AKI, fluid overload and RRT

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Disclosures and Funding

Disclosures

- Consulting agreement with Baxter Healthcare Inc.

Funding

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- Kentucky Research Fund (University of Kentucky)
- Clinical trials/registry support: STARRT-AKI, CRRTnet

Outline

- AKI risk-stratification
- Fluid therapy and fluid overload
- Basic concepts of CRRT

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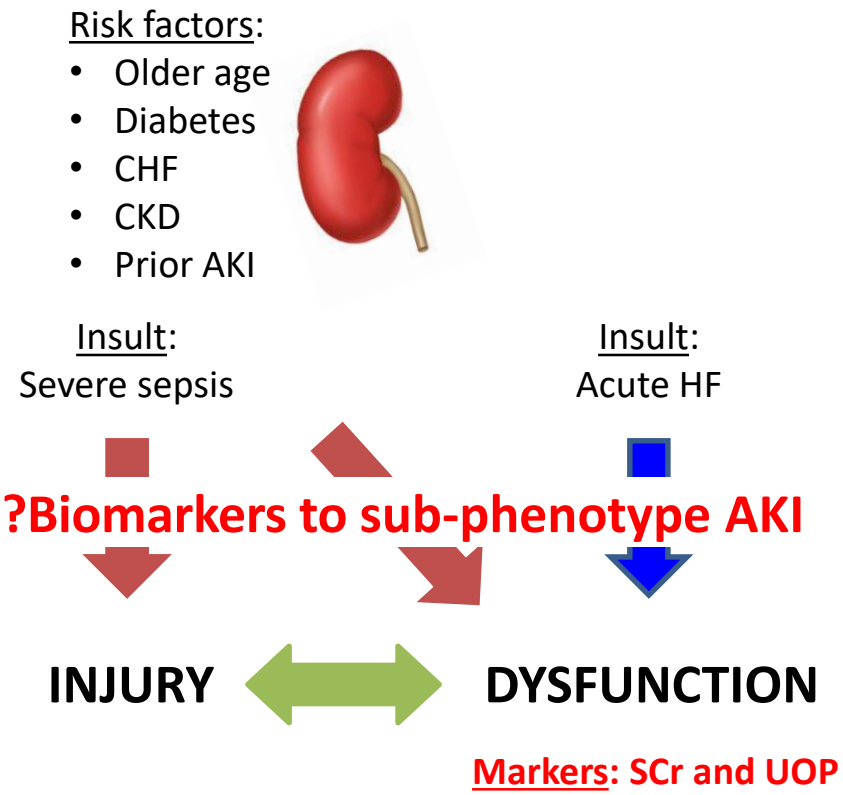
AKI in the Hospital

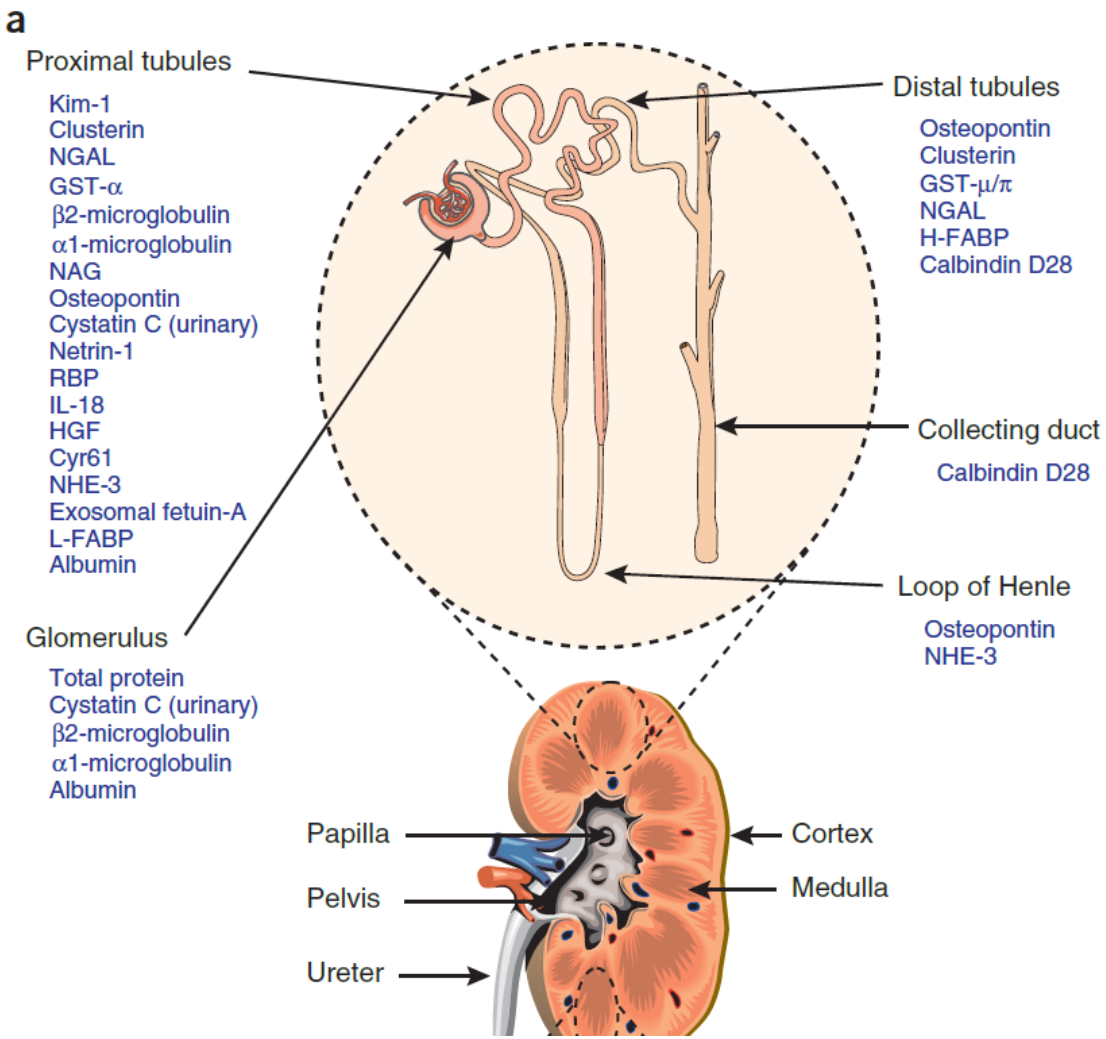
- AKI occurs in 20% of hospitalized pts (doubles in ICU pts)
- Severely ill patients with AKI have mortality rates up to 50%
- 5-10% hospitalized patients have AKID
- One third of AKI survivors will develop CKD within 2 to 5 years
- AKI survivors have higher risk for CVD and HTN

Neyra JA at https://www.kidney.org/atoz/content/AcuteKidneyInjury

Conceptual model of AKI

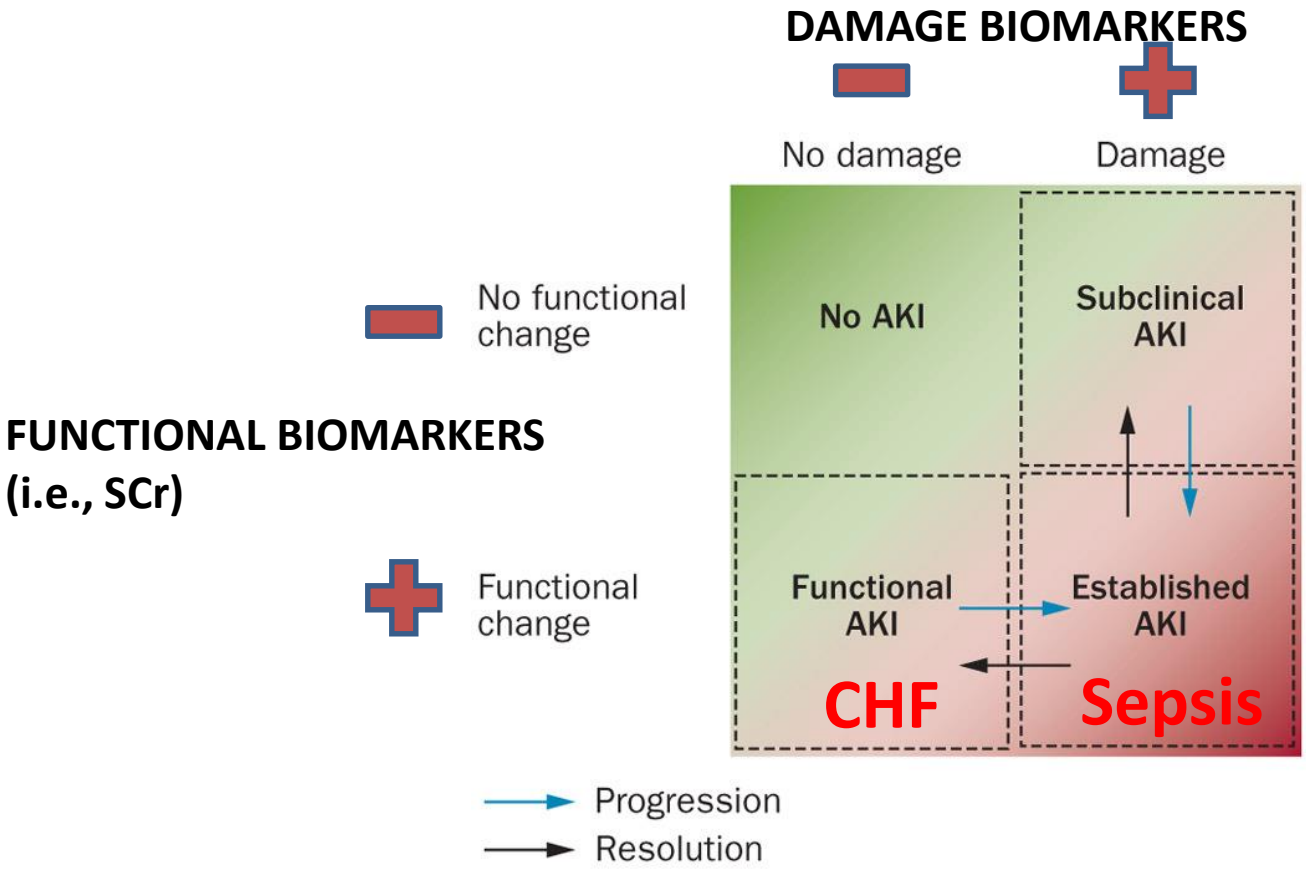


AKI Biomarkers



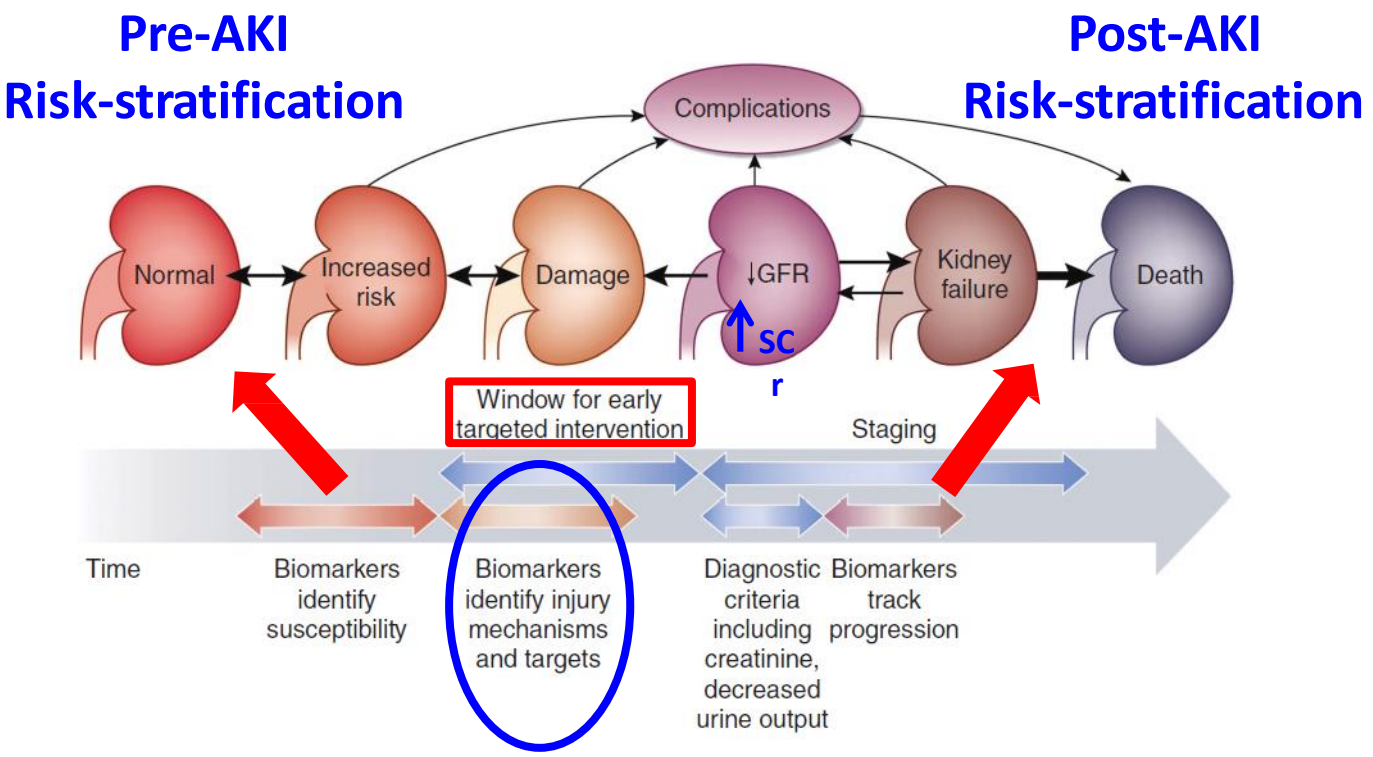
Bonventre JV et al. Nature 2010

Conceptual model of AKI



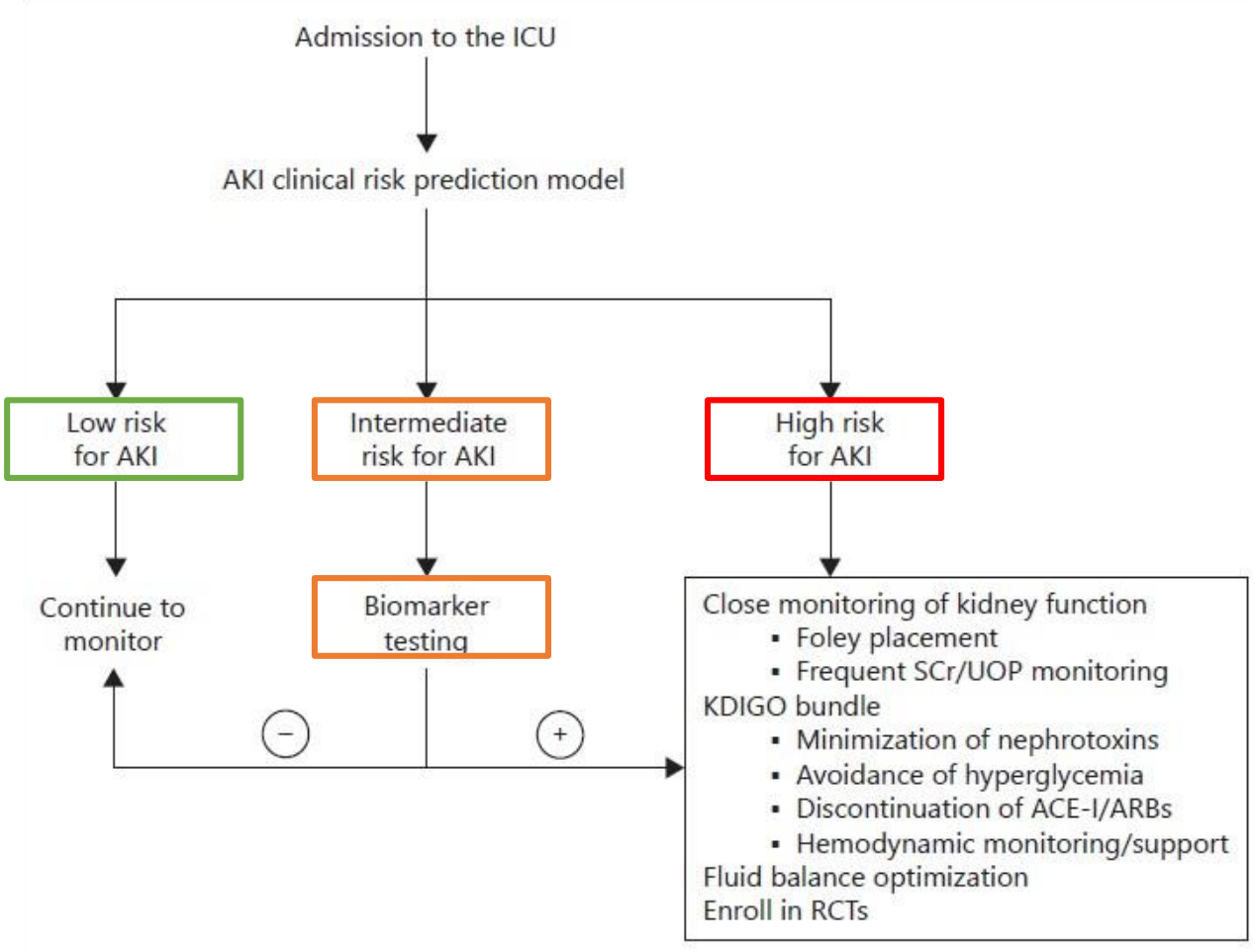
Cruz D et al. Nature Reviews Nephrology 2014

Conceptual model of AKI risk-stratification



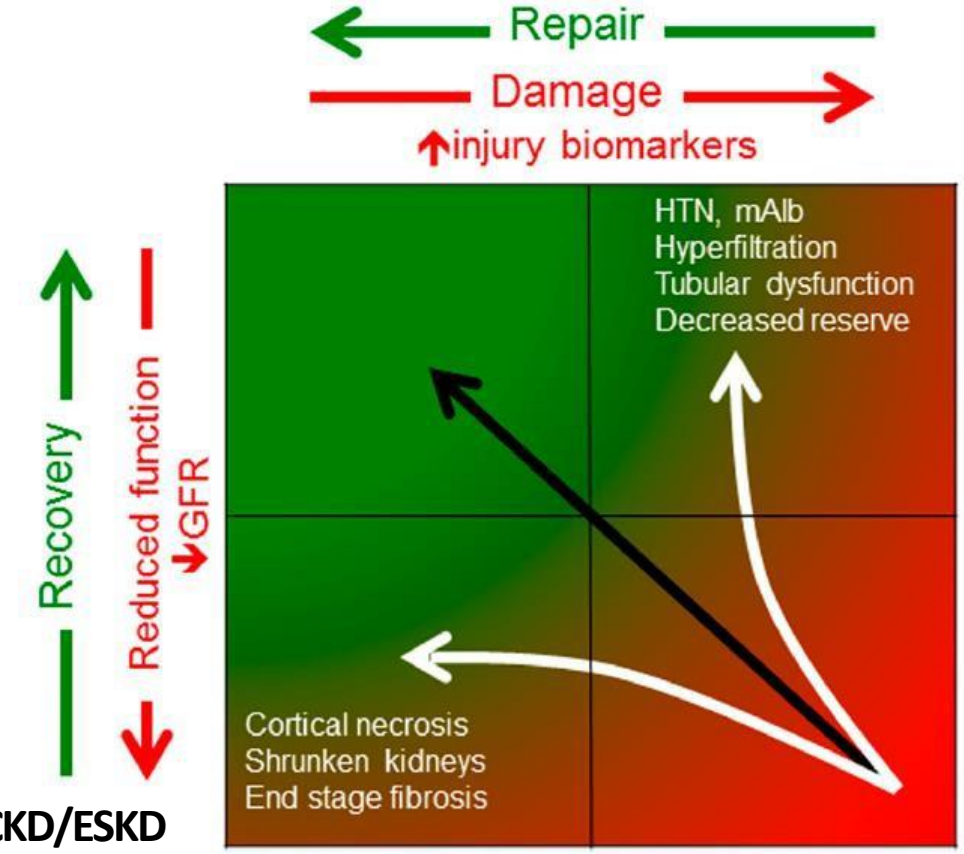
KDIGO Guidelines 2012

AKI risk-stratification: Incidence



Neyra JA et al. Nephron 2018

AKI risk-stratification: Recovery



Recurrent AKI

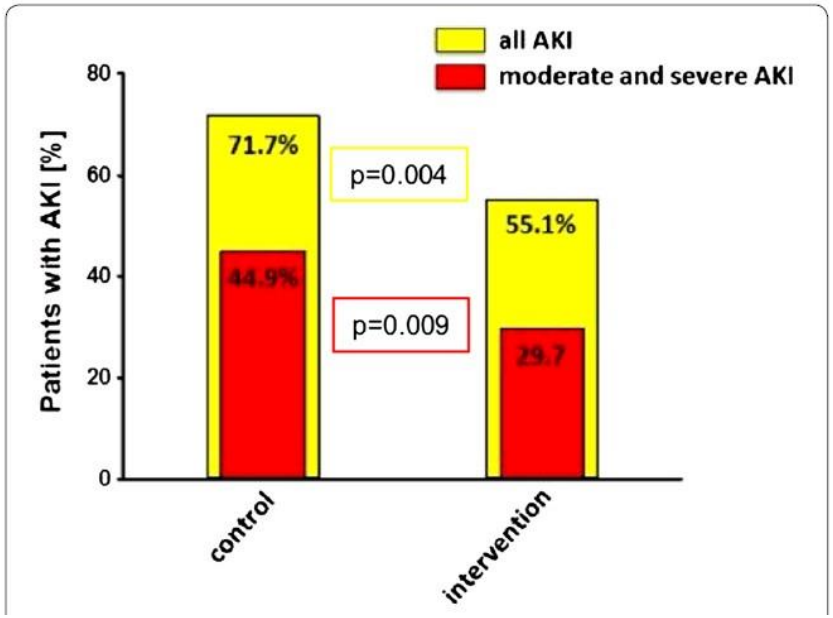
Progressive AKD → CKD/ESKD

Humphreys et al. JASN 2015

AKI risk-stratification: Intervention

Surgery — 48h — 72h

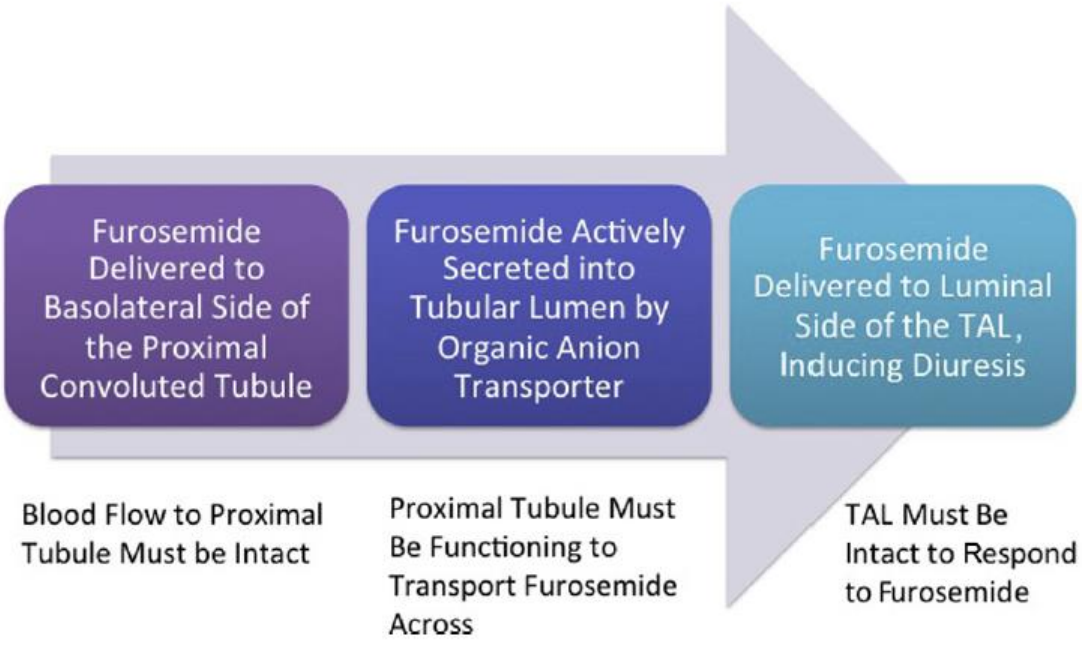
- Avoidance of nephrotoxic agents
- Withholding of ACEi and ARBs
- Close monitoring of SCr and urine output
- Avoidance of Hyperglycaemia
- Consider alternatives to radio-contrast agents
- Optimization of volume status and haemodynamic parameters



PrevAKI trial: 276 high-risk patients undergoing cardiac surgery with **TIMP2 x IGFBP7 >0.3** (4h after CPB disconnection)

Meersch et al. Intensive Care Med 2017

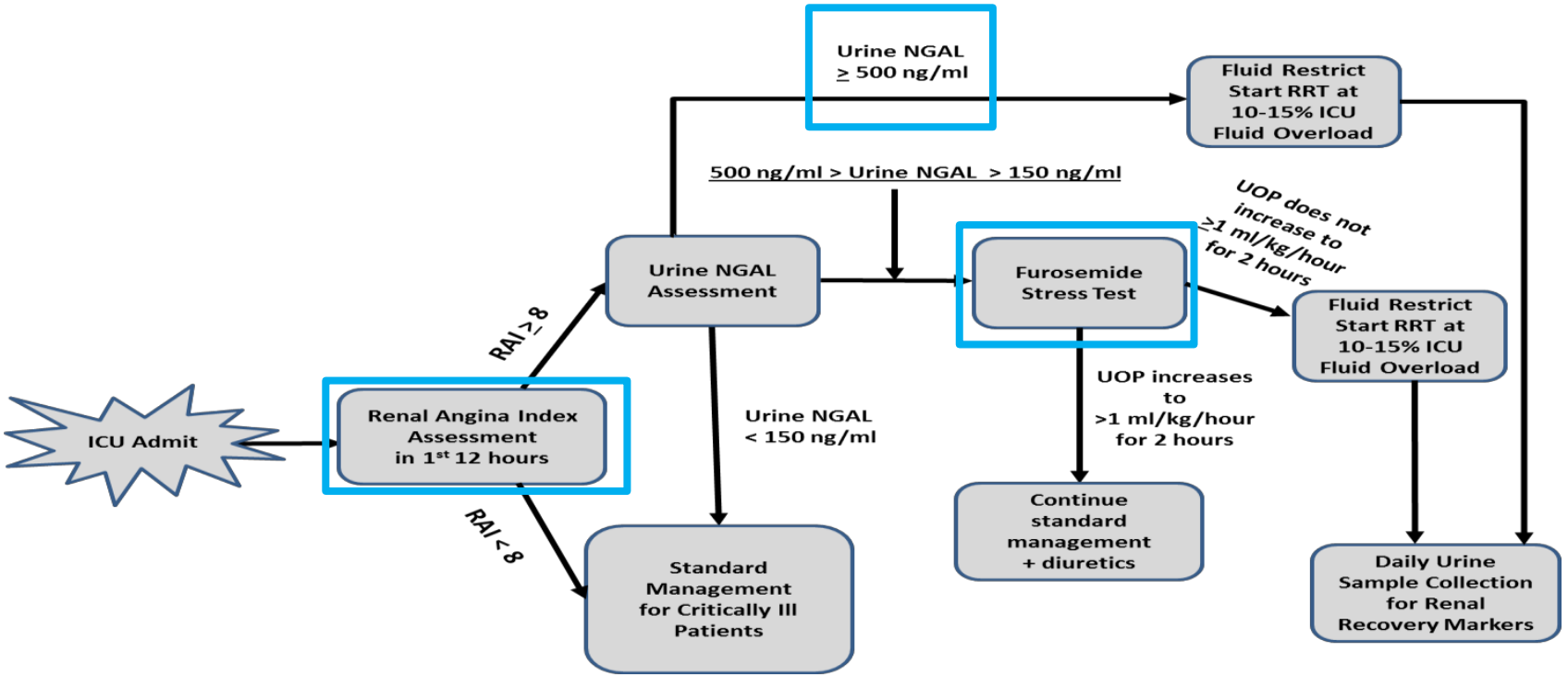
Furosemide Stress Test



- Furosemide Stress Test = 1-1.5 mg/kg for response of 200 ml x 2 hours ***for AKI progression**, outperformed biomarkers of injury (**AUC =0.87**)

Adapted from Chawla and Ronco, KI 2016

Combined model of risk-stratification



Funded by P50 DK096418-06

Courtesy of S. Goldstein

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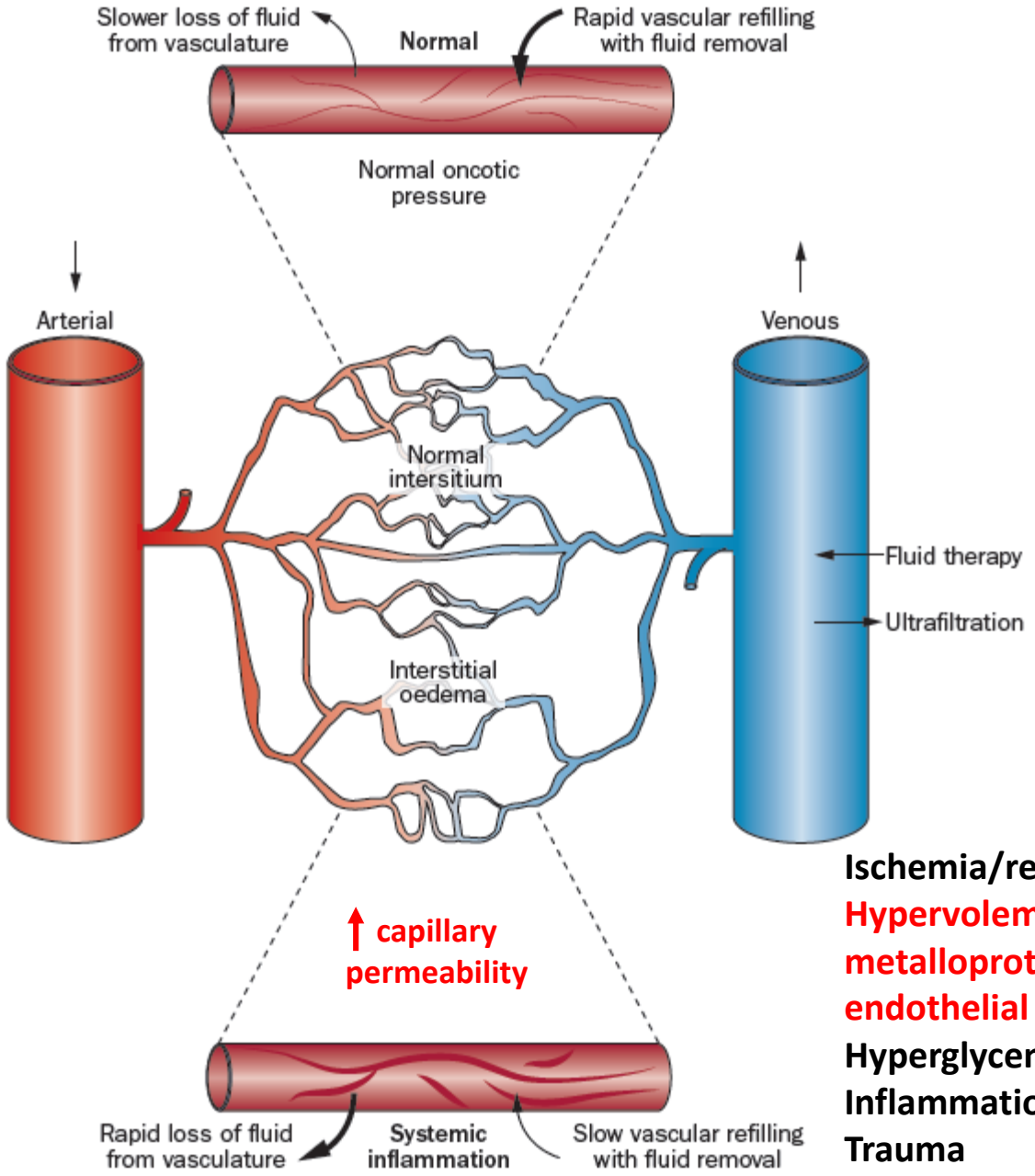
- AKI risk-stratification
- Fluid therapy and fluid overload
- Basic concepts of CRRT

What is fluid therapy?

- Fluid therapy is a key intervention to restore perfusion (O_2 delivery) in critical illness
- Fluid therapy is a key intervention in the prevention and treatment of AKI (restore MAP and CO → optimize RBF)
- Effect modifiers: myocardial performance, vascular tone, regional blood flow distribution, venous reservoir capacity and capillary permeability
- Limited window of efficacy

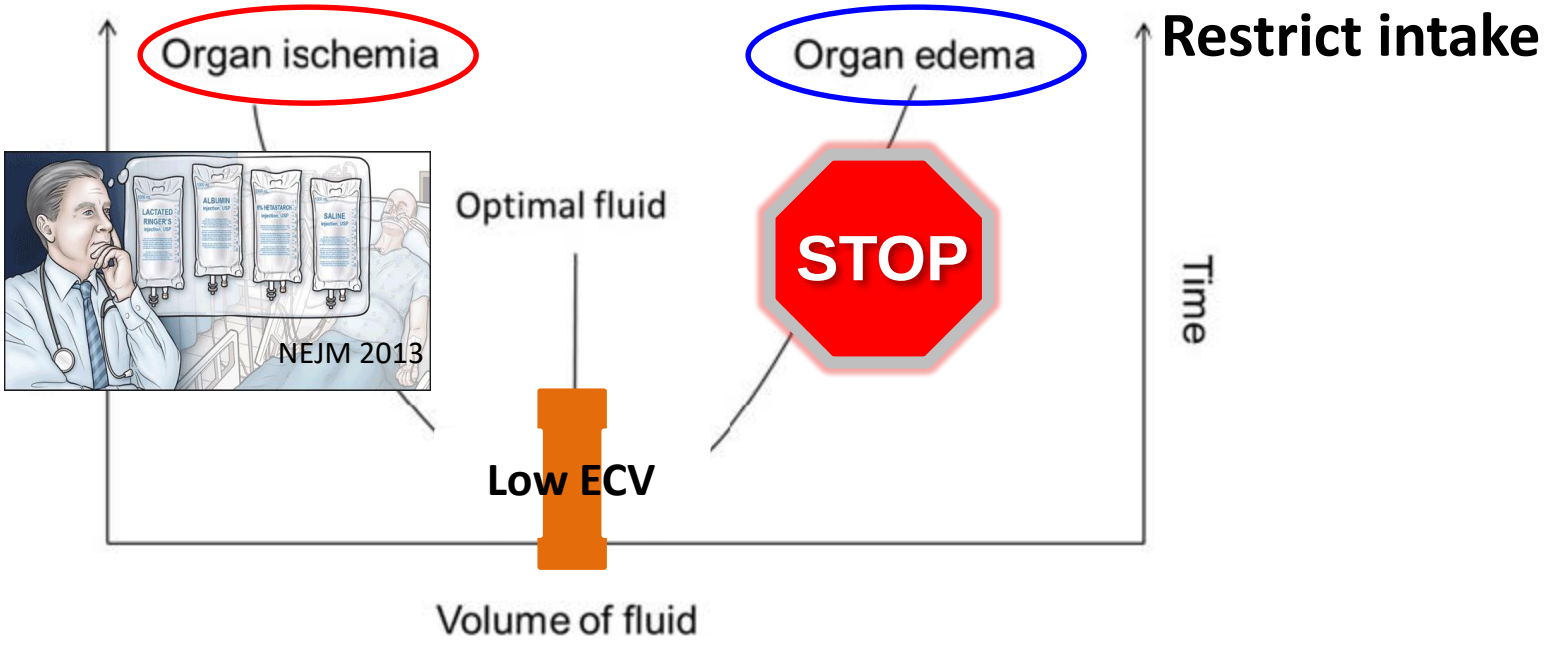


Ischemia/reperfusion
Hypervolemia: ANP → activates metalloproteinases → digest endothelial surface layer
Hyperglycemia
Inflammation
Trauma

Prowle, J. R. *et al. Nat. Rev. Nephrol.* **10**, 37–47 (2014)

Fluid Dynamics: U-shape

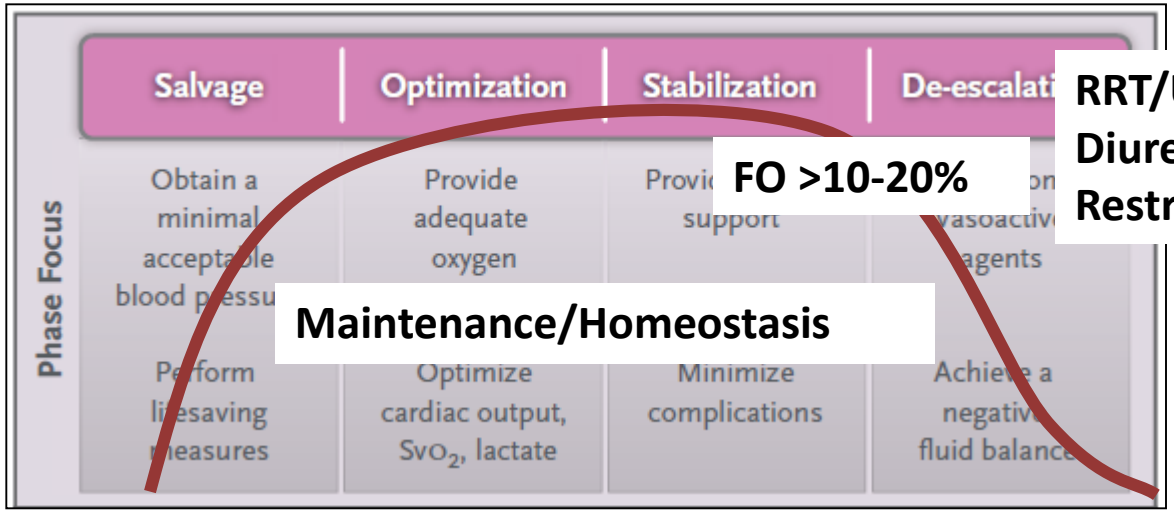
RRT/UF
Diuretics
Restrict intake



Crit Care Med 2012 Vol. 40, No. 6

ADQI 12: Goals of Resuscitation

Rescue/resuscitation **Optimize fluid balance**



RRT/UF
Diuretics
Restrict intake

Save the patient — Titration — Save the organs

type and amount

Fluid is a drug!

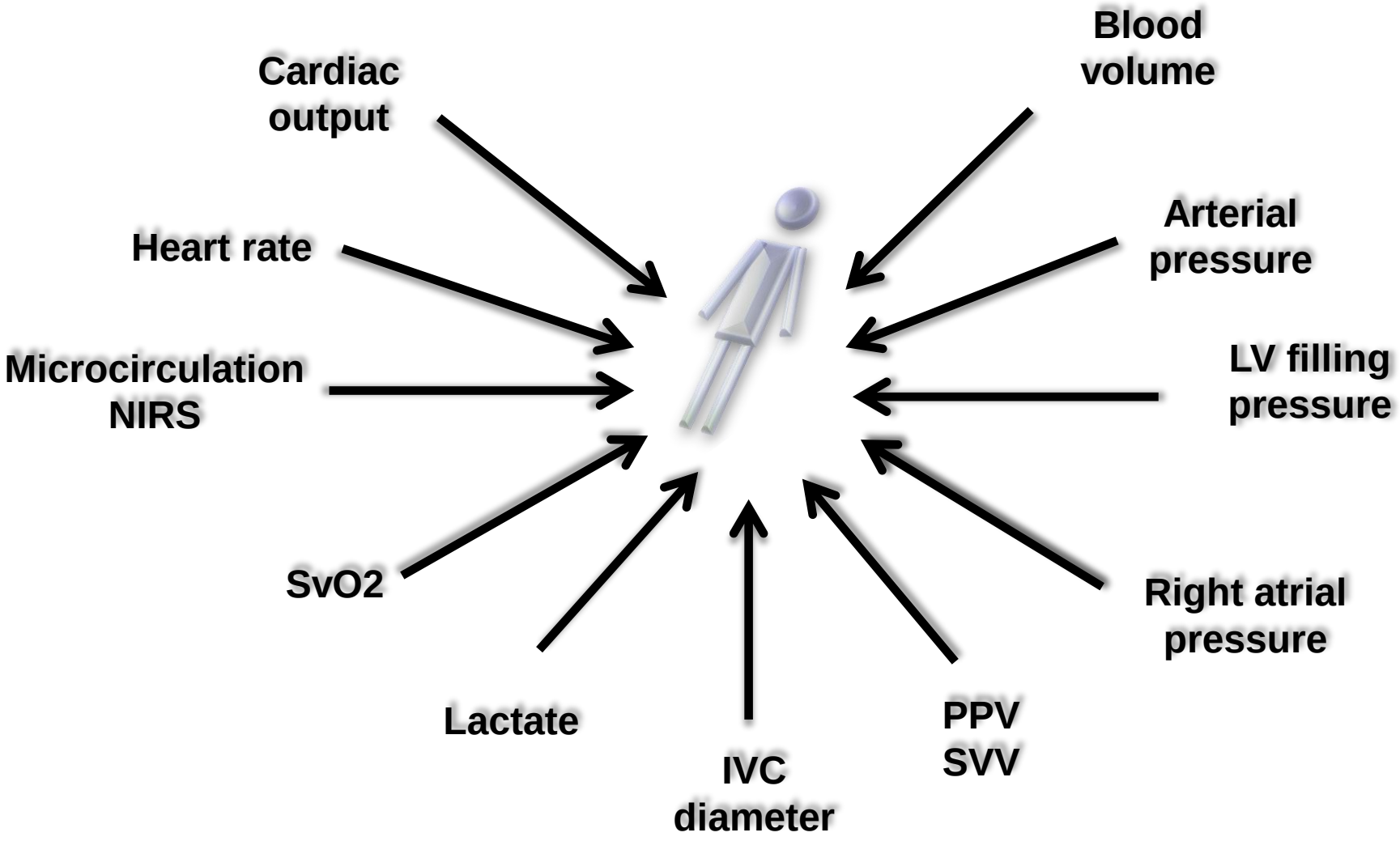
Not all hypotension needs fluid

N Engl J Med 2013;369:1726-34.

How to guide fluid therapy?

- Static tests: MAP, UOP, CVP/PCWP, CXR, lactate
- Functional tests: passive leg raising
- POCUS: TTE (subaortic VTI), lung US
- Respiratory variation tests: IVC collapse, SVV, PPV

How to guide fluid therapy?



Fluid Accumulation at Pediatric CRRT Initiation and Mortality

Author	Year	N	FO (Alive)	FO (Death)
Goldstein	2001	22	**16%**	**34%**
Gillespie	2004	77	**%FO >10% with OR death 3.02**	
Foland	2004	113	**8%**	**17%**
Goldstein (ppCRRT)	2005	116	**14%**	**25%**
Hayes	2009	76	**7%**	**22%**

A positive fluid balance is associated with a worse outcome in patients with acute renal failure

Didier Payen[1], Anne Cornélie de Pont[2], Yasser Sakr[3], Claudia Spies[4], Konrad Reinhart[3], Jean Louis Vincent[5] for the Sepsis Occurrence in Acutely Ill Patients (SOAP) Investigators

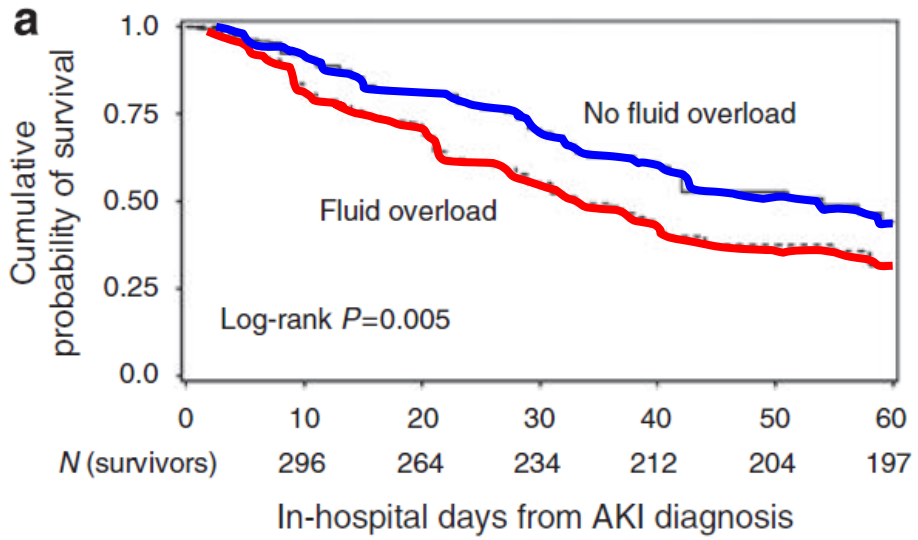
Critical Care 2008;12:R74

- Analysis of **SOAP study** patients with AKI (n =1120)
- **Survivors** had significantly lower mean daily fluid balance than non-survivors (**0.15L/day vs 0.98 L/day, *p* <0.001**)
  - Findings persisted when stratifying for timing of AKI, oliguria, and timing of RRT
- HR for 60-day mortality per +1L/24hr fluid balance was 1.21 (95% CI 1.13-1.28)

PICARD Study

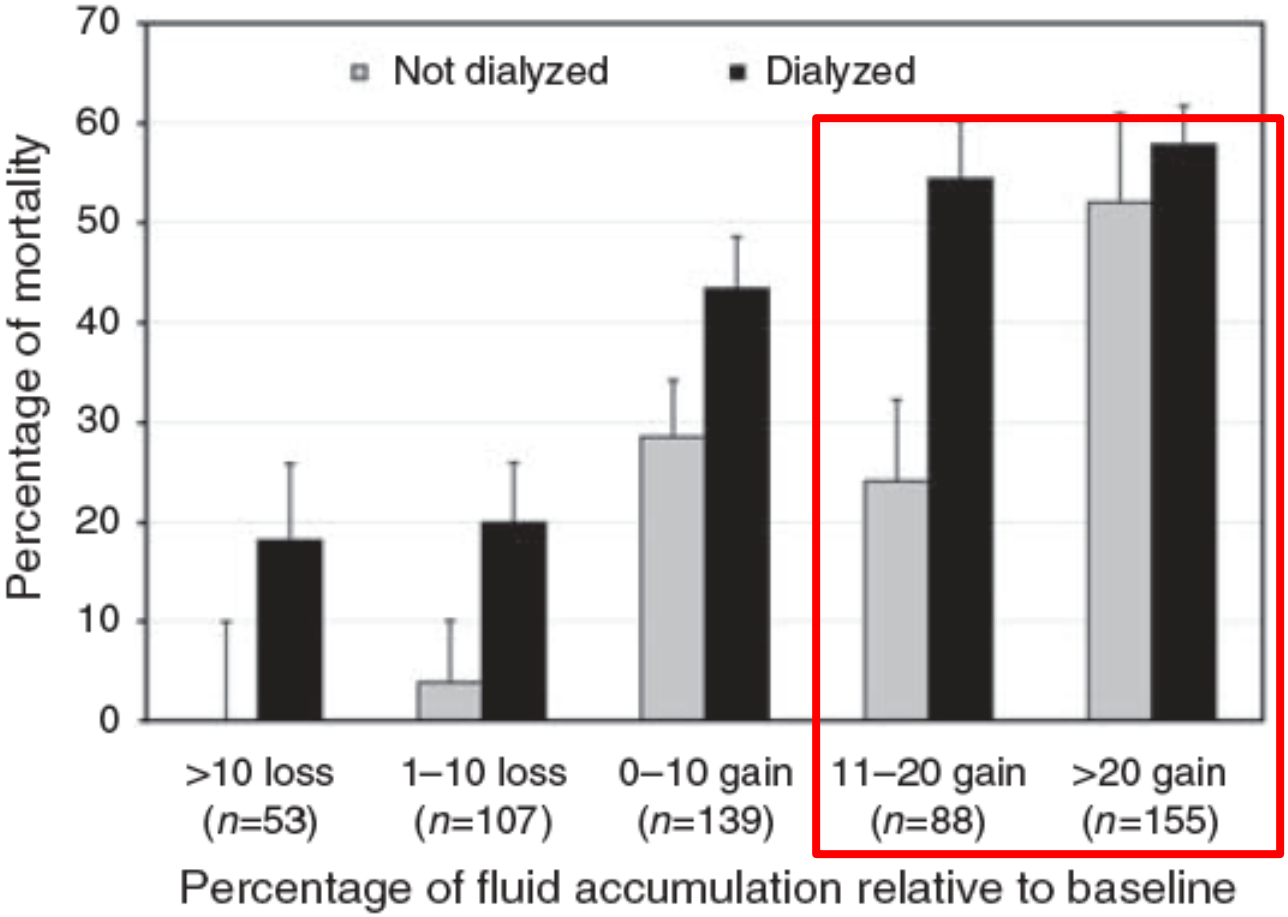
Bouchard *Kidney Int* 2009;76:422-7

- Prospective, multicenter, observational study of ICU AKI pts (n =618)
- **% FO = ∑(I-O)/admit wt x 100%**
  - Fluid balance for 3 days prior to renal consultation
  - FO defined as >10% accumulation
- FO at AKI diagnosis and RRT initiation associated with significantly higher 30d and 60d mortality



Adjusted mortality OR 2.07

Fluid overload is a risk factor for death in adult patients with AKI

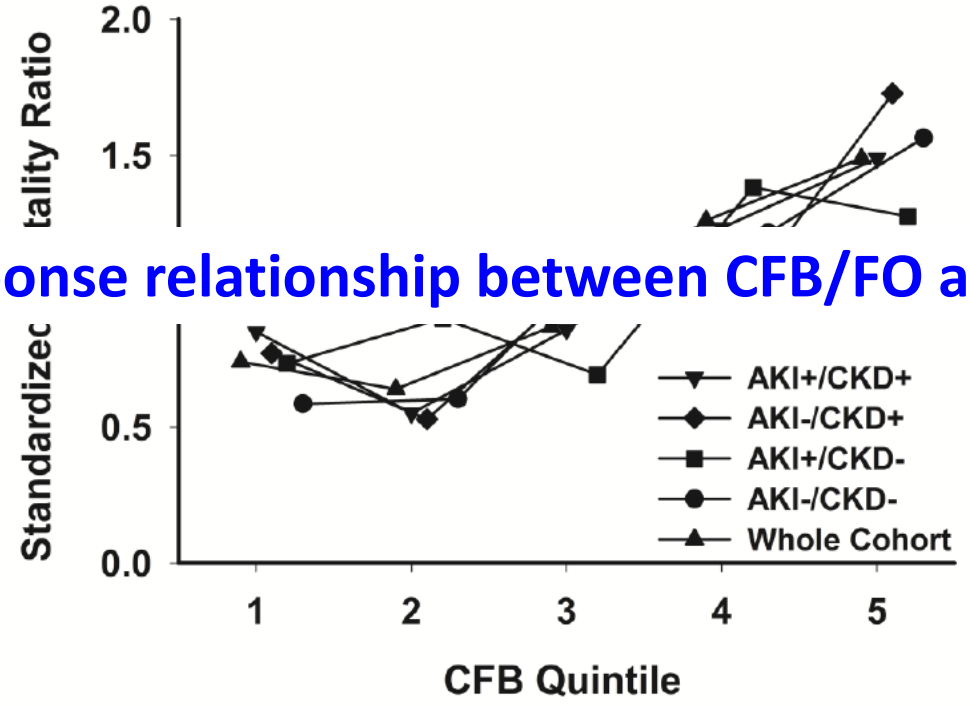


Bouchard et al, KI 2009

Cumulative Fluid Balance and Mortality in Septic Patients With or Without Acute Kidney Injury and Chronic Kidney Disease

Javier A. Neyra, MD, MSCS[1,2]; Xilong Li, PhD, MS[3]; Fabrizio Canepa-Escaro, MD[4]; Beverley Adams-Huet, MS[3]; Robert D. Toto, MD[1]; Jerry Yee, MD[5]; S. Susan Hedayati, MD, MHSc[1,6]; for the Acute Kidney Injury in Critical Illness Study Group

Critical Care Medicine 2016



Dose-response relationship between CFB/FO and mortality

Cumulative Fluid Balance and Mortality in Septic Patients With or Without Acute Kidney Injury and Chronic Kidney Disease

Javier A. Neyra, MD, MSCS[1,2]; Xilong Li, PhD, MS[3]; Fabrizio Canepa-Escaro, MD[4]; Beverley Adams-Huet, MS[3]; Robert D. Toto, MD[1]; Jerry Yee, MD[5]; S. Susan Hedayati, MD, MHSc[1,6]; for the Acute Kidney Injury in Critical Illness Study Group

Critical Care Medicine 2016

- **<u>Conclusions</u>**:

- Higher CFB 72 h of ICU admission was independently associated with hospital mortality regardless of AKI or CKD presence
- We characterized CFB cut-offs associated with hospital mortality based on AKI/CKD status, underpinning the heterogeneity of fluid regulation in sepsis and kidney disease

Fluid overload at initiation of renal replacement therapy is associated with lack of renal recovery in patients with acute kidney injury

Michael Heung[1,*], Dawn F. Wolfgram[2,*], Mallika Kommareddi[1], Youna Hu[3], Peter X. Song[3] and Akinlolu O. Ojo[1]

***Nephrol Dial Transplant* 2012**

- Analysis of pts with ATN requiring RRT (n =170), followed up to 1 year for primary outcome of renal recovery (dialysis independence)
- **FO associated with increased 1-yr mortality (adjusted OR 1.04 per 1% FO, *p* =0.01)**

Table 2. Cox regression model of risk for renal recovery within 1 year of dialysis initiation ($n = 170$)[a]

Predictor	Hazard ratio	95% CI	P-value
% FO at initiation (per 1%)	0.97	(0.95–1.00)	0.024
≥1 comorbidity	0.51	(0.30–0.89)	0.018
Baseline serum creatinine (per 1 mg/dL)	0.56	(0.37–0.87)	0.009
Use of vasopressors	0.49	(0.28–0.85)	0.011
Time between consult and initiation (per day)	0.84	(0.72–0.98)	0.025

[a]FO, Fluid overload.

Dose-Response Relationship between FO at the time of CRRT initiation and mortality

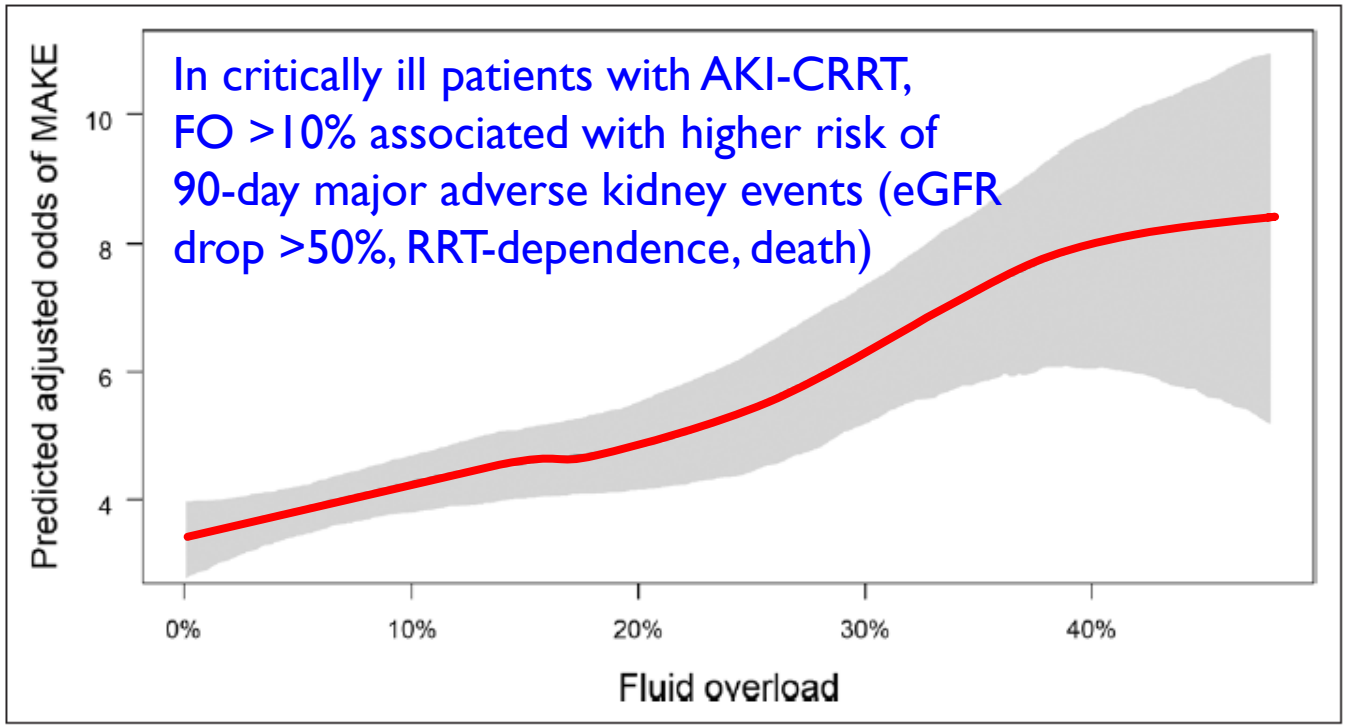


Figure 2. Cubic spline showing the effect of fluid overload (FO) on the odds of major adverse kidney events (MAKE), as calculated by logistic regression treating FO as a continuous variable, excluding patients with FO less than 0%. *Shaded area* corresponds to 95% CI.

Woodward C… Neyra JA. Critical Care Medicine 2019

Acute kidney injury in patients with acute lung injury: Impact of fluid accumulation on classification of acute kidney injury and associated outcomes*

Kathleen D. Liu, MD; B. Taylor Thompson, MD; Marek Ancukiewicz; Jay S. Steingrub, MD; Ivor S. Douglas, MD; Michael A. Matthay, MD; Patrick Wright, MD; Michael W. Peterson, MD; Peter Rock, MD; Robert C. Hyzy, MD; Antonio Anzueto, MD; Jonathon D. Truwit, MD, MBA; for the National Institutes of Health National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Network

Table 1. Development of AKI by treatment group before and after adjustment of serum creatinine for fluid balance[a]

	Liberal		Conservative		*p* Liberal vs. Conservative	
AKIN stage 3, no. (%)	75 (15%)	89 (18%)	75 (15%)	83 (17%)	.94	.56

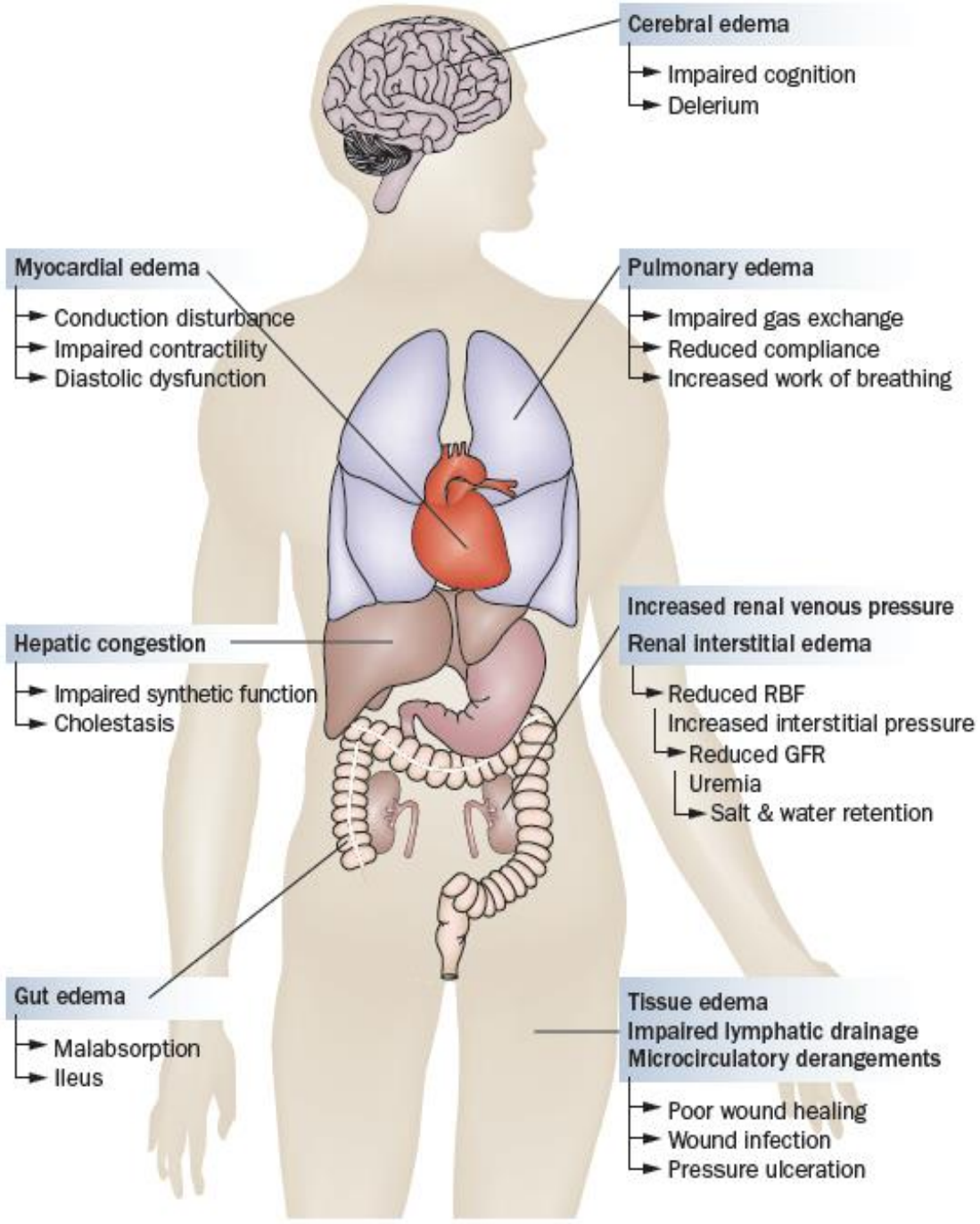
AKI stage 1 pts identified after adjustment of FB had similar mortality rates than those with AKI stage 1 independently of FB (~30% mortality rates)

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network.

[a]There was no difference in the incidence of AKI by pulmonary artery catheter vs. central venous catheter management groups.

1000 critically-ill pts from FACT trial

Crit Care Med 2011 Vol. 39, No. 12

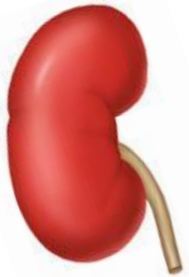


Fluid overload has many potentially deleterious effects

- Impairs oxygen and metabolite diffusion
- Disturbs cell-cell interaction
- Distorts tissue architecture
- Impedes organ perfusion, venous outflow and lymphatic drainage

Prowle *et al*, Nat Rev Neph 2010

Fluid Overload and the Kidney



- Expansion of interstitial space and increased venous pressure (e.g., ACS) may initiate and maintain AKI
- Venous congestion: increased venous pressure → increased renal subcapsular pressure → decreased RBF and GFR
- Interstitial edema ←→ inflammation

Fluid Overload and Adverse Outcomes

- FO at AKI diagnosis is associated with increased mortality
- FO at the beginning of RRT is associated with increased mortality and impaired renal recovery
- **Is FO a marker of severity of illness or has a modifiable causative role in AKI?**

Fluid Regulation

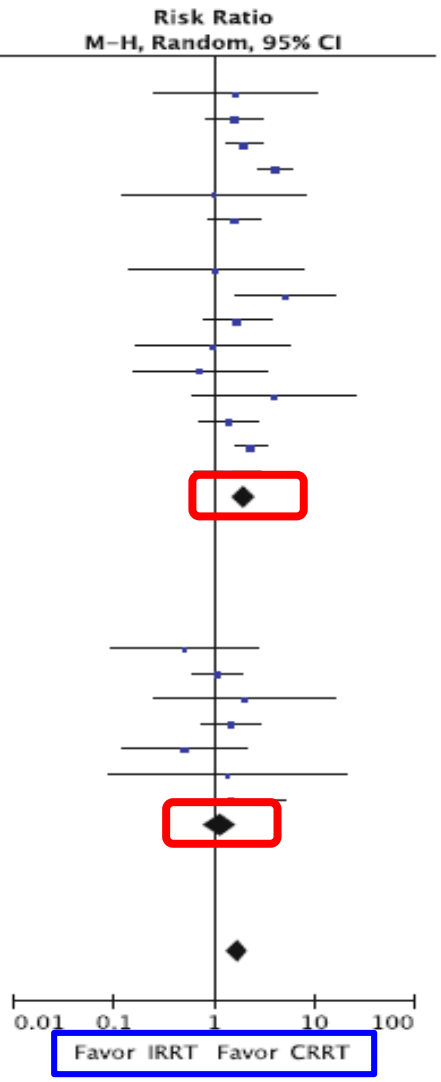
- **When FB cannot be adequately controlled in critically ill pts with AKI → RRT within the first 12-24 h to limit FO**
- Rapid transition to iHD may impact renal recovery and slow resolution of edema, even when a pt has regained hemodynamic stability

Antoine G. Schneider
Rinaldo Bellomo
Sean M. Bagshaw
Neil J. Glassford
Serigne Lo
Min Jun
Alan Cass
Martin Gallagher

Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systematic review and meta-analysis

Intensive Care Med (2013) 39:987–997
DOI 10.1007/s00134-013-2864-5

Study or Subgroup	IRRT Events	IRRT Total	CRRT Events	CRRT Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Observational						
Andrikos 2009	1	4	5	33	1.5%	1.65 [0.25, 10.81]
Bagshaw 2006	15	42	12	54	7.0%	1.61 [0.84, 3.06]
Bell 2007	26	158	78	944	9.8%	1.99 [1.32, 3.00]
CartinCeba 2009	256	555	26	229	10.3%	4.06 [2.80, 5.90]
Chang 2004	4	44	1	11	1.3%	1.00 [0.12, 8.08]
Elsevier 2010	37	175	13	98	7.7%	1.59 [0.89, 2.85]
Garcia-Fernandes 2011	0	16	0	55		Not estimable
Gonwa 2001	1	6	4	25	1.4%	1.04 [0.14, 7.71]
Jacka 2005	9	14	3	24	3.5%	5.14 [1.66, 15.89]
Lin 2009	11	54	10	83	5.7%	1.69 [0.77, 3.71]
Lins 2006	9	37	1	4	1.6%	0.97 [0.16, 5.83]
Marshall 2012	5	56	2	16	2.1%	0.71 [0.15, 3.34]
Park 2005	37	83	1	9	1.5%	4.01 [0.62, 25.86]
Swartz 2005	24	110	10	64	6.7%	1.40 [0.71, 2.73]
Uchino 2007	37	110	52	360	10.5%	2.33 [1.62, 3.35]
Waldrop 2005	7	12	6	14	5.8%	1.36 [0.63, 2.94]
Subtotal (95% CI)		**1476**		**2023**	**76.4%**	**1.99 [1.53, 2.59]**
Total events	479		224			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 24.14$, df = 14 (P = 0.04); $I^2 = 42\%$						
Test for overall effect: Z = 5.14 (P < 0.00001)						
1.1.2 RCT						
Abe 2010	2	25	3	19	1.8%	0.51 [0.09, 2.74]
Augustine 2004	8	12	8	13	7.6%	1.08 [0.60, 1.95]
Kumar 2004	3	12	1	8	1.3%	2.00 [0.25, 15.99]
Lins 2009	15	60	11	65	6.5%	1.48 [0.74, 2.96]
Mehta 2001	3	43	4	29	2.4%	0.51 [0.12, 2.09]
Uehlinger 2005	1	27	1	37	0.8%	1.37 [0.09, 20.95]
Vinsonneau 2006	6	61	4	61	3.1%	1.50 [0.45, 5.05]
Subtotal (95% CI)		**240**		**232**	**23.6%**	**1.15 [0.78, 1.68]**
Total events	38		32			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.20$, df = 6 (P = 0.78); $I^2 = 0\%$						
Test for overall effect: Z = 0.71 (P = 0.48)						
Total (95% CI)		**1716**		**2255**	**100.0%**	**1.73 [1.35, 2.20]**
Total events	517		256			
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 37.19$, df = 21 (P = 0.02); $I^2 = 44\%$						
Test for overall effect: Z = 4.36 (P < 0.0001)						
Test for subgroup differences: $Chi^2 = 5.45$, df = 1 (P = 0.02), $I^2 = 81.7\%$						



The Association Between Renal Replacement Therapy Modality and Long-Term Outcomes Among Critically Ill Adults With Acute Kidney Injury: A Retrospective Cohort Study

Ron Wald, MDCM, MPH, FRCPC[1,2]; Salimah Z. Shariff, PhD[3]; Neill K. J. Adhikari, MDCM, MSc, FRCPC[4,5]; Sean M. Bagshaw, MD, FRCPC[6]; Karen E. A. Burns, MD, MSc, FRCPC[2,5,7]; Jan O. Friedrich, MD, MSc, DPhil, FRCPC[2,5,7]; Amit X. Garg, MD, PhD, FRCPC[3,8]; Ziv Harel, MD, MSc, FRCPC[1,2]; Abhijat Kitchlu, MD[1,2]; Joel G. Ray, MD, MSc, FRCPC[2,3,9]

April 2014 • Volume 42 • Number 4

TABLE 2. O … iated on Continuo…

Outcome		p
Chronic dial…		< 0.0001
Death		0.73

CRRT = continuc…

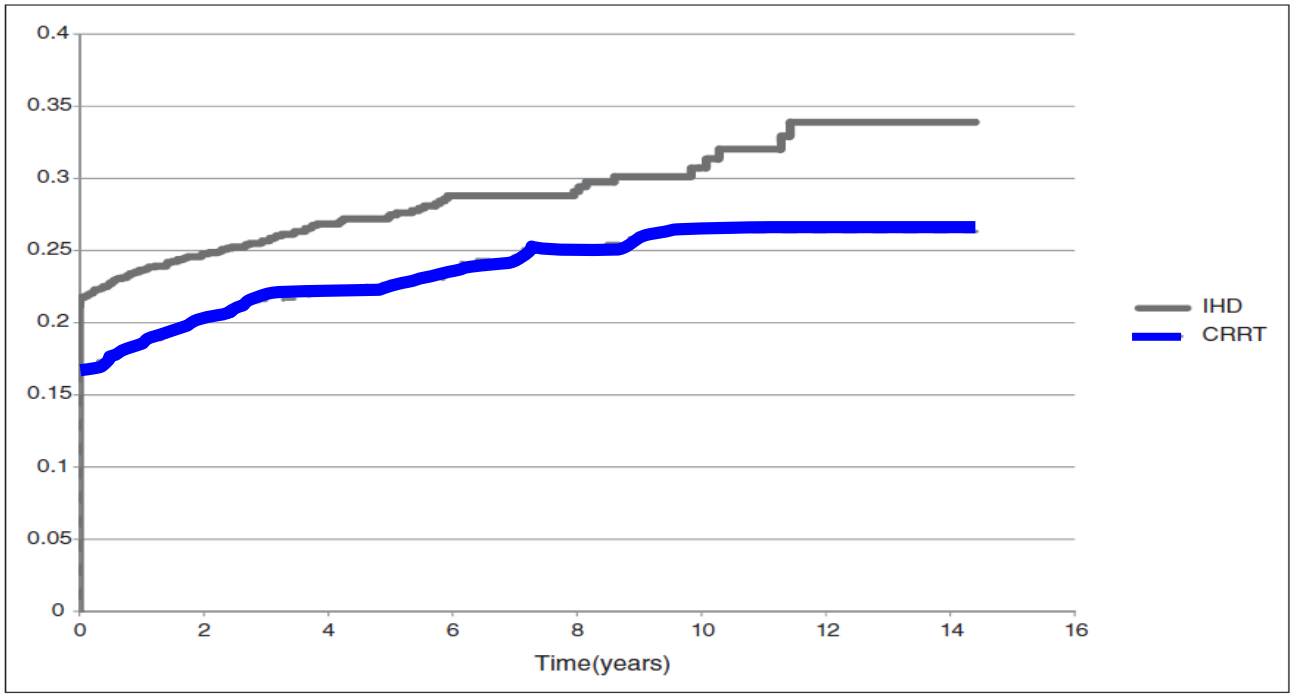


Figure 2. Cumulative risk of chronic dialysis among critically ill patients with acute kidney injury surviving to day 90 after commencement of renal replacement therapy who were initially treated with continuous renal replacement therapy (CRRT) (*dashed line*) versus intermittent hemodialysis (IHD) (*solid line*).

Outline

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Indications for the initiation of renal replacement therapy in AKI

- Classic indications
- hyperkalemia
- severe metabolic acidosis
- volume overload
- oligoanuria
- uremic complications
- drug intoxications

- Potential indications
- Hemodynamic instability
- catabolic states
- sepsis
- increased ICP

Tolwani. NEJM 2012

CRRT vs intermittent HD

	CRRT	IHD
Tx Time	Continuous	3-4hrs, Q1-2d
BFR (mL/min)	100-200	>350
DFR	2000-3000 mL/hr (33-50mL/min)	500-800 mL/min
Dialysate: Na	136 mEq/L	may vary
K	2, 3, 4 mEq/L	0-4 mEq/L
HCO3	25 (32) mEq/L	34-38 mEq/L
Phos	0, 0.75,1.5mmol/L	none
Ca	none	2.5-3.5 mEq/L
Anticoagulation	Regional (citrate)	Systemic (heparin)

CRRT vs intermittent HD

Advantages

- Greater hemodynamic stability
- *lower UFR, hypothermia, slower reduction of ECF osmolality (fluid shift), slower change in ECF electrolytes (resting membrane potentials)*
- Better fluid regulation
- Greater solute control (large Vd)
- Lower bleeding risk
- More physiologic

Disadvantages

- Requires anticoagulation
- Hypothermia
- Hypophosphatemia
- Slow correction of severe electrolyte abnormalities
- Limits patient freedom for procedures, studies, PT/OT
- RN labor intensive
- Higher cost

Is There a Survival Benefit: CRRT vs iHD?

	Design	n	CRRT	Survival	Comments
Mehta (KI 2001)	Multictr PRCT, ITT	160	CVVHDF (DFR 1L/hr, UF 400-800mL/hr)	- Unadj in-hosp mortality 65.5% vs 47.6%, p<.02 - Adj odds ratio for death = ns	- Low dose therapy - Randomization failure - High crossover - No diff in renal recovery
Augustine (AJKD 2004)	Single-ctr, PRCT, ITT	80	CVVHD (BFR 200, variable DFR)	- Hosp mortality 67.5% vs 70%, p = ns	- No diff in renal recovery - Better hemodynamic stability with CRRT - More negative fluid balance with CRRT
Uehlinger (NDT 2005)	Single-ctr, PRCT	125	CVVHDF (BFR 100-180, efflu 2000mL/hr	- Hosp mortality 47% vs 51%, p=.72	- No cross-over allowed - No diff in hemodynamic stability - No diff in renal recovery
Vinsonneau (Lancet 2006)	Multi-ctr PRCT	360	CVVHDF	- 60d survival 32.6% vs 31.5%, p=.98	- No differences in LOS, renal recovery, or hemodynamic stability - Mean IHD tx time 5.2h - IHD survival improved during study period
Lins (NDT 2009)	Multi-ctr PRCT	316	CVVH	- Hosp mortality 58.1% vs 62.5%, p=.43	- No differences in renal recovery at discharge

Potential reasons for pre-emptive "early" RRT

- **Fluid overload**
- Faster restoration of acid-base balance
- Accelerated removal of small and middle-sized molecules
- Mitigation of inflammation

Caution for “early” RRT initiation

- Many patients with severe AKI will recover renal function
- RRT-related risks
- Dialysis access-related risks
- Health care cost

TABLE 1: Comparison between recent randomized clinical trials addressing early vs delayed initiation of RRT in critically ill patients with AKI

Characteristics	AKIKI Trial	ELAIN Trial	IDEAL Trial
Participating sites	31 (France)	1 (Germany)	29 (France)
Total number of participants	620	231	488
Early RRT definition	KDIGO stage 3	KDIGO stage 2	KDIGO stage 3
Delayed RRT definition	BUN >112, K >6, pH <7.15, pulmonary edema, oliguria for >72 h	<12 h KDIGO stage 3 or absolute indications	>48 h KDIGO stage 3 or absolute indications
Timing from randomization to initiation of RRT, median	2 h (early) vs 57 h (delayed)	6 h (early) vs 25.5 h (delayed)	7.6 h (early) vs 51.5 h (delayed)
SOFA score, mean	11	16	12
CKD, %	10	41	15
Septic shock, %	67	32	100
Surgical intervention, %	21	97	–
RRT modality at initiation	HD, SLED, or CRRT	CRRT	HD, SLED, or CRRT
Primary endpoint	60-day mortality	90-day mortality	90-day mortality
Mortality – Early, %	49	39	58
Mortality – Delayed, %	50	55	54
Received RRT in delayed arm, %	51	91	62

Note: KDIGO = Kidney Disease: Improving Global Outcomes; HD = hemodialysis; SLED = sustained low-efficiency dialysis.

Neyra JA and Hauschild CE. Chest Physician 2019

Factors to Consider for RRT Initiation

Severity of AKI

- Creatinine & urea and trajectories
- Urine output / fluid status
- Electrolyte derangement
- Acid base status
- Complications of uremia

Severity of Critical Illness

- Inciting event leading to AKI
- Non-renal organ dysfunction
- Degree of fluid overload
- Pre-existing comorbidities
- Trajectory

Potential Risks of RRT

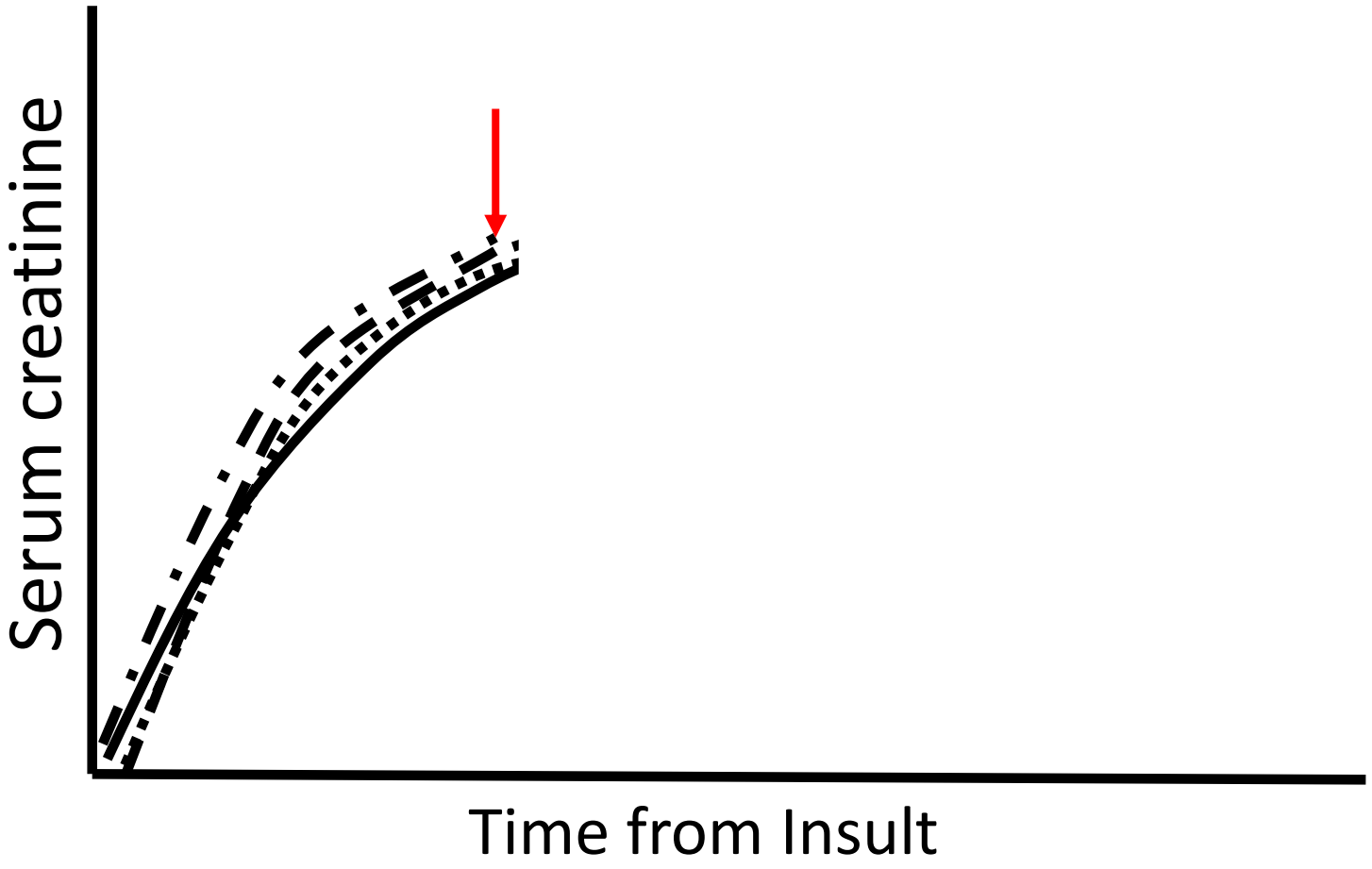
- Line insertion
- Hypotension during RRT
- Clearance of nutrients/drugs

Other Factors

- Availability of machines
- Availability of staff
- Patient's / relatives' wishes
- Futility / long-term prognosis

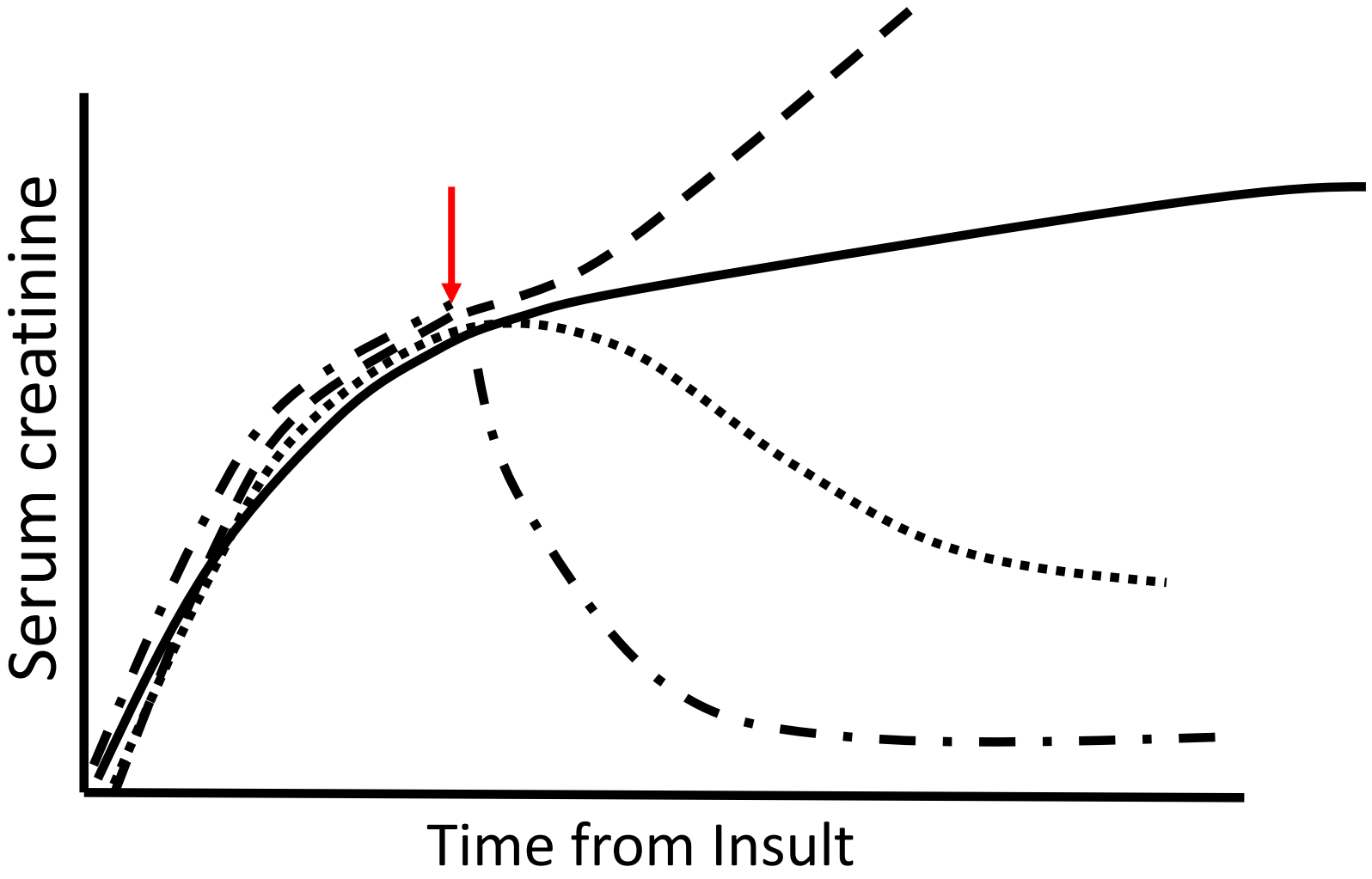
Challenges in Clinical Practice

Prediction of AKI progression



Challenges in Clinical Practice

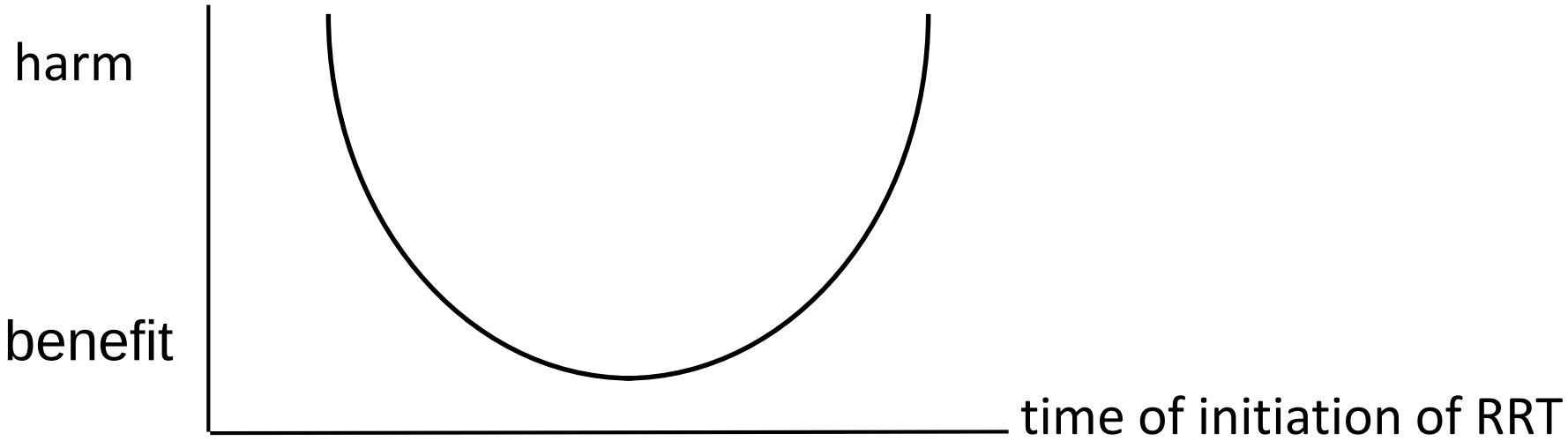
Prediction of AKI progression



Starting RRT – An Individualized Approach

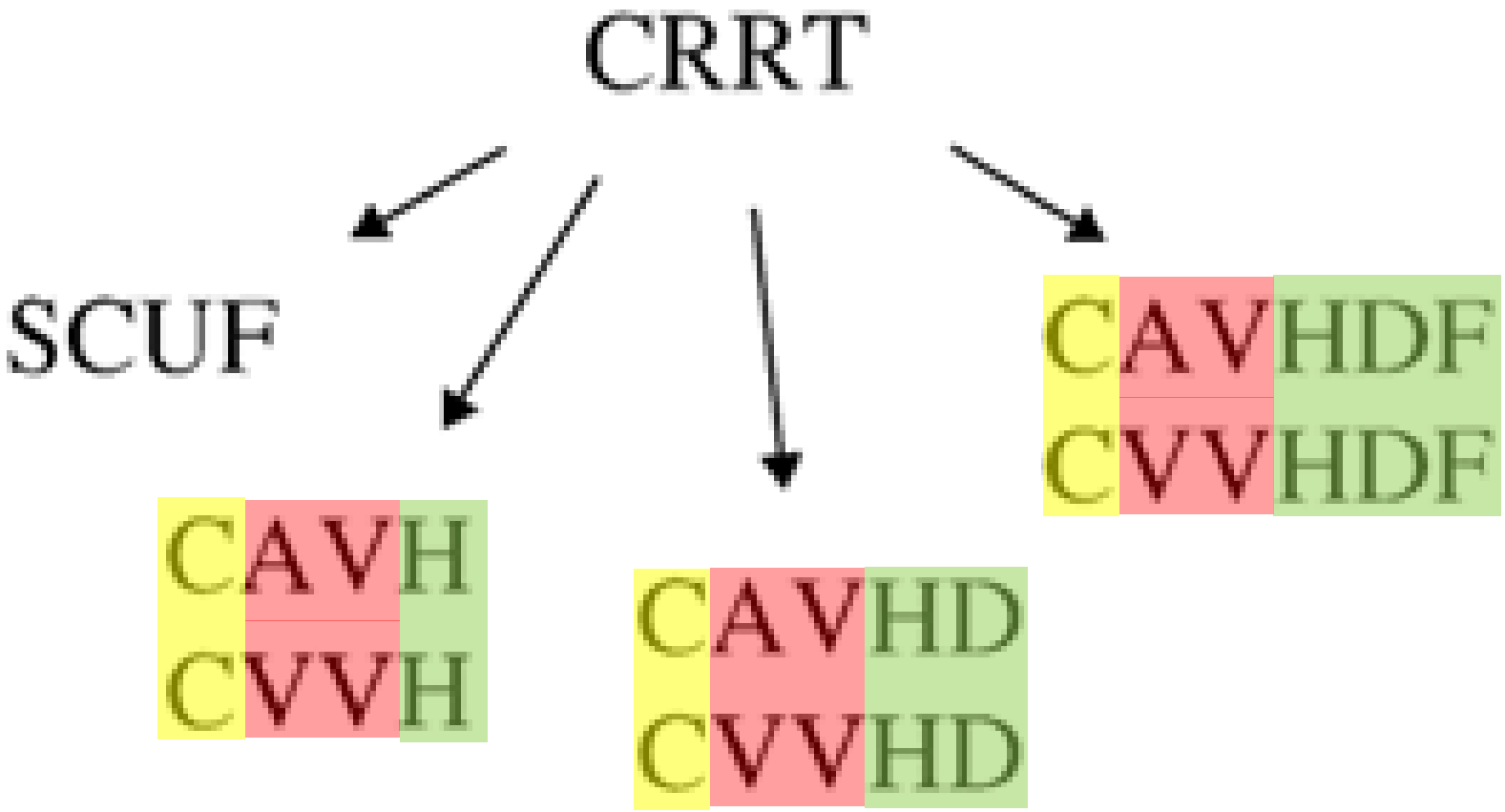
Key principles:

1. **Kidneys have limited capacity.**
2. **The degree and impact of fluid & metabolic derangement vary between patients.**



"early RRT" for one patient may be "too late" for a different patient

Nomenclature

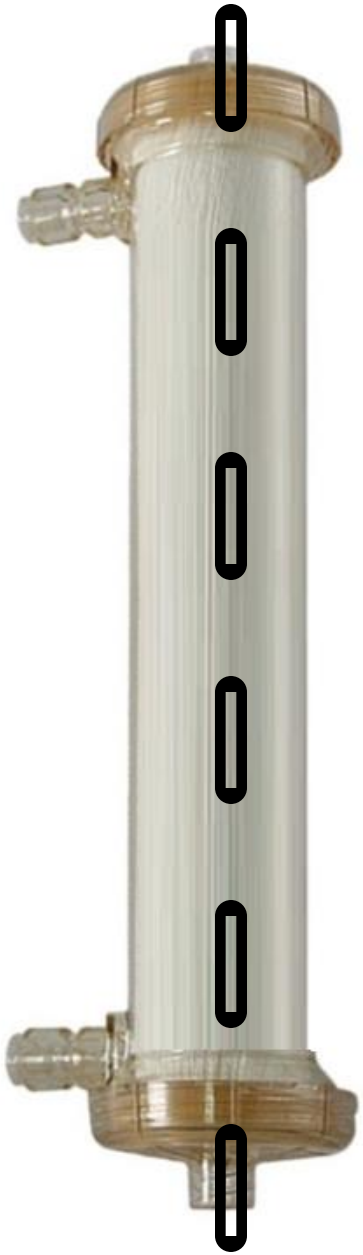


HD =hemodialysis

HF or H =hemofiltration

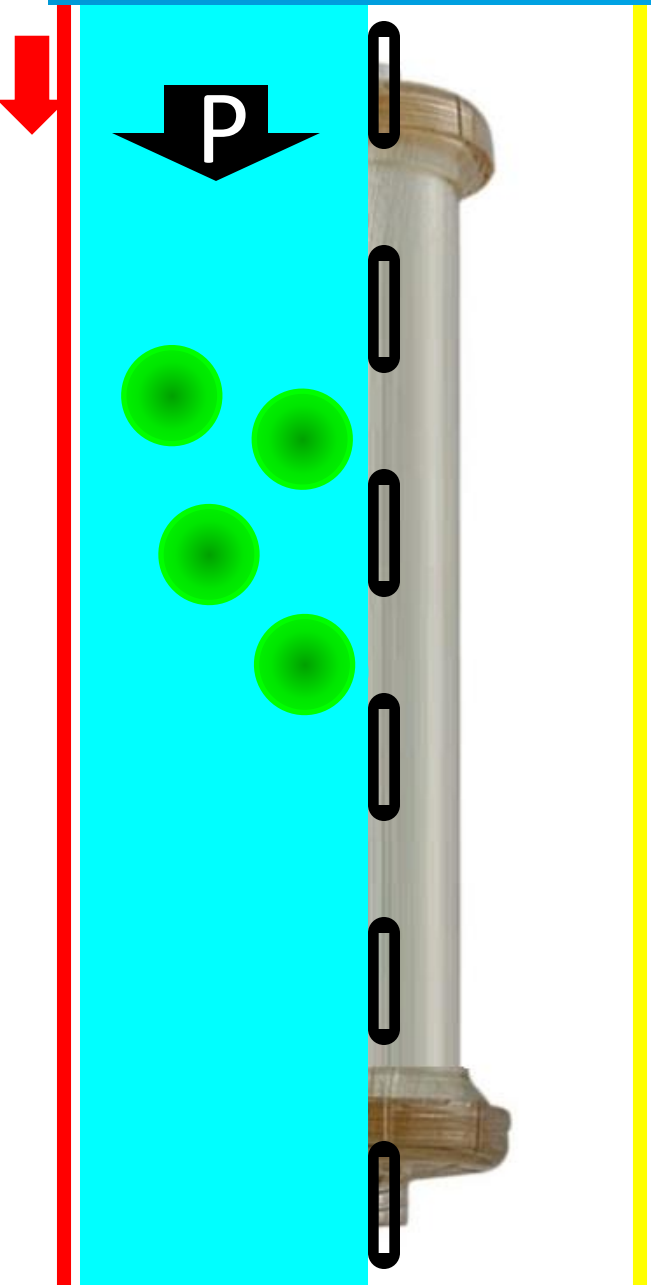
HDF =hemodiafiltration

Hemodialysis: Diffusion



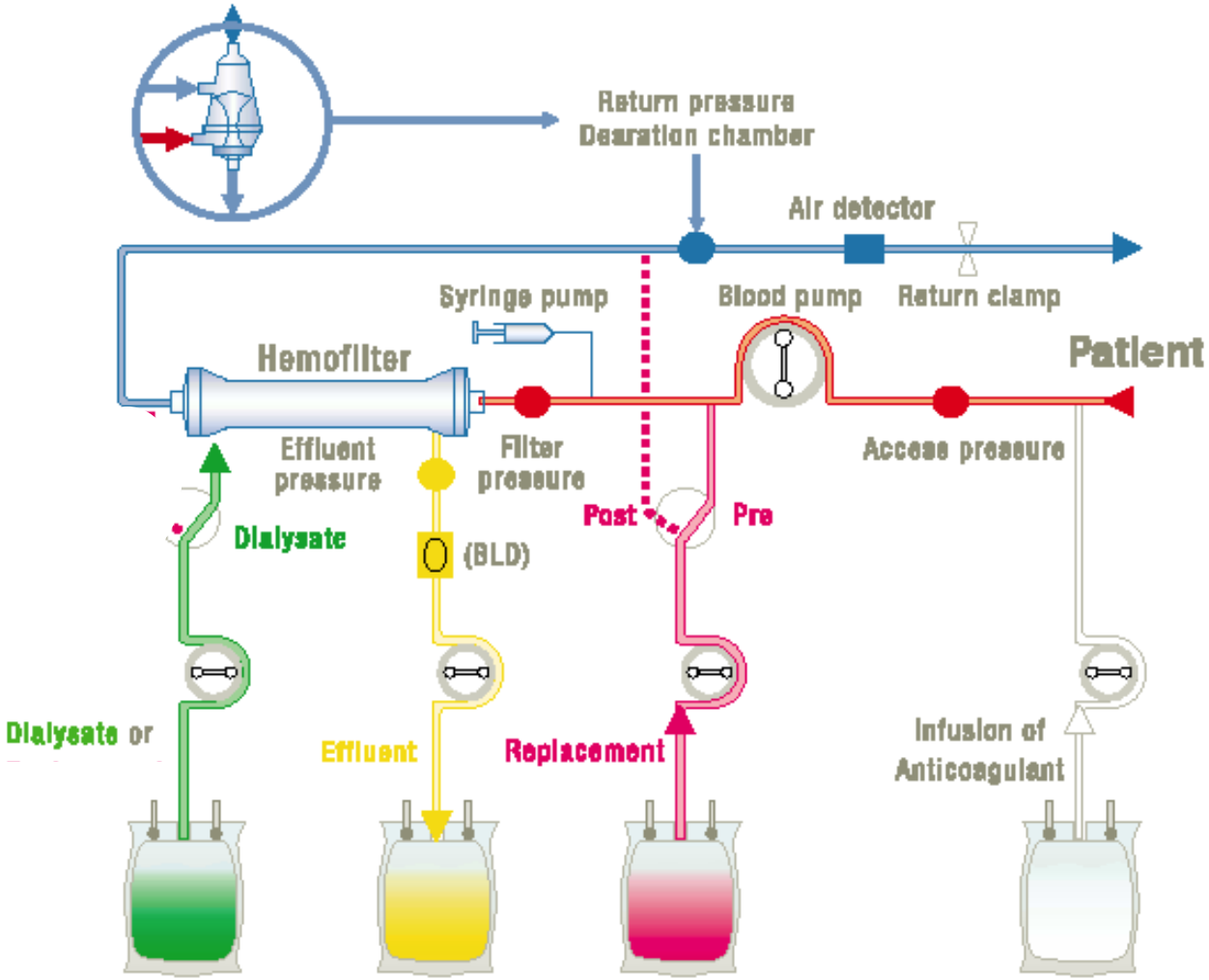
- **Diffusion**: movement of solutes down a diffusion gradient
- Uses a hemodialyzer
- **Small solutes** move more readily → **excellent clearance**
- **Larger solutes** move slower → **poor clearance**
- Solute clearance is **independent** of water flux
- Fluid removal is **not obligatory**

Hemofiltration: Convection



- **Convection**: because large solutes diffuse slowly, they are "pushed" out along with the fluid
- Uses a hemofilter
- No need for dialysate, no gradient is needed
- Solute clearance is **dependent on** fluid removal (ultrafiltration rate). **UF is obligatory**
- Because large UF is needed to convect solutes, replacement fluid is needed. **Net UF** can be adjusted

CVVHDF (Hybrid Therapy)



CRRT: Dosing → ~25-30 ml/kg/hr

- Effluent dose = $Q_D + Q_R$ + UF: ml/kg/hr
- For a 70 kg patient with Q_D =1000 ml/hr, Q_R =1000 ml/hr, UF 100 ml/hr = 30 ml/kg/hr

Study	N	Interventions	Population	Risk of Death	ARF Duration	Renal Recovery
Ronco 2000	425	20 vs 35 vs 45mL/kg/hr	75% post surgical, 12% septic	59% vs 43% vs 42% (p <0.002)		No effect
Bouman 2002	106	24- 36L/d vs 72L/d (20 vs 48mL/kg/hr)	58% post CV surgery, 100% resp failure, 100% inotrope or pressors	No effect	No effect	No effect
Saudan 2006	206	CVVHF 25mL/kg/hr vs CVVHDF 42mL/kg/hr	60% septic	61% vs 41% (p =0.03)		No effect
Tolwani 2008	200	20 vs 35mL/kg/hr	54% septic, 77.5% resp failure	No effect		No effect
Palevsky (ARF Trial Network) 2008	1124	20 vs 35mL/kg/hr AND 3X/wk IHD vs 6X/wk IHD	63% septic, 80.6% resp failure	No effect	No effect	No effect
Bellomo (RENAL) 2009	1508	25 vs 40mL/kg/hr	49.4% septic, 73.9% resp failure	No effect	No effect	No effect
Joannes-Boyau 2013	140	35 vs 70mL/kg/hr	100% septic, 97% resp failure	No effect	No effect	No effect

Access: Catheter Insertion

- Use a non-tunneled temporary HD catheter (2D)
- **Right internal jugular is preferred** (2nd fem, 3rd LIJ, last SC)
- Catheter length: RIJ 12-15 cm, LIJ 15-20 cm, Fem 19-24 cm (*diameter 12-13 Fr*)
- Catheter tip position in the SVC (caval-atrial junction, <4 cm from RA) with arterial lumen facing the mediastinum
- Do not allow catheter tip to touch atrium floor

KDIGO Guidelines 2012

AKI and ECMO

- ECMO can trigger an acute inflammatory reaction associated with diffuse endothelial dysfunction and capillary leak
  - AKI may result from:
    - Inflammatory response
    - Instability prior to ECMO cannulation
    - Changes in volume status
    - Hemoylsis: plasma-free hemoglobin

- Diuretics can be variably successful in managing fluid overload with ECMO

AKI and ECMO

- AKI is common in critically ill patients requiring ECMO
  - Incidence is 70 to 85% (RIFLE definition)
  - Registry data suggest that up to 1 out of 2 patients on ECMO need RRT
  - Likelihood of long-term ESKD in ECMO survivors requiring RRT is low

- AKI is an independent risk factor for mortality in critically ill patients on ECMO
  - Increased time on MV and longer ECMO duration

ELSO International Registry Report 2009
Askenazi et al. CJASN 2012; 7: 1328

CRRT and ECMO

Benefits

- Fluid regulation/management
- Removal of inflammatory mediators (convection)
- Control of electrolyte/acid-base abnormalities

Risks

- Labor intensive
- Air entrainment/embolism
- Pressure rises within CRRT circuit
- Microemboli
- Hemorrhage

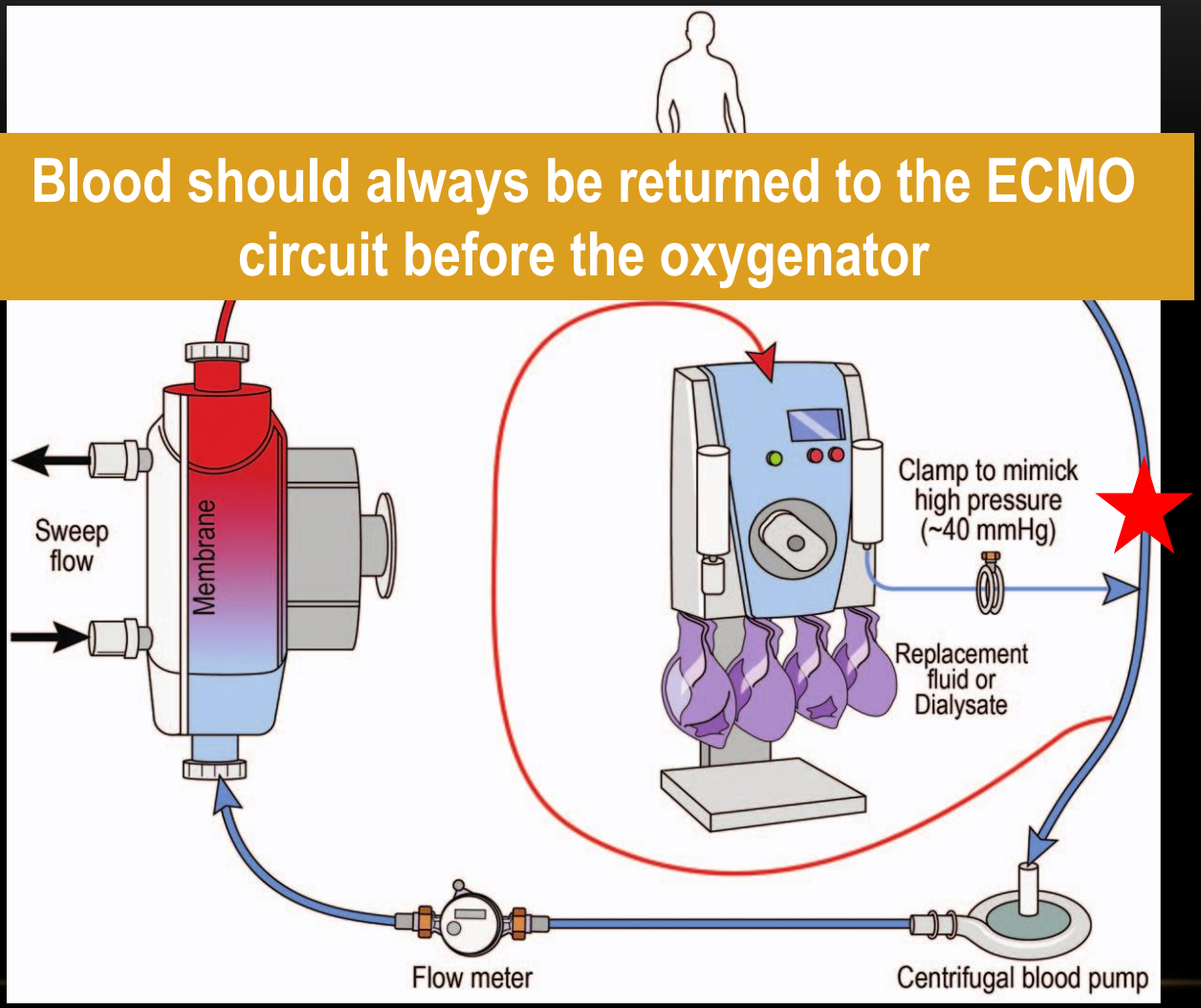
CRRT & ECMO APPROACHES

Combination of CRRT and ECMO	Specific type	Advantages	Disadvantages/risks
Integrated approach 	In-line haemofilter	Relatively easy to set up Low cost Ability to generate large volumes of ultrafiltrate No need for separate anticoagulation	No pressure monitoring Requires external pump to control ultrafiltration Less precise ultrafiltration Risk of excessive ultrafiltration Limited solute clearance Flow turbulences and risk of haemolysis
	Integration of CRRT device in ECMO circuit	Provision of ultrafiltration and solute clearance Mode of solute clearance not restricted Control of ultrafiltration No need for separate vascular access No need for separate anticoagulation	exposure of CRRT machine to pressures outside the safety range Risk of air entrapment Flow turbulences and risk of haemolysis Risk of thrombus formation on the additional connectors Generation of shunt within ECMO circuit
	Connection of CRRT device to oxygenator	Control of ultrafiltration Pressures maintained within safety range of CRRT device	Potential risk of interfering with oxygenator
Parallel systems	Separate CRRT and ECMO circuits	Provision of ultrafiltration and solute clearance Mode of solute clearance not restricted Precise fluid removal Ability to provide CRRT independent of ECMO Option of using separate anticoagulation method to keep CRRT circuit patent No need to involve ECMO team when changing CRRT circuit	Need for separate vascular access Increased difficulty caring for patient with two separate extracorporeal circuits Higher extracorporeal blood volume

Curr Opin Crit Care. 2018;24:493-503.

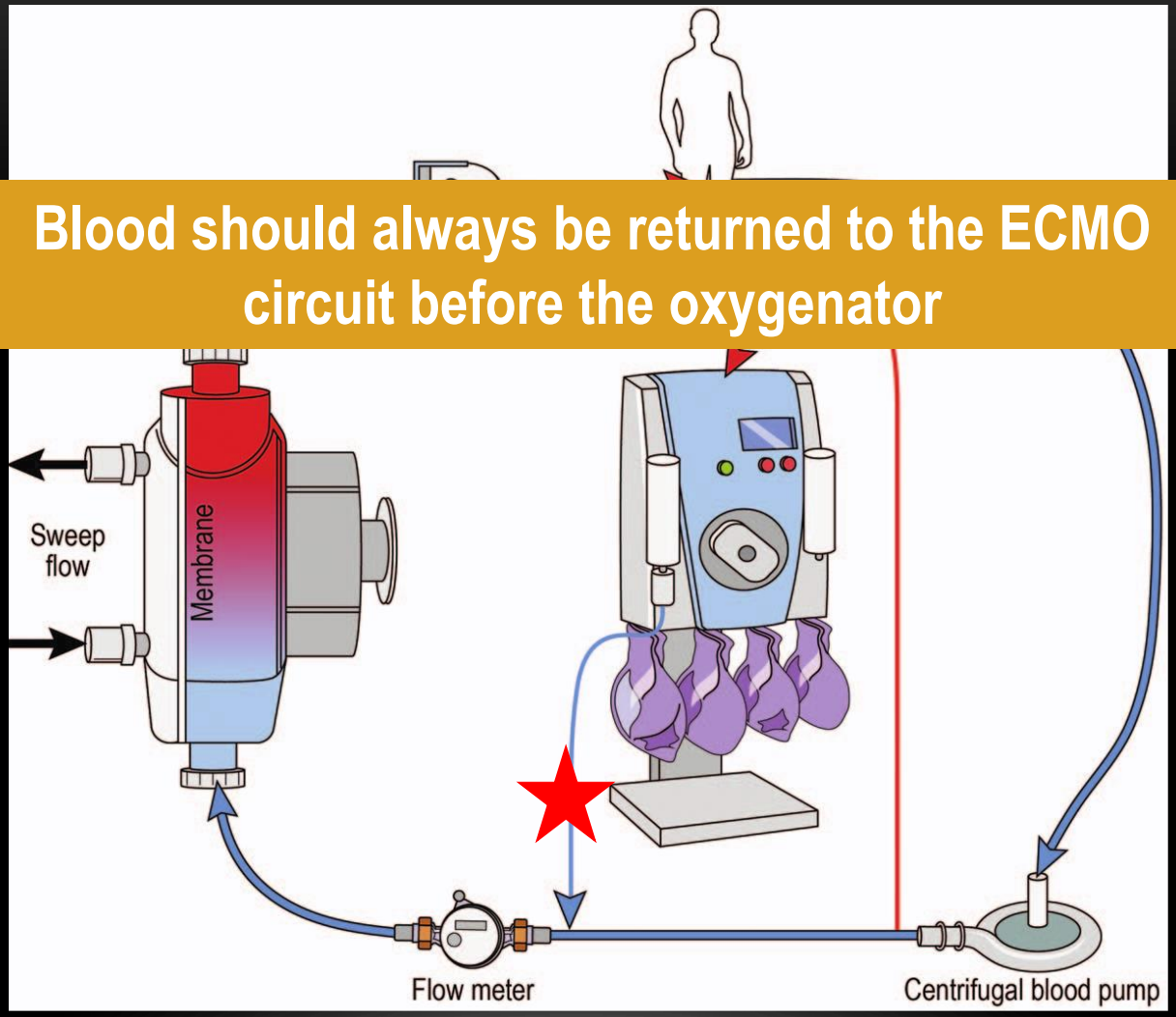
Venous Port: Negative Pressure

Blood should always be returned to the ECMO circuit before the oxygenator



Curr Opin Crit Care. 2018;24:493-503.

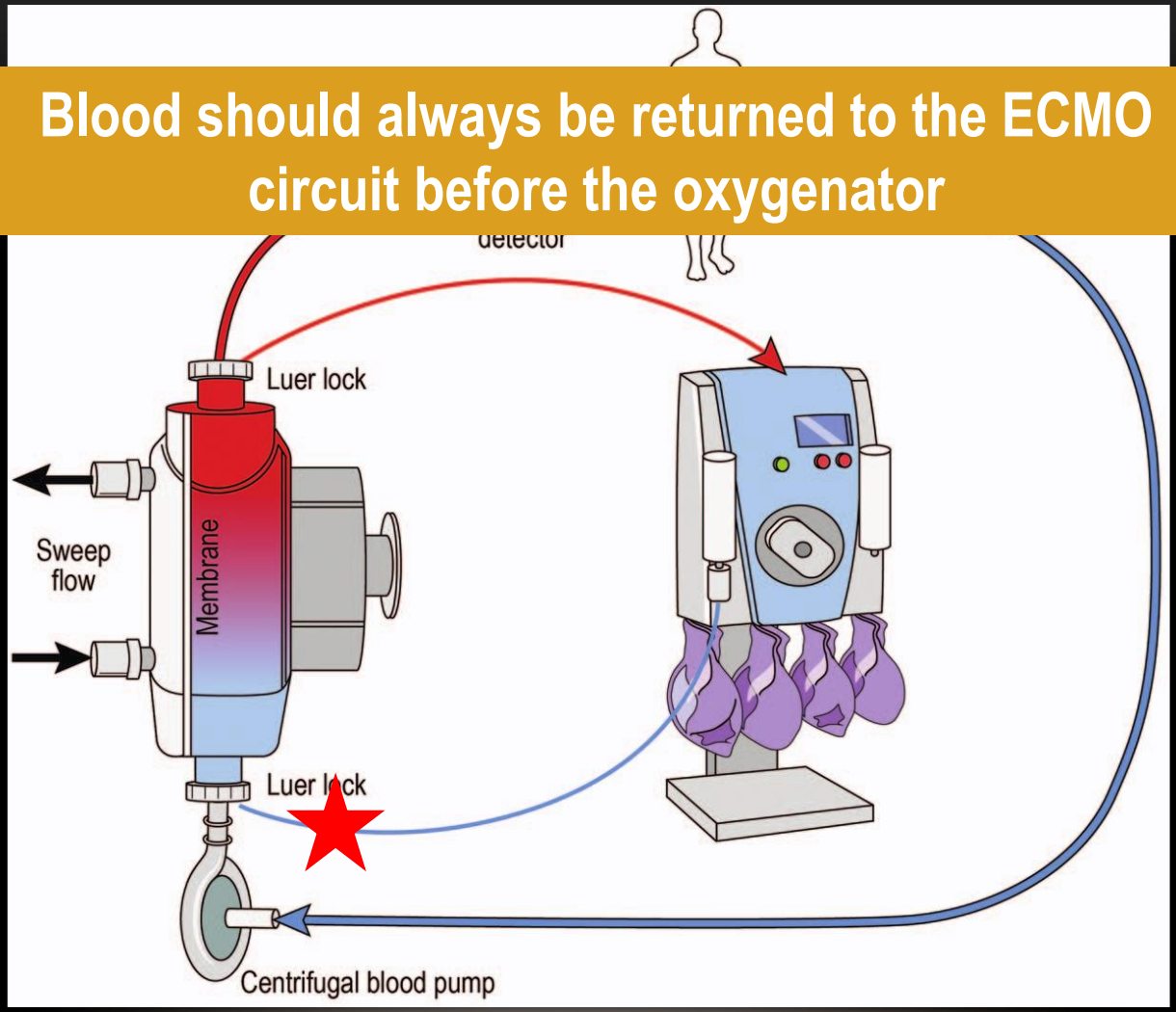
Venous Port: Positive Pressure



Curr Opin Crit Care. 2018;24:493-503.

Oxigenator Connection

Blood should always be returned to the ECMO circuit before the oxygenator



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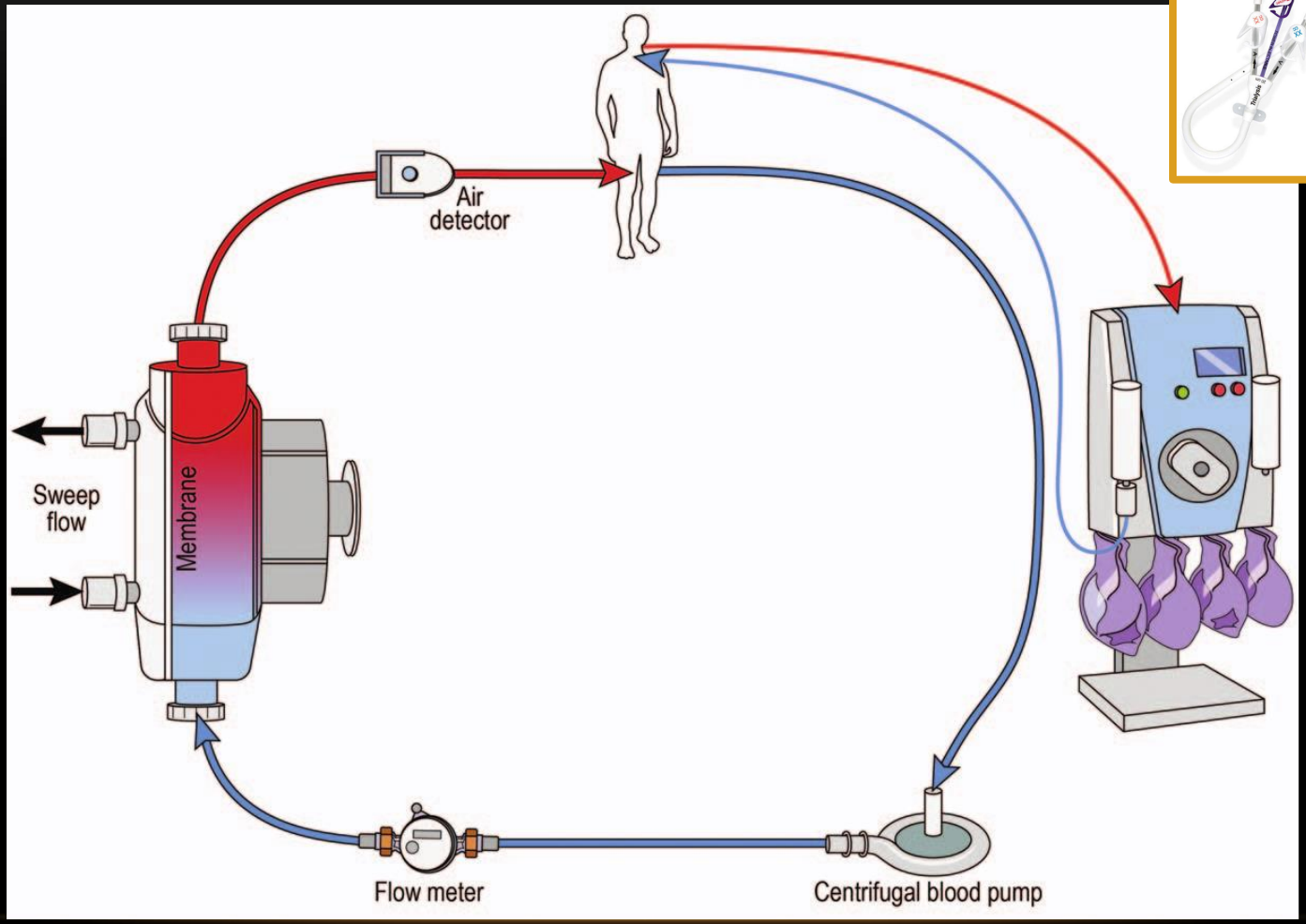
Parallel CRRT and ECMO



Curr Opin Crit Care. 2018;24:493-503.

CRRT and ECMO: UK Data (August 2017- August 2019)

	Total 119	Alive 34	Dead 85
Demographics			
Age, years ± SD	53.70 ± 13.32	48.97 ± 13.05	55.59 ± 13.03
Male, n (%)	81 (68.07)	22 (64.71)	59 (69.41)
White race, n (%)	114 (95.80)	32 (94.12)	82 (96.47)
Weight, kg ± SD	102.82 ± 31.72	109.61 ± 37.26	100.10 ± 29.01

Mortality Rate: 71.4% (ECMO), 63.2% (non-ECMO)
FO% at CRRT initiation: XX% (ECMO)

Charlson Comorbidity score, [median IQR]	3.00 [2.00-6.00]	3.00 [2.00-6.75]	3.00 [2.00-5.00]
ESRD, n (%)	14 (11.76)	7 (20.59)	7 (8.24)
Critical illness parameters			
ICU legth of stay, days, median [IQ1-IQ3]	11.50 [4.25-24.65]	23.35 [12.73-35.35]	10.00 [3.40-17.70]
CRRT days, median [IQ1-IQ3]	7.29 [2.72-14.82]	13.50 [7.69-26.38]	4.83 [2.13-12.83]
Mechanical ventilation, n (%)	117 (98.32)	33 (97.06)	84 (98.82)
SOFA at ICU admission, median [IQ1-IQ3]	11.00 [8.00-14.00]	11.00 [8.00-13.00]	12.00 [8.00-15.00]
SOFA at CRRT start, median [IQ1-IQ3]	15.00 [12.00-17.00]	13.50 [11.25-16.75]	15.00 [12.00-17.00]

Not published

UK-CRRT Quality Management Reports (Monthly)

- **~50 patients per month**
- **2017: 483 pts (7.0 days/pt)**
- **2018: 478 pts (7.9 days/pt)**
- Integrate machine utilization, technical, machine data, research, education and outcomes reports
- ~70% utilization of CRRT machines
- Identify machines to be replaced (technical issues)
- Identify operational problems and solutions

Take Home Messages

- AKI risk-stratification can be assisted by clinical and biomarker data
- FO is associated with adverse outcome and might also directly contribute to AKI
- CRRT is the preferred type of RRT for critically ill patients that are hemodynamically unstable
- “Early RRT” for one patient may be “too late” for a different patient → RRT initiation should be individualized
- When using CRRT integrated into the ECMO circuit, blood should always be returned to the ECMO circuit before the oxygenator to avoid complications

Thanks!

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