# *Le modalità disponibili in Terapia Intensiva: Intermittenti, Continue o Ibride?*

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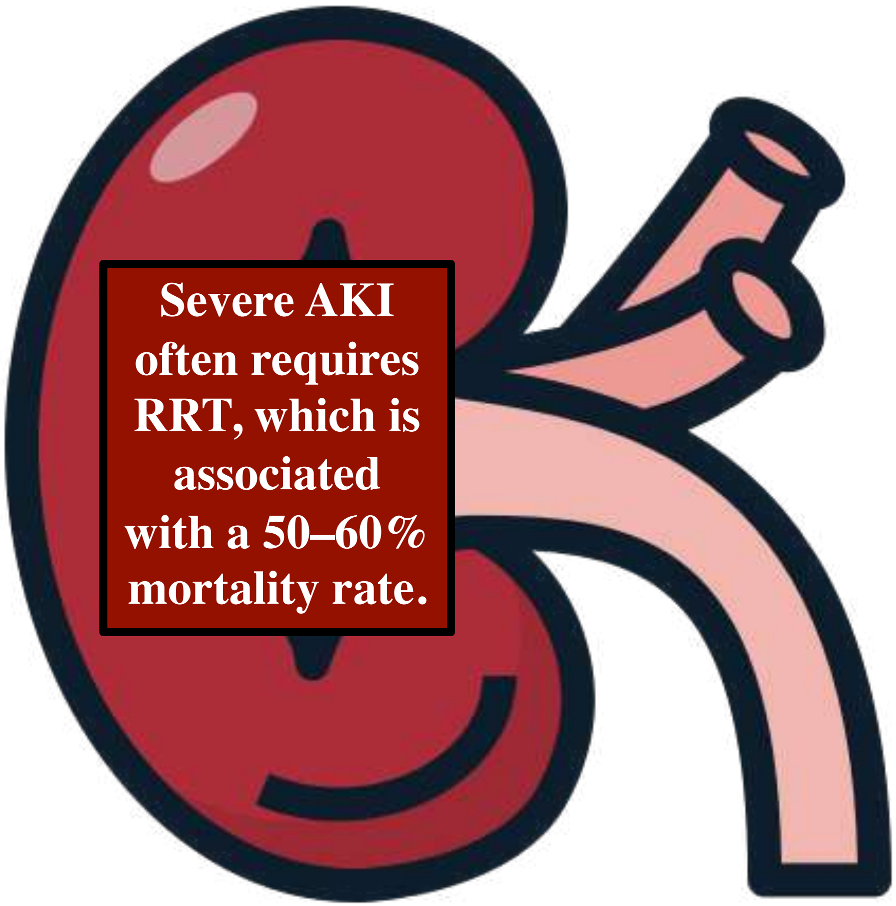
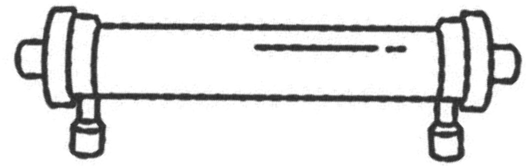
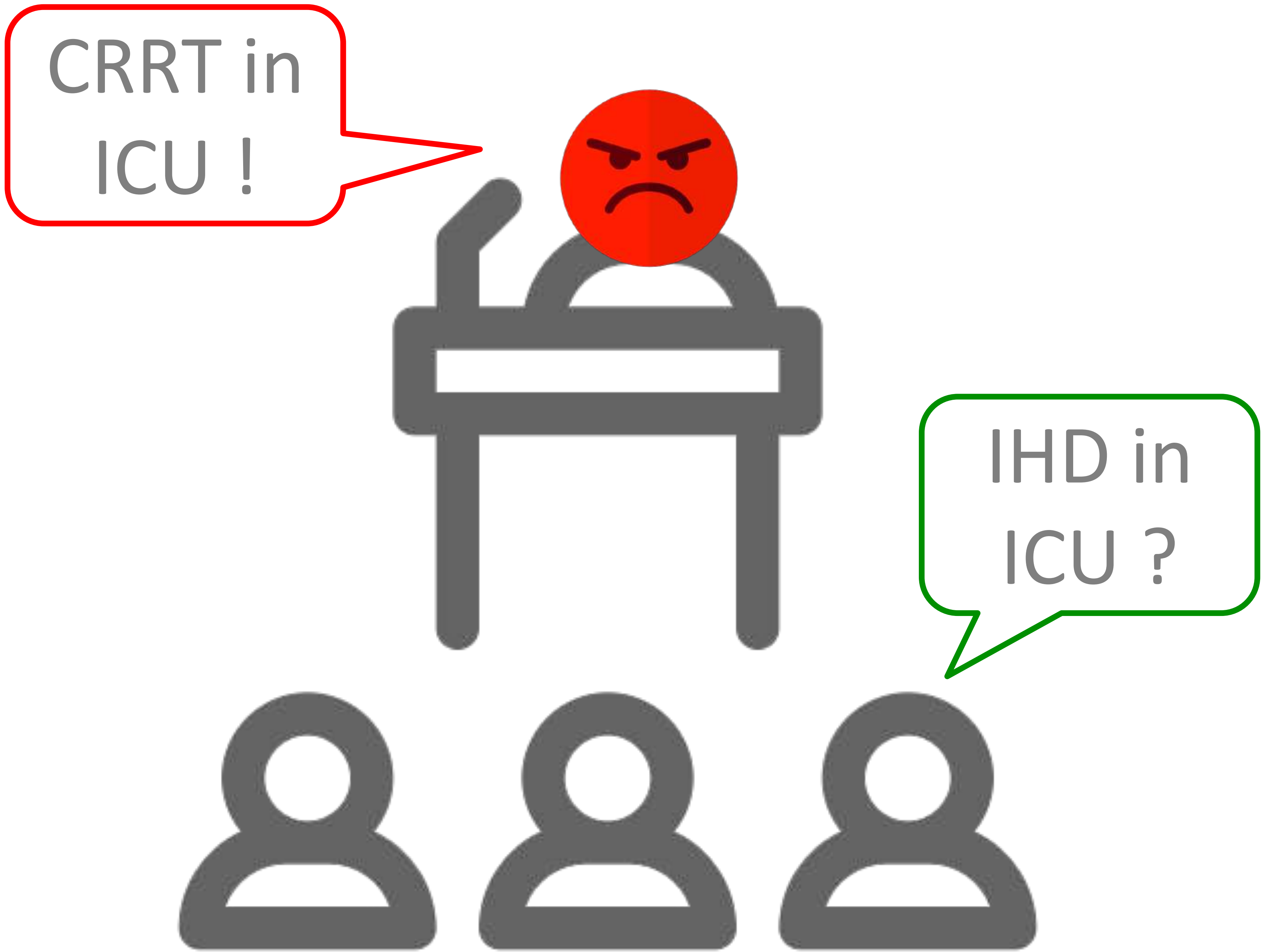


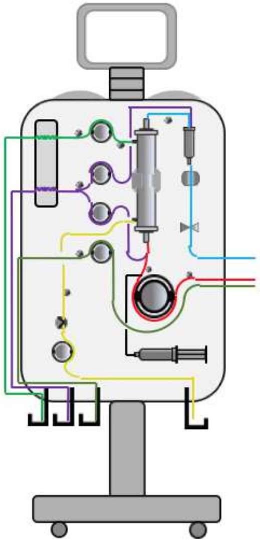
Severe AKI often requires RRT, which is associated with a 50–60% mortality rate.



IHD
SLED
CRRT
CVVH
CVVHD
CVVHDF
EARLY
DELAYED
BIOMARKERS
CITRATE
HEPARIN
NO ANTICOAGULATION
. . .

# ISICEM 2005


CRRT in ICU !
IHD in ICU ?


# Clinical course

Physiotherapy

Fluid balance

# OUTLINE . . .

- IHD, CRRT, HT (SLED, SLEDD, SLEDD-f, EDD,SCD,AVVH, AVVHDF) - nomenclature and definitions
- Evidence for the literature
- . . . And so what?

Tandukar S & Palewsky PM. CHEST (2019)

# Continuous Renal Replacement Therapy

## Who, When, Why, and How

*Srijan Tandukar, MD; and Paul M. Palevsky, MD*

# Selection of RRT Modality

Although CRRT and PIRRT are most commonly used in hemodynamically unstable patients, there is marked variation in practice.

Some centers use CRRT (or PIRRT) in all ICU patients with renal failure regardless of hemodynamic status, whereas others use IHD, albeit with adjustments in prescription, even in vasopressor-dependent patients.

Continuous Renal Replacement Therapies (CRRT)

Intermittent Hemodialysis (IHD)

Prolonged Intermittent Renal Replacement Therapies (PIRRT)

Although the benefit of a **slow, continuous modality** of renal support in hemodynamically unstable patients may seem **selfevident**, RCTs have **failed** to show differences with regard to either mortality or recovery of kidney function comparing CRRT with either IHD or PIRRT.


Mehta RL et al. Kidney Int (2001)
Augustine JJ et al. Am J Kidney Dis (2004)
Uehlinger DE et al. Nephrol Dial Transplant (2005)
Vinsonneau C et al. Lancet (2006)
Lins RL et al. Nephrol Dial Transplant (2009)
Schefold JC et al. Crit Care (2014)
Bagshaw SM et al. Crit Care Med (2008)
Pannu N et al. JAMA (2008)
Friedrich JO et al. Critical Care (2012)
Zhang L et al. Am J Kidney Dis (2015)
Kielstein JT et al. Am J Kidney Dis (2004)
Schwenger V et al. Crit Care (2012)

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# PIRRT

## Prolonged intermittent renal replacement therapy

Acute RRTs include standard **intermittent hemodialysis**, **peritoneal dialysis**, **continuous renal replacement therapies (CRRTs**), and **hybrid therapies** such **as prolonged intermittent renal replacement therapies (PIRRTs).**

Other terms used to describe PIRRT include:

- **Sustained low-efficiency (daily) dialysis** (**SLED** or **SLEDD**)
- **Sustained low-efficiency (daily) diafiltration** (**SLEDD-f**)
- **Extended daily dialysis (EDD)**
- **Slow continuous dialysis** (**SCD**)
- **Go slow dialysis**
- **Accelerated venovenous hemofiltration (AVV**H) or **hemodiafiltration (AVVHDF)**

*14 May 2020*

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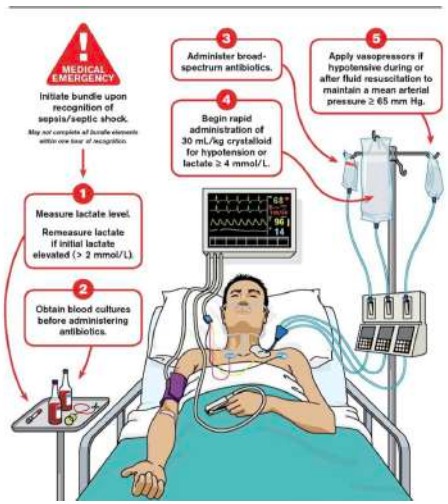
# PIRRT

PIRRT is an **alternative** to CRRT for hemodynamically unstable patients, although the evidence is weak




*14 May 2020*

# Hybrid therapies

Villa et al. Critical Care (2016) 20:283
DOI 10.1186/s13054-016-1456-5

Critical Care

REVIEW Open Access

## Nomenclature for renal replacement therapy and blood purification techniques in critically ill patients: practical applications

Gianluca Villa, Mauro Neri, Rinaldo Bellomo, Jorge Cerda, A. Raffaele De Gaudio, Silvia De Rosa, Francesco Garzotto, Patrick M. Honore, John Kellum, Anna Lorenzin, Didier Payen, Zaccaria Ricci, Sara Samoni, Jean-Louis Vincent, Julia Wendon, Marta Zaccaria, Claudio Ronco, on behalf of the Nomenclature Standardization Initiative (NSI) Alliance

**Abstract**

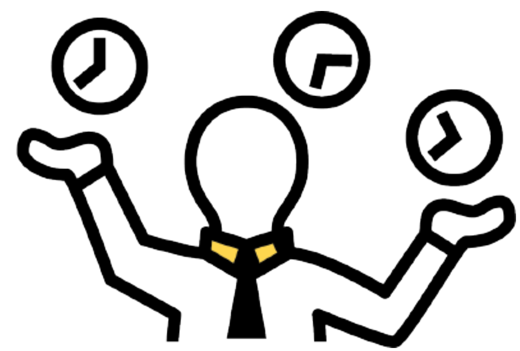
This article reports the conclusions of the second part of a consensus expert conference on the nomenclature of renal replacement therapy (RRT) techniques currently utilized to manage acute kidney injury and other organ dysfunction syndromes in critically ill patients. A multidisciplinary approach was taken to achieve harmonization of definitions, components, techniques, and operations of the extracorporeal therapies. The article describes the RRT techniques in detail with the relevant technology, procedures, and phases of treatment and key aspects of volume management/fluid balance in critically ill patients. In addition, the article describes recent developments in other extracorporeal therapies, including therapeutic plasma exchange, multiple organ support therapy, liver support, lung support, and blood purification in sepsis. This is a consensus report on nomenclature harmonization in extracorporeal blood purification therapies, such as hemofiltration, plasma exchange, multiple organ support therapies, and blood purification in sepsis.

**Keywords:** Terminology, Pump, Pressure sensor, CRRT machine, Continuous veno-venous hemodialysis, Continuous veno-venous hemofiltration, Continuous veno-venous hemodiafiltration, High volume hemofiltration, Continuous plasmafiltration coupled with adsorption, Hemoperfusion

**Abbreviations:** AKI, Acute kidney injury; AVVH, Accelerated veno-venous hemofiltration; CPE, Continuous plasma exchange; CPFA, Continuous plasmafiltration coupled with adsorption; CRRT, Continuous renal replacement therapy; CVVH, Continuous veno-venous hemofiltration; CVVHD, Continuous veno-venous hemodialysis; CVVHDF, Continuous veno-venous hemodiafiltration; CVVHFD, Continuous veno-venous high-flux dialysis; ECMO, Extracorporeal membrane oxygenation; ED, Extended dialysis; EDD, Extended daily dialysis; EDDf, Extended daily dialysis with filtration; FPSA, Fractionated plasma separation and adsorption; HVHF, High-volume hemofiltration; ICU, Intensive care unit; IHD, Intermittent hemodialysis; IHDF, Intermittent hemodiafiltration; IHF, Intermittent hemofiltration; IHFD, Intermittent high-flux dialysis; MARS, Molecular adsorbent recirculating system; MOST, Multiple organ support therapy; PIRRT, Prolonged intermittent renal replacement therapy; PMX, Polymyxin; RRT, Renal replacement therapy; SCUF, Slow continuous ultrafiltration; SLED, Sustained low-efficiency dialysis; SLEDD, Slow low-efficiency extended daily dialysis; SPAD, Single pass albumin dialysis; TMP, Transmembrane pressure; TPE, Therapeutic plasma exchange; VHVHF, Very high-volume hemofiltration

- Sustained low-efficiency dialysis (**SLED**)
- Slow low-efficiency extended daily dialysis (**SLEDD**)
- Prolonged intermittent RRT (**PIRRT**)
- Extended daily dialysis (**EDD**)
- Extended daily dialysis with filtration (**EDDf** )
- Extended dialysis (**ED**)
- “go slow dialysis”
- Accelerated veno-venous hemofiltration (**AVVH**).

- Si utilizza **generalmente** material di **IHD** (macchina, filtri, circuiti).
- La rimozione dei soluti avviene prevalemntemente con tecnica **diffusiva**.
- Esistono variant con tecnica **convettiva** (EDDf, AVVH)


PLEASE
SLOW
DOWN

## Continuous (RRT)

## Intermittent (HD)


## Hybrid therapies

. . .

# Continuous (RRT)

# Intermittent (HD)


# Hybrid therapies

| CRRT | IHD | PIRRTs | SLED |
|---|---|---|---|
| Continuous Renal Replacement Therapies | Intermittent Hemo Dialysis | Prolonged Intermittent Renal Replacement Therapies | Sustained Low Efficiency Dialysis |

Hybrid

All of these use relatively similar extracorporeal blood circuits and differ primarily with regard to duration of therapy and, consequently, the **rapidity of <u>net ultrafiltration</u> and <u>solute clearance</u>**.

**Mechanisms of solute clearance**

- Green = Diffusion
- Blue = Convection

Tandukar S & Palewsky PM. CHEST (2019) + Wang AY, Bellomo R. Curr Opin Crit Care (2018)

IHD

**Renal replacement therapy in the ICU: intermittent hemodialysis, sustained low-efficiency dialysis or continuous renal replacement therapy?**

SLED

CRRT

Wang AY, Bellomo R. Curr Opin Crit Care (2018)

# MODALITIES OF RENAL REPLACEMENT THERAPY USED IN ICU

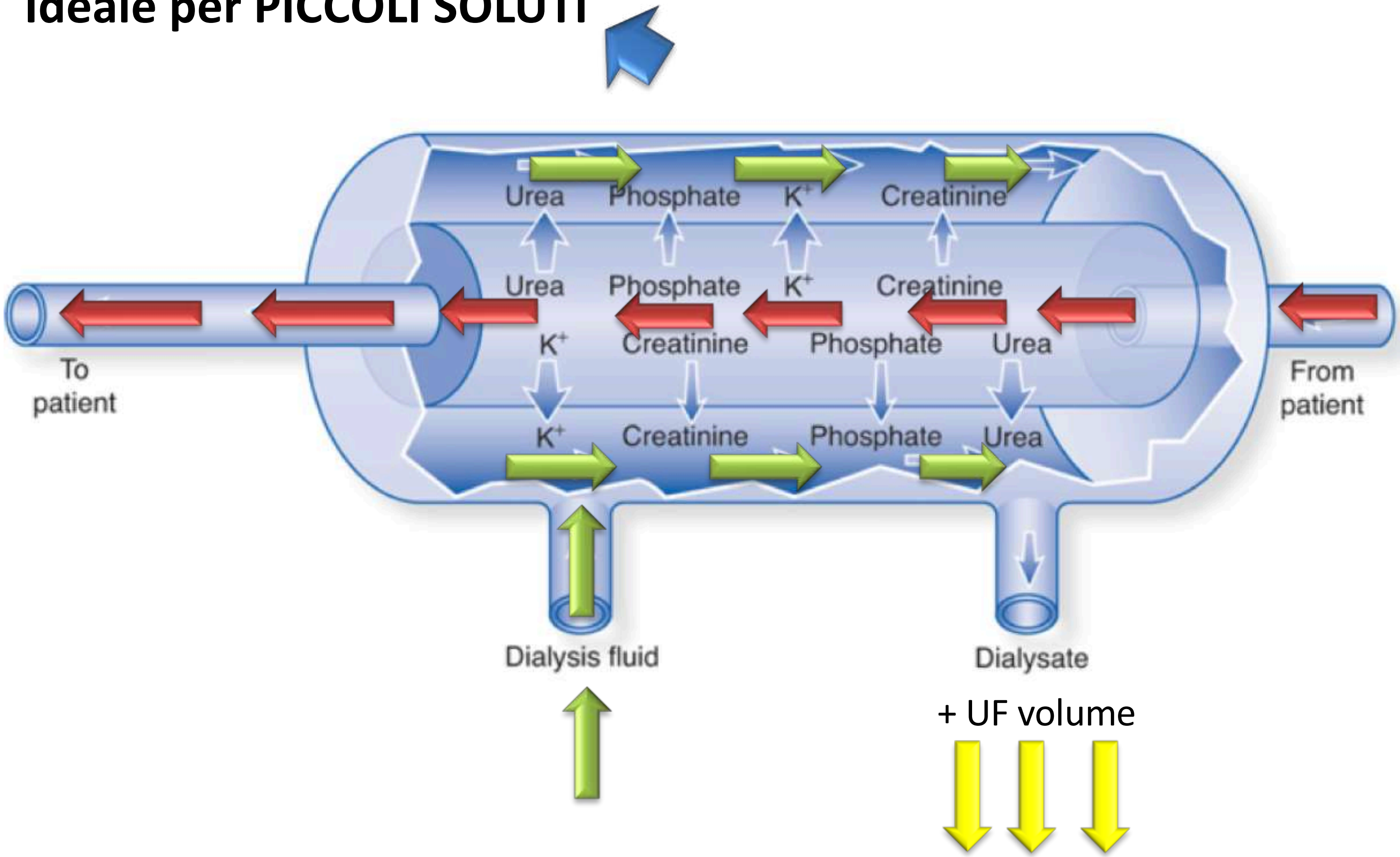
**Indications for commencement** of RRT therapy for severe AKI patients are the same for all modalities, such as fluid overload, hyperkalemia, acidosis, and uremic syndrome that are refractory to medical therapy.

*. . . there is still* ***controversy*** *on the advantages of one modality over the others on clinical outcomes of AKI patients. . .*

Wang AY, Bellomo R. Curr Opin Crit Care (2018)

# IHD – Intermittent HemoDialysis

- Meccanismo principale per la rimozione dei solute è la DIFFUSIONE
- **Ideale per PICCOLI SOLUTI**



# Intermittent hemodialysis (IHD)

- IHD is often used in the setting of **CKD** where patients receive hemodialysis three times a week
- **3–5h** each session, using higher flow rates than CRRT to maintain fluids, electrolytes, and acid–base balance
- It can also be administered for **AKI** patients, especially those who are **hemodynamically stable**
- It removes solutes by diffusion and may be more suited for patients who require **rapid removal of dialyzable substances** such as severe hyperkalemia and selected toxins

Wang AY, Bellomo R. Curr Opin Crit Care (2018)

- IHD is **less expensive** and requires **less anticoagulation**

In fact, it is likely the most commonly used acute RRT modality in the United States.

However, IHD may be associated with an **increased risk of hypotension** because of removal of large amount of fluid over a short period of time, potentially leading to **further renal ischemia**

Vinsonneau C et al. Lancet (2006)

Nonetheless, IHD can be used as an alternative option for AKI requiring RRT, especially in **resource-limiting settings**.

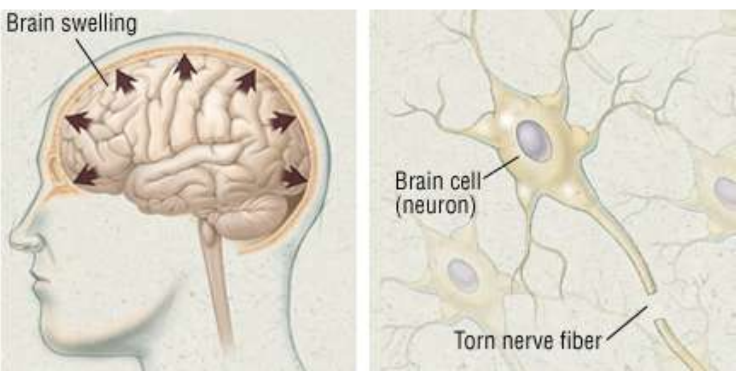
Sankarasubbaiyan S et al. IndianJ Nephrol (2013)

**Continuous therapy**, compared with IHD, tends to be associated with **less cerebral edema** because of a **more physiological and slow removal of urea and other solutes**.

Clinical Trial > J Nephrol. May-Jun 1999;12(3):173-8.

# Brain Density Changes During Renal Replacement in Critically Ill Patients With Acute Renal Failure. Continuous Hemofiltration Versus Intermittent Hemodialysis

C Ronco [1], R Bellomo, A Brendolan, V Pinna, G La Greca




Ronco C, Bellomo R, Brendolan A, et al. Brain density changes during renal replacement in critically ill patients with acute renal failure. Continuous hemofiltration versus intermittent hemodialysis.
J Nephrol 1999; 12: 173–178.

# Continuous renal replacement therapy (CRRT)

- CRRT provides continuous support

- Continuous venovenous hemofiltration (**CVVH**) → convection
- Continuous venovenous hemodialysis (**CVVHD**) → diffusion
- Continuous venovenous hemodiafiltration (**CVVHD**) → diffusion + convection

provides a . . . ***slow***, ***gentle***, and ***continuous*** kidney support

…preferentially used approach for critically ill patients with ***hemodynamic instability***

**CRRT**

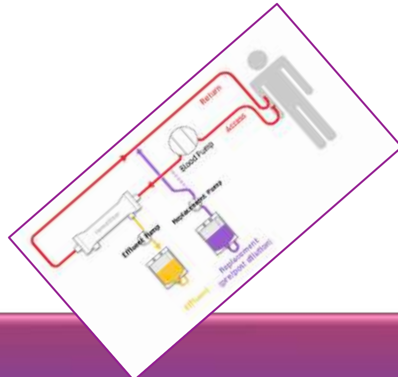
**Continuous Renal Replacement Therapies**

- Continuous venovenous hemofiltration (CVVH) – **convection**
- Continuous venovenous hemodialysis (CVVHD) – **diffusion**
- Continuous venovenous hemodiafiltration (CVVHDF) – **diffusion** and **convection**

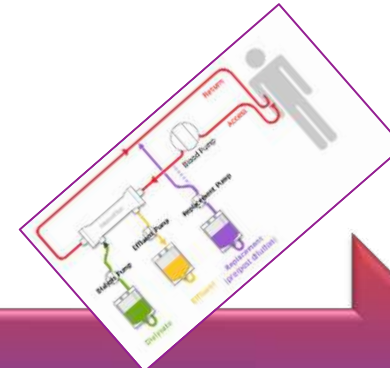

CRRT provides a **slow, gentle**, and **continuous** kidney support → **hemodynamic instability**

**More gradual fluid removal** and **solute clearance** over prolonged treatment times

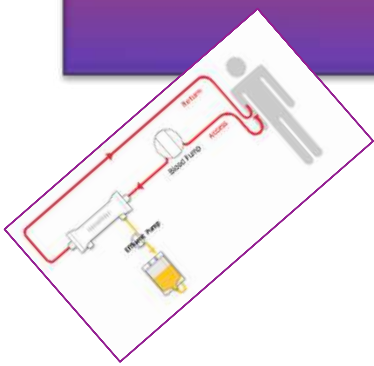
# Continuous renal replacement therapy (CRRT)



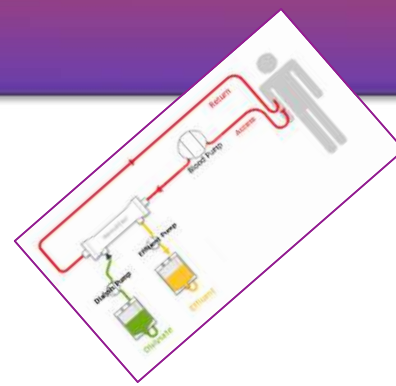
CVVHD Hep
CVVHD Citrate



SCUF



CVVH Post Hep
CVVH Pre Hep
CVVH Pre-Post Hep
CVVH Post-Citrate



CVVHDF Post Hep
CVVHDF Pre Hep
CVVHDF Pre-Post Hep
CVVHDF Post-Citrate

The modes differ in whether the primary driver of solute removal is **convection**, **diffusion**, or **both,** the **reinfusion** site (pre-post-both) and the **anticoagulation** modality (heparin, citrate → pre).

# CRRT

**Continuous**
**Renal**
**Replacement**
**Therapies**

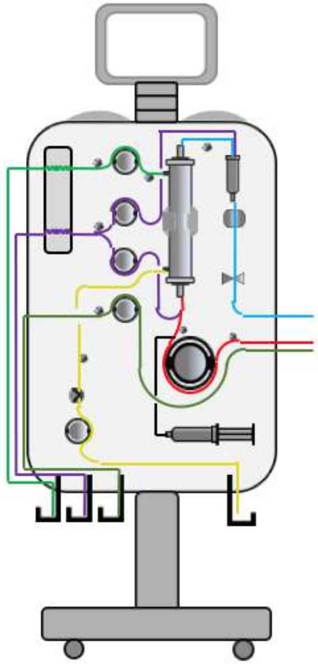

CRRT provides a **slow, gentle**, and **continuous** kidney support → **hemodynamic instability**

**More gradual fluid removal** and **solute clearance** over prolonged treatment times


Although the **Kidney Disease: Improving Global Outcomes (KDIGO)** Clinical Practice Guideline for AKI recommends the use of CRRT for patients who are **hemodynamically unstable**, the strength of this recommendation is low.

Observational data, however, do suggest that CRRT is more effective in **achieving net** **negative fluid balance** than IHD.

Tandukar S & Palewsky PM. CHEST (2019)



- **CRRT** is usually a **more appropriate modality in those ICU patients with increased intracranial pressure** (e.g. acute brain injury, fulminant hepatic failure, at risk of increased intracranial pressure).

- **CRRT**, compared with IHD or SLED, can remove **fluid steadily over a longer period of time** and is available **24 h/day** for the prevention of fluid overload, should large amounts of fluids and blood products require rapid infusion.

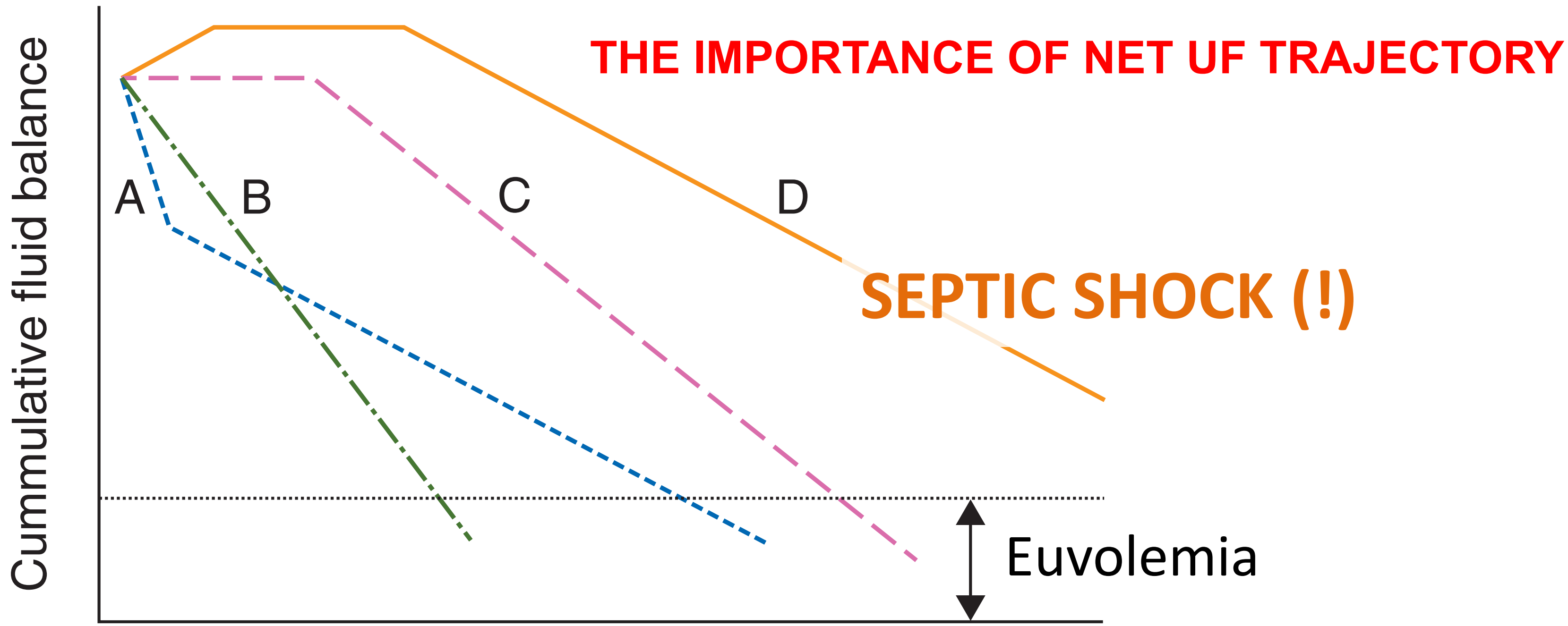
- Therefore, CRRT is also often used in the setting **of severe volume overload** or during massive transfusion in patients with AKI.

Wang AY, Bellomo R. Curr Opin Crit Care (2018)

# Indications and management of mechanical fluid removal in critical illness

M. H. Rosner[1†], M. Ostermann[2†*], R. Murugan[3], J. R. Prowle[4], C. Ronco[5], J. A. Kellum[3], M. G. Mythen[6] and A. D. Shaw[7] for the ADQI XII Investigators Group

BJA 2014




Rapid early fluid removal may be indicated in cardio-renal syndrome (A), but a slower removal may be required for haemodynamic tolerance after resolution of pulmonary oedema. Patients with single organ renal failure (B) may tolerate more rapid fluid removal than those with AKI complicating severe sepsis (C) or septic shock (D).

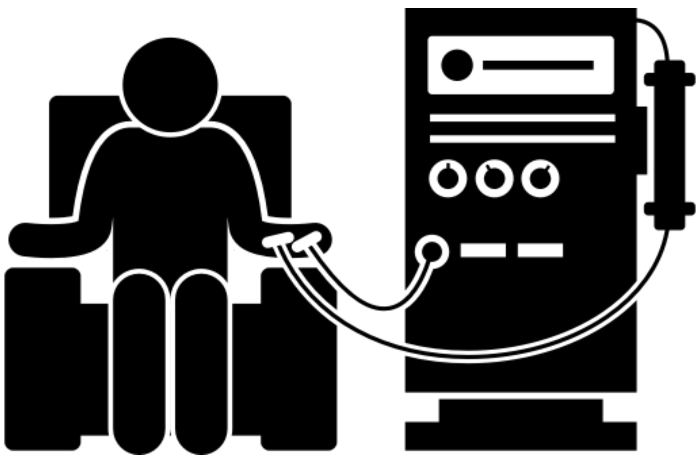
# Hybrid therapies

Sono modalità che cercano di ottimizzare i vantaggi e **minimizzare gli svantaggi di entrambe**:

- Efficiente rimozione dei soluti
- Più lenta quota di ultrafiltrazione (ultrafiltration rate) → **stabilità emodinamica**
- Minore esposizione **all'anticoagulazione**
- Più breve **durata**
- Minori costi
- Minore carico di lavoro infermieristico
- Migliore *"ICU workflow"*

**PIRRTs**

**Prolonged**
**Intermittent**
**Renal**
**Replacement**
**Therapies**



**SLED**

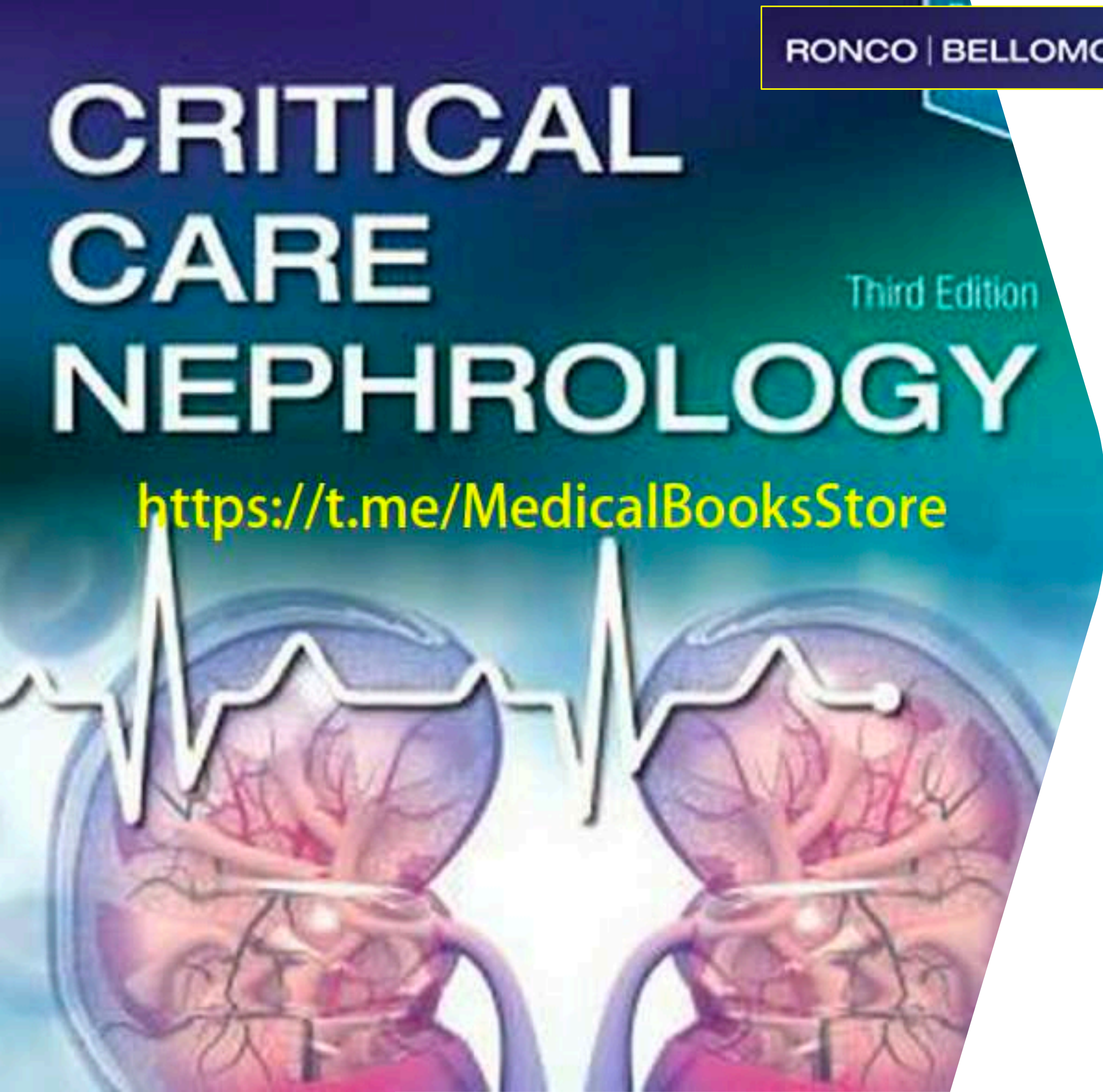
**Sustained**
**Low**
**Efficiency**
**Dialysis**

PIRRT can be performed on most **machines** that are used for standard intermittent hemodialysis.

**Standard** extracorporeal circuit tubing and hemodialyzers are used for PIRRT.

PIRRT should be performed at least **three** times per week to provide an adequate dialysis dose. The time per session ranges from **6 to 18** hours but is typically approximately **8** hours.

The length of the dialysis session depends on the **needs of the patient** (usually the volume that needs to be removed) and hemodynamic stability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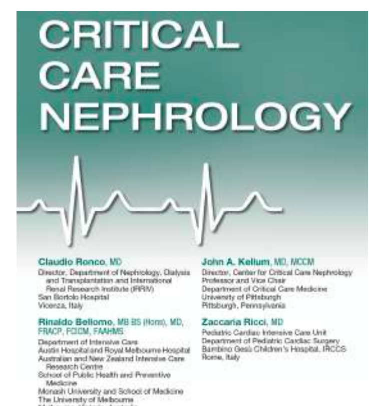
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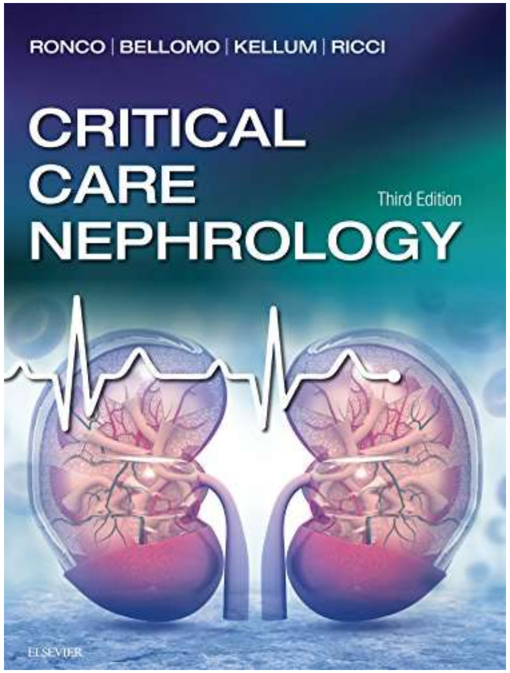



The technical elements of HT are not novel. In the extreme, it can be argued that Kolff actually performed the first HT treatments more than **50 years ago**.

However, the clinical context of **HT is novel as a conceptual and logistic compromise between the modern applications of IHD and CRRT**

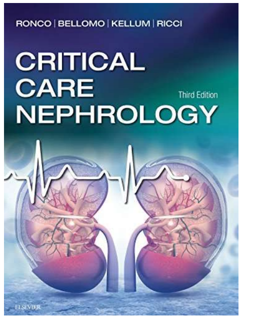
There is agreement among opinion leaders that the nomenclature must be standardized

RONCO | BELLOMO | KELLUM | RICCI

*However, this is proving difficult, owing to lack of a common perspective between nephrologists and intensivists*

- Hybrid therapy is “low efficiency” and “prolonged” to **nephrologists** . .

- but “high efficiency” and “foreshortened” to **intensivists**



Therefore, SLED can be theoretically used in **hemodynamically unstable** AKI patients.

# Intermittent versus continuous renal replacement therapy for acute renal failure in adults (Review)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**Intermittent versus continuous renal replacement therapy for acute renal failure in adults (Review)**

Rabindranath KS, Adams J, MacLeod AM, Muirhead N

Rabindranath KS, Adams J, MacLeod AM, Muirhead N.
Intermittent versus continuous renal replacement therapy for acute renal failure in adults.
*Cochrane Database of Systematic Reviews* 2007, Issue 3. Art. No.: CD003773.
DOI: 10.1002/14651858.CD003773.pub3.

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Intermittent versus continuous renal replacement therapy for acute renal failure in adults (Review)


WILEY

Rabindranath K et al. rane Database Syst Rev (2007)

- 15 trials comparing intermittent RRT (IRRT) versus CRRT
- Comparing intermittent RRT (IRRT) versus CRRT and did not show differences in ICU and in-hospital **mortality**, the number of patients who **became RRT independent**, **hemodynamically instable**, or **hypotensive**.
- Patients Patients on **CRRT** were likely to have significantly **higher mean arterial pressure** and higher risk of clotting dialysis filters

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## Extended Daily Dialysis in Acute Kidney Injury Patients: Metabolic and Fluid Control and Risk Factors for Death

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University São Paulo State-UNESP, Distrito de Rubiao Junior, Botucatu, São Paulo, Brazil

**Abstract**

Intermittent hemodialysis (IHD) and continuous renal replacement therapies (CRRT) are used as Acute Kidney Injury (AKI) therapy and have certain advantages and disadvantages. Extended daily dialysis (EDD) has emerged as an alternative to CRRT in the management of hemodynamically unstable AKI patients, mainly in developed countries.

*Objectives:* We hypothesized that EDD is a safe option for AKI treatment and aimed to describe metabolic and fluid control of AKI patients undergoing EDD and identify complications and risk factors associated with death.

*Study Selection:* This is an observational and retrospective study describing introduction of EDD at our institution. A total of 231 hemodynamically unstable AKI patients (noradrenalin dose between 0.3 and 1.0 ucg/kg/min) were assigned to 1367 EDD session. EDD consisted of 6–8 h of HD 6 days a week, with blood flow of 200 ml/min, dialysate flows of 300 ml/min.

*Data Synthesis:* Mean age was 60.6±15.8 years, 97.4% of patients were in the intensive care unit, and sepsis was the main etiology of AKI (76.2). BUN and creatinine levels stabilized after four sessions at around 38 and 2.4 mg/dl, respectively. Fluid balance decreased progressively and stabilized around zero after five sessions. Weekly delivered Kt/V was 5.94±0.7. Hypotension and filter clotting occurred in 47.5 and 12.4% of treatment session, respectively. Regarding AKI outcome, 22.5% of patients presented renal function recovery, 5.6% of patients remained on dialysis after 30 days, and 71.9% of patients died. Age and focus abdominal sepsis were identified as risk factors for death. Urine output and negative fluid balance were identified as protective factors.

*Conclusions:* EDD is effective for AKI patients, allowing adequate metabolic and fluid control. Age, focus abdominal sepsis, and lower urine output as well as positive fluid balance after two EDD sessions were associated significantly with death.

**Citation:** Ponce D, Abrão JMG, Albino BB, Balbi AL (2013) Extended Daily Dialysis in Acute Kidney Injury Patients: Metabolic and Fluid Control and Risk Factors for Death. PLoS ONE 8(12): e81697. doi:10.1371/journal.pone.0081697

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**Competing Interests:** Daniela Ponce is a PLOS ONE Editorial Board member and this does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

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### Background

The high mortality rate among critically ill acute kidney injury (AKI) patients remains an unsolved problem in intensive care units (ICU) in spite of the considerable technological progress in renal replacement therapy (RRT) [1–3]. Dialytic management of these patients is difficult because of associated hemodynamic instability and multiple organ dysfunction, with mortality rates reaching 50–70% [4].

There is no consensus in literature on the best dialysis method and intermittent hemodialysis (IHD) and continuous renal replacement therapies (CRRT) have been used in AKI. Several studies have not revealed a definitive advantage in terms of patient survival for CRRT compared with IHD [5–10].

Both conventional IHD and CRRTs have certain advantages, but also several disadvantages. IHD is often complicated by hypotension and inadequate fluid removal, and CRRT by high cost of solutions and problems with anticoagulation. A hybrid therapy called sustained low efficiency dialysis (SLED) or extended dialysis (EDD) has emerged as an alternative to CRRT in the management of hemodynamically unstable patients with AKI, mainly in developed countries [11,12].

The studies in the literature on EDD in AKI patients are few and involve a small number of patients [9,13–16]. They have demonstrated that EDD is well tolerated in critically ill patients, with comparable ultrafiltration and solute removal to CRRT and peritoneal dialysis [13,16].

This prospective study was designed to describe the introduction of EDD at our institution. We focused on metabolic and fluid control, complications and risk factors associated with death.

### Patients and Methods

#### Study Population

This was an observational and retrospective study describing our experience of introducing EDD as a new HD modality in two Brazilian University Hospitals (Botucatu School of Medicine and Bauru State of Sao Paulo). In our units, conventional IHD and peritoneal dialysis had previously been the standard of care for AKI.

Ponce D et al. PloS one (2013)

- Single-center - retrospective study
- 231 hemodynamically unstable AKI patients (NE 0.3-1.0 mcg/Kg/min) – 76.2% sepsis
- SLED (6–8h of hemodialysis 6 days a week, with blood flow of 200 ml/min, dialysate flows of 300 ml/min) – 1367 sessions.

SLED
appeared to be able to provide adequate metabolic and fluid control.

Age and focus abdominal sepsis were identified as risk factors for **death**.
Urine output and negative fluid balance were identified as **protective** factors.

AJKD

Original Investigation

2015

# Extended Daily Dialysis Versus Continuous Renal Replacement Therapy for Acute Kidney Injury: A Meta-analysis

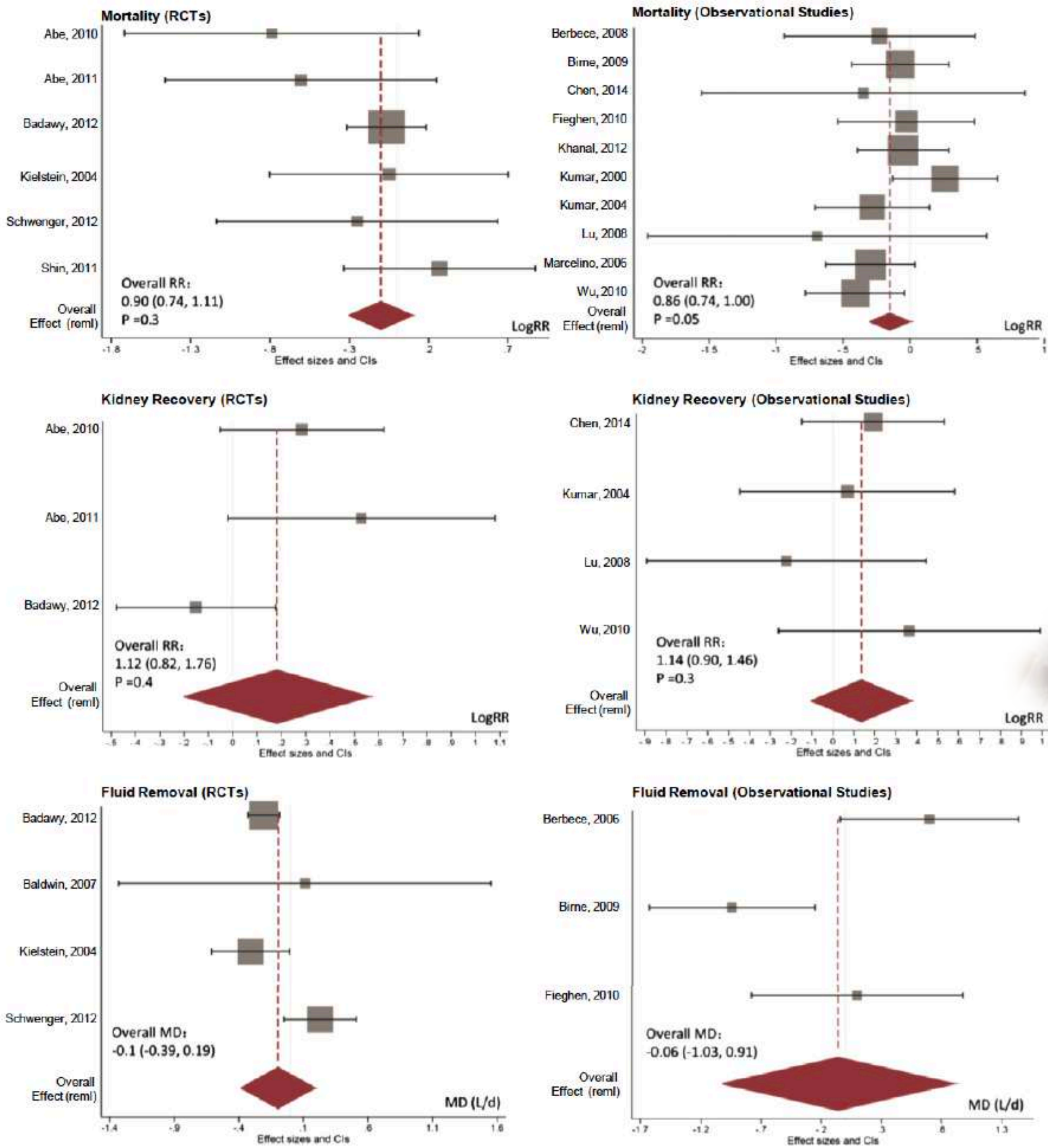
*Ling Zhang, MD,[1,2] Jiqiao Yang, MD,[3] Glenn M. Eastwood, MD,[2] Guijun Zhu, MD,[2,4] Aiko Tanaka, MD,[2] and Rinaldo Bellomo, MD, PhD[2]*

| Study | Country | Design of Study | Modality | N | Mean Age (y) | Male Sex (%) | Mean Therapy Duration (h/d) | | Main Outcomes | Funding |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | EDD | CRRT | | |
| Kielstein[6] (2004) | DE | RCT | EDD vs CVVH | 39 | 50.5 | 62.9 | 11.7 | 23.3 | Mortality, fluid removal | Industry |
| Baldwin[18] (2007) | AU | RCT | EDD vs CVVH | 16 | 69.5 | 56.3 | 7.3 | 18.4 | Fluid removal | NR |
| Abe[7] (2010) | JP | RCT | EDDF vs CVVHDF | 60 | 68.7 | 65.0 | 6.5 | 20.3 | Mortality, kidney recovery, ICU days | NR |
| Abe[19] (2011) | JP | RCT | EDDF vs CVVHDF | 50 | 65.9 | 66.0 | 6.0 | 15.2 | Mortality, kidney recovery, ICU days | NR |
| Shin[20] (2011) | KR | RCT | SLED vs CVVH | 46 | 63 | 63.0 | 10 | NR | Mortality | NR |
| Schwenger[8] (2012) | DE | RCT | SLED vs CVVH | 232 | 66.2 | 67.7 | 14.9 | 19.9 | Mortality, fluid removal, ICU days | NR |
| Badawy[21] (2012) | EG | RCT | EDD vs CVVHDF | 80 | 47.5 | 65.0 | 6-8 | NR | Mortality, fluid removal, ICU days | NR |
| Kumar[22] (2000) | US | Retrospective | EDD vs CVVH | 42 | 50 | 64.3 | 7.5 | 19.5 | Mortality | NR |
| Kumar[23] (2004) | US | Prospective | EDD vs CVVHD | 54 | 52 | 63.0 | 6.7 | 16.8 | Mortality, kidney recovery | NR |
| Berbece[24] (2006) | CA | Prospective | SLED vs CVVHDF | 34 | 58.4 | 61.8 | 7.5 | 21.3 | Mortality, fluid removal | NR |
| Marcelino[25] (2006) | PT | Retrospective | SLED vs CVVHDF | 53 | 59.1 | NR | 6.8 | 22.1 | Mortality | NR |
| Lu[29] (2008) | CN | Prospective | SLED vs CVVH | 12 | 49.7 | 66.7 | 10 | 18 | Mortality, kidney recovery | Public |
| Birne[30] (2009) | PT | Retrospective | SLED vs CVVHDF | 63 | 63.3 | 49.2 | 6-12 | NR | Mortality, fluid removal | NR |
| Fieghen[26] (2010) | CA | Retrospective | SLED vs CVVHDF | 43 | 62.1 | 76.7 | 6.8 | 19.7 | Mortality, fluid removal | NR |
| Wu[9] (2010) | TW | Retrospective | SLED vs CVVH | 101 | 67.4 | 65.3 | 8.0 | NR | Mortality, kidney recovery | NR |
| Khanal[27] (2012) | NZ | Retrospective | SLEDF vs CVVHDF | 166 | 58.5 | 62.0 | 7.2 | NR | Mortality, ICU days | NR |
| Chen[28] (2014) | CN | Retrospective | SLEDF vs CVVH | 107 | 59.5 | NR | 8.8 | 23.5 | Mortality, kidney recovery | NR |

- 17 studies (7 RCTs and 10 observational) of 1208 patients compared the effect of SLED with CRRT on clinical outcomes

Zhang L et al. AJKD (2015)

Zhang L et al. AJKD (2015)



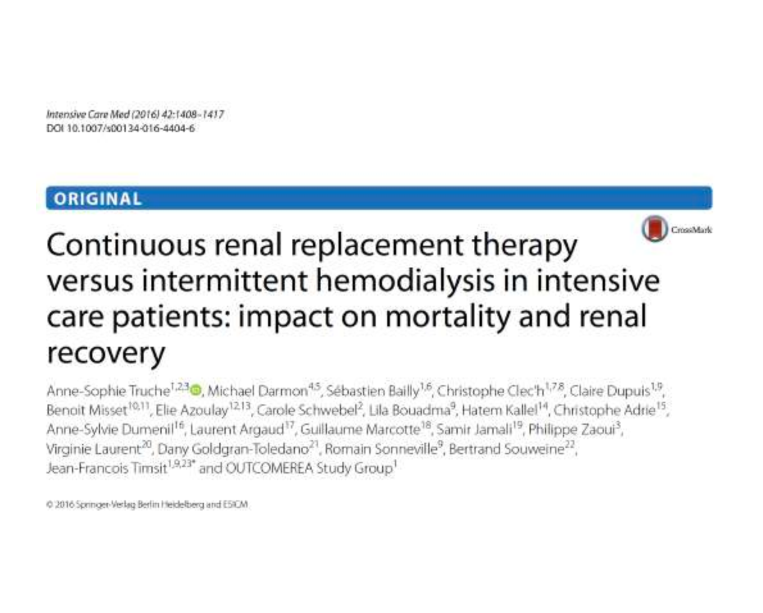

**No significant differences** in recovery of renal function, fluid removal, days of ICU stay, and biochemical clearance between SLED and CRRT.

# **OUTCOMEREA** study

- Prospective observational multicenter cohort database study
- Assessed an association of dialysis modality with 30-day mortality and dialysis dependence in patients with AKI who underwent RRT between 2004 and 2014.

- 1360 patients

- **No difference** was seen in the composite outcome of **30-day mortality** and **dialysis dependence** between the CRRT and IHD group.
- However, **CRRT** was associated with **lower mortality** and **better recovery of renal function** in patients with **higher weight gain at the initiation of RRT** and was associated with **increased mortality in patients without shock**.


*Intensive Care Med* (2016) 42:1408–1417
DOI 10.1007/s00134-016-4404-6

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], Jean-Francois Timsit[1,9,23]* and OUTCOMEREA Study Group[1]



Truche AS et al. ICM (2016)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journal homepage: www.jccjournal.org

Renal

Systematic review and meta-analysis of renal replacement therapy modalities for acute kidney injury in the intensive care unit

Danielle M. Nash, MSc [a,b,*], Sebastian Przech, BSc, MDCM [b,c,d], Ron Wald, MDCM, MPH, FRCPC [e,f,1], Daria O'Reilly, MSc, PhD [a,g,2]

ARTICLE INFO

ABSTRACT

Purpose: To compare clinical outcomes among critically ill adults with acute kidney injury (AKI) treated with continuous renal replacement therapy (CRRT), intermittent hemodialysis (IHD) or sustained low efficiency dialysis (SLED).

Nash DM et al. JCC (2017)

- 21 trials comparing RRT modalities in the ICU
- 16 studies were RCTs
- No single RRT modality carried definitive advantages on mortality and dialysis dependence at 30 days
- **However, there was a trend toward better patient and kidney survival for CRRT versus IHD**

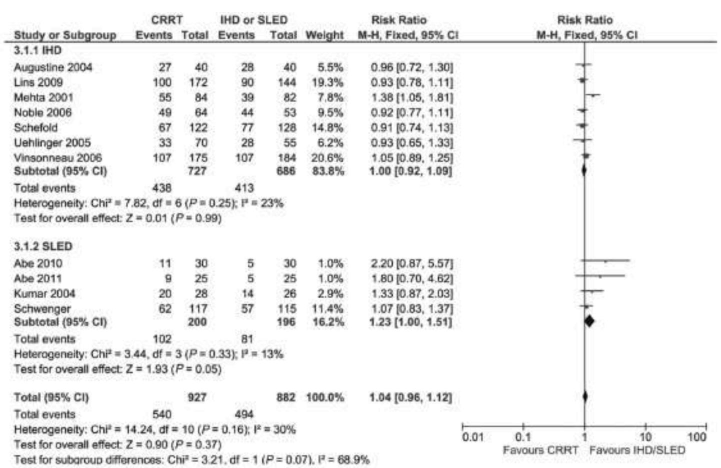


**Fig. 2.** In-hospital mortality comparing continuous renal replacement therapy and intermittent hemodialysis/sustained low efficiency dialysis.

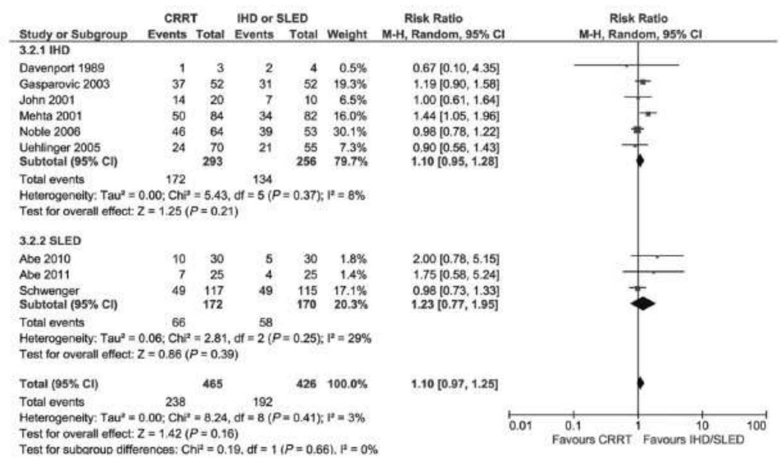


**Fig. 3.** ICU mortality comparing continuous renal replacement therapy and intermittent hemodialysis/sustained low efficiency dialysis.

# Large studies assessing effects of RRT modalities on both short-term and long-term renal outcomes of AKI patients.

## End-stage renal disease patients on renal replacement therapy in the intensive care unit: Short- and long-term outcome*

Max Bell, MD; Fredrik Granath, PhD; Staffan Schön, MD; Erland Löfberg, PhD; SWING; Anders Ekbom, PhD; Claes-Roland Martling, PhD

*Objective:* The number of patients with end-stage renal disease has increased during the last decades. Data shows that 10% of the renal replacement therapy population in the intensive care unit are patients with end-stage renal disease. We aimed to describe the short- and long-term outcome of these patients after renal replacement therapy in the intensive care unit.

*Design:* Nationwide cohort study between the years 1995 and 2004. Follow-up up to 5 years.

*Setting:* Swedish general intensive care units and Swedish hospitals.

*Patients:* Eligible subjects were end-stage renal disease patients treated with renal replacement therapy in 32 Swedish general intensive care units. In total, 245 patients were studied.

*Interventions:* None.

*Measurements and Main Results:* Short- and long-term mortality was studied. Logistic regression was used to analyze short-term mortality. Long-term mortality was compared with the mortality of end-stage renal disease patients outside the intensive care unit and the mortality in the population.

Diabetes and heart failure are significant risk factors for 90-day mortality, with an odds ratio of 1.9 and 2.0, respectively. The intensive care unit end-stage renal disease cohort had increased long-term mortality as compared with non-intensive care unit end-stage renal disease patients, relative risk of death 2.32 (confidence interval 1.84–2.92). A comparison with the mortality rate in the general population yielded a standardized mortality ratio of 25 (95% confidence interval: 19.6–31.4).

*Conclusions:* For end-stage renal disease patients in the intensive care unit, age, diabetes mellitus, and heart failure are risk factors for 90-day mortality. Long-term mortality is associated with age and heart failure. The long-term mortality of end-stage renal disease patients surviving the intensive care unit stay is significantly higher compared with end-stage renal disease patients without a known intensive care unit admission. (Crit Care Med 2008; 36: 2773–2778)

Key Words: end-stage renal disease; outcome; intensive care; renal replacement therapy; epidemiology

The number of patients with end-stage renal disease (ESRD) has increased during the last decades. Some studies indicate that the incidence of ESRD may double in the next 10 years (1). In Sweden, data from the Swedish Registry for Active Treatment of Uremia (SRAU) reveal that the prevalence of patients on dialysis and transplantation was ≈815 per million population in 2005. During the 12-yr period between 1991 and 2002 it increased by 75% (2). The number of patients on hemodialysis more than doubled from 1991 to 2005, from 1099 to 2591 patients.

The mean age of ESRD subjects has increased over the last decade (2). A large proportion of these older patients have nonrenal complicating diseases. These complications and the associated vulnerability of ESRD patients increase the risk of intensive care unit (ICU)-related organ dysfunction (3). Thus, an obvious conclusion is that an aging ESRD population, increasing in numbers, will result in more admissions to the ICU from this population. One Australian study showed that 2% of patients on chronic dialysis require ICU admission every year (4). A recent Swedish nationwide study revealed that close to 10% of the specific ICU population receiving renal replacement therapy (RRT) consisted of patients with ESRD (5).

Data on ESRD patients in the ICU is limited. Three single center studies including 38 (4), 92 (6), and 93 patients (7), respectively, detailed the validity of ICU scoring systems and outcome for this patient population. One multicentered study investigated the impact of acute renal failure (ARF) (254 cases) as compared with ESRD (57 cases) on ICU outcome (8). A recent very large database study from the United Kingdom looked into the outcome of ESRD patients and found that 1.3% of all patients admitted to the ICU were receiving chronic renal dialysis before ICU admission (3). All these investigations have focused on short-term mortality. The present study investigates the short- and the long-term outcome of a cohort of 245 ESRD patients needing RRT in the ICU. We detail their comorbidity risk factors and their original kidney disease. Furthermore, we compare the long-term mortality among

*See also p. 2939.

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This work was performed at the Department of Anesthesiology and Intensive Care, Karolinska University Hospital, Solna, Sweden and the Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden.

The authors have not disclosed any potential conflicts of interest.



DOI: 10.1097/CCM.0b013e318187815a

Bell M et al. Crit Care Med (2008)

## 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]

*See also p. 990.

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This work was conducted at the Institute for Clinical Evaluative Sciences @Western Expansion Site.

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Dr. Wald consulted for Thrasos, lectured for Alere, and received grant support from Alere. His institution received grant support from the Physician Services Incorporated Foundation (peer reviewed grant). Dr. Bagshaw has served as a paid consultant for Gambro and lectured for Alere and Spectral Diagnostics. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/CCM.0000000000000042

**Objective:** Among critically ill patients with acute kidney injury, the impact of renal replacement therapy modality on long-term kidney function is unknown. Compared with conventional intermittent hemodialysis, continuous renal replacement therapy may promote kidney recovery by conferring greater hemodynamic stability; yet continuous renal replacement therapy may not enhance patient survival and is resource intense. Our objective was to determine whether continuous renal replacement therapy was associated with a lower risk of chronic dialysis as compared with intermittent hemodialysis, among survivors of acute kidney injury.

**Design:** Retrospective cohort study.

**Setting:** Linked population-wide administrative databases in Ontario, Canada.

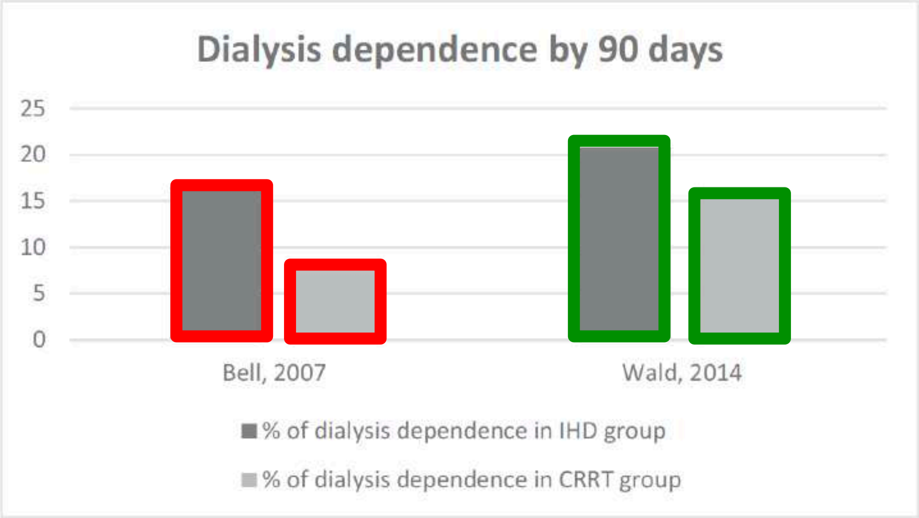
**Patients:** Critically ill adults who initiated dialysis for acute kidney injury between July 1996 and December 2009. In the primary analysis, we considered those who survived to at least 90 days after renal replacement therapy initiation.

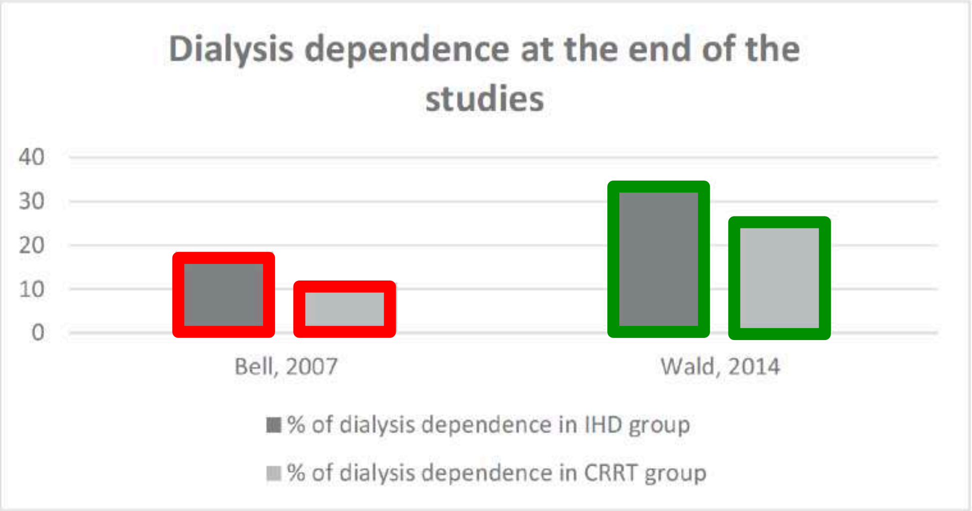
**Interventions:** Initial receipt of continuous renal replacement therapy versus intermittent hemodialysis.

**Measurements and Main Results:** Continuous renal replacement therapy recipients were matched 1:1 to intermittent hemodialysis recipients based on a history of chronic kidney disease, receipt of mechanical ventilation, and a propensity score for the likelihood of receiving continuous renal replacement therapy. Cox proportional hazards were used to evaluate the relationship between initial renal replacement therapy modality and the primary outcome of chronic dialysis, defined as the need for dialysis for a consecutive period of 90 days. We identified 2,315 continuous renal replacement therapy recipients of whom 2,004 (87%) were successfully matched to 2,004 intermittent hemodialysis recipients. Participants were followed over a median duration of 3 years. The risk of chronic dialysis was significantly lower

Wald R et al. Crit Care Med (2014)

# percentages of patients who were survived and **remained dialysis dependent**




Bell M et al. Crit Care Med (2008)

Wald R et al. Crit Care Med (2014)

Online Clinical Investigations

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

Martin Bonnassieux, MD[1,2]; Antoine Duclos, MD, PhD[3]; Antoine G. Schneider, MD, PhD[4]; Aurélie Schmidt, MS[5]; Stève Bénard, PharmD[5]; Charlotte Cancalon, MS[5]; Olivier Joannes-Boyau, MD[6]; Carole Ichai, MD, PhD[7,8]; Jean-Michel Constantin, MD, PhD[9]; Jean-Yves Lefrant, MD, PhD[10]; John A. Kellum, MD, FACP, MCCM[11]; Thomas Rimmelé, MD, PhD[1,2]; for the AzuRéa Group

*See also p. 340.

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[8]IRCAN Unit, UMR INSERM U1081 - CNRS 7284, Nice Sophia-Antipolis University, Nice, France.

[9]Department of perioperative medicine, University Hospital of Clermont-Ferrand, Clermont-Ferrand, France.

[10]Department of Critical Care Medicine, CHU Nîmes, Nîmes, France.

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A complete 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.

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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.

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

- Retrospective cohort study
- France; 291 centers
- 58 635 patients with AKI receiving RRT in ICU

Bonnassieux M et al.CCM (2018)

Online Clinical Investigations

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


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**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.


- Overall hospital mortality of 56.1%.
- Of these, 13.2% patients were still dialysis dependent at the time of discharge.
- Among these 58 635 patients, the use of IHD as the **initial** modality of dialysis was associated with lower rates of recovery of renal function at hospital discharge

Bonnassieux M et al.CCM (2018)


Final
Thoughts

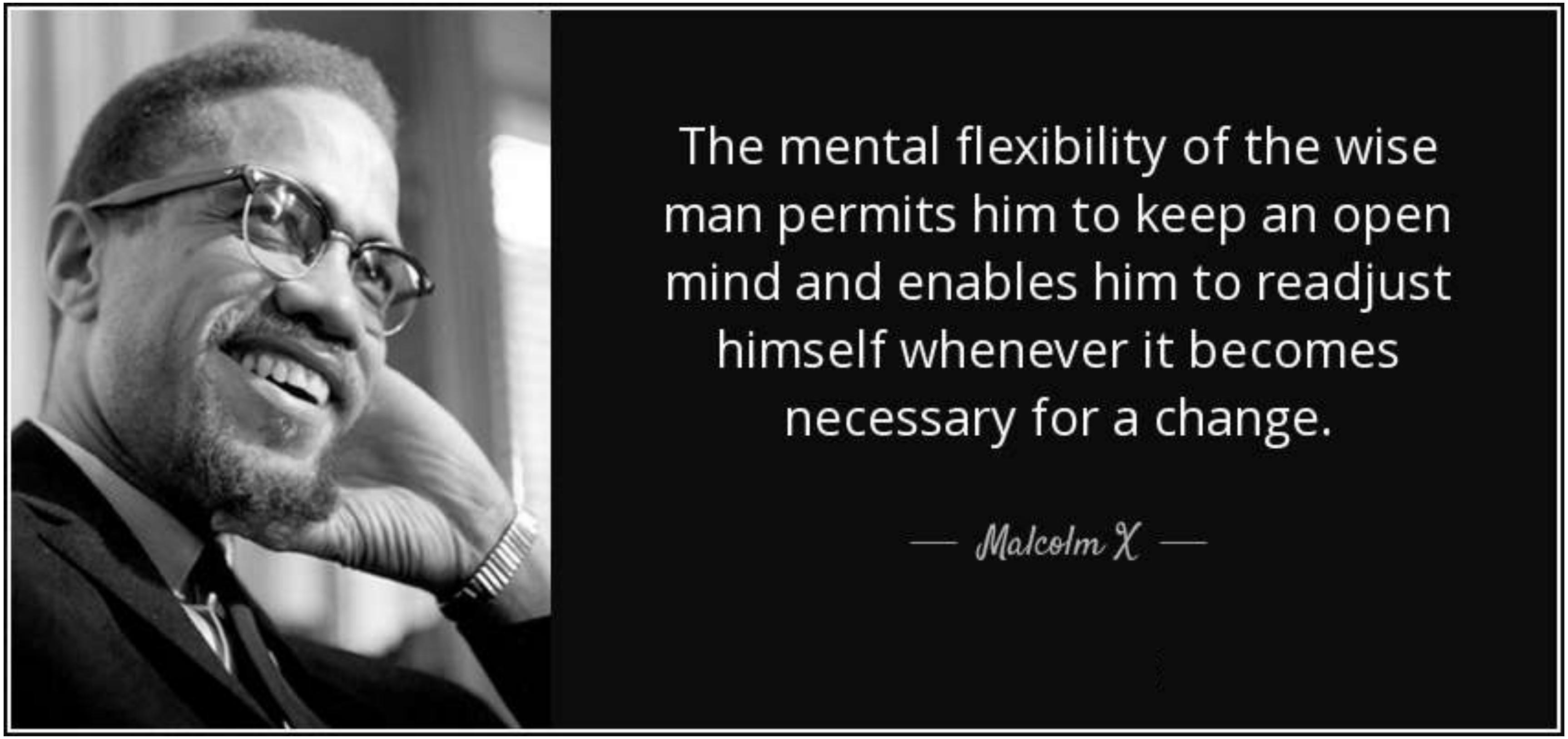
- ✓ RRT in the ICU setting: continuous or intermittent (or HYBRID, SLED, PIRRT ...)

- ✓ To date, **no modality of RRT shows clear superiority** over the others in terms of survival and recovery of renal function.

- ✓ However:
  - ✓ CRRT → a slow, gentle, and continuous kidney support → hemodynamic instability + fluid balance
  - ✓ CRRT → less cerebral edema (more physiological and slow removal of urea and other solutes).
  - ✓ **Initial** or **exclusive** use of **IHD** → decreased likelihood of renal recovery in the short and medium term compared with initial or exclusive use of CRRT.

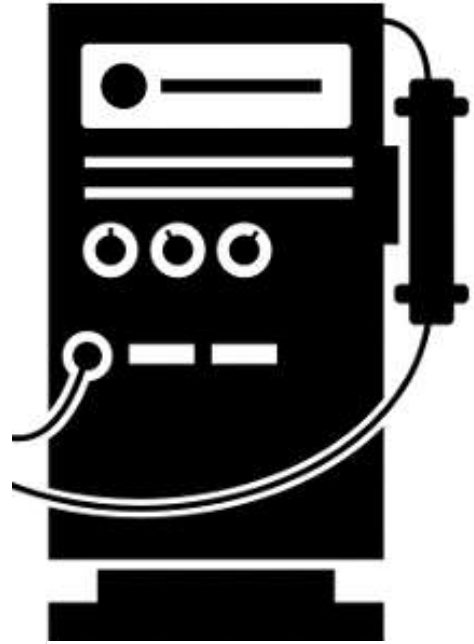
- ✓ . . . additional studies are a key priority in the field of critical care nephrology . . .

# CRITICALLY ILL PATIENT

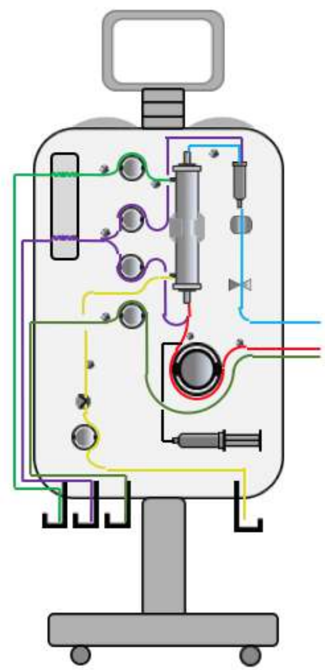

The mental flexibility of the wise man permits him to keep an open mind and enables him to readjust himself whenever it becomes necessary for a change.
— Malcolm X —


Plan A
Plan B
Plan C

*... availability ...*
*timing .... timeliness*
*... materials . . .*

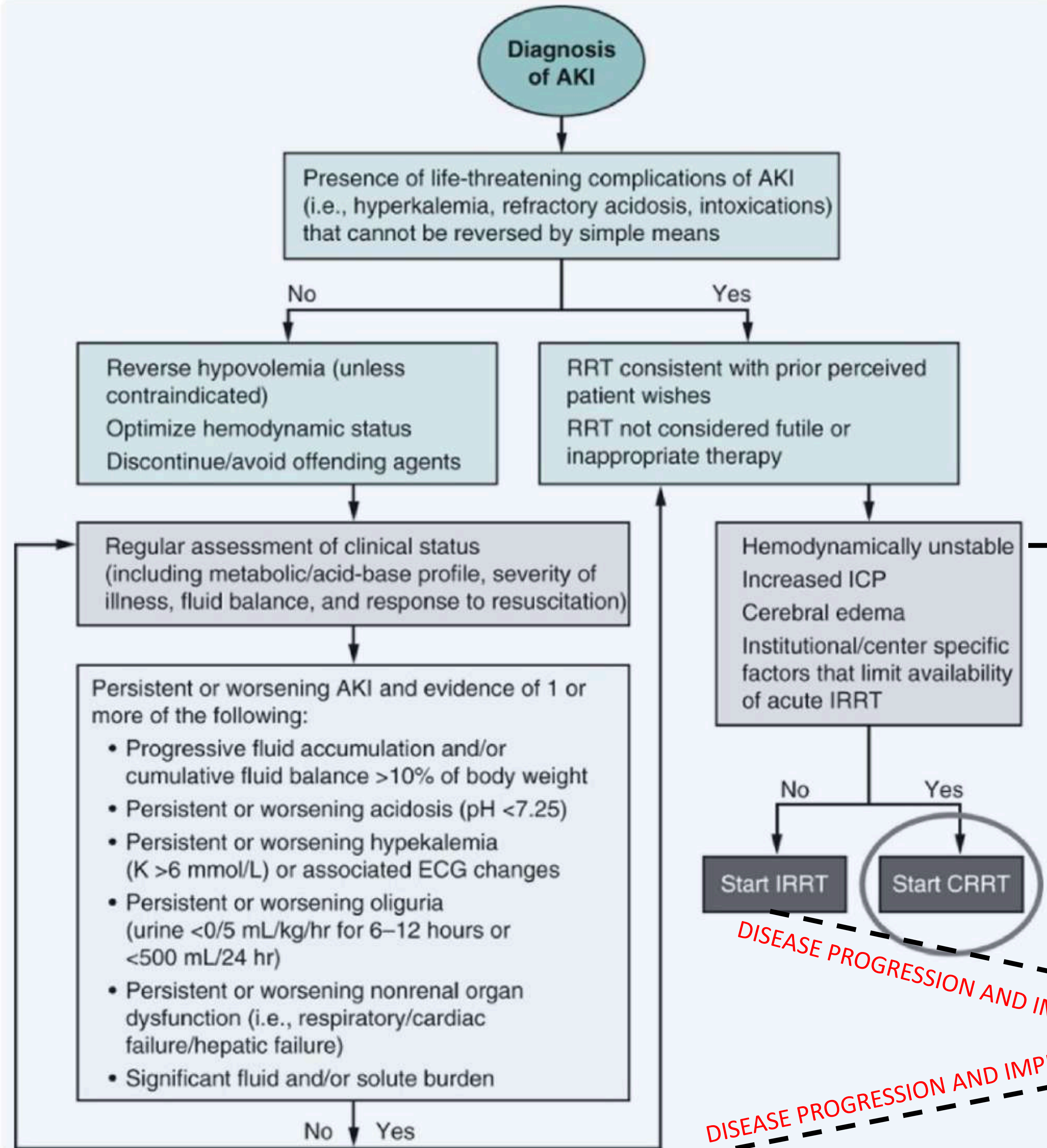


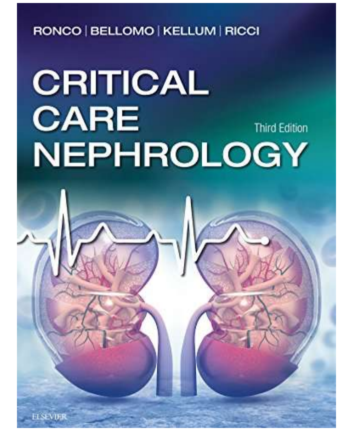
Nephrologist
Dialysis nurse
(technician)



Intensivist
ICU nurse

13-06-2020 - ICU




Oleksa G. Rewa
Sean M. Bagshaw

Start HYBRID

Why Not

DISEASE PROGRESSION AND IMPROVEMENT
DISEASE PROGRESSION AND IMPROVEMENT

Start HYBRID

# Le modalità disponibili in Terapia Intensiva: Intermittenti, Continue o Ibride?

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IRRIV International Renal Research Institute Vicenza

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| | STUDY | | | | | | |
|---|---|---|---|---|---|---|---|
| | SCHLAEPER ET AL.[19] | FINKEL AND FORINGER[12] | LONNEMANN ET AL.[15] | MARSHALL ET AL.[16] | MARSHALL ET AL.[17] | NAKA ET AL.[18] | KUMAR ET AL.[13,14] |
| Hemodialysis machine | Fresenius 2008H | Fresenius 2008H | Fresenius GENIUS | Fresenius 2008H | Fresenius 4008S ARrT-Plus | Fresenius 4008S ARrT-Plus | Fresenius 2008H |
| Hemodialyzer | Fresenius F40 | Fresenius F7 | Fresenius F60S | Fresenius F8 | Fresenius AV600S | Fresenius AV600S | Toray 1.0 |
| Membrane composition | Polysulfone | Polysulfone | Polysulfone | Polysulfone | Polysulfone | Polysulfone | Polymethyl methacrylate |
| Area ($m^2$) | 0.7 | 1.6 | 1.25 | 1.8 | 1.4 | 1.4 | 1.0 |
| Flux | High | Low | High | Low | High | High | High |
| Duration (hours) | Continuous | Continuous | 8–18 | 12 | 8–10 | 8–10 | 8 |
| Time of day | Continuous | Continuous | Nocturnal | Nocturnal | Nocturnal/Diurnal | Diurnal | Diurnal |
| Frequency | Continuous | Continuous | Daily | Daily/5–6 days per week | Daily/5–6 days per week | Daily/5–6 days per week | Daily/6 days per week |
| Blood flow rate ($Q_s$) (mL/min) | 150–200 | 150 | 70 | 200 | 200–350 | 100 | 150–200 |
| Dialysate flow rate ($Q_D$) (mL/min) | 100 | 100 | 70 | 100 | 200 | 200 | 300 |
| Filtration rate ($Q_F$) (mL/min) | 0 | 0 | 0 | 0 | 100 | 25 | 0 |
| Dialysate | Bicarbonate | Bicarbonate | Bicarbonate | Bicarbonate | Bicarbonate | Bicarbonate | Bicarbonate |