Insufficienza renale acuta
Le nuove opzioni dialitiche

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TOPICS

What is changing in renal replacement therapy (RRT) for acute kidney injury (AKI)

- New indications to RRT
- New modalities of RRT
- New anticoagulation protocols

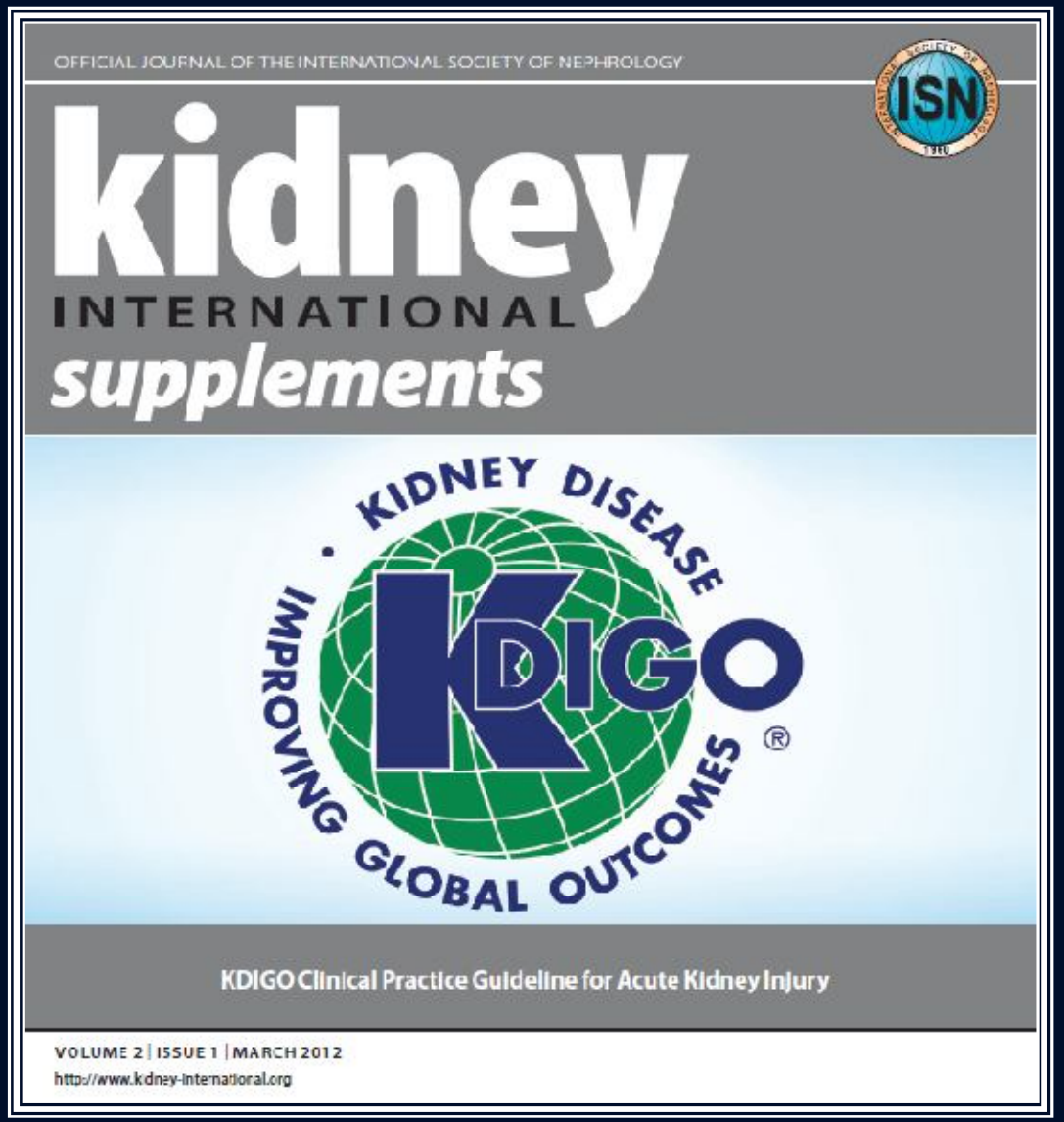
2012

volume one

USRDS Annual Data Report

Atlas of Chronic Kidney Disease in the United States

national institutes of health
national institute of diabetes & digestive & kidney diseases
division of kidney, urologic, & hematologic diseases


OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY
ISN
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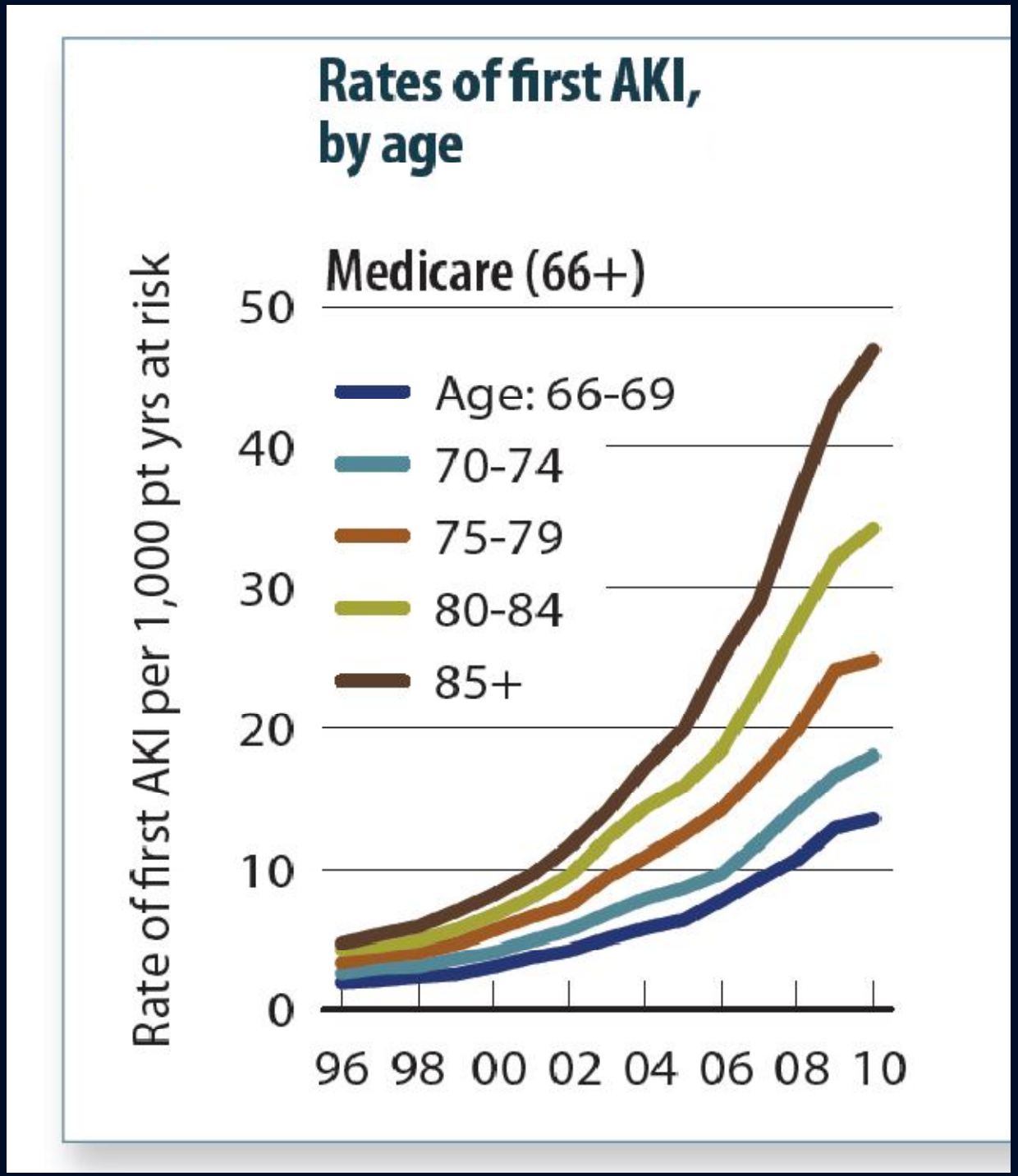
supplements
KIDNEY DISEASE
IMPROVING GLOBAL OUTCOMES
KDIGO
KDIGO Clinical Practice Guideline for Acute Kidney Injury
VOLUME 2 | ISSUE 1 | MARCH 2012
http://www.kidney-international.org



The incidence of AKI is increasing

2012 USRDS Annual DATA Report

Why an epidemic of AKI?

- **Patients are changing:** elderly people with increasing burden of acute and chronic comorbidities
- **Medicine is changing:** more invasive procedures, complex surgery, nephrotoxic drugs etc.
- **Awareness of AKI is changing:** early diagnosis more sensitive diagnostic criteria

Increased morbility and mortality risk in survivors from AKI

Uremic memory: the role of acute kidney injury in long-term outcomes

Ladan Golestaneh[1], Michal L. Melamed[1] and Thomas H. Hostetter[1]

Most epidemiologic data, thus far, have focused on short-term outcomes of acute kidney injury (AKI). Lo *et al.* correlate AKI with long-term outcomes. The concept of 'uremic memory' sheds light on the importance of AKI and its permanent imprint. The focus of research should be on prevention of an episode of AKI, when possible.

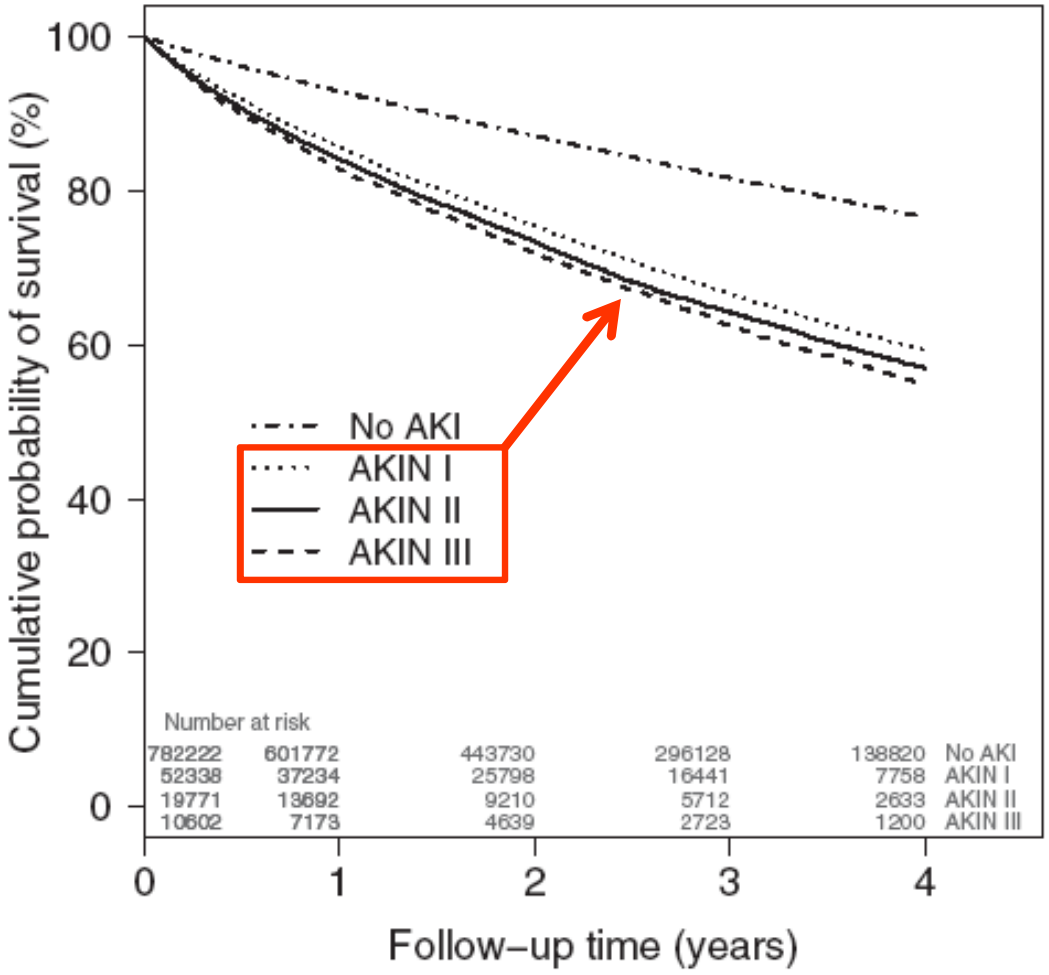
Kidney International (2009) **76,** 813–814. doi:10.1038/ki.2009.314

Long-term negative adverse effects of AKI as the consequence of the “uremic” memory

Acute Kidney Injury Associates with Increased Long-Term Mortality

Jean-Philippe Lafrance and Donald R. Miller

Center for Health Quality, Outcomes, and Economic Research, Edith Nourse Rogers Memorial Veterans Hospital, Bedford, Massachusetts; and Boston University School of Public Health, Boston, Massachusetts

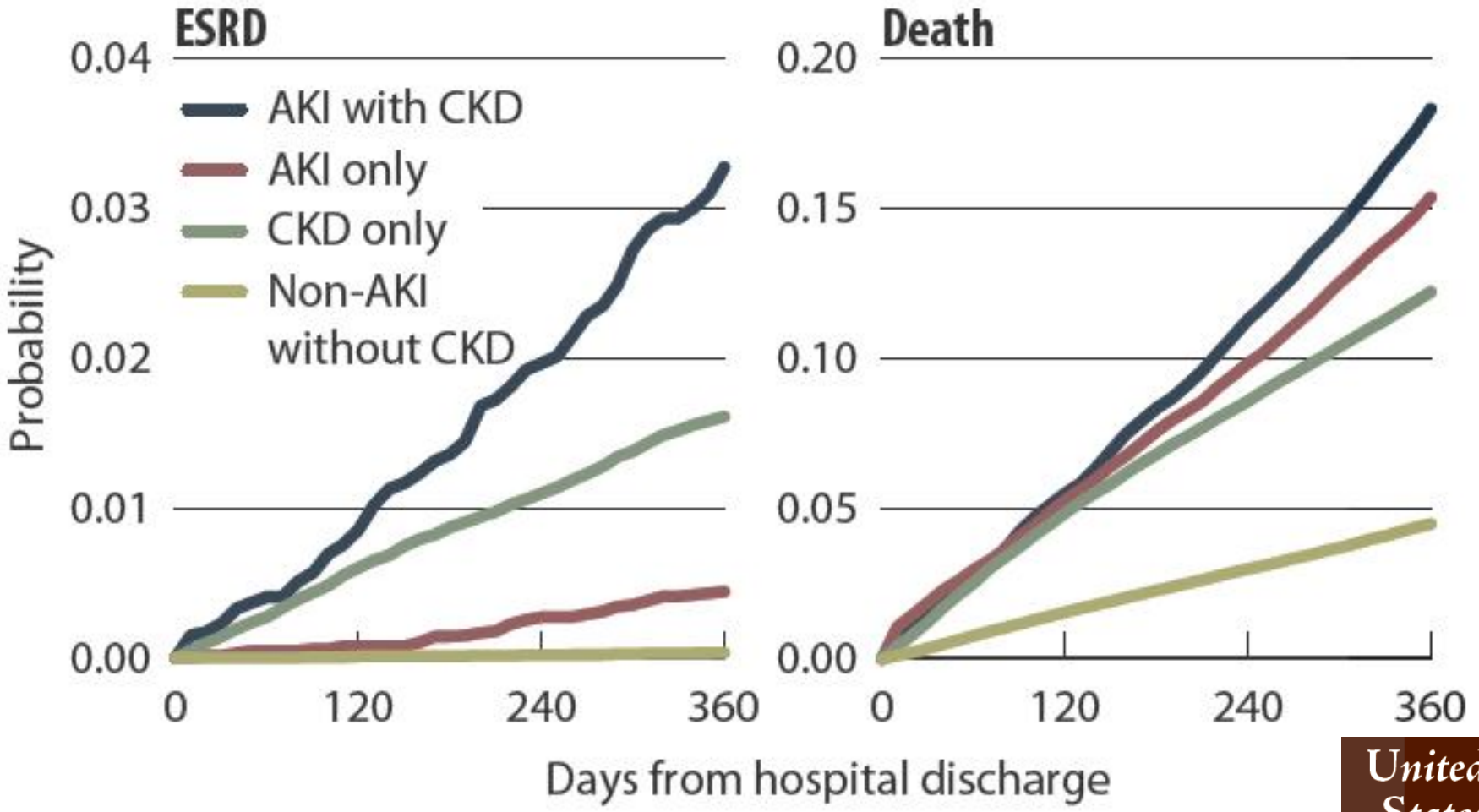


Whatever is the severity of AKI, mortality is increased even following patient dismission

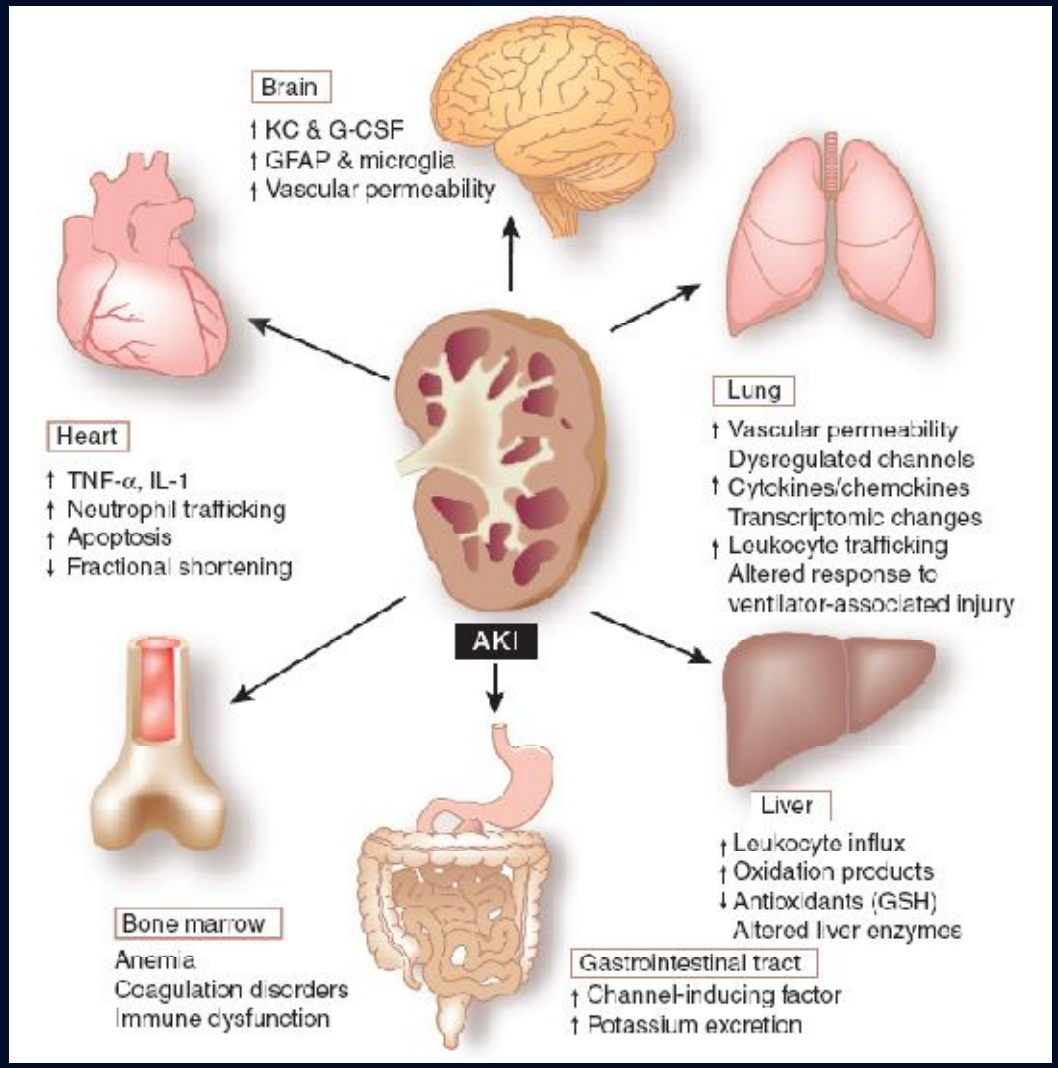
Figure 1. Unadjusted Kaplan-Meier survival curves by AKIN categories are shown. Time is calculated from 90 d after discharge of the index admission. AKIN categories are defined by the ratio of the highest creatinine to the lowest creatinine. AKIN I is a ratio ≥1.5 and <2, AKIN II is a ratio ≥2 and <3, and AKIN III is a ratio ≥3. Log-rank test: $P < 0.001$.

J Am Soc Nephrol 21: 345–352, 2010.

[8]20$_i$ Probability of ESRD & death after live hospital discharge, by AKI & CKD status, 2006



AKI-induced distant organ effects: The systemic complications of AKI as the consequence of a “nephro-centric” inflammatory syndrome

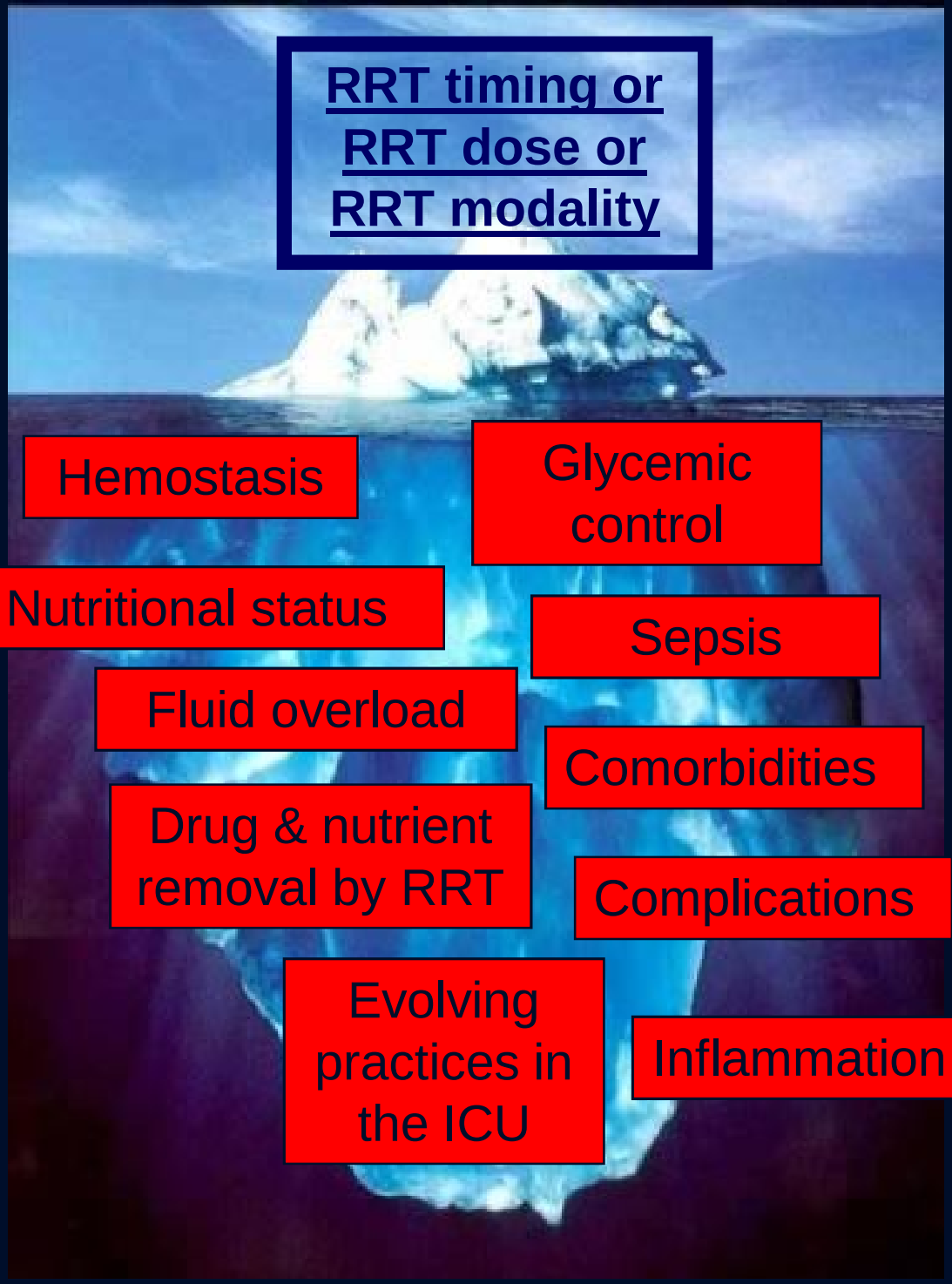


Scheel PJ et al, Kidney Int 2008; 74:849-851

Factors affecting prognosis in patients with AKI on RRT

Factors directly related to RRT

Factors indirectly related to RRT



TOPICS

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- **New indications to RRT**
- New modalities of RRT
- New anticoagulation protocols

Starting RRT in AKI

- Conventional and/or urgent indications
- Clinical and logistic factors influencing the decision to start RRT
- Expanded indications and evolving practices in the ICU

Conventional and/or urgent indications for starting RRT in AKI (biochemical/clinical)

- Severe hyperkalemia refractory to medical treatment and/or with severe EKG alterations
- Pulmonary edema and oliguria
- Severe metabolic acidosis
- Progressive azotemia
- Overt uremic signs (encephalopathy, pericarditis, bleeding diathesis etc.,)
- Concomitant intoxication with dialyzable drug or toxin

Factors influencing biochemical/clinical decision to start RRT in AKI

Factors		
Patient-Specific	Clinician-Specific	Organizational
Kidney function/reserve	Goals of therapy	Country/ Institution
Comorbid disease and physiologic reserve	Relative indications and clinician threshold for initiation	ICU Type
Primary diagnosis: severity of illness and trajectory	Local practice patterns	Machine and nursing availability
AKI: severity and trend	Prescribing service	Health costs

Baghshaw SM et al., Crit Care 2009; 13:317

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (*Not Graded*)

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

Kidney International Supplements (2012) **2**, 1

Renal Support: Expanded Indications

Volume removal or prevention of excessive accumulation

Immuno-modulation or restoring immune homeostasis in sepsis

Chemotherapy-induced organ injury, transfusion support

Refractory respiratory acidosis in ARDS

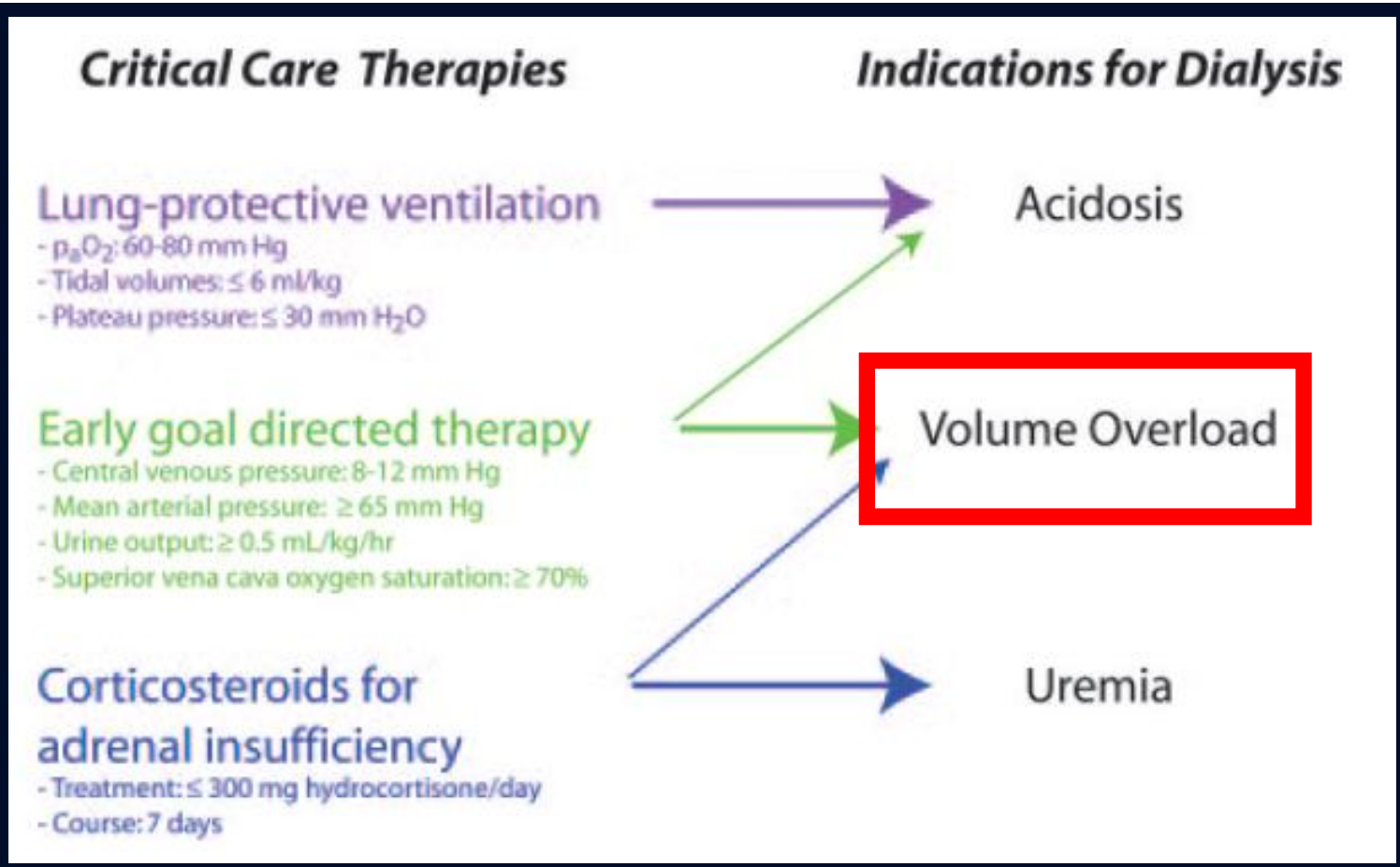
Hypercatabolism

Dialysis without AKI

Evolving Practices in Critical Care and Potential Implications for Management of Acute Kidney Injury

Kathleen D. Liu,* Michael A. Matthay,† and Glenn M. Chertow*‡

Division of Nephrology, Department of Medicine, †Departments of Medicine and Anesthesiology and Cardiovascular Research Institute, and ‡Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, California



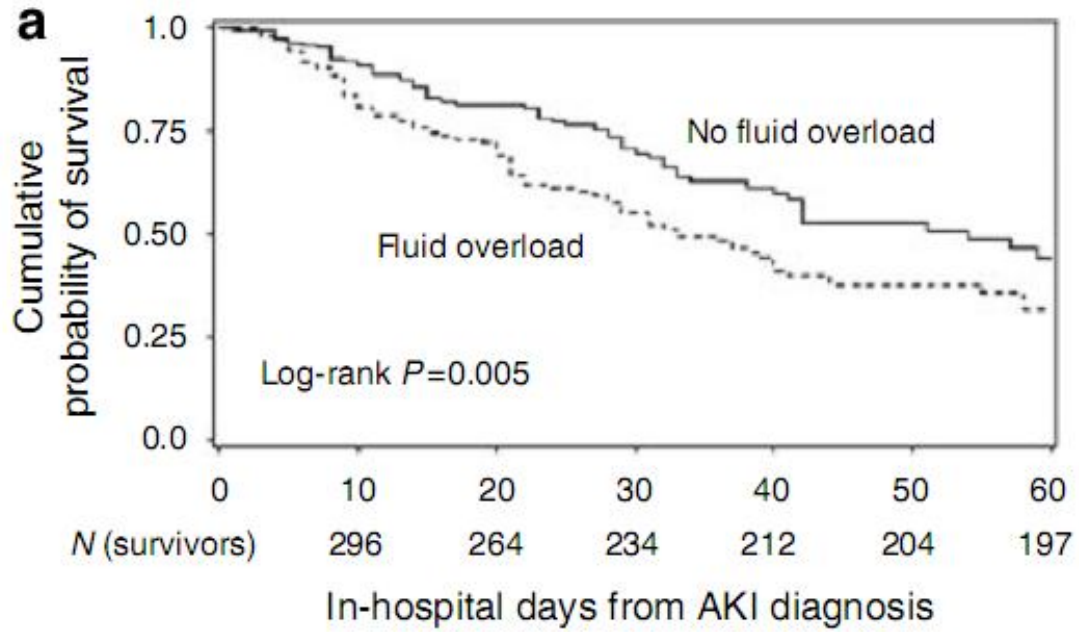
Clin J Am Soc Nephrol 1: 869–873, 2006.

The nephrologist' view of ICU patients

The intensivist' view of ICU patients

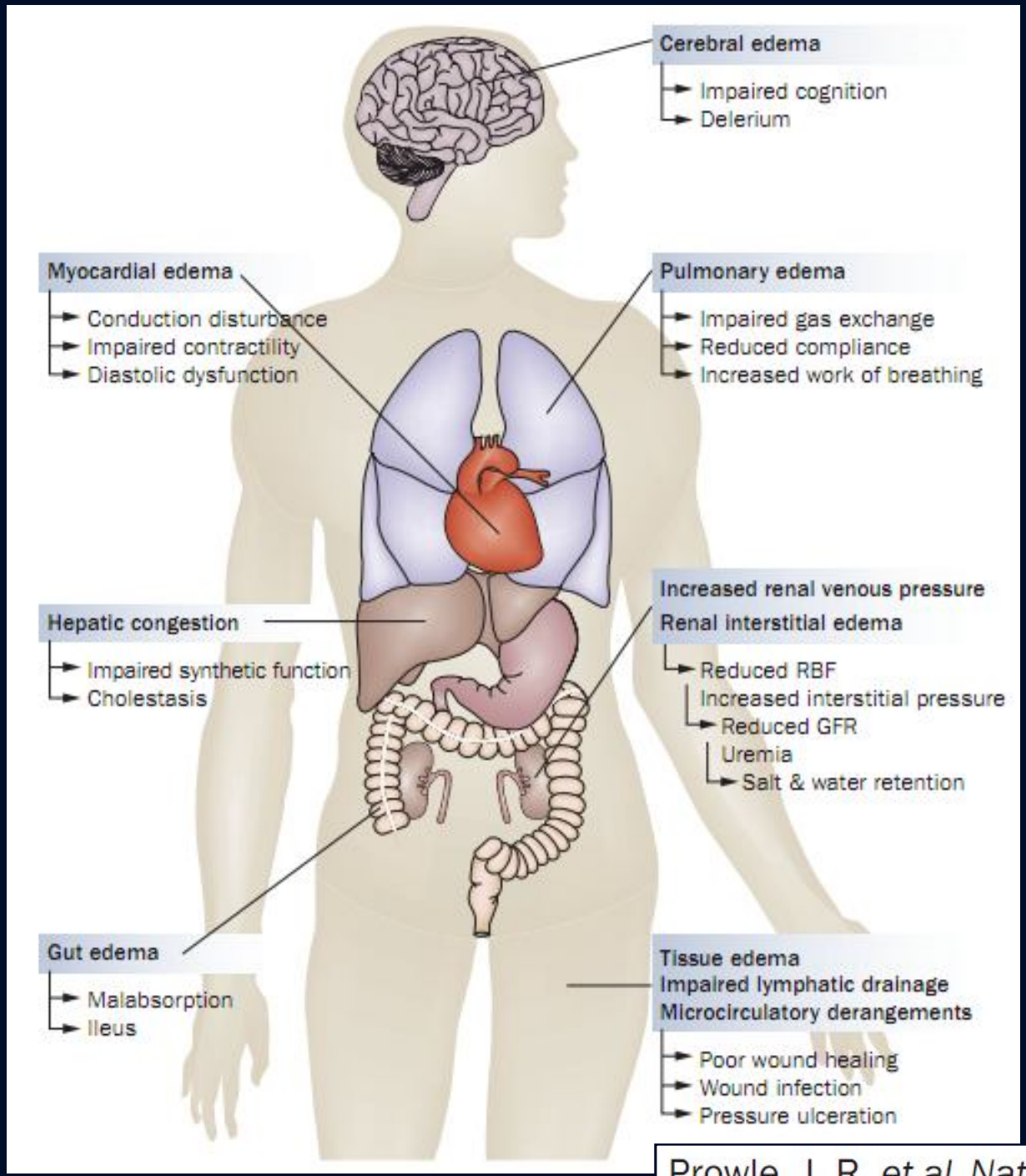
Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

Josée Bouchard[1], Sharon B. Soroko[1], Glenn M. Chertow[2], Jonathan Himmelfarb[3], T. Alp Ikizler[4], Emil P. Paganini[5] and Ravindra L. Mehta[1], Program to Improve Care in Acute Renal Disease (PICARD) Study Group



Increased mortality risk associated with fluid overload in AKI

Bouchard J et al., Kidney Int 2009; 76:422-427



Pathological sequelae of fluid overload

Prowle, J. R. *et al. Nat. Rev. Nephrol.* **6**, 107–115 (2010)

Extracorporeal Blood Purification Techniques in Sepsis

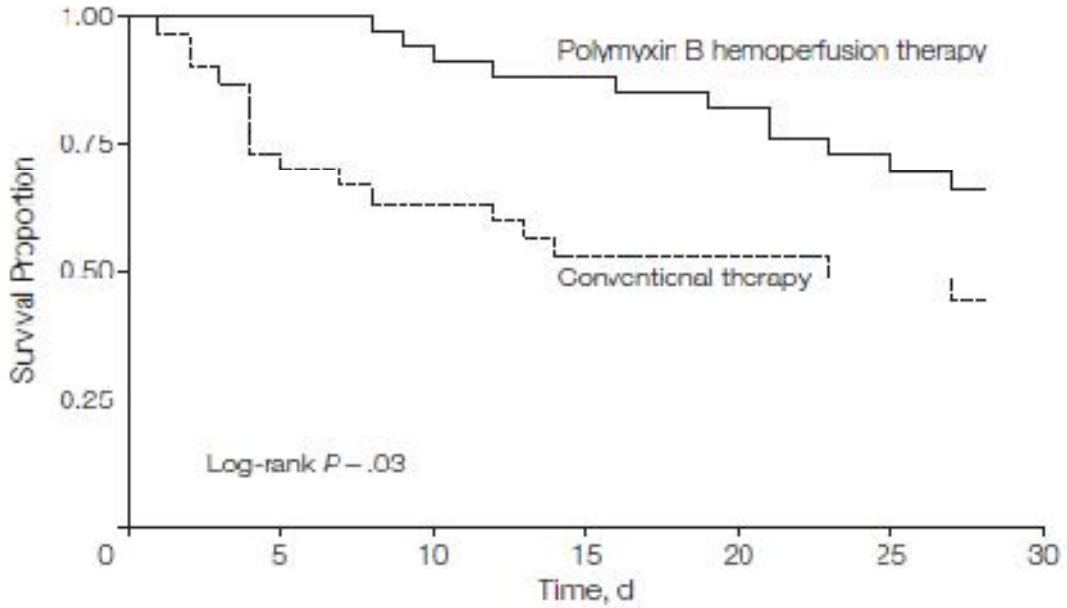
Technique	Aim	Principle	Reported Results
High-volume hemofiltration (HVHF)	Nonselective removal of inflammatory mediators	Convection	Reduces vasopressor requirements, reduces concentrations of inflammatory mediators in blood, and observed mortality lower than predicted mortality
High cutoff membranes (HCOM)	Nonselective removal of inflammatory mediators	Convection	Reduces vasopressor requirements, high clearance of inflammatory mediators moderates leukocyte proliferation, normalizes PMN phagocytosis
Polymyxin-B column (PMX-F)	Selective removal of endotoxin	Adsorption	Reduces vasopressor requirement, increases blood pressure, ameliorates organ dysfunction, reduces short-term mortality
Coupled plasma filtration adsorption (CPFA)	Nonselective removal of inflammatory mediators	Plasma adsorption	Reduces concentrations of inflammatory mediators in blood, restores leukocyte responsiveness
Cytokine adsorbing columns	Nonselective removal of inflammatory mediators	Plasma adsorption	Reduces cytokine levels, improvement in respiratory parameters
Renal assist device (RAD)	Substitute the filtration, transport, metabolic, endocrine and immunologic functions of the kidney	Cell-based therapy	Ameliorates the cytokine profile, improves calcium, phosphate, urea, and creatinine levels
Extracorporeal immune support system (EISS)	Attenuation of excessive antiinflammatory response	Cell-based therapy	Reduces vasopressor requirement, reduces concentrations of endotoxin and inflammatory markers (eg CRP, procalctonin) in blood
Leukocyte inhibition module (LIM)	Attenuation of excessive proinflammatory response	Antibody-based therapy	No studies in sepsis

Abbreviations: CRP, C-reactive protein; PMN, polymorphonuclear

Early Use of Polymyxin B Hemoperfusion in Abdominal Septic Shock

The EUPHAS Randomized Controlled Trial

Figure 3. Estimation of Survival Rate According to Treatment Group



No. at risk

Polymyxin B hemoperfusion therapy	34	34	32	30	27	22	18
Conventional therapy	30	22	19	15	15	12	11

Patients in the polymyxin B hemoperfusion group were treated with 2 sessions of direct hemoperfusion with polymyxin B in addition to standard conventional therapy.

JAMA. 2009;301(23):2445-2452

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- **New modalities of RRT**
- New anticoagulation protocols

Diagnostic & Therapeutic Corner

Dialysis in Intensive Care Unit Patients with Acute Kidney Injury: Continuous Therapy is Superior

Claudio Ronco* and Rinaldo Bellomo†

*Department of Nephrology Ospedale San Bortolo, Vicenza, Italy, and †Department of Intensive Care, Austin Hospital, Melbourne, Australia

Clin J Am Soc Nephrol 2: 597–600, 2007. doi: 10.2215/CJN.00430107

Continuous dialysis is not superior to intermittent dialysis in acute kidney injury of the critically ill patient

Jonathan Himmelfarb

Nature Clinical Practice Nephrology 2007; 3:120-121

Continuous RRT (CRRT)

vs

Conventional Intermittent RRT

Vanholder *et al. Critical Care* 2011, **15**:204
http://ccforum.com/content/15/1/204

REVIEW

Pro/con debate: Continuous versus intermittent dialysis for acute kidney injury: a never-ending story yet approaching the finish?

Raymond Vanholder[1]*, Wim Van Biesen[1], Eric Hoste[2] and Norbert Lameire[1]

Conclusions – towards slow long-extended daily dialysis

A possible solution to the debate might be represented by an hybrid between conventional intermittent modalities of RRT and CRRT

Prolonged Intermittent Renal Replacement Modalities

Acronyms in the literature

- **SLED** (sustained low efficiency dialysis)
- **EDD** (extended daily dialysis)
- **SLEDD** (slow long extended daily dialysis)
- **SLEDD-f** (sustained low efficiency daily diafiltration)
- **PIRRT** (prolonged intermittent renal replacement therapy)

SLED is a flexible approach to RRT for AKI in the ICU that takes most of its advantages from the strenghts of both intermittent and continuous modalities of RRT

- Efficient solute removal
- Hemodynamic stability
- Fluid removal capacity
- Flexibility and logistics
- Costs
- Reduced exposition to systemic anticoagulation

Mortality with SLED

Original Article

NDT
Nephrology Dialysis Transplantation

Mortality rate comparison after switching from continuous to prolonged intermittent renal replacement for acute kidney injury in three intensive care units from different countries

Mark R. Marshall[1,2], Julie M. Creamer[3], Michelle Foster[3], Tian M. Ma[2], Susan L. Mann[2], Enrico Fiaccadori[4], Umberto Maggiore[4], Brent Richards[3,5], Vanessa L. Wilson[6], Anthony B. Williams[1,7] and Alan P.N. Rankin[7]

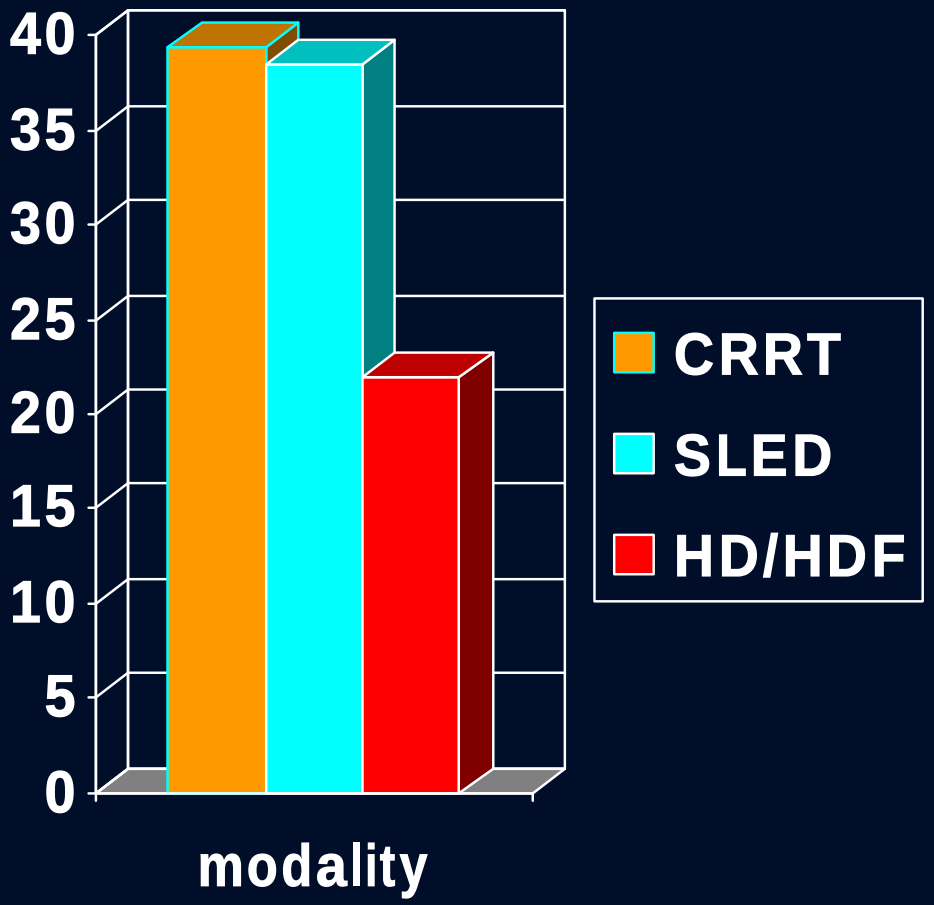
[1]Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand, [2]Department of Renal Medicine, Middlemore Hospital, Manukau, New Zealand, [3]Department of Intensive Care, Gold Coast Hospital, Southport, Australia, [4]Department of Internal Medicine and Nephrology, Parma University Hospital, Parma, Italy, [5]Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia, [6]Fresenius Medical Care—South Asia Pacific, Milsons Point, Sydney, Australia and [7]Department of Intensive Care Medicine, Middlemore Hospital, Manukau, New Zealand

No difference in mortality between two different time periods (before and after the transition from CRRT to SLED) in three different ICUs (Australia, New Zealand, Italy)

Marshall MK et al. Nephrol Dial Transpl 2011, 26:2169-75

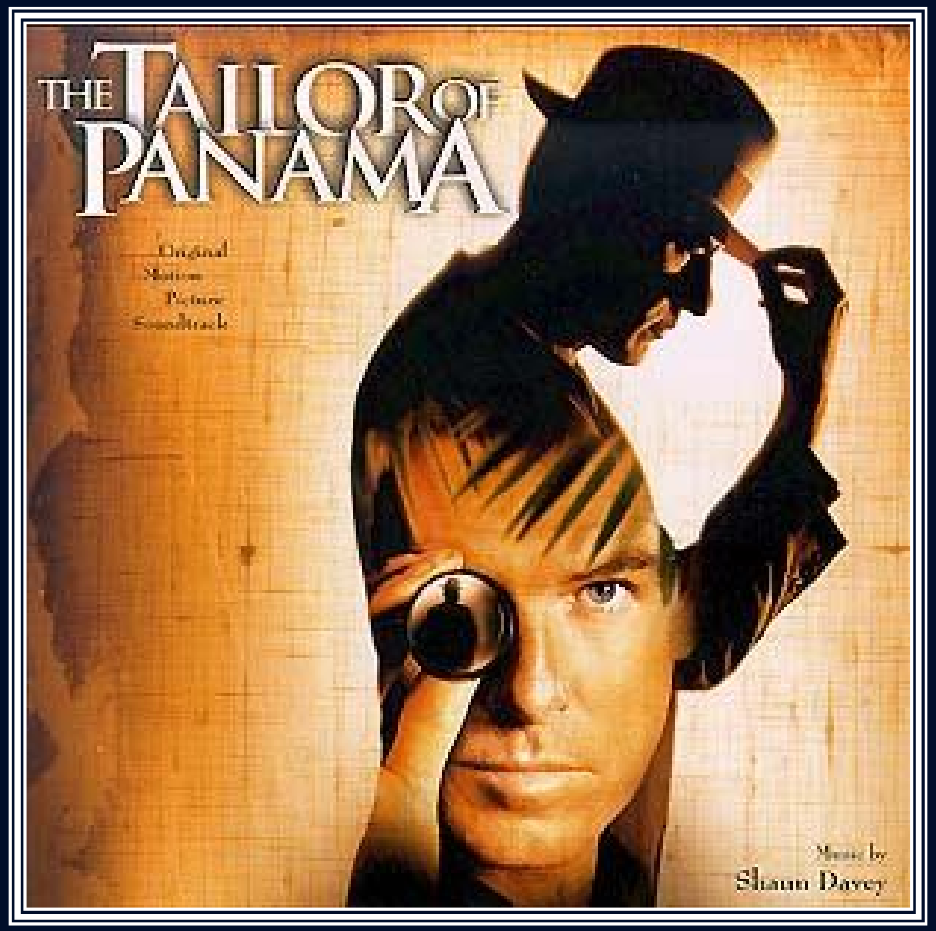
Modality of RRT in the ICU

(79 ICU from Piemonte, Italy)

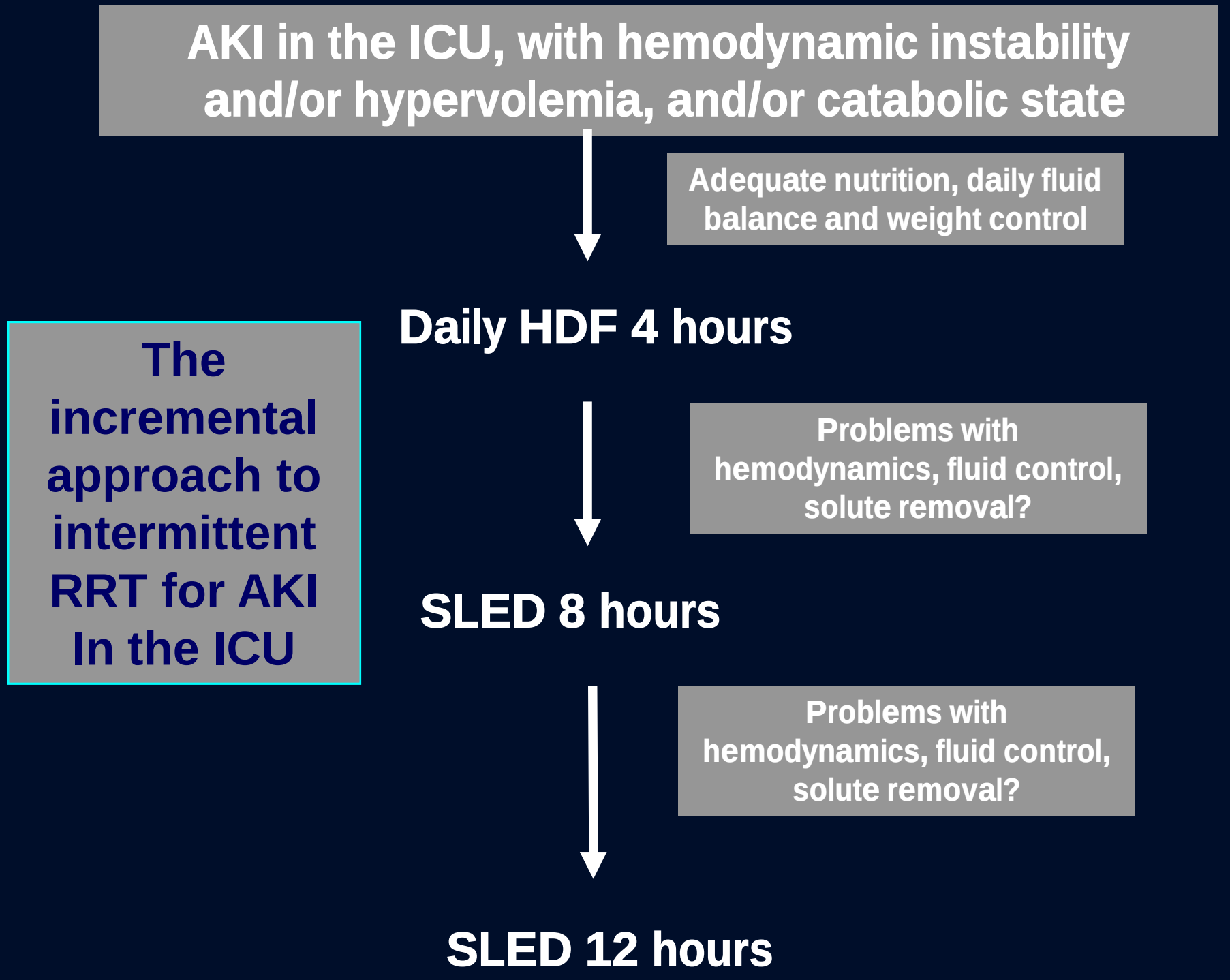


- **RRT for a total of 7,842 days was provided in 79 ICUs for 1,118 patients.**
- **RRT median duration (5.76 days/patient)**

JNEPHROL 2011; 24(02): 165-176



An approach to RRT in AKI tailored to the patient needs


AKI in the ICU, with hemodynamic instability and/or hypervolemia, and/or catabolic state
Adequate nutrition, daily fluid balance and weight control
Daily HDF 4 hours
Problems with hemodynamics, fluid control, solute removal?
SLED 8 hours
Problems with hemodynamics, fluid control, solute removal?
SLED 12 hours
The incremental approach to intermittent RRT for AKI In the ICU

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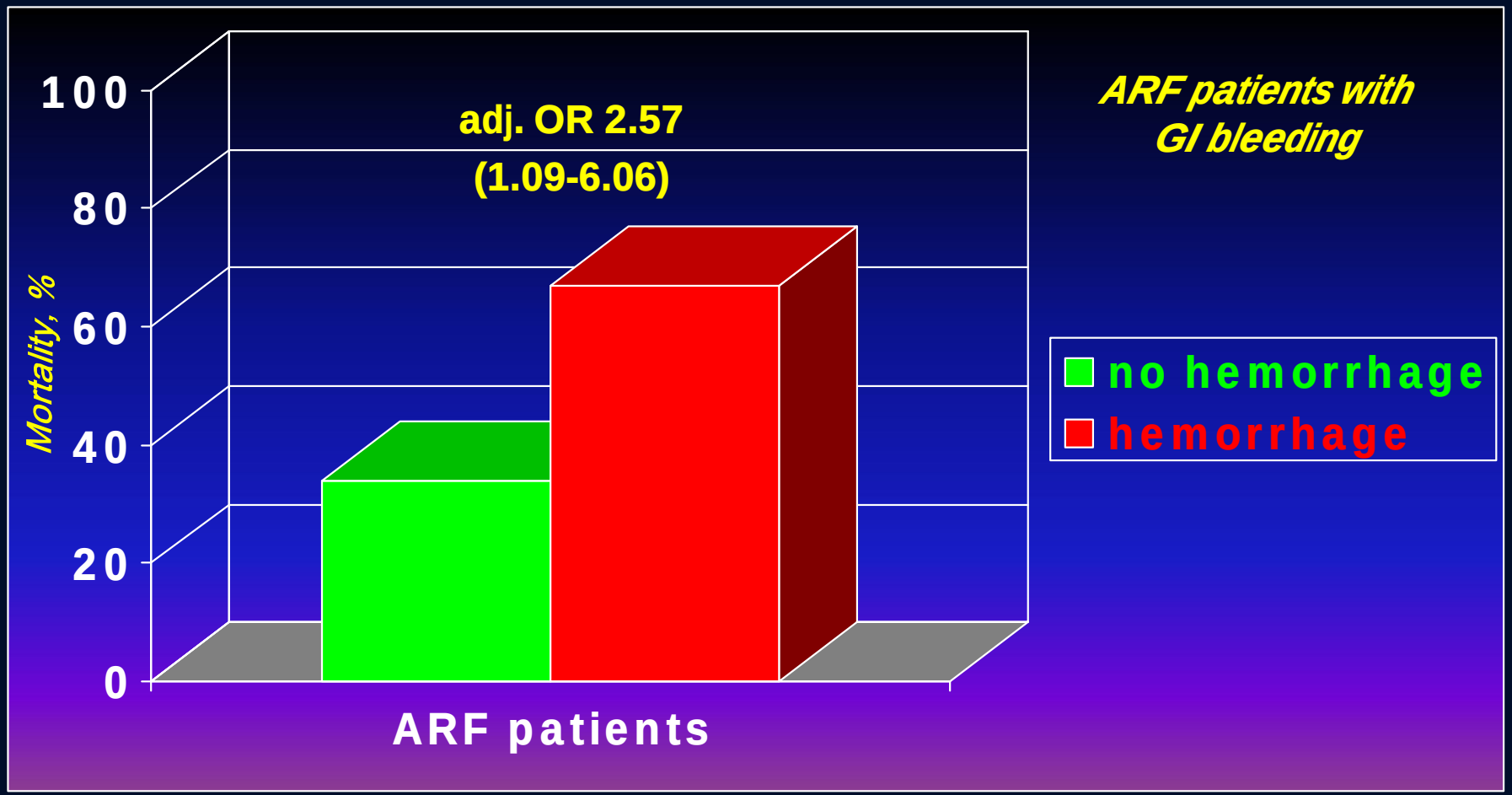
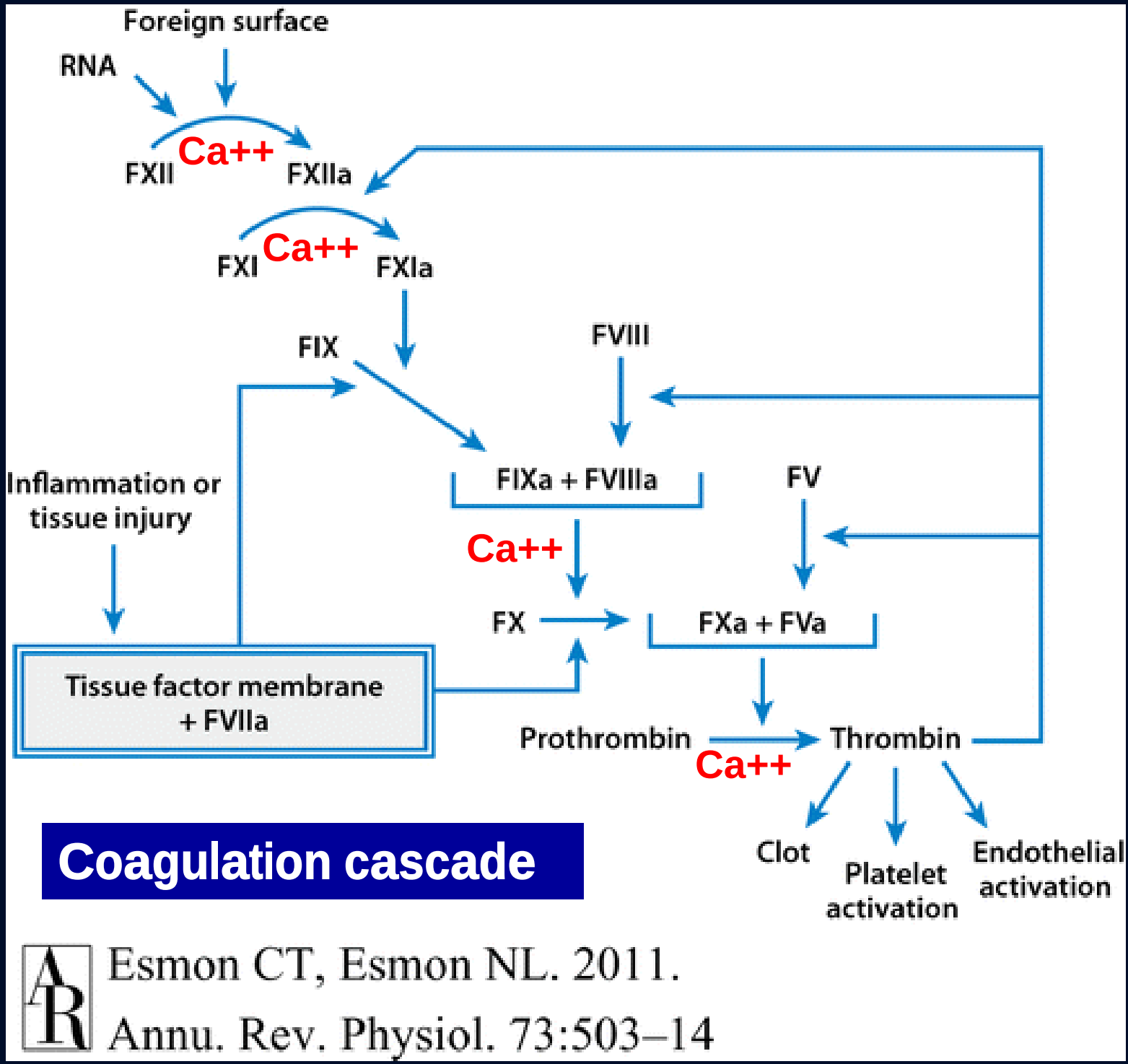
- New modalities of RRT
- **New anticoagulation protocols**

Clinically important GI bleeding significantly increases the risk of death in ARF patients



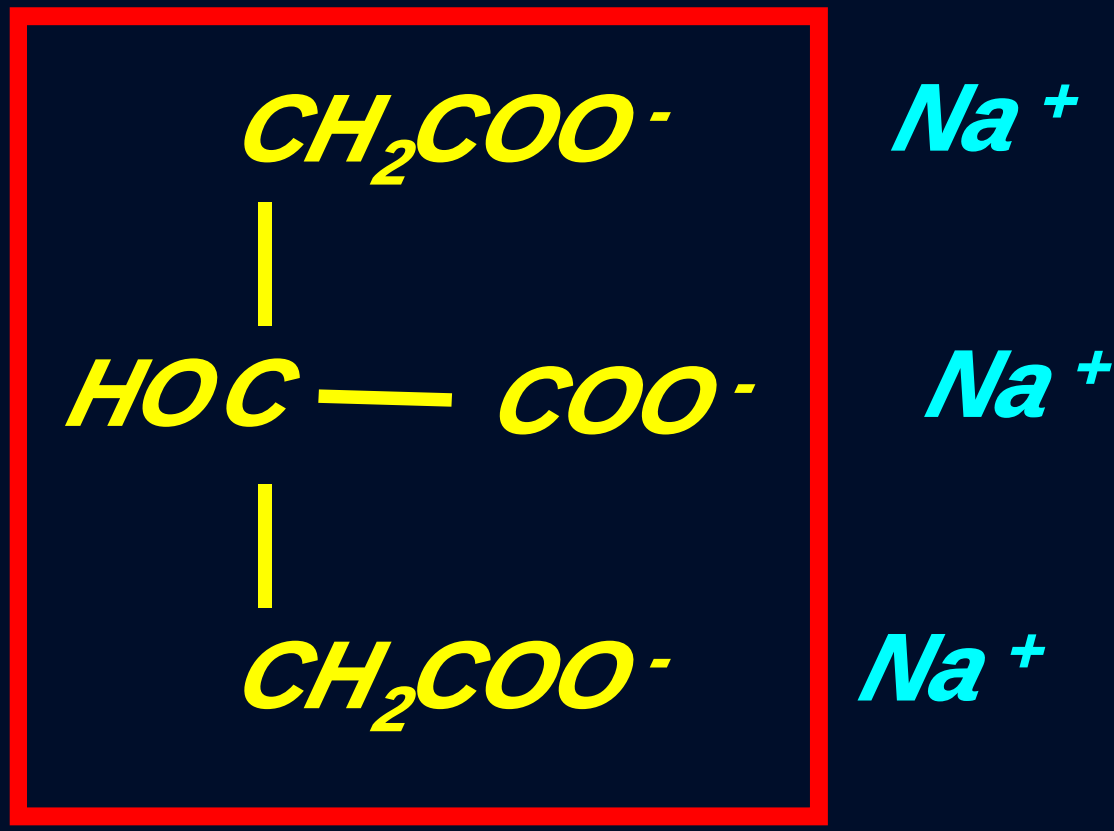
Fiaccadori E et al., Kidney Int 2001; 59:1510-19



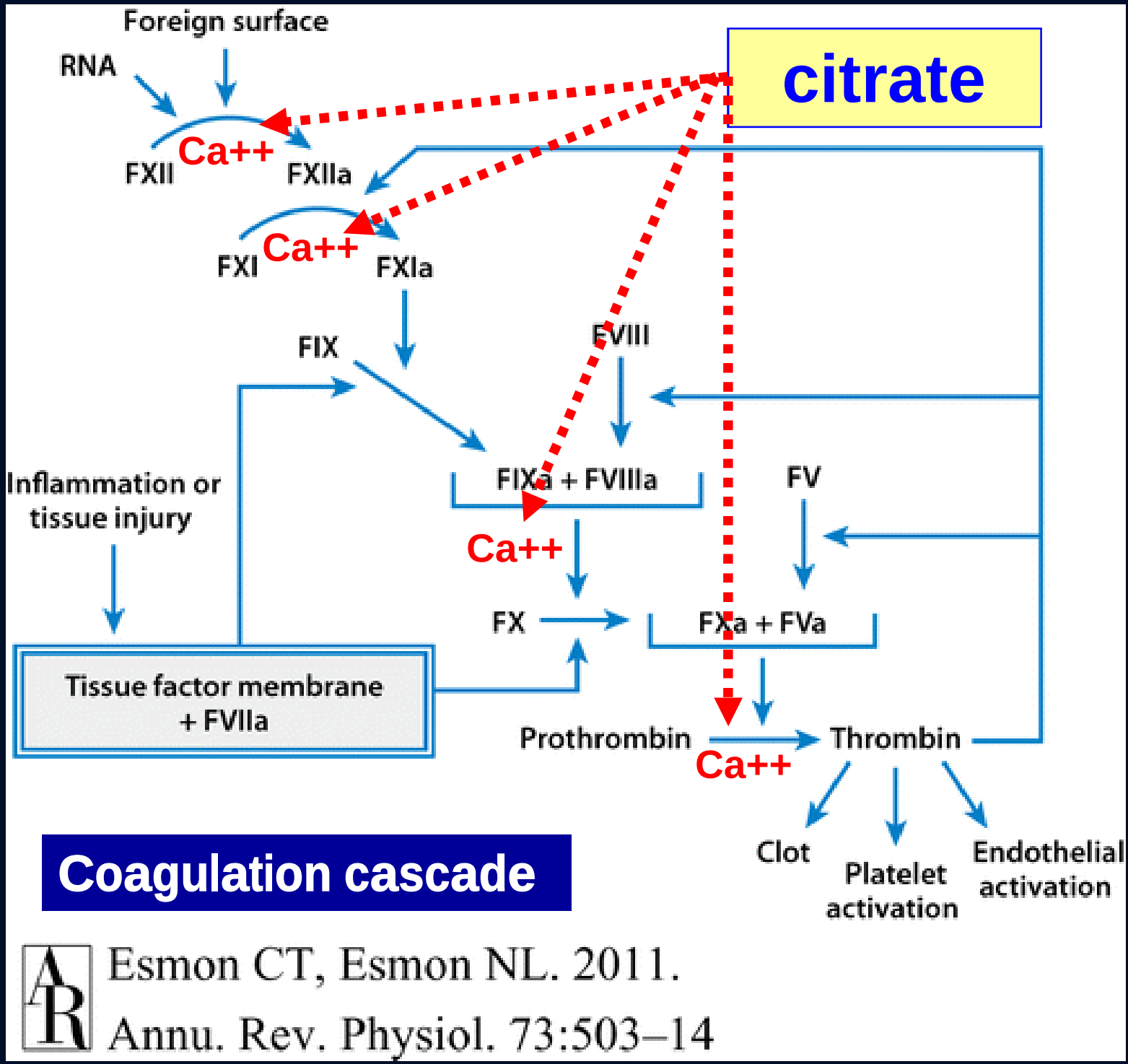
Coagulation cascade

Esmon CT, Esmon NL. 2011.
Annu. Rev. Physiol. 73:503–14

Trisodium citrate



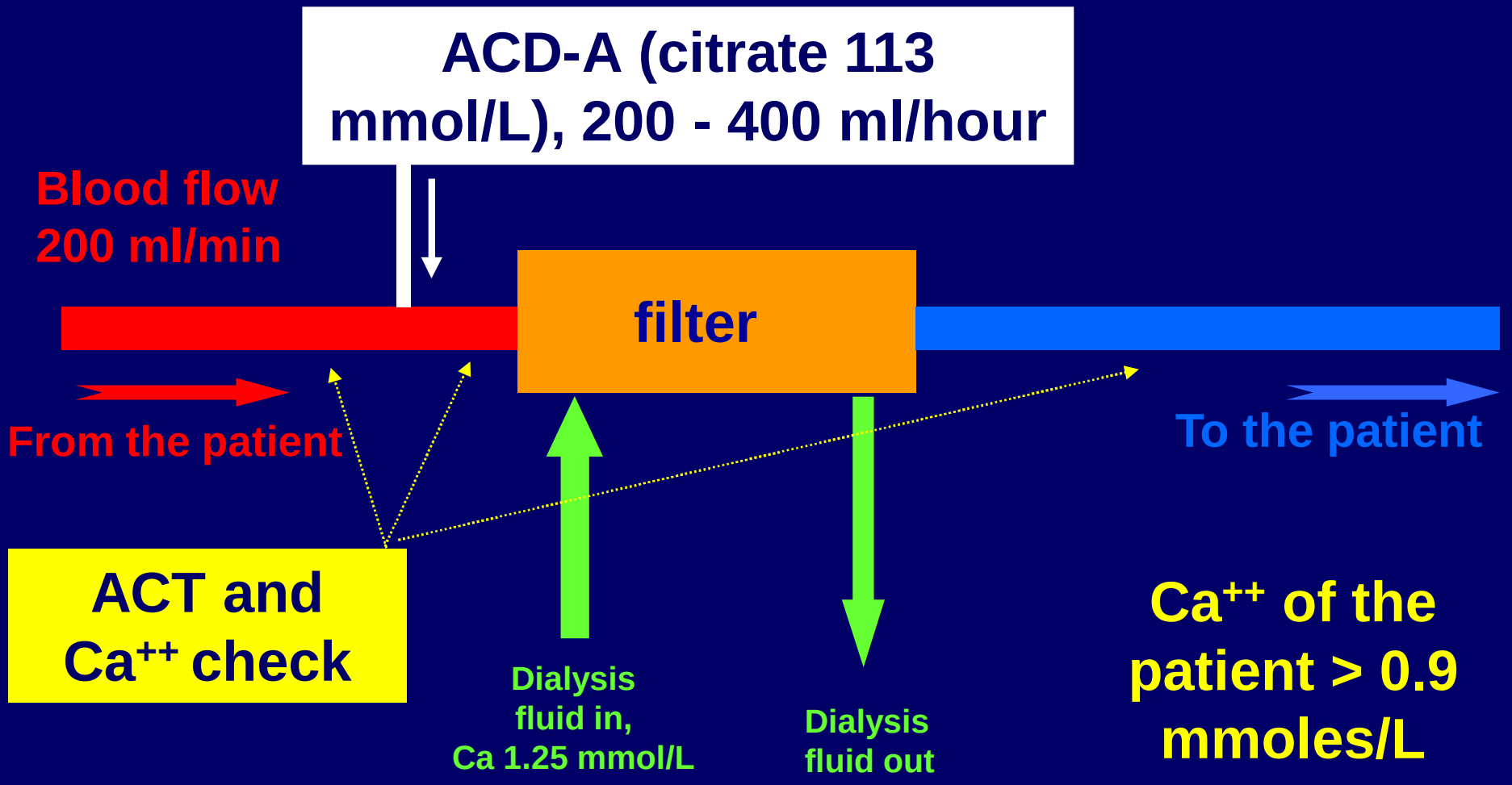
MW 258 Da



Coagulation cascade

Esmon CT, Esmon NL. 2011.
Annu. Rev. Physiol. 73:503–14

Sustained, low-efficiency dialysis (SLED) with citrate

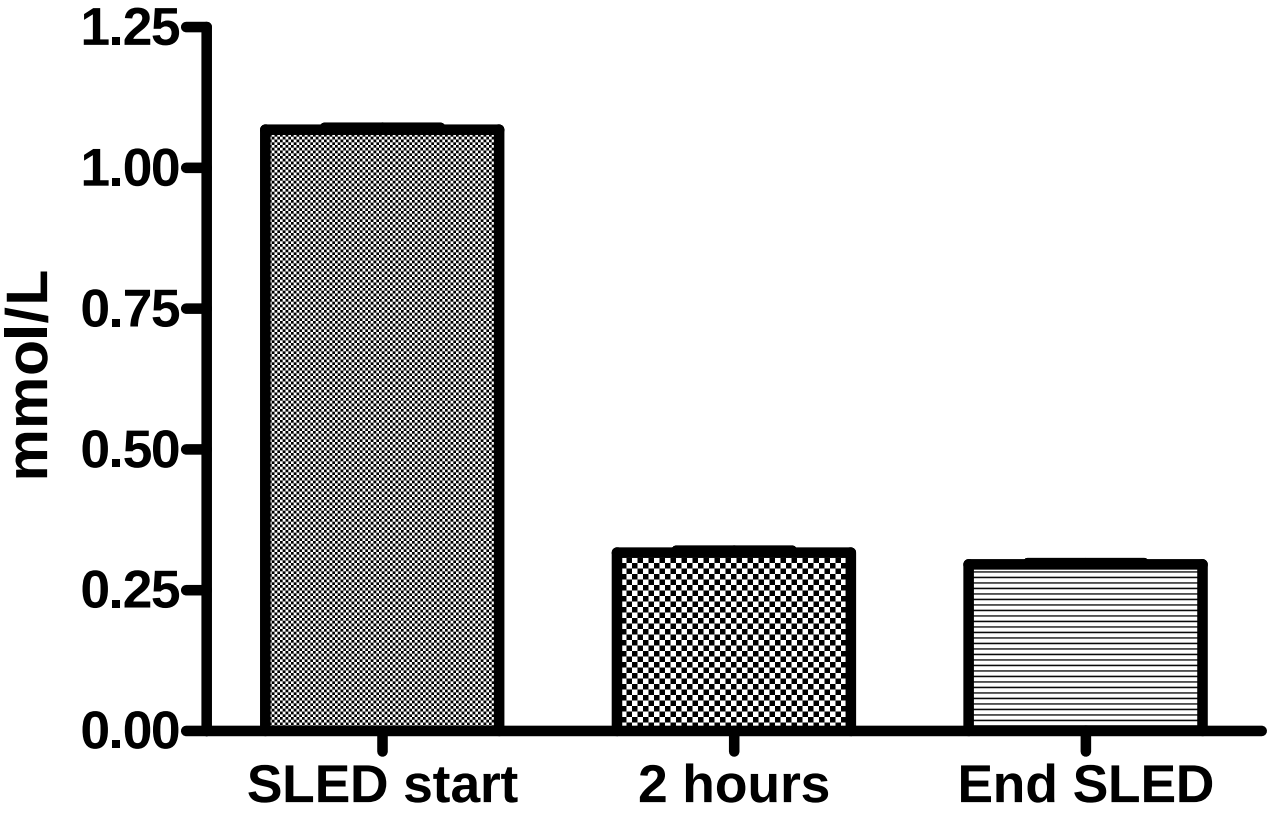


- Dialysis fluid rate 300 ml/min
- Daily treatments, 8 to 12 hours
- Standard dialysis machine
- polisulfone filters, 1.7 m2, KUF 20 ml/mmHg/h

Patients

- 40 ICU patients with AKI and need for RRT
- General ICU, Heart Surgery ICU, Renal ICU
- 26 m, age 74 ± 11,
- APACHE II 25.7 ± 2.2
- Mechanical ventilation 35/40
- Sepsis 27/40
- Mortality 16/40
- 290 SLED sessions (8-10 hours)

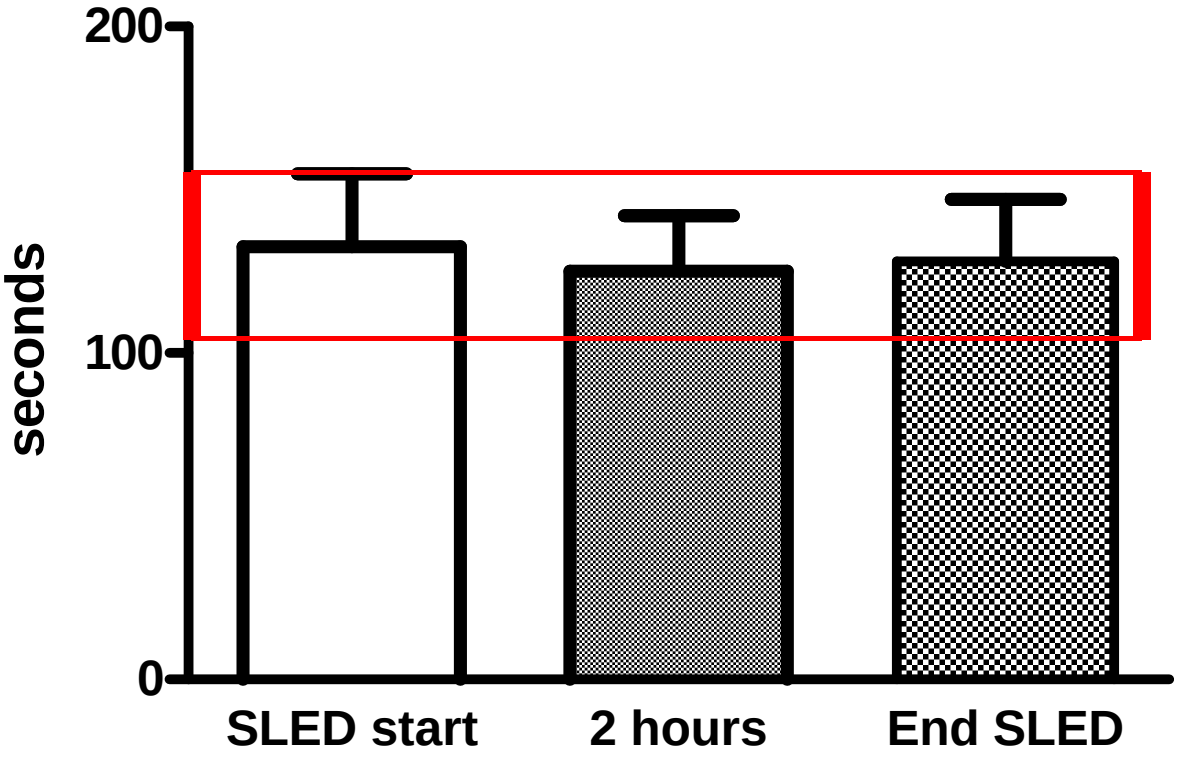
Serum Ca^{++} levels in the blood before the filter



n = 281

Target Ca^{++} levels for circuit anticoagulation 0.25-0.45 mmol/L

ACT values levels in the patient

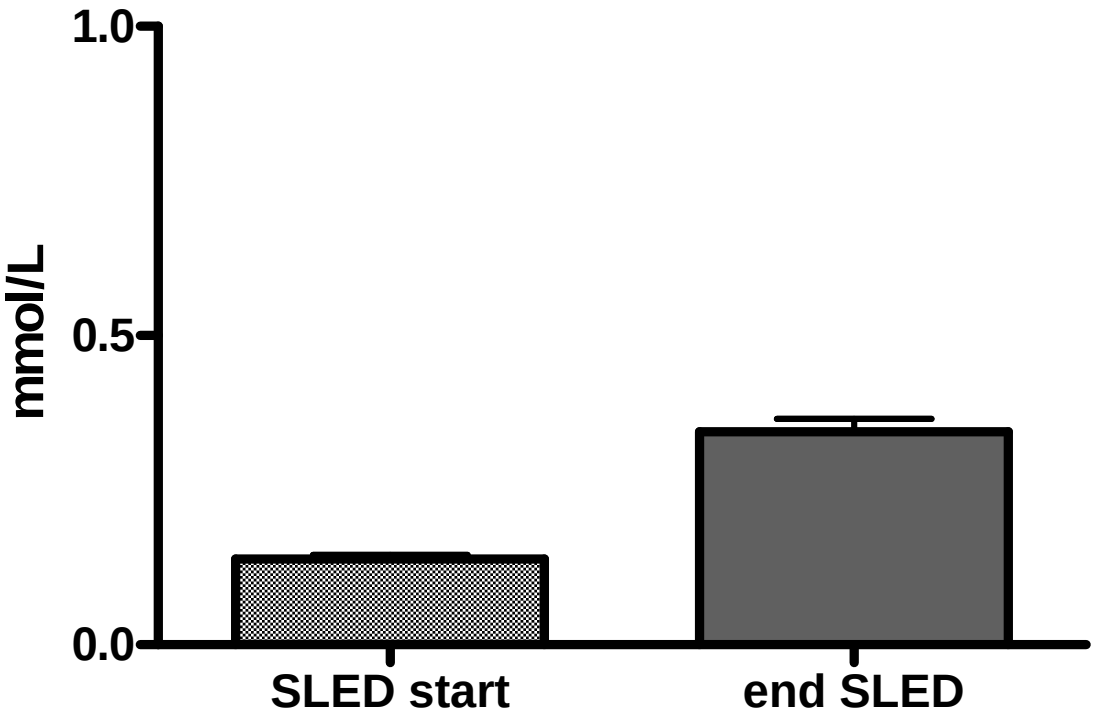


SLED start
2 hours
End SLED

n = 253

Normal range for ACT 100-150 sec

Citrate levels in patients



n = 70
p < 001

citrate levels in healthy control subjects 0.12 ± 0.05 mol/L

citrate levels for anticoagulation 2-4 mmol/L

Causes of SLED discontinuation

	n. SLED	% SLED
Scheduled	265/290	91.4
Impending circuit coagulation	15/290	5.2
Circuit coagulation	2/290	0.7
Malfunct CVC	3/290	1.0
Urgent procedure or surgery	2/290	0.7
Refractory hypotension	3/290	1.0

(290 SLED in 40 patients with AKI in the ICU, 8-10 hours)

Complications

- Calcium administration 3/40
- Major hemorrhagic complications in 2/40 (5%)

Take home messages

- New indications for RRT in patients with AKI
- No formal demonstration of superiority of one RRT modality as compared to the others; however more prolonged modalities of RRT may allow an easier control of metabolic and fluid status of the patient, reducing hemodynamic instability risk
- A possible approach to RRT in AKI might be to integrate in an hybrid RRT modality (SLED) the advantages of both conventional intermittent and continuous RRT modalities (CRRT)
- SLED with citrate might represent a reasonable compromise between the need for an efficient treatment and the need to control the hemorrhagic risk