

CRRT e Anticoagulazione Una scelta ponderata: come mantenere la pervietà e il perfetto funzionamento del circuito. Diversi regimi di anticoagulazione

Stefano Romagnoli, MD, PhD



Dip. di Scienze della Salute – Università di Firenze
Dip. di Anestesia e Rianimazione - AOU Careggi - Firenze

UO di Nefrologia, Dialisi e Trapianto Renale
Ospedale San Bortolo - ULSS 8 Berica
International Renal Research Institute Vicenza (IRRV)



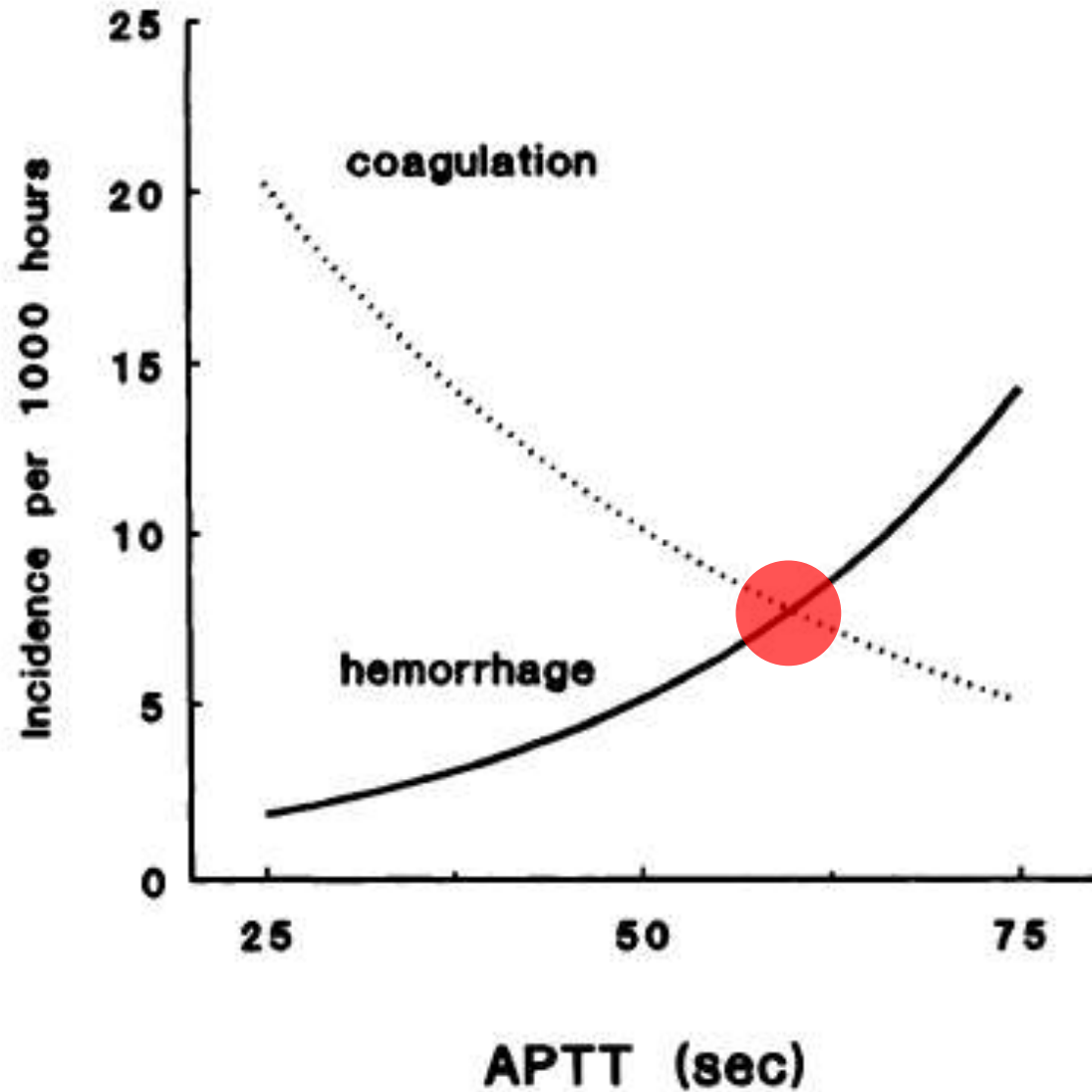
CRRT
Questione di EQUIPE!

Videoconferenza LIVE per
INFERMIERI
NEFROLOGI
INTENSIVISTI ...
e tutti i Medici in Formazione Specialistica!
XI Edizione



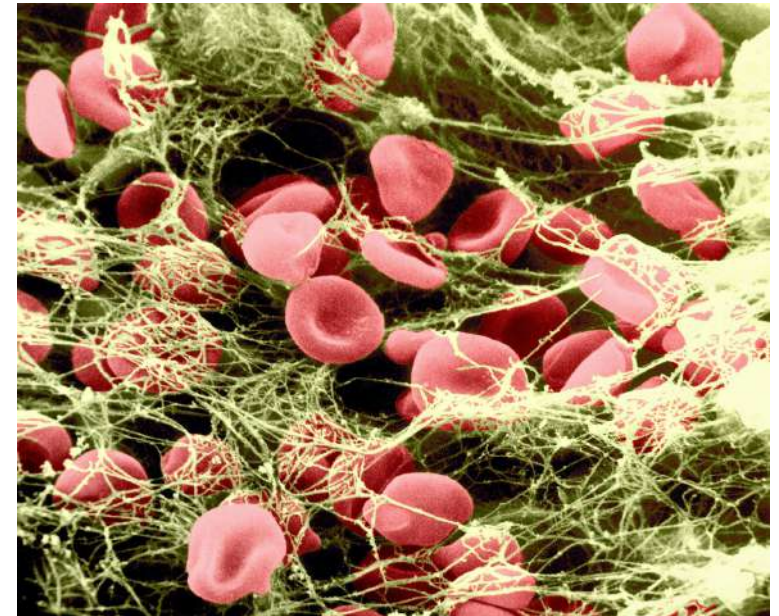
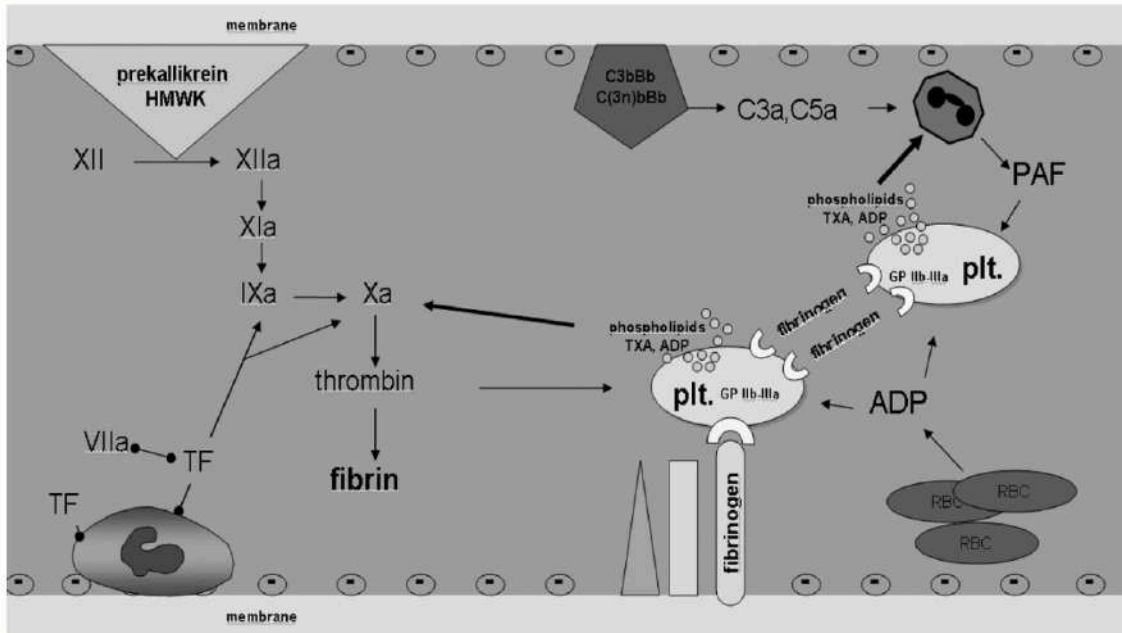
15-16 giugno 2020

Heparin Use in Continuous Renal Replacement Procedures: The Struggle Between Filter Coagulation and Patient Hemorrhage¹



Review

Clinical review: Patency of the circuit in continuous renal replacement therapy



'artificial kidney failure' (AKF)

- In most situations, it is related to progressive **clotting** and/or clogging of extracorporeal circuits components.

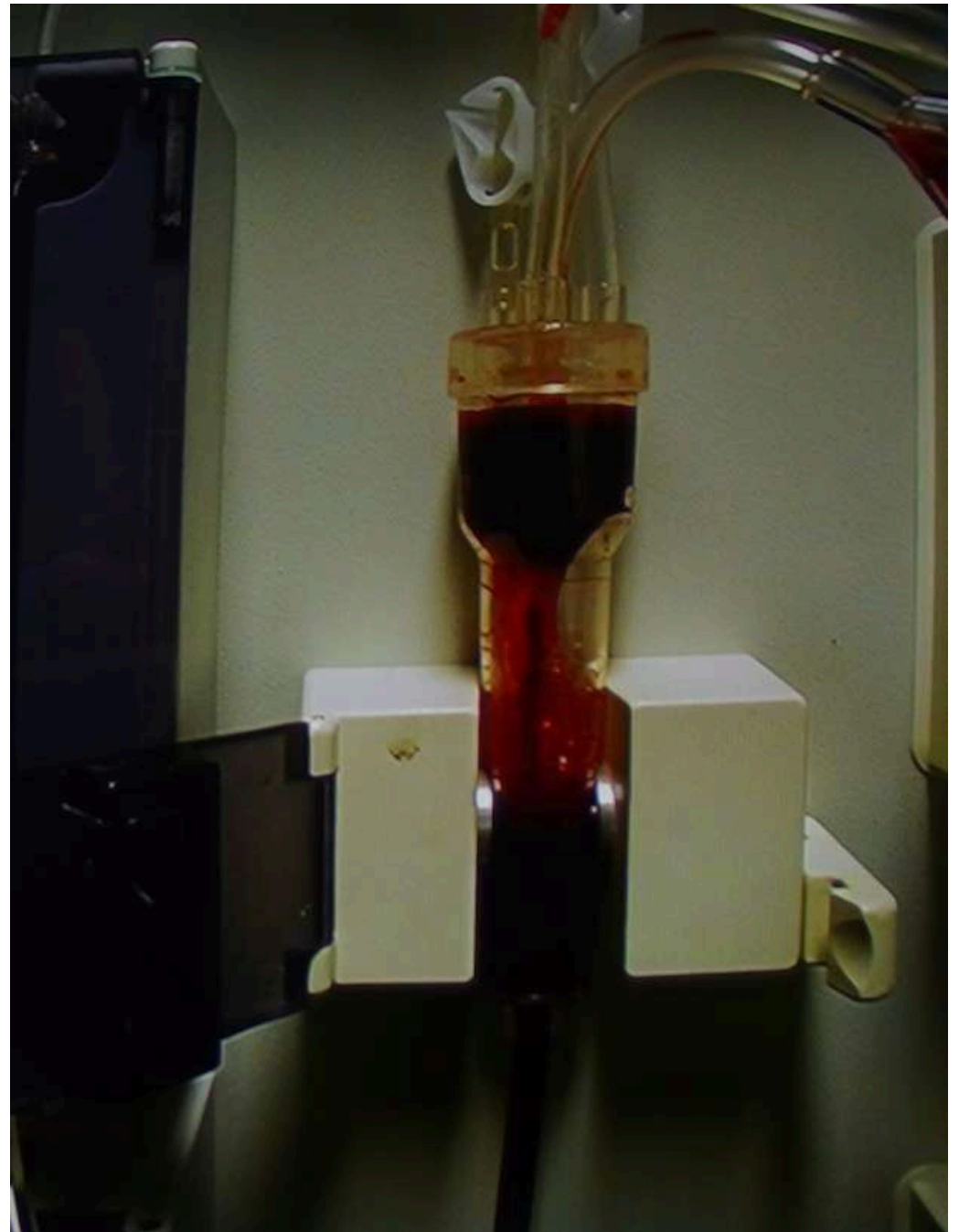
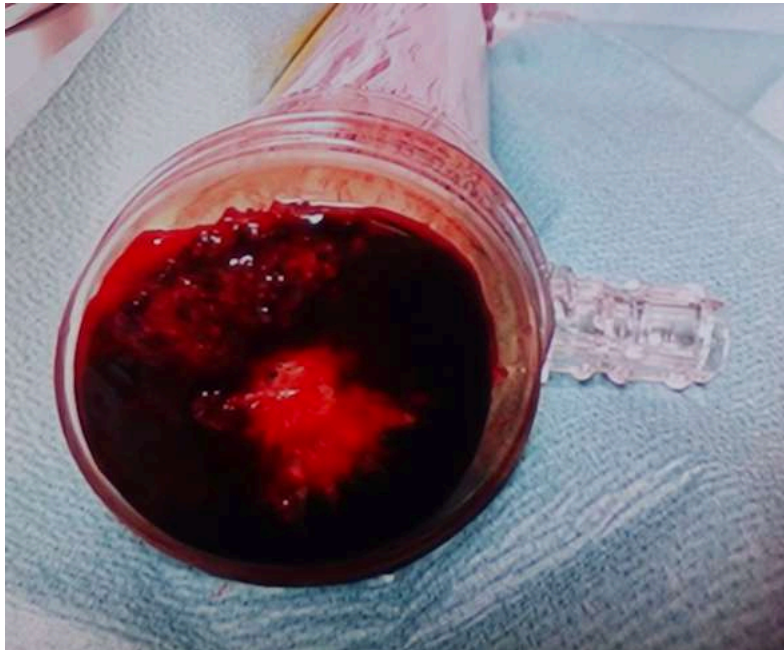


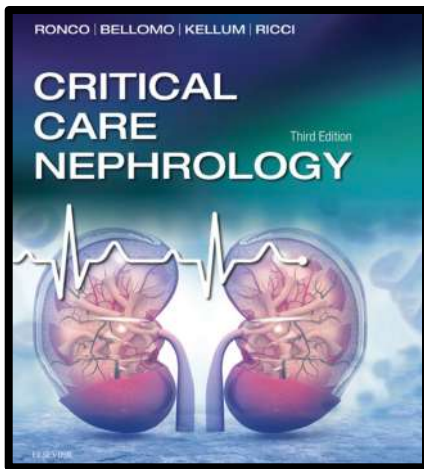
Blood circulation through an extracorporeal circuit is associated with intense activation of the coagulation cascade.



- Clotting can occur as a slow and progressive process or rapidly.
- Clots are most frequently observed at the **venous chamber level** (blood gas interface and relative stasis) and **within the hemofilter**.

- Delivery failure
- Blood loss
- Increased workload
- Increased costs





- Develop your own **expertise** with your protocols.
 - If the circuit clots, it can be replaced. If the patient bleeds, a more serious and adverse outcome may occur.
-
- To loose a filter to protect a patient is entirely acceptable.
 - To loose a patient to protect a filter is NOT.



Kidney Disease: Improving Global Outcomes (2012)

In patients with AKI requiring RRT, the contact of blood with the foreign surface of the extracorporeal circuit results in activation of both the intrinsic and the extrinsic pathway of plasmatic coagulation and activation of platelets.⁵⁷¹ Prevention of dialyzer/hemofilter clotting often requires some form of anticoagulation, which may represent a particular challenge in patients with AKI. The need for continuous anticoagulation represents a potential drawback of CRRT.

OFTEN; SOME; CHALLENGE



Kidney Disease: Improving Global Outcomes (2012)

- In a patient with **AKI requiring RRT**, base the decision to use anticoagulation for RRT on assessment of the patient's **potential risks and benefits** from anticoagulation (Not Graded)
- We **recommend using anticoagulation** during RRT in AKI if a patient does not have an increased bleeding risk or impaired coagulation and is not already receiving systemic anticoagulation. (1B)

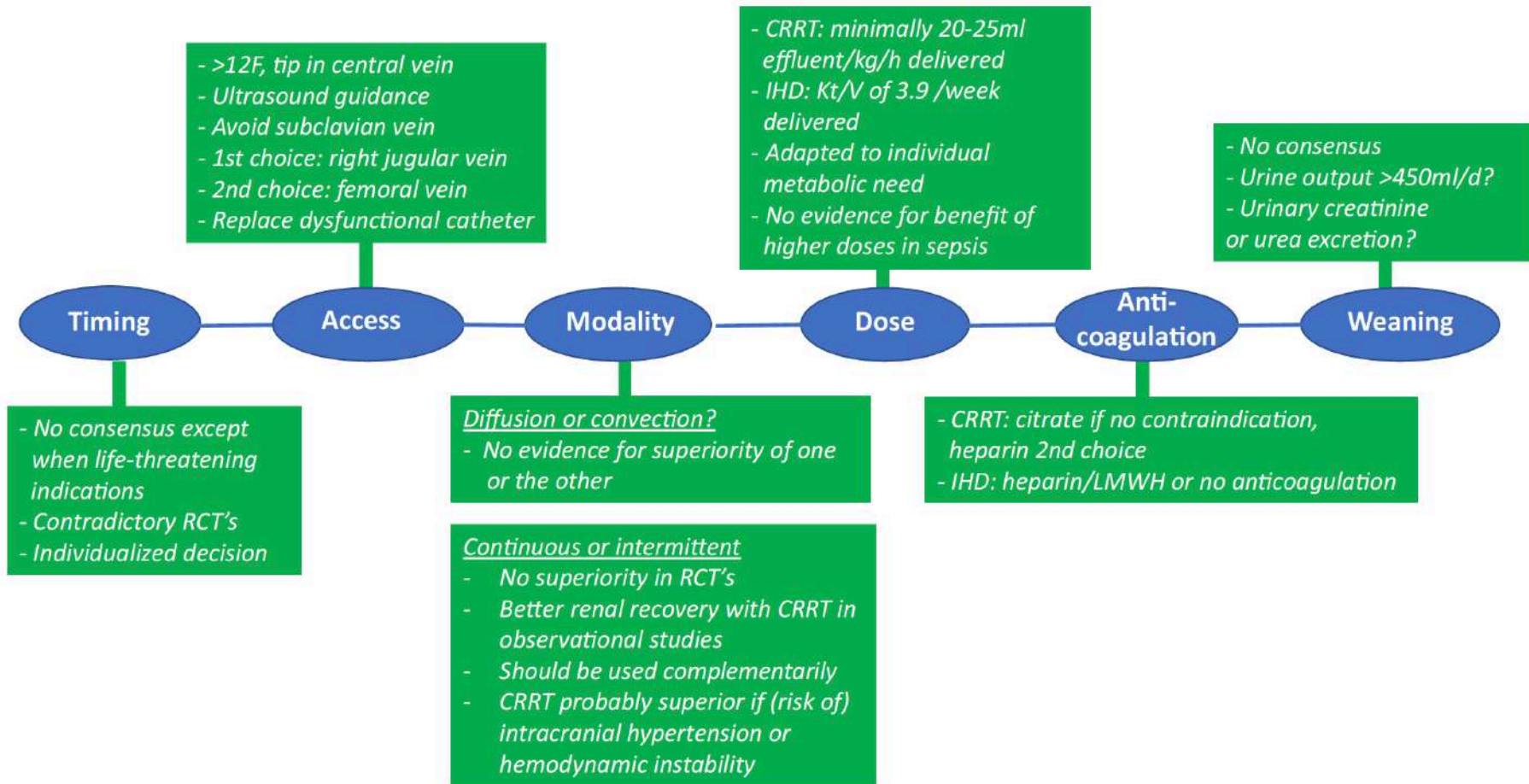




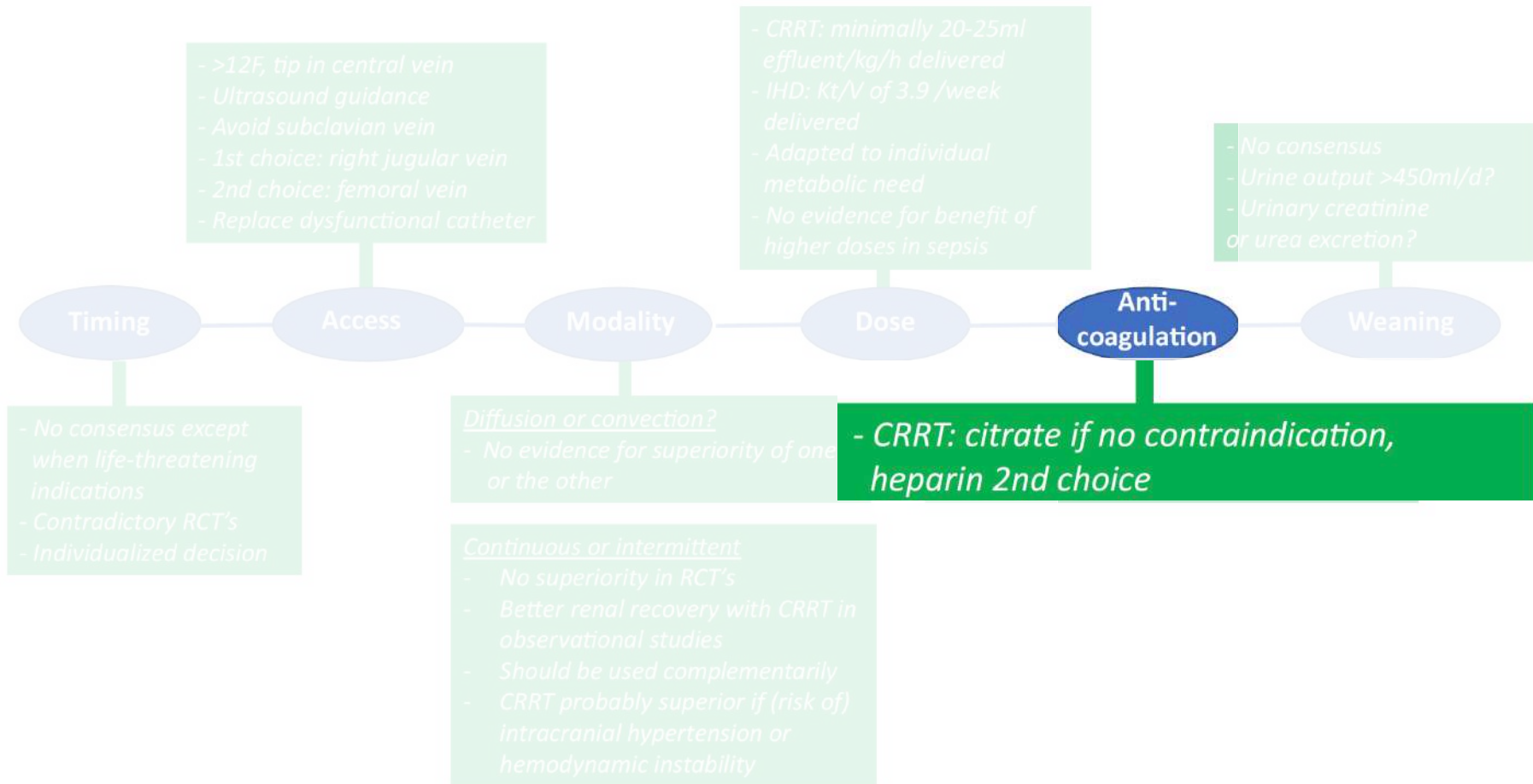
Kidney Disease: Improving Global Outcomes (2012)

- For patients **without an increased bleeding risk** or impaired coagulation and not already receiving effective systemic anticoagulation, we suggest the following:
 - For anticoagulation in CRRT, we suggest using **regional citrate anticoagulation** rather than heparin in patients who do not have contraindications for citrate.
 - For anticoagulation during CRRT in patients who have **contraindications for citrate**, we suggest using either unfractionated or low-molecular-weight **heparin**, rather than other anticoagulants.

The intensive care medicine agenda on acute kidney injury



The intensive care medicine agenda on acute kidney injury



Anticoagulation OPTIONS for CRRT

1

Regional Anticoagulation

2

Systemic Anticoagulation

3

Anticoagulation Free

Continuous Renal Replacement Therapy

Who, When, Why, and How

Anticoagulation for CRRT

- Clotting of the extracorporeal circuit is the most common complication during CRRT.
- Practice patterns regarding the use of anticoagulation vary widely, with estimates of **30% to 60% of patients undergoing CRRT without anticoagulation.**

VA/NIH Acute Renal Failure Trial Network, Palevsky PM et al. N Engl J Med (2008)
Uchino S et al. Intensive Care Med (2007)
- Although the use of anticoagulation is often avoided in patients who are coagulopathic, thrombocytopenic, or are having active hemorrhage, anticoagulation-free treatment may also be successful in the absence of coagulopathy and thrombocytopenia

Regional Anticoagulation



**Regional
CITRATE
anticoagulation
(RCA)**

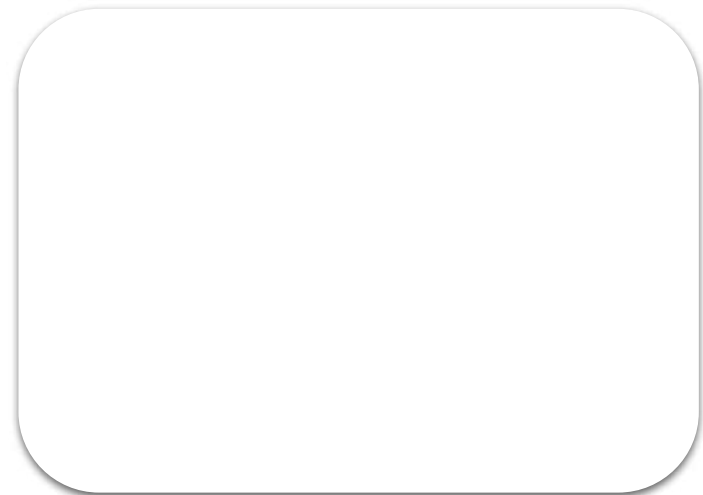
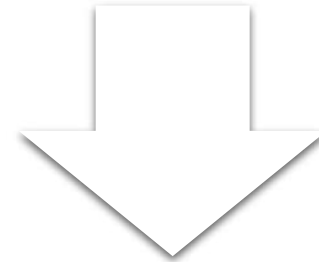


**Regional
Heparin-
Protamine
anticoagulation**

Regional Anticoagulation



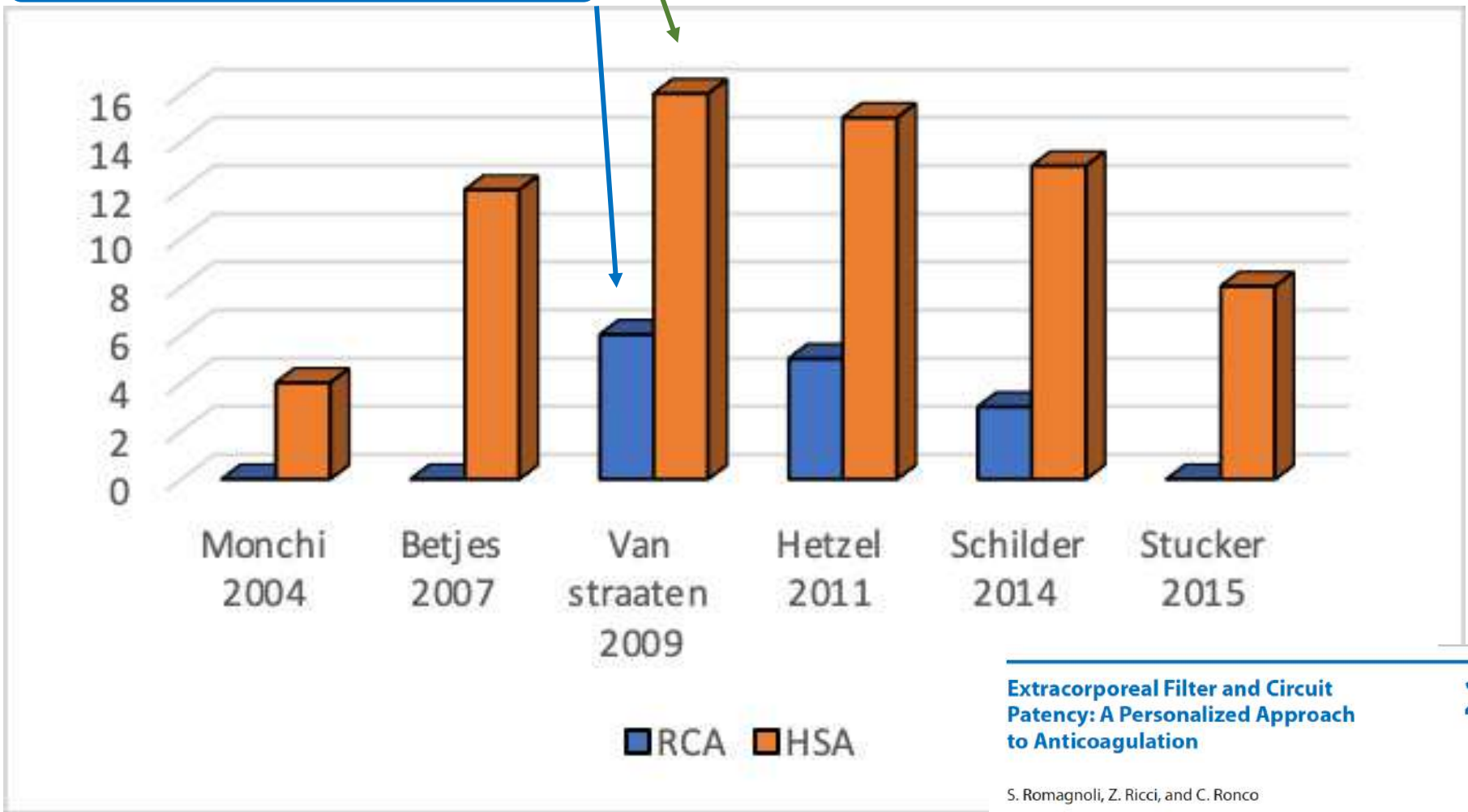
**Regional
CITRATE
anticoagulation
(RCA)**



Regional Anticoagulation

Systemic Anticoagulation

Bleeding complications



Extracorporeal Filter and Circuit Patency: A Personalized Approach to Anticoagulation

Regional Citrate Anticoagulation (RCA)

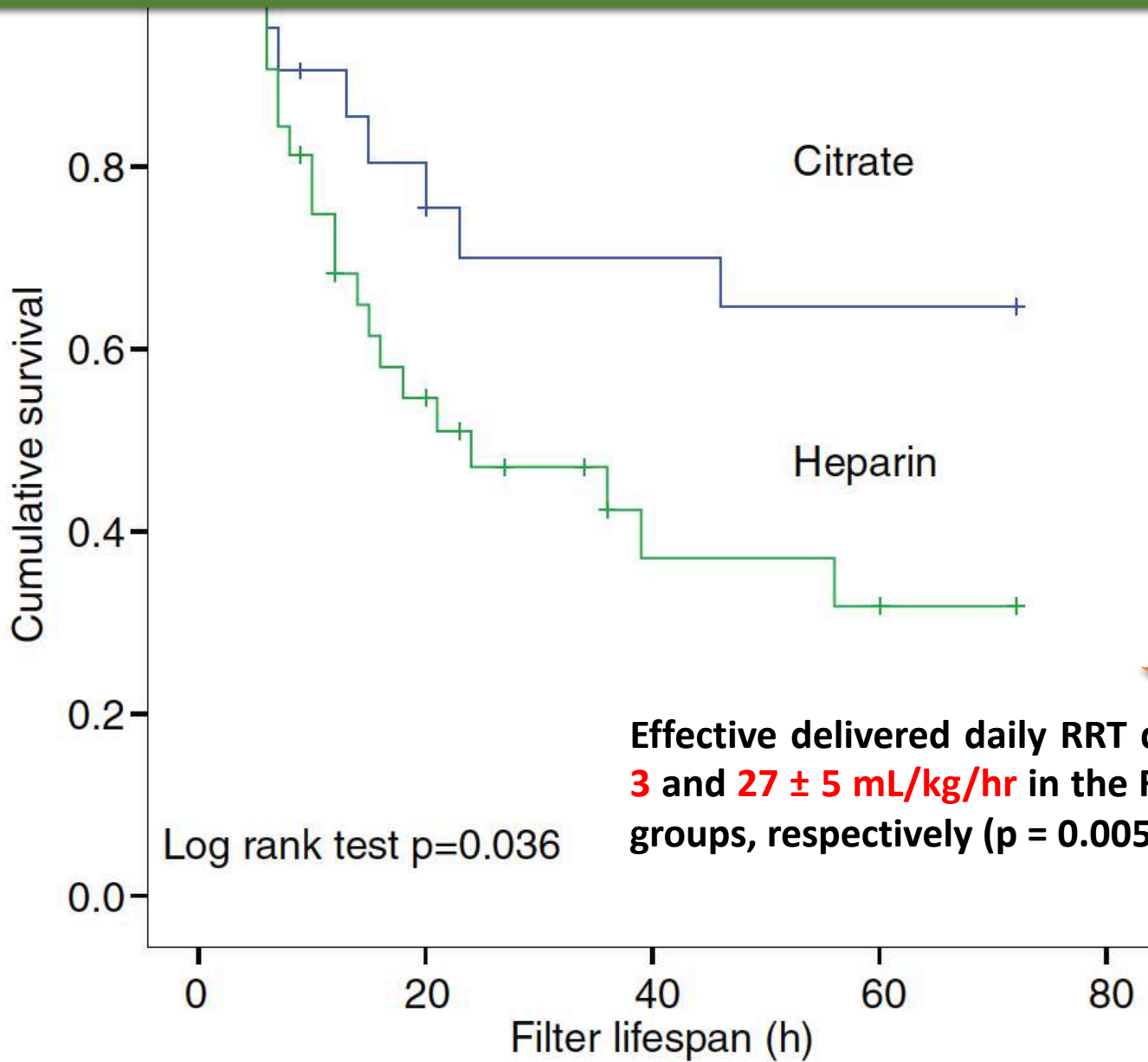
- ↗ Filter life without systemic anticoagulation
- 👍 Patients with moderate to high risk of bleeding
- ↘ Bleeding rates
- ↘ Transfusion rates
- ↘ Incidence of HIT
- ↘ Costs
- Similar overall mortality vs. systemic anticoagulation (heparin-based)

Pickkers P et al. Intensive Care Med (2017)

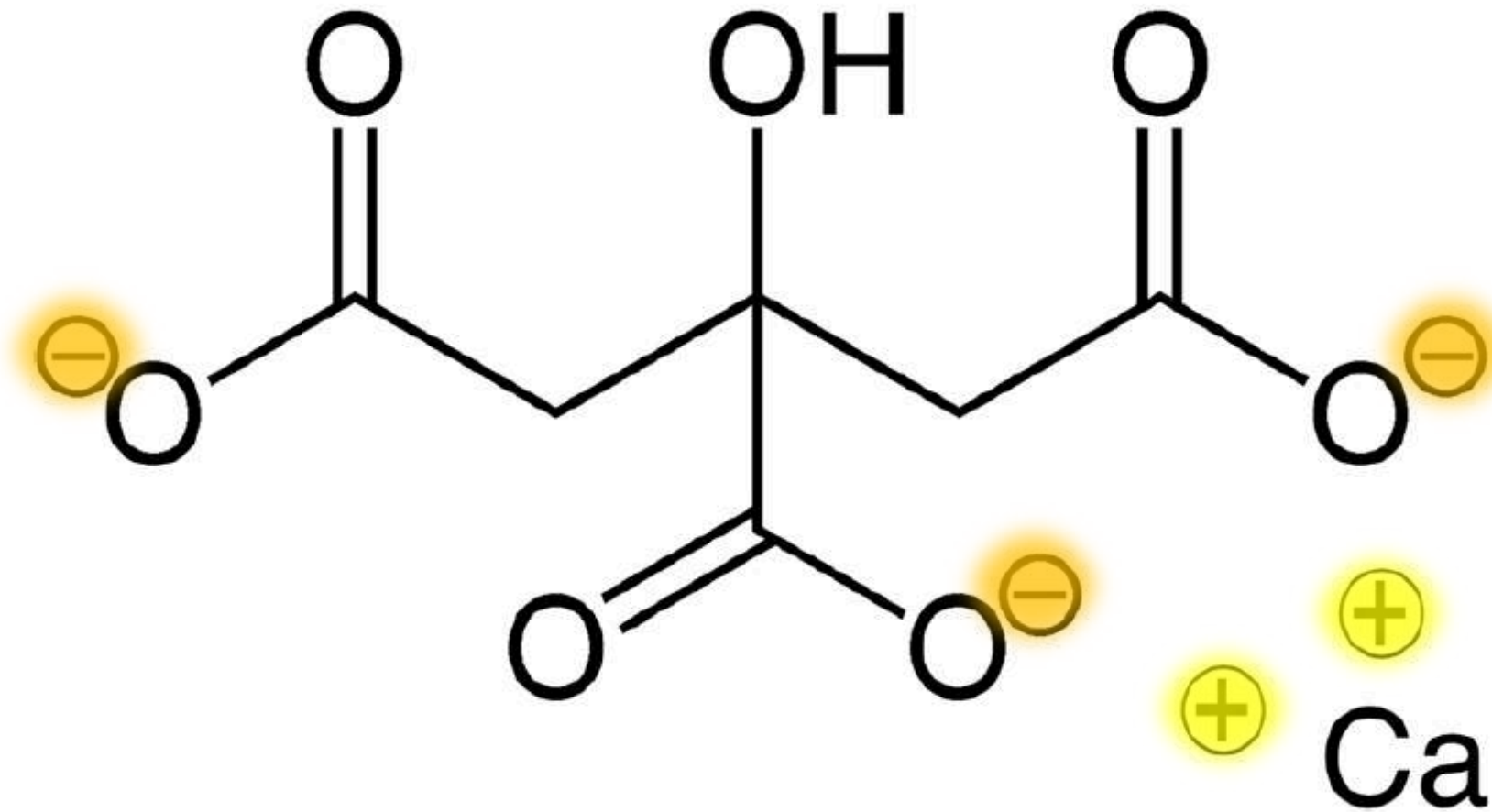
Ahmed AR et al. Critical Care Research and Practice (2019)

Bai M, et al. Intensive Care (2015)

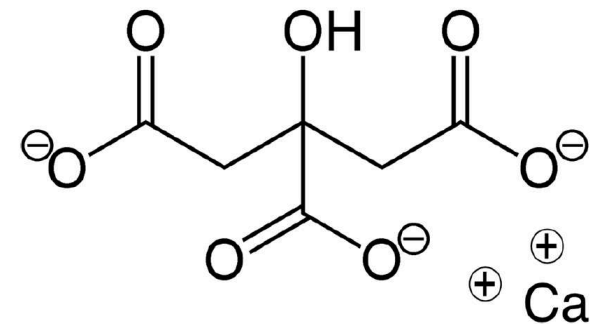
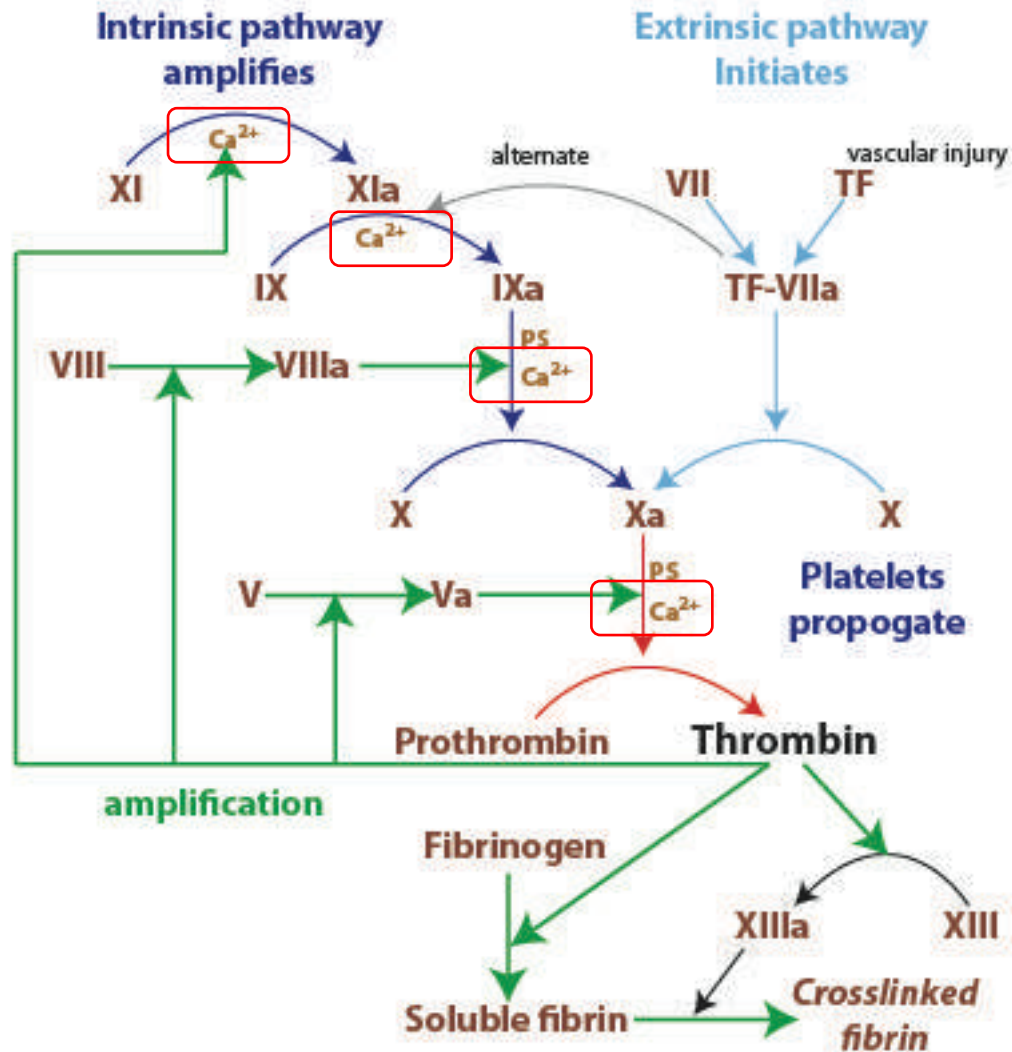
RCA: filter life → delivered RRT dose



CITRATE

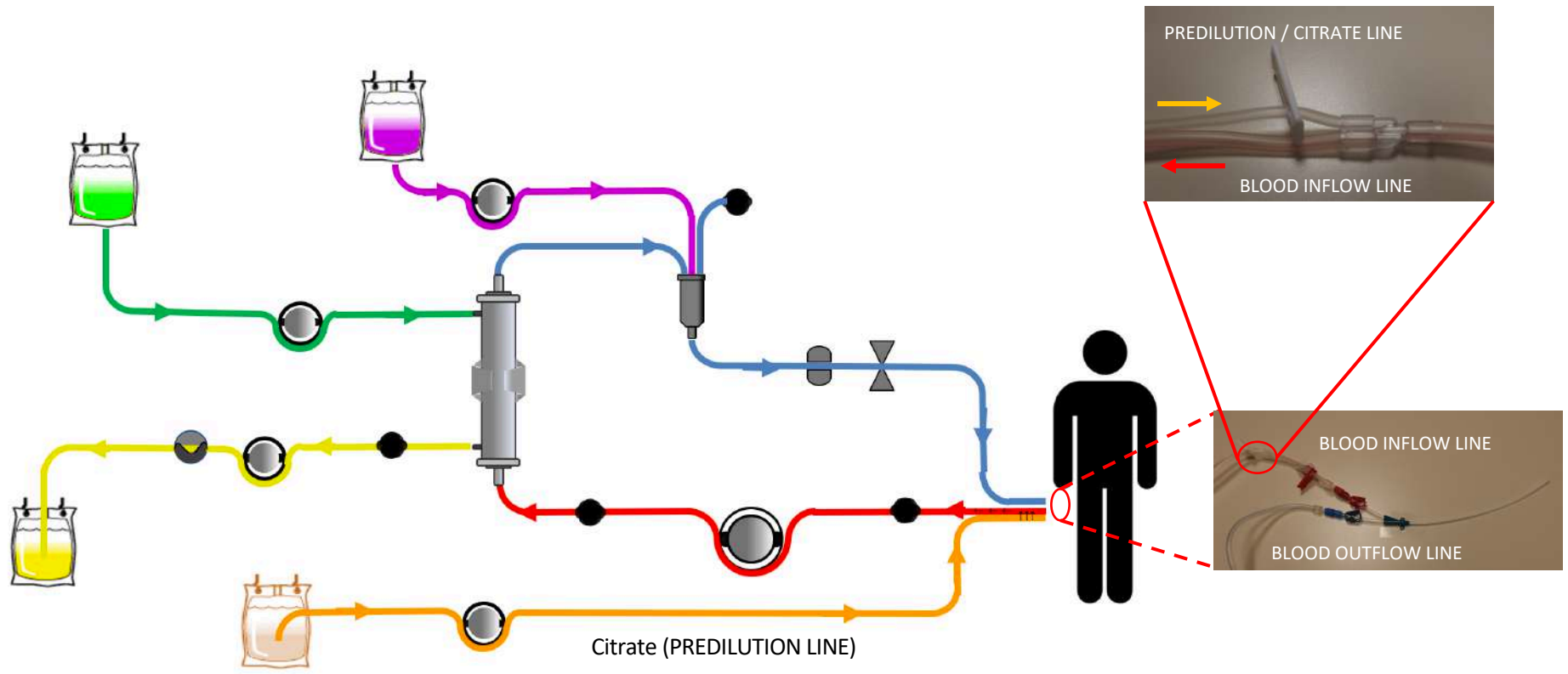


The anticoagulant effect of sodium **citrate** relies on forming a complex with **ionized calcium**, thus removing an essential component of the coagulation cascade.



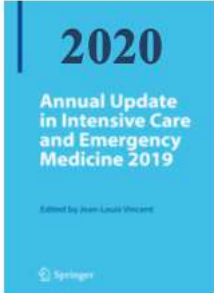
Citrate forms a complex with the Ca⁺⁺ ions, making them unavailable as co-factor within the clotting cascade



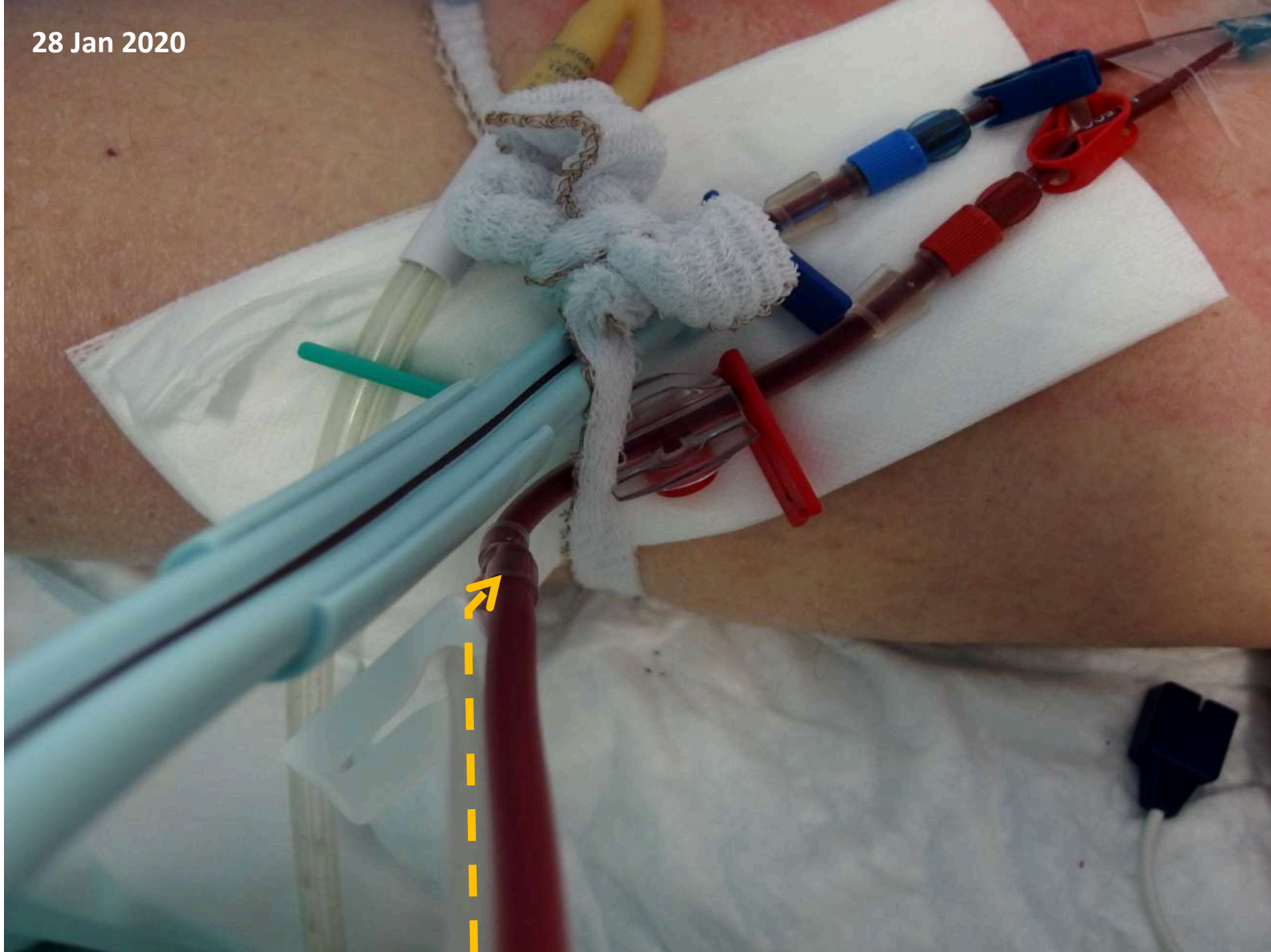


Continuous Veno-Venous Hemo Diafiltration

Romagnolis, Ricci Z, Ronco C.
 Annual Update in Intensive Care and Emergency Medicine (2020)



28 Jan 2020



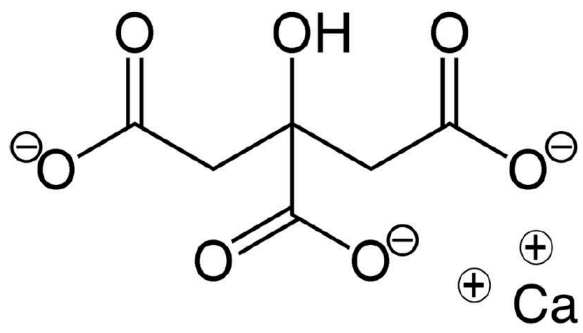
Blood is removed via the **inflow line** and citrate is added

Citrate complexes with calcium and prevent clotting

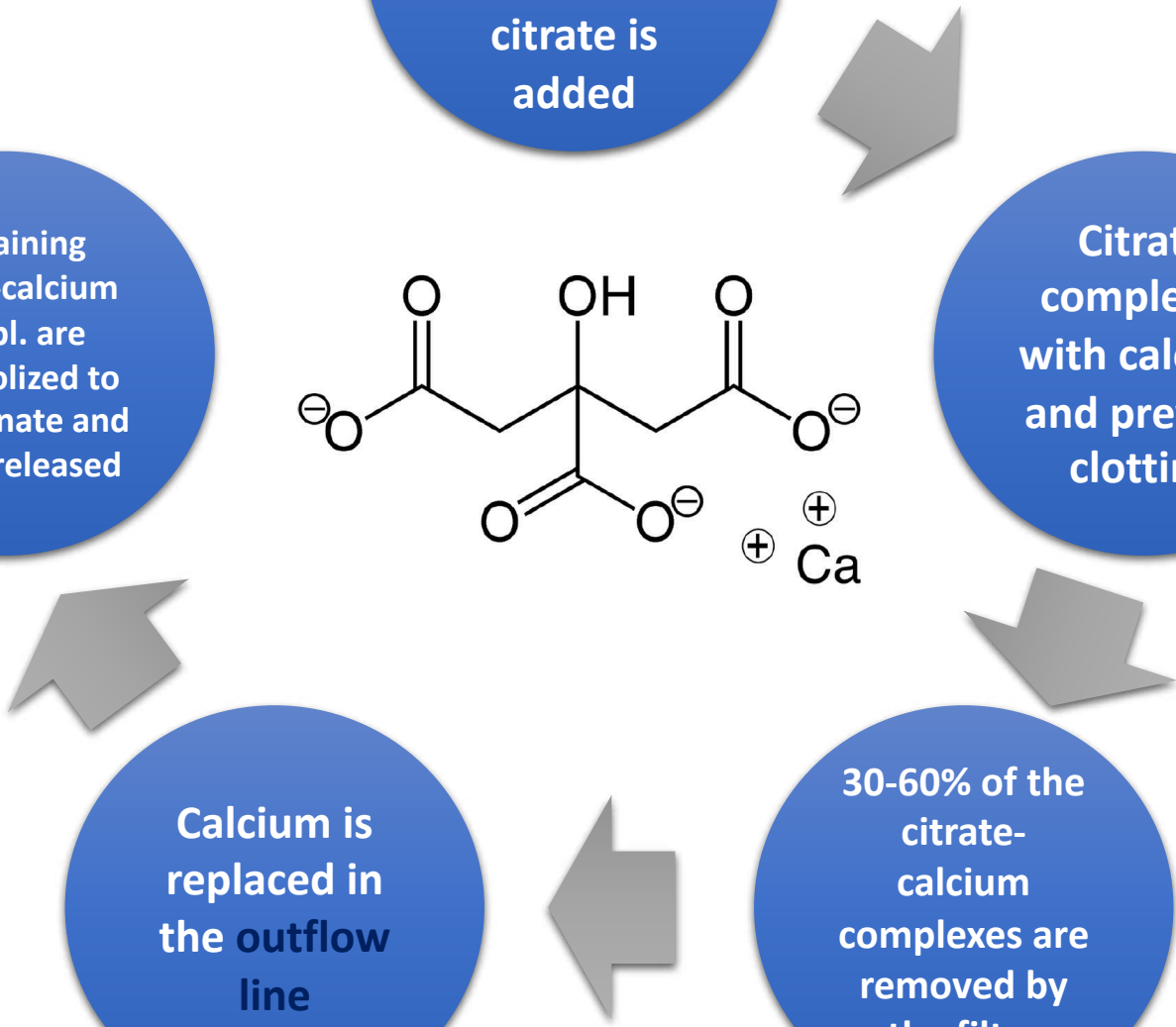
30-60% of the citrate-calcium complexes are removed by the filter

Calcium is replaced in the **outflow line**

Remaining citrate-calcium compl. are metabolized to bicarbonate and Ca^{++} is released

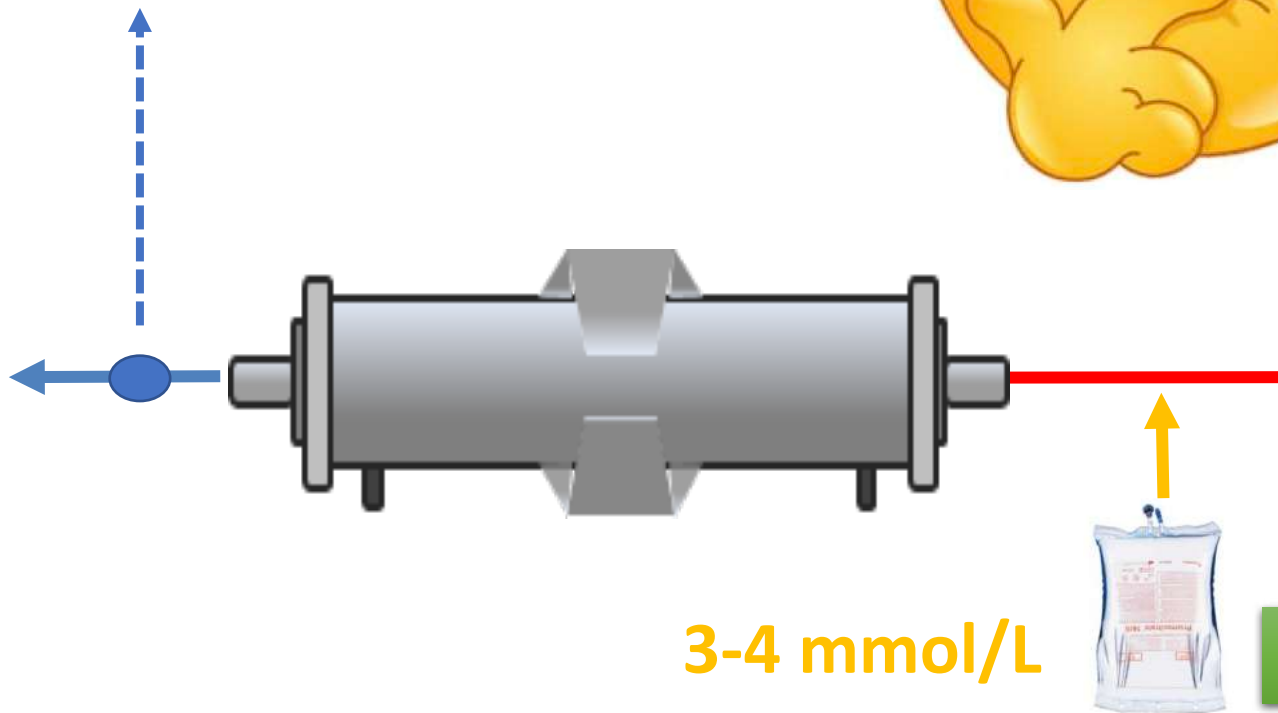


298 Da
High hydrosolubility
Sc = 1

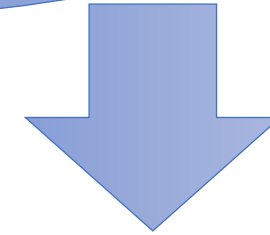
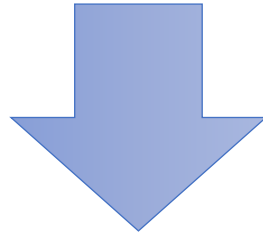


Regional Citrate Anticoagulation (RCA)

Ca⁺⁺ (post-filter)
0.25 - 0.4 mmol/L
or
1.0 - 1.6 mg/dL

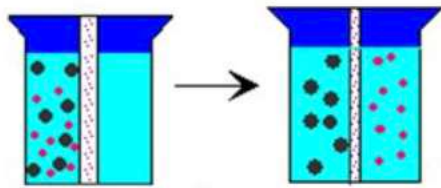


Citrate

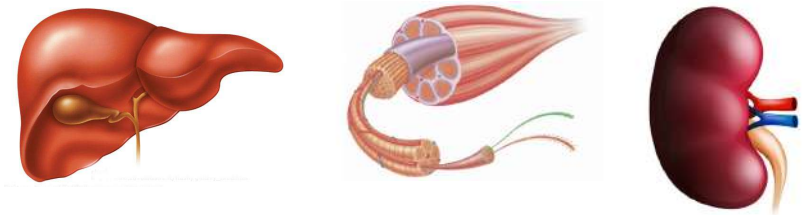


Citrate is partially removed by filtration or dialysis.

(Mariano F, et al. *Nephrol Dial Transplant* 2011; 26: 3882–3888)



The remaining amount, infused into the patient, is rapidly metabolized in the citric acid (Krebs) cycle, especially in the liver, muscle, and renal cortex

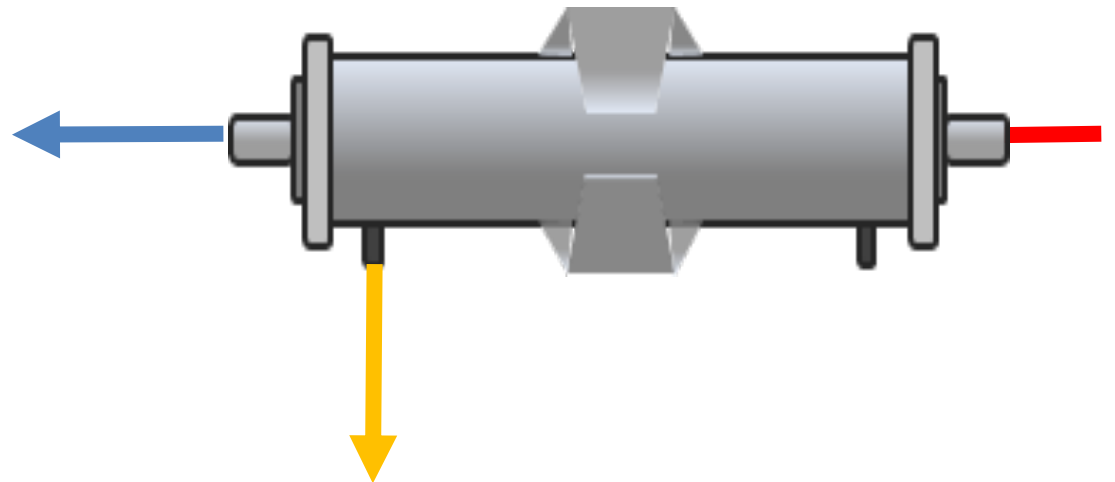


The ensuing regional hypocalcemia in the filter inhibits thrombin generation.

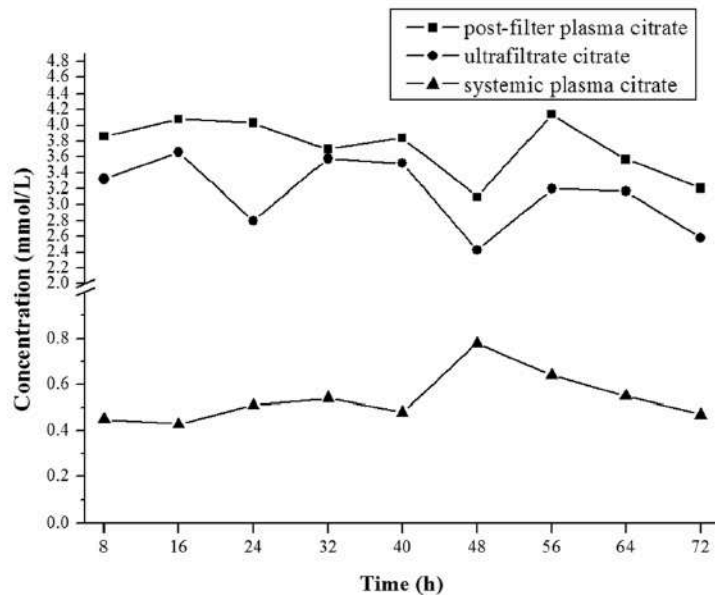


[0.45-0.62 mmol/L]

[3.44-4.01 mmol/L]


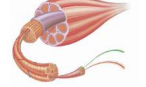



[2.69-3.48 mmol/L]



A mode of CVVH with regional citrate anticoagulation compared to no anticoagulation for acute kidney injury patients at high risk of bleeding

REGIONAL CITRATE

- There is no systemic anticoagulation as a result of:
 - Any citrate-calcium complex → patient's blood →    → **1 cit = 3 bicarbonate** ions
 - During this metabolism, **Calcium is released** contributing to normalizing of the coagulation
 - 1 mmol citrate → 2.48 kJ (593 cal/mmol citrate)

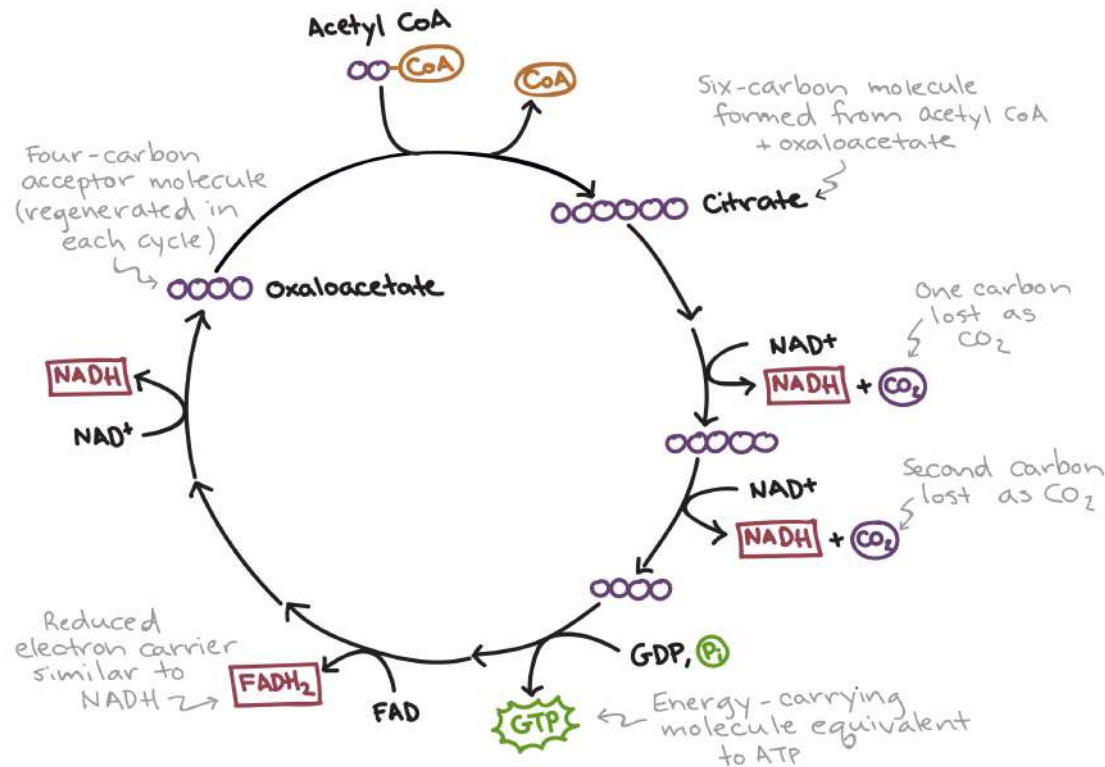
Am J Clin Nutr 2017; 105:1559-63

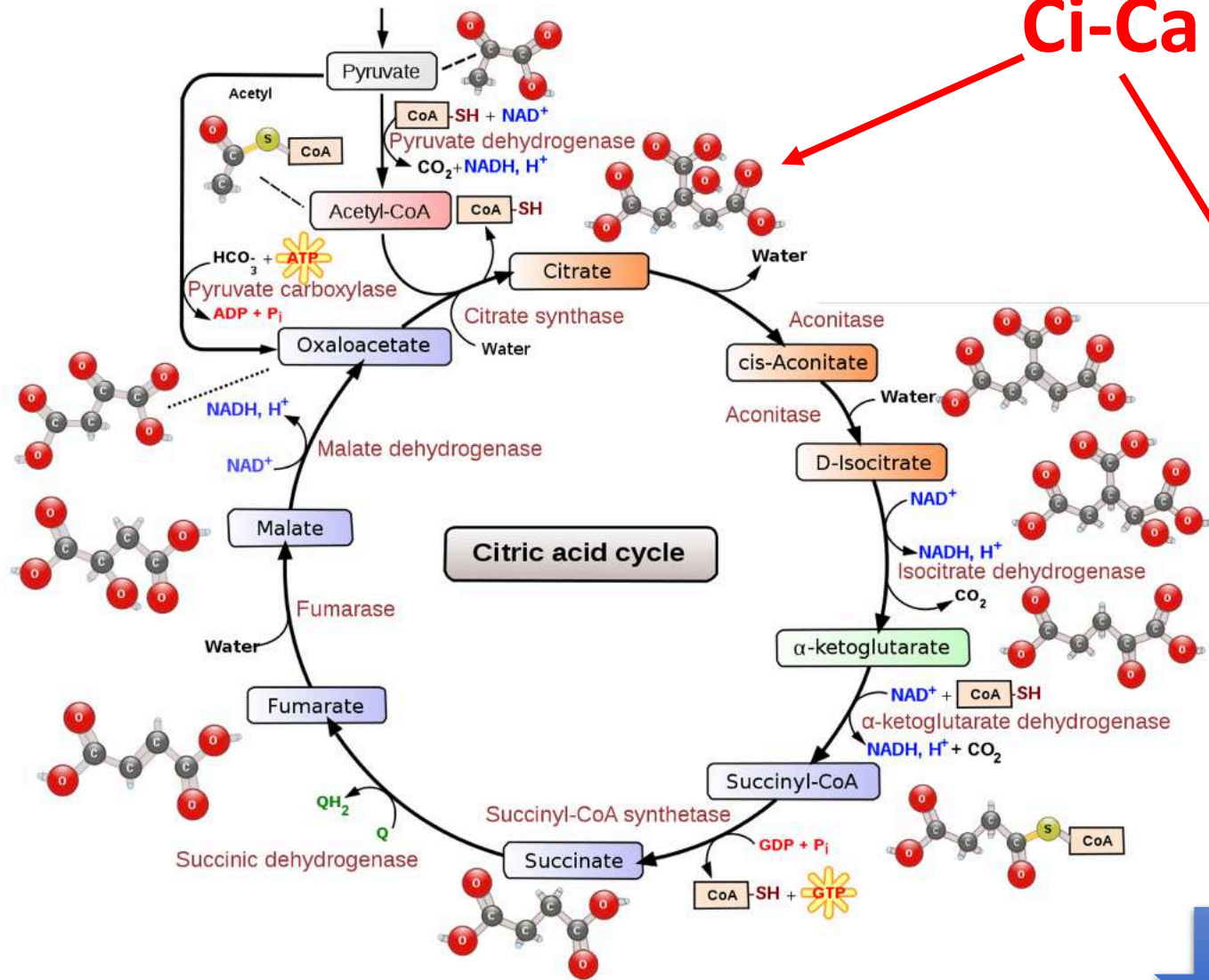
- Pay attention to ... Magnesium (Mg^{++})

The citrate **metabolic load** to the patient is:

$$[\text{Citrate}]_{\text{pre}} - [\text{Citrate}]_{\text{eff}}$$

With the more commonly reported citrate protocols, the citrate load is approximately **10–20 mmol/h**.





Ci-Ca

Ca⁺⁺

Na⁺

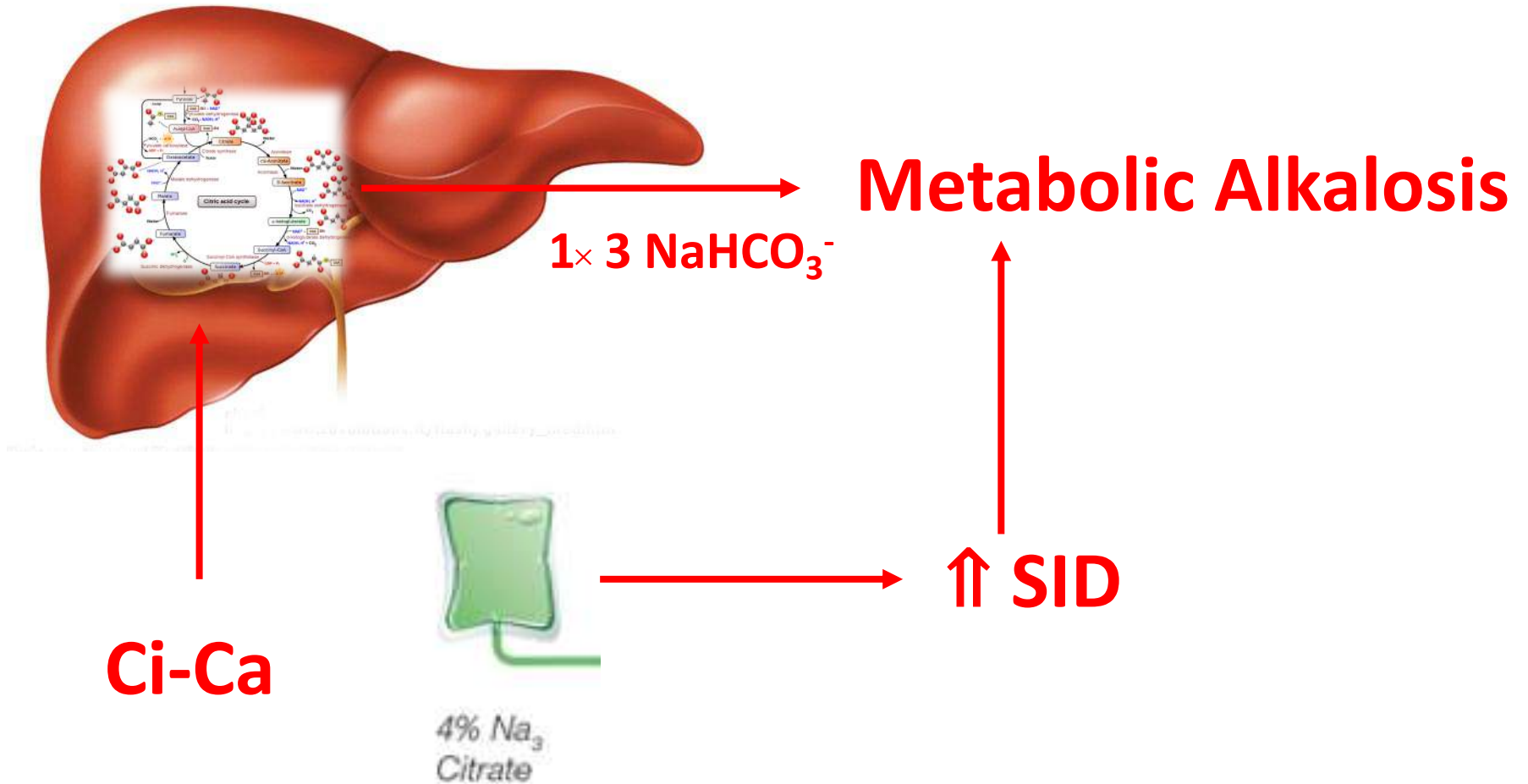
Citric acid cycle



Half life 5'
2.48kJ – 593 cal/mmol citrate

O₂ dependent

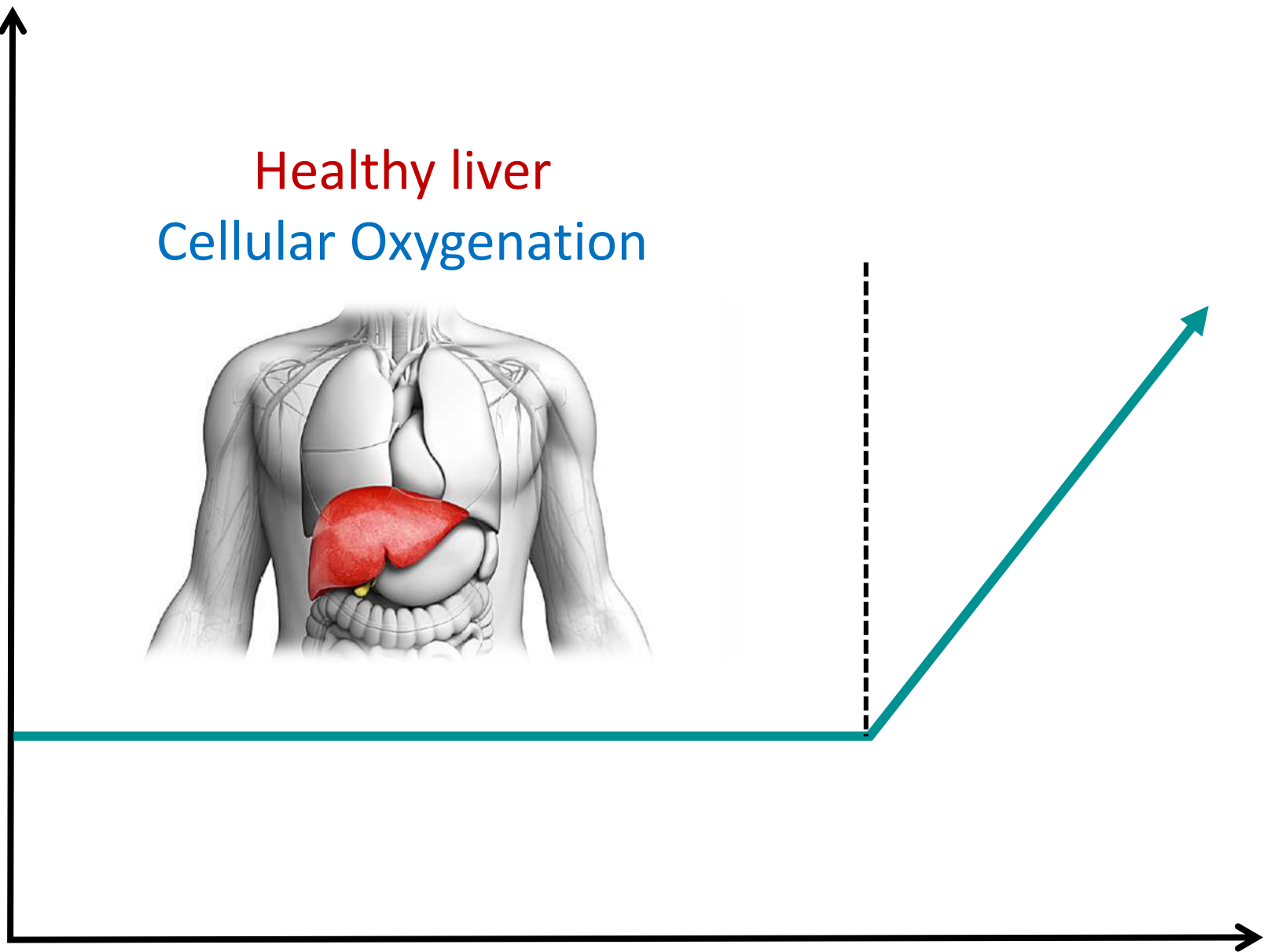
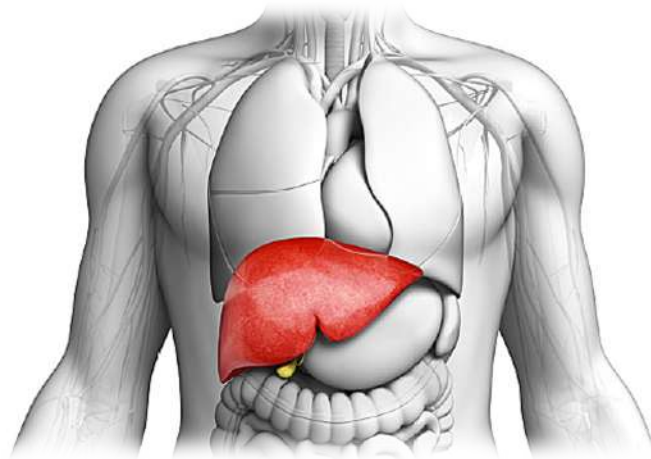
Acid-base effects



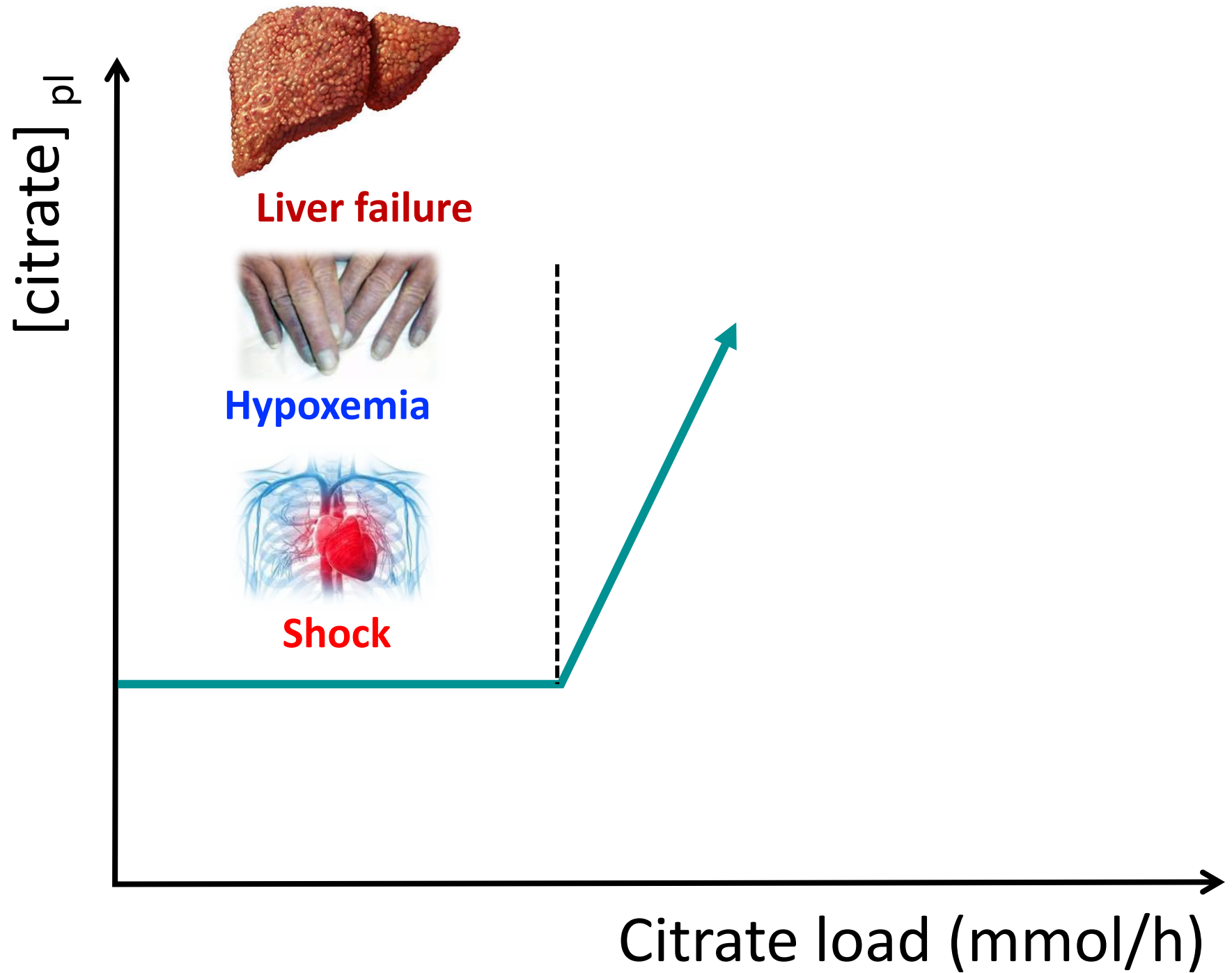
Ci-Ca accumulation → **Metabolic Acidosis**

[citrate]_{pl}

Healthy liver
Cellular Oxygenation

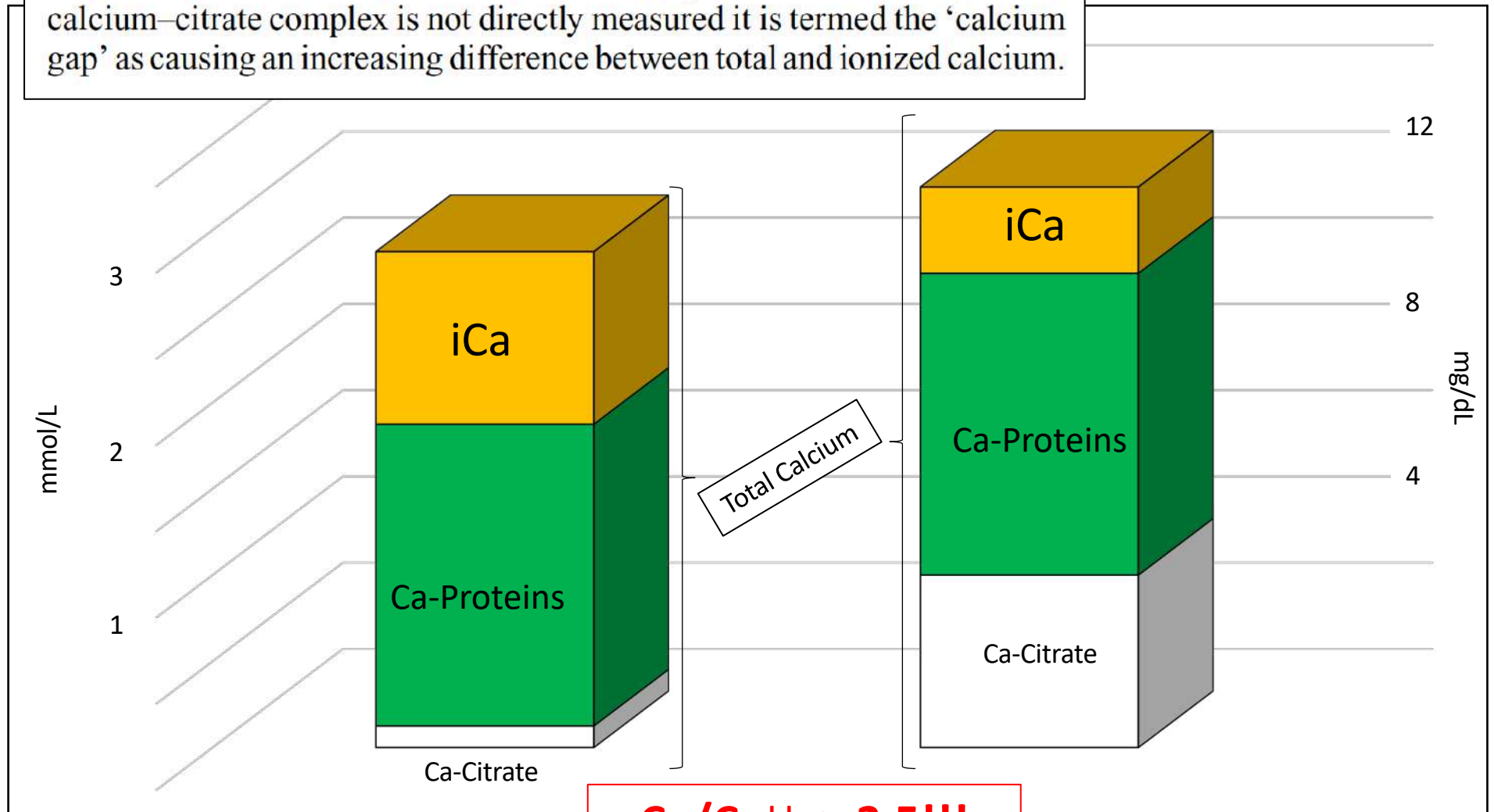


Citrate load (mmol/h)



If citrate cannot be metabolized, then the total serum calcium concentration appears to increase, with a corresponding fall in ionized calcium due to the increase in calcium complexed with citrate, as the calcium–citrate complex is not directly measured it is termed the ‘calcium gap’ as causing an increasing difference between total and ionized calcium.

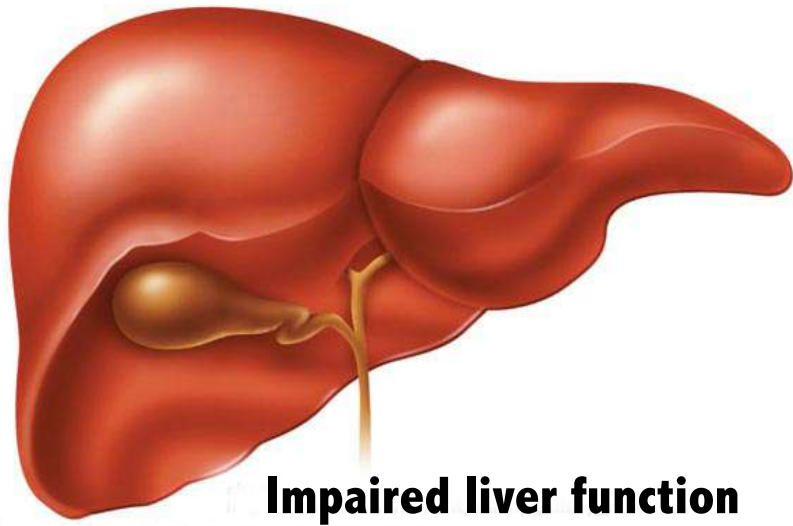
Davenport A et al. NTD (2009)



Ca/Ca⁺⁺ > 2.5!!!

...accurately predict the citrate accumulation (systemic citrate concentration **1 mmol/L**) with high sensitivity and specificity (89 and 100%, respectively)

Bakker AJ, et al. Clin Chem Lab Med (2006)



Impaired liver function



Hypoxemia



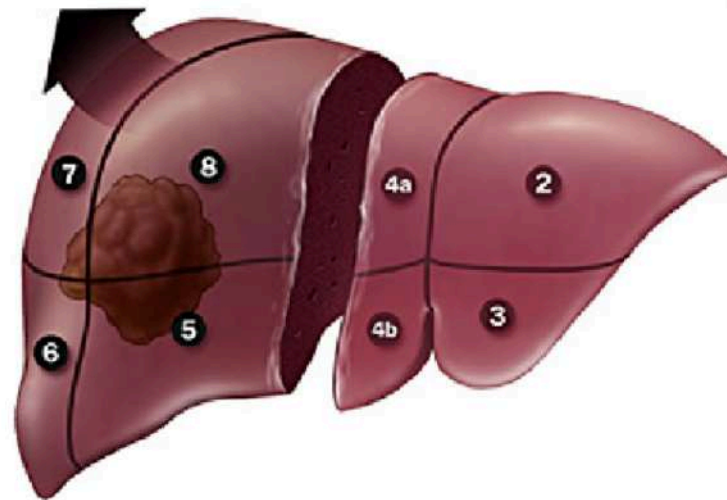
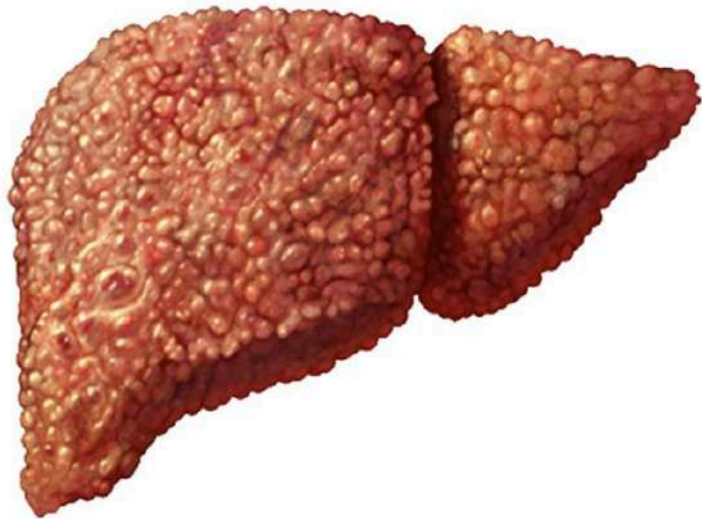
Shock

Khadzhyonov D, et al J Crit Care (2014)

Ricci D et al. Contrib Nephrol (2017)

However, there is increasing evidence that at least **impaired liver function need not be considered as an absolute contraindication** for RCA.

Several studies have reported that RCA can be safely used even in this population.



Fiaccadori E, et al. J Nephrol 2015; 28: 151–164.
Slowinski T, et al. Crit Care 2015; 19: 349.
Schultheiß C, et al. Crit Care 2012; 16:R162.
Kribben A, et al. 2012; 142: 782–789.e3.

Anticoagulation OPTIONS for CRRT

1

Regional Anticoagulation

Rigid Protocol

1.5

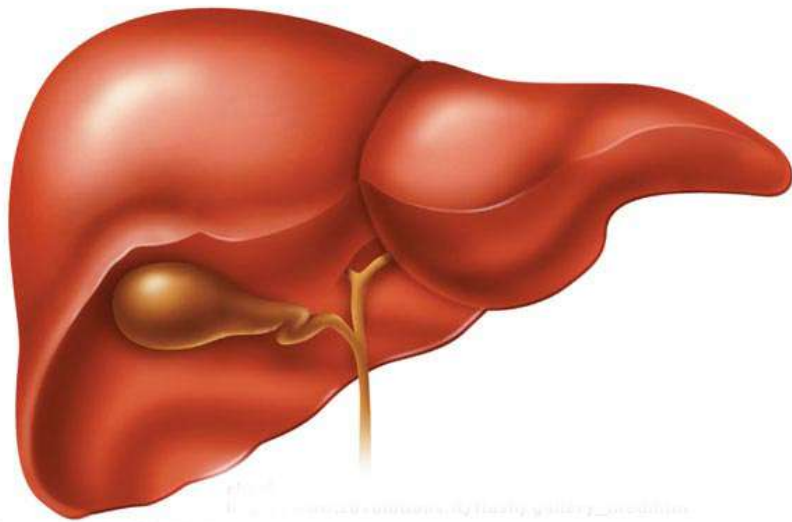
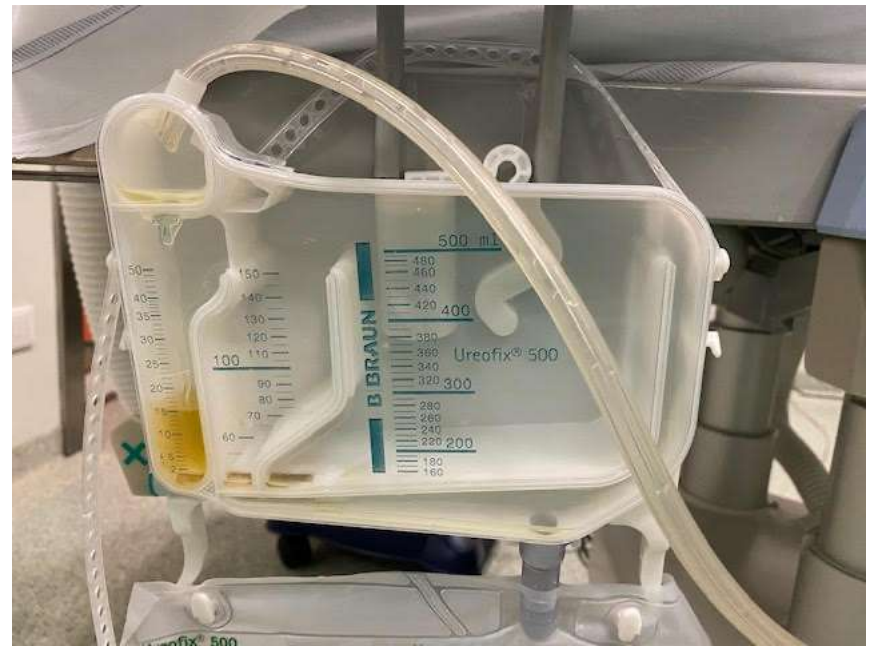
RCA management and handling

3

Anticoagulation Free

28 Jan 2020





Prescrizione

Anticoagulazione

Metodo	Cit/Cal
Soluzione con citrato	Prismocitrate 18/0 Citrato: 18 mmol/l Acido citrico: 0 mmol/l Volume sacca: 5000 ml
Dose citrato	2.0 mmol/l sangue
Citrato PBP	1200 ml/h
Accum. citrato paz.	12.7 mmol/h
Soluzione con calcio	Calcio Cloruro Calcio: 680 mmol/l
Post reinfusione	Calcio: 1.75 mmol/l
Comp. calcio	130 %
Ematocrito (HCT)	34 %
Flusso siringa	10.0 ml/h
Flusso di calcio	6.8 mmol/h

REGOL.

Pressioni (mmHg)

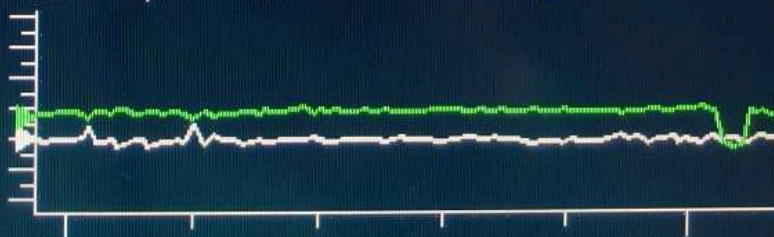


Info

TMP

Caduta press.: 17

PTM: 65



STOP

CAMBIO
SACCHE

CAMBIO
SIR/LINEA

REGOLAZ.
CAMERA

STRUM.
SISTEMA

STORIA

AIUTO

Prescrizione

Anticoagulazione

Sangue 180 ml/min

Citrato PBP 1200 ml/h

Dialisato 1900 ml/h

Reinfusione 500 ml/h

Post

Rimoz. fluido paz. 50 ml/h

Effluente 3660 ml/h

Dose effluente 43 ml/kg/h

Dose conv. (UFR) 18 ml/kg/h

Frazione filtrazione 22 %

REGOL.

Pressioni (mmHg)

Accesso -84

-233 300

Filtro 155

10 450

Effluente 52

-500 500

Rientro 107

54 350



Info

TMP

Caduta press.: 14

PTM: 62



STOP

CAMBIO
SACCHE

CAMBIO
SIR/LINEA

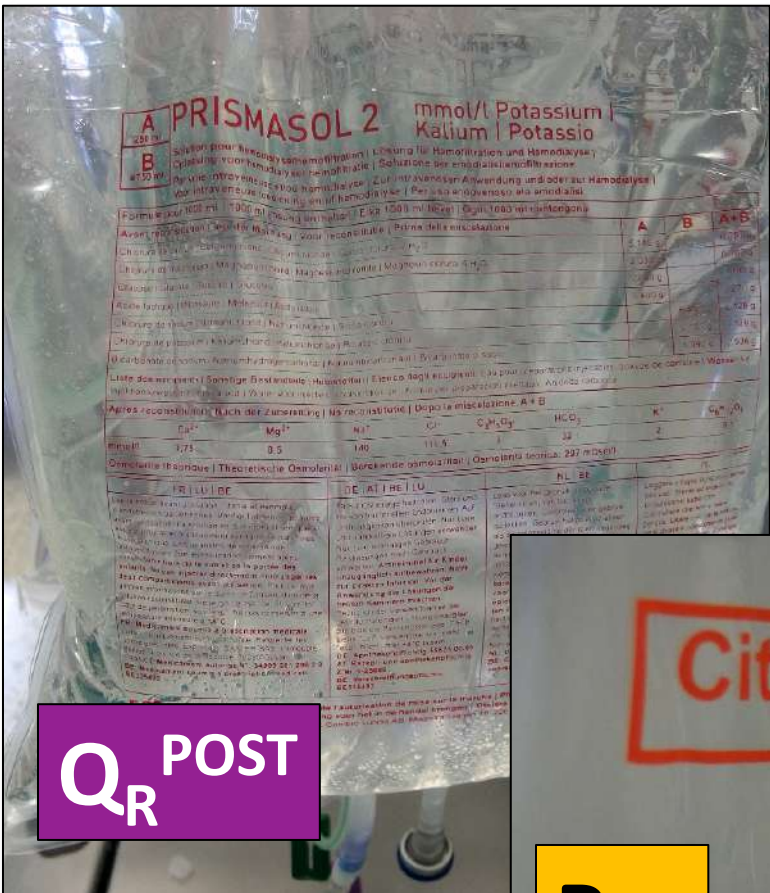
REGOLAZ.
CAMERA

STRUM.
SISTEMA

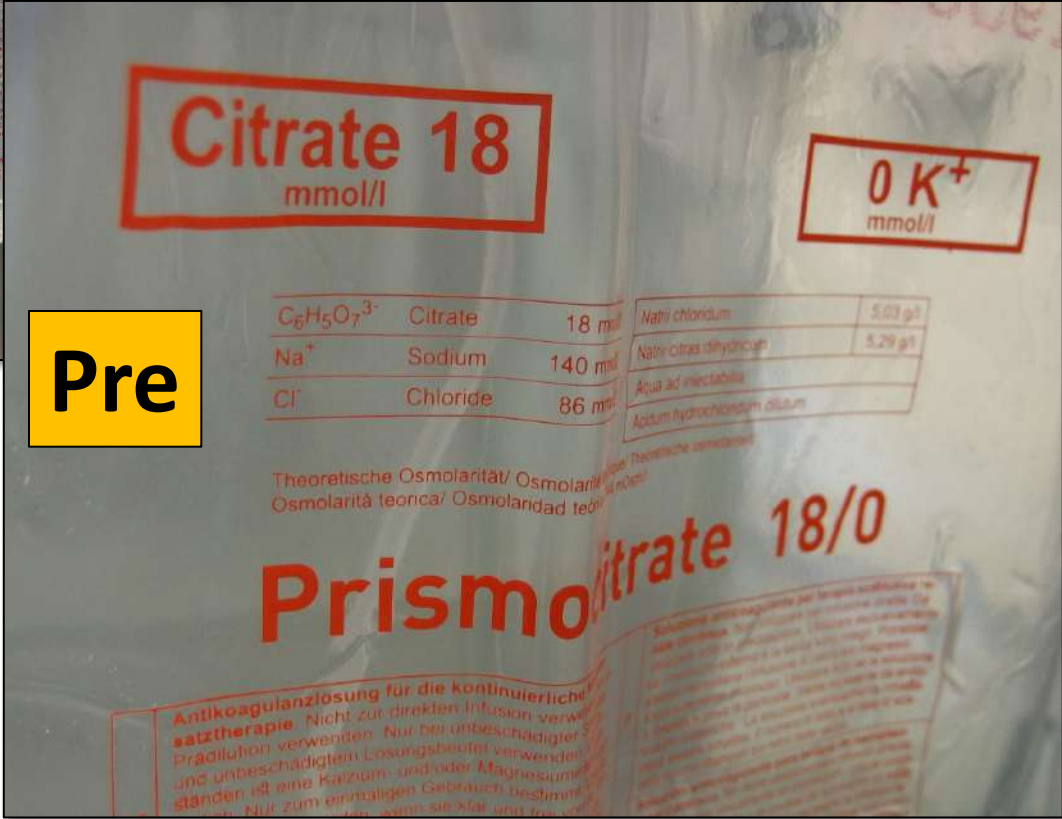
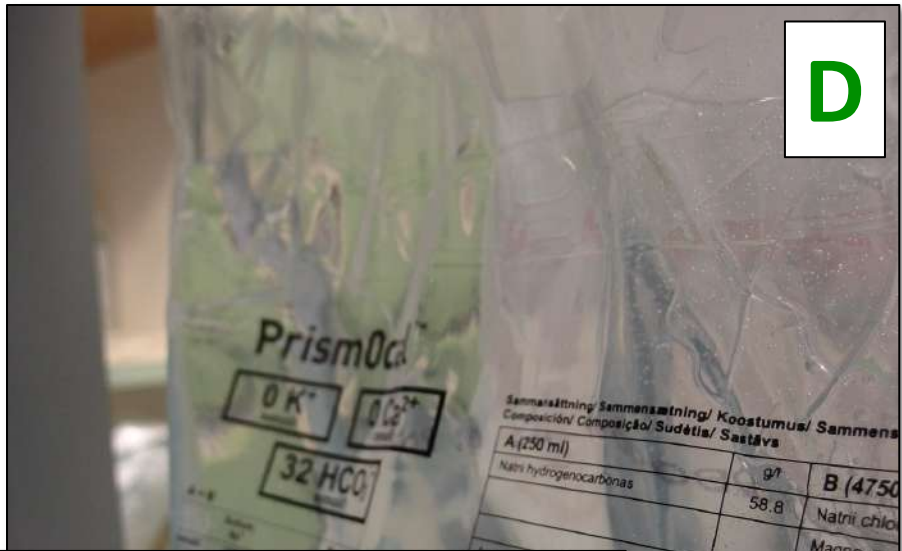
STORIA

AIUTO

D



QR POST



Pre

Stato

alessandretti guido

85 kg

22:44 ▶ 22:44 ⌚ 20:09

▶ CVVHD ✎ CVVHDF

Prescrizione

Anticoagulazione

Metodo Cit/Cal
Soluzione con citrato Prismocitrate 18/0
Citrato: 18 mmol/l
Acido citrico: 0 mmol/l
Volume sacca: 5000 ml

Dose citrato 0.0 mmol/l sangue

Citrato PBP 0 ml/h

Accum. citrato paz. 0.0 mmol/h

Soluzione con calcio Calcio Cloruro
Calcio: 680 mmol/l

Post reinfusione Calcio: 1.75 mmol/l

Comp. calcio 150 %

Ematocrito (HCT) 34 %

Flusso siringa 0.0 ml/h

Flusso di calcio 0.0 mmol/h

REGOL.

Pressioni (mmHg)



Caduta press.: 45

PTM: 15



STOP

CAMBIO
SACCHE

CAMBIO
SIR/LINEA

REGOLAZ.
CAMERA

STRUM.
SISTEMA

STORIA

AUTO

Stato

alessandretti guido
85 kg

22:44 22:44 20:04

CWHD CVHDF

Prescrizione

Anticoagulazione

Sangue	200 ml/min
Citrato PBP	0 ml/h
Dialisato	1900 ml/h
Reinfusione	500 ml/h
	Post
Rimoz. fluido paz.	0 ml/h
Effluente	2400 ml/h
Dose effluente	28 ml/kg/h
Dose conv. (UFR)	6 ml/kg/h
Frazione filtrazione	7 %

REGOL.

Pressioni (mmHg)



Info

TMP

Caduta press.: 19

PTM: 27



STOP

CAMBIO
BACCHE

CAMBIO
SIR/LINEA

REGOLAZ
CAMERA

STRUM.
SISTEMA

STORIA

AUTO



The **new software** is in fact able to adapt citrate infusion to blood flow changes, thus limiting the risk of an inappropriate citrate/blood flow ratio.



OMNI – PROTOCOLLO CITRATO CVVHD (CHUV LOSANNA)

Calcio Post Filtro (circuito)

- 5 minuti dopo l'inizio terapia (CVVHD)
- 5 minuti dopo ogni modifica della dose
- Successivamente ogni 6 – 8 ore

Calcio ionizzato paziente

- Prima di iniziare la terapia
- 1 ora dopo
- Ogni 3 ore durante le prime 12 ore
- Ogni 6 ore quando il Calcio è stabile

Calcemia totale paziente

- Prima di iniziare la terapia
- Ogni 6 ore

Il Flusso di Citrato è sempre vincolato al Flusso Sanguigno

- La quantità di citrato è sempre un rapporto: citrato / litri di sangue
- **Impostare a inizio trattamento una dose di 4 mmol di citrato per litro di sangue**
- La dose di calcio è prescritta considerando l'effluente
- L'effluente è la somma del calo peso + dializzato
- **Impostare a inizio trattamento una dose di 1,7 mmol/l di calcio nell'effluente**



Moreover, with CRRT monitors the citrate dose **can be modified at any time during the treatment** in the event of a documented or suspected citrate overload.

Last, **modulation of the convective and/or diffusive CRRT** dose may prevent the development of citrate accumulation, due to the substantial removal of citrate with the effluent fluid

Automatic Dialysis and Continuous Renal Replacement Therapy: Keeping the Primacy of Human Consciousness and Fighting the Dark Side of Technology

Zaccaria Ricci^a Stefano Romagnoli^b Claudio Ronco^{c,d}

Blood Purif 2017;44:271–275



PrismOcal B22
5000 ml



Na⁺ 140 mmol/L
K⁺ 4 mmol/L
Mg⁺⁺ 0.75 mmol/L
Cl⁻ 120 mmol/L
HCO₃⁻ 22 mmol/L
Lattato 3 mmol/L
Glucosio 6.1 mmol/L
Osm 294 mOsm/L

Calcium – Free
NaHCO₃ 22 mmol/l

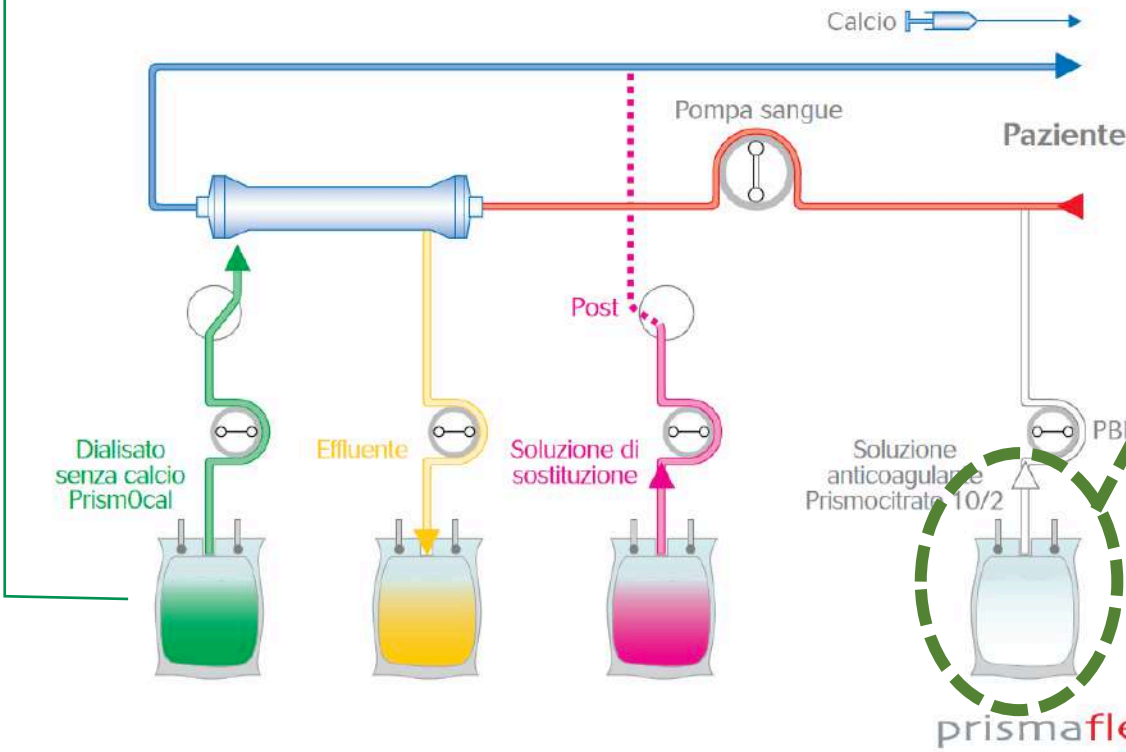
CVVHDF



Prismocitrate 18/0
18 mmol/l
5000 ml



Baxter



NaCl 5.03 g/L
Sodio citrate 5.29 g/L
Citrato 18 mmol/L
Na⁺ 140 mmol/L
Osm 244 mOsm/L

Protocollo CVVHDF con Citrato con Prismaflex

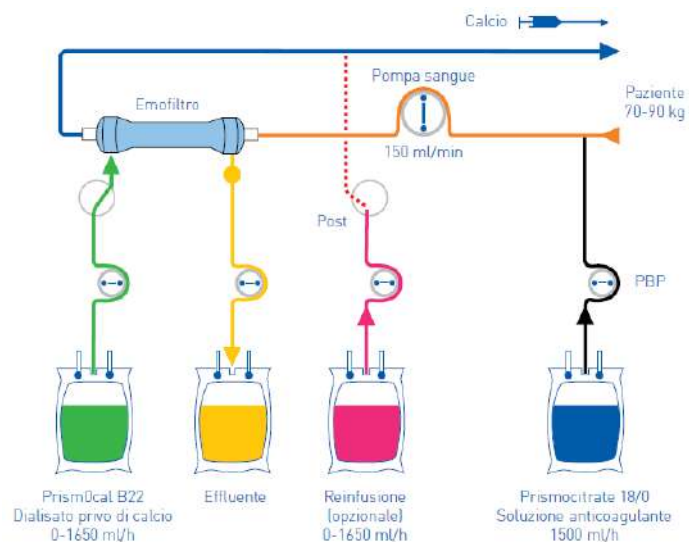
(con Prismocitrate® 18/0)

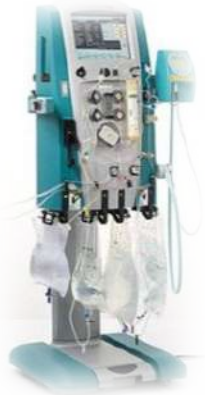


IMPOSTAZIONE FLUSSI	Peso Paziente [Kg]									
	50	60	70	80	90	100	110	120	130	
FLUSSO SANGUE [ml/min]	100	110	120	130	140	150	160	170	180	
Infusione PBP (pre diluizione) ⁽¹⁾ Prismocitrate® 18/0 o Regiocit [ml/h]	1000	1100	1200	1300	1400	1500	1600	1700	1800	
DIALISATO senza calcio PrismOcal® B22 o Biphozyl [ml/h]	1000	1100	1200	1300	1400	1500	1600	1700	1800	
REINFUSIONE post diluizione ⁽²⁾ PRISMASOL 2 / 4, Phoxilium® o Biphozyl [ml/h]	200	400	500	500	500	600	700	800	1000	



IMPOSTAZIONE ANTICOAGULANTE	
Dose Citrato	3 mmol/L sangue
Compensazione Calcio ⁽³⁾	100 %





Calcio ionizzato sistemico Range: 1,00 – 1,20 mmol/L o 4,00 – 4,80 mg/dL	Entro i primi 30 min	A 2 ore dalla partenza	Almeno ogni 6 ore (vedi schema)
Calcio ionizzato post filtro Range: 0,25 – 0,50 mmol/L o 1,00 – 2,00 mg/dL	Entro i primi 30 min		Almeno ogni 24 ore (vedi schema)

COMPENSAZIONE % DELLA CALCEMIA PAZIENTE TRAMITE SIRINGA PRISMAFLEX

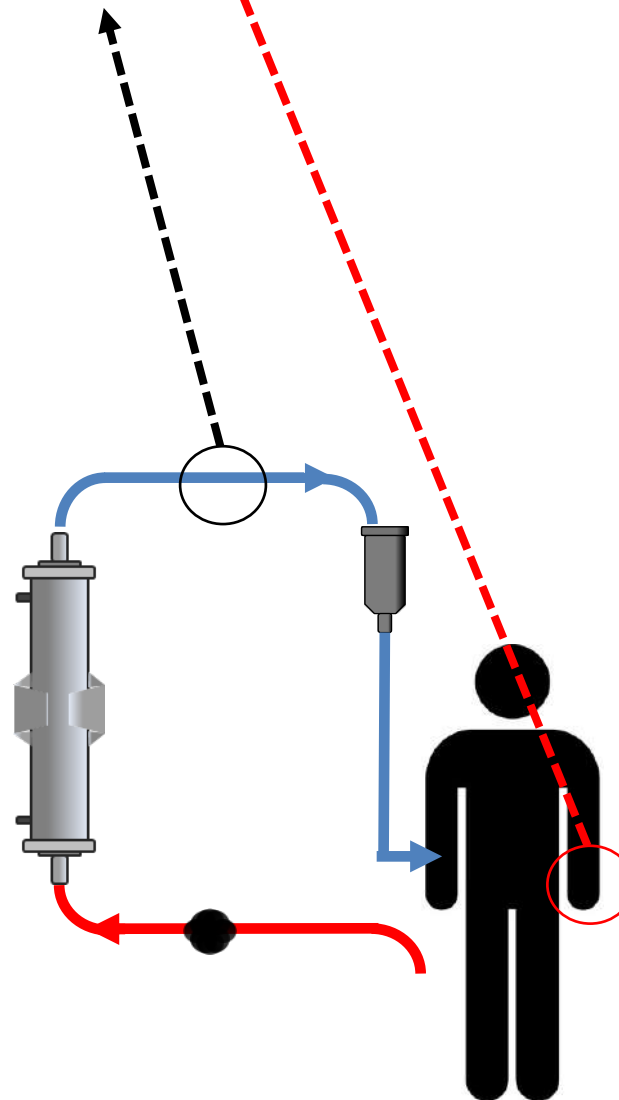
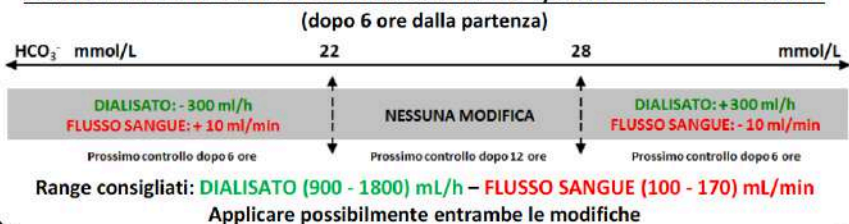


In caso di grave ipocalcemia si suggerisce di valutare un'ipotetica intolleranza mediante il rapporto Ca Tot. / Ca⁺⁺

AGGIUSTAMENTO DEL CALCIO IONIZZATO POST FILTRO



AGGIUSTAMENTO DELL'ACCUMULO DI CITRATO e/o BILANCIO BICARBONATI





OMNI – PROTOCOLLO CITRATO CVVHD (CHUV LOSANNA)



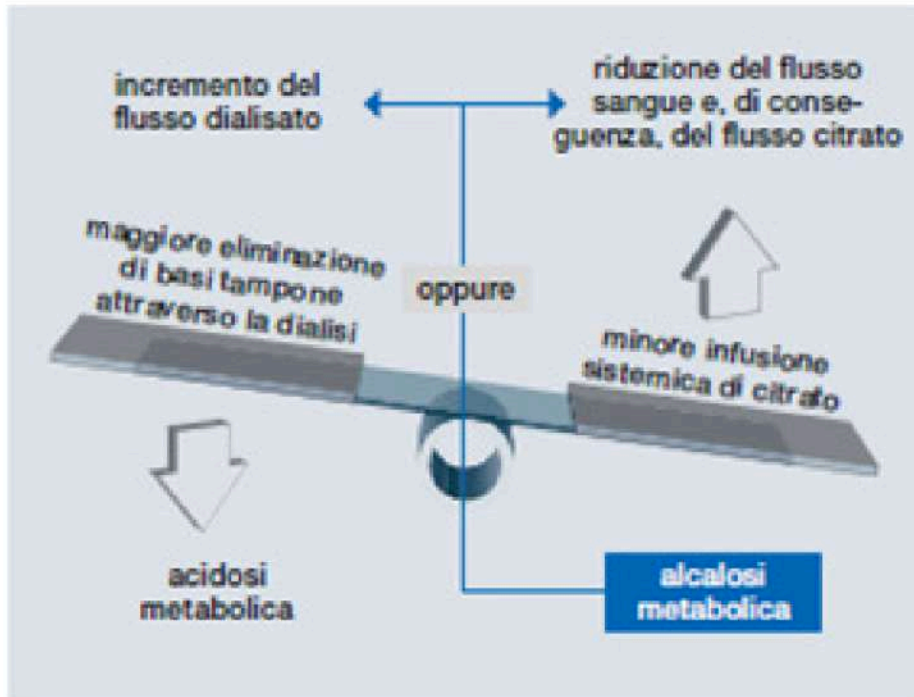
B. BRAUN
SHARING EXPERTISE

Peso paziente (Kg)	Flusso Dialisato (ml/h)	Flusso Sangue (ml/min)
60	1600	80
60 - 79	2000	100
80 - 99	2600	130
100 - 119	3000	150
120 - 149	3600	180

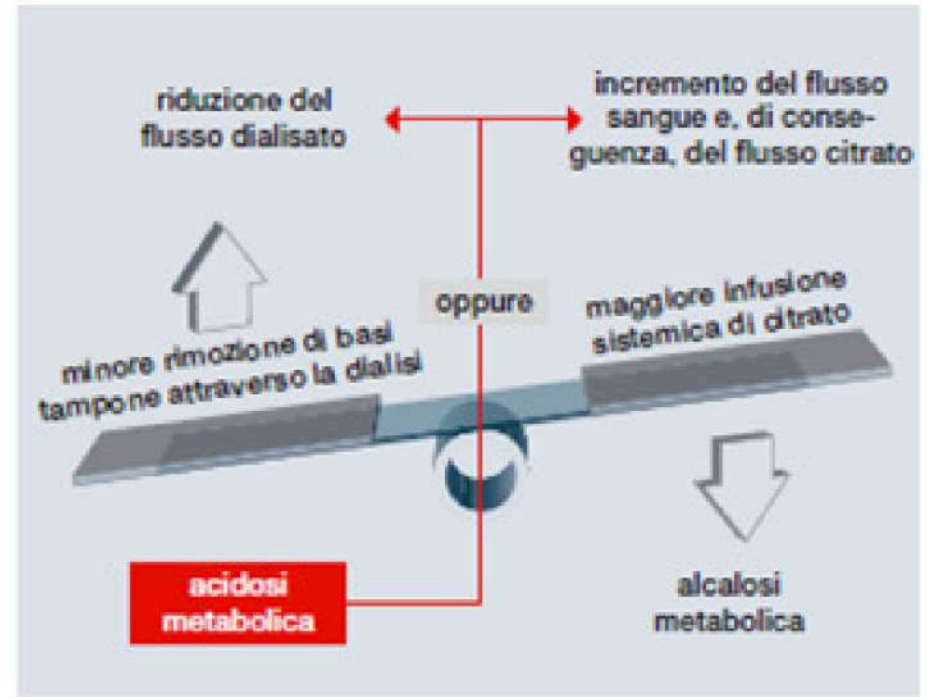
•Trisodio citrato **4%**
 •Siringa B.Braun Omnifix da 50cc contenente:
30 ml Calcio Cloruro 10% (680mmol/l) più
20 ml di soluzione fisiologica => **408 mmol/l**
 Rapporto Flusso Dialisato/Flusso sangue 20:1
 Dialisato senza calcio a 4K

Calcio ionizzato POST FILTRO (mmol/l)	Modifica dose CITRATO (Citrato/Sangue)	Calcio ionizzato SISTEMICO (mmol/l)	Modifica dose CALCIO (Calcio/Effluente)
> 0,45	Aumentare di 0,3 mmol/l e informare il medico	> 1,45	Diminuire di 0,6 mmol/l e informare il medico
0,41 – 0,45	Aumentare di 0,2 mmol/l	1,31 – 1,45	Diminuire di 0,4 mmol/l
0,35 – 0,40	Aumentare di 0,1 mmol/l	1,21 – 1,30	Diminuire di 0,2 mmol/l
0,25 – 0,34	Nessuna modifica	1,12 – 1,20	Nessuna modifica
0,20 – 0,24	Ridurre di 0,1 mmol/l	1,05 – 1,11	Aumentare di 0,2 mmol/l
0,15 – 0,19	Ridurre di 0,2 mmol/l	0,95 – 1,04	Aumentare di 0,4 mmol/l
< 0,15	Ridurre di 0,3 mmol/l	< 0,95	Aumentare di 0,6 mmol/l e informare il medico

ALCALOSI METABOLICA



ACIDOSI METABOLICA

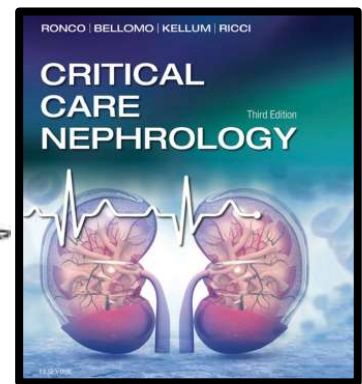


Citrate accumulation or overload (*management*)

- 1) Decreasing Q_B (decreases intake) through blood flow–citrate coupling or
- 2) Increasing Q_D (CVVHD) or Q_R^{POST} (CVVH) (increases removal), or
- 3) Decreasing the targeted citrate concentration within the filter.



Nonanticoagulant Measures Reducing Circuit and Access Clotting



Catheter design

- Increase diameter
- High inner diameter (thin material)
- Avoid side holes
- Use short-gun tip



Catheter position

- Chose individually
- Chose position with lowest pressures
- Choose straight direction : right jugular, left or right femoral vein
- Prevent kinking
- Tip of jugular vein catheter in right atrium
- Tip of femoral vein catheter in inferior caval vein

CRRT mode

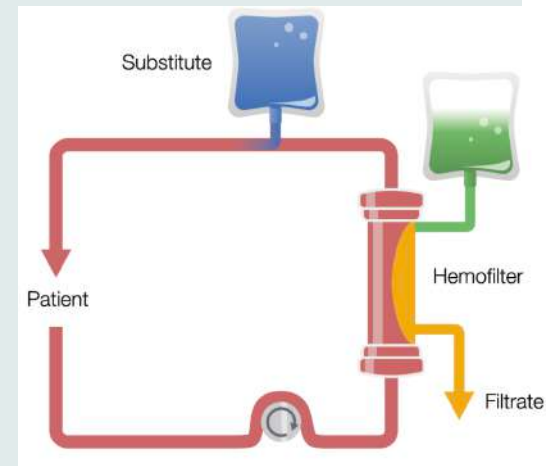
- Avoid or reduce hemoconcentration
 - Hemodialysis
 - Hemofiltration with low filtration fraction
 - Predilution hemofiltration

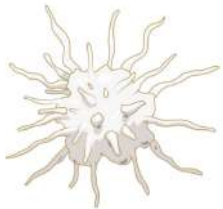
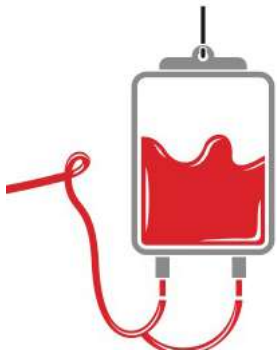
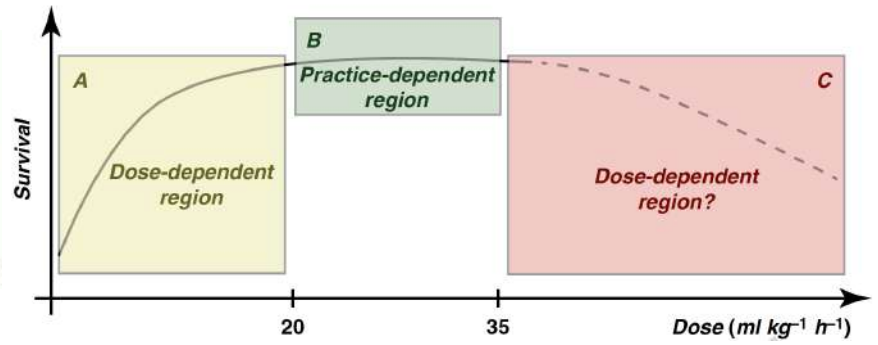
Circuit

- Avoid blood flows < 100mL/min

Venous access during CRRT interruptions

- Use a citrate lock





Continuous Renal Replacement Therapy


Who, When, Why, and How

Vascular Access

- In adults, catheter design and position must be sufficient to sustain blood flow rates of 200 to 300 mL/min.
- KDIGO Clinical Practice Guidelines for AKI recommend the right internal jugular vein as the preferred location for catheter placement, followed by the femoral and the left internal jugular veins

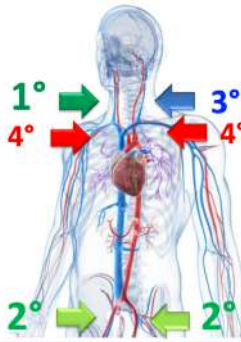
Position/site

Kidney Disease: Improving Global Outcomes (2012)



5.4.2: When choosing a vein for insertion of a dialysis catheter in patients with AKI, consider these preferences (*Not Graded*):

- First choice: right jugular vein;
- Second choice: femoral vein;
- Third choice: left jugular vein;
- Last choice: subclavian vein with preference for the dominant side.



<http://kdigo.org/home/guidelines/acute-kidney-injury/>

In the **femoral** location, catheters **shorter than 25cm** or with lower flow capacity may predispose to **catheter dysfunction**.

Parenti JJ et al. *Crit Care Med* 2010; 38:1118–1125
Bellomo R et al. *Blood Purif* 2016; 41:11–17



- The recommended femoral catheter length is therefore just **above 24 cm**

KDIGO 2012; Dugué AE et al. Clin J Am Soc Nephrol CIASN 2012;7:70–7

- Strategies to minimize the risk of clotting of the extracorporeal circuit include the following:
 - Higher Q_b rates
 - Minimization of **filtration fraction** (the ratio of ultrafiltration to plasma flow)
 - Minimization of filtration fraction (the ratio of ultrafiltration to plasma flow) by using CVVHD rather than CVVH or infusing replacement fluids **prefilter** during CVVH and CVVHDF (Predilution)
 - **Predilution**: replacement fluids prefilter during CVVH and CVVHDF
 - Ensuring optimal **catheter function**
 - **Responding promptly to machine alarms to minimize interruptions in blood flow**
 - Increasing the frequency of **scheduled replacement** of the extracorporeal circuit

VA/NIH Acute Renal Failure Trial Network, Palevsky PM et al. N Engl J Med (2008)
RENAL Replacement Therapy Study Investigators, Bellomo R, et al. N Engl J Med (2009)

Final Thoughts

- **RCA**
 - ✓ Per se is safe and effective
 - ✓ Prolongs filter running time
 - ✓ Decreases bleeding risk (vs. systemic anticoag.)
 - ✓ Decreases workload & associated cost
- Patients at risk for citrate accumulation
 - ✓ Severe liver failure
 - ✓ Severe hypoxemia
 - ✓ Shock
- For patients at **risk** for citrate accumulation (liver failure, hypoxemia, shock) + contraindications to systemic anticoagulation (after surgery, complex endovascular procedures ...)
 - ✓ Consider anticoagulation free approach
 - ✓ Personalize the strategies when the clinical scenario changes

CRRT e Anticoagulazione Una scelta ponderata: come mantenere la pervietà e il perfetto funzionamento del circuito. Diversi regimi di anticoagulazione

Stefano Romagnoli, MD, PhD



Dip. di Scienze della Salute – Università di Firenze
Dip. di Anestesia e Rianimazione - AOU Careggi - Firenze

UO di Nefrologia, Dialisi e Trapianto Renale
Ospedale San Bortolo - ULSS 8 Berica
International Renal Research Institute Vicenza (IRRV)



UNIVERSITÀ
DEGLI STUDI
DI PADOVA



CRRT
Questione di EQUIPE!

Videoconferenza LIVE per
INFERMIERI
NEFROLOGI
INTENSIVISTI ...
e tutti i Medici in Formazione Specialistica!
XI Edizione



15-16 giugno 2020