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Hybrid therapy in the ICU

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Conflict of interest

Studies funded by grants from French Ministry of Health and French Ministry of research

Christophe Vinsonneau

REVIEW

Current state of the art for renal replacement therapy in critically ill patients with acute kidney injury

Sean M. Bagshaw[1*], Michael Darmon[2], Marlies Ostermann[3], Fredric O. Finkelstein[4], Ron Wald[5], Ashita J. Tolwani[6], Stuart L. Goldstein[7], David J. Gattas[8], Shigehiko Uchino[9], Eric A. Hoste[10,11] and Stephane Gaudry[12]

Extracorporeal RRT

Peritoneal dialysis

Parameter	Modality			
	IRRT	Hybrid IRRT SLED/EDD/PIRRT	CRRT	PD
Duration (h)	4–6	6–16	24	24
Frequency	Daily/alternate days	Daily/alternate days	Daily	Daily
Solute transport	Diffusion	Diffusion or convection or both	Diffusion or convection or both	Diffusion

“Hybrid therapies” encompass many names

- Extended daily dialysis (EDD)
- Sustained low efficiency dialysis (SLED)
- Prolonged intermittent renal replacement therapy (PIRRT)
- But principle is the same….

Provocative statement

Hybrid therapies do not exist !!

Provocative statement

Hybrid therapies do not exist !!

Hybrid therapies

=

Intermittent RRT done properly (for ICU patients)

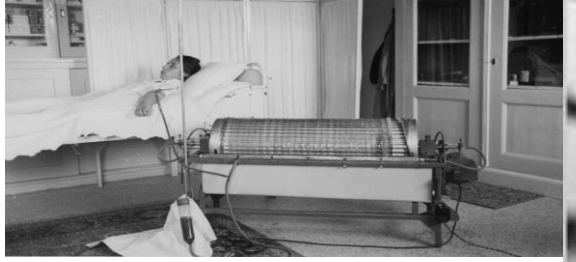
Progress in Internal Medicine

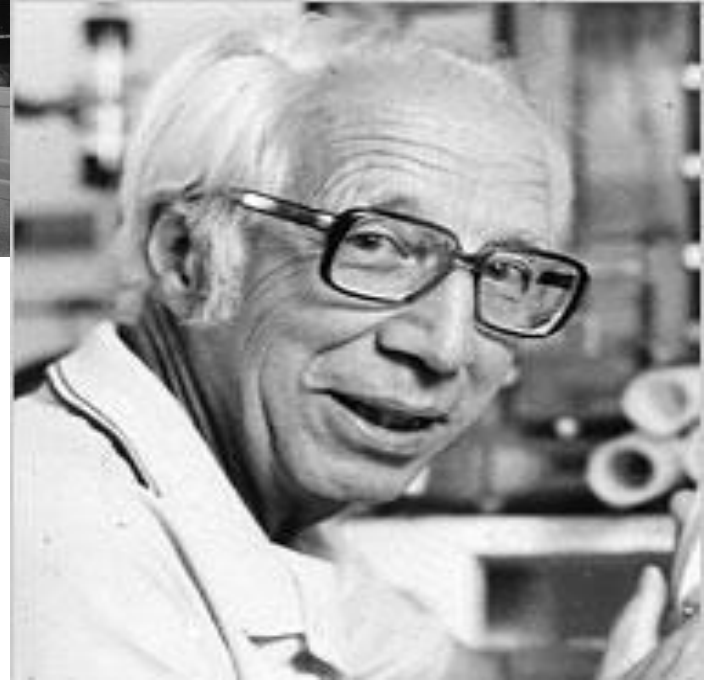
DIALYSIS IN TREATMENT OF UREMIA

Artificial Kidney and Peritoneal Lavage

W. J. KOLFF, M.D.
CLEVELAND

1954

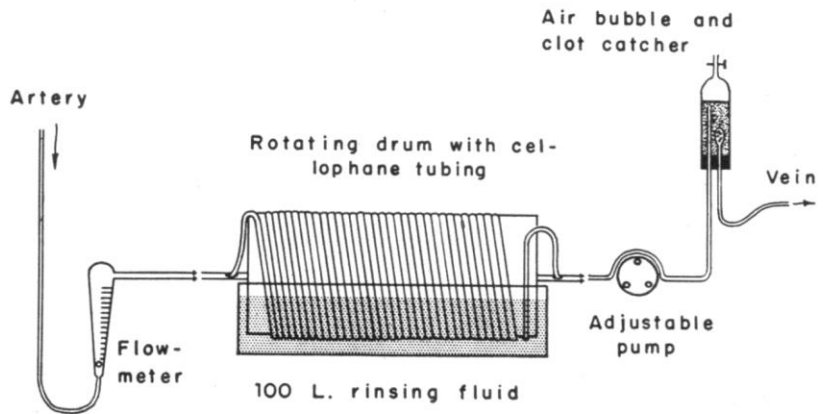




First **hemodialysis** treatment by W.J. Kolff:
. Duration of the treatment : **11.5 hours**
. Blood flow: **116 ml/min**

Willem Johan "Pim" Kolff
February 14, 1911, Leiden
February 11, 2009

***Kolff* performed hybrid therapies**

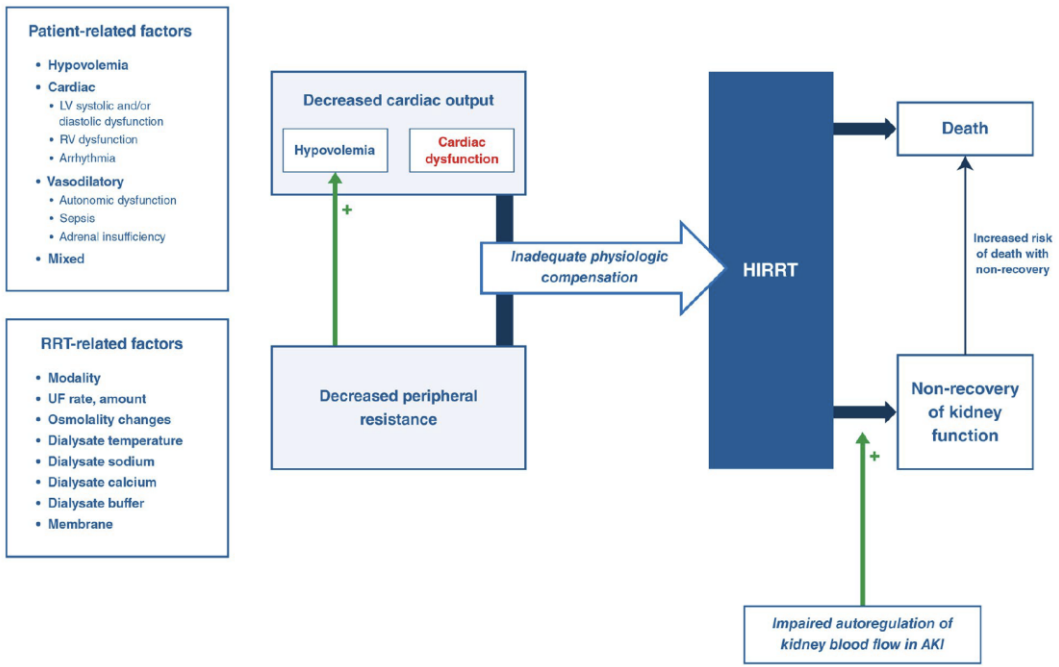


Intensive Care Med (2019) 45:1333–1346
https://doi.org/10.1007/s00134-019-05707-w

REVIEW

Mechanisms for hemodynamic instability related to renal replacement therapy: a narrative review

Adrianna Douvris[1], Khalid Zeid[2], Swapnil Hiremath[1], Sean M. Bagshaw[3], Ron Wald[4], William Beaubien-Souligny[4], Jennifer Kong[1], Claudio Ronco[5] and Edward G. Clark[1*]



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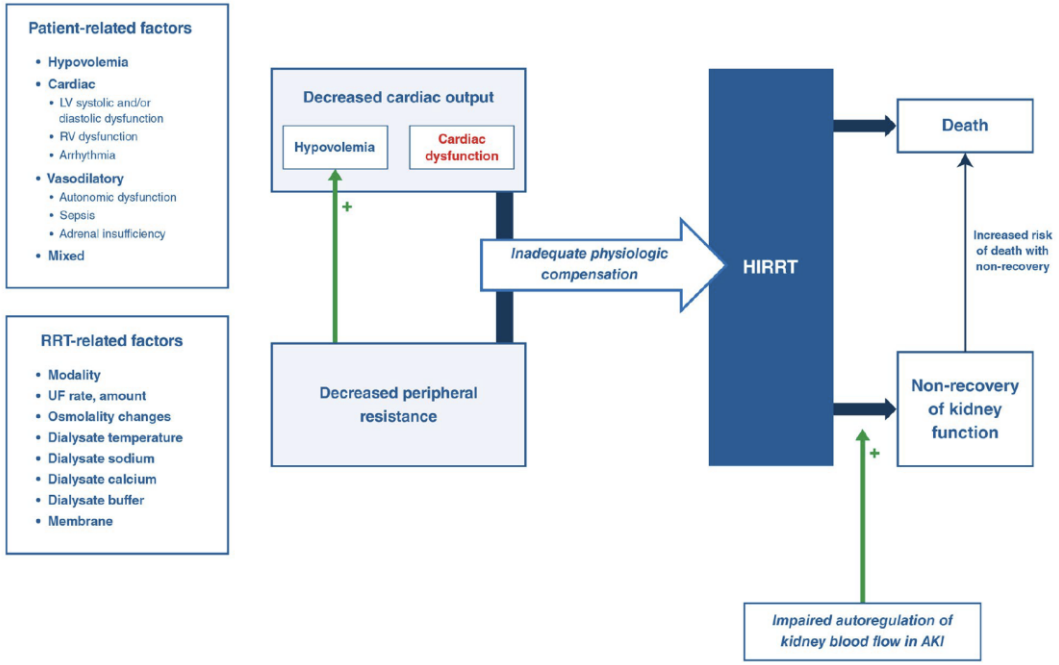


Critical Care Nephrology and Acute Kidney Injury

Prolonged Intermittent Kidney Replacement Therapy

Zoey Levine and Anitha Vijayan

« ….compared with IHD, *hybrid therapy* offers **more hemodynamic stability**, particularly in patients who remain highly vulnerable to hypotension from aggressive ultrafiltration over a shorter duration of treatment…. »

Critical Care Nephrology
and Acute Kidney Injury

Prolonged Intermittent Kidney Replacement Therapy

Zoey Levine and Anitha Vijayan

"Reducing the efficiency of solute clearance (thereby reducing osmotic shifts) and **extending the duration of treatment** (thereby lowering the ultrafiltration rate) make PIRRT less likely to provoke hemodynamic instability during RRT (HIRRT) relative to IHD."

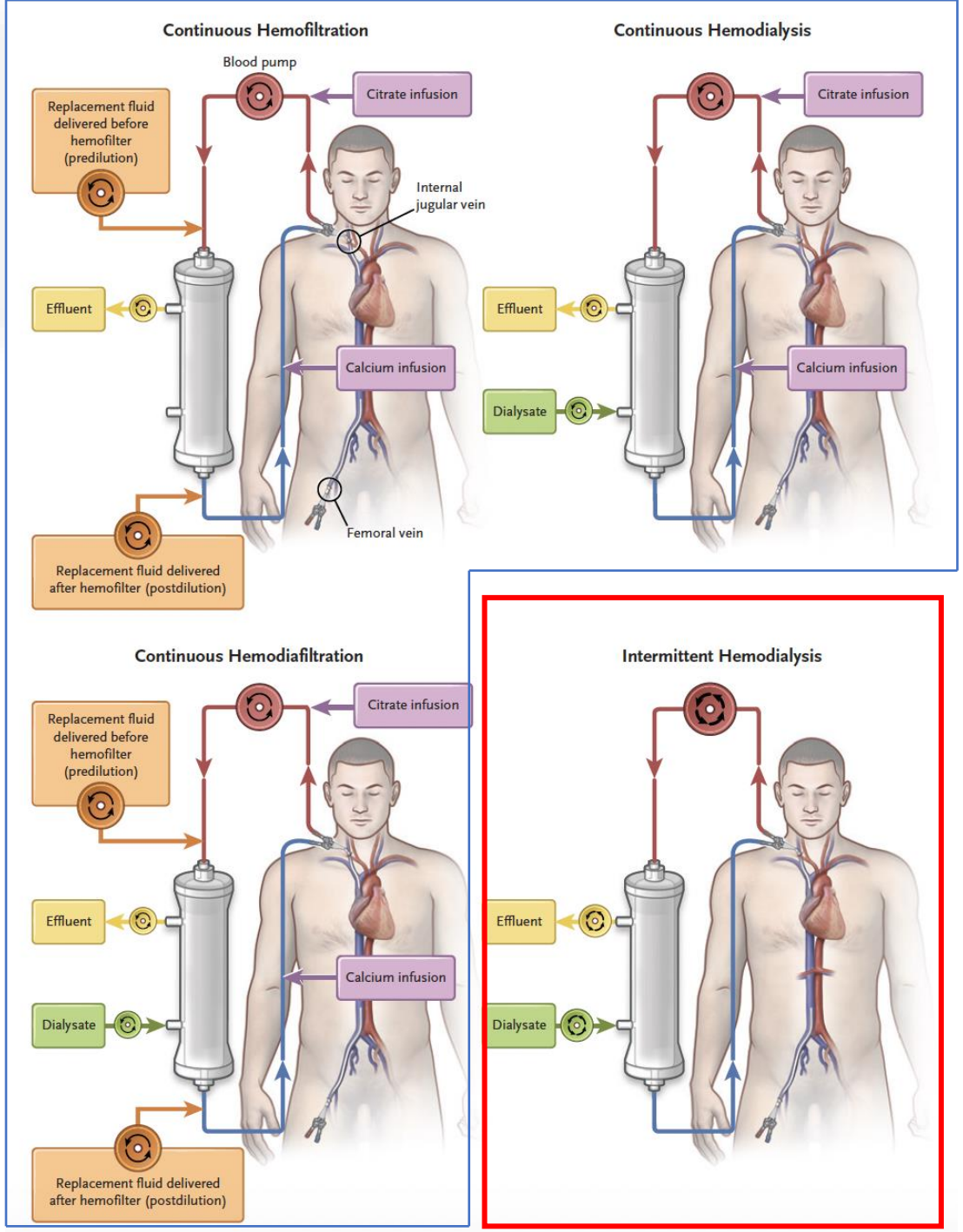
REVIEW ARTICLE

Julie R. Ingelfinger, M.D., *Editor*

Extracorporeal Kidney-Replacement Therapy for Acute Kidney Injury

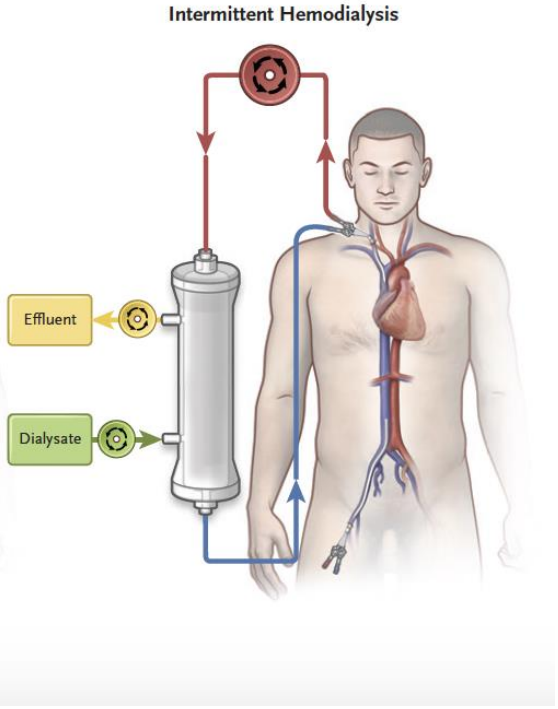
Stéphane Gaudry, M.D., Ph.D., Paul M. Palevsky, M.D., and Didier Dreyfuss, M.D.

CRRT



IHD

IHD



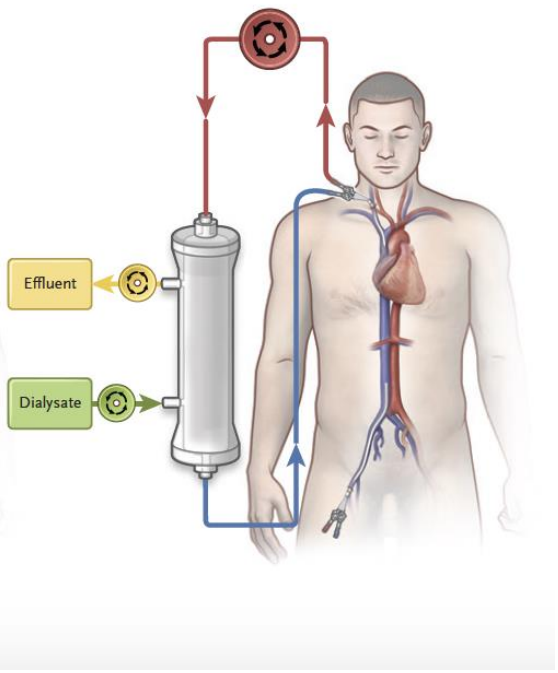
Advantages

- Widely available
- Better for **transportation** (CT scan, operating theater)
- Better for **rehabilitation**
- Rapid correction of metabolic abnormalities
- No anticoagulation option

Disadvantage

Hemodynamic instability ?

IHD



REVIEW

Current state of the art for renal replacement therapy in critically ill patients with acute kidney injury

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Strategies to **improve hemodynamic tolerance of IRRT**

Disadvantage

Hemodynamic instability ?

Strategies to **improve hemodynamic tolerance of IRRT**

INTERVENTION	PHYSIOLOGICAL EFFECT	STRATEGY
Isovolemic initiation	Preserve intravascular volume, prevent hypovolemia	Fill circuit with 0.9% saline
Reduced dialysate temperature	Preserve vasomotor tone	Decrease dialysate temp by 1 to 2 °C
Reduced dialysate flow rate	Preserve plasma osmolality and prevent rapid shift in plasma osmolality	Decrease to 50-100 ml/min
Dialysate [Na+] profiling	Preserve plasma osmolality, promote vascular refill	Progressive increase dialysate [NA+]> 145 mmol/l
Prefential use bicarbonate buffer	Preserve myocardial contractility	Avoid acid-based dialysis buffer
Conservative UF	Preserve intravascular volume, prevent hypovolemia	Start with isolated dialysis; gentle UF; extend session to achieve fluid balance goals

What do current guidelines recommend?

- KDIGO: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients. (2B)

- French guidelines: Continuous and intermittent RRT techniques can be used equally, taking into account their availability and the experience of the team. Strong agreement

Paul Palevsky

CRITICAL CARE NEPHROLOGY AND ACUTE KIDNEY INJURY

Debate: Intermittent Hemodialysis versus Continuous Kidney Replacement Therapy in the Critically Ill Patient: Moderator Commentary

Palevsky, Paul M. MD[1,a]

CJASN 2023

"Merely stating that **IHD and CRRT** provided equivalent outcomes is misleading if it is not acknowledged that **similar outcomes may not be achievable with the short, rapid treatments that characterize most inpatient hemodialysis in US**. Treatment duration will need to be extended **from 3-4 hours to 5-5$^{1/2}$ hours** to achieve similar outcomes"

Definition

Form of KRT that offers either **diffusive or convective clearance** that is **longer than a standard hemodialysis** session of 3–4 hours, **but not 24-hour duration** like continuous KRT (CKRT)

PIRRT could be performed using
hemodialysis machines or CKRT machines

First description

AJKD 2000

Extended Daily Dialysis: A New Approach to Renal Replacement for Acute Renal Failure in the Intensive Care Unit

Victoria A. Kumar, MD, Maureen Craig, RN, MSN, Thomas A. Depner, MD, and Jane Y. Yeun, MD

Disadvantages of CVVH:

- Intensive nursing requirements
- Continuous anticoagulation
- Patient immobility
- Expense

Extended daily dialysis: n=25

CVVH: n= 17

	EDD	CVVH
Total no. of treatment days	367	113
Median duration of daily treatment (h)	7.5 (6-8)	19.5 (13.4-24)
Median no. of treatments performed per patient	9 (3-39)	6 (3-15)

First description

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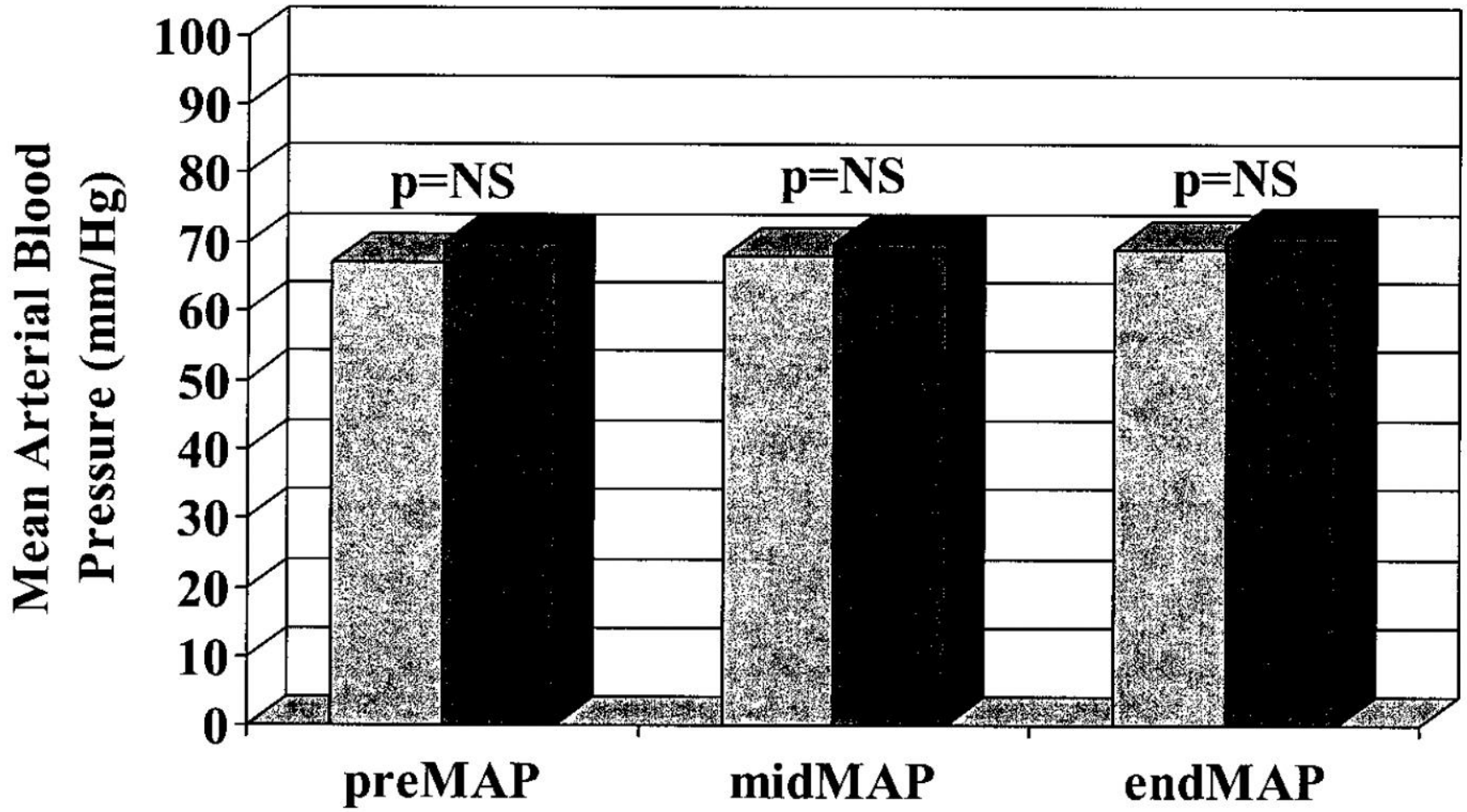

First description

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Victoria A. Kumar, MD, Maureen Craig, RN, MSN, Thomas A. Depner, MD, and Jane Y. Yeun, MD

Patients treated with EDD required significantly less heparin
4,000 U/d vs 21,100 U/d; P=0.001

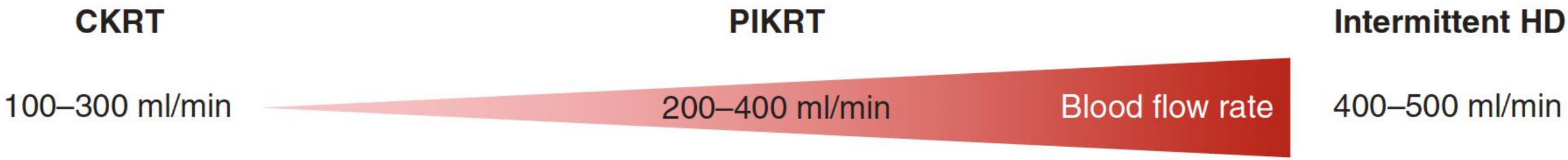
Prolonged Intermittent Kidney Replacement Therapy

Zoey Levine and Anitha Vijayan

Table 1. Prolonged intermittent KRT: Nomenclature and commonly used KRT machines

Acronym	Procedure	KRT Machines
Diffusion only		
SLED (12,13,47)	Sustained low-efficiency dialysis	Fresenius 2008, Gambro AK200S, Gambro Integra
ED (48), EDD (5)	Extended dialysis or Extended daily dialysis	Fresenius 2008, Fresenius Genius
SLED-BD (23)	Sustained low-efficiency dialysis with batched dialysate	Fresenius Genius
E-HFD (49)	Extended high-flux hemodialysis	Fresenius Genius
Convection only		
AVVH (14,15)	Accelerated venovenous hemofiltration	NxStage System One
Diffusion and convection		
S-HDF (16)	Sustained hemodiafiltration	Nikkiso DBB-02
SLEDD-f (50)	Sustained low-efficiency daily diafiltration	Fresenius 4008S ArRT-Plus
PDIKRT (51)	Prolonged daily intermittent KRT	Fresenius 4008S ArRT-Plus

Treatment parameters



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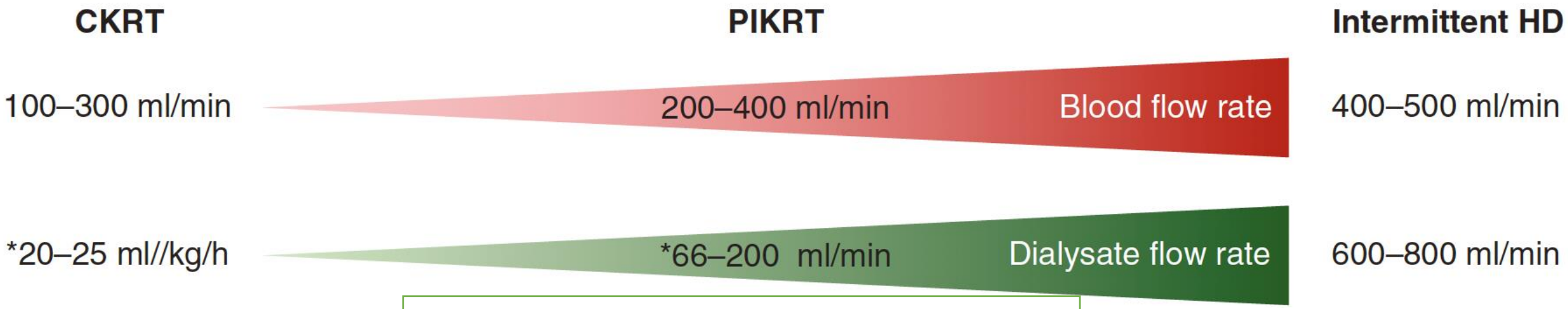
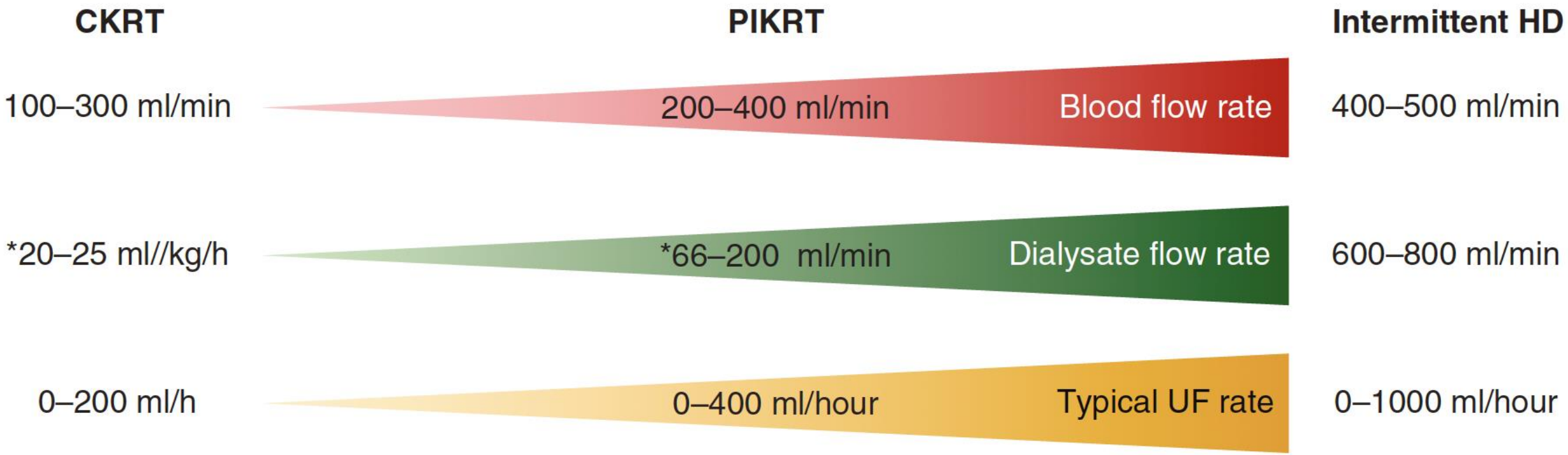
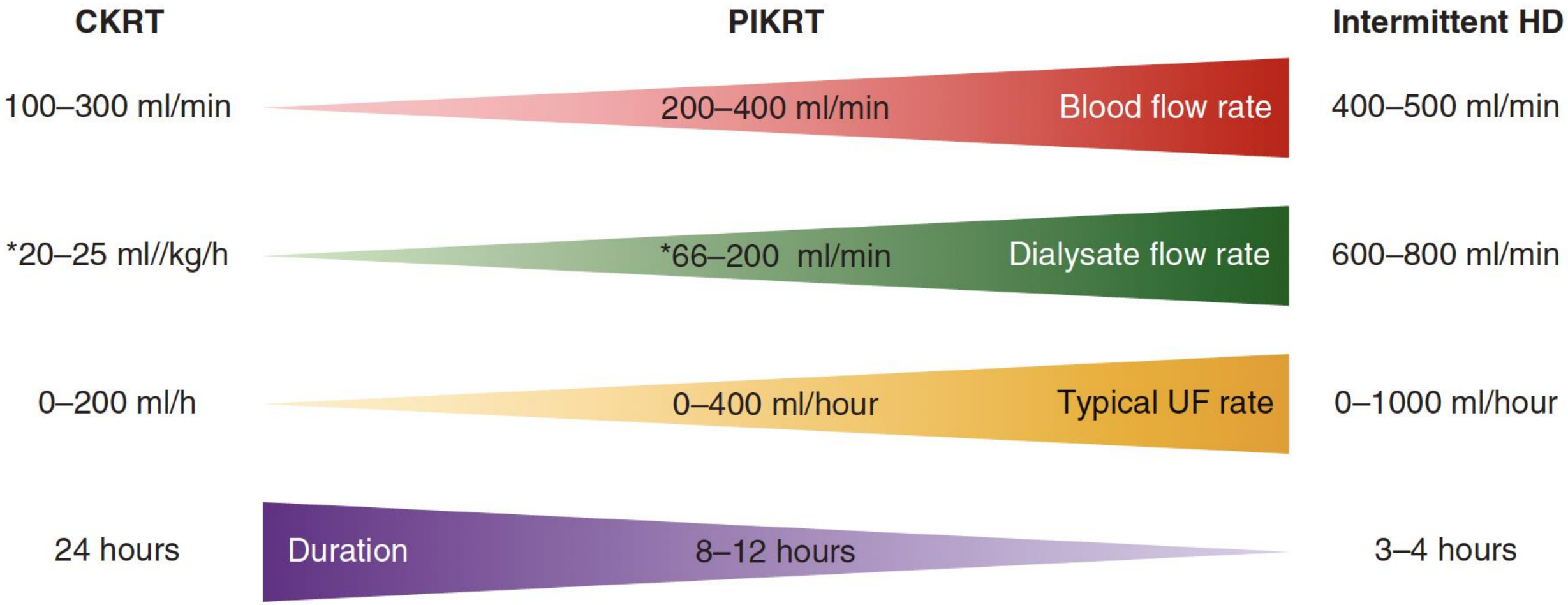


Diffusive technique: Dialysate flow rate
Convective technique: Replacement fluid flow rate
Both technique: Combination

Treatment parameters



Treatment parameters



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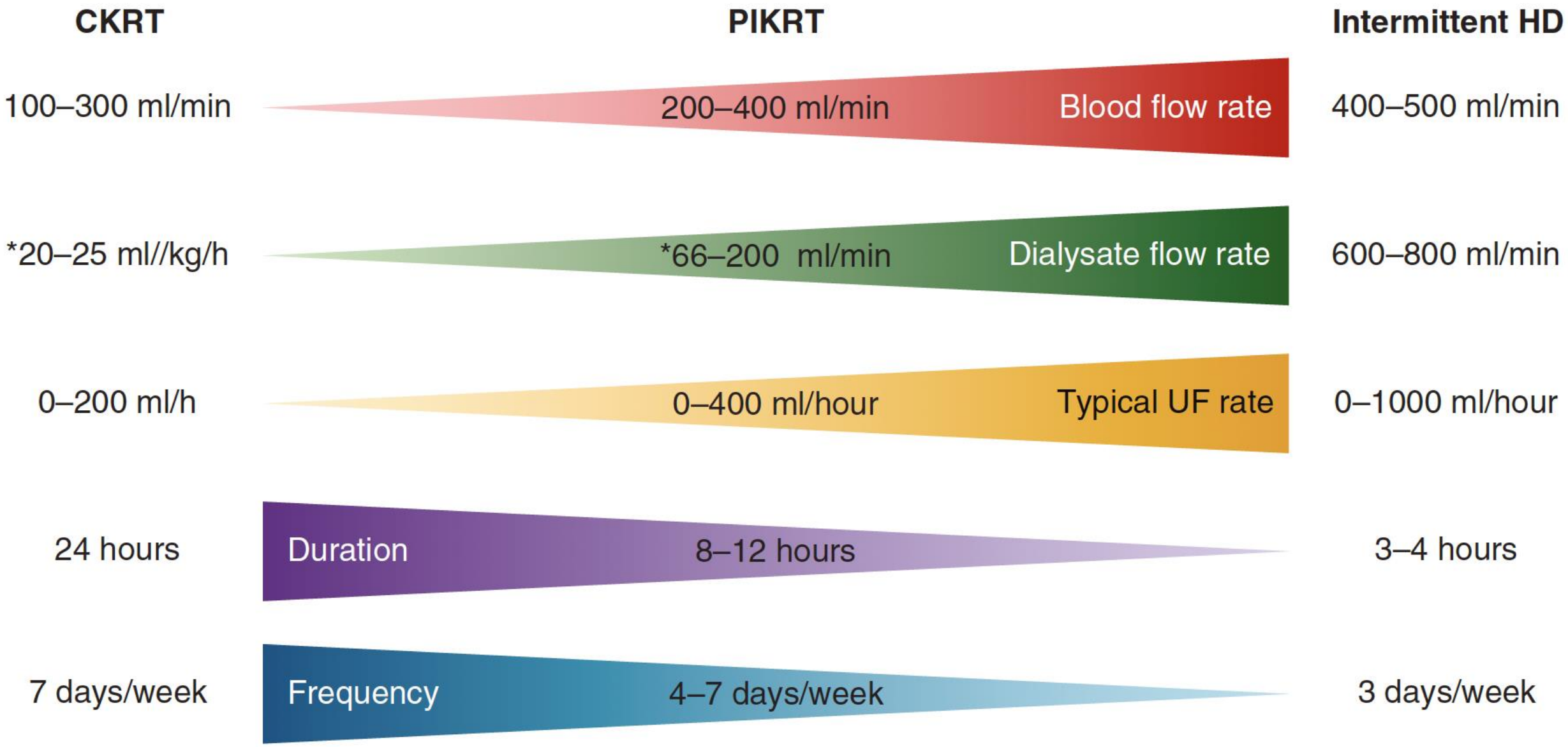


Are hybrid therapies frequently used ?

ORIGINAL ARTICLE

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

STARRT AKI

- Multicenter, International, RCT
- 165 hospitals in 15 countries
- **2927 adults ICU** patients with **severe AKI**

Characteristic	Accelerated strategy (N=1418)	Standard strategy (N=903)	P value
RRT modality – no. (%)			0.53
CRRT	968 (68.4)	621 (70.6)	
IHD	383 (27.0)	223 (25.3)	
SLED	65 (4.6)	36 (4.1)	

A Prospective International Multicenter Study of AKI in the Intensive Care Unit

Josée Bouchard, Anjali Acharya,† Jorge Cerda,‡ Elizabeth R. Maccariello,§ Rajasekara Chakravarthi Madarasu,‖ Ashita J. Tolwani,¶ Xinling Liang,** Ping Fu,†† Zhi-Hong Liu,‡‡ and Ravindra L. Mehta§§*

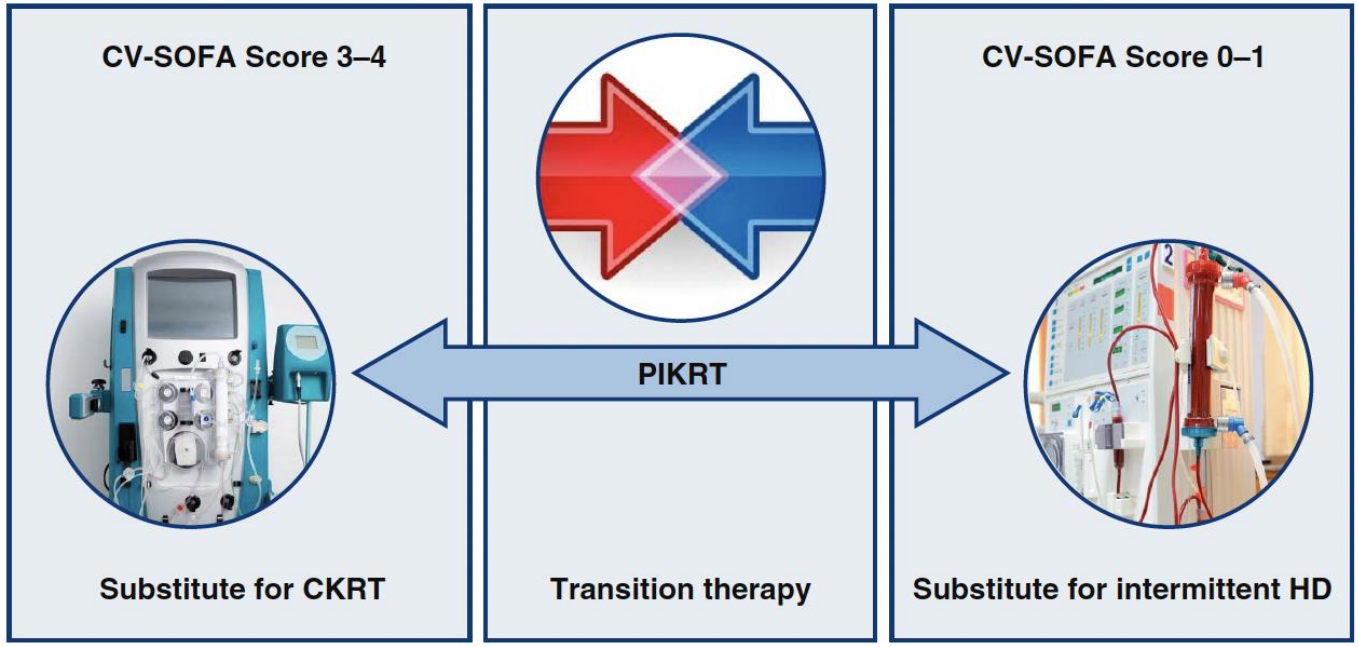
Clin J Am Soc Nephrol 10: 1324–1331, 2015

SLED was most often used in emerging countries

45.2% versus 4.3% ; P=0.001

Potential indications of PIRRT

1. As a **substitute for CRRT** to treat hemodynamically unstable patients with AKI
2. As a **substitute for IHD**
3. For **de-escalation of treatment** in the ICU

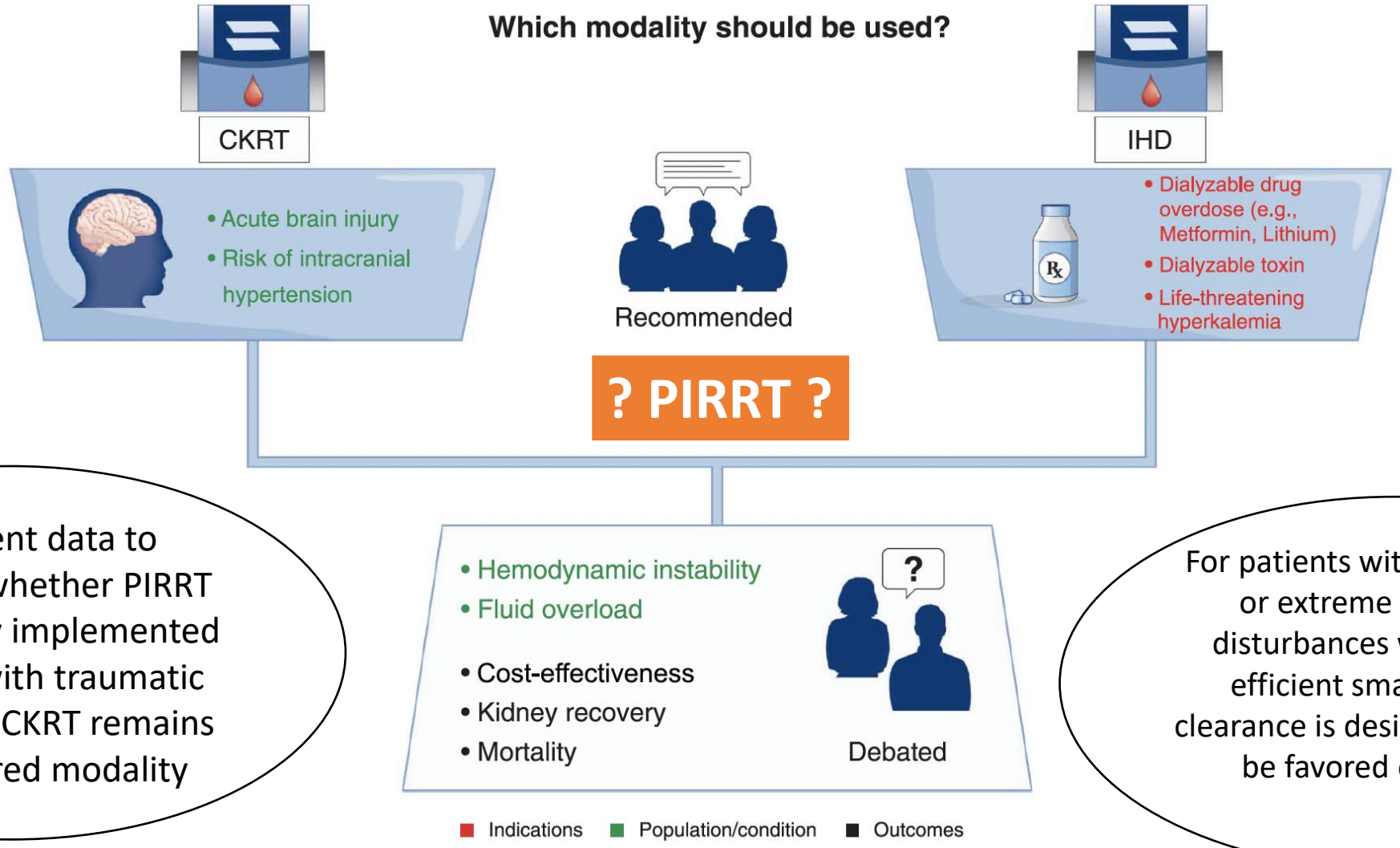


Critical Care Nephrology and Acute Kidney Injury

CJASN 2023

Debate: Intermittent Hemodialysis versus Continuous Kidney Replacement Therapy in the Critically Ill Patient: The Choice Should Be Evidence Based

Khalil Chaïbi,[1,2] Didier Dreyfuss,[2,3,4] and Stéphane Gaudry[1,2,5]



Insufficient data to determine whether PIRRT can be safely implemented in patient with traumatic brain injury. CKRT remains the preferred modality

For patients with intoxications or extreme electrolyte disturbances where highly efficient small molecule clearance is desired, IHD should be favored over PIRRT

Advantages of hybrid therapies (or IRRT….) compared to CRRT

They facilitate the performance of **diagnostic imaging**, **rehabilitation**, and other procedures

SYSTEMATIC REVIEW

The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review

Claire J. Tipping[1,2], Meg Harrold[4,5], Anne Holland[2,6], Lorena Romero[7], Travis Nisbet[3] and Carol L. Hodgson[1,2*]

Conclusion: Active mobilisation and rehabilitation in the ICU has no impact on short- and long-term mortality, but may improve mobility status, muscle strength and days alive and out of hospital to 180 days.

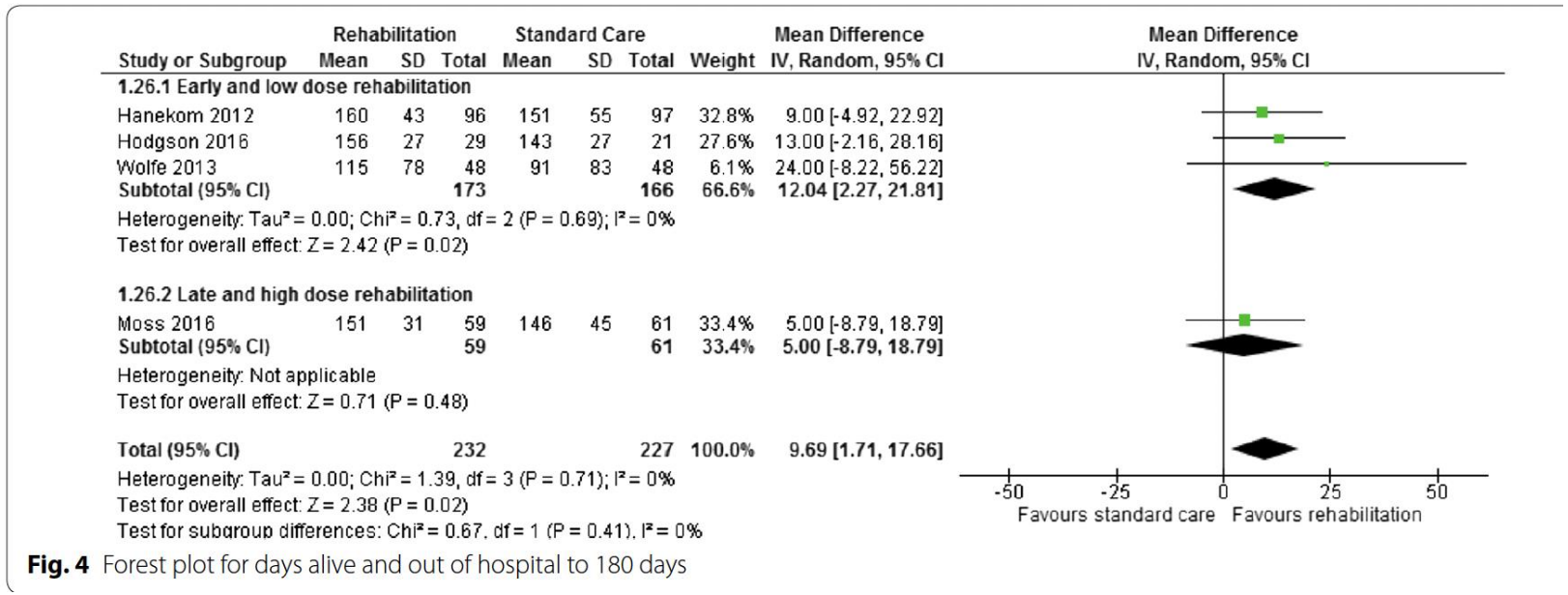


Fig. 4 Forest plot for days alive and out of hospital to 180 days

Advantages of hybrid therapies (or IRRT….) compared to CRRT

They facilitate the performance of **diagnostic imaging**, **rehabilitation**, and other procedures

There is **less need for anticoagulation**

Regional citrate anticoagulation is possible if CRRT machine is used.

Advantages of hybrid therapies (or IRRT….) compared to CRRT

They facilitate the performance of **diagnostic imaging**, **rehabilitation**, and other procedures

There is **less need for anticoagulation**

Regional citrate anticoagulation is possible if CRRT machine is used.

It is **cost-effective**

Costs by modality

	SLED ($)	CRRT citrate ($)	CRRT heparin ($)
Supply cost/day	69.75	402.80	334.95
HD RN cost/day	168.75[a]	37.50	37.50
Total cost/day	238.50	440.30	372.45
Total cost/week	1431	3089	2607

Berbece and Richardson *Kidney Int* 2006

Advantages of hybrid therapies (or IRRT….) compared to CRRT

They facilitate the performance of **diagnostic imaging**, **rehabilitation**, and other procedures

There is **less need for anticoagulation**

Regional citrate anticoagulation is possible if CRRT machine is used.

It is **cost-effective**

It allows for utilization of **one machine for up to 3 patients/day**

Reducing the risk of Shortage of RRT for COVID-19 patients

Impending Shortages of Kidney Replacement Therapy for COVID-19 Patients

David S. Goldfarb,[1,2] Judith A. Benstein,[2] Olga Zhdanova,[2,3] Elizabeth Hammer,[2] Clay A. Block,[4] Nina J. Caplin,[2,3] Nathan Thompson,[2,3] and David M. Charytan[2]

CJASN 15: 880–882, 2020. doi: https://doi.org/10.2215/CJN.05180420

"An informal survey of our intensive care units (ICUs) this week demonstrates that **20%–40% of intubated ICU patients have AKI that necessitates KRT**"

We initiated the use of **acute peritoneal dialysis**, a modality rarely used in American ICUs in recent years, to remove pressures from our CKRT supply

We must now highlight the possibility that before a deficiency of ventilators become an issue in caring for patients with COVID-19, provision of KRT may face critical shortages.

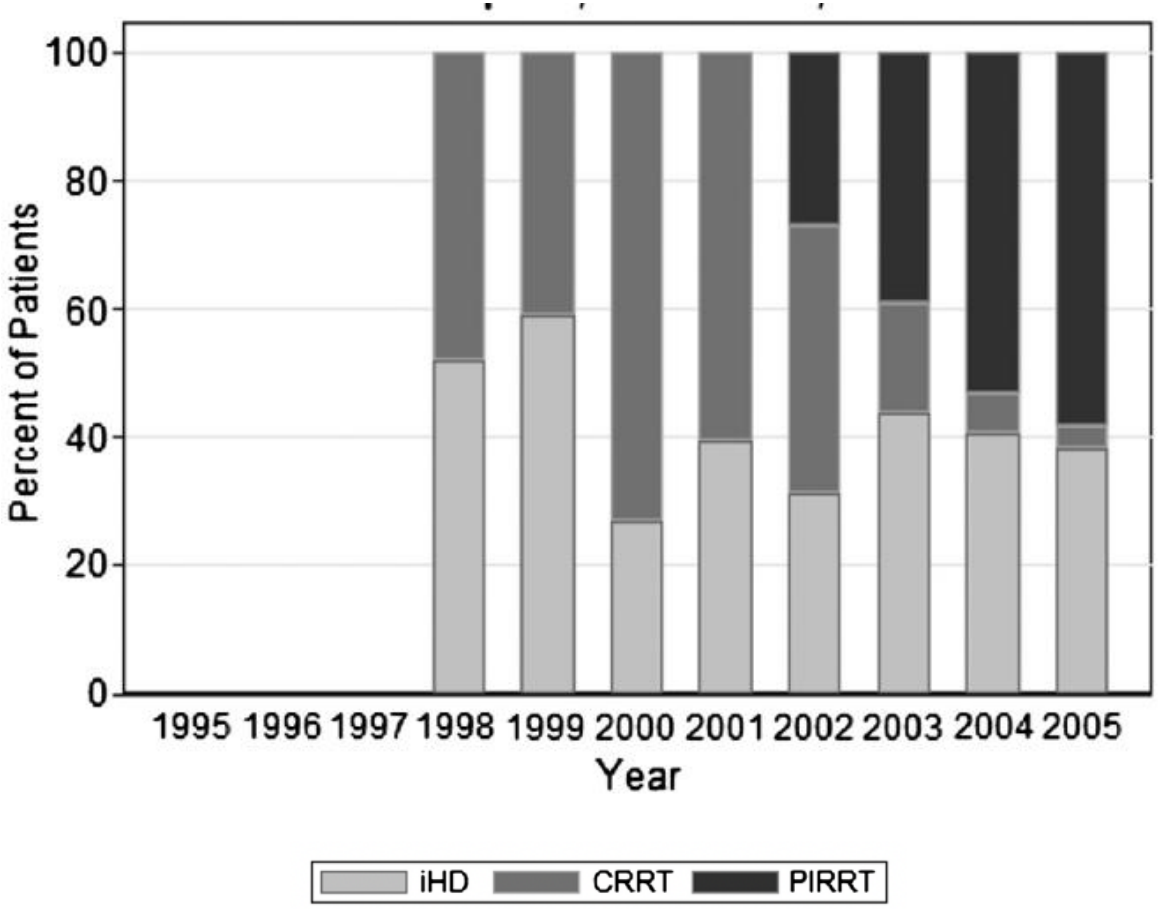
Comparison between hybrid therapies and CRRT ?
Clinical studies

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

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

NDT 2011

- Retrospective study
- 3 ICUs
- 1347 patients



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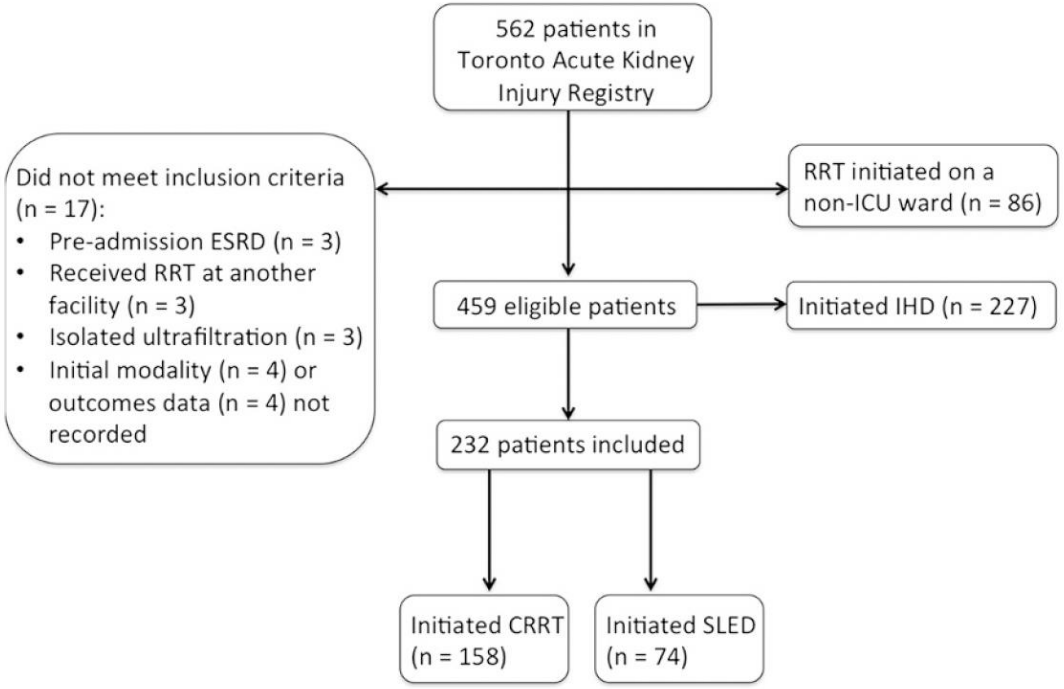
Results. The change from CRRT to PIRRT was not associated with any increase in mortality rate, with an adjusted IRR of 1.02 (0.61–1.71). The IRR was virtually identical in the three ICUs (P-value = 0.63 for the difference in the IRR between ICUs).

RESEARCH ARTICLE Open Access

Outcomes of sustained low efficiency dialysis versus continuous renal replacement therapy in critically ill adults with acute kidney injury: a cohort study

Abhijat Kitchlu[1], Neill Adhikari[2,3], Karen E. A. Burns[2,4,5], Jan O. Friedrich[2,4,5], Amit X. Garg[6,7], David Klein[2,4,5], Robert M. Richardson[1] and Ron Wald[1,4*]



- Cohort study
- SLED (target 8 h/session, blood flow 200 mL/min, predominantly without anticoagulation) (n=74)
- vs CRRT (n=158)

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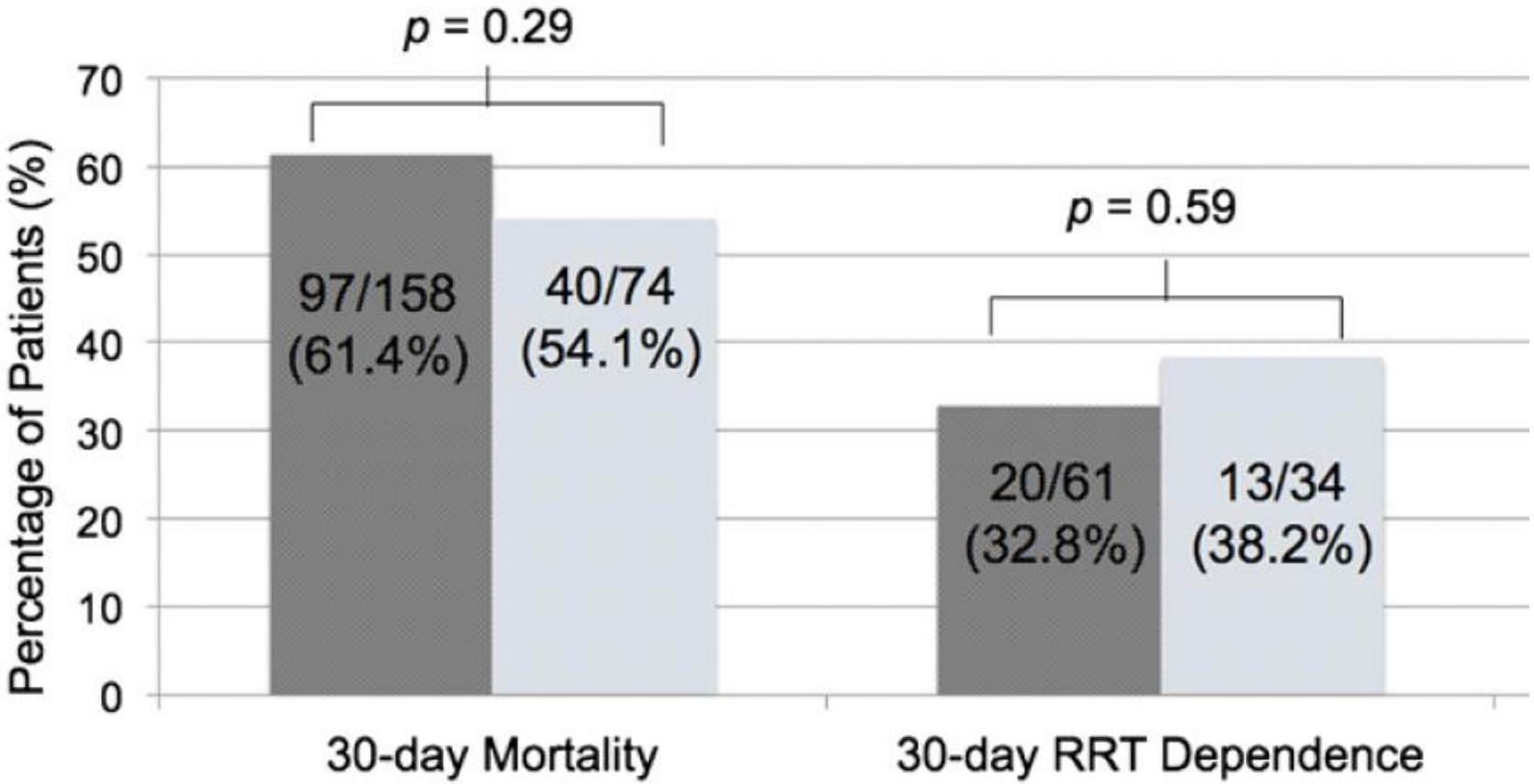

Schwenger et al. Critical Care 2012, 16:R140
http://ccforum.com/content/16/4/R140

CRITICAL CARE

RESEARCH Open Access

Sustained low efficiency dialysis using a single-pass batch system in acute kidney injury - a randomized interventional trial: the REnal Replacement Therapy Study in Intensive Care Unit PatiEnts

Vedat Schwenger[1*†], Markus A Weigand[2†], Oskar Hoffmann[3], Ralf Dikow[1], Lars P Kihm[1], Jörg Seckinger[1], Nexhat Miftari[1], Matthias Schaier[1], Stefan Hofer[4], Caroline Haar[4], Peter P Nawroth[5], Martin Zeier[1], Eike Martin[4] and Christian Morath[1]

SLED vs CRRT: RCT

- Single-centre RCT, n=232

  SLED vs **CVVH** (Prisma)
- SLED (12 hr intended, 14.9 hrs delivered)
- CVVH (24 hr intended, 19.9 hrs delivered)

Schwenger et al *Crit Care* 2012

Schwenger et al. Critical Care 2012, 16:R140
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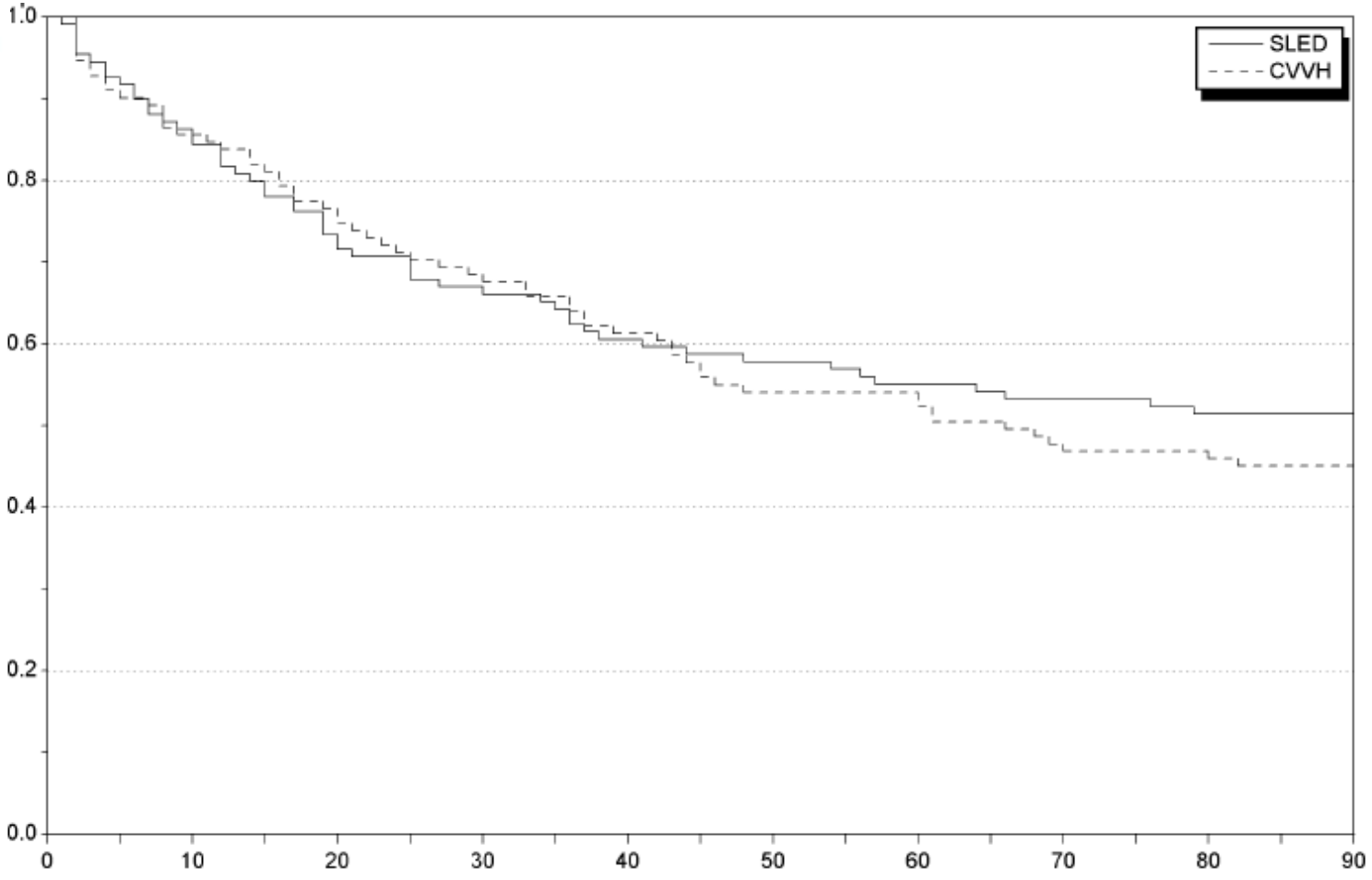
Primary outcome

SLED vs CRRT
90-day mortality



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Secondary outcomes

- **Hemodynamic stability** did not differ
- SLED-BD group had significantly **fewer days of mechanical ventilation** (17.7 vs. 20.9; P = 0.047)
- SLED-BD group had significantly **fewer days in the ICU** (19.6 vs. 23.7, P = 0.04).
- Patients treated with SLED **needed fewer blood transfusions** (1,375 vs. 1,976 , P = 0.02)

Schwenger et al. Critical Care 2012, 16:R140
http://ccforum.com/content/16/4/R140

CRITICAL CARE

RESEARCH Open Access

Sustained low efficiency dialysis using a single-pass batch system in acute kidney injury - a randomized interventional trial: the REnal Replacement Therapy Study in Intensive Care Unit PatiEnts

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Table 4 Dialysis equipment and nursing time per patient.

	SLED (n = 115)	CVVH (n = 117)	*P**
Number of membranes used	14.3 ± 15.3	7.56 ± 8.54	< 0.001
Number of dialysis catheters used	1.74 ± 1.44	1.70 ± 1.89	0.294
Nursing time spent (minutes)			
< 1	9.36 ± 14.7	14.3 ± 41.9	0.131
1 to 5	3.64 ± 4.63	6.75 ± 13.2	0.136
> 5	7.24 ± 9.51	12.1 ± 17.0	< 0.001

*One-tailed Wilcoxon test. SLED: sustained low efficiency dialysis; CVVH: continuous veno-venous hemofiltration.

Models of nursing support for PIKRT in the ICU

ICU Nursing Model

- Usually performed using CKRT equipment
- ICU nurse is responsible for set-up and take-down
- ICU nurse is responsible for monitoring patient throughout the procedure and troubleshooting alarms
- May require one-on-one ICU nursing

Models of nursing support for PIKRT in the ICU

ICU Nursing Model

- Usually performed using CKRT equipment
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Dialysis Nursing Model

- Usually performed with an intermittent HD machine
- Dialysis nurse is responsible for set-up and take-down
- Dialysis nurse is responsible for monitoring patient throughout the procedure and troubleshooting alarms
- One dialysis nurse may oversee 2 or 3 patients in the same ICU

Models of nursing support for PIKRT in the ICU

ICU Nursing Model	ICU and Dialysis Nurse: Collaborative Model	Dialysis Nursing Model
• Usually performed using CKRT equipment • ICU nurse is responsible for set-up and take-down • ICU nurse is responsible for monitoring patient throughout the procedure and troubleshooting alarms • May require one-on-one ICU nursing	• Can be performed using either CKRT or intermittent HD equipment • Dialysis nurse is responsible for set-up and take-down • ICU nurse is responsible for monitoring patient throughout the procedure and troubleshooting alarms • May not require one-on-one ICU nursing • One dialysis nurse can oversee several patients in the hospital	• Usually performed with an intermittent HD machine • Dialysis nurse is responsible for set-up and take-down • Dialysis nurse is responsible for monitoring patient throughout the procedure and troubleshooting alarms • One dialysis nurse may oversee 2 or 3 patients in the same ICU

To sumarize

- Hybrid therapies = a kind of IHD done (properly) for ICU patients
- **Many advantages:** hemodynamically well tolerated, facilitate diagnostic imaging and early mobilisation, no need anticoagulation, cost-effective, one machine for 3 patients/d
- **Few limits:** no guidelines for dose and frequency, no data on medication (antibiotics) dosing, risk of hypophosphatemia and hypokalemia
- **Need more high quality studies**

MINISTÈRE
DES SOLIDARITÉS
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PHRC 2022

ICRAKI trial

non-inferiority multicenter open-label randomized controlled trial

- Adults under invasive MV or receiving catecholamine infusion
- RRT indication(s)
  - severe hyperK+, severe metabolic acidosis, severe pulmonary edema
  - AKI stage 3 with serum urea concentration >40 mmol/L or oligo-anuria>3 days

RANDOMIZATION

CRRT group

IHD group

Primary endpoint
major adverse kidney event 90 days after randomization (MAKE90)
death *or* RRT *or* serum creatinine > 25% basal value

Number of participants: 1000
ICU centers: n=26


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Thank you