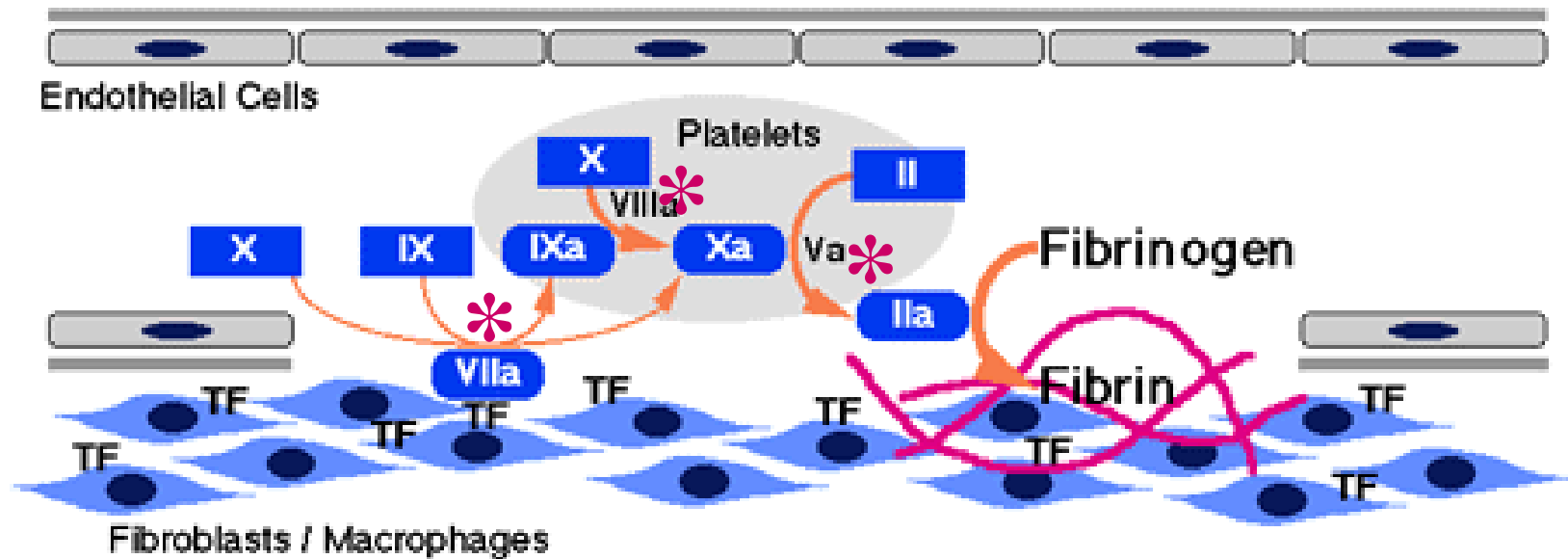
gebonden-Ca

ionCa ↓

gebonden-Ca

Ca-citraat + Na

Ca⁺⁺: essentielle co-factor *



*ion-Ca < 0.30 mmol/l →
remming van stolling*

Na₃citraat

ionCa⁺⁺ ↓

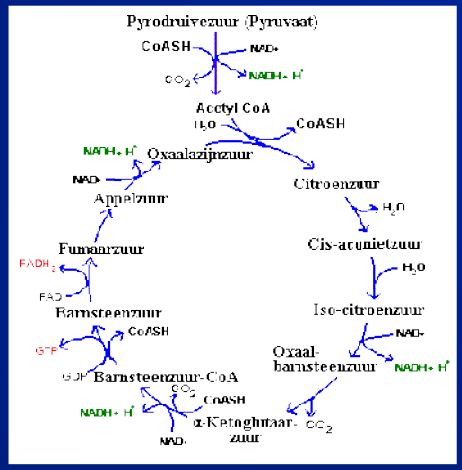


Ca-citraat

citraat

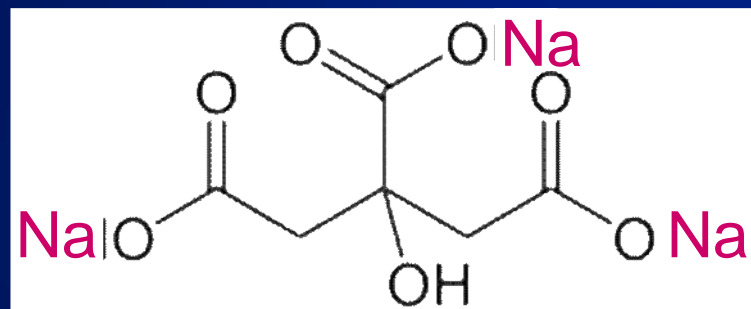
**regionale
antistolling**

calcium



Citraat is ook een buffer!

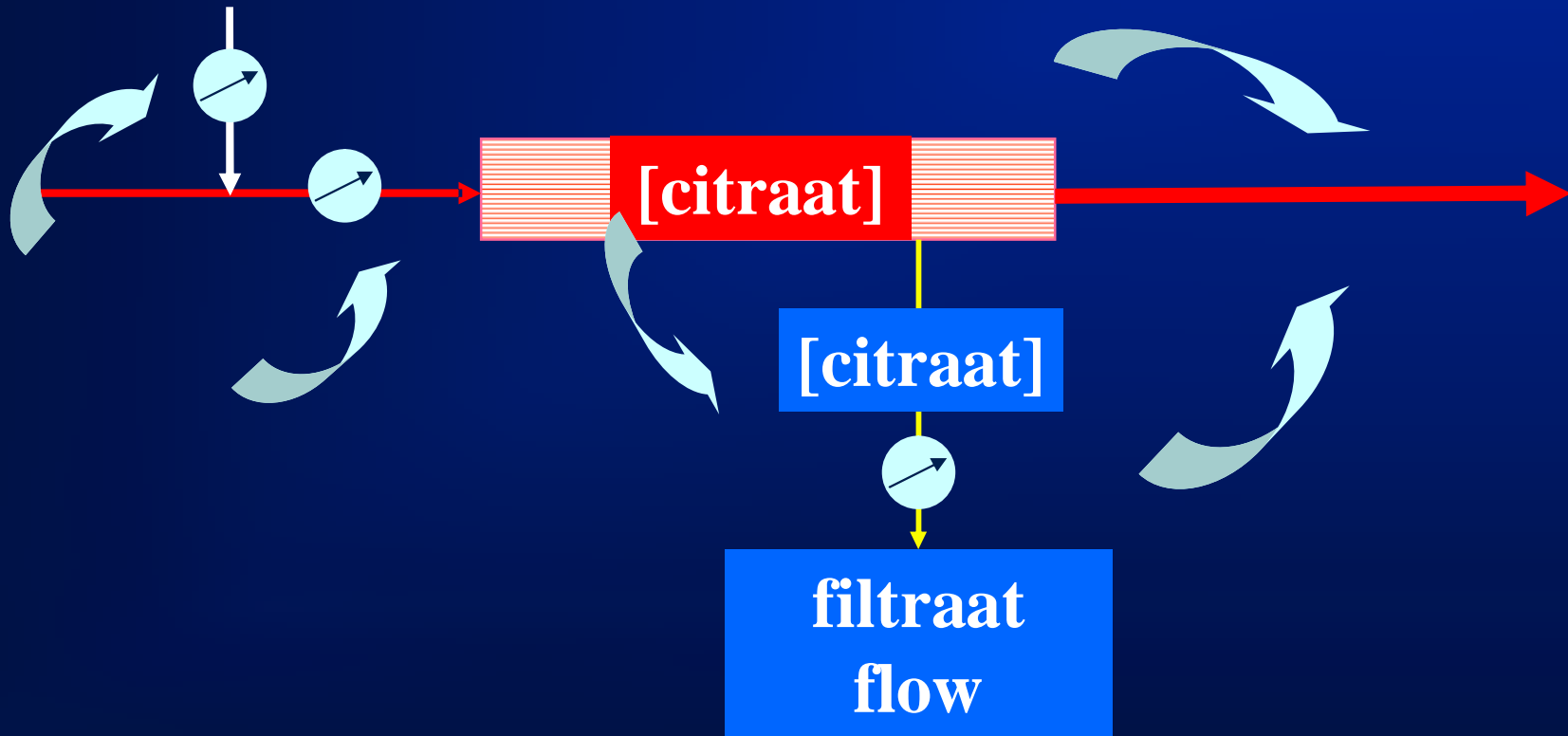
1 mol Na₃citraat → 3 mol Na⁺ + 3 mol HCO₃⁻



Hoeveel buffer komt er nu in de patient?

citraat (buffer) → patient

Na₃citraat



Hoe doe ik citraat?

Predilutie CVVH

Predilutie CVVH

substitutie

Sodium	140 mmol/l	
Potassium	3 mmol/l	
Citrate	13,3 mmol/l	(39,9 mEq/l)
Chloride	104 mmol/l	
Magnesium	0,5 mmol/l	(1,0 mEq/l)
Glucose	5 mmol/l	



Pallson, 1999

VUMC, Amsterdam

Filtraat

1900-2700 ml/u

**Monitoring
ionCa⁺⁺**

Standaard instellingen

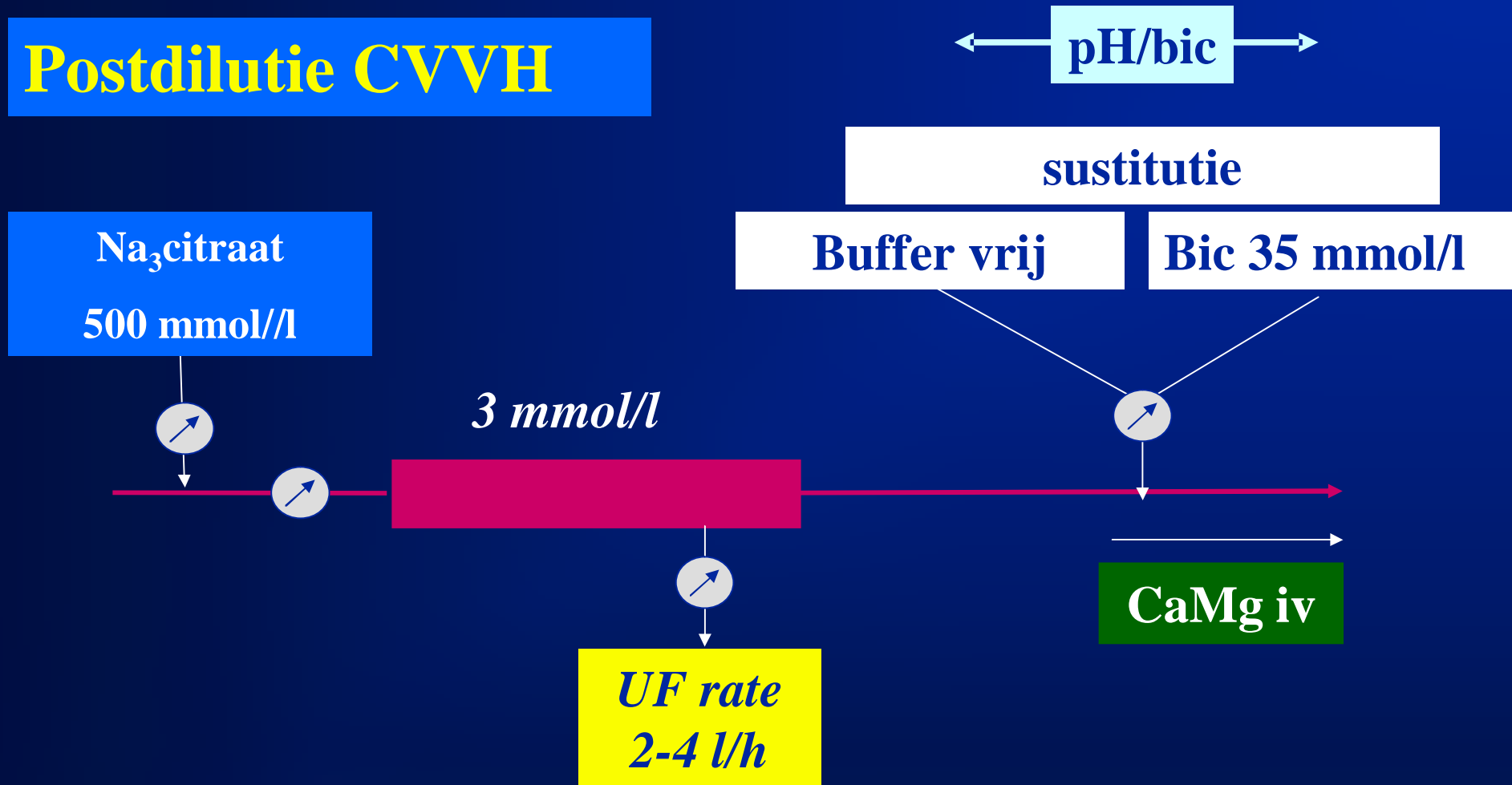
Table 2: Algorithm for blood flow, substitution flow and calcium-supplementation; for calcium infusion, calcium gluconate (0.225 mmol/ml) is used.

Blood flow (ml/min)	Substitution flow (ml/h)	Calciuminfusion (ml/h)
140	1900	9.5
160	2100	10.5
180	2400	12
200	2700	13.5

aangepast aan serum ionCa⁺⁺

Postdilutie CVVH

Postdilutie CVVH



HM Oudemans-van Straaten

CVVH Postdilutie

Na₃citraat
500 mmol/l

3 mmol/l

QC ~ QB

UF flow
2-4 l/h

geen postfilter
Ca⁺⁺ meting

CaMg iv

Na 109 mmol/l
K 2 mmol/L
Cl 109 mmmol/L
Ca 1.81 mmol/L
Mg 0.52 mmol/L

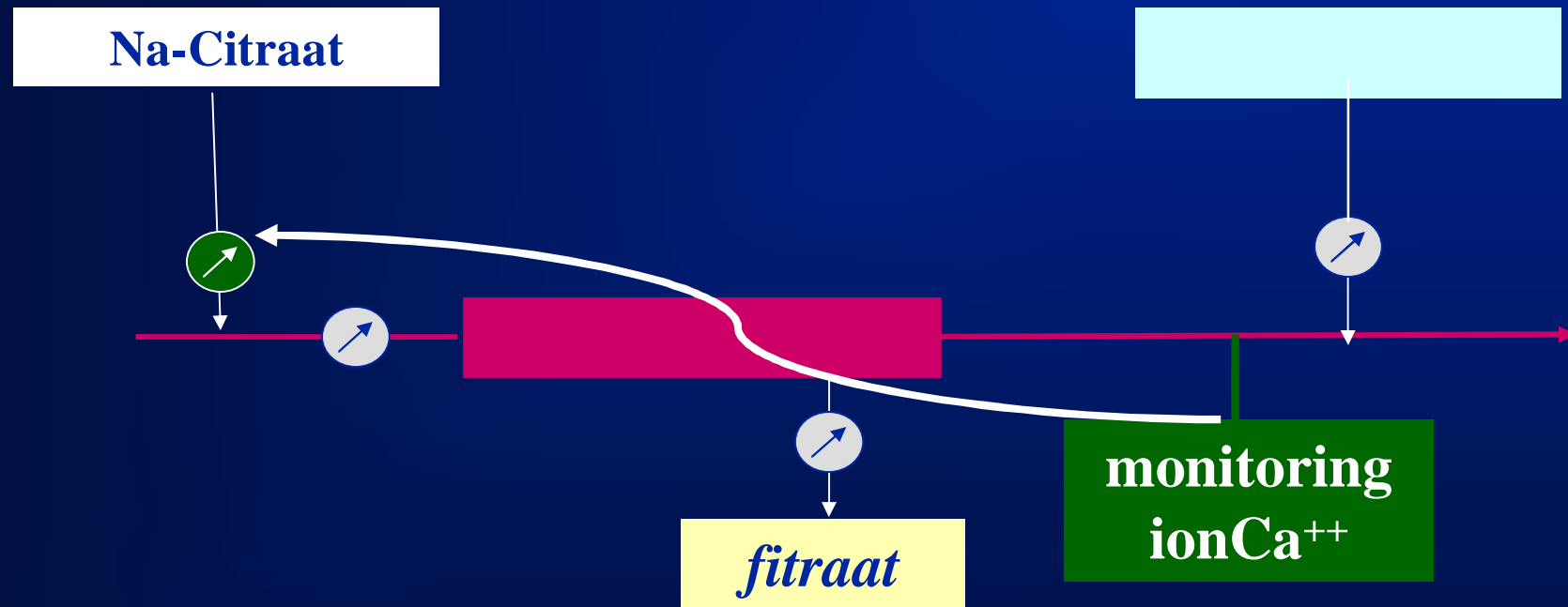
buffer vrij

Na 140 mmol/L
K 2 mmol/L
Cl 107 mmol/L
Mg 1 mmol/L
Ca 1.25 mmol/L

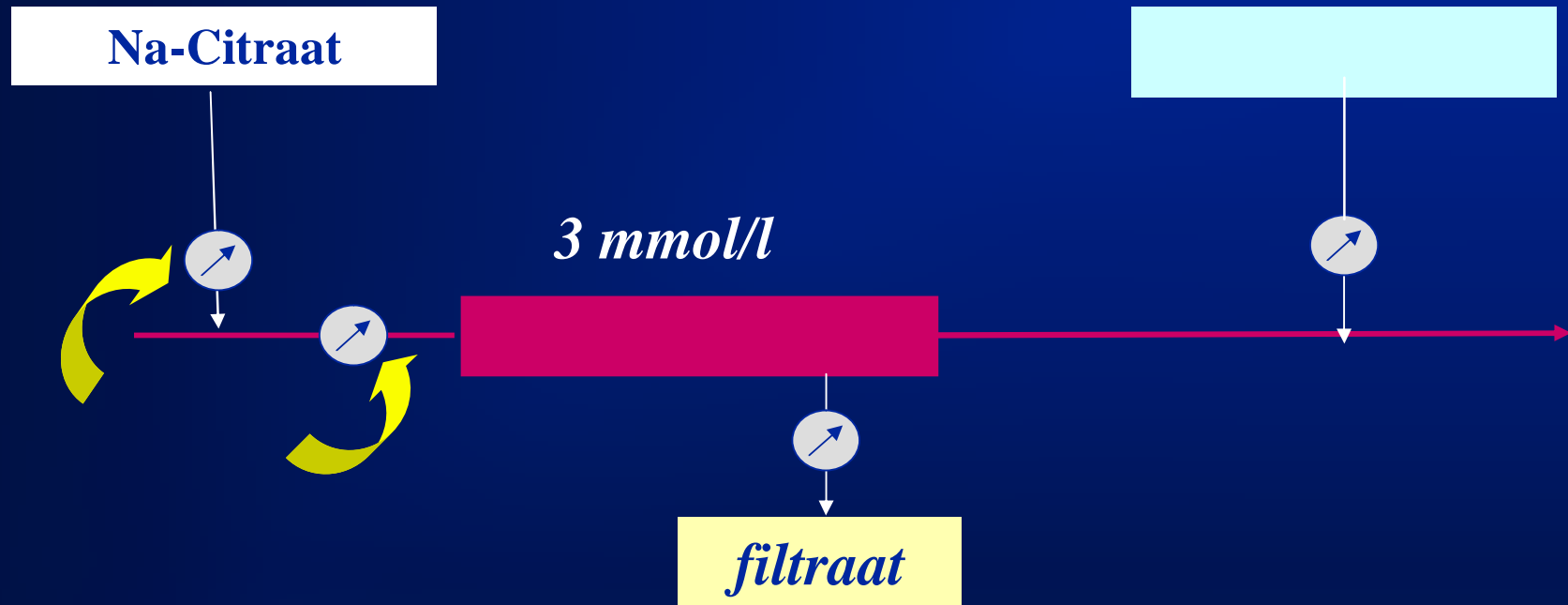
bic 35 mmol/L

Hoe passen we de antistolling aan?

Citrate flow \leftrightarrow postfilter ionCa⁺⁺



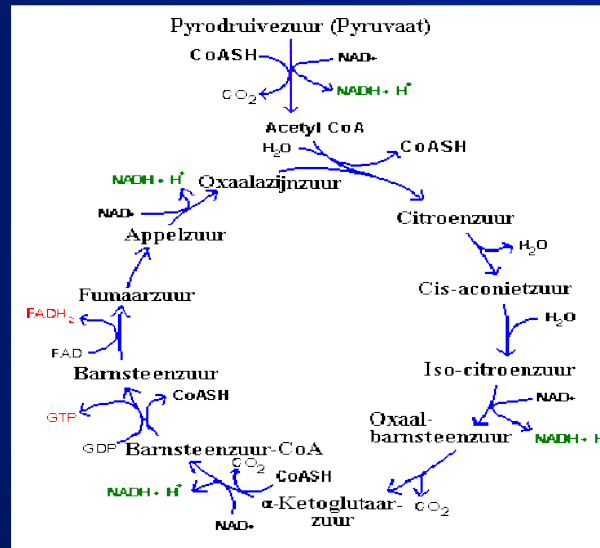
Citraat flow \leftrightarrow bloed flow



[citraat]_{filter} 3.1 mmol/l

FF ml/u	BF ml/min	CF ml/u	CaMg ml/u
2400	160	60	4
2600	170	64	8
2800	190	71	8
3000	200	74	8
3200	220	82	12
3400	230	84	16
3600	240	89	16
3800	250	94	20
4000	270	100	20

Verdragen ernstig zieke patiënten citraat?



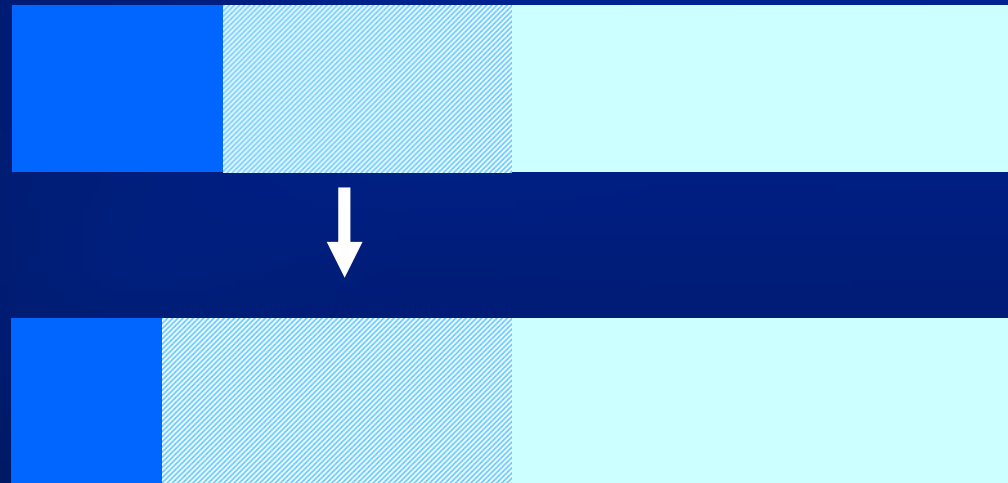
Metabole omzetting

Beperking citraat:

lever falen

lever en spierperfusie ↓

*als citraat niet
wordt omgezet:*



Metabool falen

- meest gevoelig
- meest specifiek

→ ion Ca^{++} ↓

→ tot/ion Ca^{++} > 2.25-2.5

- citraat wordt niet als buffer gebruikt

→ metabole acidose

→ lactaat ↑, anion gap ↑

Meier-Kriese H, Crit Care med 2001;29:748
Bakker A, Clin Chem Lab Med 2006;44:962-966

Patienten met lever/metabool falen

- *start CRRT met citraat*
- *monitor systemisch tot/ion Ca^{++} na 2h*
- *reduceer citraat dosering bij accumulatie (Ca-ratio > 2,25)*
- *vervang meer bicarbonaat, afhankelijk van pH*

Lab contrôles

iedere 6u

- pH, bicarbonate, PCO_2
- ion Ca^{++}
- Na, K

iedere 12u

- tot Ca^{++}
- fostaat

geen APTT

postfilter ion Ca^{++}

- om antistolling te optimaliseren
niet noodzakelijk

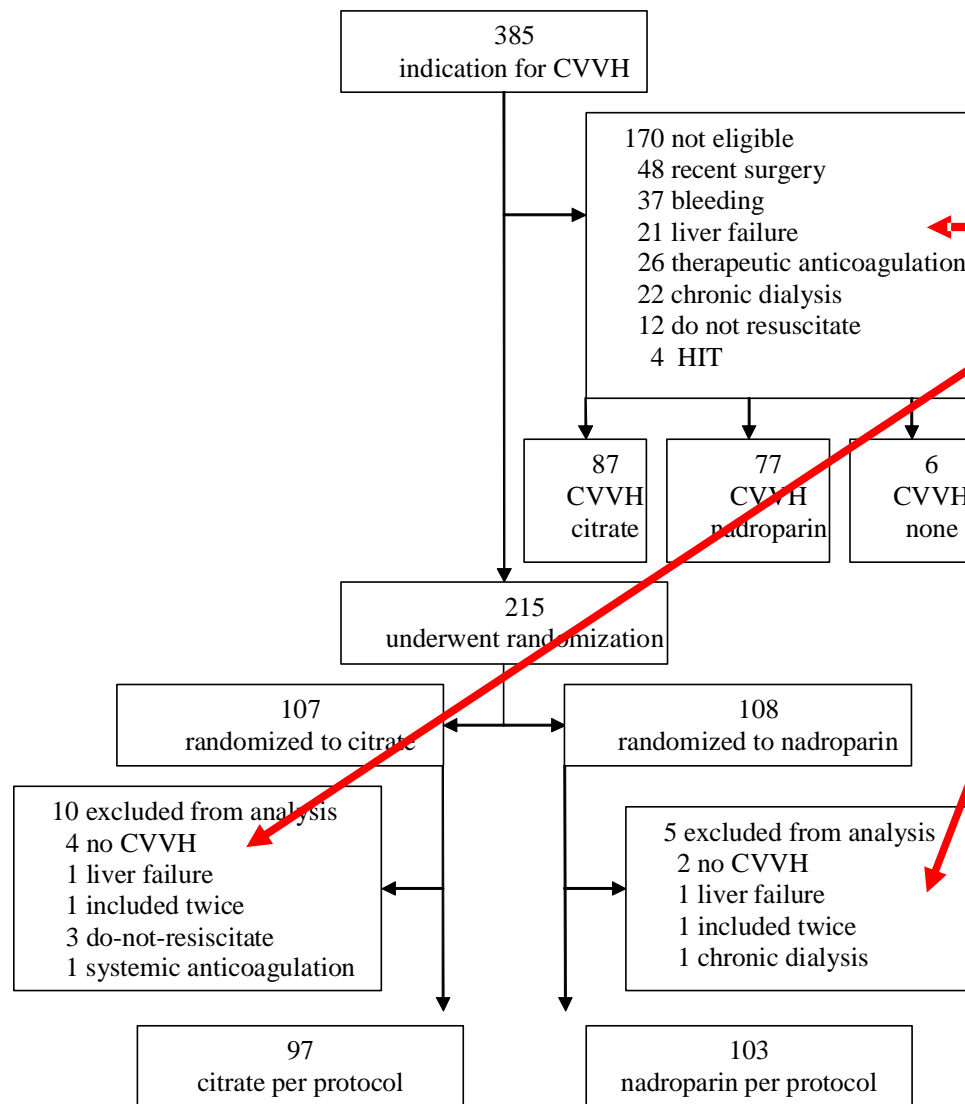
Voordelen van citrate?

gerandomiseerde studies

citraat ↔ heparine

Citraat vs. heparine

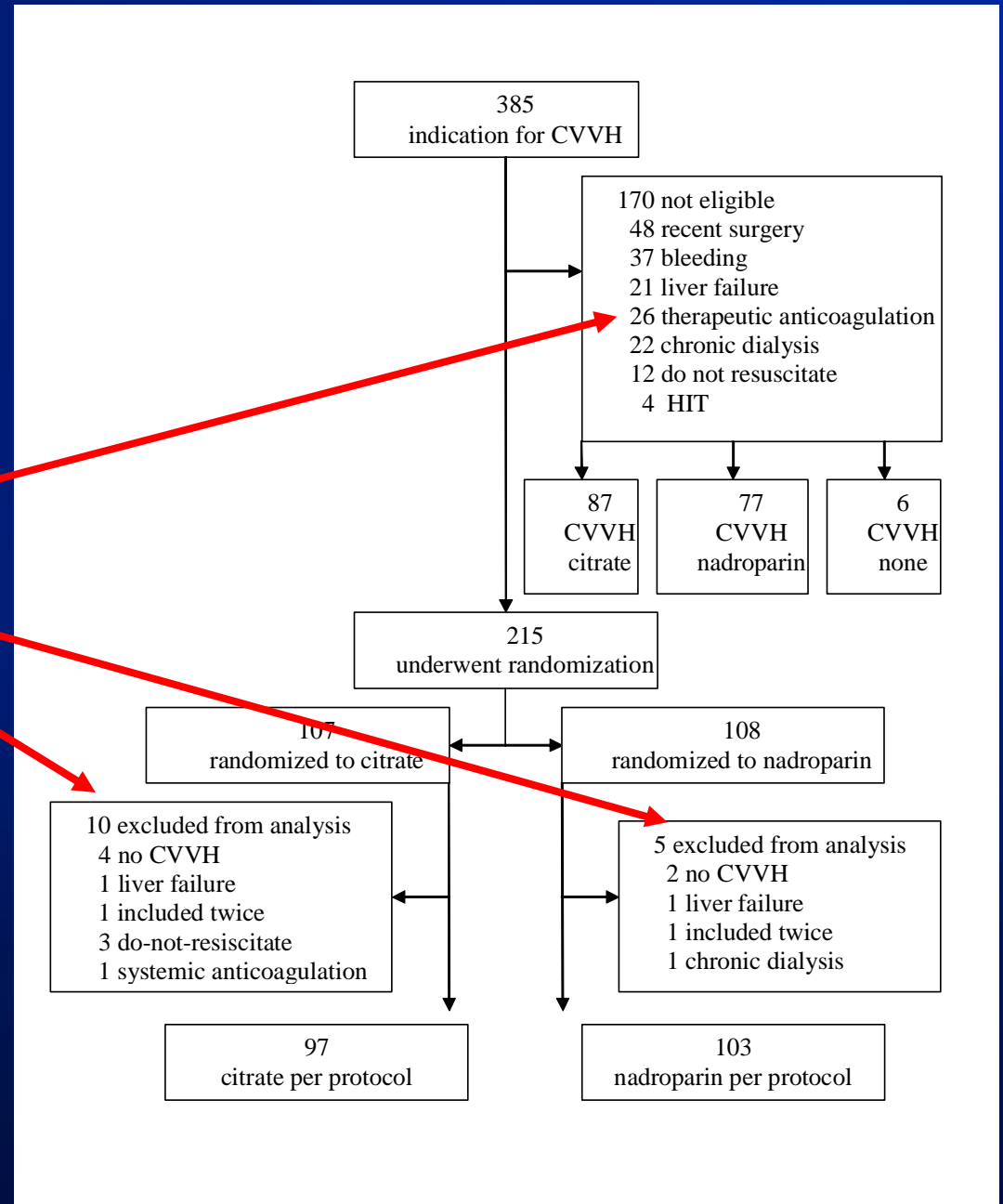
- **tolerantie**
- **bloedingen**
- **transfusie**
- **overleving filter**
- **overleving patient**



- 6% uitgesloten ivm leverfalen
- 23% uitgesloten ivm (kans op) bloedingen

Tolerantie

- 6% uitgesloten ivm leverfalen
- 23% uitgesloten ivm (kans op) bloedingen



Tolerantie

vroegtijdig staken van het studie-anticoagulans

citraat n = 97	nadroparine n = 101	
2 %	19 %	p = 0.000
1 stapeling citraat 1 snelle stolling	16 bloeding 4 trombocytopenie	

Bloedingen

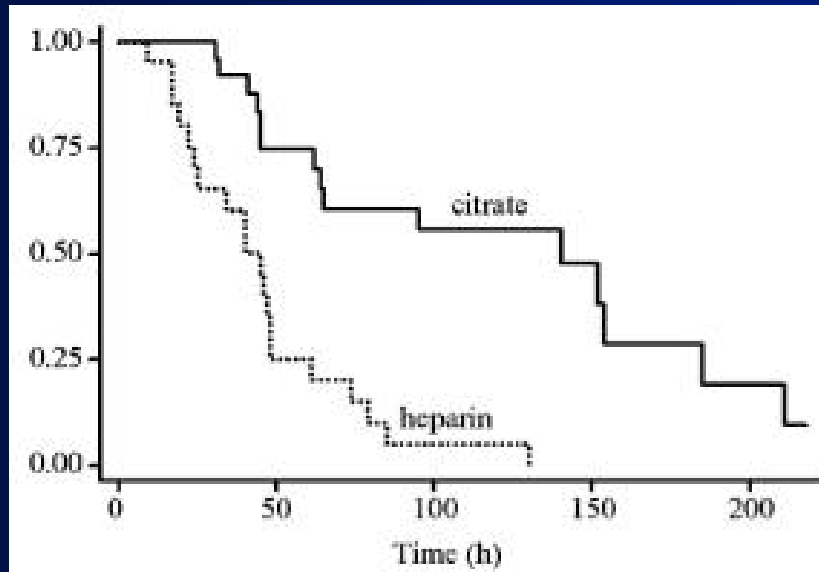
	Design	Citraat	Heparine	P
Monchi 2004	R cross-over N=30	0	1	
Kutsogiannis 2005	RCT N=30	RR 0.17 (0.03-1.04)		0.06
Betjes 2007	RCT N=48	0%	33%	<0.01
Oudemans in press	RCT N=200	6%	16%	0.08

Bloedtransfusie

	Design	Citraat	Heparine	P
Monchi 2004	R cross-over N=30	0.2 0-2.0	1.0 0-4.0	p < 0.001
Betjes 2007	RCT N=48	0.43	0.88	0.01
Oudemans in press	RCT N=200	0.27 0-0.63	0.36 0-0.83	0.31

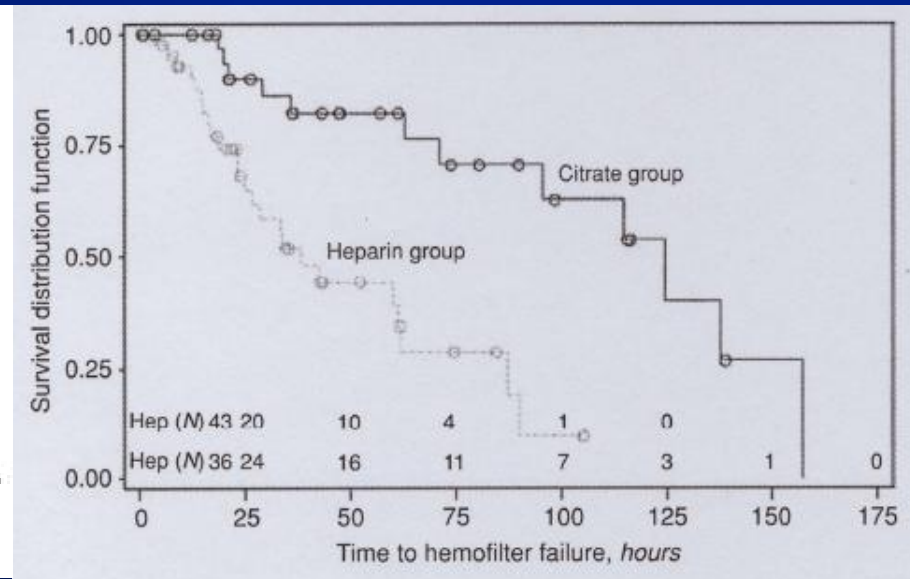
Overleving circuit

Cross-over, N = 20



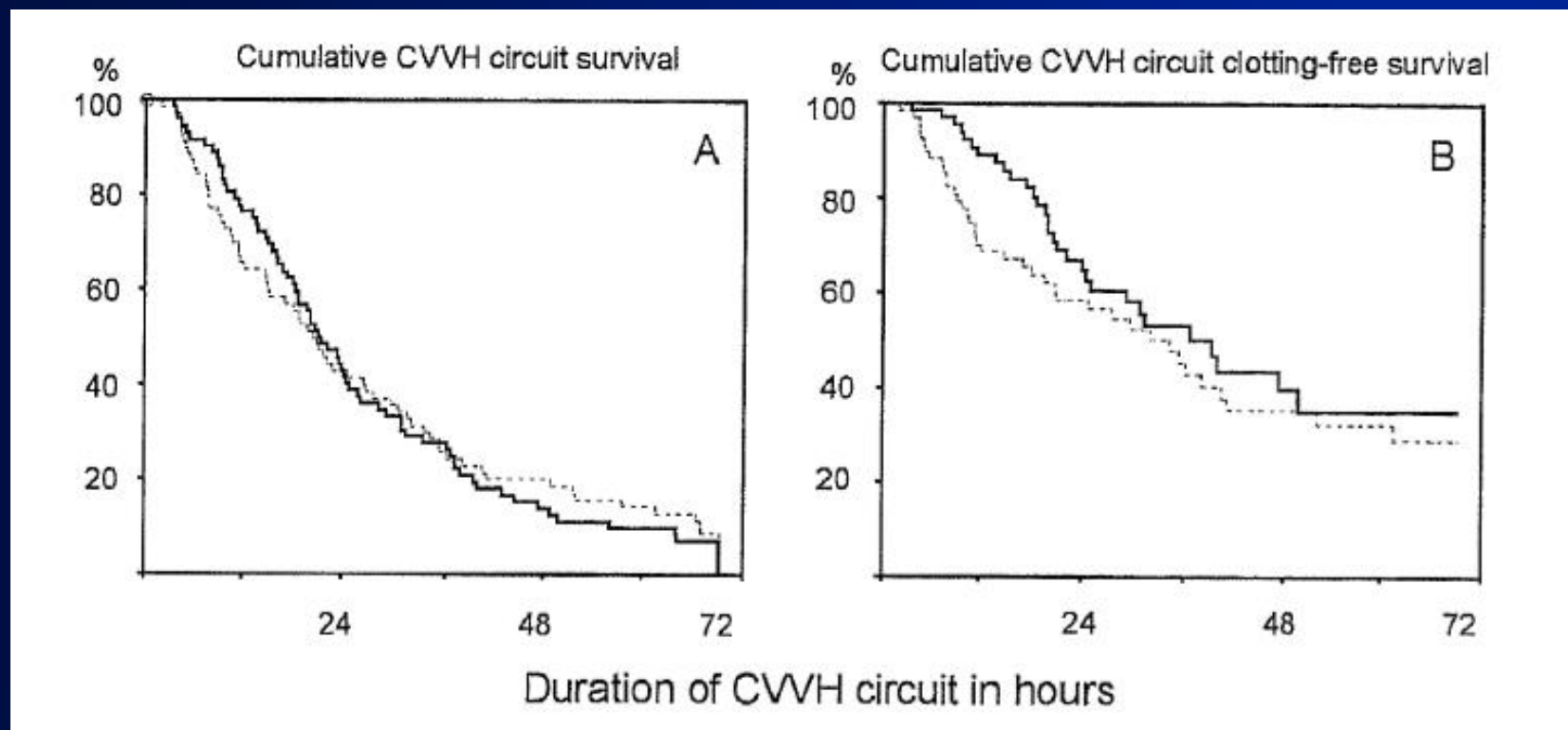
Monchi M,
Intensive Care Med 2004; 30:260

RCT, N = 36



Kutsogiannis DJ,
Kidney Int 2005;67:2361

Overleving circuit *citrate (n=21) vs. heparin (n=27)*

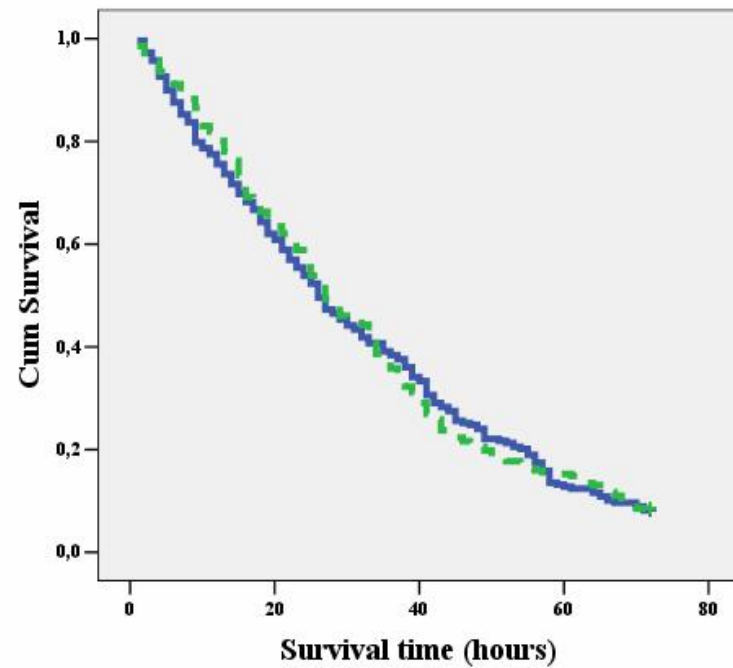


Betjes MGH, J Nephrol 2007;20:602

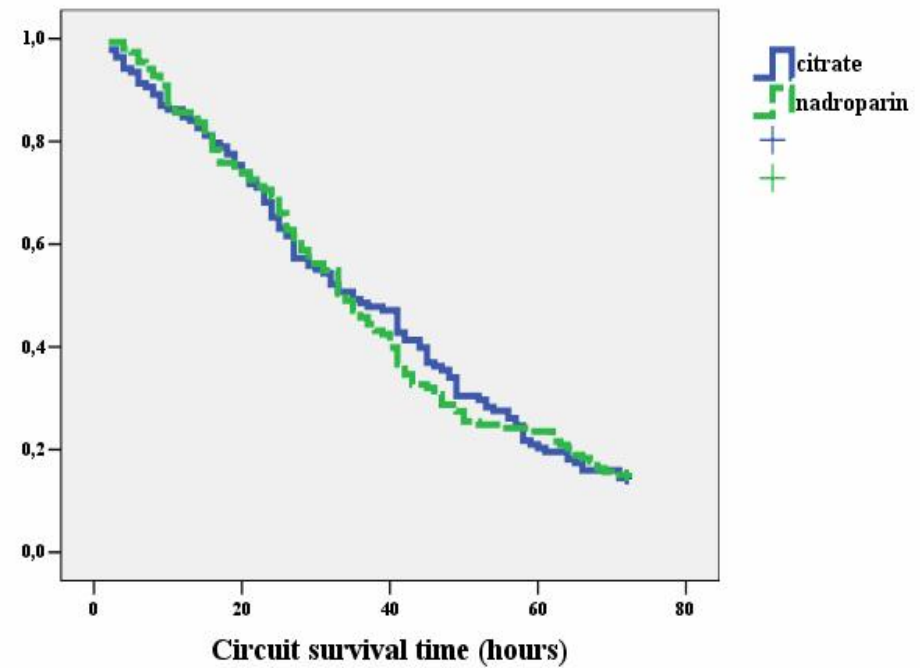
Overleving circuit

200 patienten

All circuits



Circuits discontinued for high filter pressures



Overleving patient

Gerandomiseerde studie

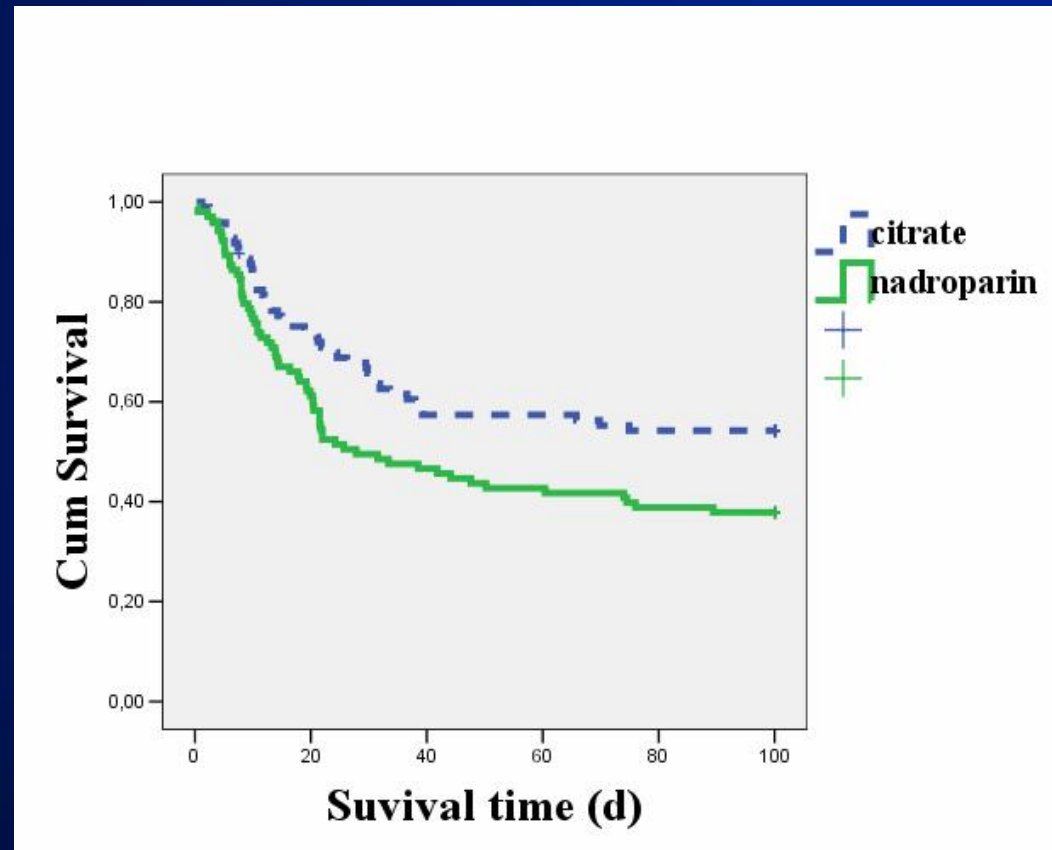
citraat vs. nadroparine voor CVVH

	citraat <i>n=97</i>	nadroparine <i>n=103</i>
leeftijd (jaren)	73 (64-79)	73 (67-79)
AP II	28 (7.9)	28 (6.9)
int-CS-chir (%)	44-32-24	46-31-23
sepsis	43%	49%
SOFA _{start HF}	11 (10-13)	11 (10-14)
RIFLE _{start HF}	3 (2-3)	3 (2-3)
UF flow (ml/kg/u)	36± 17	33± 13

3-maands overleving

citraat vs. nadroparine voor CVVH

Log Rank (Mantel-Cox) $p = 0.02$

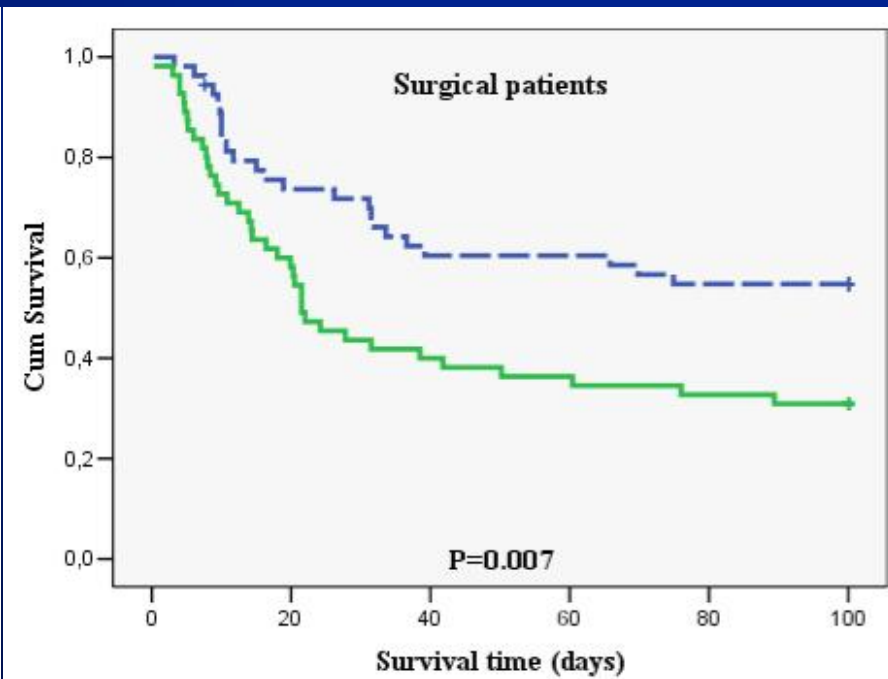
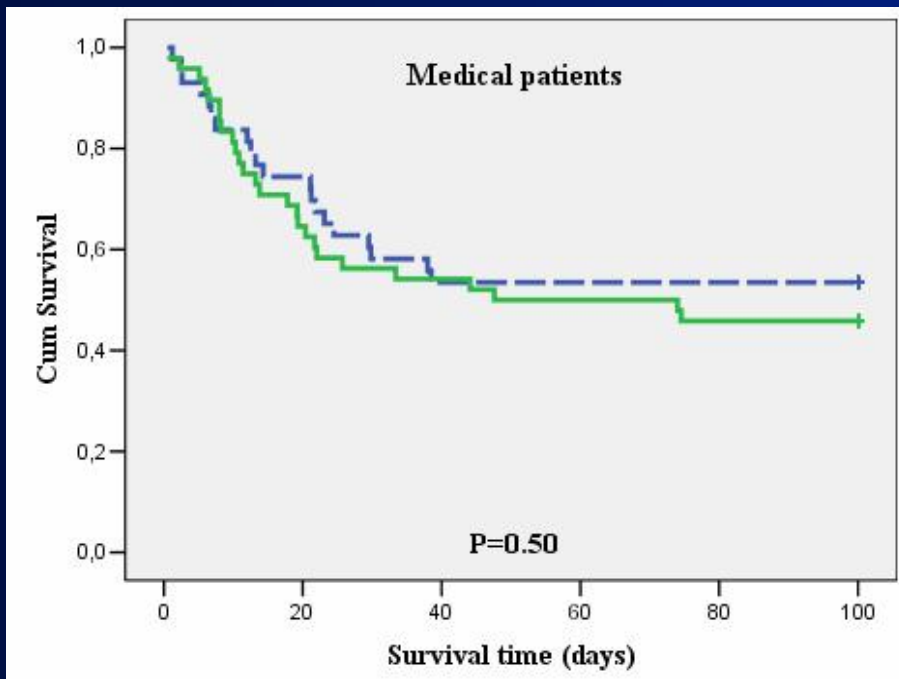


Interne ↔ chirurgische Patienten

Log Rank (Mantel-Cox)

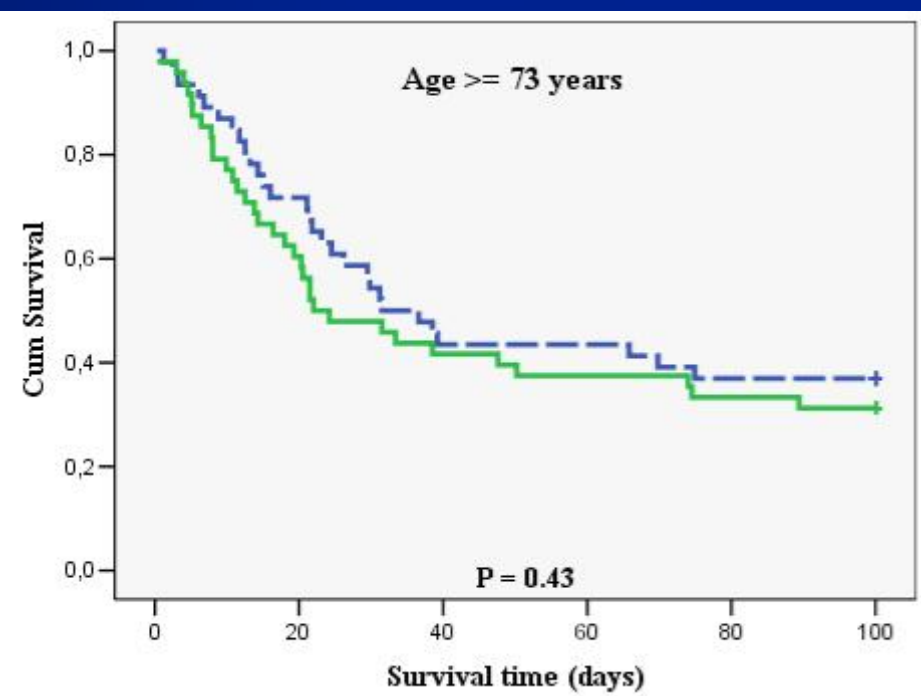
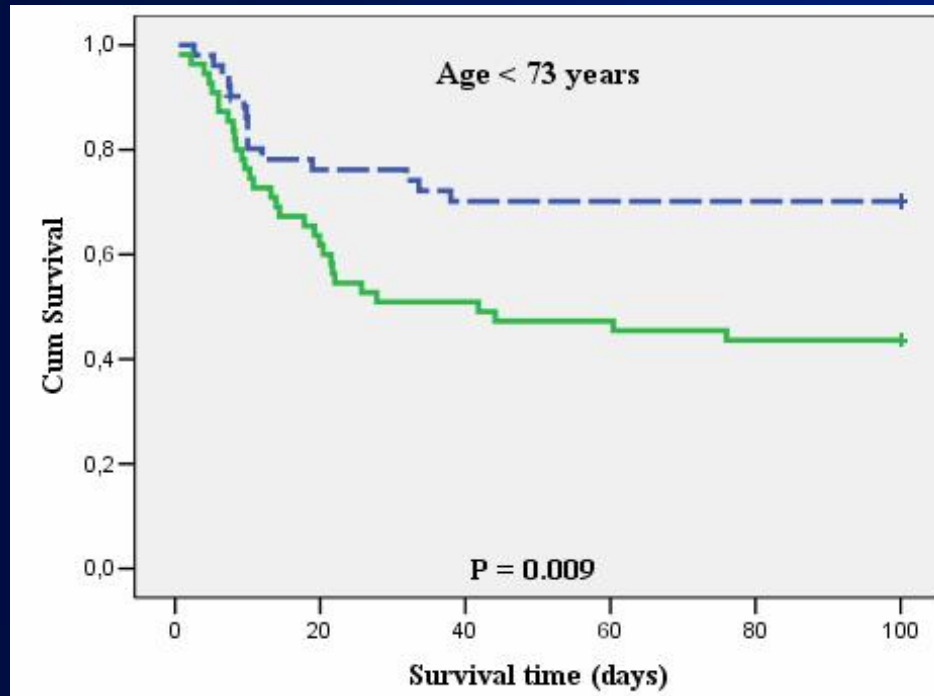
n = 102

n = 98



Jongere ↔ oudere patiënten

Log Rank (Mantel-Cox)

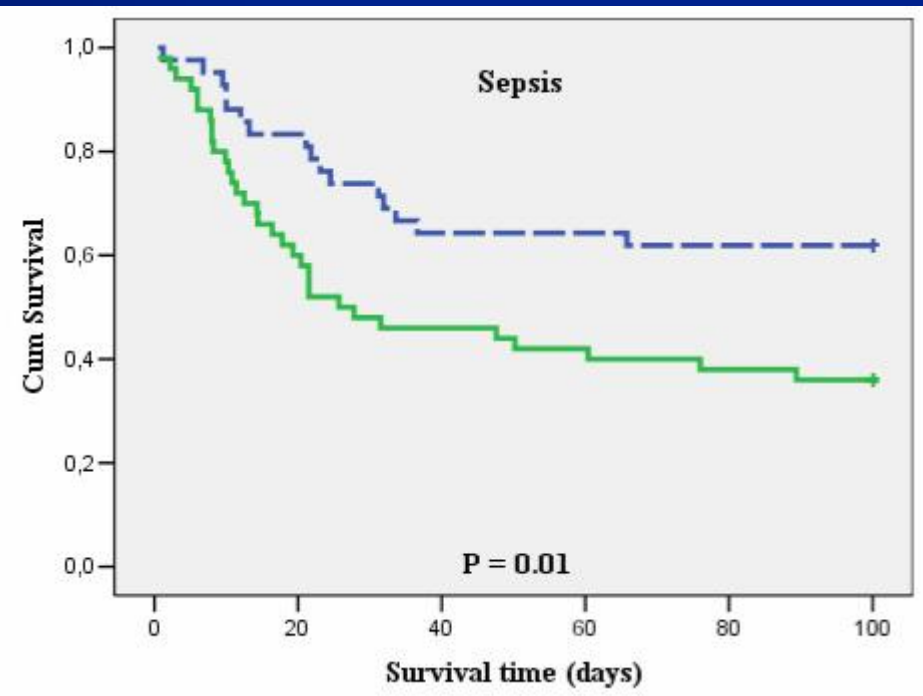
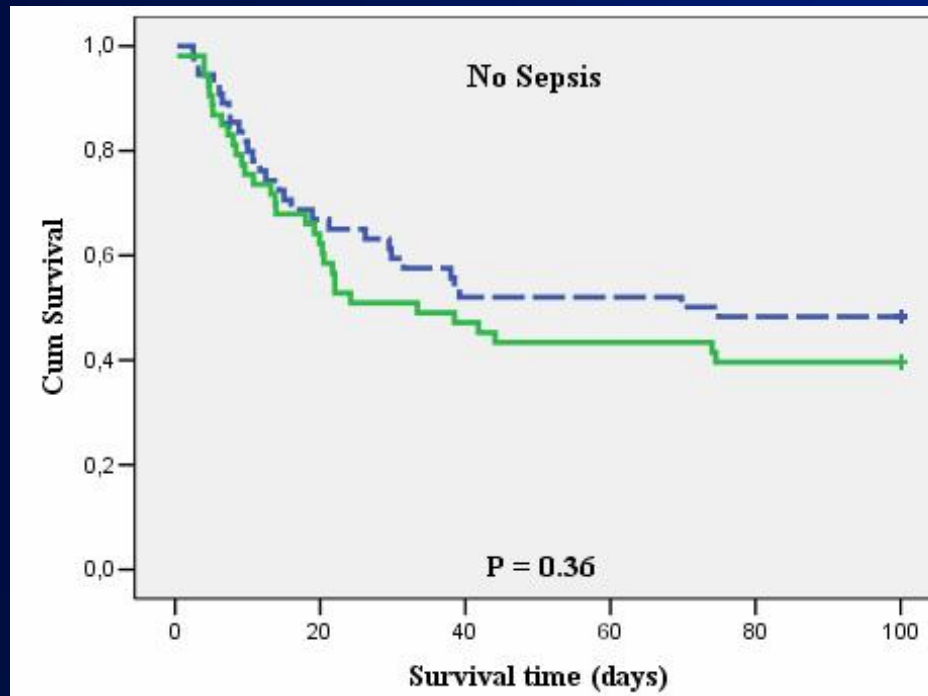


Niet-septische ↔ septische patiënten

Log Rank (Mantel-Cox)

n=92

n=108

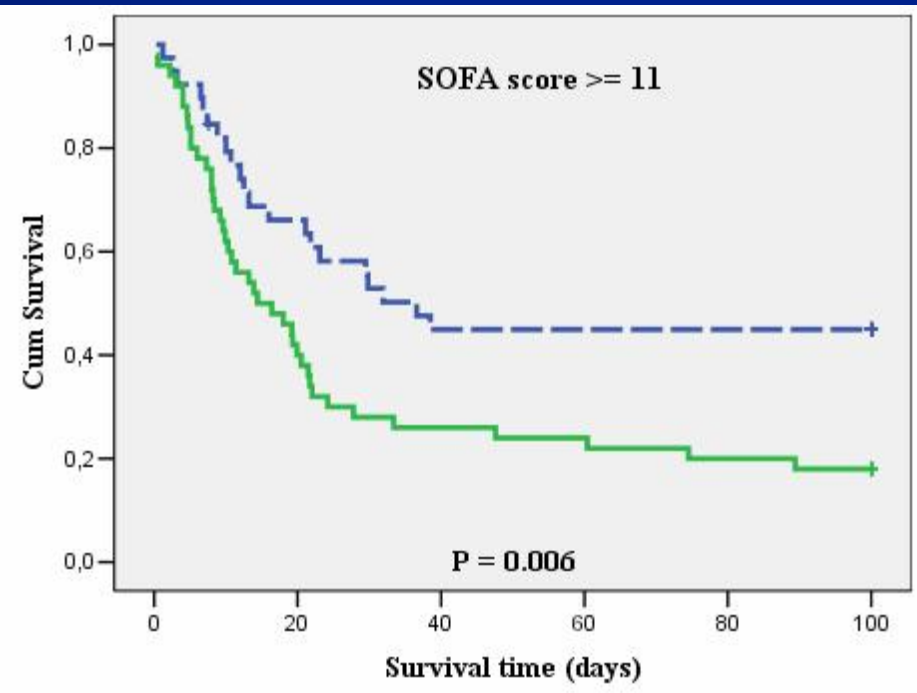
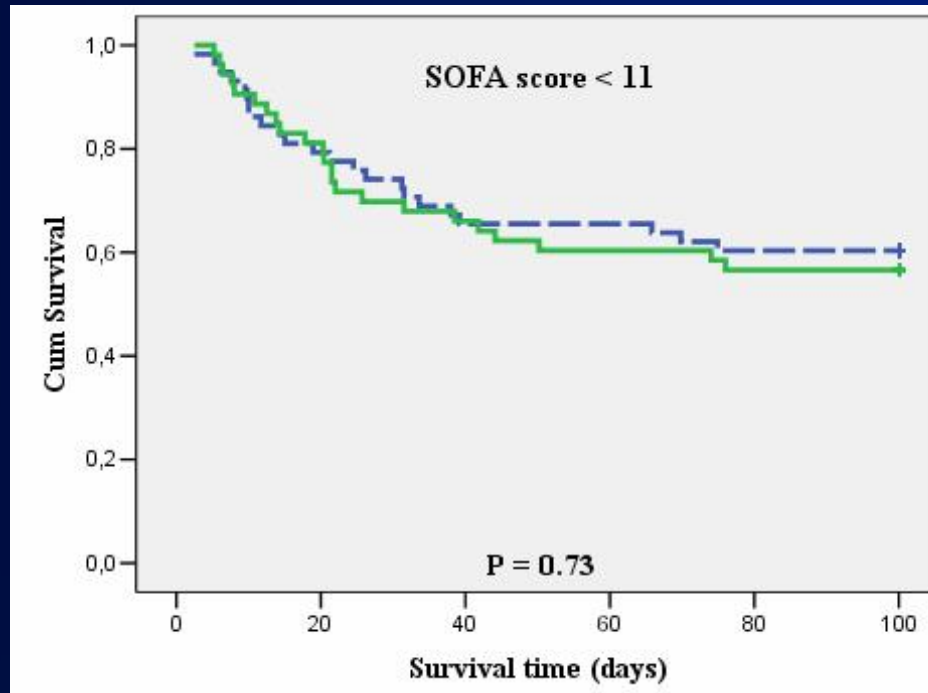


Minder ↔ meer orgaan falen

Log Rank (Mantel-Cox)

n=107

n=93



Citraat

- **wordt beter verdragen dan heparine**
- **gunstig resultaat**
 - **filteroverleving**
 - **bloedingen**
 - **overleving van de patient**

Citraat

zorg voor:

*een goed protocol
training en begrip*