Acute RRT Modalities: Comparisons and Considerations
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Acute kidney injury is common among hospitalized patients globally.1

AKI affects an estimated 20% of hospitalized patients worldwide1,*. 

AKI is a serious condition

AKI is associated with an increased risk of morbidity and mortality2–6

AKI is associated with an increased risk of CKD, including ESRD7–9

*Multicentre meta-analysis of 154 studies (n=3,585,911), primarily in hospital settings, that adopted a KDIGO-equivalent AKI definition between 2004 and 2012. Pooled rates.1
**Fluid overload** is one condition that may **adversely** impact AKI patient prognosis\(^{10,11}\)

Consequences of fluid overload may lead to organ dysfunction\(^{13}\)

Fluid overload at RRT initiation for AKI has been associated with an increased risk of mortality\(^{11,*}\)

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**FLUID OVERLOAD IN PATIENTS WITH AKI IS A SERIOUS CONDITION** \(^{14–16}\)

*Prospective, observational cohort study of 296 adults treated with RRT in 17 Finnish ICUs from Sep 2011–Feb 2012.\(^{11}\)*
AKI is associated with **substantial financial burden** \(^{17-19,*}\)

### AKI status impacts daily costs \(^{18}\)

**Patients with AKI have significantly higher daily costs compared with patients without AKI** \(^{18,†}\)

<table>
<thead>
<tr>
<th>Acute medical condition</th>
<th>Adjusted mean cost difference, in 2012 USD (95% CI) (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI-D (^b)</td>
<td>11,016 (10,468, 11,564)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4822 (4696, 5068)</td>
</tr>
<tr>
<td>VTE</td>
<td>3782 (3611, 3953)</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>1802 (1676, 1929)</td>
</tr>
<tr>
<td><strong>AKI</strong> (^c)</td>
<td><strong>1795 (1692, 1899)</strong></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1705 (1584, 1825)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1427 (1281, 1573)</td>
</tr>
<tr>
<td>MI</td>
<td>14 (–91, 119)</td>
</tr>
<tr>
<td>GI bleed</td>
<td>–860 (–961, –759)</td>
</tr>
</tbody>
</table>

\(^a\)Compared with reference group without the condition of interest.

\(^b\)Compared with patients without AKI.

\(^c\)Includes patients with dialysis-requiring AKI (AKI-D).

**THE INCREMENTAL COST OF AKI-D OR AKI IS HIGHER THAN FOR MANY OTHER CONDITIONS FOUND IN HOSPITALIZED PATIENTS** \(^{19,‡}\)

### AKI is expensive even relative to other acute medical conditions \(^{19}\)

**Acute medical condition**

**Adjusted mean cost difference, in 2012 USD (95% CI) \(^a\)**

- **AKI-D**
  - 11,016 (10,468, 11,564)
- Sepsis
  - 4822 (4696, 5068)
- VTE
  - 3782 (3611, 3953)
- Acute pancreatitis
  - 1802 (1676, 1929)
- **AKI**
  - **1795 (1692, 1899)**
- Pneumonia
  - 1705 (1584, 1825)
- Stroke
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- MI
  - 14 (–91, 119)
- GI bleed
  - –860 (–961, –759)

\(^a\)Compared with reference group without the condition of interest.

\(^b\)Compared with patients without AKI.

\(^c\)Includes patients with dialysis-requiring AKI (AKI-D).

**WHILE EXPENDITURES MAY VARY BY COUNTRY, AKI is a COSTLY CONDITION** \(^{17-19}\)

\(^*\)Costs for hospitalisation due to AKI may vary from country to country.

\(^†\)Multicentre, retrospective cohort study of 659,945 adult hospital admissions across central China in 2013.\(^{18}\)

\(^‡\)2012 multicentre, retrospective study of 29,763,649 adult US hospitalisations without ESRD.\(^{19}\)
Various renal replacement modalities are available for the management of AKI.\(^{20-24}\)

**RRT MODALITIES FOR AKI**

**RRT for AKI**

**Continuous therapies**
- **PD**
  - Therapy delivered continuously through intraperitoneal solution dwells throughout the day

**CRRT**
- Intended therapy delivery of 24 hours/day

**Intermittent therapies**
- **PIRRT**
  - Longer treatments compared with IHD
  - Typically delivered in sessions of 6–12 hours performed 3–7 days/week

- **IHD**
  - Conventional hemodialysis
  - Typically delivered in sessions of 3–6 hours performed 3–7 days/week

**ACUTE RRT IS DELIVERED AS EITHER A CONTINUOUS OR INTERMITTENT THERAPY.**\(^{20}\)
Modalities **differ** in their typical characteristics\(^{25}\)

**Typical RRT modality characteristics and settings for a 70-kg AKI patient\(^{25-27}\)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CVVH</th>
<th>CVVHD</th>
<th>CVVHDF</th>
<th>SLED*</th>
<th>IHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow ((Q_B), mL/min)</td>
<td>150–250</td>
<td>150–250</td>
<td>150–250</td>
<td>100–300</td>
<td>200–300</td>
</tr>
<tr>
<td>Predominant solute transport principle</td>
<td>+</td>
<td>+</td>
<td>+ +</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ultrafiltrate (mL/h)</td>
<td>1500–2000</td>
<td>variable</td>
<td>1000–1500</td>
<td>variable</td>
<td>variable</td>
</tr>
<tr>
<td>Dialysate flow ((Q_D), mL/h)</td>
<td>0</td>
<td>1500–2000</td>
<td>1000–1500</td>
<td>6000–18,000</td>
<td>18,000–30,000</td>
</tr>
<tr>
<td>Replacement fluid for zero balance (mL/h)</td>
<td>1500–2000</td>
<td>0</td>
<td>1000–1500</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urea clearance (mL/min)</td>
<td>25–33</td>
<td>25–33</td>
<td>25–33</td>
<td>80–90</td>
<td>200–500</td>
</tr>
</tbody>
</table>

* SLED is a type of PIRRT.\(^{21}\)

\(Q_B\), \(Q_D\), and urea clearance tend to be **lower** in **continuous** therapies than in **intermittent** therapies\(^{25-27}\)
Individual patient needs can be addressed by considering the characteristics of the various RRT modalities\(^{28}\).

Relative features, risks, and burdens of different RRT modalities\(^{28}\):

- **CRRT**
  - Hemodynamic stability
  - Stability of intracranial pressure

- **PIRRT / SLED**
  - Rate of fluid removal
  - Rapidity of metabolic and acid-base correction
  - Risk of osmolar shifts

- **IHD**
  - Speed of small solute clearance, including potassium, drugs

**EACH RRT MODALITY HAS POTENTIAL BENEFITS AND LIMITATIONS FOR THE MANAGEMENT OF PATIENTS WITH AKI**\(^{28}\).
RRT MODALITY CONSIDERATIONS

Selection of RRT modality requires careful consideration of many patient- and ICU-specific factors.\textsuperscript{25,28}

Overview of modality considerations

- **CLINICAL CONSIDERATIONS:** FLUID OVERLOAD AND HEMODYNAMIC INSTABILITY
- **CLINICAL CONSIDERATIONS:** LONG-TERM OUTCOMES
- **MACHINE AND PRESCRIPTION CONSIDERATIONS**
- **SOLUTION CONSIDERATIONS**
- **LONG-TERM COST CONSIDERATIONS**
- **EQUIPMENT FOOTPRINT AND MOBILITY CONSIDERATIONS**
Clinical considerations: fluid overload and hemodynamic instability

Fluid overload in AKI patients can be treated by fluid removal during RRT, but rapid fluid removal that does not allow time for plasma refill may lead to hemodynamic instability.\(^{25,29}\)

Avoiding rapid fluid removal to prevent hypovolaemia may improve AKI patient outcomes.\(^{25,29}\)

Modality comparisons\(^{30}\)

<table>
<thead>
<tr>
<th></th>
<th>CRRT</th>
<th>PIRRT/SLED</th>
<th>IHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance per hour</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Clearance per 24 hours</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Fluid status</td>
<td>Stable</td>
<td>Fluctuating</td>
<td>Stable</td>
</tr>
<tr>
<td>Serum levels</td>
<td>Stable</td>
<td>Fluctuating</td>
<td>Stable</td>
</tr>
</tbody>
</table>

CRRT MAY OFFER MORE PRECISE FLUID MANAGEMENT VS IHD OR PIRRT/SLED.\(^{25,30}\)

CRRT IS A PREFERRED RRT BY MANY CLINICIANS FOR AKI PATIENTS WHO ARE HEMODYNAMICALLY UNSTABLE.\(^{25,29}\)
Clinical considerations: long-term outcomes

AKI is associated with an increased risk of long-term dialysis dependence, acute RRT modality type may impact this risk.

Patients on chronic dialysis at day 90 by initial RRT modality

- CRRT: 22%
- IHD: 27%

CHRONIC DIALYSIS HAZARD RATIO (95% CI) FOR CRRT vs IHD WAS 0.75 (0.65–0.87), P<0.0001

Modality comparisons

**CONTINUOUS**
- CRRT
  - Patients are less likely to require chronic dialysis following initial AKI episode compared with patients treated with IHD

**INTERMITTENT**
- PIRRT
  - Insufficient evidence
- IHD
  - It has been reported that patients are more likely to require chronic dialysis following initial AKI episode compared with patients treated with CRRT

USE OF **CRRT** FOR AKI MANAGEMENT HAS BEEN ASSOCIATED WITH A LOWER RISK of CHRONIC DIALYSIS COMPARED WITH IHD.

*Retrospective multicentre cohort study of critically ill adults with AKI between 1996 and 2009. 2004 patients originally treated with CRRT and 2004 patients originally treated with IHD were propensity matched and rates of dialysis dependence were compared.

**Note:** CRRT = Continuous Renal Replacement Therapy, IHD = Intermittent Hemodialysis, AKI = Acute Kidney Injury
**RRT MODALITY CONSIDERATIONS**

**Machine and prescription considerations**

RRT machines deliver **different** dose intensities over **different** durations of therapy\(^{21,22,25}\)

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**Kinetic modeling of urea clearance by different RRT modalities**\(^{35}\)

![Graph showing urea clearance over time for CVVH, SLED, and Daily HD]

- **CVVH**: Typically run in 6–12 h sessions delivered 3–7 times/week. Intended to run 24 h/day. Slow but continuous urea clearance helps avoid spikes in BUN levels.
- **SLED**: Intermittent nature does not allow for continuous urea clearance, which could result in variable BUN levels.
- **Daily HD**: Intermittent therapy, typically run in 3–6 h sessions delivered 3–7 times/week. Continuous urea clearance helps avoid spikes in BUN levels.

**Modality comparisons**\(^{21,22,35}\)

*Unlike IHD or PIRRT, CRRT is run on machines that deliver continuous solute removal*\(^{22,35}\)

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A SAWTOOTH PATTERN WAS OBSERVED WHEN USING INTERMITTENT THERAPIES TO REMOVE UREA, WHILE CONTINUOUS THERAPY MAINTAINED A CONSISTENT BUN LEVEL OVER TIME\(^{35}\)
Solution considerations

Typically, CRRT solutions are **commercially** prepared, while IHD and PIRRT use **local water sources** to prepare dialysate.29,36,37

Preparing solutions on-line from local water sources **necessitates** water **treatment** and routine water **quality monitoring** to assure clean water standards are met.36–38

Modality **comparisons**29,36–40

<table>
<thead>
<tr>
<th>CONTINUOUS</th>
<th>INTERMITTENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRRT</td>
<td>PIRRT</td>
</tr>
<tr>
<td>Because no on-line solutions are typically used, <strong>no water treatment systems</strong> are required.</td>
<td>If a centralized water treatment system is unavailable in the ICU, individual water quality monitoring is necessary.</td>
</tr>
<tr>
<td>Monitoring water quality is not applicable.</td>
<td>If a centralized water treatment system is not used, <strong>staff need to monitor dialysate quality</strong> for individual patients.</td>
</tr>
<tr>
<td></td>
<td><strong>Disinfection requirements</strong> may limit treatment duration to &lt;12 hours41.</td>
</tr>
</tbody>
</table>

**WATER TREATMENT AND QUALITY TESTING MAY CONTRIBUTE TO INCREASED MONITORING WHEN USING SOLUTIONS PREPARED ON-LINE FOR IHD and PIRRT**39,42
Long-term cost considerations

Because initial RRT modality may impact the risk of chronic dialysis, long-term costs of AKI may also be influenced by initial treatment modality.

Cumulative costs of dialysis dependence by initial AKI treatment modality

Mean 5-year total cost/patient of AKI-D\(^{†}\) was $37,780 for CRRT as the initial modality compared with $39,448 for IRRT\(^{43}\)

\(^{†}\)Including cost of dialysis dependence. Cost in 2013 USD.

Modality comparisons

Continuous

CRRT

Total costs may be lower due, in part, to a lower risk of chronic dialysis

Intermittent

PIRRT

Insufficient evidence to compare to CRRT or IHD

IHD

Total costs may be higher due, in part, to a higher risk of chronic dialysis

THE LONG-TERM COST OF AKI MAY BE LOWER FOR PATIENTS INITIALLY TREATED WITH CRRT COMPARED TO THOSE TREATED WITH IHD\(^{43}\)

*Health outcomes and healthcare costs were simulated and averaged for a cohort of 1000 patients initiated on CRRT and a cohort of 1000 patients initiated on IRRT. All costs were inflated to 2013 USD.\(^{43}\)
### Equipment footprint and mobility considerations

Water treatment systems required for IHD and PIRRT add to physical **space** requirements and water lines may limit RRT mobility in ICUs without central water treatment systems.\(^{37,40}\)

In ICUs without central water treatment systems, portable **water treatment devices** may be necessary,\(^{40}\) which can occupy as much as 0.13–0.16 \(m^2\) of floor space.\(^{44,45}\)

### Modality comparisons\(^{36,37,40,41,46–49}\)

<table>
<thead>
<tr>
<th>Continuous</th>
<th>Intermittent</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRRT</td>
<td>PIRRT</td>
</tr>
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<td>IHD</td>
<td></td>
</tr>
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</table>

Because the CRRT machine is the **only component** that contributes to the therapy’s physical footprint, treatment mobility may be increased.

- No **space considerations** for water treatment systems are necessary.

Both the IHD machine and water treatment systems contribute to the therapy’s physical footprint, which may impact treatment mobility in ICUs without central water treatment systems.

- In situations where a central water treatment system is not utilised, the **greater physical footprint** of the machine + water treatment system may impact ICU spacing.

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**WATER TREATMENT EQUIPMENT MAY ADD TO THE FOOTPRINT OF IHD AND PIRRT SYSTEMS, POTENTIALLY DECREASING TREATMENT MOBILITY AND IMPACTING SPACING CONSIDERATIONS** \(^{40,47–49}\)
AKI is a **common** and **costly** condition among ICU patients,\(^1,17–19\) and is associated with increased risks of **morbidity and mortality**\(^2–9\).

Acute RRT is delivered as **either** a **continuous** or a **intermittent** therapy, each of which have unique characteristics, settings, and limitations\(^20,25–28\).

**Selection of RRT modality** requires careful consideration of many patient- and ICU-specific factors\(^25,28\).

**CRRT** is a preferred renal replacement therapy by many clinicians for patients with AKI who are hemodynamically unstable\(^25,28\).
ACRONYMS/ABBREVIATIONS/REFERENCES

AKI, acute kidney injury; AKI-D, dialysis-requiring AKI; BUN, blood urea nitrogen; CI, confidence interval; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; CVVH, continuous veno-venous hemofiltration; CVVHD, continuous veno-venous hemodialysis; CVVHDF, continuous veno-venous hemodiafiltration; dl, decilitre; EDHF, extended daily hemofiltration; ESRD, end-stage renal disease; Feb, February; GI, gastrointestinal; h, hour; HD, hemodialysis; ICU, intensive care unit; IHD, intermittent renal replacement therapy; K+, potassium ion; KDIGO, Kidney Disease Improving Global Outcomes; kg, kilogram; m2, square meters; mg, milligram; MI, myocardial infarction; min, minute; mL, milliliter; PD, peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy; NH3, ammonia; Qb, blood flow rate; Qcr, dialysis flow rate; RRT, renal replacement therapy; Sep, September; SLED, sustained or slow low-efficiency dialysis; SLEDD, sustained or slow low-efficiency daily dialysis; US, United States; USD, United States dollar; vs, versus; VTE, venous thromboembolism


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