37th Vicenza Course on AKI & CRRT

May 28-30, 2019

CRRT
Clinical complications & management

M Ostermann

Disclosures

Speaker honoraria: Alere, Fresenius, Mitsubishi Pharma

Advisory role: Gilead, Fresenius, Biomerieux

Research funding: Fresenius Medical Care, LaJolla Pharma

Risks and benefits of acute RRT

Metabolic control

Fluid removal

Clearance (toxins/drugs)

Central line insertion

Risks of anticoagulation

Loss of electrolytes

Loss of nutrients

Challenges of drug dosing

Work load

Healthcare costs

Common side effects of RRT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 22, 2009 VOL. 361 NO. 17

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*

1508 patients on CVVHDF for AKI

Side effects	Low dose CRRT	High dose CRRT
Hypophosphataemia	65.1%	54%
Hypokalaemia	23.4%	24.4%
Arrhythmia	42%	45.5%

Common side effects of RRT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 3, 2008 VOL. 359 NO. 1

Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

The VA/NIH Acute Renal Failure Trial Network*

1124 patients received RRT for AKI

Common side effects of RRT

Adverse events

Side effects	Low intensity RRT	High intensity RRT
Any adverse event	51%	49.9%

New Engl J Med 2008;359;1

Common side effects of RRT

Adverse events

Side effects	Low intensity RRT	High intensity RRT
Any adverse event	51%	49.9%
Catheter related complications	13.5%	12.3%

New Engl J Med 2008;359;1

Common side effects of RRT

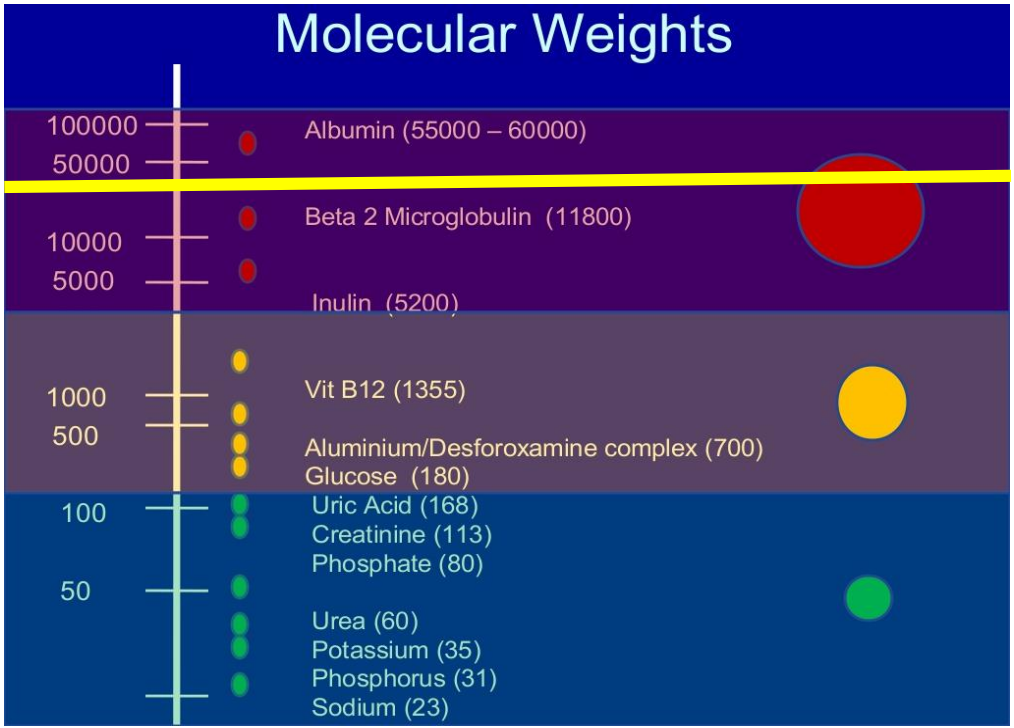
Adverse events

Side effects	Low intensity RRT	High intensity RRT
Any adverse event	51%	49.9%
Catheter related complications	13.5%	12.3%
Haemodynamic instability	51.9%	48.6%
Hypokalaemia	7.5%	4.5%
Hypophosphataemia	17.6%	10.9%

New Engl J Med 2008;359;1

Hidden side effects of RRT

Nutrient losses during RRT



Membrane cut-off 30000 – 50000 Da

Molecular weight: amino acids average 110 Da [range 75-204]
vitamins <2000 Da
trace elements <500 Da

Amino acid losses during RRT

Amino acid losses during RRT

APPLIED NUTRITIONAL INVESTIGATION

Impact of Increasing Parenteral Protein Loads on Amino Acid Levels and Balance in Critically Ill Anuric Patients on Continuous Renal Replacement Therapy

C. D. Scheinkestel, FRACP, FJFICM, F. Adams, BSc, L. Mahony, BSc, M. Bailey, BSc, MSc, A. R. Davies, FRACP, FJFICM, I. Nyulasi, MSc, and D. V. Tuxen, FRACP, FJFICM, MD

11 critically ill ventilated anuric patients on CRRT

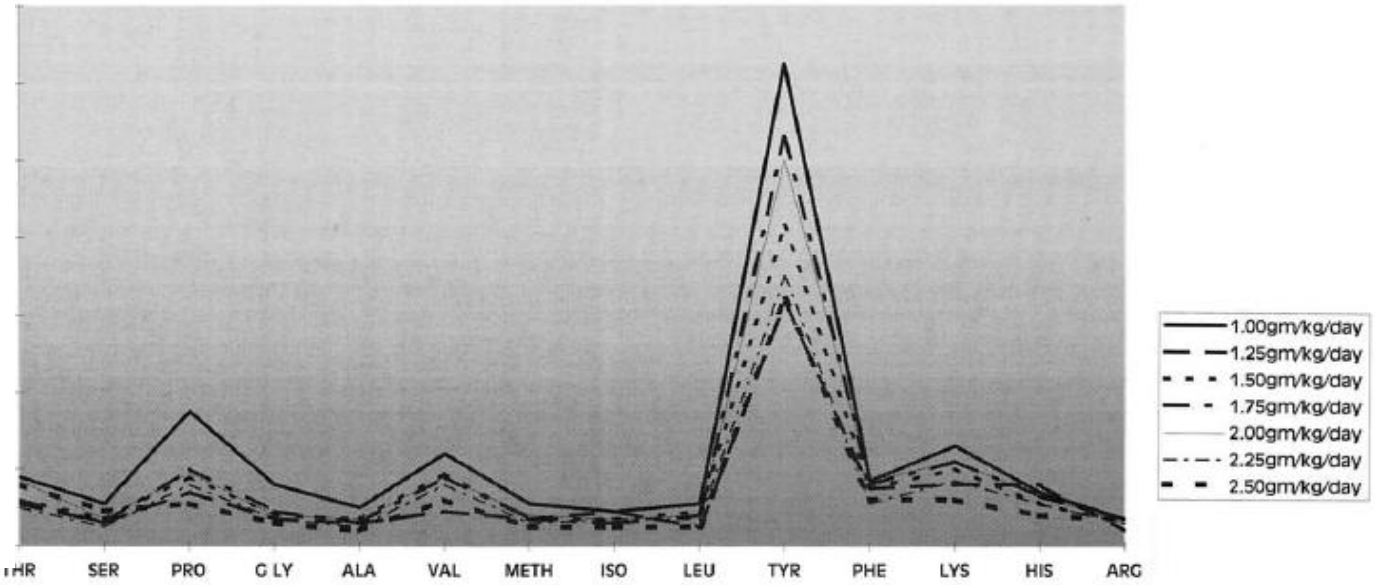
Continuous infusion of TPN with constant caloric but increasing protein concentration (by increments of 0.25g/kg/day)

CRRT prescription: dialysis based, blood flow 100-175ml/min
dialysis flow 2L/h

Nutrition 2003;19:733-740

Amino acid losses during RRT

% of infused AA lost in effluent

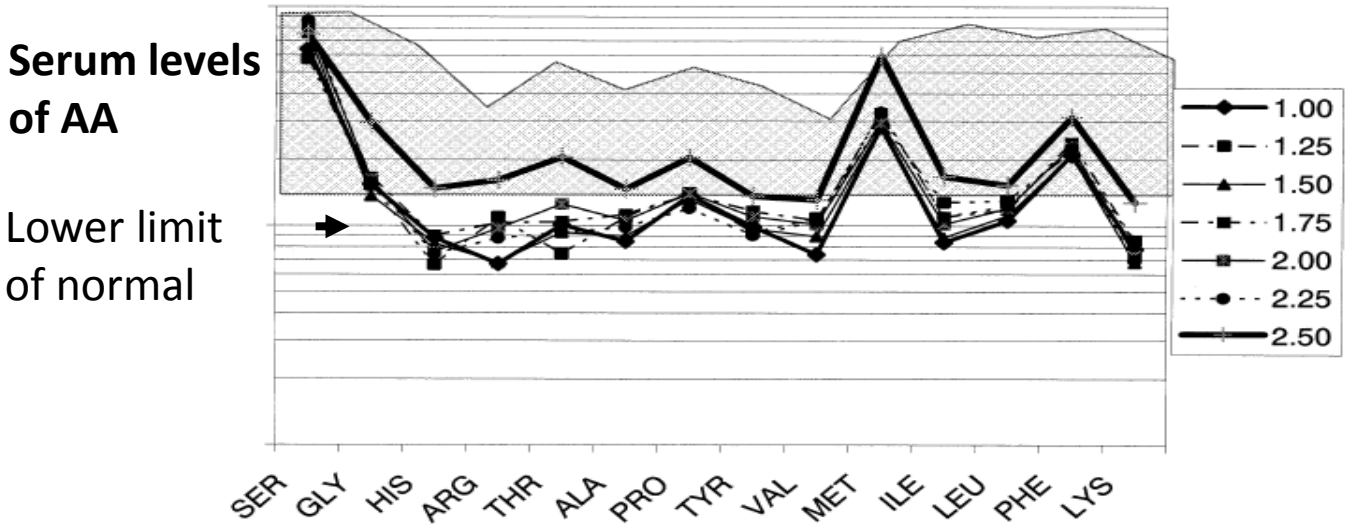


Mean 17% of total infused AAs lost in effluent (but Tyrosine: loss 87%)

Total amino acid loss: ~ 0.2g/L filtrate (~10-15g/day)

Nutrition 2003;19:733-740

Amino acid losses during RRT



- 14 – 57% of AA were below lower limit if protein intake <2.5g/kg/d
- Essential AA threonine, valine and isoleucine and indispensable AA arginine and tyrosine were constantly at low level

Nutrition 2003;19:733-740

Loss of trace elements during RRT

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

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

Prospective trial

11 AKI patients on CVVHDF for 48 hours

All patients received enteral or parenteral nutrition, plus micronutrient supplementation

Measurement of Copper, Selenium, Zinc & Thiamine in serum & effluent

Am J Clin Nutr 2004;80:410-416

Loss of trace elements during RRT

Results: Serum levels

Trace element	Baseline	Post trial	p	Reference
Zinc [µmol/L]	8.68 ± 0.66			12.7 – 20.3
Selenium [µmol/L]	0.76 ± 0.20			0.8 – 1.6
Copper [µmol/L]	0.76 ± 0.20			0.8 – 1.6
Thiamine [nmol/L]	382 ± 109			100 - 300

Am J Clin Nutr 2004;80:410-416

Loss of trace elements during RRT

Results: Serum levels

Trace element	Baseline	Post trial	p	Reference
Zinc [µmol/L]	8.68 ± 0.66	6.10 ± 0.66	0.05	12.7 – 20.3
Selenium [µmol/L]	0.76 ± 0.20	0.71 ± 0.18	<0.001	0.8 – 1.6
Copper [µmol/L]	0.76 ± 0.20	0.71 ± 0.18	0.008	0.8 – 1.6
Thiamine [nmol/L]	382 ± 109	264 ± 136	NS	100 - 300

Analysis of effluent

All 4 micronutrients were detectable.

Am J Clin Nutr 2004;80:410-416

Loss of trace elements during RRT

Conclusions:

1. Low trace elements before CRRT

2. CRRT resulted in significant losses of Se, Cu, Zn and thiamine.

3. Prolonged CRRT would have resulted in selenium and thiamine depletion despite supplementation

Am J Clin Nutr 2004;80:410-416

Loss of trace elements & vitamins during RRT

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

Comparison of 8 critically ill patients on CVVHF, 9 critically ill and 9 healthy controls (24hr)

Measurement of Vit C, Vit E, selenium, zinc, chromium and copper in serum

Story et al. Crit Care Med 1999; 27: 220-223

Loss of trace elements & vitamins during RRT

Results:

- Compared with healthy volunteers, CVVH patients had significantly lower blood concentrations of Vit C, Vit E, selenium and zinc.

- No significant differences in serum level between both critically ill cohorts.

Story et al. Crit Care Med 1999; 27: 220-223

Drug clearance during RRT

Antibiotic dosing during RRT

Variability of antibiotic concentrations in critically ill patients receiving CRRT: A multicentre pharmacokinetic study*

24 critically ill adult patients with AKI receiving ciprofloxacin, meropenem, piperacillin/tazobactam, or vancomycin during CRRT

Conclusions:

- Significant variability in antibiotic trough concentrations
- Dosing of antibiotics failed to achieve the target trough antibiotic concentration during 25% of the dosing intervals.

DM Roberts et al. Crit Care Med 2012; 40: 1523–1528

Effect of RRT on renal recovery

Effect of RRT on renal recovery

EXPERT CONSENSUS DOCUMENT

Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup

NATURE REVIEWS | NEPHROLOGY VOLUME 13 | APRIL 2017

Important question:

Can practice of RRT affect chances of renal recovery after AKI?

Effect of RRT on renal recovery

RRT characteristics
Modality
Fluid purity
Anticoagulation
Haemodynamic stability
Mode of clearance
Ultrafiltration rate
Fluid balance
Dialysate temperature
Dialysate composition
Dose of RRT
Other RRT factors

Chawla et al. Nat Rev Nephrol 2017;13

Effect of RRT on renal recovery

RRT characteristics	Effect on renal recovery
Modality	Intermittent RRT may delay recovery
Fluid purity	Possible effect
Anticoagulation	No evidence
Haemodynamic stability	Hypotension might delay recovery
Mode of clearance	No evidence
Ultrafiltration rate	Possible delay if UF causes hypotension
Fluid balance	Possible delay with positive FB
Dialysate temperature	Less hypotension with cooler dialysate
Dialysate composition	Higher dialysate [Na] may prevent low BP
Dose of RRT	No evidence
Other RRT factors	Wrong drug dosing may delay recovery

Chawla et al. Nat Rev Nephrol 2017;13

Management of complications

Electrolyte losses → supplementation

Medications → therapeutic drug monitoring / pharmacist

Nutrient losses → adjustment of nutrition

BUT: no evidence that it improves outcome

conflicting advice in official guidelines

ESPEN: “to consider supplementation”

ASPEN & KDIGO: not mentioned

DIVI & OGIV: specific recommendations

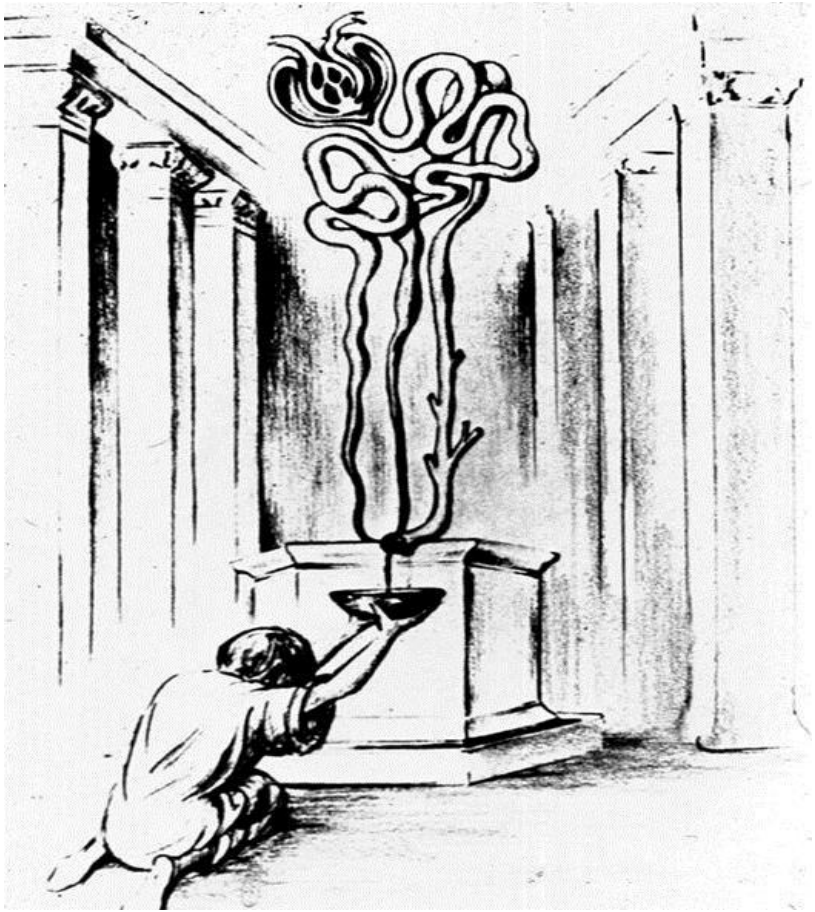
Renal non-recovery → RRT quality standards

Conclusions

The complications of RRT include

- **high risk of adverse events**
- **unrecognised losses of amino acids, trace elements and vitamins**
- **challenges in drug dosing and risk of under-dosing**
- **lack of universally accepted standards of RRT**
- **high likelihood that practice of RRT contributes to non-recovery**

Management consists of attention to detail, supplementation where possible and adherence to quality standards



Thank you