Intermittent Dialysis *vs* CRRT

Unraveling the best strategies for patients

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Zanjan

1403/2024

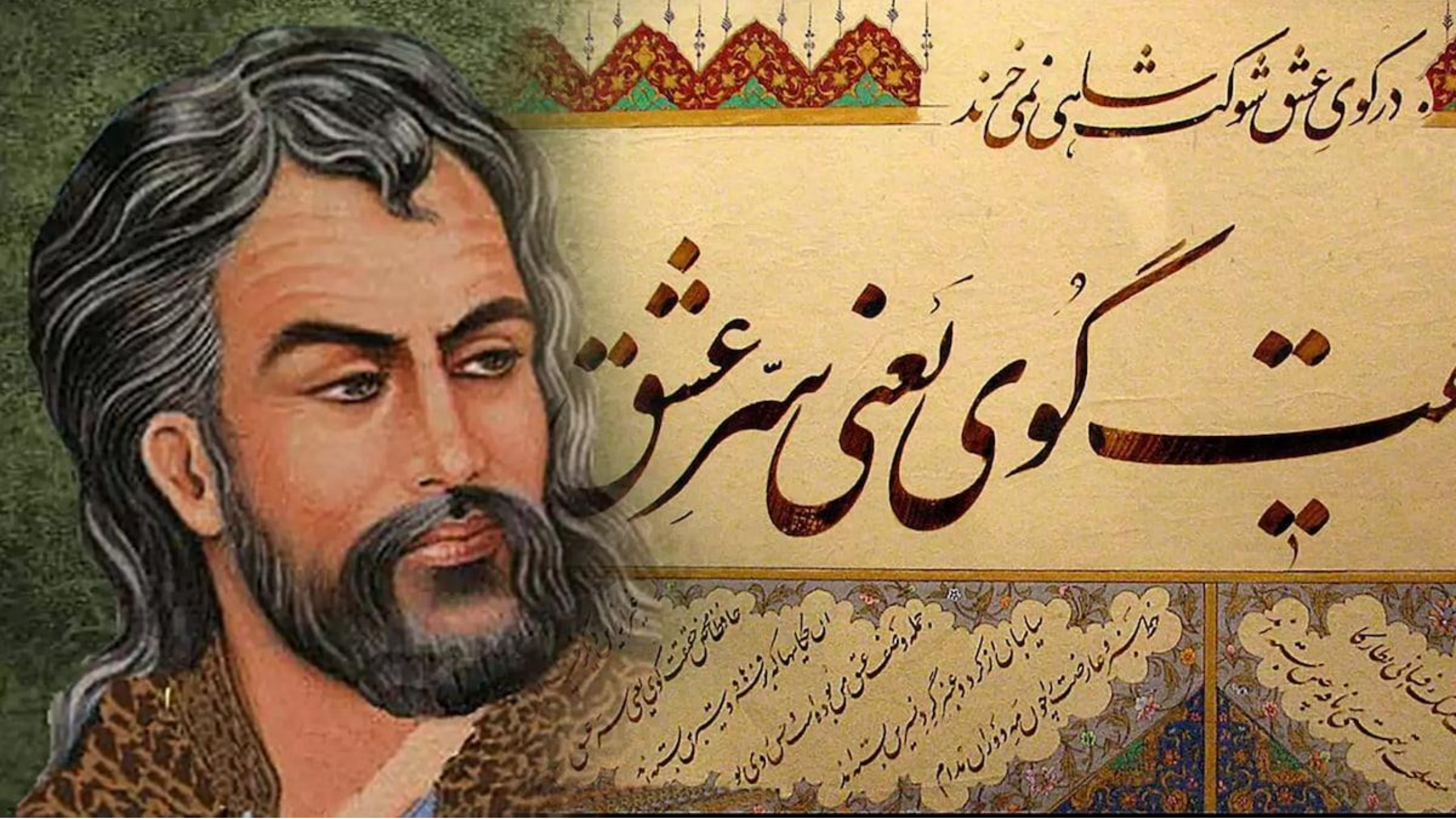
United Nations Educational, Scientific and Cultural Organization

Sustainable Development Goals

Bangkok Office

International Day of the Girl Child

11 OCTOBER


در کوی عشق شوکت شاهی نمی خرند
گُوی یعنی سرّ عشق

الا ای ساقی ادر کاسا و ناولها
که عشق آسان نمود اول ولی افتاد مشکلها

حافظ

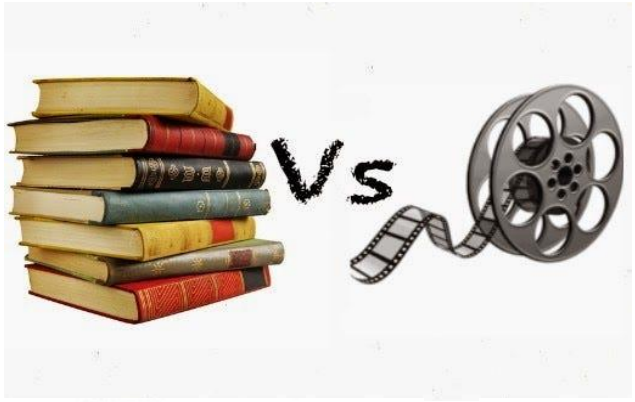
Disclosure Statement

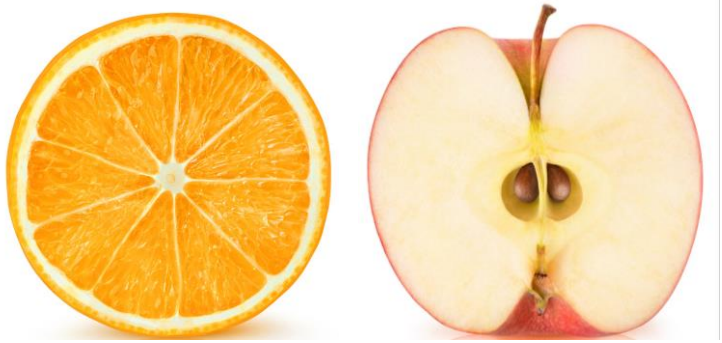
I have no financial disclosure or conflict of interest with this presentation

IRRT *vs* CRRT

Direct comparison between two valuable things

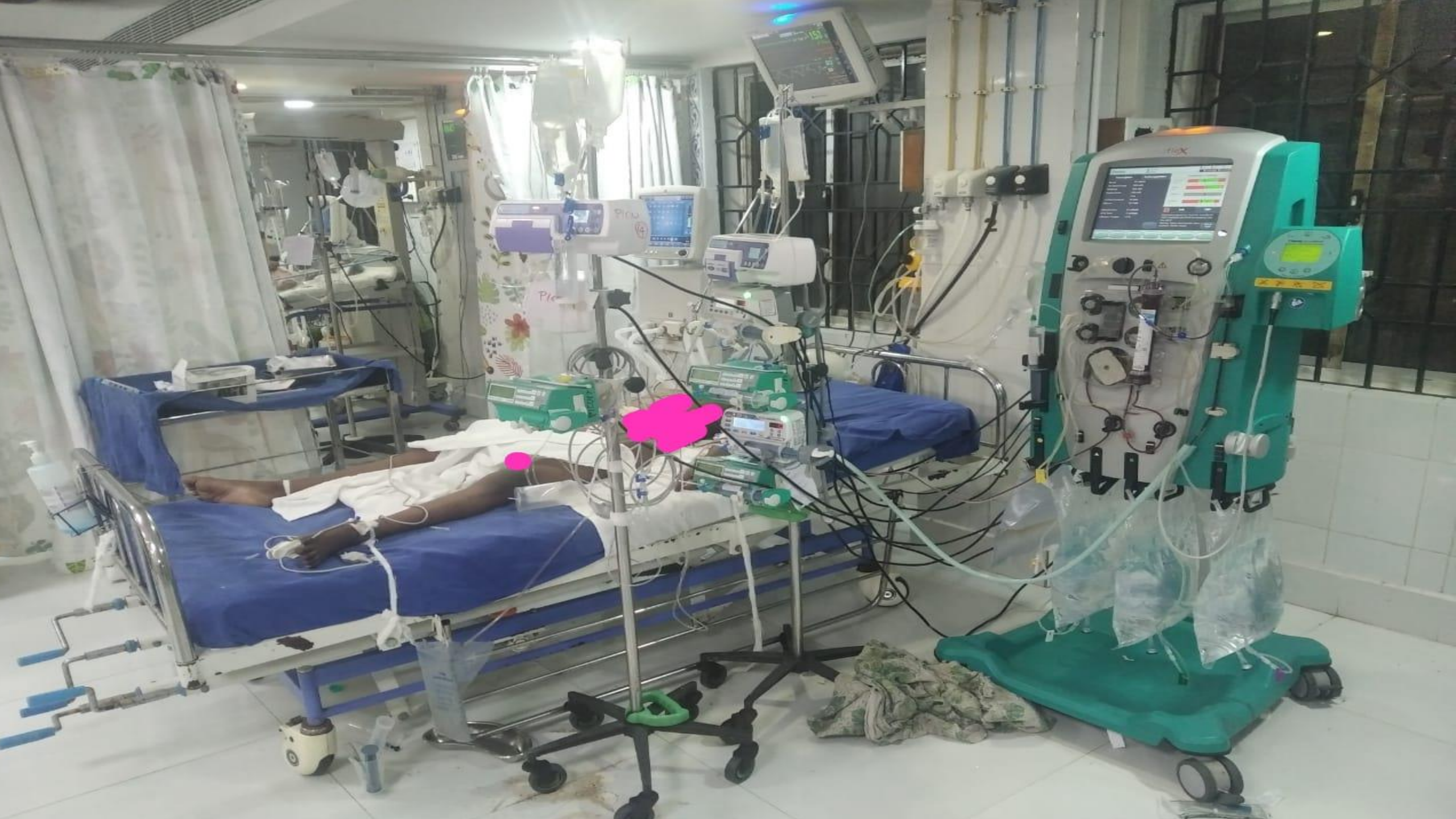
- **Oversimplify**
- **Ignores** the **context**, **purpose**, and **unique strengths** of each option.
- **Not about choosing** which is **better**
- **Right choice** in **different situations**.
- **Complementary & Not Competitive**
- **How and when** to use each option (**best outcome**).
- Appreciating **specific benefits**





IRRT *&/or* CRRT

Importance of RRT in CIP,
where the kidney is often compromised



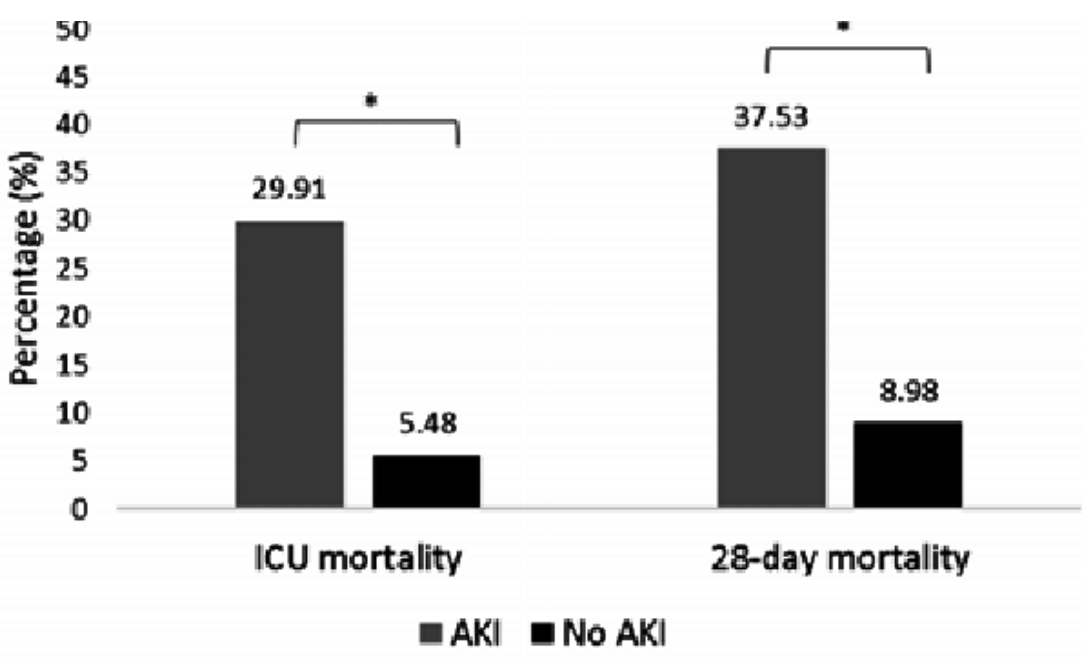
RRT in ICU

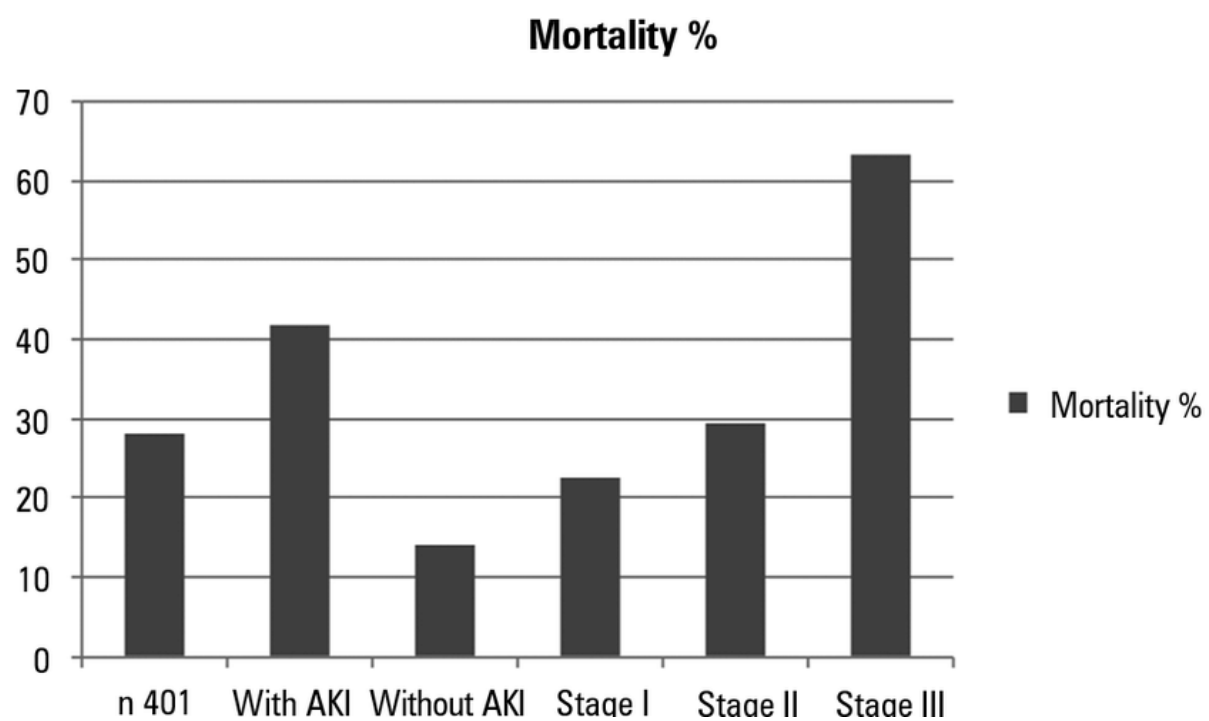
Causes

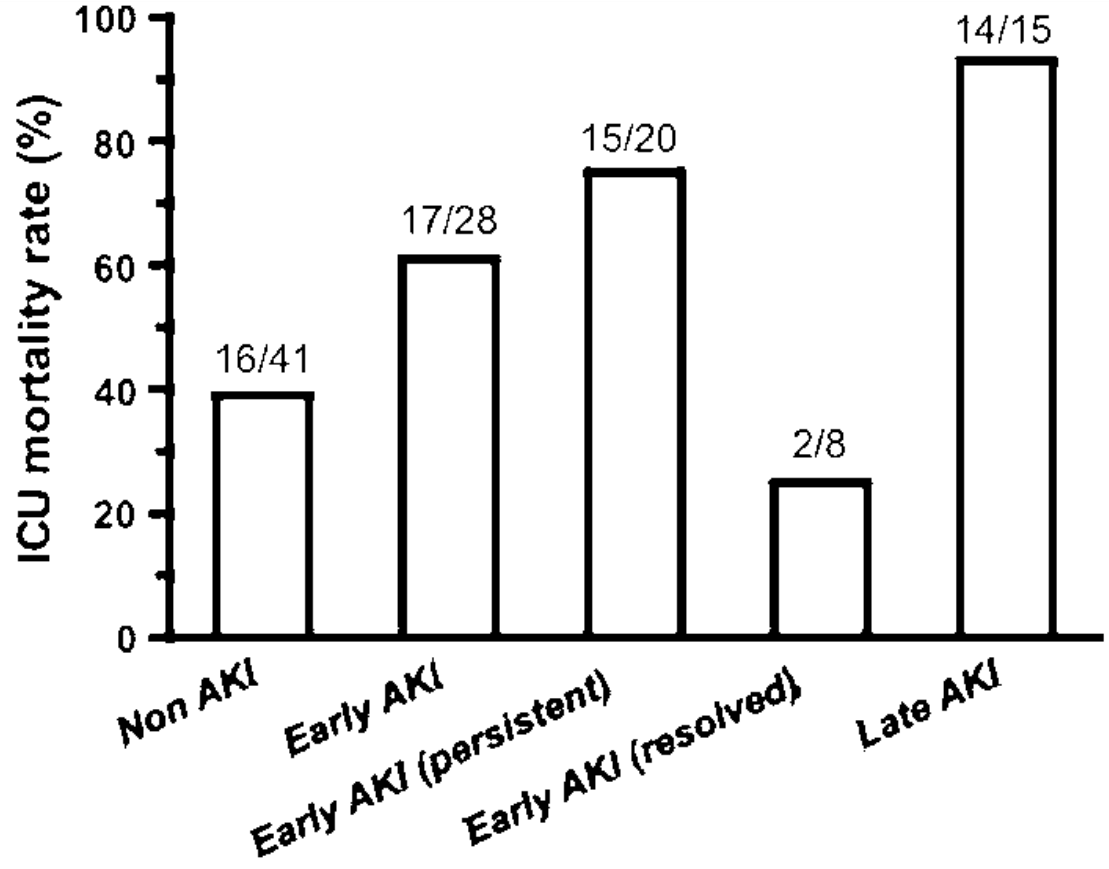
1. Acute Kidney Injury (AKI)
2. Fluid Overload
3. Electrolyte Imbalances
4. Multiorgan Failure
5. Toxin Removal
6. Acute Respiratory Distress Syndrome (ARDS)
7. Tumor Lysis Syndrome (TLS)

Statistics

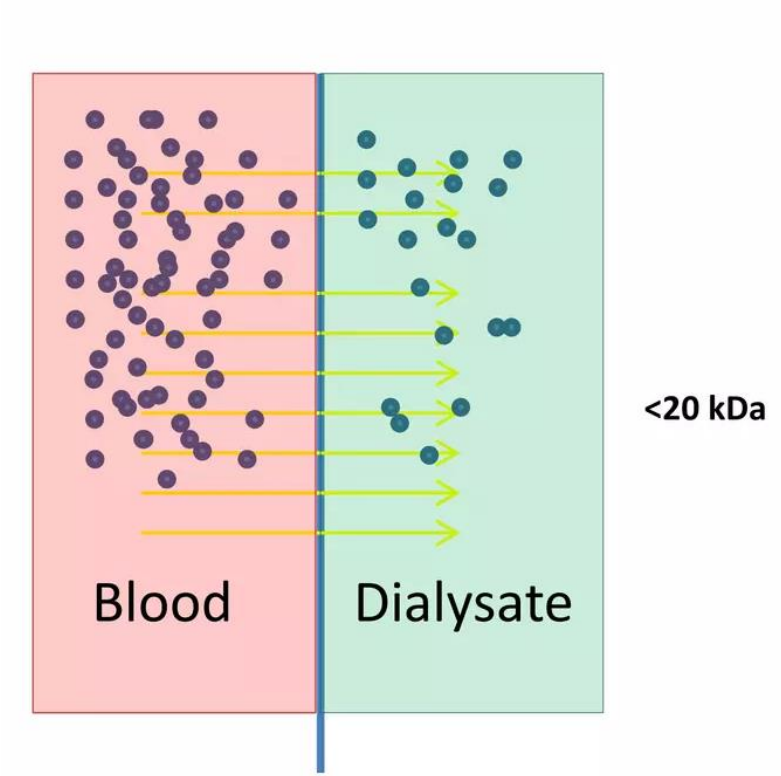
- **RRT in ICU** = 5-10% (CRRT: 60-80% & IRRT: 20-40%)
- **ICU pts + AKI + RRT** = 5-10%
- **ICU pts =** AKI in 25-60%
- **ICU pt + AKI** = 30-60% mortality
- **ICU pt + AKI + RRT** = 50-80% mortality
- **ICU pt + AKI** = 30-50% incomplete recovery = CKD
- **ICU pt + AKI** = 2-5 % no recovery = ESRD


Percentage (%)
50
45
40
35
30
25
20
15
10
5
0
*
*
29.91
5.48
37.53
8.98
ICU mortality
28-day mortality
AKI
No AKI


Mortality %
70
60
50
40
30
20
10
0
n 401
With AKI
Without AKI
Stage I
Stage II
Stage III
Mortality %

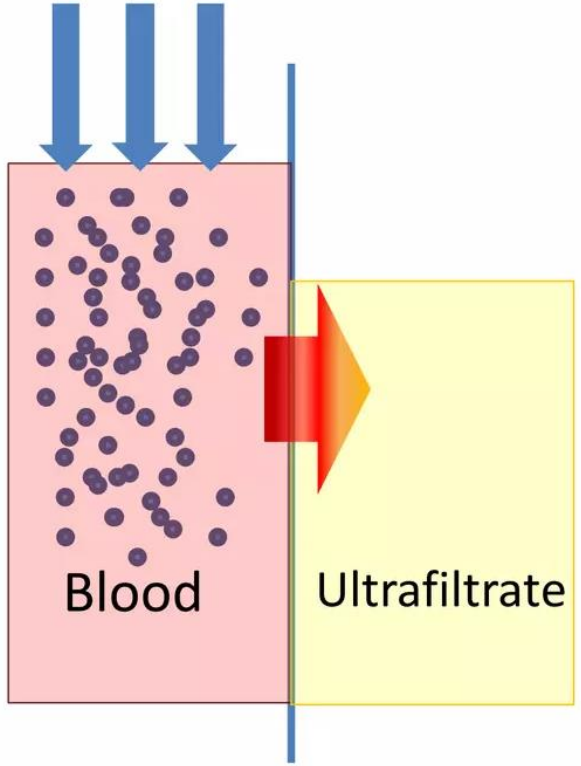

ICU mortality rate (%)
100
80
60
40
20
0
16/41
17/28
15/20
2/8
14/15
Non AKI
Early AKI
Early AKI (persistent)
Early AKI (resolved)
Late AKI

Diffusion

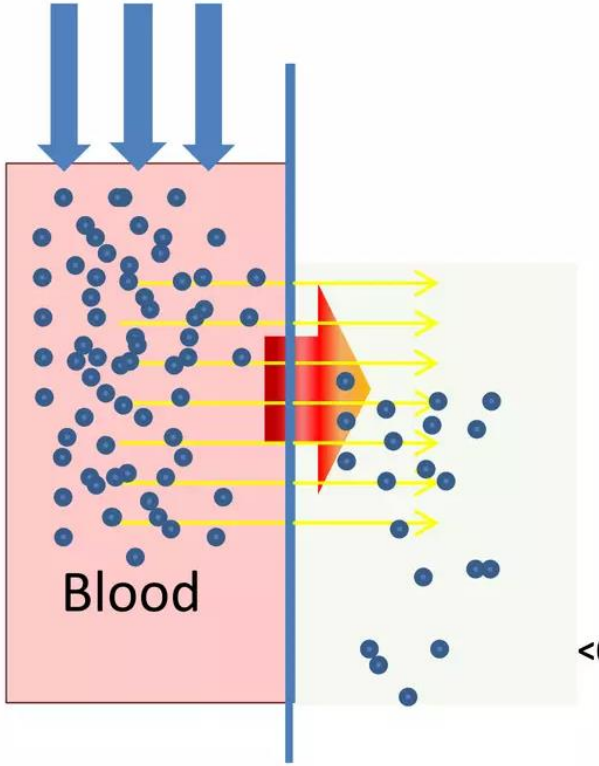


<20 kDa

Ultra-filtration

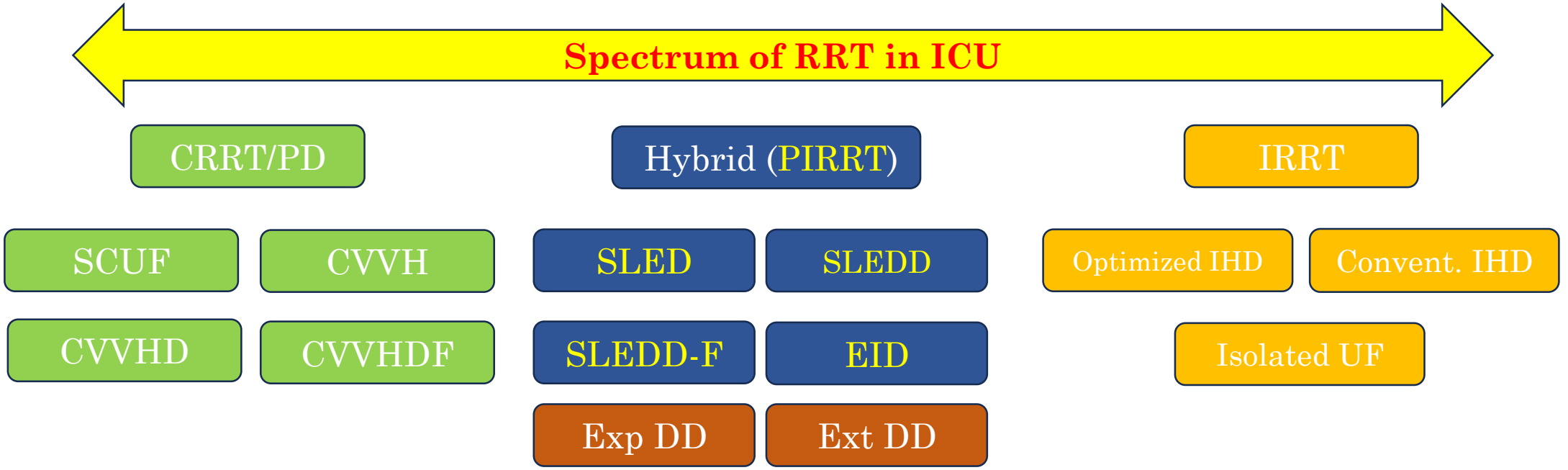


Convection



<60 kDa

Spectrum of RRT in ICU



Intermittent hemodialysis (IHD)

Advantages

- Efficiently removes toxins and liquids.
- Accessible and widely available
- Shorter treatment time compared to continuous therapy
- Greater schedule flexibility.
- Limited dosis of Anticoagulation
- Low cost and less labor intensive

Disadvantages

- It can cause hypotension, muscle cramps and fatigue which can be deleterious in patients with cirrhosis.
- Limits mobility and lifestyle.
- Large fluid removal rate
- Limited Clearence of larger solutes

Continuous renal replacement therapy (CRRT)

Advantages

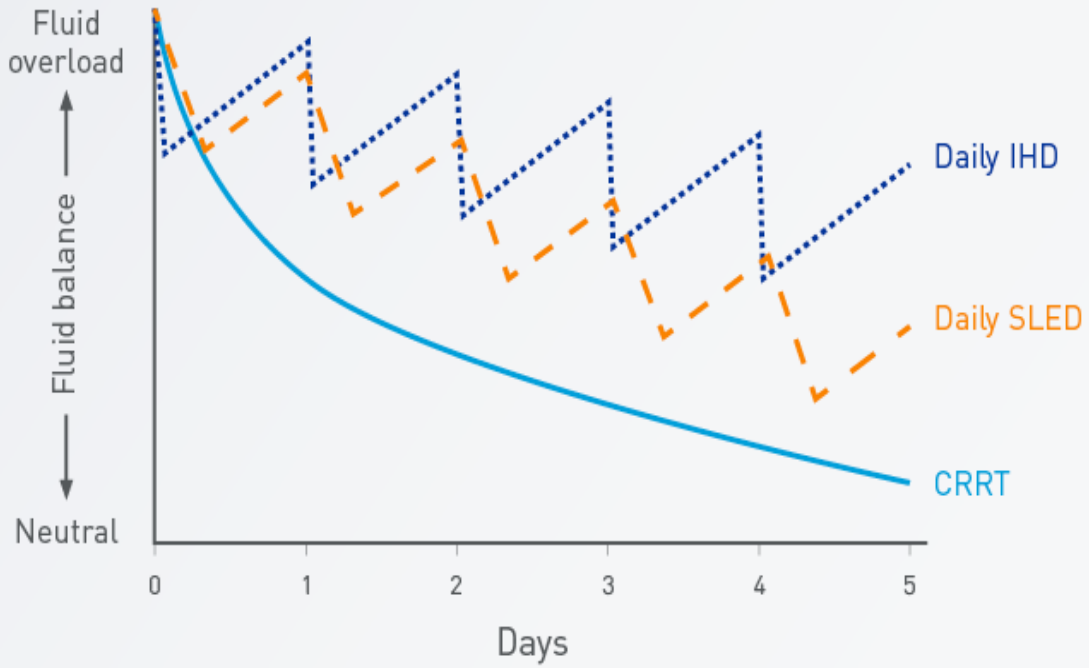
- Slow fluid removal
- Reduced fluctuations in fluid and toxin levels.
- Minimun effects on hemodynamics
- Removal of larger solutes (myoglobins, cytokines)
- Possible low cerebral impact.

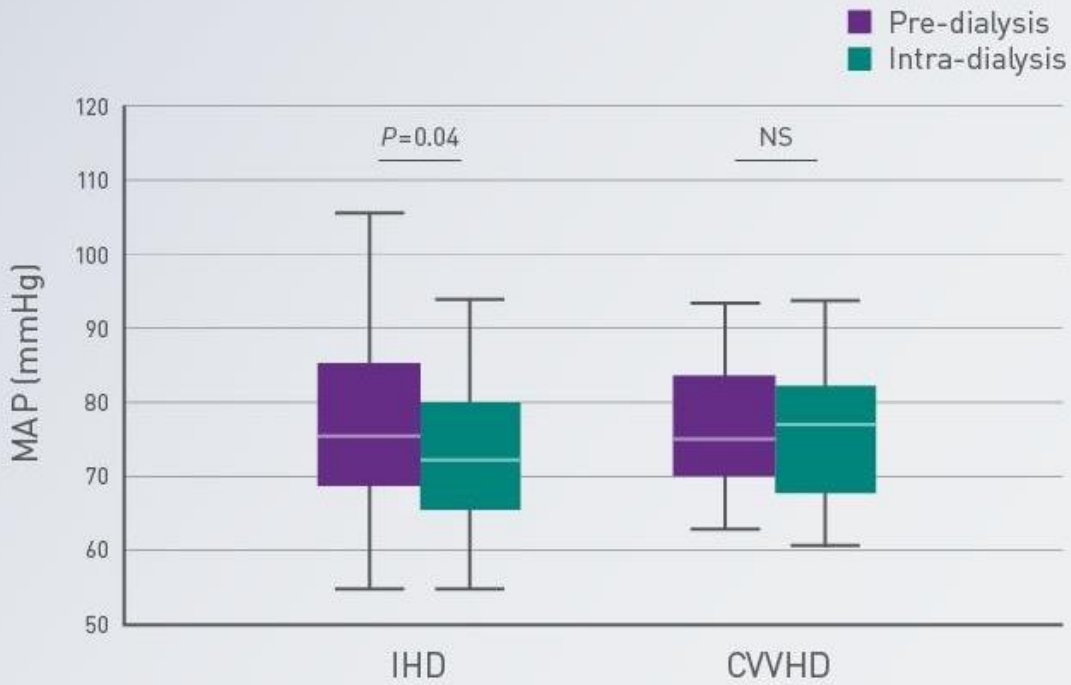
Disadvantages

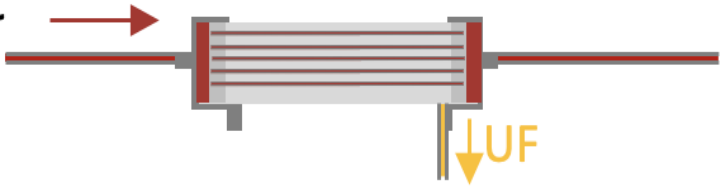
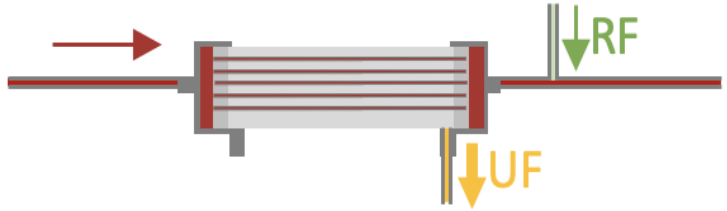
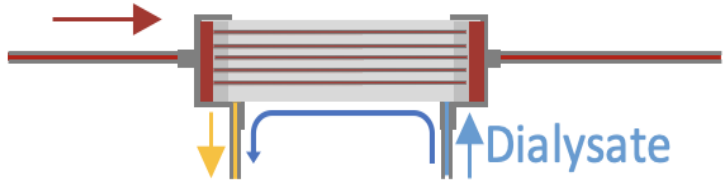
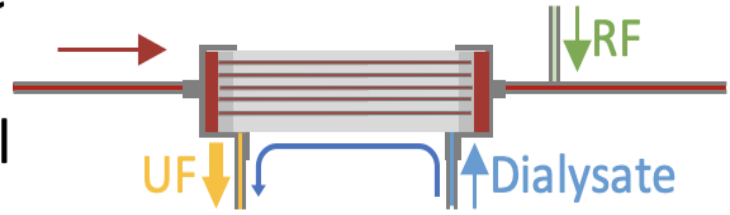
- Higher costs and labor-intense
- Requires specialized equipment and training.
- Possible need for continuous anticoagulation therapy.
- Can be less convenient and time-consuming.

CRRT in AKI: Indications & Contra-indications

Absolute indications (in the absence of contraindications for CRRT)	Refractory hyperkalemia
	Refractory metabolic acidosis
	Refractory pulmonary edema due to volume overload not responding to diuretics
	Symptomatic uremia or its complications (bleeding, pericarditis, encephalopathy, etc.)
	Overdose or toxicity of dialyzable drugs (salicylates, ethylene glycol, methanol, etc.)
Relative indications (in the absence of life-threatening complications of AKI)	Hemodynamic instability
	Advanced dysfunction of organs other than the kidneys (brain, heart, lung, liver, and gastrointestinal tract)
	Need for administration of a large volume of fluid (massive volume challenge, massive transfusion, medications, nutritional support, etc.)
	Severity of the underlying disease
Contraindications	Patient or legal representative does not want CRRT
	No infrastructure or skilled manpower to administer CRRT
Relative contraindications	Futile prognosis
	Patient receiving palliative care


Fluid overload
Fluid balance
Neutral
0
1
2
3
4
5
Days
Daily IHD
Daily SLED
CRRT


Pre-dialysis
Intra-dialysis
MAP (mmHg)
120
110
100
90
80
70
60
50
P=0.04
NS
IHD
CVVHD

CRRT Mode	Description	Schematic
SCUF	Slow continuous UF; UF removes fluid but provides almost no clearance and does not correct pH; no replacement fluid required. Corrects volume overload **only**.	
CVVH (a.k.a. **CVVHF**)	Continuous venovenous **hemofiltration**. Provides ***convective*** clearance by filtering a large volume of blood; Replacement fluid restores volume lost. Corrects uremia, lytes, pH and can remove volume.	
CVVHD	Continuous venovenous **hemodialysis**. Provides ***diffusive*** clearance by running **dialysate** opposite blood flow. No replacement fluid used. Gently corrects uremia, lytes, pH	
CVVHDF	Continuous venovenous **hemodiafiltration**. High clearance achieved using both **UF** & **dialysate** flow (both ***convection*** & ***diffusion***). Replacement fluid used. Allows fluid removal and correction of electrolyte/pH. Good for toxin removal.	

Optimized (ICU) vs Conventional IHDx in ICU

Optimized (ICU) IHDx

- Diffusion
- Std machine
- Qb 200-350
- Qeff 400-600
- Time 4-6 h
- Frequency x4-5/week
- Fluid removal rate 2-5 L/session (0.75-1.5 L/hr)
- Access AVF AVG Catheter
- Easy

Conventional IHDx

- Diffusion
- Std machine
- Qb 400-500
- Qeff 600-800
- Time 3-4 h
- Frequency x3/week
- Fluid removal rate 2-5 L/session (0.5-1 L /hr)
- Access AVF,AVG, Catheter
- Easy

Strategies to improve IRRT tolerance

Table 3 Strategies to improve hemodynamic tolerance when utilizing intermittent RRT in critically ill patients with AKI [4]

Intervention	Physiologic effect	Strategy
Isovolemic initiation	Preserve intravascular volume and prevent relative and/or absolute hypovolemia	Fill circuit with 0.9% saline
Reduced dialysate temperature	Preserve vasomotor tone and prevent temperature-induced decreases in systemic vascular resistance	Decrease dialysate temperature by 0.5–1.5 °C
Reduced dialysate flow rate	Preserve plasma osmolality and prevent rapid shifts in plasma osmolality	Decrease to 50–100 ml/min
Dialysate [Na^+] profiling	Preserve plasma osmolality, promote vascular refill, and prevent rapid shifts in plasma osmolality	Progressive increase in dialysate [Na^+] to >145 mmol/l
Preferential use of bicarbonate buffer	Preserve myocardial contractility	Avoid acetate-based dialysis buffer
Maintain normal systemic ionized [Ca^{2+}]	Preserve myocardial contractility and vasomotor tone	Maintain systemic Ca_i^{2+} > 1.0 mmol/l
Conservative ultrafiltration	Preserve intravascular volume and prevent iatrogenic relative and/or absolute hypovolemia	Start with isolated dialysis; gentle ultrafiltration; extend treatment session to achieve fluid balance goals

EDD / EDD

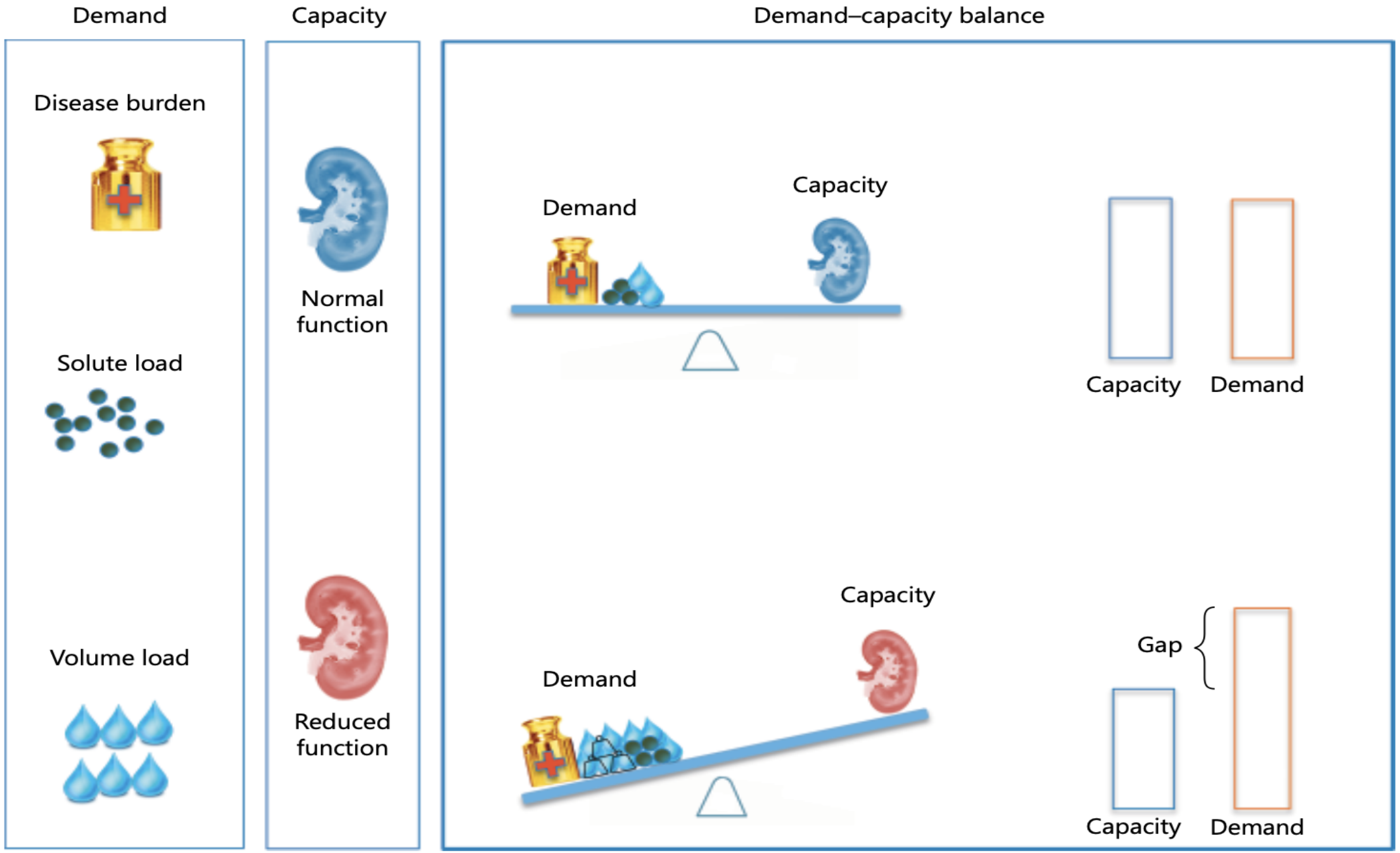
Aspect	Extended Daily Dialysis (EDD)	Expanded Daily Dialysis (EDD)
Duration	Typically 6-12 hours per session.	Typically 4-6 hours per session.
Frequency	Daily or near-daily sessions, depending on the patient's needs.	Daily or near-daily sessions, focusing on solute clearance.
Flow Rates	Lower flow rates, aimed at gentler clearance.	Higher flow rates for more efficient clearance.
Hemodynamic Stability	Better for hemodynamically unstable patients.	Suitable for more stable patients, but still requiring careful monitoring.
Solute Clearance Efficiency	Slower solute removal, more controlled fluid management.	Faster solute clearance, more intensive fluid removal.
Clinical Application	Used for patients needing slow, controlled dialysis but not full CRRT.	Used for patients needing more rapid solute removal than IHD, without requiring full CRRT.
Resource Use	Less resource-intensive than CRRT, but requires longer therapy times.	Requires more advanced machines and higher flow rates for efficiency.

Hybrid / PIRRT

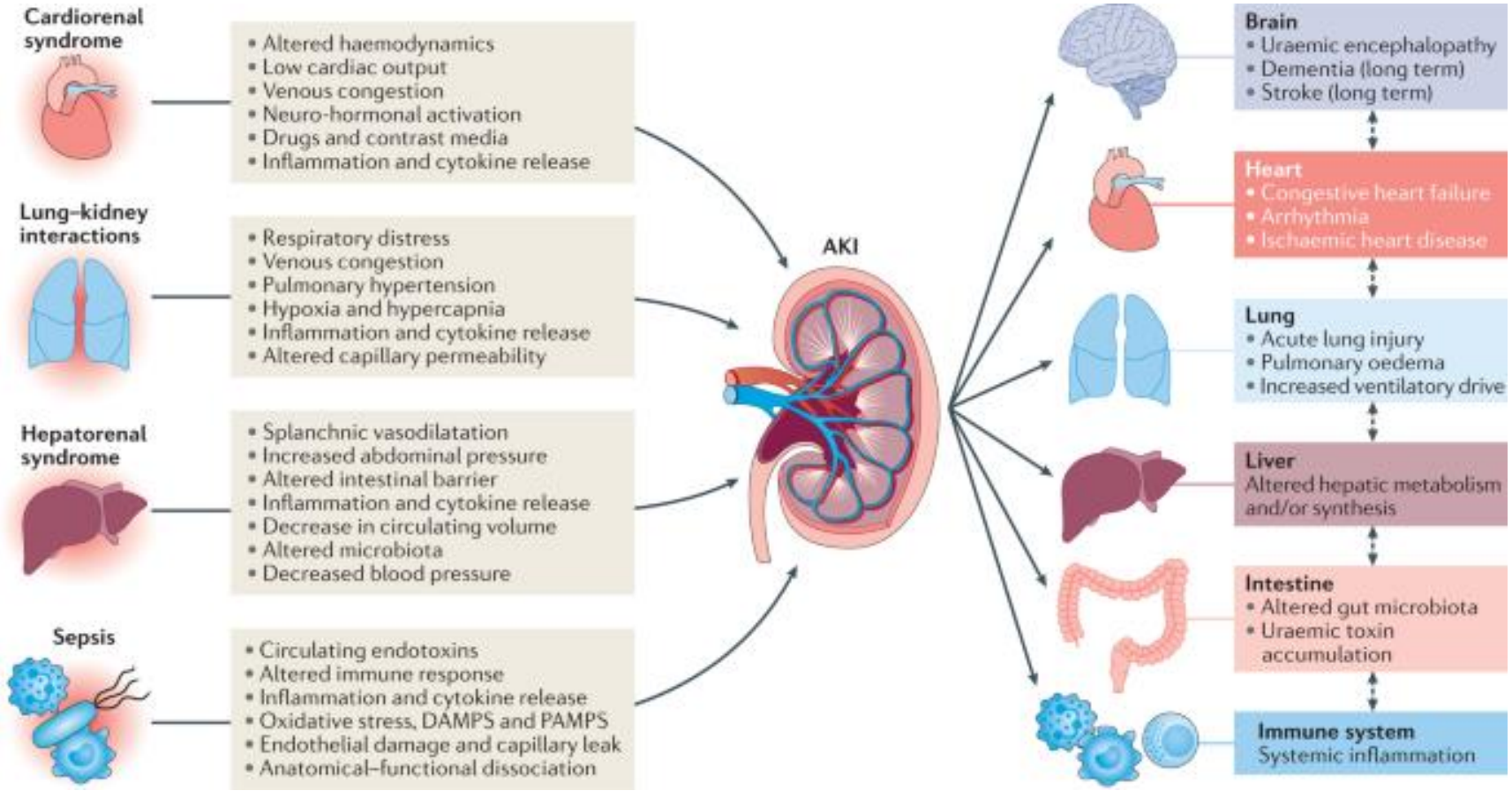
Aspect	PIRRT (SLED/SLEDD/EID)	CRRT	IHD
Duration	6-18 hours per session.	Continuous (24/7).	3-4 hours per session.
Frequency	Daily or every other day.	Continuous.	3-4 times per week (or as needed).
Flow Rates	Lower blood and dialysate flow rates.	Very low flow rates for slow, gentle removal.	High flow rates for rapid clearance.
Hemodynamic Stability	Better hemodynamic tolerance than IHD, but less than CRRT.	Best for unstable patients.	Less hemodynamic stability (risk of hypotension).
Solute Clearance Efficiency	Moderate.	Slower, more controlled.	Rapid.
Fluid Removal Control	Continuous but over a shorter period, with more flexibility.	Continuous and precise.	Rapid, with higher risk of fluid imbalance.
Resource Use	Moderate (less than CRRT, more than IHD).	High (requires continuous monitoring and resources).	Low to moderate (shorter treatment times).
Patient Immobility	Moderate (6-18 hours per session).	High (24/7 connection).	Low (patients mobile between sessions).

Deciding RRT modes in ICU

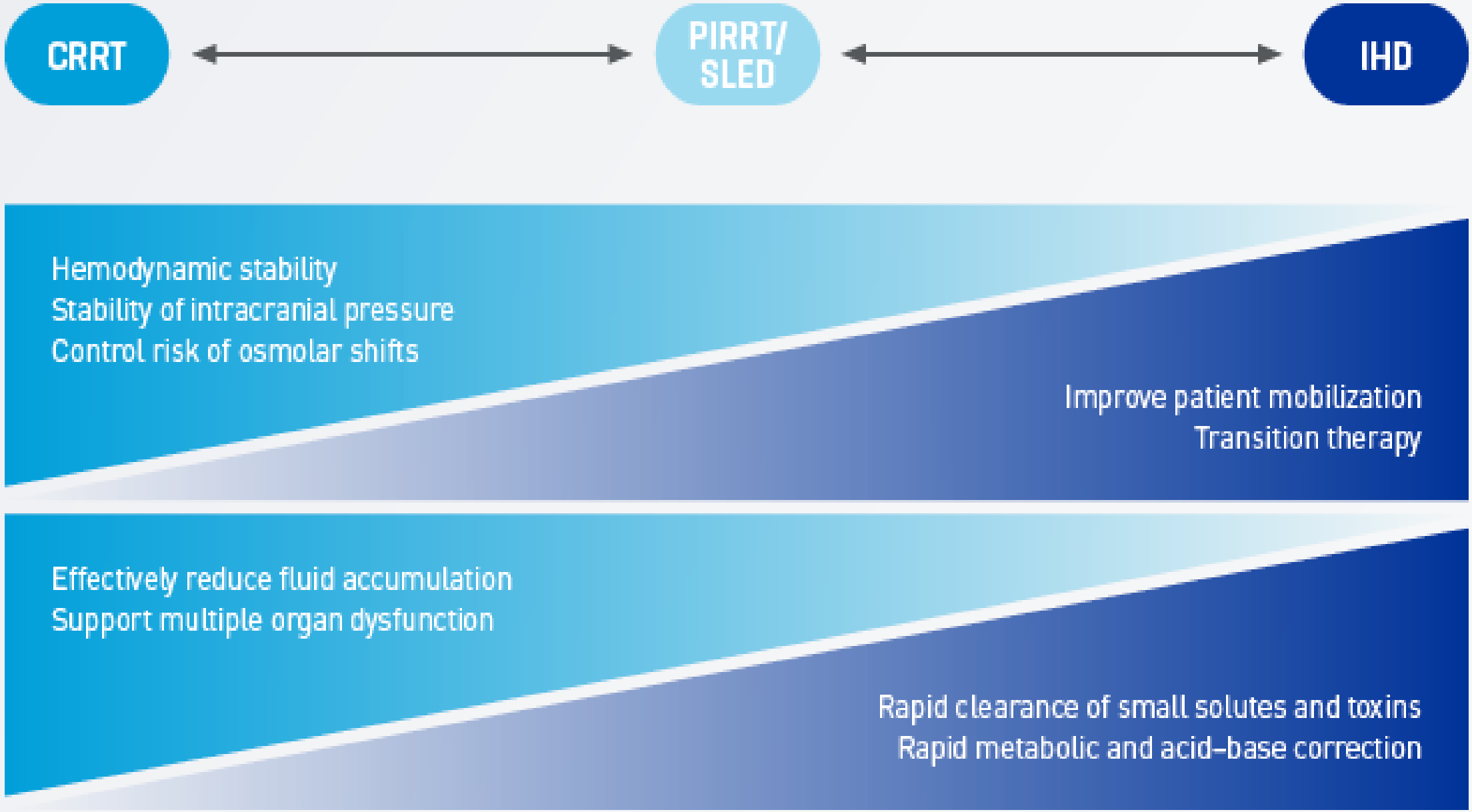

DEMAND
SUPPLY

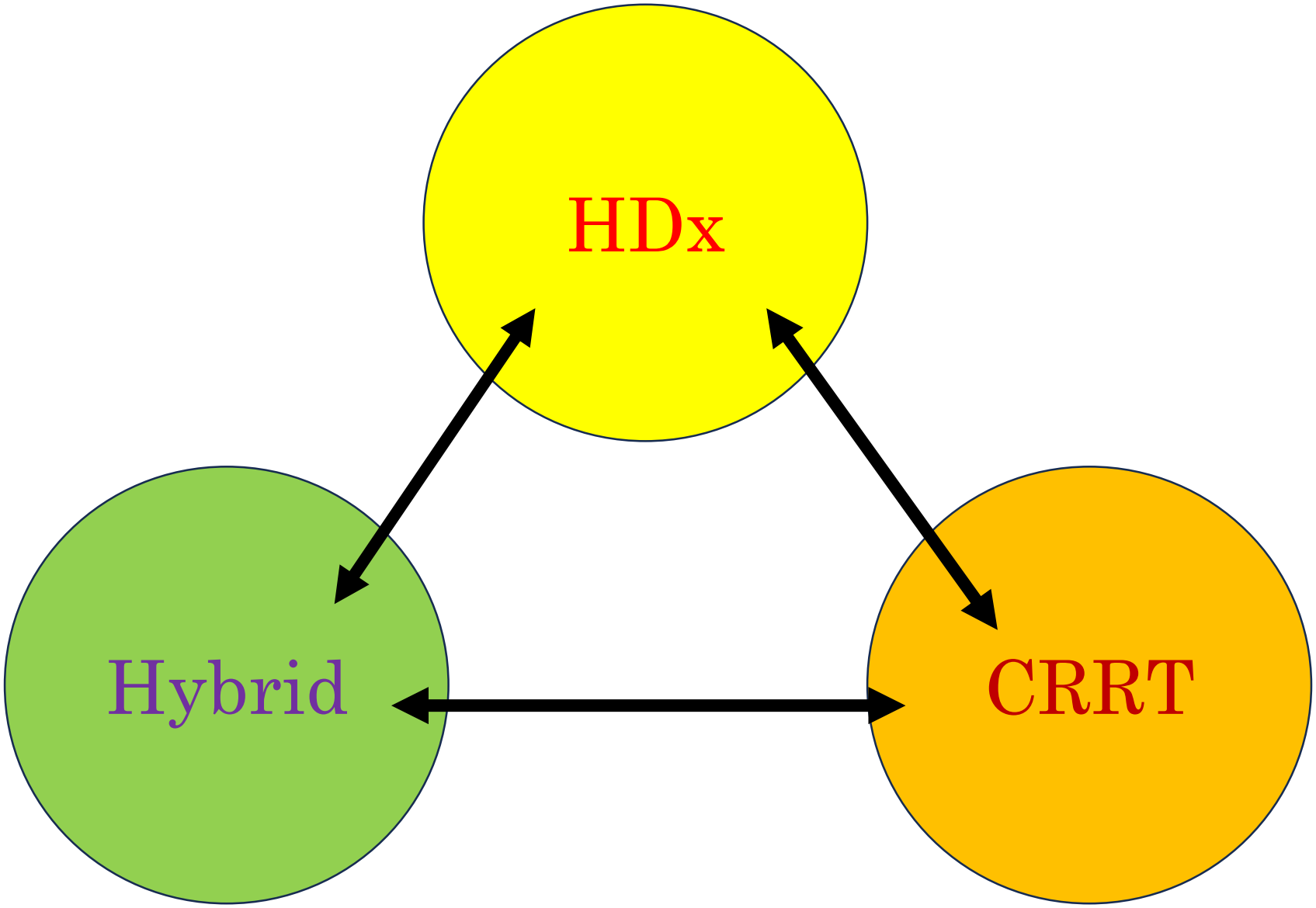

Demand
Capacity
Demand–capacity balance
Disease burden
Solute load
Volume load
Normal function
Reduced function
Demand
Capacity
Capacity
Demand
Demand
Capacity
Gap
Capacity
Demand

From causes to consequences



Design the ”goal”


CRRT
PIRRT/
SLED
IHD
Hemodynamic stability
Stability of intracranial pressure
Control risk of osmolar shifts
Improve patient mobilization
Transition therapy
Effectively reduce fluid accumulation
Support multiple organ dysfunction
Rapid clearance of small solutes and toxins
Rapid metabolic and acid–base correction


HDx
Hybrid
CRRT

Outcome Studies

Study	Type	*n*	Comparison	Mortality*	Renal recovery‡	Comment
Lins *et al.* (2009)[30]	Multicenter RCT	316	CVVHF vs IHD	58% vs 63% (*P*=ns)	35% vs 29% (*P*=ns)	Some hemodynamically unstable patients excluded
Vinsonneau *et al.* (2006)[29]	Multicenter RCT	359	CVVHDF vs IHD	32% vs 33% at day 60 (*P*=ns)	63% vs 60% (*P*=ns)	Change in relative survival during time-course of study
Uehlinger *et al.* (2005)[28]	Single-center RCT	125	CVVHDF vs IHD	47% vs 51% (*P*=ns)	50% vs 42% (*P*=ns)	Study terminated early
Augustine *et al.* (2004)[27]	Single-center RCT	80	CVVHD vs IHD	68% vs 70% (*P*=ns)	13% vs 10% (*P*=ns)	—
Kielstein *et al.* (2004)[26]	Single-center RCT	39	CVVHF vs extended daily dialysis	40% vs 40% (*P*=ns)	Not reported	Survival was not the primary outcome
Mehta *et al.* (2001)[24]	Multicenter RCT	166	CVVHDF vs IHD	66% vs 48% (*P*=0.02)	30% vs 48% (*P*=ns)	Unbalanced randomization favoring IHD
John *et al.* (2001)[25]	Single-center RCT	30	CVVHF vs IHD	70% vs 70% (*P*=ns)	Not reported	Survival was not the primary outcome

Only prospective randomized controlled trials published in peer-reviewed journals in English are included. *In-hospital mortality unless stated otherwise. ‡Percentage alive and off renal replacement therapy at hospital discharge. Abbreviations: CVVHD, continuous venovenous hemodialysis; CVVHDF, continuous venovenous hemodiafiltration; CVVHF, continuous venovenous hemofiltration; IHD, intermittent hemodialysis; ns, nonsignificant (*P*>0.05); RCT, randomized controlled trial.

Chander *et al. BMC Nephrology* (2024) 25:1
https://doi.org/10.1186/s12882-023-03435-4

BMC Nephrology

RESEARCH Open Access

Mortality and mode of dialysis: meta-analysis and systematic review

Subhash Chander[1*], Sindhu Luhana[2], FNU Sadarat[3], Om Parkash[4], Zubair Rahaman[3], Hong Yu Wang[1], FNU Kiran[5], Abhi Chand Lohana[6], FNU Sapna[7] and Roopa Kumari[8]

Abstract

Background The global use of kidney replacement therapy (KRT) has increased, mirroring the incidence of acute kidney injury and chronic kidney disease. Despite its growing clinical usage, patient outcomes with KRT modalities remain controversial. In this meta-analysis, we sought to compare the mortality outcomes of patients with any kidney disease requiring peritoneal dialysis (PD), hemodialysis (HD), or continuous renal replacement therapy (CRRT).

Methods The investigation was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). PubMed (MEDLINE), Cochrane Library, and Embase databases were screened for randomized trials and observational studies comparing mortality rates with different KRT modalities in patients with acute or chronic kidney failure. A random-effects model was applied to compute the risk ratio (RR) and 95% confidence intervals (95%CI) with CRRT vs. HD, CRRT vs. PD, and HD vs. PD. Heterogeneity was assessed using I^2 statistics, and sensitivity using leave-one-out analysis.

Results Fifteen eligible studies were identified, allowing comparisons of mortality risk with different dialytic modalities. The relative risk was non-significant in CRRT vs. PD [RR = 0.95, (95%CI 0.53, 1.73), $p = 0.92$ from 4 studies] and HD vs. CRRT [RR = 1.10, (95%CI 0.95, 1.27), $p = 0.21$ from five studies] comparisons. The findings remained unchanged in the leave-one-out sensitivity analysis. Although PD was associated with lower mortality risk than HD [RR = 0.78, (95%CI 0.62, 0.97), $p = 0.03$], the significance was lost with the exclusion of 4 out of 5 included studies.

Conclusion The current evidence indicates that while patients receiving CRRT may have similar mortality risks compared to those receiving HD or PD, PD may be associated with lower mortality risk compared to HD. However, high heterogeneity among the included studies limits the generalizability of our findings. High-quality studies comparing mortality outcomes with different dialytic modalities in CKD are necessary for a more robust safety and efficacy evaluation.

Keywords Hemodialysis, Peritoneal dialysis, CRRT, Continuous kidney replacement therapy

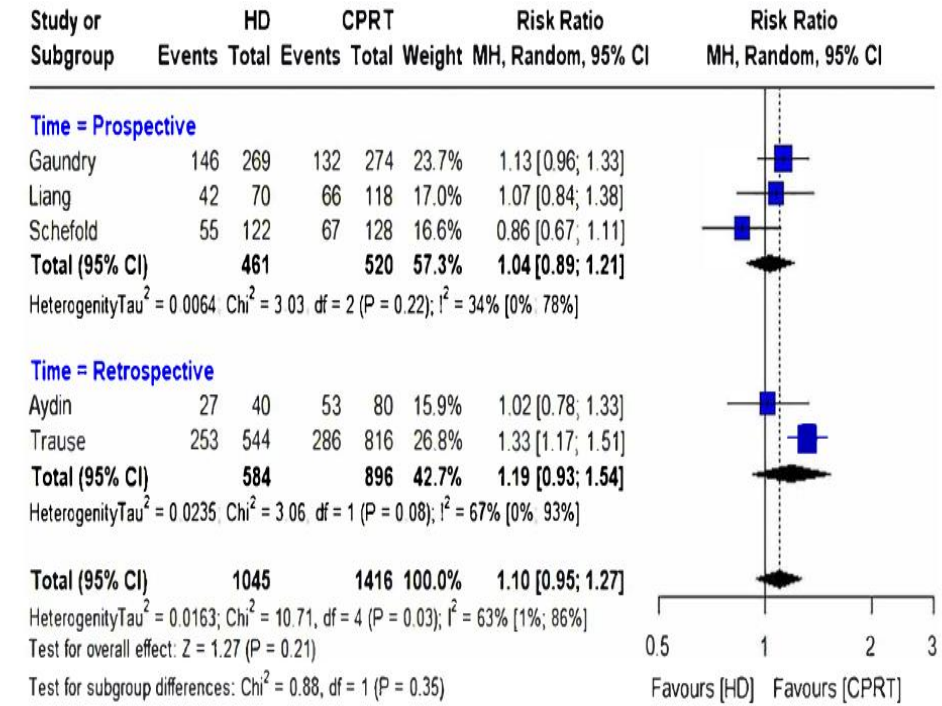


Fig. 8 Forest plot comparing mortality rates between hemodialysis (HD) and continuous renal replacement therapy (CRRT)

Gaudry *et al. Critical Care* (2022) 26:93
https://doi.org/10.1186/s13054-022-03955-9

Critical Care

RESEARCH Open Access

Continuous renal replacement therapy *versus* intermittent hemodialysis as first modality for renal replacement therapy in severe acute kidney injury: a secondary analysis of AKIKI and IDEAL-ICU studies

Stéphane Gaudry[1,2,3,4*], François Grolleau[5], Saber Barbar[6], Laurent Martin-Lefevre[7], Bertrand Pons[8], Éric Boulet[9], Alexandre Boyer[10], Guillaume Chevrel[11], Florent Montini[12], Julien Bohe[13], Julio Badie[14], Jean-Philippe Rigaud[15], Christophe Vinsonneau[16], Raphaël Porcher[5], Jean-Pierre Quenot[17,18,19†] and Didier Dreyfuss[3,20†]

Abstract

Background: Intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT) are the two main RRT modalities in patients with severe acute kidney injury (AKI). Meta-analyses conducted more than 10 years ago did not show survival difference between these two modalities. As the quality of RRT delivery has improved since then, we aimed to reassess whether the choice of IHD or CRRT as first modality affects survival of patients with severe AKI.

Methods: This is a secondary analysis of two multicenter randomized controlled trials (AKIKI and IDEAL-ICU) that compared an early RRT initiation strategy with a delayed one. We included patients allocated to the early strategy in order to emulate a trial where patients would have been randomized to receive either IHD or CRRT within twelve hours after the documentation of severe AKI. We determined each patient's modality group as the first RRT modality they received. The primary outcome was 60-day overall survival. We used two propensity score methods to balance the differences in baseline characteristics between groups and the primary analysis relied on inverse probability of treatment weighting.

Results: A total of 543 patients were included. Continuous RRT was the first modality in 269 patients and IHD in 274. Patients receiving CRRT had higher cardiovascular and total-SOFA scores. Inverse probability weighting allowed to adequately balance groups on all predefined confounders. The weighted Kaplan–Meier death rate at day 60 was 54·4% in the CRRT group and 46·5% in the IHD group (weighted HR 1·26, 95% CI 1·01–1·60). In a complementary analysis of less severely ill patients (SOFA score: 3–10), receiving IHD was associated with better day 60 survival

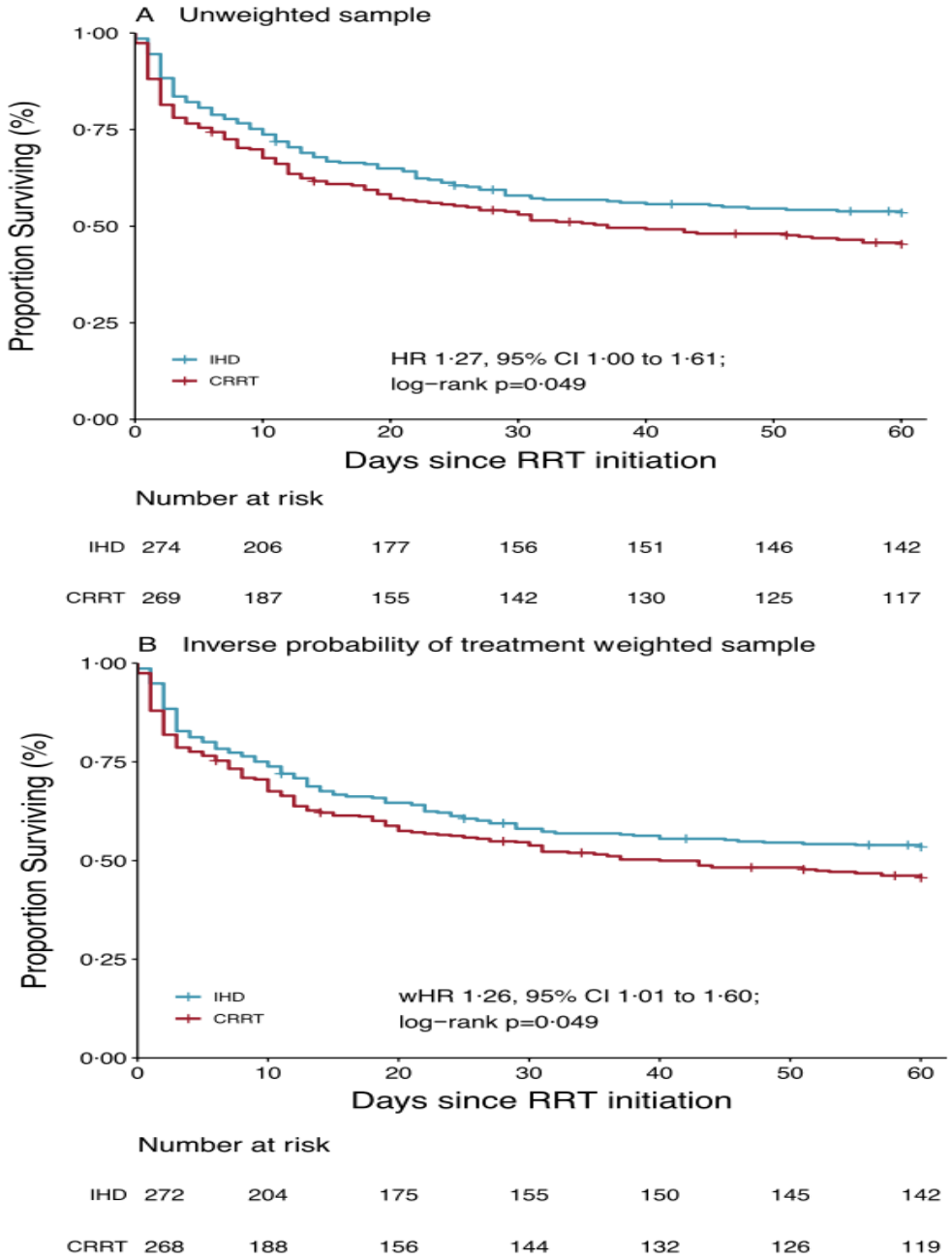
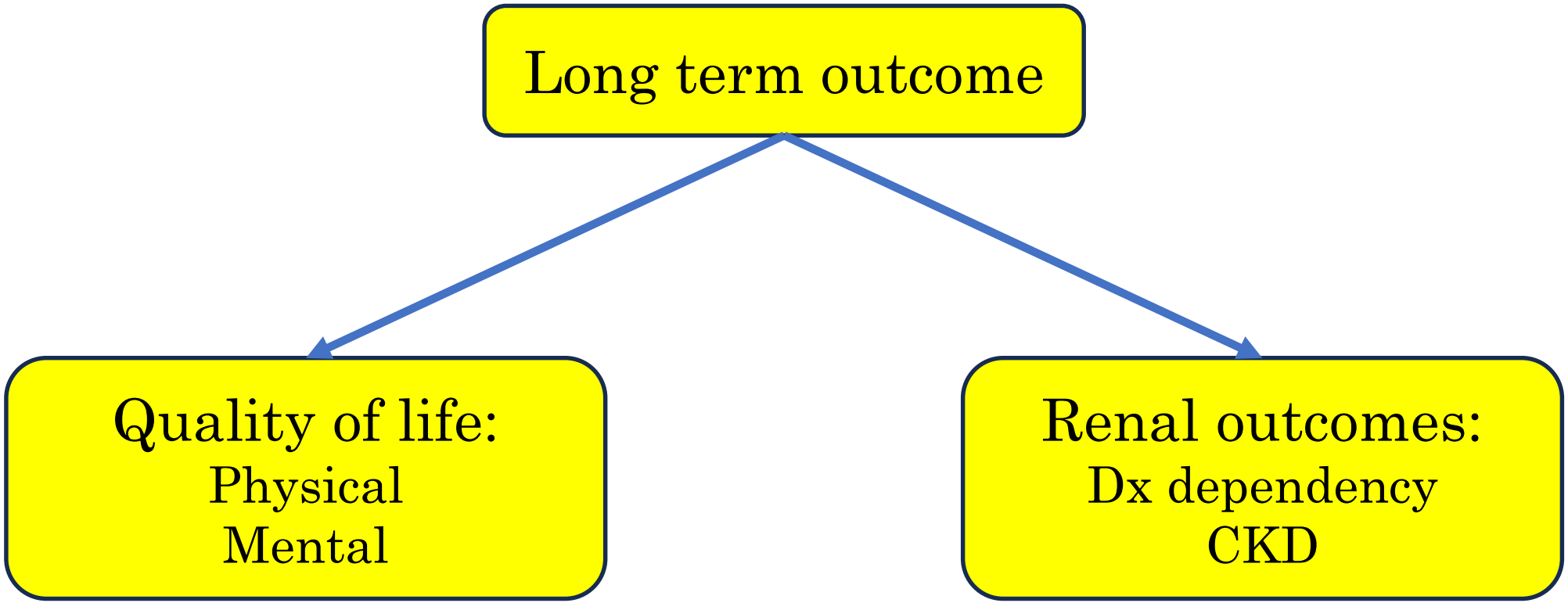
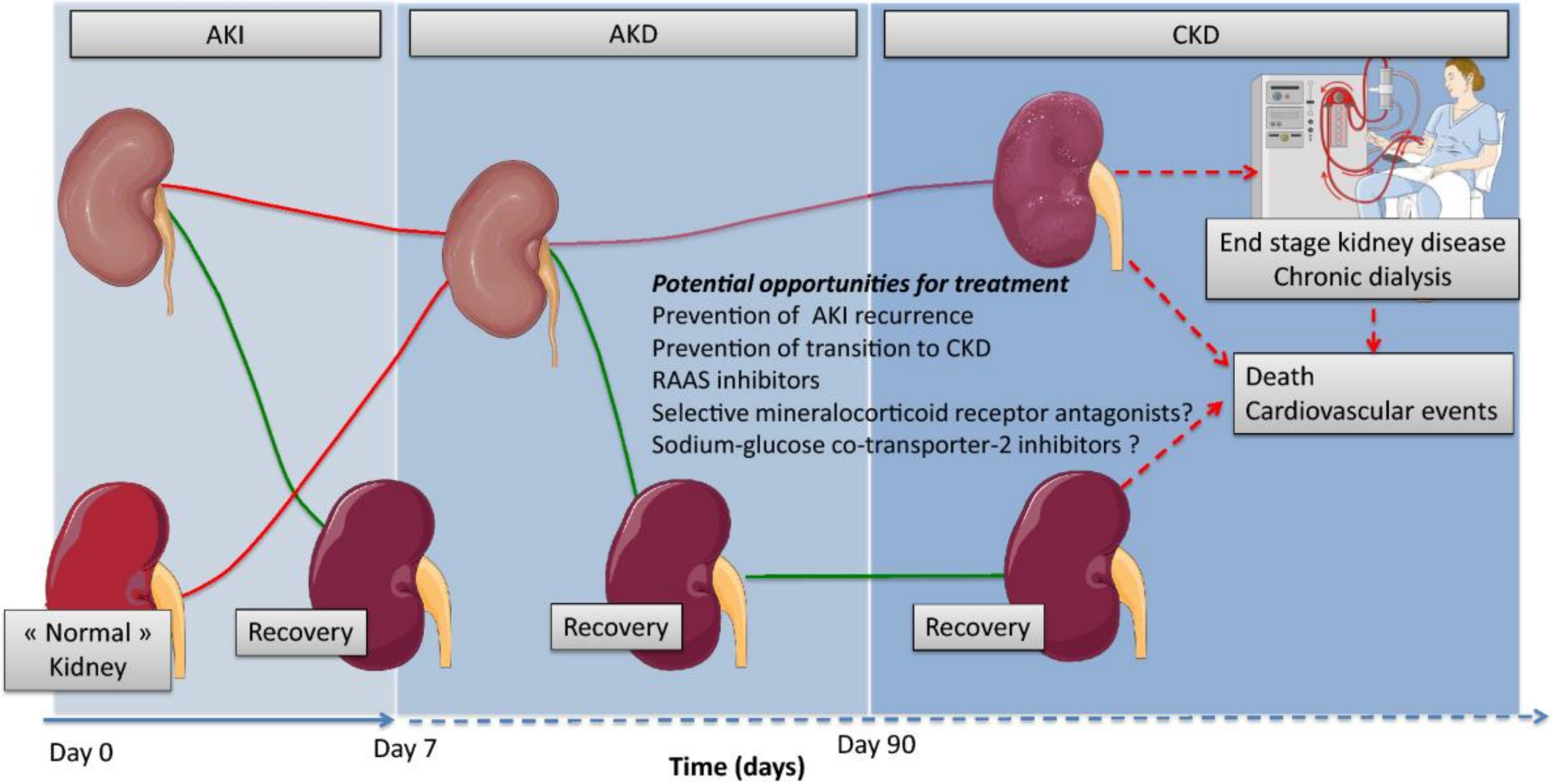
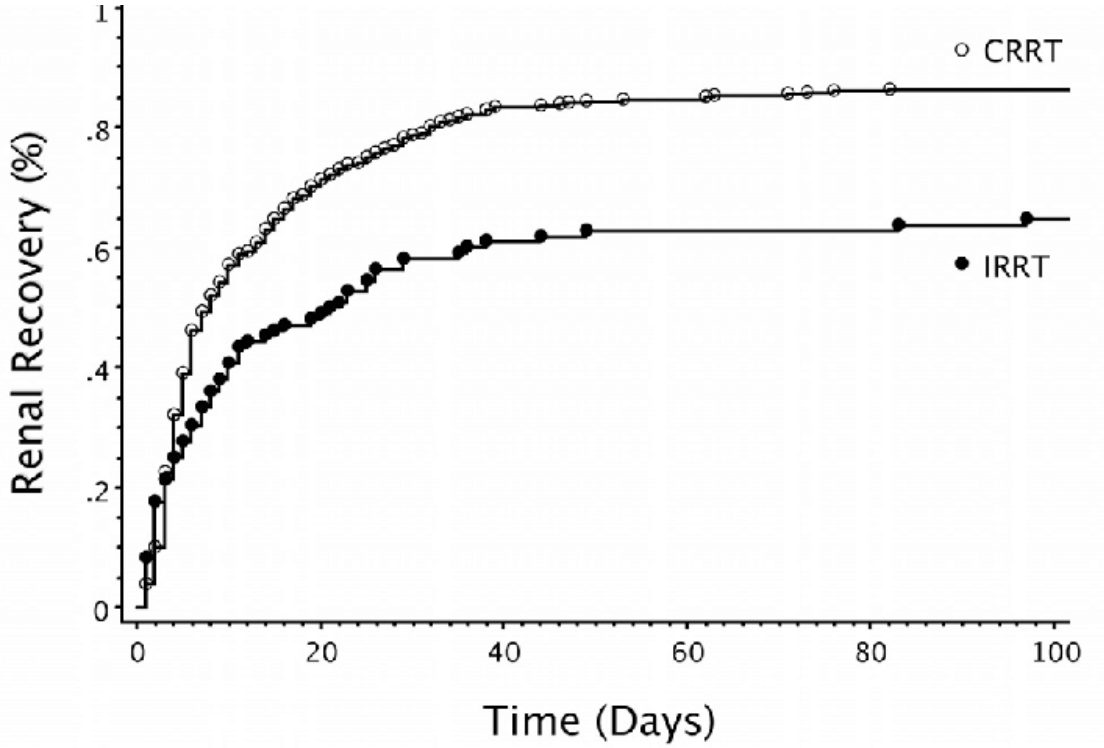


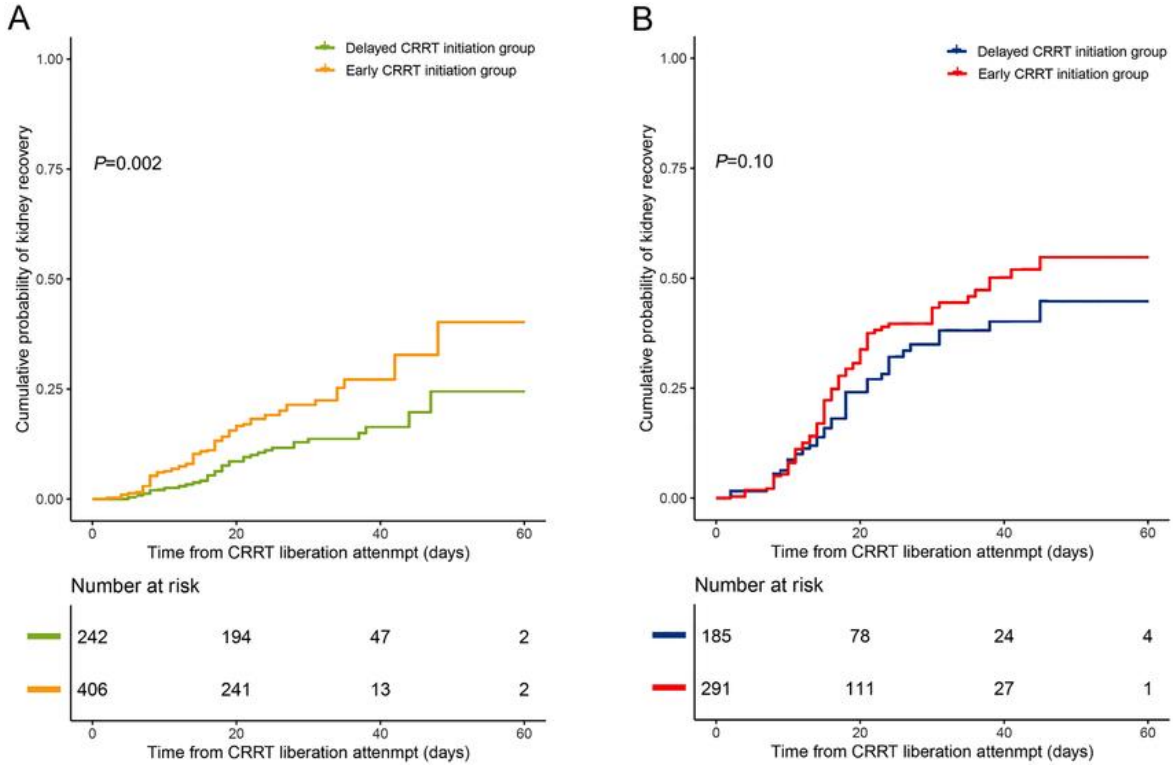
Fig. 2 Primary outcome: probability of survival in the unweighted sample (**A**) and in the IPTW sample (**B**). *HR* hazard ratio, *IHD* intermittent hemodialysis, *CRRT* continuous renal replacement therapy

Long term outcomes




AKI
AKD
CKD
End stage kidney disease
Chronic dialysis
Death
Cardiovascular events
Potential opportunities for treatment
Prevention of AKI recurrence
Prevention of transition to CKD
RAAS inhibitors
Selective mineralocorticoid receptor antagonists?
Sodium-glucose co-transporter-2 inhibitors ?
« Normal »
Kidney
Recovery
Recovery
Recovery
Day 0
Day 7
Day 90
Time (days)

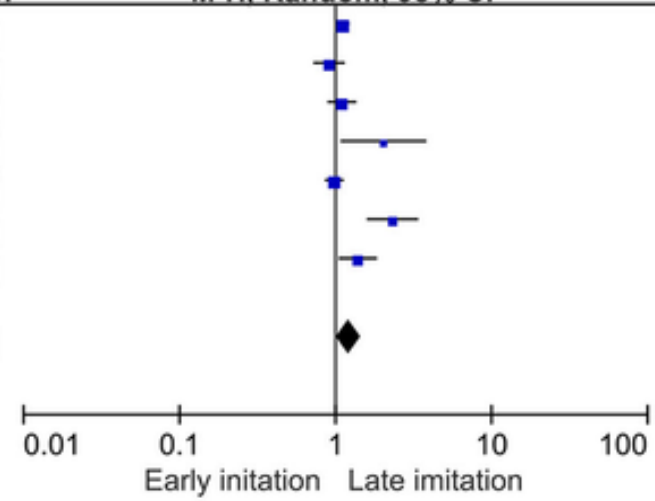




Study or Subgroup	Early initation Events	Total	Late imitation Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Christiansen 2017	125	141	129	162	19.6%	1.11 [1.01, 1.23]
Combes 2015	60	112	66	112	15.5%	0.91 [0.72, 1.15]
Gettings 1999	16	16	11	12	16.1%	1.10 [0.89, 1.36]
Shiao 2009	22	51	10	47	5.8%	2.03 [1.08, 3.82]
Shum 2012	15	16	44	46	18.5%	0.98 [0.85, 1.13]
Tian 2014	18	23	26	77	10.8%	2.32 [1.59, 3.39]
Zarkbock 2016	60	112	46	119	13.7%	1.39 [1.04, 1.84]
Total (95% CI)		**471**		**575**	**100.0%**	**1.21 [1.01, 1.45]**
Total events	316		332			

Heterogeneity: Tau² = 0.04; Chi² = 29.56, df = 6 (P < 0.0001); I² = 80%

Test for overall effect: Z = 2.11 (P = 0.03)



French study, Retrospective; 25750 pts “alive @ Hosp discharge” , RRT for AKI

Renal Replacement Therapy Modality in the ICU and Renal Recovery at Hospital Discharge

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[11]Center for Critical Care Nephrology, The CRISMA (Clinical Research, Investigation, and Systems Modeling of Acute Illness) Center, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA.

A complet list of board members of the AzuRéa Group is as follows: Pierre-François Perrigault, Matthieu Jabaudon, Bernard Allaouchiche, Marc Leone, Jean-Christophe Orban, Matthieu Legrand, Sébastien Perbet, Claire Roger, Jean-Michel Julia, Serge Molliex, Russell Chabanne, François Antonini, Sophie Kauffmann, Pierre-Eric Danin, Thomas Godet, Olivier Langeron, Arnaud Friggeri, Thomas Geeraerts, Laurent Muller, Jacques Ripart, Olivier Baldesi, Saber Barbar, Jérôme Morel, Alain Lepape, Pierre-Marie Bertrand, Jean-Etienne Bazin, Ali Mofredj, Béatrice Riu-Poulenc, Karim Lakhal, Vincent Minville, Emmanuel Futier Philippe Guerci, Emmanuel Novy, Pierre Bouzat, Qin Lu, and Karim Debbat.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Dr. Bonnassieux disclosed that the study received financial support from Gambro-Hospal-Baxter, however, Gambro-Hospal-Baxter had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the article. Dr. Schneider's institution received funding from Gambro-Hospal-Baxter, Fresenius Medical Care, and BBraun Avitum. Drs. Schmidt, Bénard, Cancalon's, and Ichai institutions received funding from Gambro-Hospal-Baxter. Dr. Joannes-Boyau's institution received funding from Asahi Kasei, and he received funding from Gambro-Hospal-Baxter, BBraun, Merck Sharp and Dohme, and Fresenius Medical Care. Dr. Constantin has received consulting fees or speaker honorarium from Gambro-Hospal-Baxter. Dr. Kellum received funding from Baxter and NxStage. Dr. Rimmelé received consulting fees or speaker honorarium from Gambro-Hospal-Baxter and Fresenius Medical Care. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/CCM.0000000000002796

Objectives: Acute kidney injury requiring renal replacement therapy is a major concern in ICUs. Initial renal replacement therapy modality, continuous renal replacement therapy or intermittent hemodialysis, may impact renal recovery. The aim of this study was to assess the influence of initial renal replacement therapy modality on renal recovery at hospital discharge.

Design: Retrospective cohort study of all ICU stays from January 1, 2010, to December 31, 2013, with a “renal replacement therapy for acute kidney injury" code using the French hospital discharge database.

Setting: Two hundred ninety-one ICUs in France.

Patients: A total of 1,031,120 stays: 58,635 with renal replacement therapy for acute kidney injury and 25,750 included in the main analysis.

Interventions: None.

Measurements Main Results: PPatients alive at hospital discharge were grouped according to initial modality (continuous renal replacement therapy or intermittent hemodialysis) and included in the main analysis to identify predictors of renal recovery. Renal recovery was defined as greater than 3 days without renal replacement therapy before hospital discharge. The main analysis was a hierarchical logistic regression analysis including patient demographics, comorbidities, and severity variables, as well as center characteristics. Three sensitivity analyses were performed. Overall mortality was 56.1%, and overall renal recovery was 86.2%. Intermittent hemodialysis was associated with a lower likelihood of recovery at hospital discharge; odds ratio, 0.910 (95% CI, 0.834–0.992) p value equals to 0.0327. Results were consistent across all sensitivity analyses with odds/hazards ratios ranging from 0.883 to 0.958.

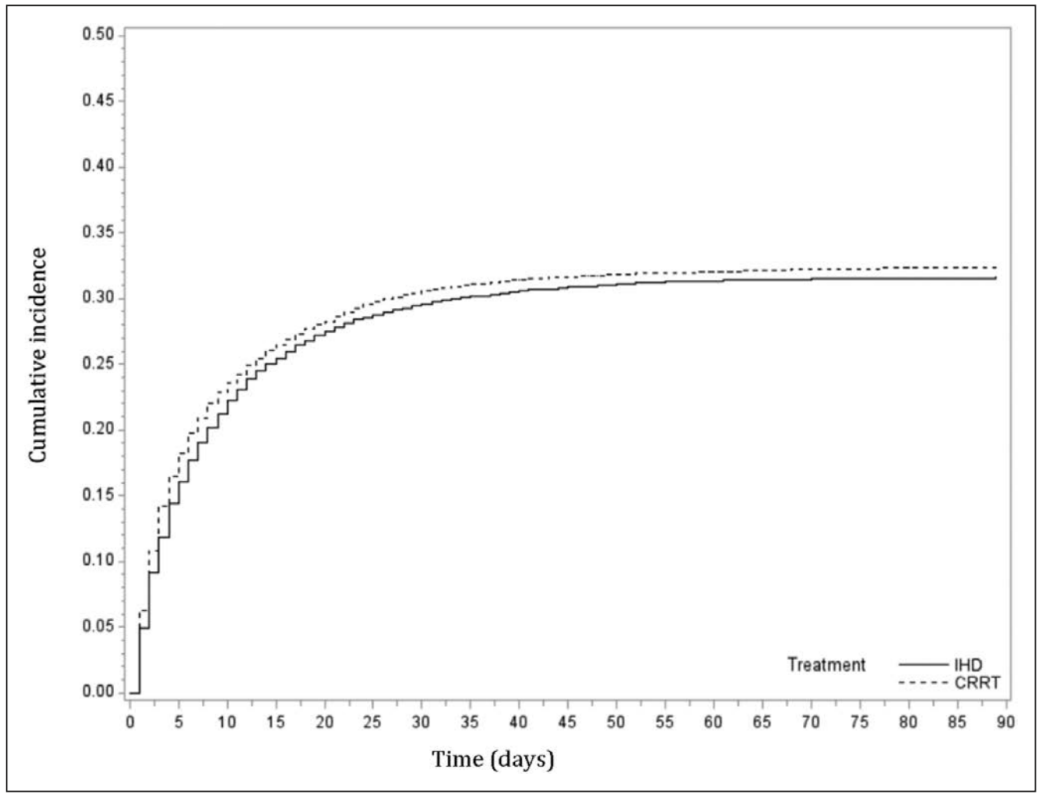
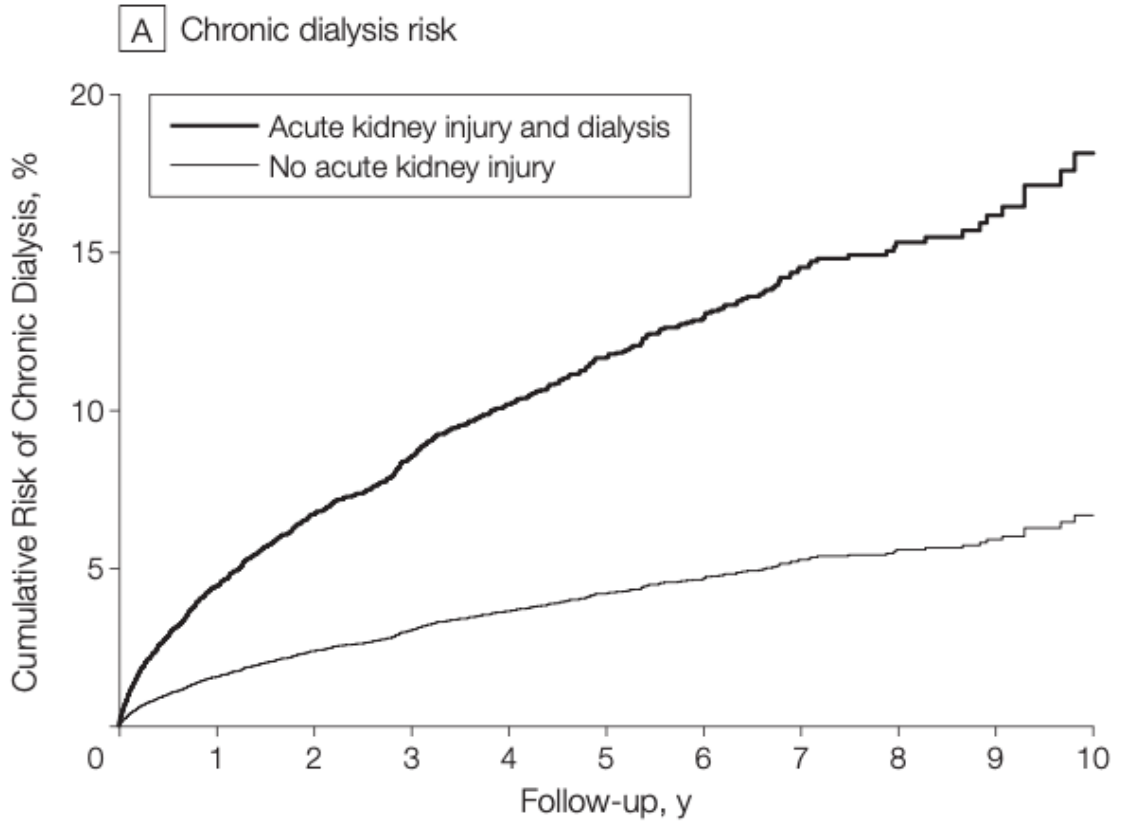


Figure 2. Cumulative incidence of survival and renal recovery at 90 d. CRRT = continuous renal replacement therapy, IHD = intermittent hemodialysis.

AKI leads to CKD after yrs from ICU stay



No. at risk											
Acute kidney injury and dialysis	3769	2761	2116	1683	1305	964	676	462	294	158	58
No acute kidney injury	13598	10224	7850	6080	4639	3383	2342	1555	905	473	169

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

SYSTEMATIC REVIEW

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

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Abstract *Purpose:* Choice of renal replacement therapy (RRT) modality may affect renal recovery after acute kidney injury (AKI). We sought to compare the rate of dialysis dependence among severe AKI survivors according to the choice of initial renal replacement therapy (RRT) modality applied [continuous (CRRT) or intermittent (IRRT)]. *Methods:* Systematic searches of peer-reviewed publications in MEDLINE and EMBASE were performed (last update July 2012). All studies published after 2000 reporting dialysis dependence among survivors from severe AKI requiring RRT were included. Data on follow-up duration, sex, age, chronic kidney disease, illness severity score, vasopressors, and mechanical ventilation were extracted when available. Results were pooled using a random-effects model. *Results:* We identified 23 studies: seven randomized controlled trials (RCTs) and 16 observational studies involving 472 and 3,499 survivors, respectively. Pooled analyses of RCTs showed no difference in the rate of dialysis dependence among survivors (relative risk, RR 1.15 [95 % confidence interval (CI) 0.78–1.68], $I^2 = 0$ %). However, pooled analyses of observational studies suggested a higher rate of dialysis dependence among survivors who initially received IRRT as compared with CRRT (RR 1.99 [95 % CI 1.53–2.59], $I^2 = 42$ %). These findings were consistent with adjusted analyses (performed in 7/16 studies), which found a higher rate of dialysis dependence in IRRT-treated patients [odds ratio (OR) 2.2–25 (5 studies)] or no difference (2 studies). *Conclusions:* Among AKI survivors, initial treatment with IRRT might be associated with higher rates of dialysis dependence than CRRT. However, this finding largely relies on data from observational trials, potentially subject to allocation bias, hence further high-quality studies are necessary.

Keywords Hemofiltration · Hemodialysis · Continuous renal replacement therapy · Acute kidney injury · Intensive care unit · Meta-analysis

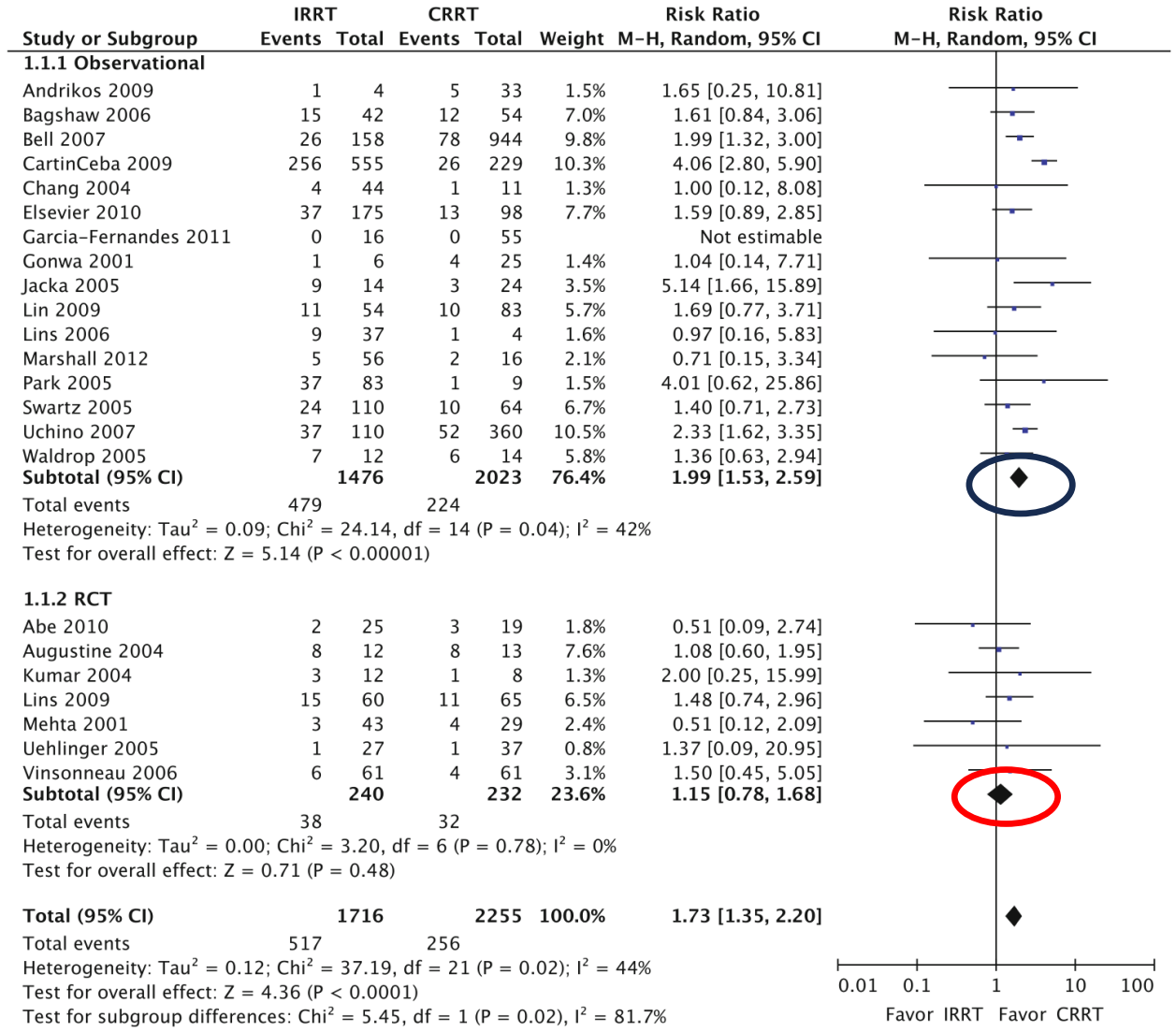


Fig. 2 Forest plot for dialysis dependence among survivors. Stratified by study design. *M–H* Mantel–Haenszel

ORIGINAL

Continuous renal replacement therapy versus intermittent hemodialysis in intensive care patients: impact on mortality and renal recovery

Anne-Sophie Truche[1,2,3], Michael Darmon[4,5], Sébastien Bailly[1,6], Christophe Clec'h[1,7,8], Claire Dupuis[1,9], Benoit Misset[10,11], Elie Azoulay[12,13], Carole Schwebel[2], Lila Bouadma[9], Hatem Kallel[14], Christophe Adrie[15], Anne-Sylvie Dumenil[16], Laurent Argaud[17], Guillaume Marcotte[18], Samir Jamali[19], Philippe Zaoui[3], Virginie Laurent[20], Dany Goldgran-Toledano[21], Romain Sonneville[9], Bertrand Souweine[22] and Jean-Francois Timsit[1,9,23*]

Abstract

Purpose: The best renal replacement therapy (RRT) modality remains controversial. We compared mortality and short- and long-term renal recovery between patients treated with continuous RRT and intermittent hemodialysis.

Methods: Patients of the prospective observational multicenter cohort database OUTCOMEREA™ were included if they underwent at least one RRT session between 2004 and 2014. Differences in patients' baseline and daily characteristics between treatment groups were taken into account by using a marginal structural Cox model, allowing one to substantially reduce the bias resulting from confounding factors in observational longitudinal data analysis. The composite primary endpoint was 30-day mortality and dialysis dependency.

Results: Among 1360 included patients with RRT, 544 (40.0 %) and 816 (60.0 %) were initially treated by continuous RRT and intermittent hemodialysis, respectively. At day 30, 39.6 % patients were dead. Among survivors, 23.8 % still required RRT. There was no difference between groups for the primary endpoint in global population (HR 1.00, 95 % CI 0.77–1.29; $p = 0.97$). In patients with higher weight gain at RRT initiation, mortality and dialysis dependency were

"Composite outcomes" "Death + RRT dependency"

- CRRT : 30 d mortality = 46%
- IRRT : 30 d mortality = 35%

- CRRT : Dx dependency = 21.8%
- IRRT : Dx dependency = 24.9%

- Results of the "composite (30 d mortality + Dx dependency) outcome" = there is **NO significant difference** for the primary endpoint (**alive w/o RRT**) HR 1.00

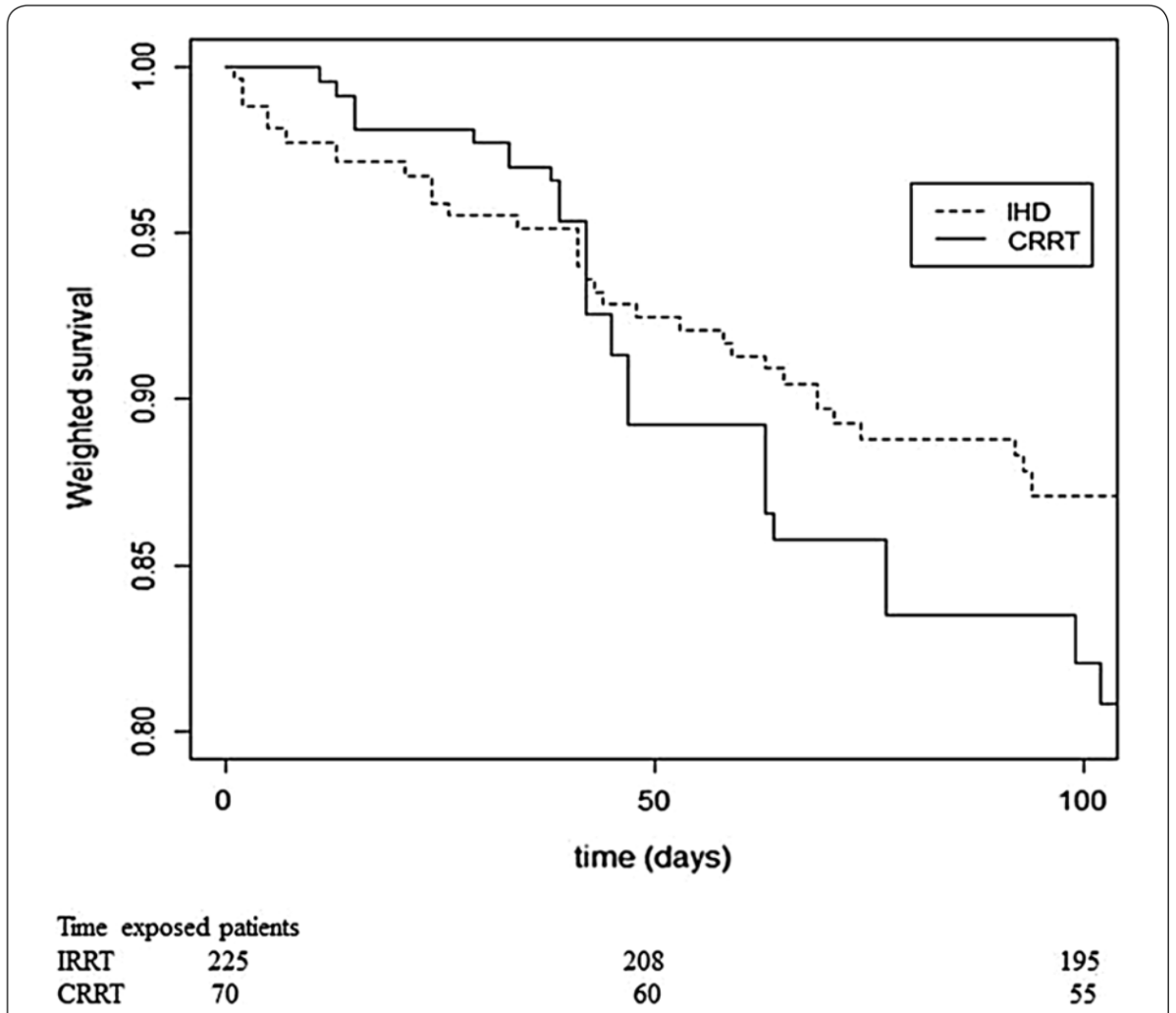


Fig. 3 Six-month mortality according to main type of renal replacement therapy received during the first 7 days: survival curves are weighted with patient IPTW estimators. Survival curve initial time is ICU discharge. *IHD* intermittent hemodialysis, *CRRT* continuous renal replacement therapy, *ICU* intensive care unit

ISICEM 2015
Rinaldo Bellomo

- IHD decrease the chance that a survivor of severe AKI will become Dx free & delays recovery to Dx independence.
- Intensive IHD decrease/delays the chance of becoming Dx independent even more (dose-related toxicity)
- IHD is a nephrotoxin just like starch, AMG, NSAIDs, Ampho.,…
- In ICU pts, IHD is an injurious historic phenomenon
- There should be no place for IHD in ICU.

What is Fluid Accumulation Syndrome ?

Definition FAS: Fluid accumulation (any degree, expressed as percentage from baseline body weight) with new onset organ failure

1. PATHOPHYSIOLOGY

- Peripheral vasodilatation
- Myocardial depression
- Increased metabolism
- DO2/VO2 imbalance
- Capillary leak (EGL degradation)

Organ congestion, impaired urinary output, fluid overload.

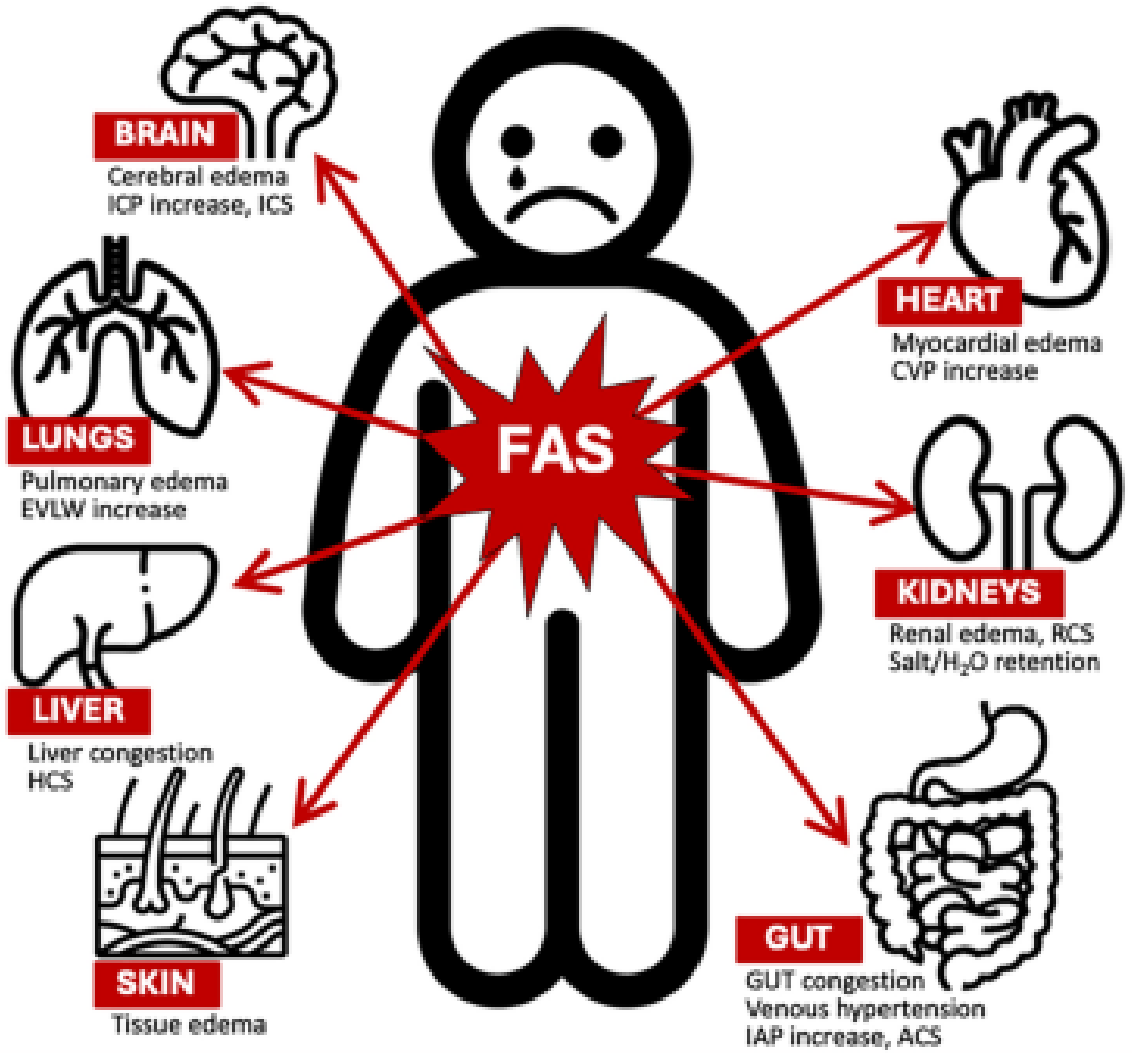
2. DIAGNOSIS

- Clinical examination (edema, cumulative fluid balance, weight)
- Ultrasonography, echocardiography
- Chest radiographs
- Advanced monitoring (TPTD, BIA)

3. PREVENTION

Minimize fluid intake:

- Restrict IV fluids unless absolutely necessary
- Early use of norepinephrine to reduce fluid accumulation
- Use concentrated parenteral/ enteral nutrition formulas
- Limit sodium and chloride administration



4. TREATMENT

Pharmacological:

- Loop diuretics (furosemide or bumetanide)
- Combination diuretic therapy (spironolactone, acetazolamide, indapamide)
- High-dose albumin administration

Mechanical:

- Renal replacement therapy (RRT) for net ultrafiltration
- Compression stockings to improve lymphatic drainage

Supportive:

- Lower IAP
- Improve abdominal wall compliance

5. DE-RESUSCITATION

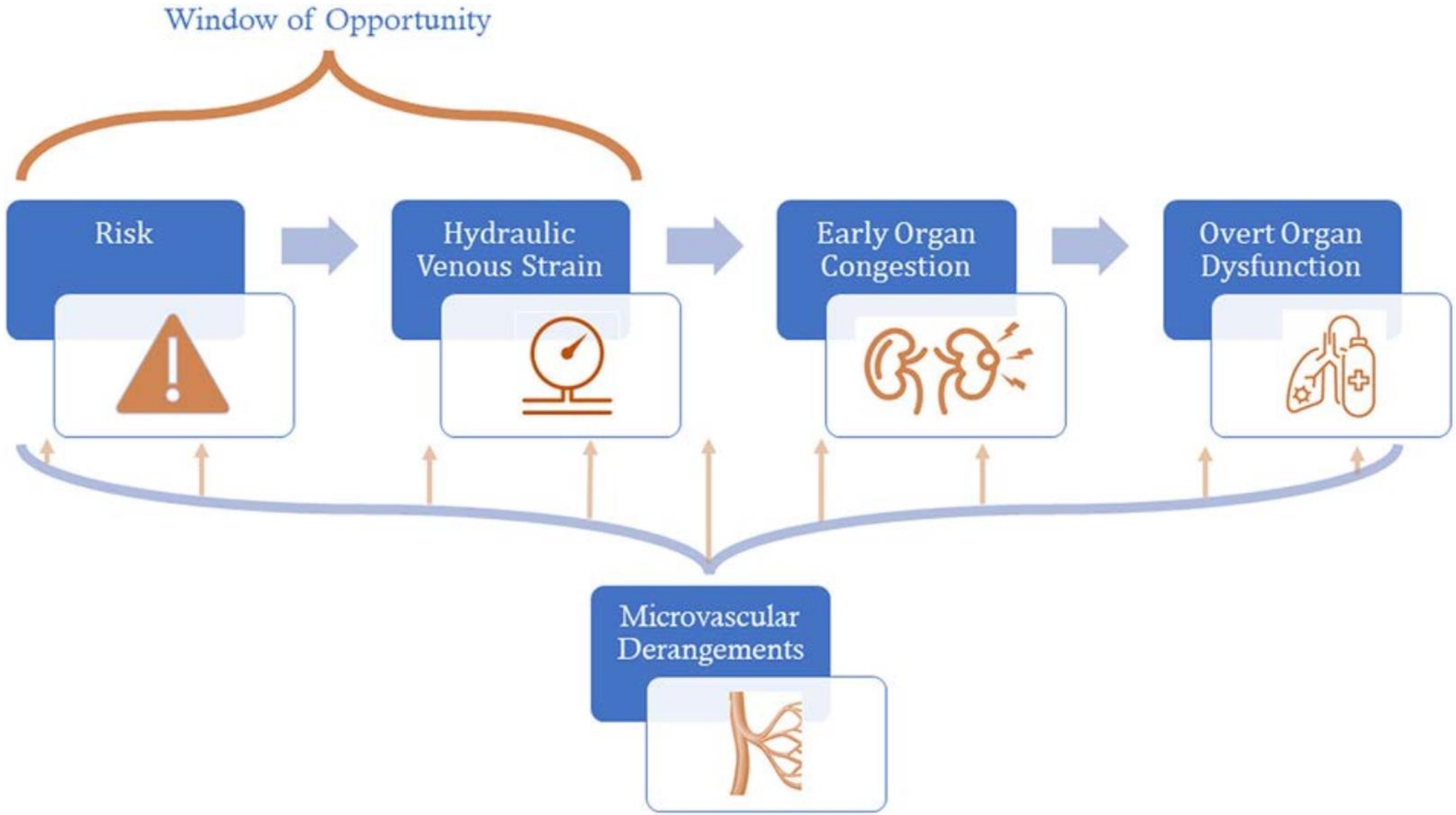
Goal: Active fluid removal in fluid overloaded patients while maintaining hemodynamic stability.

Methods:Pharmacological (diuretics) or Mechanical (RRT) or combination

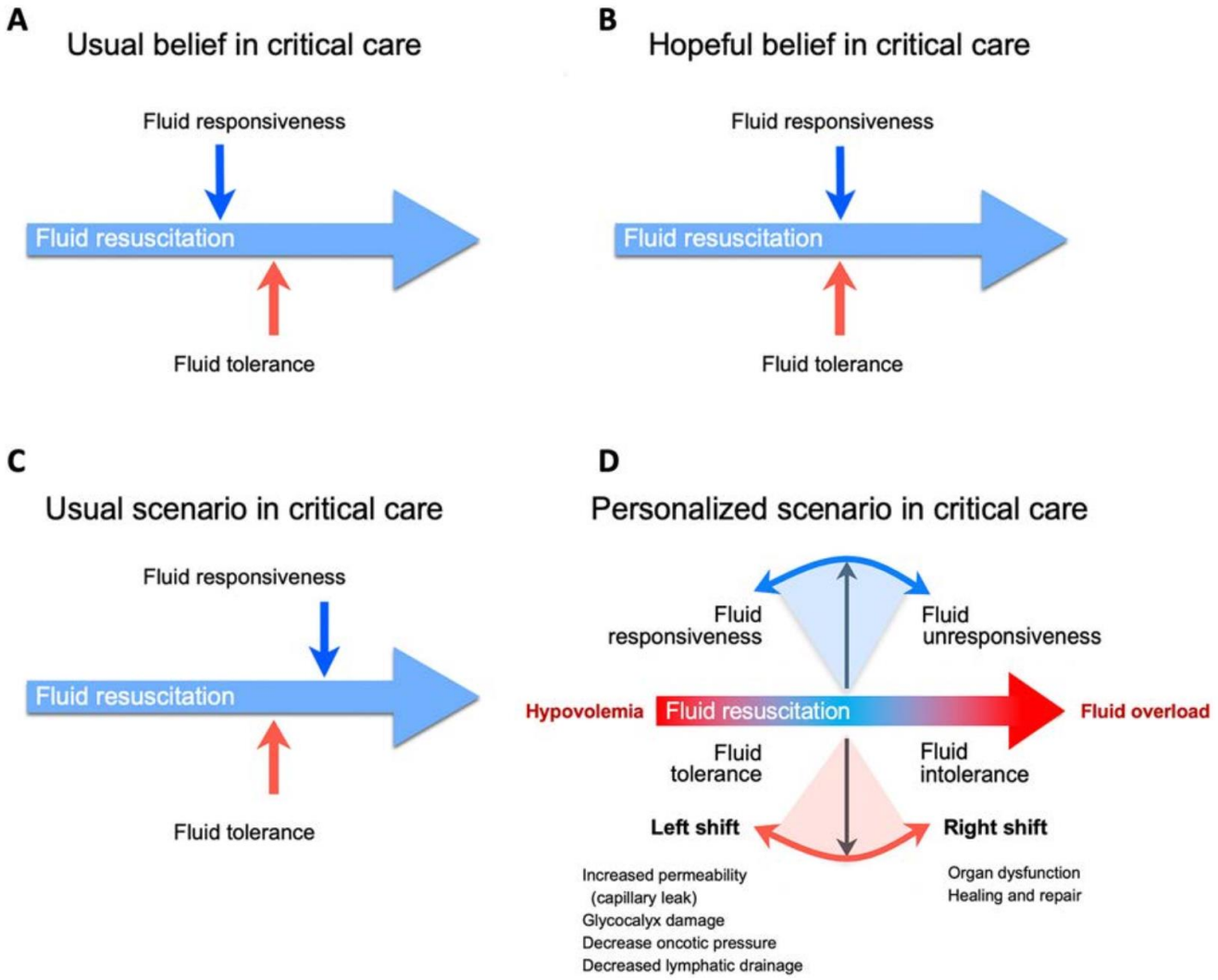
When to Start/Stop: Based on fluid responsiveness, signs of tissue hypoperfusion, and clinical context.

6. TAKE HOME MESSAGES

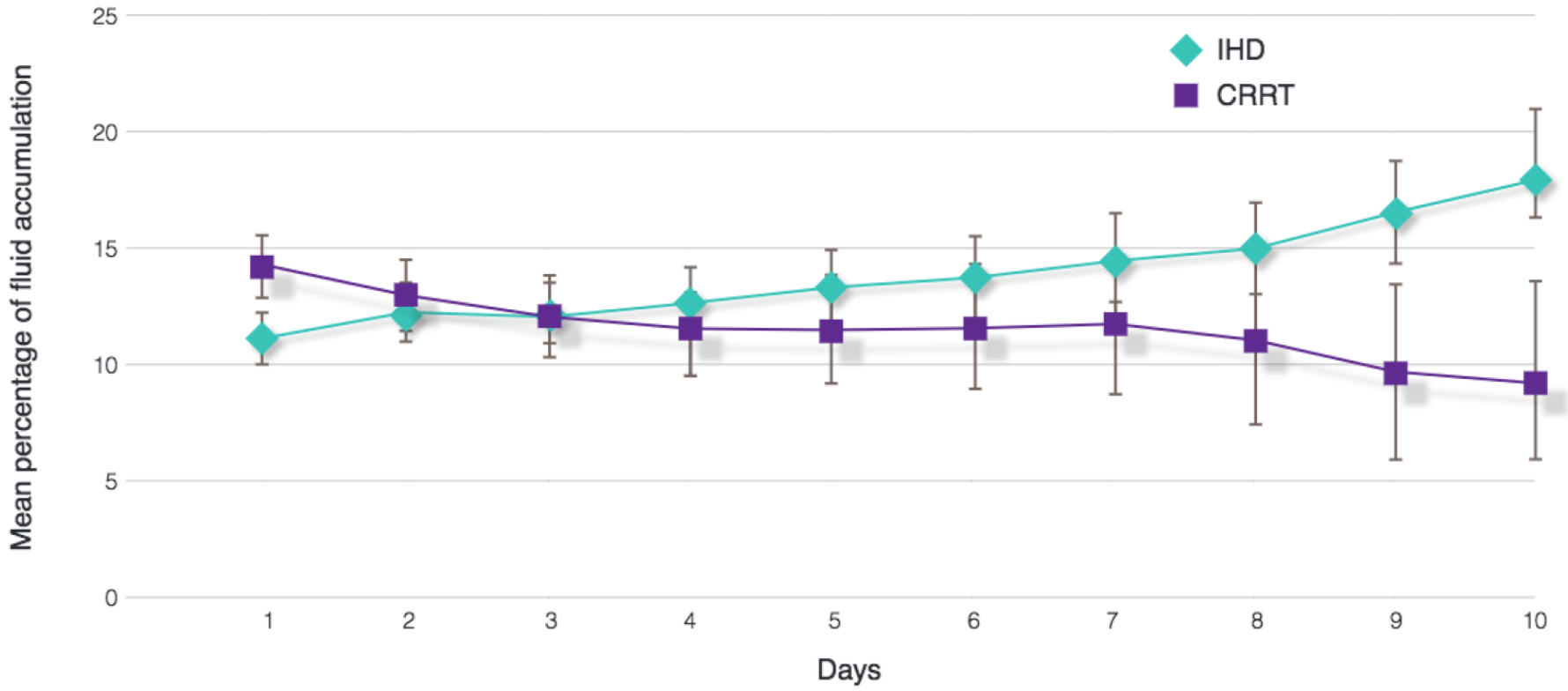
- Fluid management in sepsis should not be "one-size-fits-all"
- Regular monitoring and tailored treatment strategies are crucial
- Early prevention is better than treatment and can significantly improve outcomes.


Window of Opportunity
Risk
Hydraulic Venous Strain
Early Organ Congestion
Overt Organ Dysfunction
Microvascular Derangements

Fluid Responsiveness *vs* Fluid Tolerance



Fluid Balance Homeostasis



Vaara et al. Critical Care 2012, 16:R197
http://ccforum.com/content/16/5/R197

CRITICAL CARE

RESEARCH Open Access

Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: data from the prospective FINNAKI study

Suvi T Vaara[1*], Anna-Maija Korhonen[1], Kirsi-Maija Kaukonen[1], Sara Nisula[1], Outi Inkinen[2], Sanna Hoppu[3], Jouko J Laurila[4], Leena Mildh[1], Matti Reinikainen[5], Vesa Lund[6], Ilkka Parviainen[7] and Ville Pettilä[1,8], for The FINNAKI study group

Abstract

Introduction: Positive fluid balance has been associated with an increased risk for mortality in critically ill patients with acute kidney injury with or without renal replacement therapy (RRT). Data on fluid accumulation prior to RRT initiation and mortality are limited. We aimed to study the association between fluid accumulation at RRT initiation and 90-day mortality.

Methods: We conducted a prospective, multicenter, observational cohort study in 17 Finnish intensive care units (ICUs) during a five-month period. We collected data on patient characteristics, RRT timing, and parameters at RRT initiation. We studied the association of parameters at RRT initiation, including fluid overload (defined as cumulative fluid accumulation > 10% of baseline weight) with 90-day mortality.

Results: We included 296 RRT-treated critically ill patients. Of 283 patients with complete data on fluid balance, 76 (26.9%) patients had fluid overload. The median (interquartile range) time from ICU admission to RRT initiation was 14 (3.3 to 41.5) hours. The 90-day mortality rate of the whole cohort was 116 of 296 (39.2%; 95% confidence interval 38.6 to 39.8%). The crude 90-day mortality of patients with or without fluid overload was 45 of 76 (59.2%) vs. 65 of 207 (31.4%), $P < 0.001$. In logistic regression, fluid overload was associated with an increased risk for 90-day mortality (odds ratio 2.6) after adjusting for disease severity, time of RRT initiation, initial RRT modality, and sepsis. Of the 168 survivors with data on RRT use at 90 days, 34 (18.9%, 95% CI 13.2 to 24.6%) were still dependent on RRT.

Conclusions: Patients with fluid overload at RRT initiation had twice as high crude 90-day mortality compared to those without. Fluid overload was associated with increased risk for 90-day mortality even after adjustments.

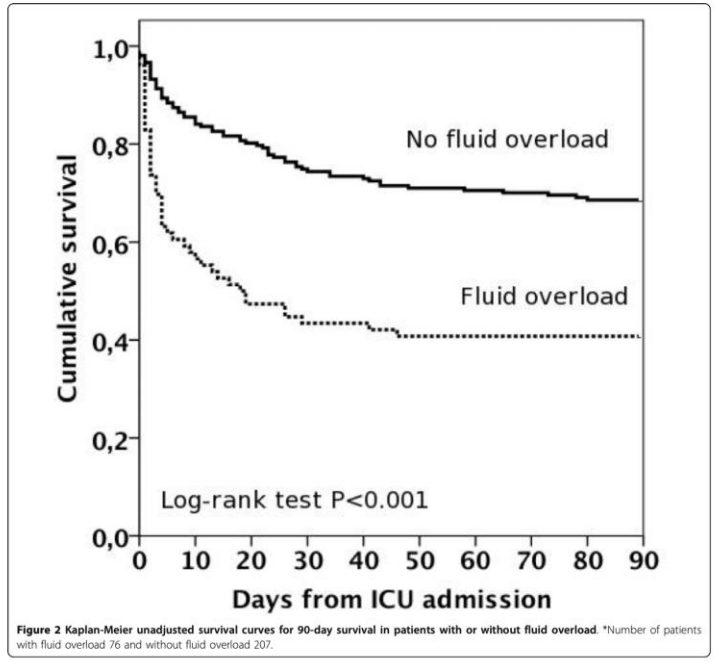


Figure 2 Kaplan-Meier unadjusted survival curves for 90-day survival in patients with or without fluid overload. *Number of patients with fluid overload 76 and without fluid overload 207.

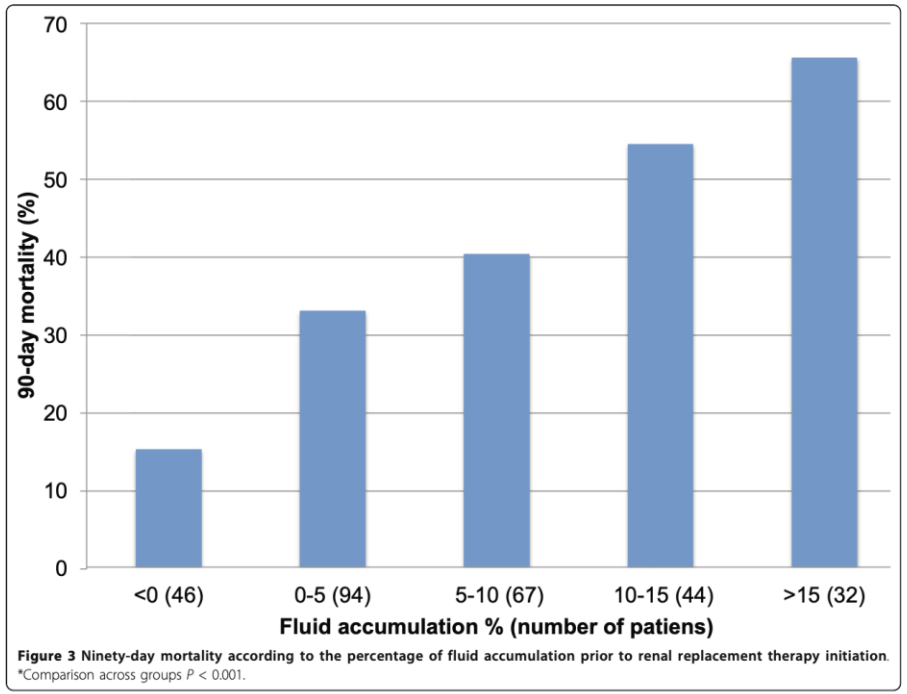


Figure 3 Ninety-day mortality according to the percentage of fluid accumulation prior to renal replacement therapy initiation. *Comparison across groups $P < 0.001$.

Wang et al. Critical Care (2015) 19:371
DOI 10.1186/s13054-015-1085-4

CRITICAL CARE

RESEARCH Open Access

Fluid balance and mortality in critically ill patients with acute kidney injury: a multicenter prospective epidemiological study

Na Wang[1,2†], Li Jiang[1†], Bo Zhu[1], Ying Wen[1], and Xiu-Ming Xi[1*] The Beijing Acute Kidney Injury Trial (BAKIT) Workgroup

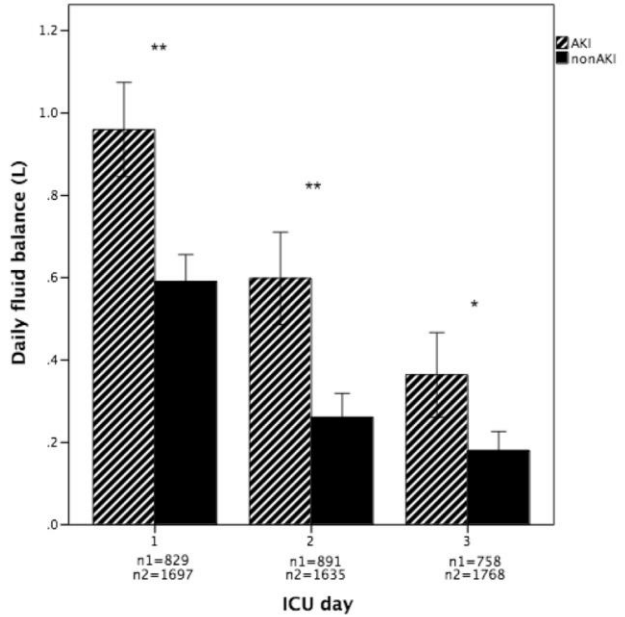


Fig. 2 Daily fluid balance in acute kidney injury (AKI) and non-AKI in the first 3 days of intensive care unit (ICU) stay (mean ± standard error of the mean). *$P = 0.007$; **$P < 0.001$. n1 represents patients with AKI; n2 represents patients without AKI

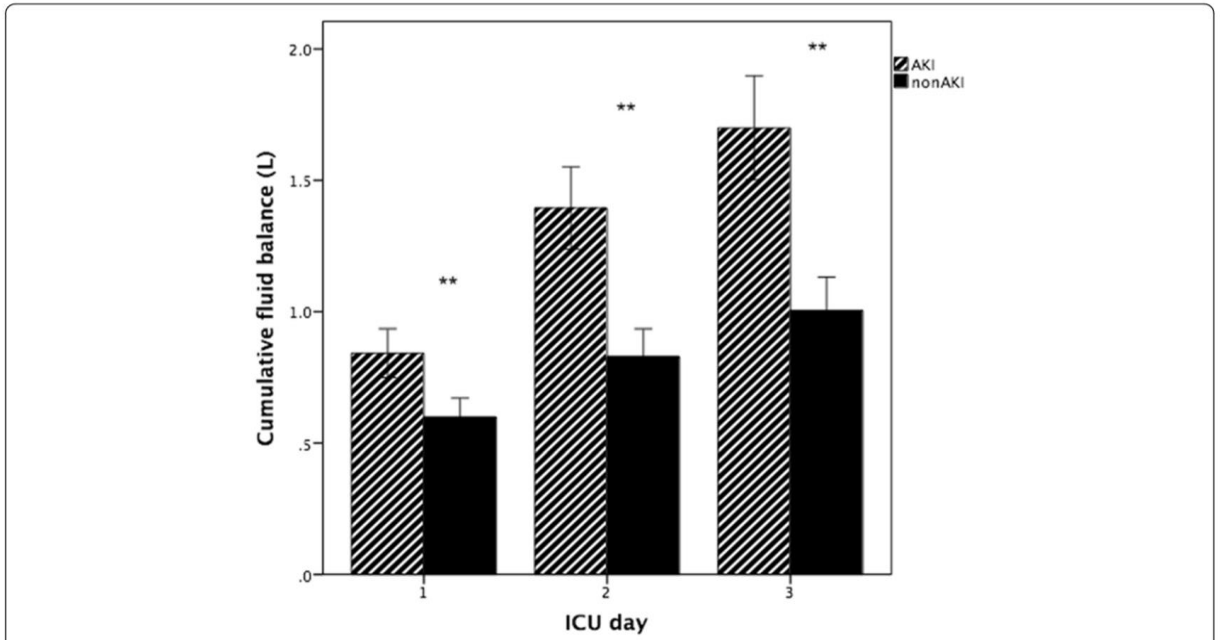


Fig. 3 Cumulative fluid balance in acute kidney injury (AKI) and non-AKI at 24, 48, and 72 h of intensive care unit (ICU) stay (mean ± standard error of the). **$P < 0.001$

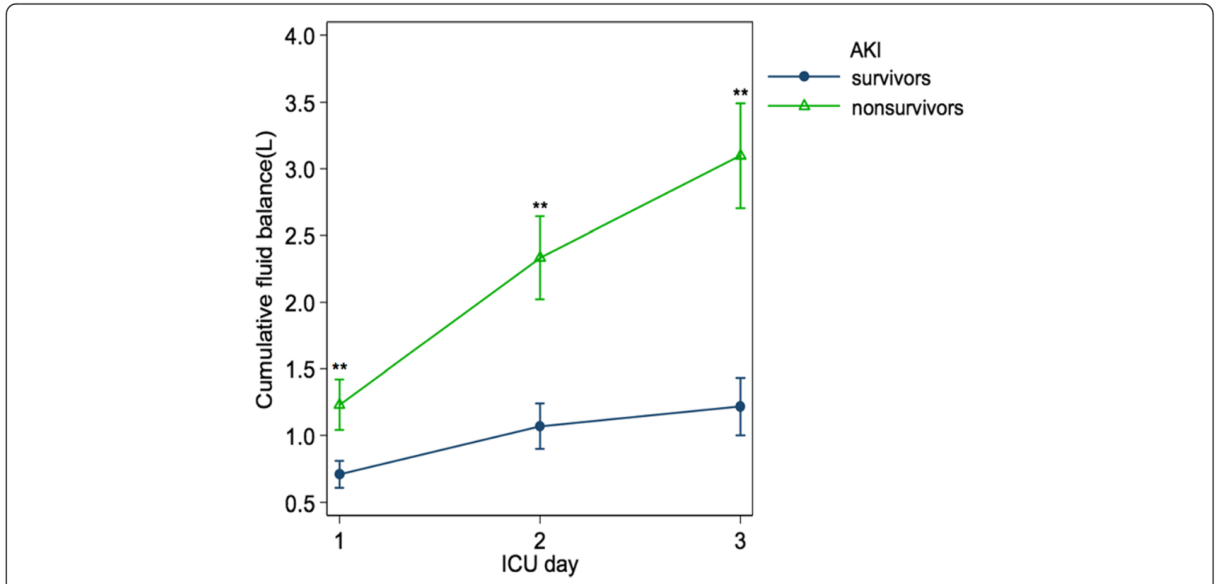


Fig. 4 Cumulative fluid balance in acute kidney injury (AKI) survivors and non-survivors in the first 3 days of their intensive care unit (ICU) stay (mean ± standard error of the mean). **$P < 0.001$

Blood Purification

ADQI Consensus

Blood Purif 2016;42:266–278
DOI: 10.1159/000448528

Published online: August 26, 2016

Precision Fluid Management in Continuous Renal Replacement Therapy

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on behalf of the Acute Disease Quality Initiative (ADQI) Consensus Group

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Key Words
Fluid · Management · Continuous renal replacement therapy · Precision medicine · Hemodialysis

Abstract
Fluid management during continuous renal replacement therapy (CRRT) in critically ill patients is a dynamic process that encompasses 3 inter-related goals: maintenance of the patency of the CRRT circuit, maintenance of plasma electrolyte and acid–base homeostasis and regulation of patient fluid balance. In this article, we report the consensus recommendations of the 2016 Acute Disease Quality Initiative XVII conference on 'Precision Fluid Management in CRRT'. We discuss the principles of fluid management, describe various prescription methods to achieve circuit integrity and introduce the concept of integrated fluid balance for tailoring fluid balance to the needs of the individual patient. We sug-

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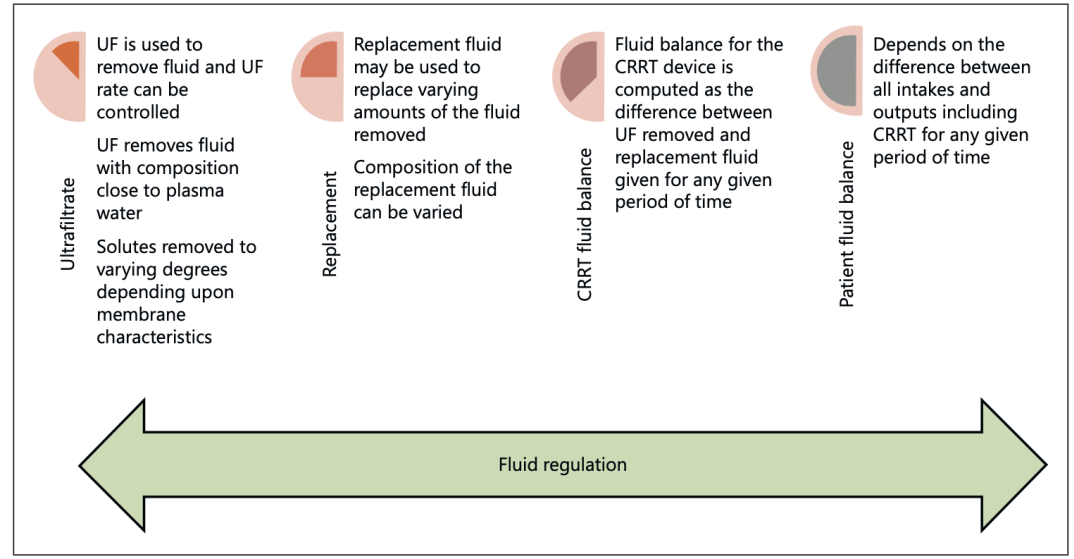
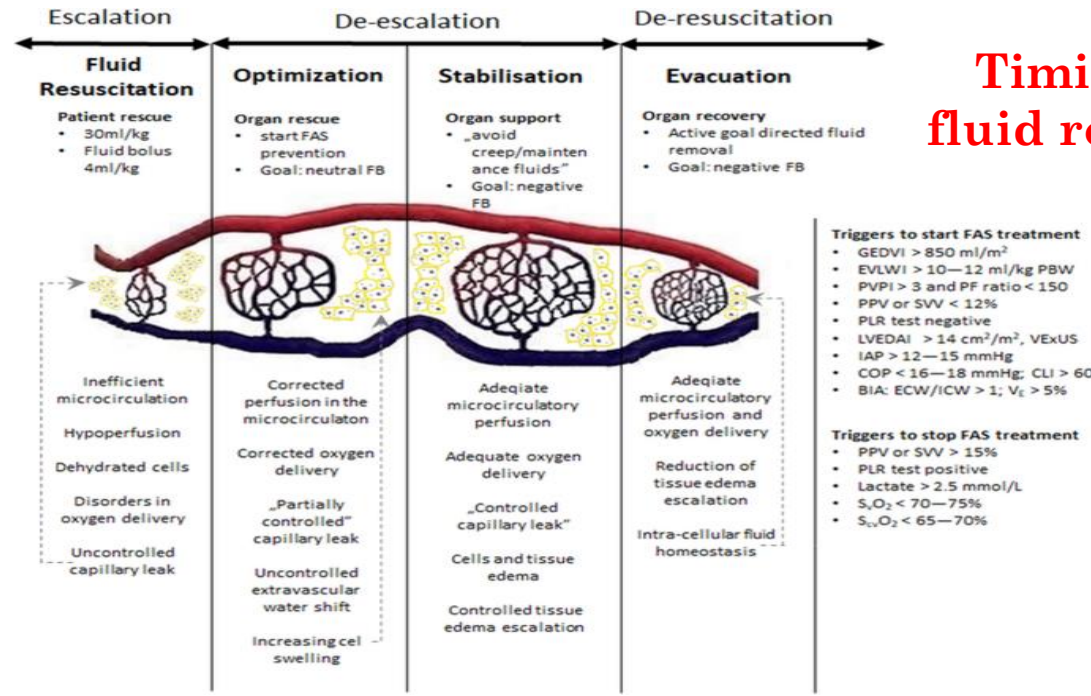


Fig. 2. Principles of fluid management in CRRT. Fluid regulation encompasses all components of fluid management in the patient undergoing CRRT and includes: CRRT machine balance (UF and replacement fluid use) and patient fluid balance. Reprinted with permission from www.ADQI.org.



Timing of fluid removal

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Critical Care

RESEARCH Open Access

Fluid removal associates with better outcomes in critically ill patients receiving continuous renal replacement therapy: a cohort study

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Abstract

Background: Fluid overload is associated with morbidity and mortality in patients receiving renal replacement therapy (RRT). We aimed to explore whether fluid overload at initiation of RRT was independently associated with mortality and whether changes in cumulative fluid balance during RRT were associated with outcome.

Methods: We retrospectively analysed the data of patients who were admitted to the multidisciplinary adult intensive care unit (ICU) in a tertiary care centre in the UK between 2012 and 2015 and received continuous RRT (CRRT) for acute kidney injury for at least 24 h. We collected baseline demographics, body mass index (BMI), comorbidities, severity of illness, laboratory parameters at CRRT initiation, daily cumulative fluid balance (FB), daily prescribed FB target, fluid bolus and diuretic administration and outcomes. The day of the lowest cumulative FB during CRRT was identified as nadir FB.

Results: Eight hundred twenty patients were analysed (median age 65 years; 49% female). At CRRT initiation, the median cumulative FB was + 1772 ml; 89 patients (10.9%) had a cumulative FB > 10% body weight (BW). Hospital survivors had a significantly lower cumulative FB at CRRT initiation compared to patients who died (1495 versus 2184 ml; $p < 0.001$). In the 7 days after CRRT initiation, hospital survivors had a significant decline in cumulative FB (mean decrease 473 ml per day, $p < 0.001$) whilst there was no significant change in cumulative FB in non-survivors (mean decrease 112 ml per day, $p = 0.188$). Higher severity of illness at CRRT initiation, shorter duration of CRRT, the number of days without a prescribed FB target and need for higher doses of noradrenaline were independent risk factors for not reaching a FB nadir during CRRT. Multivariable analysis showed that older age, lower BMI, higher severity of illness, need for higher doses of noradrenaline and smaller reductions in cumulative FB during CRRT were independent risk factors for ICU and hospital mortality. Cumulative FB at CRRT initiation was not independently associated with mortality.

Conclusion: In adult patients receiving CRRT, a decrease in cumulative FB was independently associated with lower mortality. Fluid overload and need for vasopressor support at CRRT initiation were not independently associated with mortality after correction for severity of illness.

Keywords: Renal replacement therapy, Acute kidney injury, Fluid balance, Fluid management, Ultrafiltration, Fluid removal

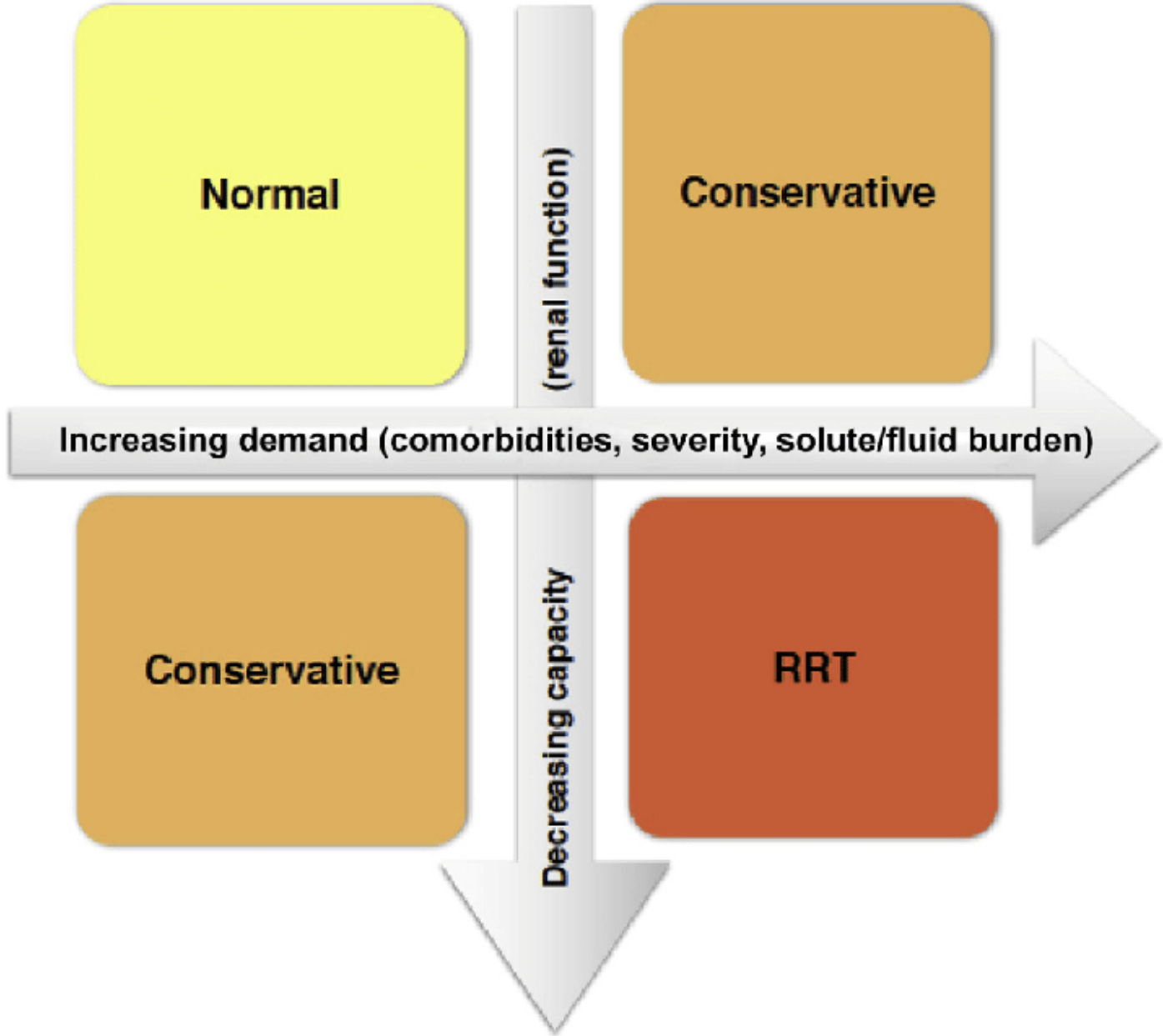
Table 2 Cumulative fluid balance in survivors and non-survivors

Parameters	ICU non-survivors ($n = 264$**)	ICU survivors ($n = 556$**)	*p* value	Hospital non-survivors ($n = 331$**)	Hospital survivors ($n = 489$**)	*p* value
Cumulative FB on day of CRRT initiation						
Cum FB (ml) *	2170 [739–5451]	1581 [263–4254]	< 0.001	2184 [707–5323]	1495 [238–404]	< 0.001
Cum FB (% BW)*	2.9 [0.9–7.2]	2.1 [0.3–5.7]	0.001	2.9 [0.9–7.2]	2.0 [0.3–5.4]	< 0.001
Cum FB ≤ 5% BW, *n* (%)	167 (30)	390 (70)	0.034	211 (38)	346 (62)	0.032
Cum FB > 5% BW, *n* (%)	90 (38)	149 (62)		110 (46)	129 (54)	
Cum FB ≤ 10% BW, *n* (%)	222 (31)	485 (69)	0.132	276 (39)	431 (61)	0.037
Cum FB > 10% BW, *n* (%)	35 (39)	54 (61)		45 (51)	44 (49)	
Cum FB ≤ median FB (1772 ml), *n* (%)	112 (27)	298 (73)	0.003	142 (35)	268 (65)	0.001
Cum FB > median FB (1772 ml), *n* (%)	152 (37)	258 (63)		189 (46)	221 (54)	
Cumulative FB at nadir during CRRT						
Cum FB (ml) *	1115 [– 656 to 3493]	– 275 [– 4401 to 1714]	< 0.001	990 [– 1078 to 3239]	–361 [– 4729 to –1709]	< 0.001
Cum FB (% BW)*	1.6 [– 0.8 to 4.7]	– 0.3 [– 4.9 to –2.5]	< 0.001	1.2 [– 1.6 to 4.0]	–0.6 [– 5.5 to –2.1]	< 0.001
Delta cumulative FB (i.e. maximum change in cumulative FB between initiation of CRRT and nadir)						
Delta FB (ml) *	541 [0–3461]	2479 [183–6242]	< 0.001	882 [0–3651]	2688 [286–6512]	< 0.001
Delta FB (% BW)*	0.9 [0–4.7]	3.1 [0.3–7.7]	< 0.001	1.4 [0–5.0]	3.3 [0.3–8.0]	< 0.001
Time to nadir of cumulative FB* **						
1 to 3 days	54 (26)	152 (74)	0.746	73 (35)	133 (65)	0.577
> 3 days	98 (25)	294 (75)		130 (33)	262 (67)	

Case Study

Case 1

- A 65-year-old male patient is admitted to the ICU with **septic shock** due to pneumonia.
- He has a history of **HTN and T2DM**.
- On day 3 of his ICU stay, he develops **AKI** with rapidly rising creatinine levels and decreasing UOP.
- BP remains unstable despite **vasopressor support**, and he is **intubated** and mechanically ventilated.
- The physician is now faced with a decision regarding renal replacement therapy.
- Should CRRT or IRRT be initiated, and when?


Normal
Conservative
(renal function)
Increasing demand (comorbidities, severity, solute/fluid burden)
Conservative
RRT
Decreasing capacity

Key RCTs: Early- vs late-initiation dialysis in AKI

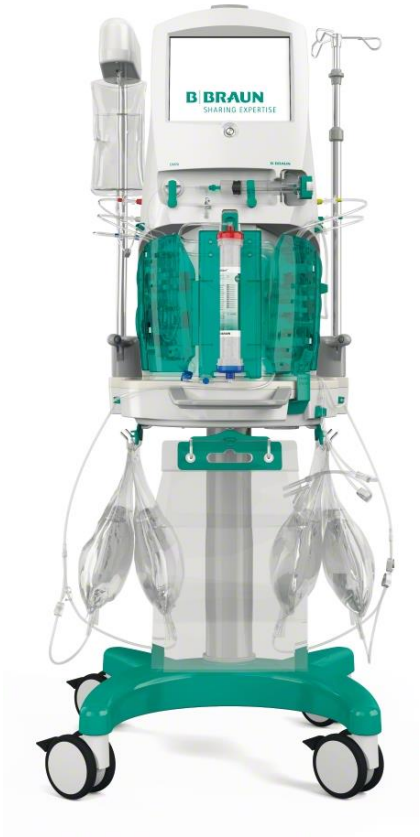
KidneyNews

	ELAIN	AKIKI	IDEAL-ICU	STARRT-AKI	AKIKI 2
Study setting	Germany, one center	France, multicenter	France, multicentric	Multicentric	France, multicentric
AKI eligibility	KDIGO stage 2 AKI + NGAL >150 ng/mL	KDIGO stage 3 AKI + on ventilator/pressors	RIFLE (failure) AKI early septic shock	KDIGO stage 2/3 + critically ill	KDIGO stage 3 AKI + oliguria >72 h, BUN >40
KRT–early/late	<8 h/8–12 h	<6 h/>72 h (or BUN >40/complications)	<12 h/>48 h	<12 h/>72 h or complications	Above/complications or BUN >50
Participants, No.	231	620	488	2927	278
% KRT (early vs late)	100% vs 91%	98% vs 51%	97% vs 62%	97% vs 62%	98% vs 79%
Mortality	90 day (39% vs 54%)	60 day (48% vs 50%)	90 day (58% vs 54%)	90 day (44% vs 44%)	60 day (44% vs 55%)
RCT favors	**Early KRT**	**No difference**	**No difference**	**No difference**	**No difference**
Other key results	**Favors early KRT** (time on KRT; kidney recovery; hospitalization duration)	**Favors delayed KRT** (fewer CRBSI; earlier diuresis post-AKI)	**Mixed results** Delayed (38% did not need KRT); early (fewer emergencies)	**Favors delayed KRT** (fewer adverse effects; KRT dependence)	**Mixed results** Delayed (fewer mortality 60 days); more delayed (fewer need KRT)
Features/ limitations	Mostly surgical patients; most early cases would have self-recovered	Advanced AKI patients; both IHD and CRRT used	Used RIFLE criteria; nonblinded; stopped early for futility	Heterogeneity in groups; KRT decision at physician discretion	Compares late vs very late (not early); BUN levels to start KRT
References	Zarbock et al. (2)	Gaudry et al. (3)	Barbar et al. (4)	Bagshaw et al. (5)	Gaudry et al. (6)

No difference in early vs late initiation of dialysis in AKI (early KRT – fewer AKI complications; delayed KRT – fewer need KRT)

@BeheraVineet

Which modes ?



Case 2

- A 65-year-old male patient presents with **septic shock** due to pneumonia and a history of HTN, type 2 diabetes, and stage 3 CKD.

- Despite initial stabilization with **fluids, antibiotics, and vasopressor therapy**, his condition deteriorates.

- On day 3 of ICU admission, his creatinine rises from 2.1 to 4.5 mg/dL, his UOP drops to less than 200 mL/day, and he exhibits severe metabolic acidosis with a pH of 7.15.

- His BP remains low despite **high-dose norepinephrine**, and he shows signs of **fluid overload** with significant peripheral edema.

- After consultation with nephrology, the decision to start RRT is made, but the team faces a choice: **CRRT or IHD**?

Case 3

- **Evolving Complexity**
- A 65-year-old male with a history of hypertension, type 2 diabetes, and stage 3 chronic kidney disease (CKD) is admitted to the ICU with septic shock secondary to pneumonia.

- After aggressive resuscitation, the patient develops acute kidney injury (AKI), characterized by rising serum creatinine (2.1 mg/dL to 4.5 mg/dL), hyperkalemia (6.2 mmol/L), metabolic acidosis (pH 7.15, lactate 5.5 mmol/L), and oliguria (<200 mL/day).

- He remains hemodynamically unstable on high-dose vasopressors.

- The ICU team considers initiating renal replacement therapy (RRT).
-
- While **CRRT** seems the initial best choice, the patient's evolving condition warrants continuous reassessment.

- The decision between CRRT, **SLED** (as a hybrid option), and **IHD** must be revisited at multiple stages of care.

Concluding Thoughts

- The decision between CRRT, IRRT, and hybrid therapies is far from static, it is a **dynamic, patient-centered process** that evolves with the patient's clinical course.
- Selecting the **right RRT modality** based on the patient's current condition and **disease trajectory**.
- Factors such as **hemodynamic stability, underlying comorbidities, fluid balance, and long-term kidney recovery** guide the choice of therapy.
- **Therapies should be: Tailored & Dynamic for Optimal Outcomes**
- The different modalities should be viewed as **"complementary therapies"**

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