BaltAnestIC 2023

11th International Baltic Congress of Anaesthesioogy and Intensive care
September 28–30, 2023, Tartu, Estonia Estonian National Museum

“Haemodialysis only for creatinine, is it?”

Haemodialysis and nutrition - are they connected?

Friday, September 29th, 2023 at 12.20 (20min)

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Unil | Université de Lausanne

CHUV Centre hospitalier universitaire vaudois

Mette M. Berger - Disclosure

Advisory Board/Consultant	Baxter, Fresenius Kabi
Stock shareholder, Bonds	none
Lecturer honoraria	Abbott, Aguettant, Baxter, DSM, Fresenius Kabi, Nestlé

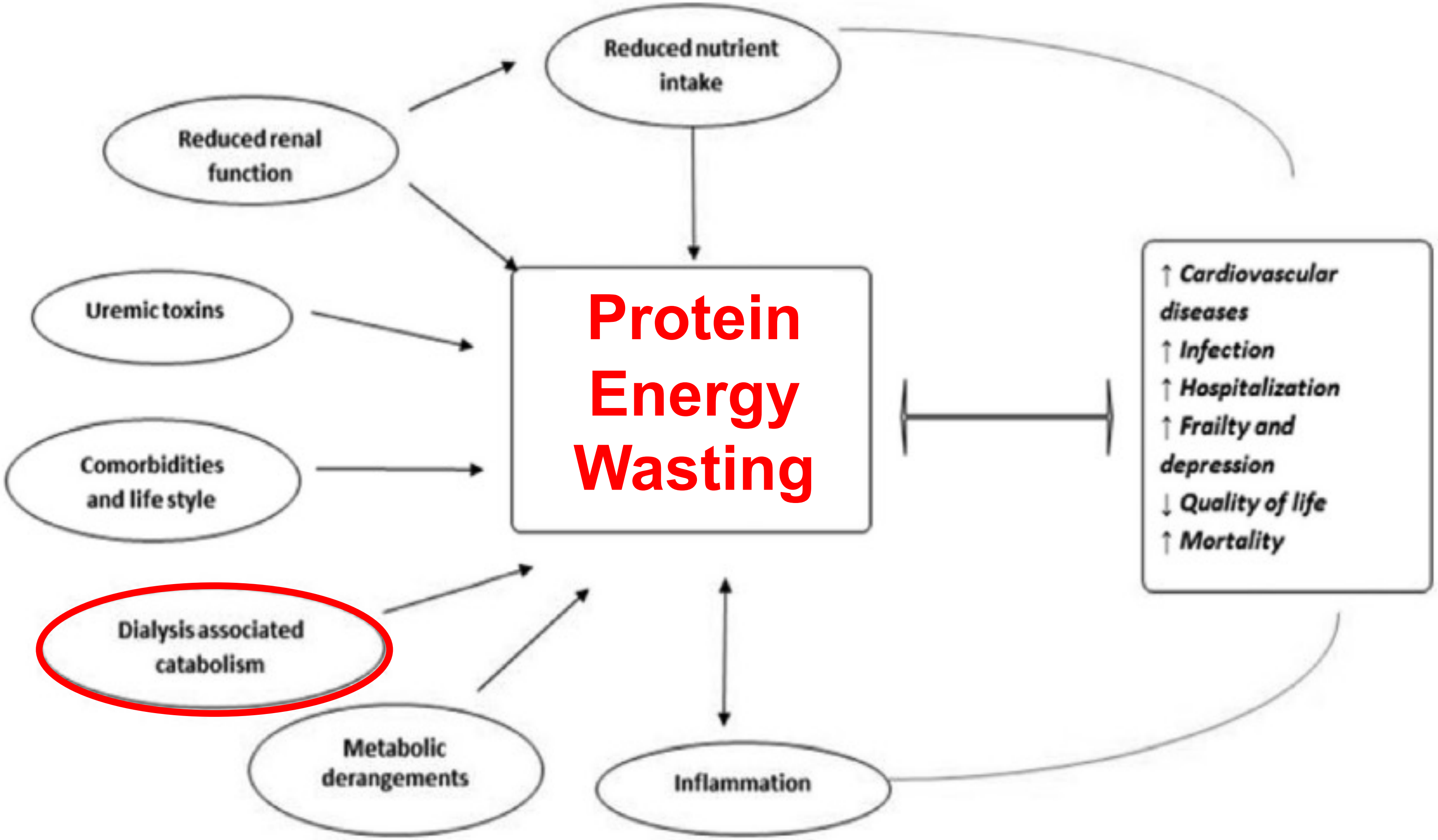
Member of guideline groups :ESPEN ICU nutrition
ESICM ICU nutrition
ESPEN Micronutrients

ESPEN Guideline

ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease

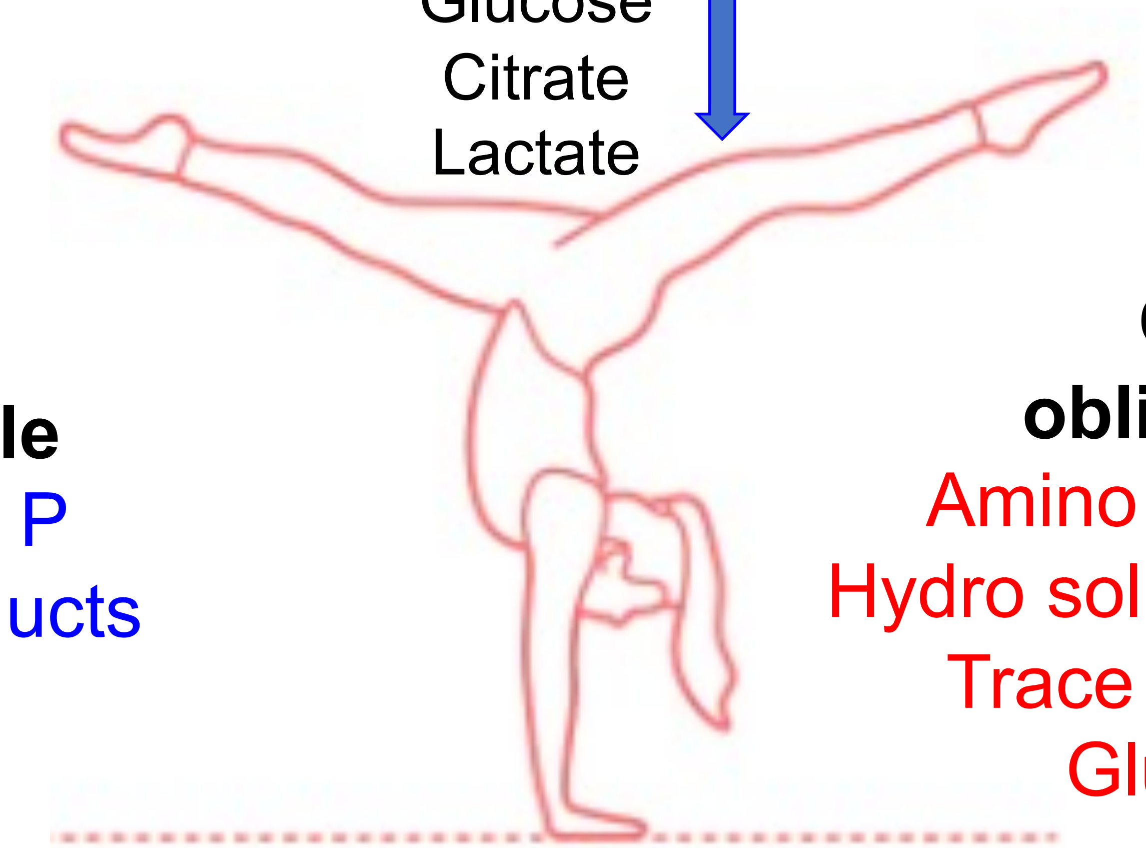
Clinical Nutrition 40 (2021) 1644–1668

Enrico Fiaccadori [a, *, 1], Alice Sabatino [a, 1], Rocco Barazzoni [b], Juan Jesus Carrero [c], Adamasco Cupisti [d], Elisabeth De Waele [e], Joop Jonckheer [f], Pierre Singer [g], Cristina Cuerda [h]



Vicious circle of malnutrition in CKD

Metabolic impact of Renal Replacement Therapy



In

Often not perceived

Glucose

Citrate

Lactate

Out

desirable

Urea, K, P

Waist products

Water

Out

obligatory

Amino acids (all)

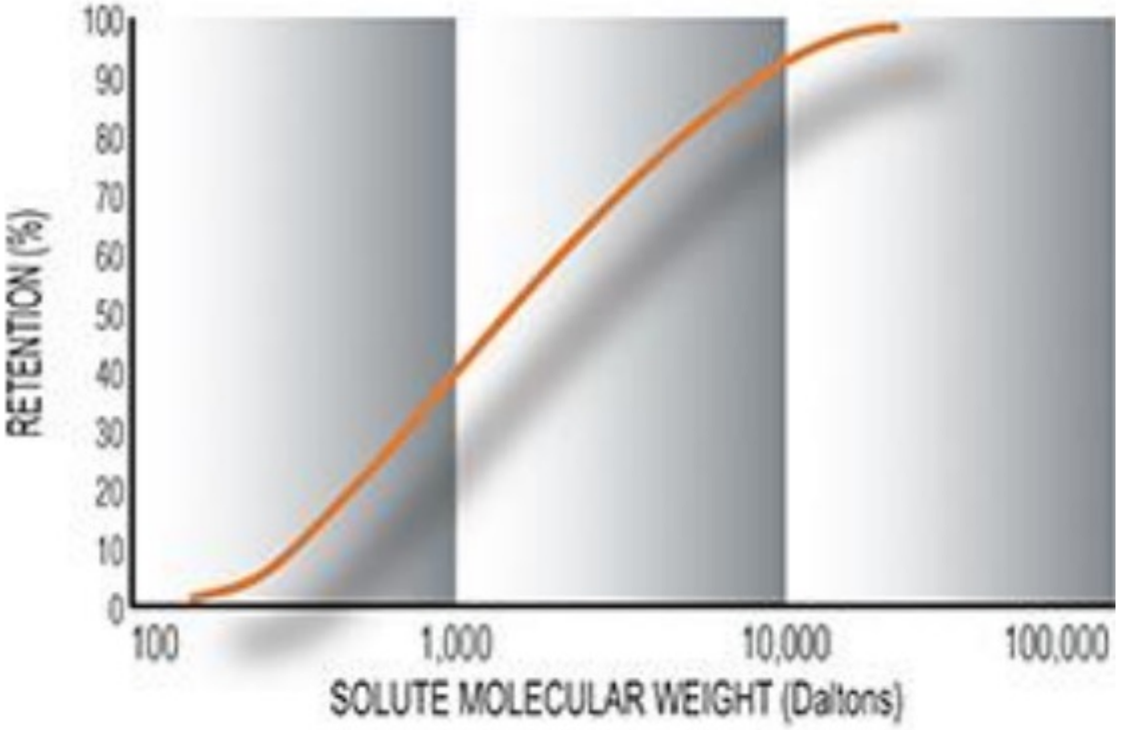
Hydro soluble vitamins

Trace elements

Glucose

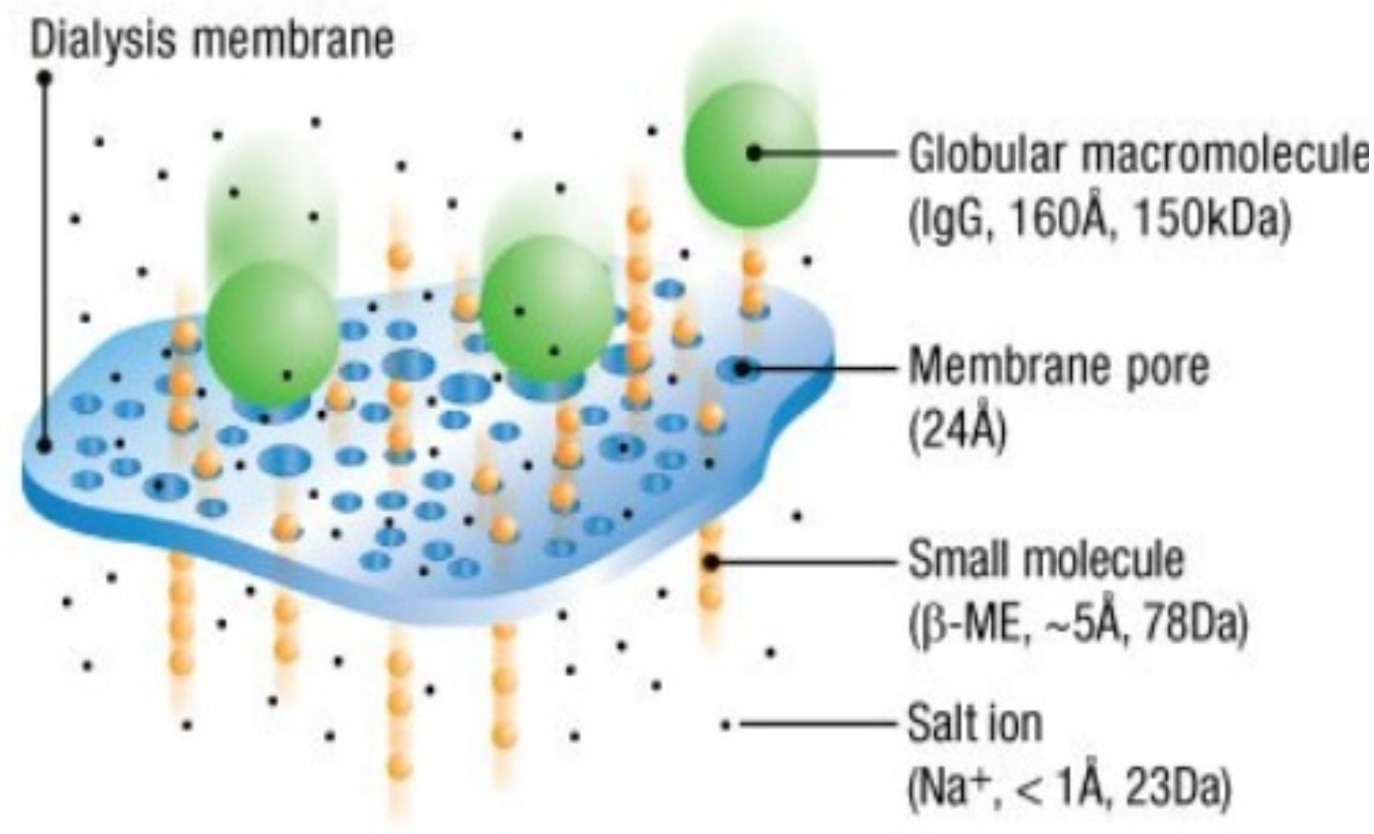
Dialysis principle and operating

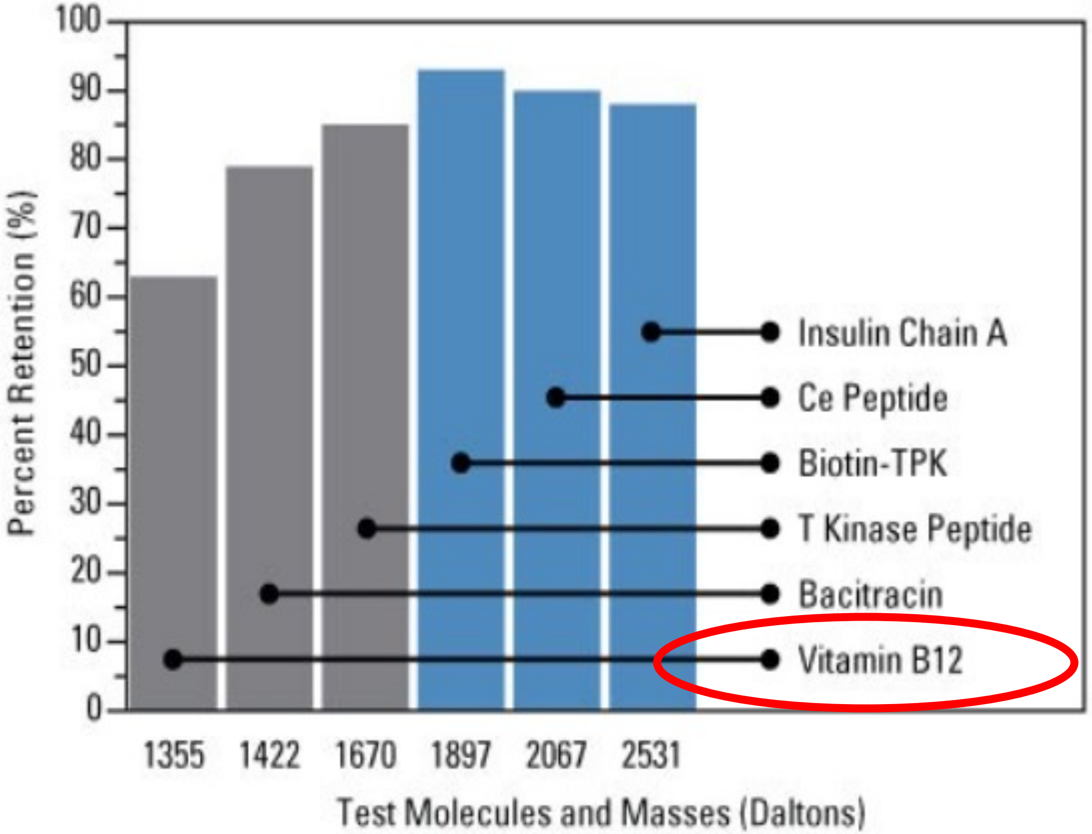
The dialysis membrane consists of a spongy matrix of crosslinked polymers
The pore rating referred to as Molecular Weight Cut Off (MWCO), is an indirect measure of the retention performance.
The membrane MWCO is determined as the **solute size** that is retained by at least 90%. However, since a solute's permeability is **also dependent upon molecular shape, degree of hydration, ionic charge and polarity**, it is recommended to select a MWCO that is half the size of the MW of the species to be retained and/or twice the size of the MW of the species intended to pass through



Molecular weight cut-off (MWCO) specifications and rates of buffer exchange with Slide-A-Lyzer Dialysis Devices and Snakeskin Dialysis Tubing

by Paul Haney et al, ThermoFisher 2013





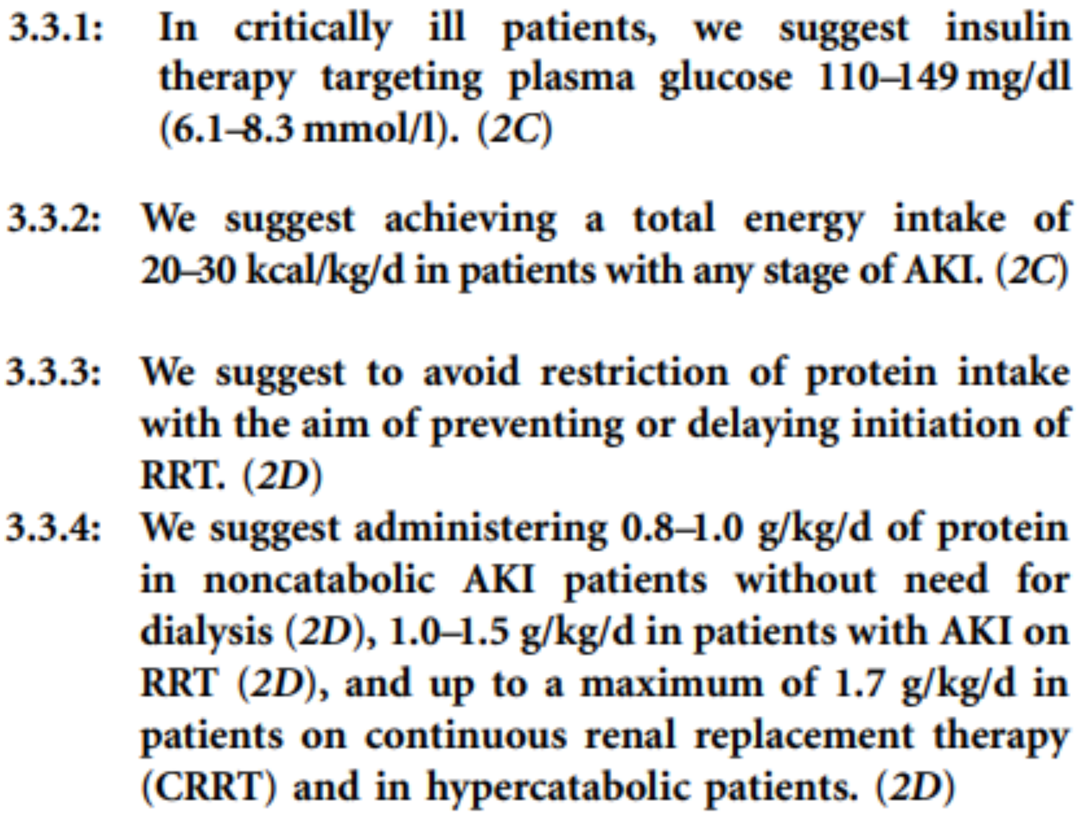
Micronutrient & other molecule sizes

Fibroblast growth factor 23		31 Da	
Urea	CH_4N_2O	60 Da	
Niacin - B3	C6H5NO2	123 Da	
Glutamine	C5H10N2O3	146 Da	
L-Carnitine	C7H15NO3	161Da	
Ascorbic acid	C6H8O6	176 Da	
Pantothenic acid	C9H17NO5	219 Da	
Retinol	C20H30O	286 Da	Lipo.
Thiamine – B1	C12H17N4OS	265 Dalton	
Biotin – B8	C10H16N2O3S	244 Dalton	
Vit.D Cholecalciferol	C27H44O	385 Da	Lipo.
Alpha-Tocopherol	C29H50O2	431 Da	Lipo.
Folic acid:	C19H19N7O6	441 Da	
Phylloquinone	C31H46O2	451 Da	Lipo.
Cobalamin B12	C63H88CoN14O14P	1355 Da	retention 63%
Myoglobin		17’200 Dalton	
Albumin		68’500 Dalton	

KDIGO Clinical Practice Guideline for Acute Kidney Injury

KDIGO Clinical Practice Guideline

Chapter 3.3:



3.3.1: In critically ill patients, we suggest insulin therapy targeting plasma glucose 110–149 mg/dl (6.1–8.3 mmol/l). (*2C*)

3.3.2: We suggest achieving a total energy intake of 20–30 kcal/kg/d in patients with any stage of AKI. (*2C*)

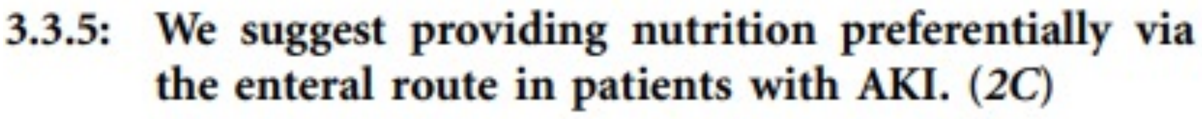
3.3.3: We suggest to avoid restriction of protein intake with the aim of preventing or delaying initiation of RRT. (*2D*)

3.3.4: We suggest administering 0.8–1.0 g/kg/d of protein in noncatabolic AKI patients without need for dialysis (*2D*), 1.0–1.5 g/kg/d in patients with AKI on RRT (*2D*), and up to a maximum of 1.7 g/kg/d in patients on continuous renal replacement therapy (CRRT) and in hypercatabolic patients. (*2D*)

Nutritional protein administration should not be restricted as a means to attenuate the rise in BUN associated with declining GFR.

Due to their continuous nature and the high filtration rates, **CRRT** techniques can better control azotemia and fluid overload associated with nutritional support but may also **result in additional losses of water-soluble, low-molecular weight substances, including nutrients**. Normalized protein catabolic rates of 1.4 to 1.8 g/kg/d have been reported in patients with AKI receiving CRRT.

In CRRT, about 0.2 g amino acids are lost per liter of filtrate, amounting to a total daily loss of 10–15 g amino acids. In addition, 5–10 g of protein are lost per day, depending on the type of therapy and dialyzer membrane. Similar amounts of protein and amino acids are typically lost by peritoneal dialysis (PD). Nutritional support should account for the losses related to CRRT, including PD, by providing a maximum of 1.7 g amino acids/kg/d.

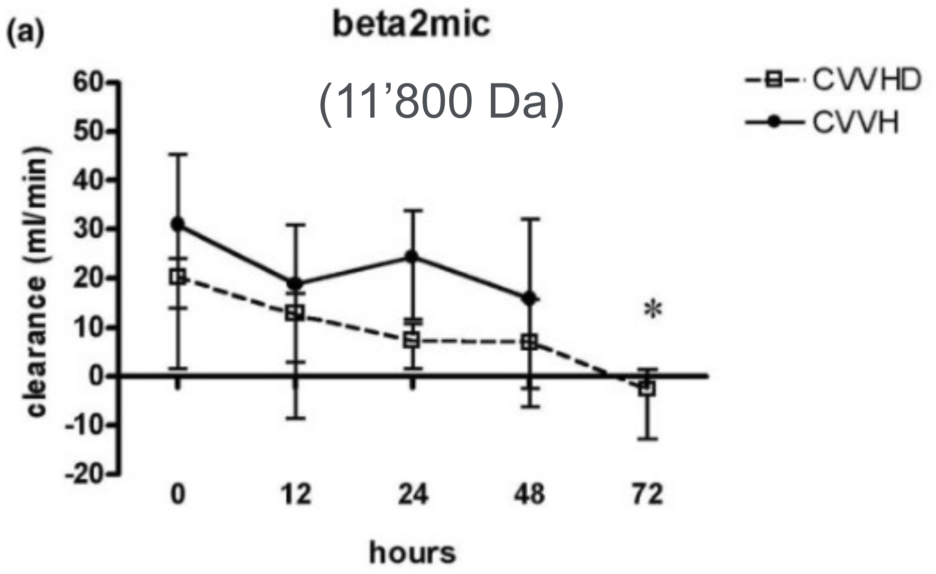


3.3.5: We suggest providing nutrition preferentially via the enteral route in patients with AKI. (*2C*)

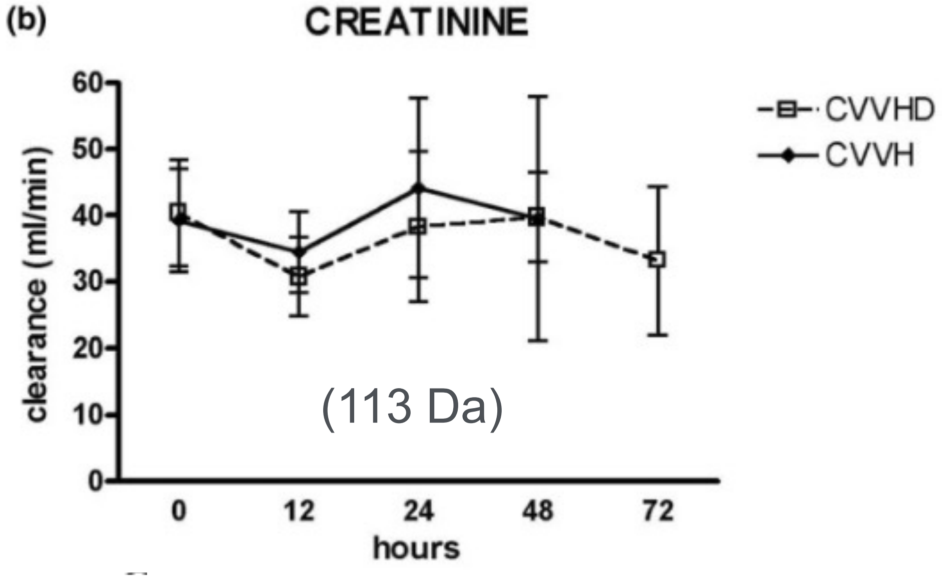
Solute removal during continuous renal replacement therapy in critically ill patients: convection versus diffusion

Ricci & Ronco, Crit Care. 2006; 10(2): R67.

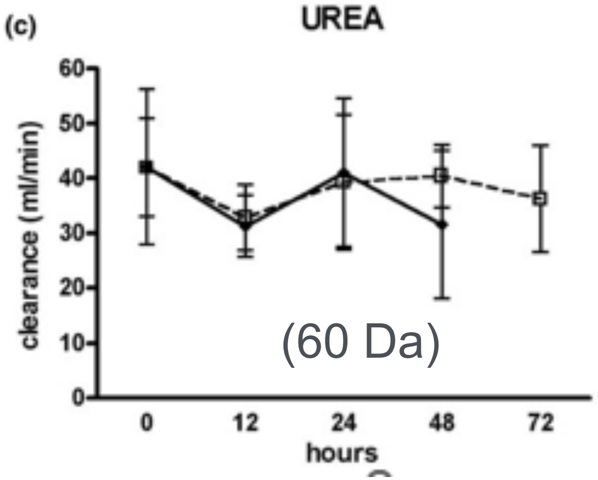
Behaviour of (a) β2 microglobulin (beta2mic), (b) creatinine and (c) urea clearance over time for continuous veno-venous hemofiltration (CVVH) and continuous veno-venous dialysis (CVVHD). Beta2mic removal decreased significantly with respect to baseline during CVVHD at T4 (72 hours).



clearance



During CRRT, many variables may affect the effective delivery of treatment dose: the molecular weight of different solutes is certainly an important aspect



Removal of large middle molecules via haemodialysis with medium cut-off membranes at lower blood flow rates: an observational prospective study

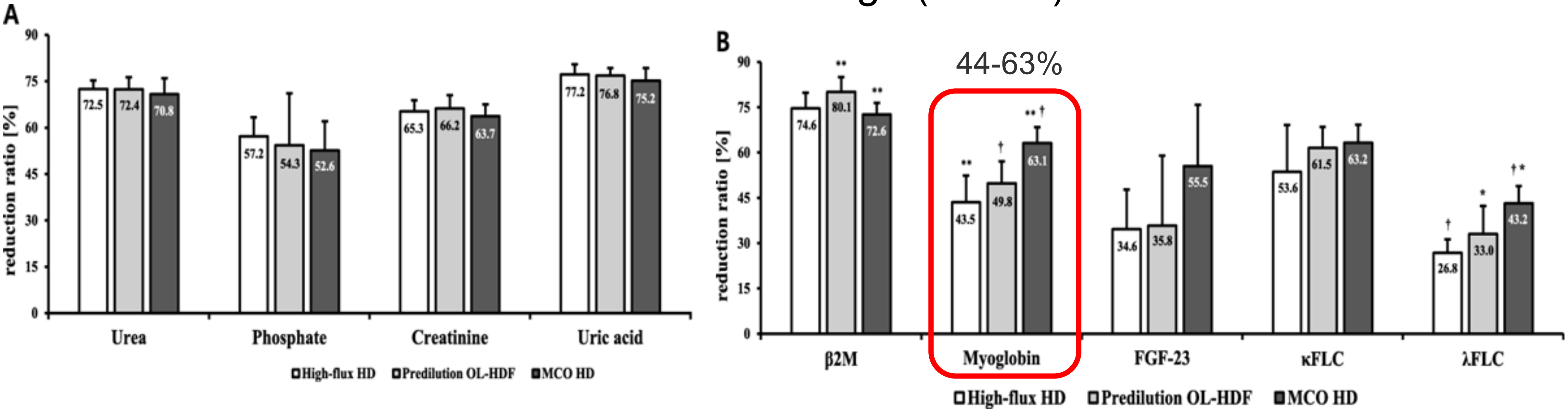
Tae Hoon Kim, et al BMC Nephrology 2020; 21:2

Treatment efficacy assessed by calculating the reduction ratio (RR) for β2-microglobulin (β2M), myoglobin, κ and λ free light chains (FLCs), and fibroblast growth factor (FGF)-23 and measuring clearance for FLCs.

Results: All 3 treatments showed comparable RRs for urea, phosphate, creatinine, and uric acid.

Reduction ratio (%) for the various uraemic toxins according to treatment modalities.

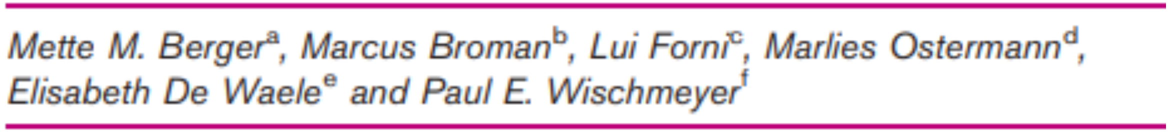
a Small water-soluble molecules. b Large (middle) molecules.

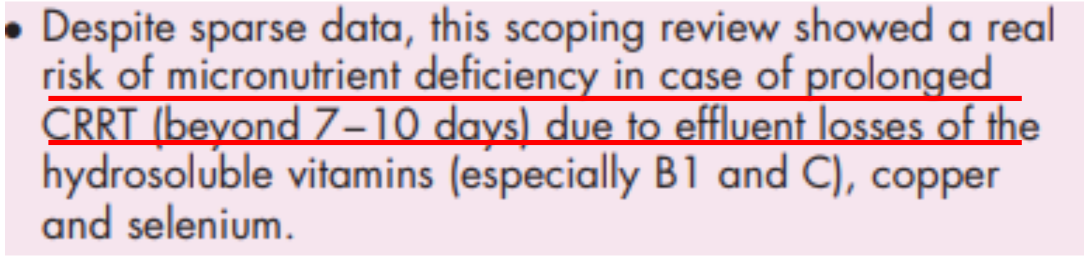


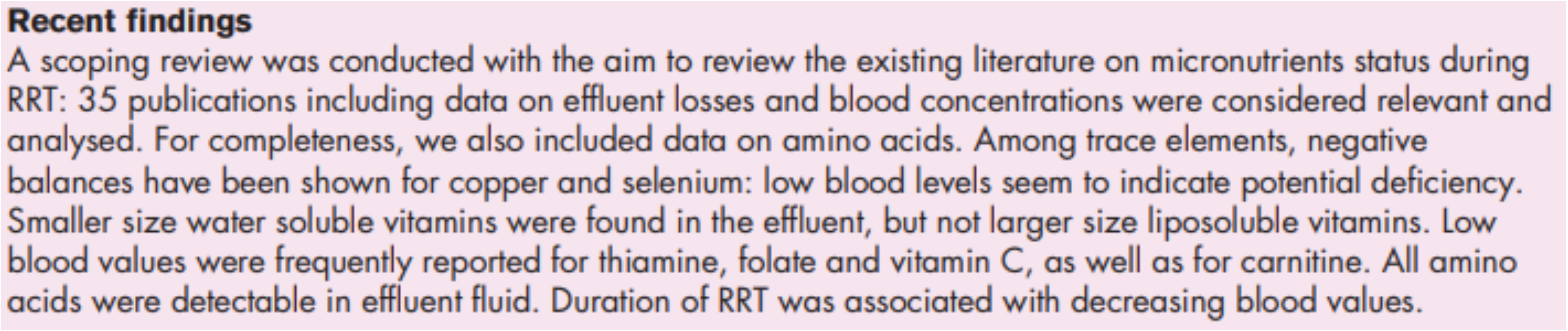
44-63%


Nutrients and micronutrients at risk during renal replacement therapy: a scoping review

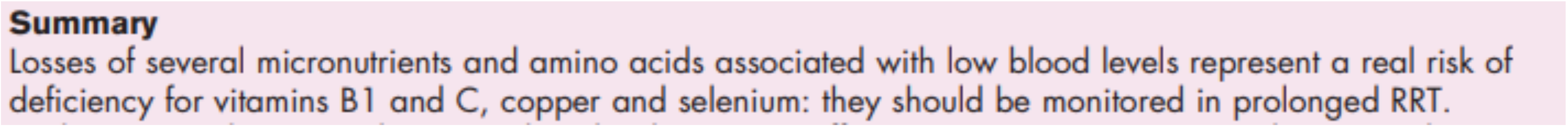
Curr Opin Crit Care 2021, 27:367–377


Mette M. Berger[a], Marcus Broman[b], Lui Forni[c], Marlies Ostermann[d], Elisabeth De Waele[e] and Paul E. Wischmeyer[f]


- Despite sparse data, this scoping review showed a real risk of micronutrient deficiency in case of prolonged CRRT (beyond 7–10 days) due to effluent losses of the hydrosoluble vitamins (especially B1 and C), copper and selenium.


Recent findings

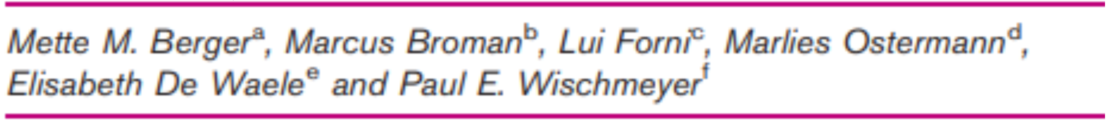
A scoping review was conducted with the aim to review the existing literature on micronutrients status during RRT: 35 publications including data on effluent losses and blood concentrations were considered relevant and analysed. For completeness, we also included data on amino acids. Among trace elements, negative balances have been shown for copper and selenium: low blood levels seem to indicate potential deficiency. Smaller size water soluble vitamins were found in the effluent, but not larger size liposoluble vitamins. Low blood values were frequently reported for thiamine, folate and vitamin C, as well as for carnitine. All amino acids were detectable in effluent fluid. Duration of RRT was associated with decreasing blood values.


Summary

Losses of several micronutrients and amino acids associated with low blood levels represent a real risk of deficiency for vitamins B1 and C, copper and selenium: they should be monitored in prolonged RRT.

Nutrients and micronutrients at risk during renal replacement therapy: a scoping review

Curr Opin Crit Care 2021, 27:367–377



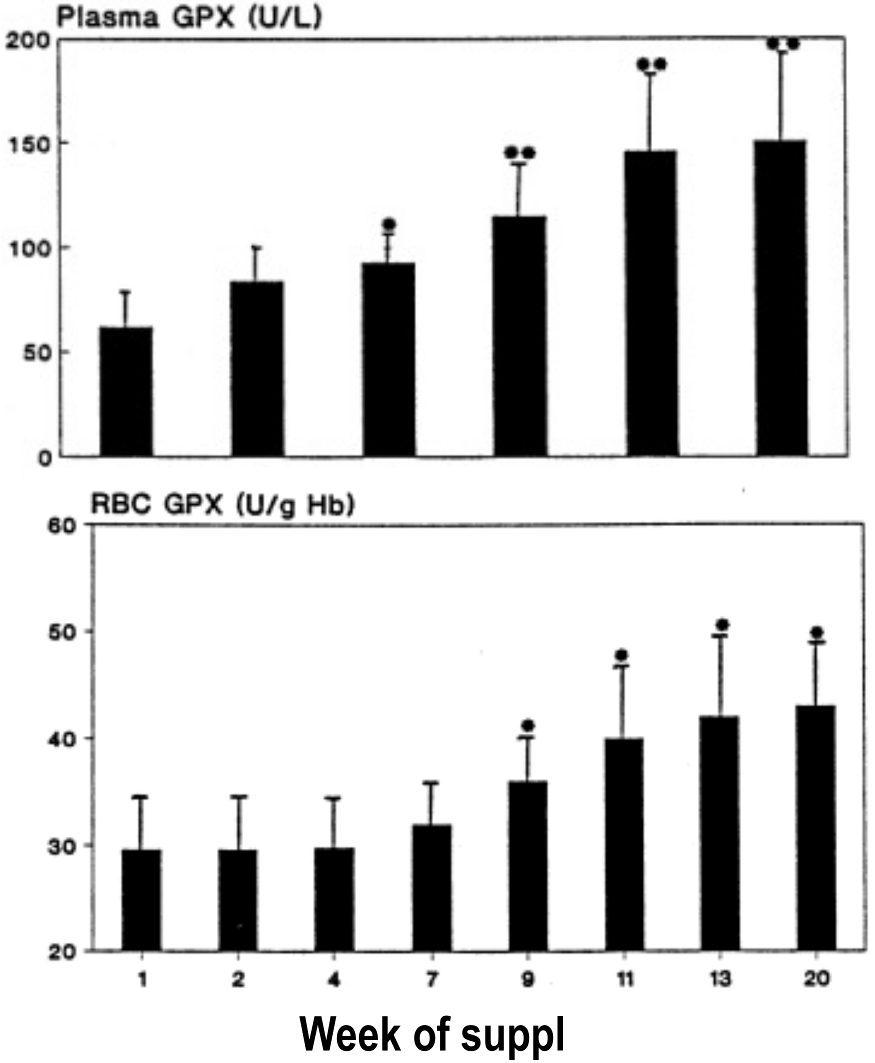
Mette M. Berger[a], Marcus Broman[b], Lui Forni[c], Marlies Ostermann[d], Elisabeth De Waele[e] and Paul E. Wischmeyer[f]

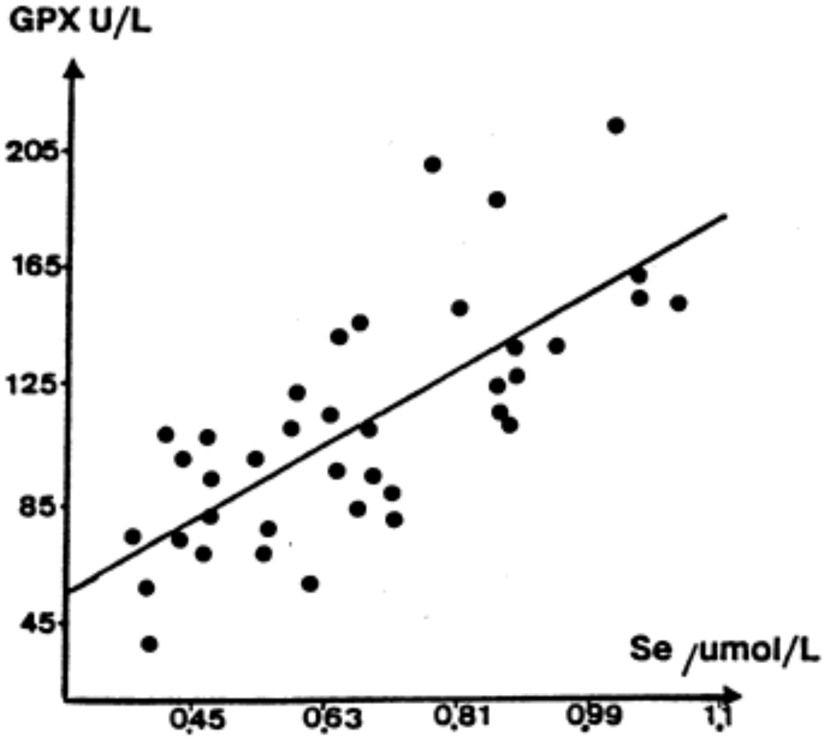
- Observation of low blood levels of some micronutrients in several studies points to depletion: monitoring blood levels of Cu, Se, B1 is encouraged from 2nd week on.
- Amino acid losses have been repeatedly shown, contributing significantly to negative nitrogen balances and to malnutrition.
- Adsorption to the filter of several micronutrients has been demonstrated and limits the results on balance studies including only effluent losses.
- Carnitine is lost in the effluents, contributing to the development of the carnitine deficiency that is observed in patients on RRT.
- The water-soluble micronutrient needs are increased. A well tolerated option is to deliver one dose of intravenous multi-trace element and multi-vitamin products per day from the second week on: prospective studies are required to determine optimal doses, and specific tailored repletion products might be required

Reversing Se & Zinc deficiency in chronic HD patients by IV supplements

Richard et al, Biol Tr Elem Res, 39:149, 1993

Pl. glutathione-peroxidase vs plasma Se





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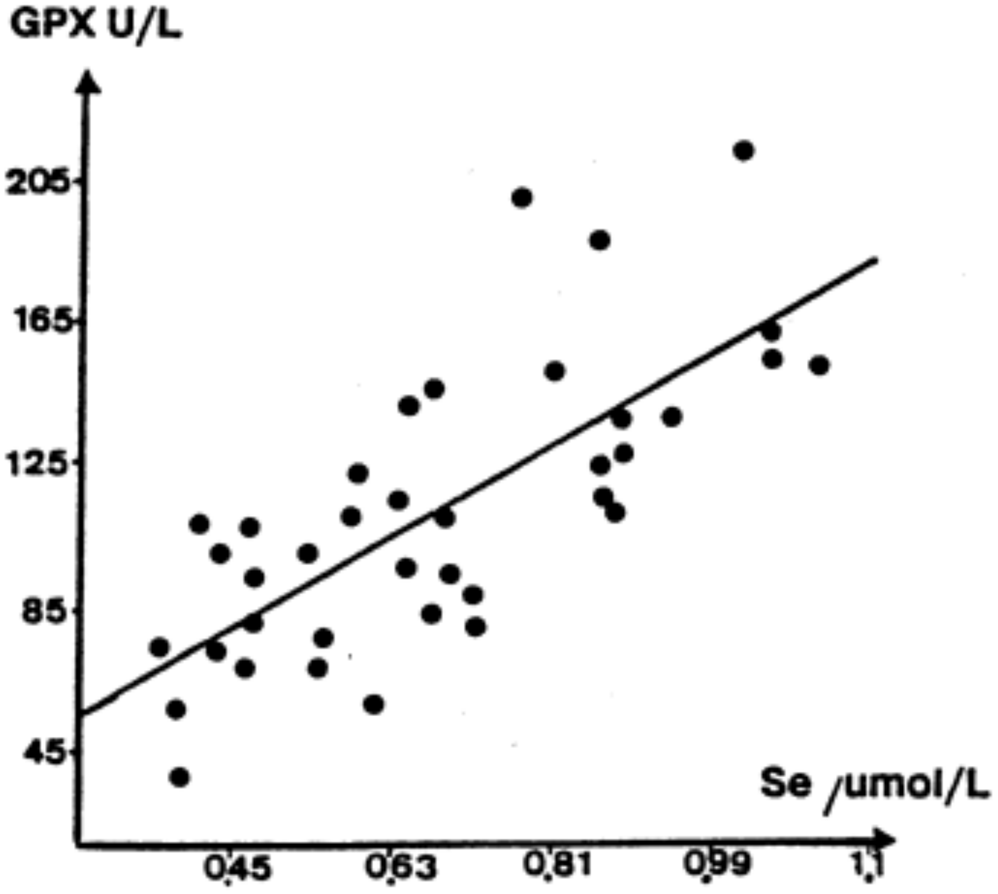
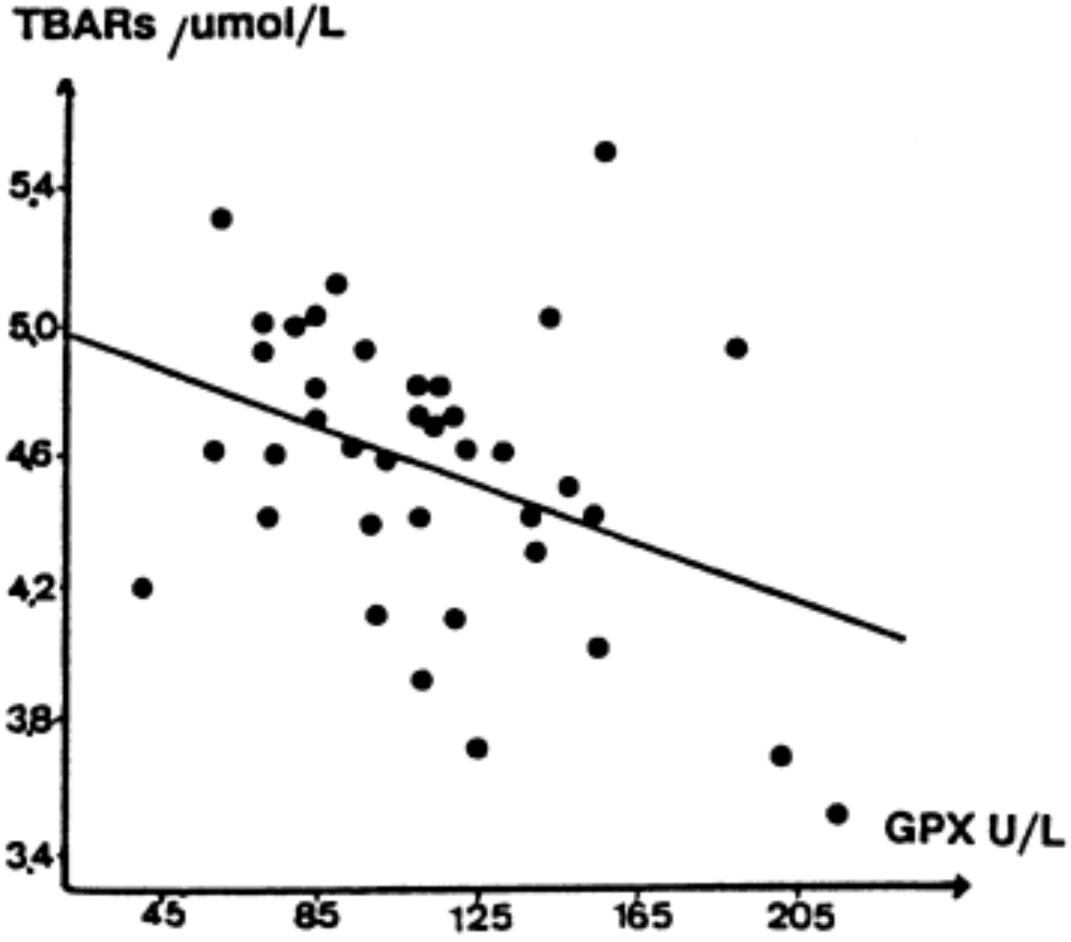
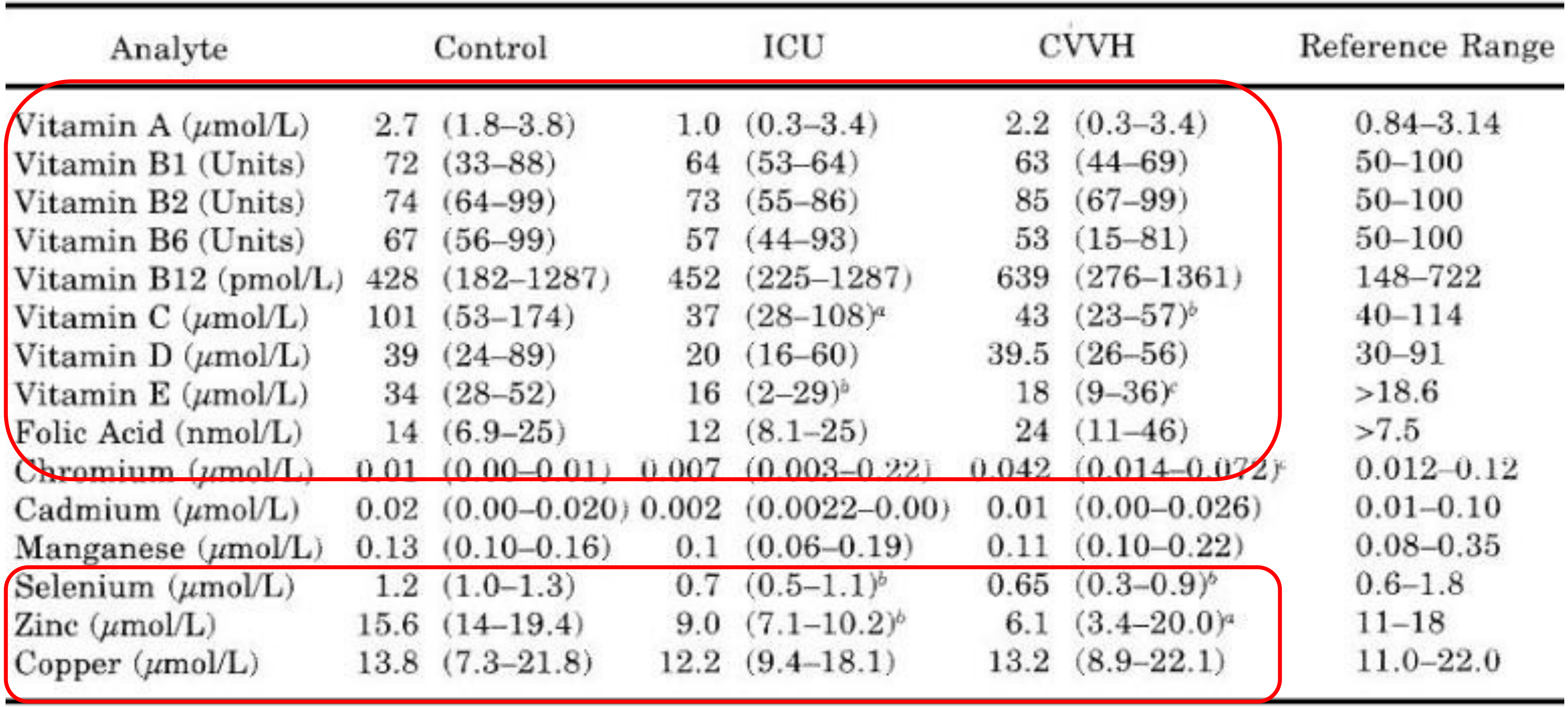




Trace element and vitamin concentrations and losses in critically ill patients treated with CVVF

Story DA et al CCM, 27:220, 1999



Analyte	Control		ICU		CVVH		Reference Range
Vitamin A (μmol/L)	2.7	(1.8–3.8)	1.0	(0.3–3.4)	2.2	(0.3–3.4)	0.84–3.14
Vitamin B1 (Units)	72	(33–88)	64	(53–64)	63	(44–69)	50–100
Vitamin B2 (Units)	74	(64–99)	73	(55–86)	85	(67–99)	50–100
Vitamin B6 (Units)	67	(56–99)	57	(44–93)	53	(15–81)	50–100
Vitamin B12 (pmol/L)	428	(182–1287)	452	(225–1287)	639	(276–1361)	148–722
Vitamin C (μmol/L)	101	(53–174)	37	(28–108)[a]	43	(23–57)[b]	40–114
Vitamin D (μmol/L)	39	(24–89)	20	(16–60)	39.5	(26–56)	30–91
Vitamin E (μmol/L)	34	(28–52)	16	(2–29)[b]	18	(9–36)[c]	>18.6
Folic Acid (nmol/L)	14	(6.9–25)	12	(8.1–25)	24	(11–46)	>7.5
Chromium (μmol/L)	0.01	(0.00–0.01)	0.007	(0.003–0.22)	0.042	(0.014–0.072)[c]	0.012–0.12
Cadmium (μmol/L)	0.02	(0.00–0.020)	0.002	(0.0022–0.00)	0.01	(0.00–0.026)	0.01–0.10
Manganese (μmol/L)	0.13	(0.10–0.16)	0.1	(0.06–0.19)	0.11	(0.10–0.22)	0.08–0.35
Selenium (μmol/L)	1.2	(1.0–1.3)	0.7	(0.5–1.1)[b]	0.65	(0.3–0.9)[b]	0.6–1.8
Zinc (μmol/L)	15.6	(14–19.4)	9.0	(7.1–10.2)[b]	6.1	(3.4–20.0)[a]	11–18
Copper (μmol/L)	13.8	(7.3–21.8)	12.2	(9.4–18.1)	13.2	(8.9–22.1)	11.0–22.0

Blood concentrations

Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients[1–3]

Am J Clin Nutr 2004; 80: 410

Mette M Berger, Alan Shenkin, Jean-Pierre Revelly, Eddie Roberts, M Christine Cayeux, Malcolm Baines, and Rene L Chioléro

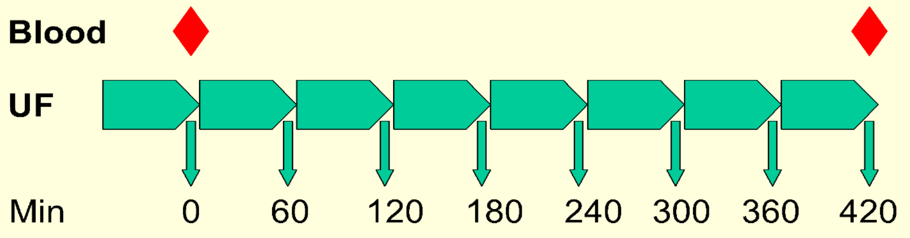
Micronutrient balances during CVVHDF - chuv

Methods

CVVHDF using alternatively commercial bicarbonate (BIC) and lactate (LAC) replacement solutions on 2 consecutive days in ICU patients with acute renal failure

Filter: AN69 (Hospal)

Fig.1. Scheme of the sampling during the 8 hrs



11 ICU patients enrolled: 19 sessions

MOF in all patients: mortality 54% (n=6)

- Replacement solutions contained no Copper, no thiamine, but small quantities of Se and significant amounts of Zinc
- Cu, Se, Zn and thiamine were detectable in the effluent of all patients
- Balances were negative for Cu, Se and thiamine (no difference BIC vs LAC), positive for Zn

Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients[1–3]

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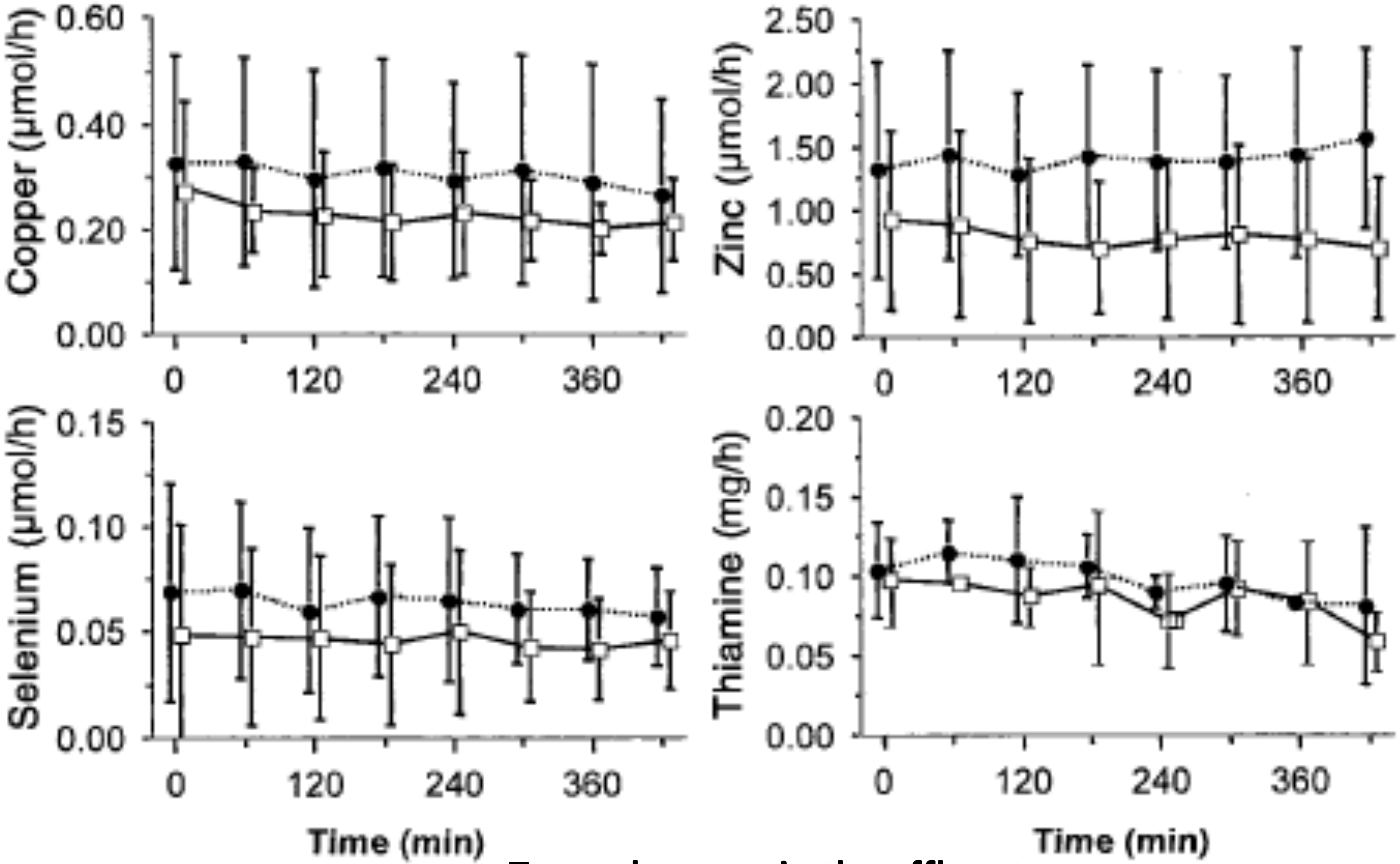


Bic

Lactate

Trace elements in the effluents

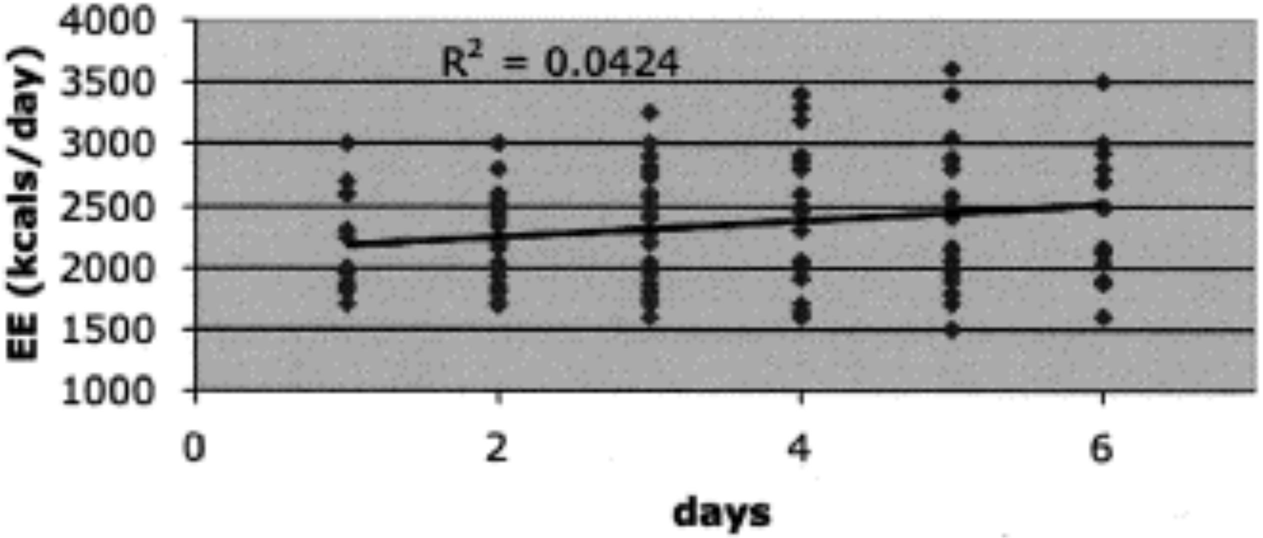
Replacement solution composition

mmol/liter	***Lactate-*** *buffered*	***Bicarbonate-*** *buffered*	***Hemosol B0***	***Kalilactasol***
Sodium	142	140	140	142
Chloride	103	110	109.5	109
Calcium	2	1.75	1.75	1,75
Potassium	0	0	0	2
Magnesium	0.75	0.5	0.5	0,75
Glucose	5.6	5.6	**0**	6.1
Lactate	44.5	3	3	40
Bicarbonate	0	34.5	32	0

PRCT : caloric and protein needs of critically ill, anuric, ventilated patients requiring CRRT

Scheinkestel et al, Nutrition 2003, 19:909

Energy expenditure with time



50 patients aged 50±17 years, APACHE 26 ± 8

EE on D2: **2153 ±380** kcal/d and increased by 56 ±4 kcal/d throughout the 6-d period to **2431 ±498** kcal/d ($P < 0.0001$)

EN or PN feeding **- isocaloric**

Previous work: 2.5 g $\cdot$kg^{-1} $\cdot$d^{-1} protein intake → plasma aa within norms

- 10 patients randomized to **2.0 g $\cdot$kg$^{-1}\cdot$d^{-1}** throughout (control).
- 40 patients (trial group) received **escalating doses of protein**:

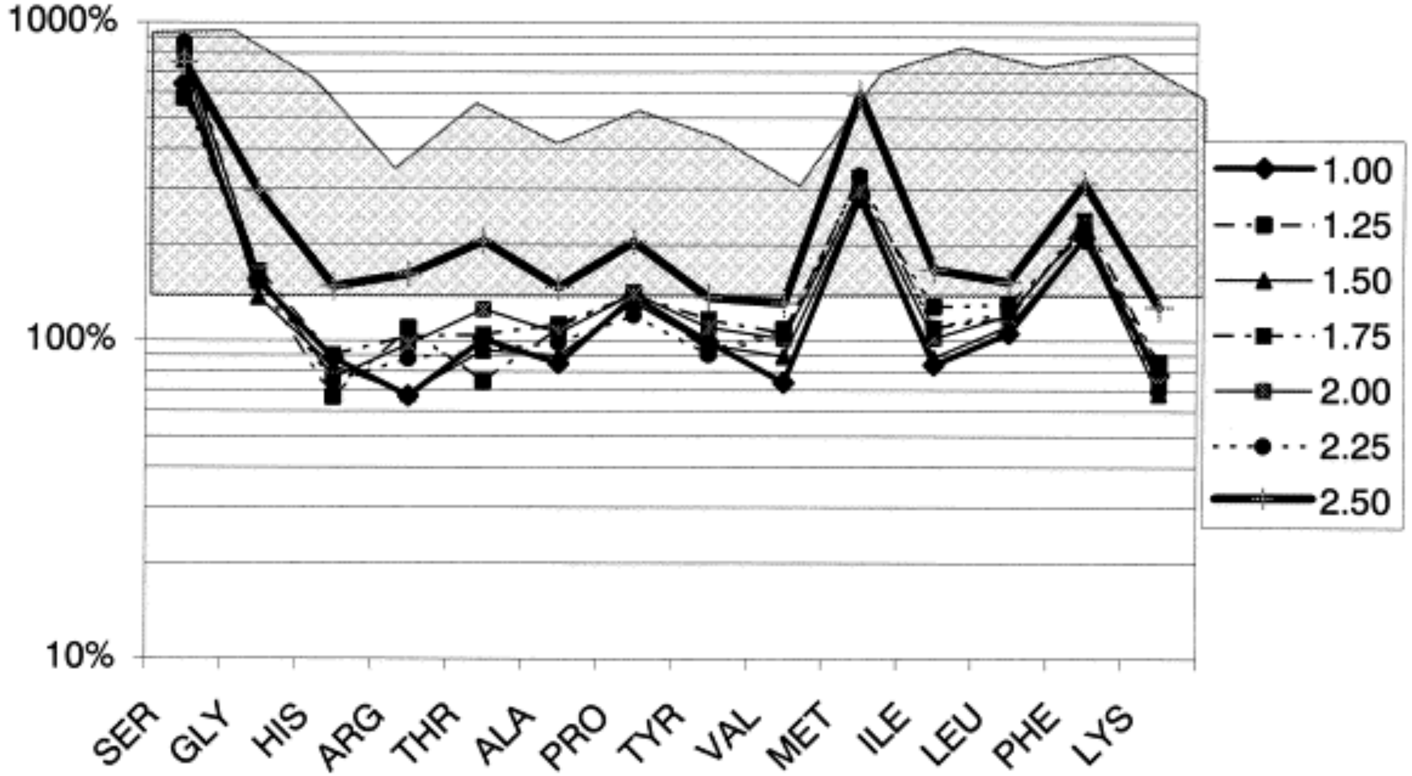
1.5 g $\cdot$kg$^{-1}\cdot$d^{-1} for 2 d, 2.0 g $\cdot$kg^{-1} $\cdot$d^{-1} for 2 d, and then 2.5 g $\cdot$kg^{-1} $\cdot$d^{-1} for the final 2 d

Alfred, Melbourne

Impact of increasing parenteral protein loads on amino acid levels and balance in critically ill anuric patients on CVVH.

Scheinkestel et al, Nutrition. 2003;19:733-40.

100% represents the lower limit of normal for each AA

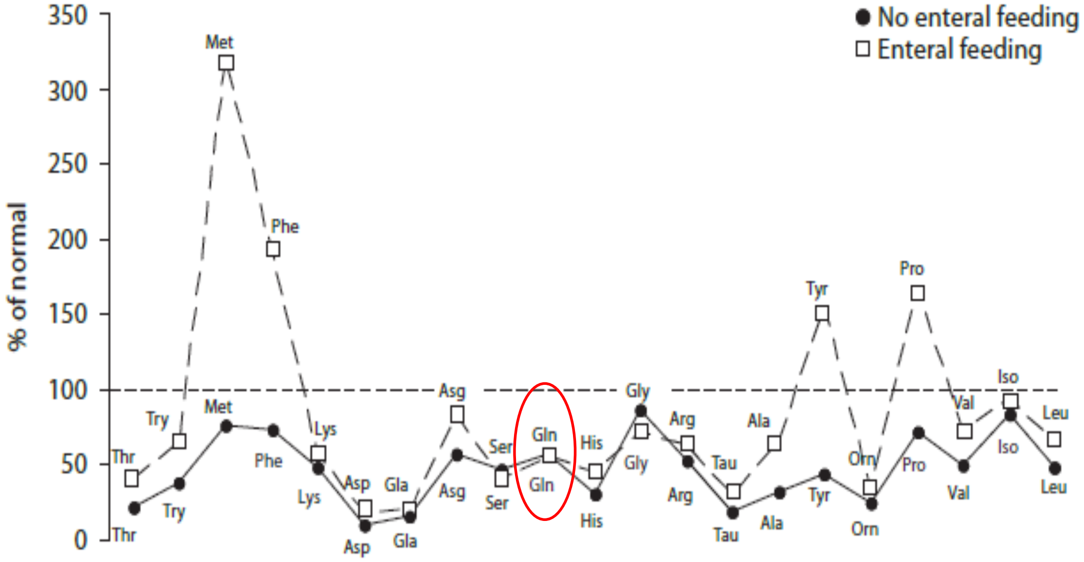


Levels of individual AAs in each feeding regimen (1 to 2.5 g·kg^{-1}·d^{-1} of protein input). The blood levels of the essential AA threonine, valine, and isoleucine, “acquired indispensable AAs” arginine and tyrosine, and non-essential alanine changed according to the amount fed. Lowest protein intakes → AA up to 33% below the lower limit of normal

Amino Acid Balance with Extended Daily Diafiltration in Acute Kidney Injury

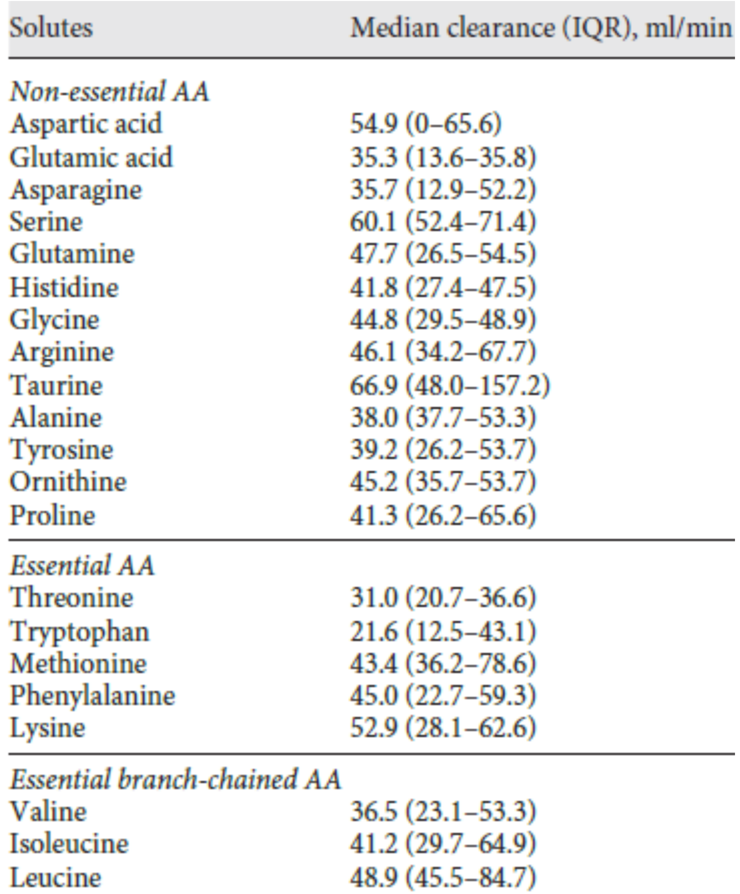
Chua HR et al Blood Purif 2012;33:292

AA balance with extended daily diafiltration (EDDF) in 7 patients



Variation in serum AA concentrations in subgroup with enteral feeding versus subgroup without.

AA loss with EDDF: much individual variability, and contributed to a strongly negative daily nitrogen balance of –10.7 (IQR –16.6 to –1.4) g/day

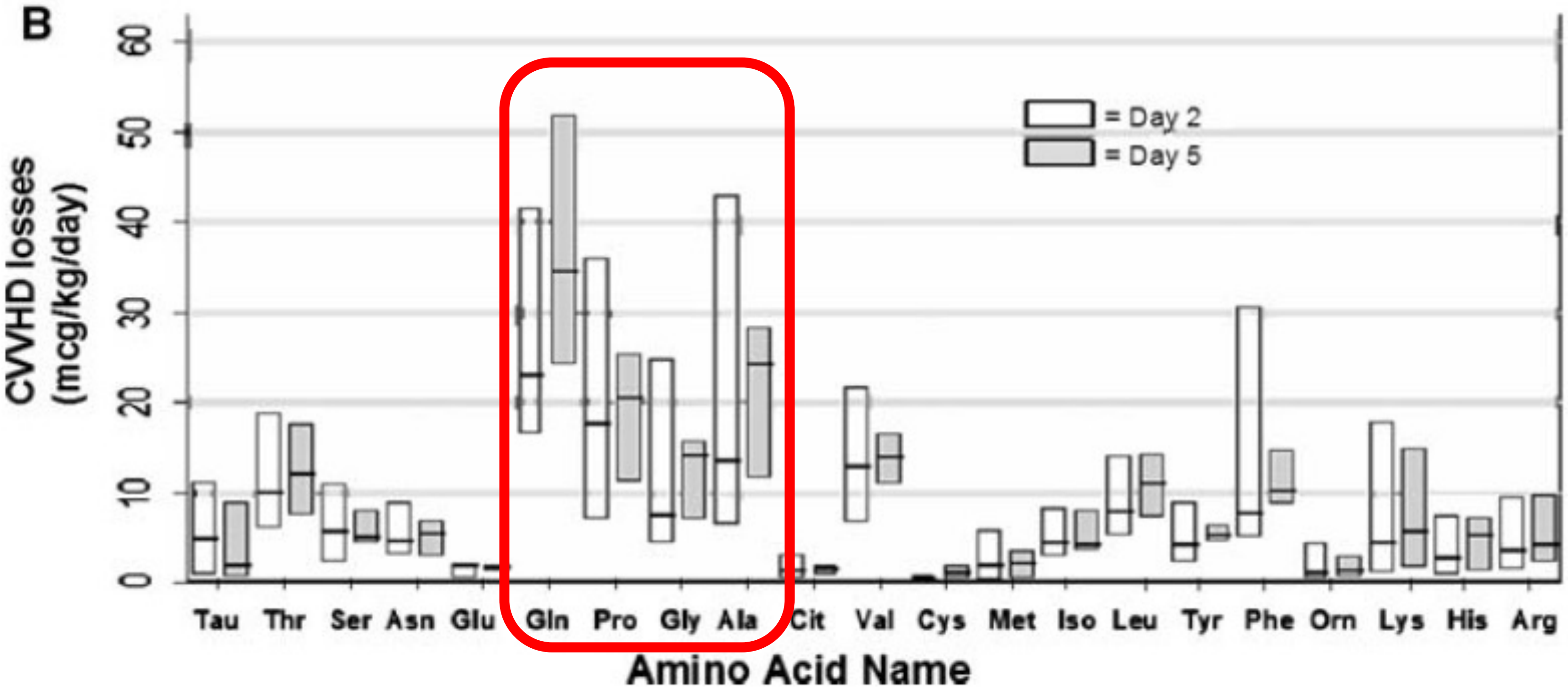


Solutes	Median clearance (IQR), ml/min
Non-essential AA	
Aspartic acid	54.9 (0–65.6)
Glutamic acid	35.3 (13.6–35.8)
Asparagine	35.7 (12.9–52.2)
Serine	60.1 (52.4–71.4)
Glutamine	47.7 (26.5–54.5)
Histidine	41.8 (27.4–47.5)
Glycine	44.8 (29.5–48.9)
Arginine	46.1 (34.2–67.7)
Taurine	66.9 (48.0–157.2)
Alanine	38.0 (37.7–53.3)
Tyrosine	39.2 (26.2–53.7)
Ornithine	45.2 (35.7–53.7)
Proline	41.3 (26.2–65.6)
Essential AA	
Threonine	31.0 (20.7–36.6)
Tryptophan	21.6 (12.5–43.1)
Methionine	43.4 (36.2–78.6)
Phenylalanine	45.0 (22.7–59.3)
Lysine	52.9 (28.1–62.6)
Essential branch-chained AA	
Valine	36.5 (23.1–53.3)
Isoleucine	41.2 (29.7–64.9)
Leucine	48.9 (45.5–84.7)

Continuous renal replacement therapy amino acid, trace metal and folate clearance in critically ill children

Zappitelli et al, Intensive Care Med, 2009; 35:698

Amino acid losses on Days 2 and 5 of CVVH

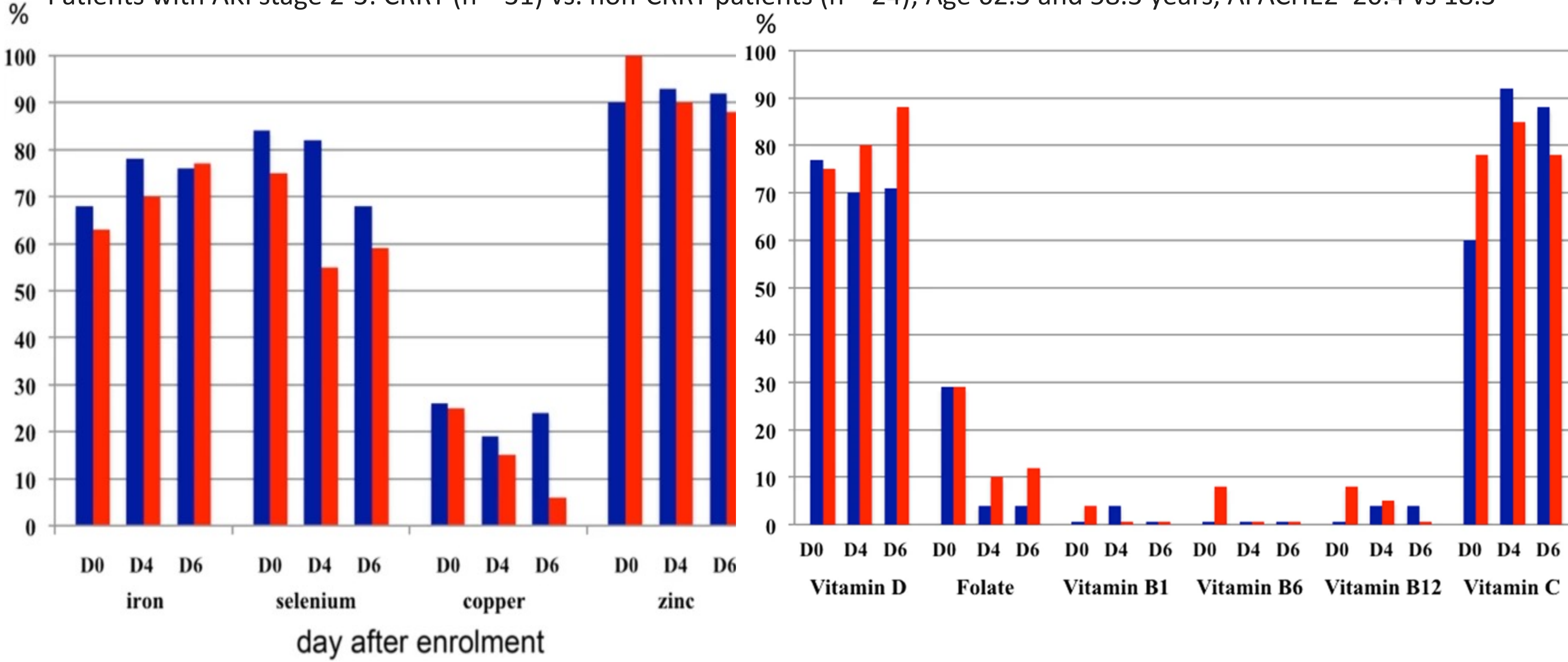


Glutamine

Micronutrients in critically ill patients with severe acute kidney injury – a prospective study

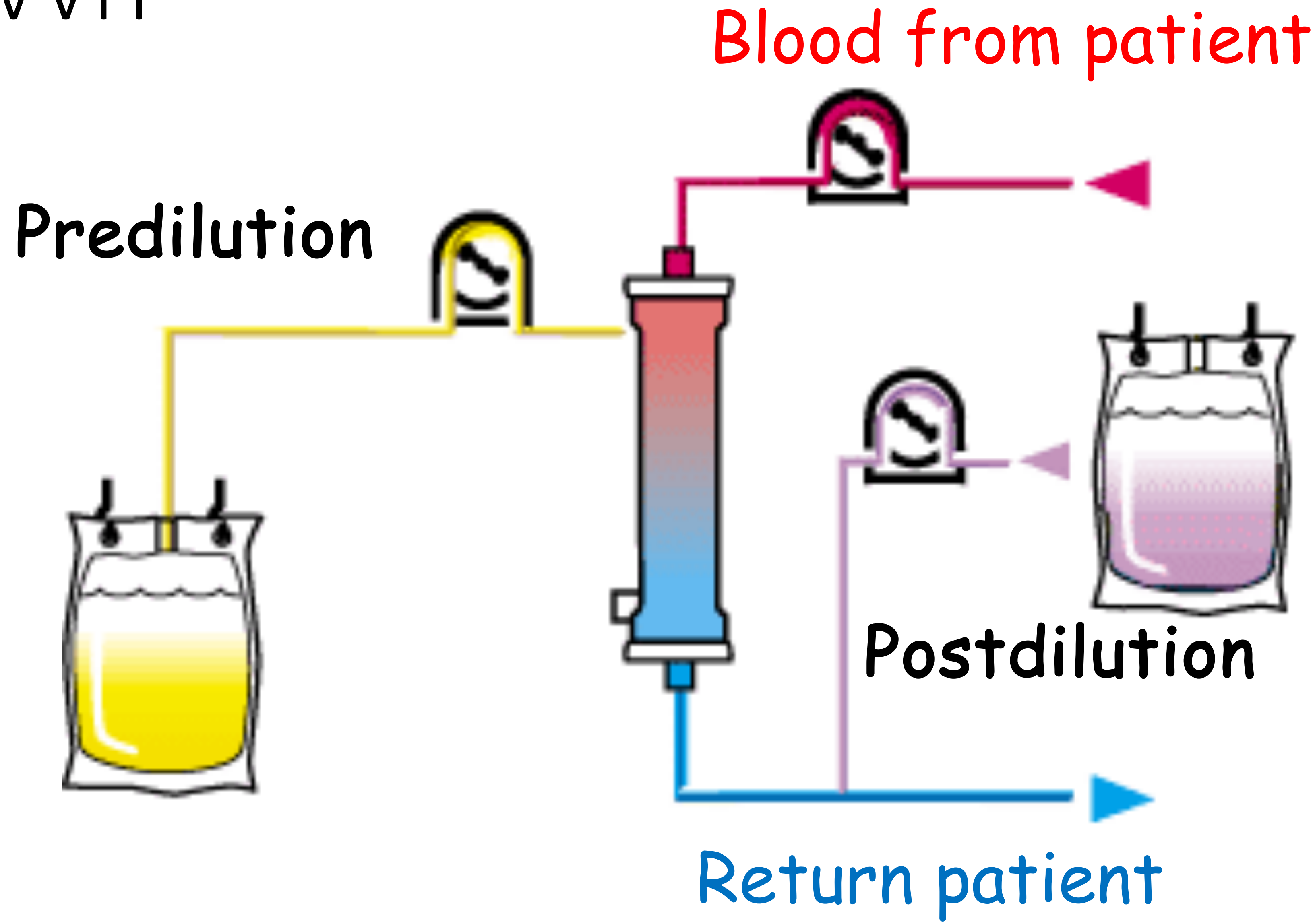
Ostermann M et al, Scientific reports, 2020; 10:1505

Patients with AKI stage 2-3: CRRT (n = 31) vs. non-CRRT patients (n = 24); Age 62.3 and 58.3 years, APACHE2 20.4 vs 18.3



Proportion of patients with plasma concentrations of trace elements and vitamins below the reference range.
CRRT patients in blue; severe AKI patients who were not treated with CRRT in red

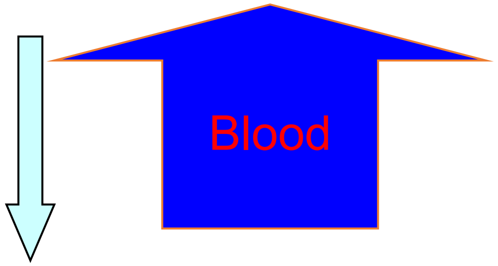
CVVH


Blood from patient
Predilution
Postdilution
Return patient

Outputs translated into renal function equivalents

	ml/min	ml/hour	L/24h
Blood flow	200-300 →	12’000-18’000 (12-18 L/H)	**288-432**
Substitution	25-50	←1’500-3’000	**36-72**

Equivalent to GFR
25-50 ml/ min



Substitution solutions: contaminated with Zn

No micronutrient adjunctions for stability reasons

Critical Care BMC

Bench-to-bedside review: Citrate for continuous renal replacement therapy, from science to practice

Heleen M Oudemans-van Straaten & Marlies Ostermann

Crit Care. 2012; 16(6): 249.

Citrate can even be used in patients with significant liver disease provided that monitoring is intensified and the dose is carefully adjusted.

The use of citrate may also be associated with less inflammation due to hypocalcemia-induced suppression of intracellular signaling at the membrane and avoidance of heparin, which may have proinflammatory properties.

Potential sources of CRRT-derived energy: citrate, glucose (in ACD) and lactate.

Respective energy equivalents: 2.48 kJ (0.59 kcal), 3.06 kJ (0.73 kcal), 1.37 kJ (0.33 kcal) per mmole.

Net energetic gain depends on the dose infused and the amount removed by CRRT.

Citrate provides about 350 kcal/day (1,466 kJ) during CVVHD and about 500 kcal/day (1,294 kJ) during postdilution CVVH.

Lactate-containing replacement fluids with citrate (CRRT at 2 L/h)→ ≅ 550 kcal (2,303 kJ)

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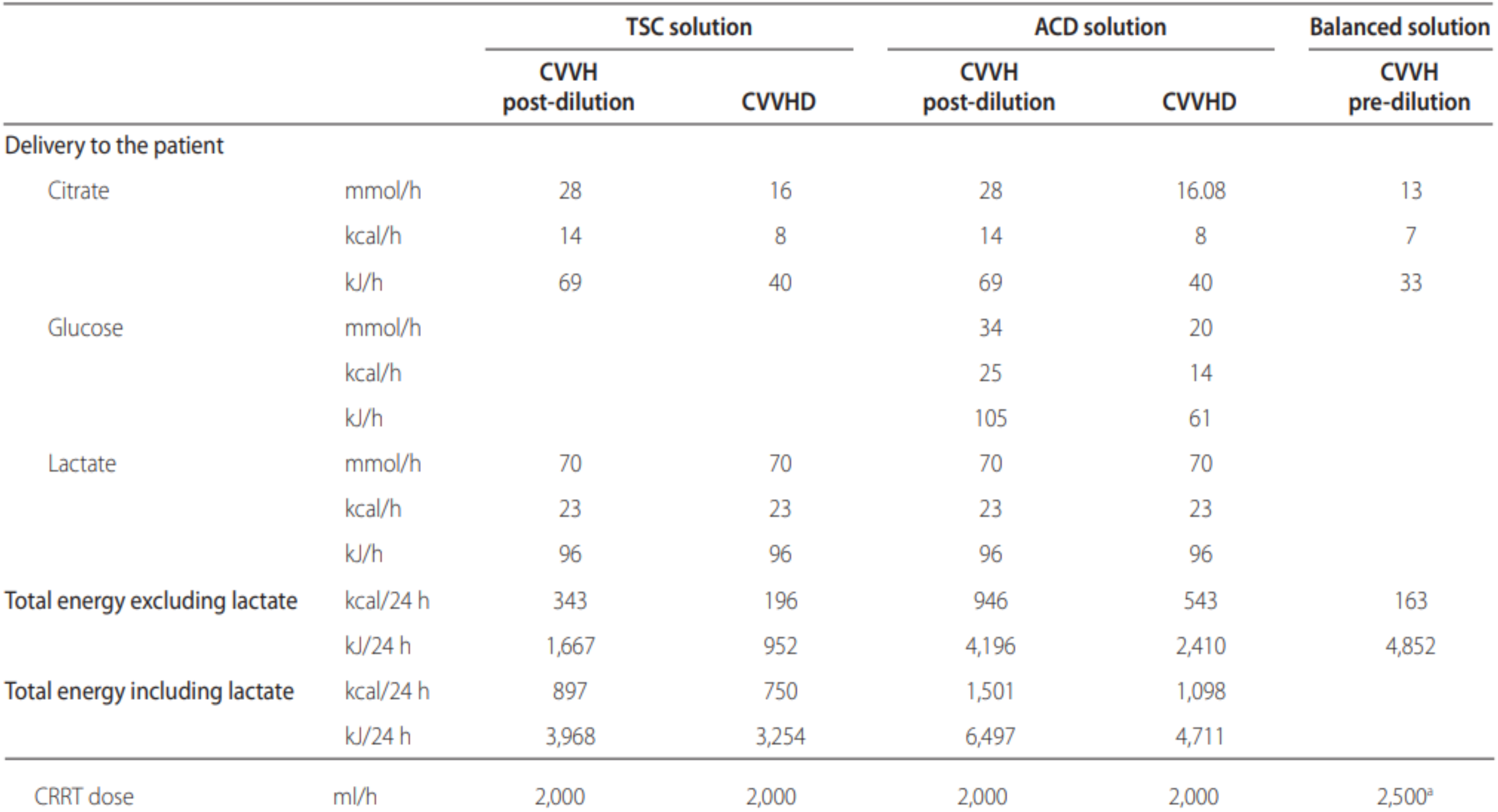


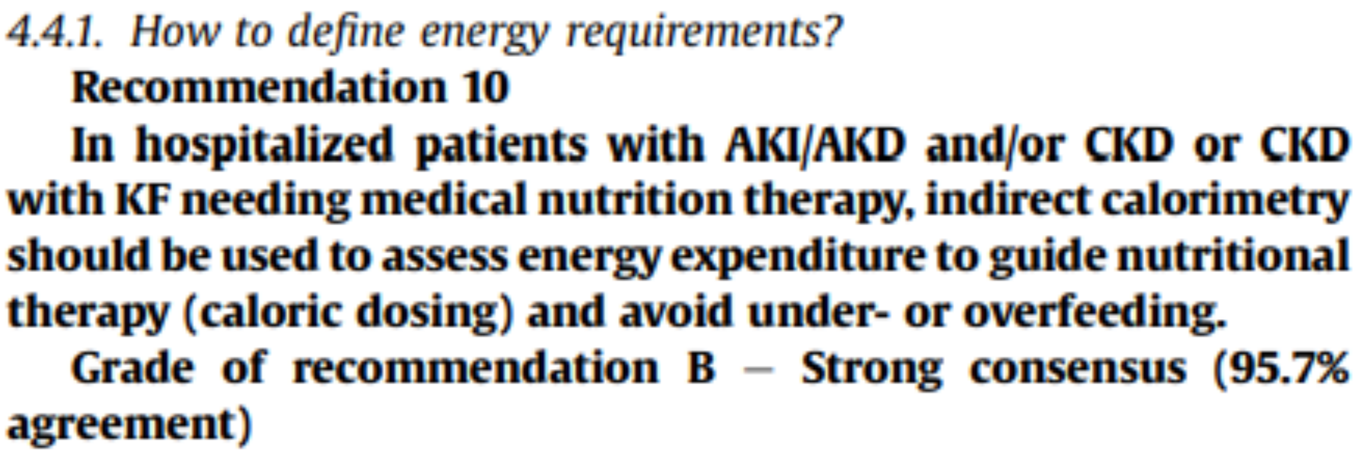
		TSC solution		ACD solution		Balanced solution
		CVVH post-dilution	CVVHD	CVVH post-dilution	CVVHD	CVVH pre-dilution
Delivery to the patient						
Citrate	mmol/h	28	16	28	16.08	13
	kcal/h	14	8	14	8	7
	kJ/h	69	40	69	40	33
Glucose	mmol/h			34	20	
	kcal/h			25	14	
	kJ/h			105	61	
Lactate	mmol/h	70	70	70	70	
	kcal/h	23	23	23	23	
	kJ/h	96	96	96	96	
Total energy excluding lactate	kcal/24 h	343	196	946	543	163
	kJ/24 h	1,667	952	4,196	2,410	4,852
Total energy including lactate	kcal/24 h	897	750	1,501	1,098	
	kJ/24 h	3,968	3,254	6,497	4,711	
CRRT dose	ml/h	2,000	2,000	2,000	2,000	2,500[a]

ESPEN Guideline

ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease

Clinical Nutrition 40 (2021) 1644–1668

Enrico Fiaccadori [a, *, 1], Alice Sabatino [a, 1], Rocco Barazzoni [b], Juan Jesus Carrero [c], Adamasco Cupisti [d], Elisabeth De Waele [e], Joop Jonckheer [f], Pierre Singer [g], Cristina Cuerda [h]



4.4.1. How to define energy requirements?

Recommendation 10

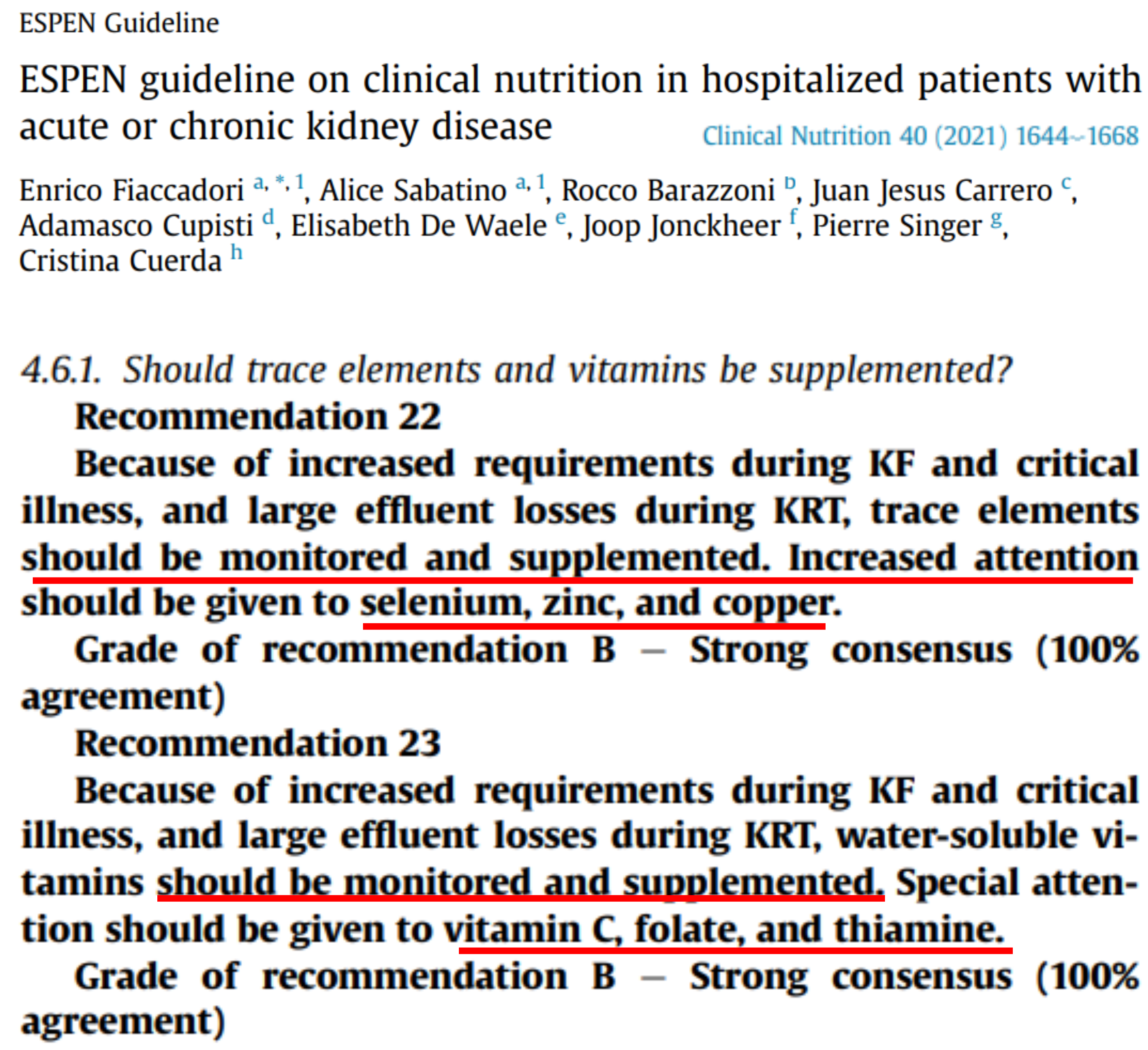
In hospitalized patients with AKI/AKD and/or CKD or CKD with KF needing medical nutrition therapy, indirect calorimetry should be used to assess energy expenditure to guide nutritional therapy (caloric dosing) and avoid under- or overfeeding.

Grade of recommendation B – Strong consensus (95.7% agreement)

Use body composition
- BIA

Past guidelines on ICU patients with AKI have recommended 20-0 kcal/kg/d of non-protein calories, or 20e30 kcal/ kg/d total calories . These indications reasonably include the mean energy needs at the population level and can be used as a general starting point when indirect calorimetry is not available.

However, in many cases, no mention if the actual, preadmission, or ideal body weight should be considered for calculations. Considering that patients with AKI frequently have fluid overload and suffer sudden fluid shifts related to KRT, it is even more difficult to define the reference body weight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4.6.1. Should trace elements and vitamins be supplemented?

Recommendation 22

Because of increased requirements during KF and critical illness, and large effluent losses during KRT, trace elements should be monitored and supplemented. Increased attention should be given to selenium, zinc, and copper.

Grade of recommendation B – Strong consensus (100% agreement)

Recommendation 23

Because of increased requirements during KF and critical illness, and large effluent losses during KRT, water-soluble vitamins should be monitored and supplemented. Special attention should be given to vitamin C, folate, and thiamine.

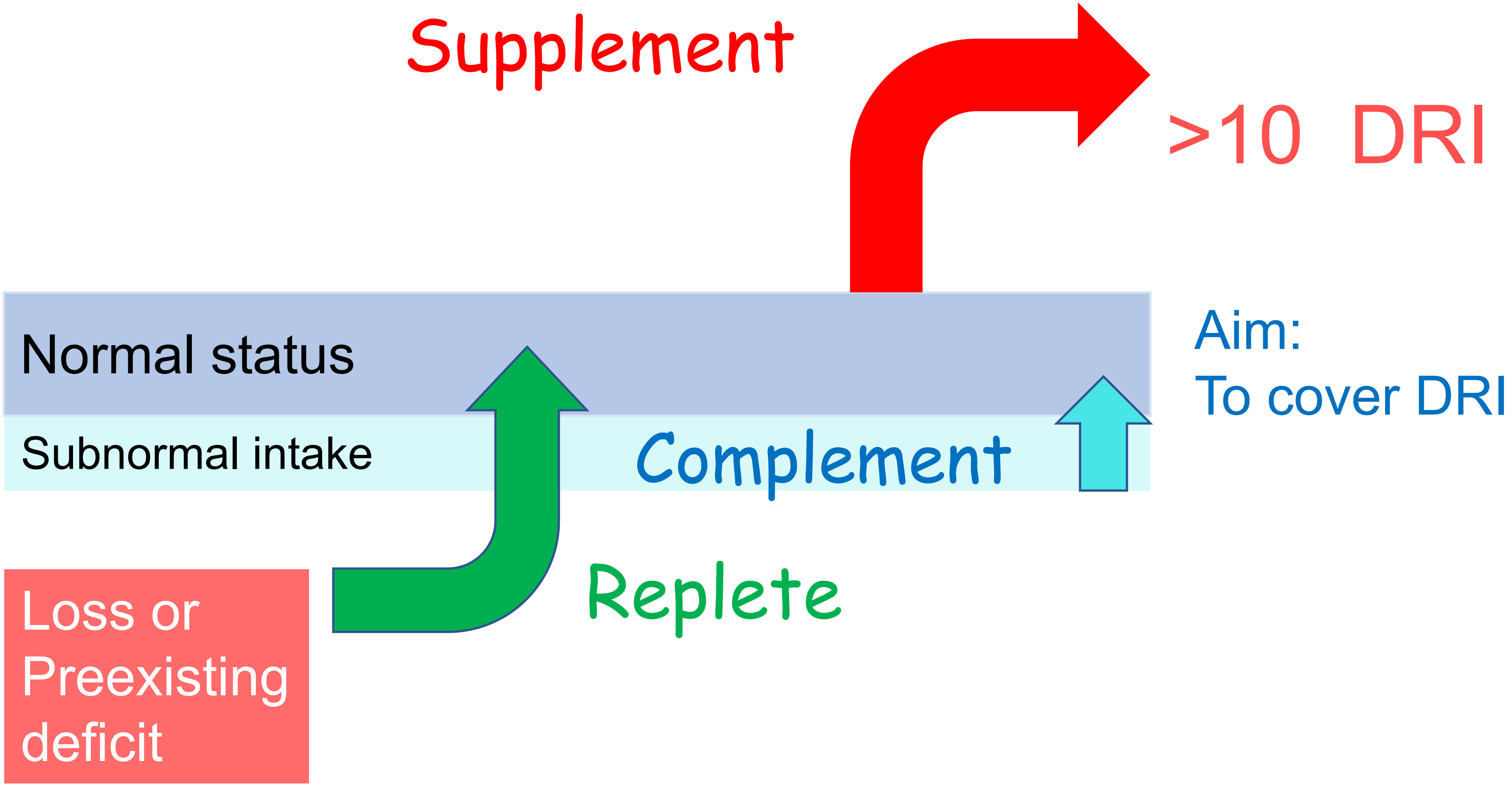
Grade of recommendation B – Strong consensus (100% agreement)

During critical illnesses, vitamins, and trace elements may impact on immunomodulation, wound healing and may have antioxidant properties.

Even though optimal dosing of micronutrients in critically ill patients is still a matter of debate, it appears quite clear that the start of KRT as CKRT in patients with AKI or AKI on CKD or CKD with KF represents an additional variable negatively affecting serum micronutrient levels

In conclusion, given the blood assay limitations and the lack of evidence of clinical advantages derived from micronutrients supplementation, supplementation of micronutrients should be guided by their serum levels and KRT losses.

Complement, Replete or Supplement?
Three different situations with different objectives



Supplement

>10 DRI

Normal status

Subnormal intake

Complement

Aim:
To cover DRI

Replete

Loss or Preexisting deficit

Haemodialysis and nutrition - Conclusion

- Our life-saving therapy has life-threatening aspects, if not addressed
- Energy balance ← intakes from citrate & lactate and losses (glucose), is significantly modified
- Specific indirect calorimetry studies are few and indicate high EE, individual monitoring and adjustment is required
- While removing excess of electrolytes and waist products, it automatically removes other small to medium size molecules: MNs and amino acids.
- Addressing protein needs: they are higher than standard ICU patients
- Preventing MN deficit? 1-2-3 times PN multi-MN products?
- Knowledge remains limited and further studies are required

Thank you !! ☺

from Lac Léman seen from Vevey Switzerland