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MEETING REPORT

Renal Support for Acute Kidney Injury in the Developing World

Rajeev A. Annigeri[1], Marlies Ostermann[2], Ashita Tolwani[3], Armando Vazquez-Rangel[4], Daniela Ponce[5], Arvind Bagga[6], Rajasekara Chakravarthi[7] and Ravindra L. Mehta[8], for the Acute Dialysis Quality Initiative (ADQI) Consensus Group

[1]Department of Nephrology, Apollo Hospitals, Chennai, India; [2]Department of Nephrology & Critical Care, Guy's & St Thomas' Hospital, London, UK; [3]Division of Nephrology, University of Alabama, Birmingham, Alabama, USA; [4]Department of Nephrology, Instituto Nacional de Cardiologia, Mexico City, Mexico; [5]Department of Medicine, Botucatu School of Medicine, Sao Paulo, Brazil; [6]Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India; [7]Reknown Nephrology Associates, Hyderabad, India; and [8]Division of Nephrology and Hypertension, Department of Medicine, University of California-San Diego, San Diego, California, USA

There is wide variation in the management of acute kidney injury (AKI) and the practice of renal replacement therapy (RRT) around the world. Clinicians in developing countries face additional challenges due to limited resources, reduced availability of trained staff and equipment, cultural and socioeconomic aspects, and administrative and governmental barriers. In this article, we report the consensus recommendations from the 18th Acute Dialysis Quality Initiative conference in Hyderabad, India. We provide the minimal requirements for provision of acute RRT in developing countries, including patient selection, choice of RRT modality and monitoring, transition, and termination of acute RRT. We also discuss areas of uncertainty and propose themes for future research. These recommendations can serve as a foundation for clinicians to implement renal support for AKI in low resource settings.

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Acute kidney injury (AKI) has been recognized as a major public health problem.[1,2] The epidemiology, management, and prognosis of AKI vary considerably worldwide. Renal replacement therapy (RRT) is acutely applied to 20% to 25% of critically ill patients with AKI, but major variations in practice have been seen. In 2016, the Acute Disease Quality Initiative (ADQI) published consensus recommendations for the management of continuous renal replacement therapy (CRRT) to develop best clinical practice and standards of care.[3–6] However, clinicians in developing countries face additional challenges due to limited resources, reduced availability of trained staff and equipment, cultural and socioeconomic aspects, and administrative and governmental barriers, all of which affect patient selection, choice of RRT modality, and management of RRT.[7,8] Although some facilities for RRT are available in most metropolitan cities in these regions, children usually receive hemodialysis or peritoneal dialysis in adult units, whereas input from a dedicated pediatric team involved in multidisciplinary care are limited. Guidelines and recommendations for acute RRT need to incorporate these particular aspects of the condition.

Methods

This consensus meeting followed the established ADQI process, as previously described.[9] The broad objective of ADQI is to provide expert-based statements and interpretation of current knowledge for use by clinicians according to professional judgment, as well as identify evidence care gaps to establish research priorities. The 18th ADQI Consensus Conference focused on "Management of AKI in the Developing World," convening a diverse panel for a 2-1/2 day meeting in Hyderabad, India from September 27 to 30, 2016. The consensus-building process was informed by preconference, conference, and postconference activities. Before the conference, the workgroup searched PubMed for English language articles on dialysis support for AKI. This search included the terms "acute

Correspondence: Dr. Rajeev A. Annigeri, Apollo Hospitals, Department of Nephrology, 21, Greams Lane, Off Greams Road, Chennai, Tamil Nadu 600006, India. E-mail: r_annigeri@yahoo.com; drrajeevannigeri@hotmail.com

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kidney injury" and "acute renal failure," combined with "renal replacement therapy," "continuous venovenous hemodialysis," "continuous venovenous haemofiltration," "hemodialysis," "peritoneal dialysis," "sustained low efficiency dialysis," "CRRT," "PIRRT," "SLED" and "extracorporeal therapy."

A preconference series of emails that involved the work group members was used to identify the current state of knowledge and enable the formulation of key questions. At the in-person meeting, the work group developed consensus statements through a series of alternating breakout and plenary sessions. In each breakout session, the work group refined the key questions, identified the supporting evidence, and generated consensus statements. Work group members presented the results for feedback to all ADQI participants during the plenary sessions, and then revised the drafts based on the plenary comments until a final version was accepted. We developed recommendations and consensus of expert opinion with evidence, where possible, to distill the current literature. To address important unanswered questions, we articulated a research agenda.

Following the conference, this summary report was generated, revised, and approved by all members of the work group.

Q1: What Are the Minimal Infrastructure Requirements for RRT?

Consensus Statements

1.1. We recommend the availability of an essential core team of trained personnel, consisting of at least 1 physician and healthcare professional dedicated to managing the dialysis therapy. If intermittent hemodialysis (IHD), prolonged intermittent renal replacement therapy (PIRRT), sustained low efficiency dialysis (SLED), and/or CRRT are used, a technician for machine maintenance should be available.

1.2. We recommend the availability of peritoneal dialysis (PD) catheters and vascular access catheters for PD and hemodialysis (HD) techniques.

1.3. We recommend the availability of appropriate fluid bags and tubing in case of PD, and appropriate filters, circuits, and fluids in case of extracorporeal RRT.

1.4. We recommend that the essential core team and equipment be available at all times.

1.5. We recommend that units managing children who need acute RRT have the appropriate infrastructure, equipment, and trained personnel to provide appropriate standards of care.

Context

Barriers to providing RRT in developing countries or resource-limited regions can be due to regional impediments, RRT-related aspects, and patient-related factors (Table 1). Examples of regional barriers include environmental challenges, logistics, and inadequate administrative or policy support by the government or institution. Delivery of RRT can be hindered by decreased availability of equipment, lack of trained healthcare personnel, absence of a regulatory framework to ensure quality of dialysis, decreased availability of laboratory tests for monitoring of RRT, and financial costs.[8] Inadequate technical support leads to poor equipment maintenance, frequent machine breakdowns, and interruptions or delay in treatment. Patient barriers to RRT include cultural beliefs and socioeconomic aspects that influence the decision to start RRT and the type of modality, including the ability to pay for such services. Important geographic factors are the availability of transportation and the distance patients would have to travel to receive RRT, because RRT is usually only obtainable in larger cities for those who can afford to pay.

For RRT to be safe and effective, a minimal infrastructure has to be in place. This can only be achieved with full local commitment, a viable financial model, and the availability of skilled staff and equipment.

Table 1. Barriers at several levels for receiving renal replacement therapy in developing countries

Population
Sociocultural: Customs, health beliefs, accessibility and beliefs in other health systems
Policy and financial: Lack of legislation to provide health care
Medical and scientific: Lack of scientific data from the developing countries, scepticism to accept the scientific data derived from developed countries
Socioeconomic: Lack of infrastructure, such as continuous provision of electricity, good quality water, and sanitation
Healthcare system
Lack of administrative support at the level of hospital, local, state, and national governments
Lack of physicians trained to provide RRT
Density of physicians and geographic distance from centers providing RRT
Existence of several different health systems, especially indigenous systems
Healthcare provider
Lack of infrastructure to provide RRT
Wide variation in the quality of care and infrastructure to provide RRT
Lack of trained personnel to provide RRT at all times; limited training to manage RRT in children
Lack of technical support to maintain and service the dialysis machines
High cost of RRT
Lack of laboratory facilities and high cost of laboratory tests
Late referral of patients to centres providing RRT
Patients
Fear and anxiety of the patient and family regarding RRT
Health insurance availability, access and coverage
Financial constraints

RRT, renal replacement therapy.

All dialytic devices need to function properly at all times, and trained personnel and equipment should be available on a 24-hour basis.[10]

An essential core of trained personnel has to have the expertise to prescribe, provide, manage and monitor the dialytic therapy. The number of personnel should be sufficient to ensure adequate patient care and safety. If the dialytic therapy involves the use of IHD, PIRRT, or CRRT machines, a qualified technician or engineer for maintenance and regular preventive servicing of the machines should be available. Portable water and engineering systems for the production of pure water need to be in place.[10] The water used to produce the dialysate should be treated to achieve the standards of the Association for the Advancement of Medical Instrumentation.[11]

Essential equipment for the delivery of PD includes catheters with appropriate fluid bags and tubing. Adapting nasogastric tubes for PD should be discouraged. For IHD, PIRRT, and CRRT, vascular access catheters should be available, as well as appropriate dialyzers, circuits, fluids, and emergency electric power supply for life-saving equipment in case of power failure. Written protocols for all procedures, including cleaning and disinfection of surfaces and equipment should be available.

Reusing dialyzers and tubes is common practice in developing countries and usually follows manual reprocessing. A study from Sri Lanka showed that the reuse of hemodialyzers in patients with end-stage renal failure (ESRF) resulted in 40% cost saving of consumables and a reduction in the hourly dialysis expense by one-third.[12] However, concerns have been raised about reduced dialyzer efficiency and an increased mortality risk with reuse of dialyzers.[13] Regions that reuse tubing and dialyzers should have an appropriate protocol for reprocessing, facilities for cleaning, and reliable monitoring systems. Only dialyzers labeled for multiple uses should be used. The chemical quality of water used for dialyzer reprocessing should meet the same Advancement of Medical Instrumentation standards as for dialysate.[11] Agents used for disinfecting dialyzers are sodium hypochlorite, formaldehyde, glutaraldehyde, or peracetic acid. Technicians and other personnel responsible for the reprocessing of dialyzers should receive proper training, including training for infection control.

Most children in developing countries receive HD in adult units, often with limited input from a pediatric multidisciplinary team trained in the relevant medical, nursing, developmental, and psychosocial issues. It is recommended that units managing children who need acute RRT should have the appropriate infrastructure and equipment, as well as trained personnel to ensure standards of care.[14] Physicians taking care of children in developing countries should receive appropriate training and acquire requisite knowledge and skills to meet the specific needs of children on RRT.[14]

Saving Young Lives is an initiative of 3 international societies (i.e., the International Society of Nephrology, International Pediatric Nephrology Association, and International Society for Peritoneal Dialysis) and the Sustainable Kidney Care Foundation. With a focus on education and training, it has successfully developed sustainable programs for treatment of AKI in sub-Saharan Africa and South East Asia.[15]

Research Recommendations

- **To compile a registry for dialysis availability in different regions and countries of the world that can be used to study practice patterns, identify barriers to the use of dialysis, and determine outcomes in low resource regions.**
- **To develop strategies for training of healthcare workers to provide RRT in low resource regions.**
- **To develop more techniques for reliable, affordable, and cost-effective RRT.**

Q2: Who Should Be Considered for RRT?

Consensus Statements

2.1. We recommend RRT should be initiated emergently when life-threatening changes in fluid, electrolytes, and acid-base balance are unresponsive to medical therapy.

2.2. We recommend RRT should be considered when metabolic and fluid demands exceed total kidney capacity.

2.3. We suggest that factors such as patient preference, quality of life, comorbid conditions, severity of acute illness, expected prognosis, urine output, logistics, and social and cultural issues should be considered when deciding whether to start RRT.

2.4. We suggest that in severely ill patients a shared decision-making process with the physician, patient, and family should be undertaken to decide whether to start RRT.

2.5. We suggest that a palliative care program should be available for supportive care.

Context

Multiple factors should be taken into consideration when deciding whether to initiate RRT for AKI (Figure 1). It is well accepted that dialysis should be initiated emergently in patients with life-threatening indications, such as severe hyperkalemia, severe acidosis, pulmonary edema, and uremic complications refractory to medical management.[16] However, beyond these absolute indications, the Kidney Disease Improving Global Outcome (KDIGO) clinical practice

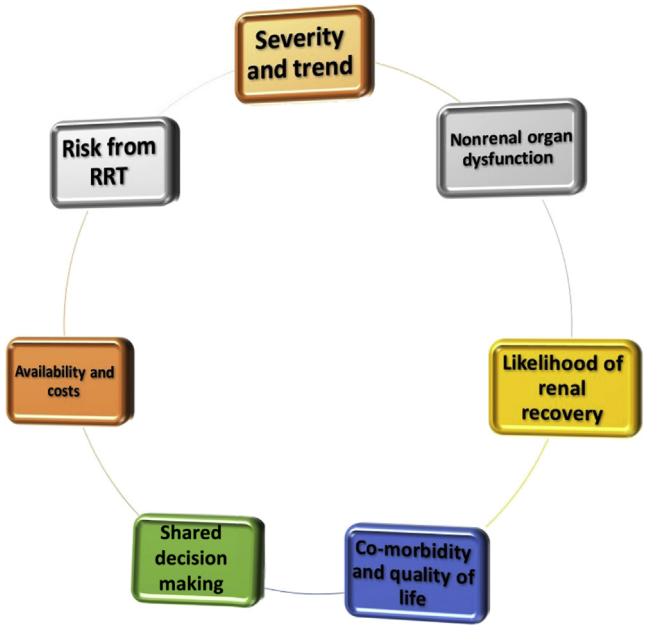

Figure 1. Factors to consider for renal replacement therapy (RRT) initiation in acute kidney injury.

guidelines recommend considering the broader clinical context of the patient.[16] This includes taking into account the severity of the underlying disease, degree of dysfunction of other organs, severity of fluid overload, solute burden and urine output, and the likelihood of recovery of kidney function.[4,16] In the last 2 years, 3 randomized controlled trials (RCTs) compared early initiation of RRT versus late initiation of RRT.[17–19] In 2 studies, 36% and 50% of the patients assigned to late RRT had spontaneous renal recovery without ever receiving RRT,[17,19] which highlights that efforts should be made to identify patients with a high probability of early renal recovery in whom RRT may be avoidable.[20] The decision to start acute RRT should be individualized, and RRT should be considered when the capacity of the kidneys cannot meet the demands being placed on them[4,21] (Figure 2).

Other factors relevant to the decision-making process are patient preference, quality of life, comorbid conditions, expected prognosis, logistics, and social and cultural issues. In developing countries or resource-limited regions, physicians may be faced with the ethical dilemma of the appropriateness of starting RRT in patients with a poor prognosis due to significant acute and chronic comorbid conditions. If the patient is critically ill or has otherwise a poor prognosis, a shared decision process with the patient and family should be undertaken. When it is unclear if a patient will benefit from dialysis, a time-limited trial may be used to determine the benefit of treatment versus the burden of treatment.[22] For those who decide not to start dialysis, it is important to have formal

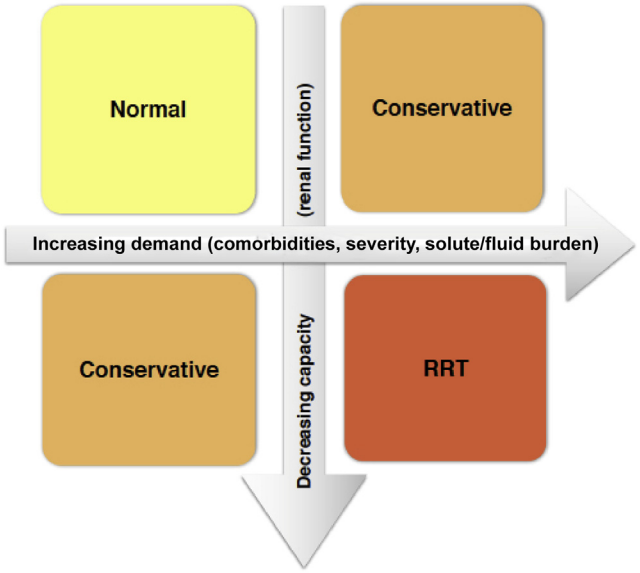

Figure 2. Demand versus capacity paradigm. The upper left quadrant represents the normal condition in which metabolic and fluid demand on the kidneys is low, and the kidneys have full capacity. The upper right quadrant represents the situation in which renal capacity is preserved but demand is high, and the lower left quadrant represents the situation in which renal capacity is decreased but the demand on the kidney is also low; in these 2 situations the kidneys can be managed conservatively without renal replacement therapy (RRT). The right lower quadrant represents the situation in which the demand on the kidneys is high and the capacity and/or function of the kidneys is low. In this situation, RRT should be initiated.

conservative care programs available. Palliative care should be offered to all patients with AKI regardless of whether they start or decline RRT. A formal palliative program should consist of a team of clinicians and trained personnel who provide expert management of pain and other symptoms, emotional and spiritual support, and guidance with difficult treatment choices. The goal of palliation would be to improve quality of life for both the patient and the family, and to help the patient and family understand the treatment options and goals.

Research Recommendations

- **To develop a clinical decision system that helps healthcare workers deciding when and how to implement RRT.**
- **To determine reproducible criteria for the demand to capacity paradigm to inform the decision to start RRT.**

Q3: How Should RRT Be Delivered in AKI Patients?

Q3a: What Are the Goals of RRT?

Consensus Statements.

3a.1. We recommend the short-term goal of RRT for AKI is to support the kidneys' capacity to overcome the metabolic and fluid demands and to

achieve control of azotemia, acid-base and electrolyte derangement, and fluid overload.

3a.2. We recommend the long-term goals of RRT for AKI are to improve survival and promote renal recovery.

Context. The concept of demand capacity balance in AKI was originally described by Macedo and Mehta,[21] and recently recommended in a consensus ADQI meeting.[4] The demand is determined by severity of the acute illness, and the solute and fluid burden. The demand capacity balance is dynamic in nature and varies with the course of critical illness. When renal capacity decreases and fails to cope with the demands, initiation of RRT should be considered (Figure 2).

The aim of acute RRT is to support native kidney function in controlling acid base and electrolyte derangements, as well as fluid overload, and to reduce the effects of AKI on nonrenal organs. Monitoring of serum creatinine, electrolytes, and cumulative fluid balance is necessary to adjust RRT according to the needs of the patient.

The long-term goals are patient survival and renal recovery. The latter is relevant to low-resource settings. To date, there are insufficient data to recommend specific RRT techniques to facilitate renal and patient recovery.[23] There is also a lack of evidence on the optimal timing and mode of discontinuation[4] (see Q4: When Should RRT Be Transitioned or Stopped?)

Recommendations for Future Research

- **To evaluate whether fluid overload at initiation and during RRT affects renal recovery.**
- **To investigate whether the degree of control of azotemia during RRT affects mortality and renal recovery.**
- **To investigate the optimal method of delivering acute RRT in clinical settings relevant to developing countries, including poisoning or obstetric AKI.**
- **To include renal recovery as an outcome in clinical trials and cost utility analyses of RRT, especially if conducted in developing countries.**

Q3b: What Is the Most Appropriate Type of RRT?

Consensus Statements.

3b.1. We suggest that the choice of the initial RRT modality is primarily based on the local availability and experience with a specific treatment and the patient's clinical status.

3b.2. We recommend IHD for life-threatening emergent indications.

3b.3. We recommend IHD and PIRRT when mobilization is the priority, and fluid and metabolic control can be obtained.

3b.4. In patients with acute brain injury or increased intracranial pressure, we recommend the use of CRRT or PD, if available.

3b.5. We recommend the use of CRRT, PD, or PIRRT in situations where fluctuations in fluid balance and solutes are poorly tolerated.

3b.6. For patients with an increased catabolic state, we suggest CRRT, PIRRT, or IHD over PD.

3b.7. All dialysis modalities provide particular benefits and should be used accordingly to optimize care. Transition of modality should be considered when the patient's condition allows, and adequate infrastructure and trained personnel are available.

Context. Current RRT modalities for AKI include IHD, PIRRT (including SLED), CRRT, and PD. Table 2 shows the advantages and disadvantages of the different techniques. There are at least 10 RCTs that compared IHD versus CRRT.[24–31] However, several studies were limited by restricted patient selection, protocol deviations, and the need for crossover treatment. Three systematic reviews and meta-analyses were also published, all of which found no significant differences in mortality or recovery of kidney function between patients treated with intermittent or continuous modalities.[32–34] The most recent meta-analysis by the Cochrane Collaboration, which included 15 RCTs in 1550 critically ill patients with AKI, concluded that there was no significant difference in mortality in hospital and in the intensive care unit (ICU), length of hospitalization, and chances of renal recovery in survivors between patients treated with CRRT and IHD.[34] However, in patients who received CRRT, the mean arterial pressure (MAP) was significantly higher at the end of the treatment, and the number of patients who required escalation of vasopressor therapy was significantly lower.

Table 2. Advantages and disadvantages of dialysis modalities

Factors	IHD	PIRRT	CRRT	PD
Need for vascular access	+++	+++	+++	–
Need for anticoagulation	+	++	+++	–
Need for peritoneal integrity	–	–	–	+++
Impact on diaphragm movement	–	–	–	+
Speed of toxin removal	+++	++	+	+
Risk of cerebral edema	+++	++	+	+
Hemodynamic tolerance	+	++	+++	+++
Solute and balance stability	+	++	+++	+++
Removal of nutrients and drugs	+	++	+++	++
Complexity	+++	+++	++	+
Time for mobilization	+++	++	+	++
Financial costs	++	++	+++	+

+, weakly relevant; ++, moderately relevant; +++, very relevant; –, not relevant; CRRT, continuous renal replacement therapy; IHD, intermittent hemodialysis; PD = peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy.

Based on these data, the KDIGO Clinical Practice Guidelines for AKI in adults recommends considering continuous and intermittent RRT modalities as complementary, except for 2 specific patient groups for whom CRRT is recommended over standard intermittent RRT: patients with intracranial hypertension and/or acute brain injury, and patients with hemodynamic instability.[16]

Hybrid treatments, such as PIRRT and SLED, incorporate the advantages of both CRRT and IHD and are used worldwide in many ICUs.[35–37] They may be considered for hemodynamically unstable patients in situations where other forms of CRRT are not available, but data on comparative efficacy and harm are limited.[38–41] A systematic review and meta-analysis including 17 studies from 2000 to 2014 (7 RCTs and 10 observational studies involving 533 and 675 patients, respectively) focused on the impact of PIRRT and CRRT on mortality and renal recovery.[42] Meta-analysis of the RCTs only showed no difference in mortality between both modalities (relative risk [RR]: 0.90; 95% confidence interval [CI]: 0.74–1.11; $P = 0.3$). However, when using data from observational studies, PIRRT was associated with lower mortality compared with CRRT (RR: 0.86; 95% CI: 0.74–1.00; $P = 0.05$). In RCTs and observational studies, there were no significant differences in recovery of kidney function, fluid removal, days in the ICU, and biochemical efficacy. The meta-analysis concluded that PIRRT was associated with similar outcomes to CRRT.

Some studies suggested that the choice of initial RRT modality might affect renal recovery and risk of dialysis dependence after AKI, which has implications for patients and families, as well as healthcare systems, in terms of survival, quality of life, and financial costs.[42–46] A meta-analysis included 7 RCTs and 16 observational studies and showed that based on pooled analysis of data from observational studies, dialysis dependence was higher among survivors who initially received IHD versus CRRT (RR: 1.99; 95% CI: 1.53–2.59).[46] However, analysis of the RCTs only demonstrated no difference in dialysis dependence among survivors (RR: 1.15; 95% CI: 0.78–1.68).

Experience with PD in AKI is limited, except in the pediatric setting and in regions with limited resources.[47–54] Gravity-driven PD is particularly attractive because it provides RRT without the need for machines and electricity. In most countries, PD is underused despite advantages such as lower costs (as little as US $150 to save 1 life).[51] Technical advances (i.e., flexible and cuffed catheters, automatic cycling, and high and continuous flow PD) have made PD an acceptable alternative to other forms of acute RRT.[48] The International Society for Peritoneal Dialysis (ISPD) firmly recommends that PD is a suitable modality for patients with AKI, especially in developing countries.[55] Recent reports have confirmed a fall in mortality and complication rates in units where acute PD is performed regularly.[47–53]

IHD is the preferred treatment in situations in which immediate removal of small solutes is required, such as severe hyperkalemia, poisoning, and tumor lysis syndrome. IHD and PIRRT have a particular role in situations in which rehabilitation and mobilization are priorities, and fluid and metabolic fluctuations can be tolerated.[4]

Continuous types of RRT are recommended for patients who may not tolerate rapid shifts in fluid balance, including those with severe hemodynamic instability.[4,16] However, PIRRT might also have a role in this situation, in particular because there was no significant difference in mortality, hemodynamic stability, and solute clearance in studies that compared PIRRT with CRRT.[37–41]

Intracranial hypertension and/or acute brain injury are specific situations in which CRRT or PD are preferred over IHD.[16] The KDIGO guideline cited observational studies that reported increases in intracranial pressure with IHD[56] and increases in brain water content after IHD, whereas such changes were not observed after CRRT.[57] Since then, further case reports raised concerns about the potential risk of brain herniation due to rapid changes in osmolytes, falls in cerebral oxygen saturation, and negative effects on cerebrovascular autoregulation with IHD, all of which support the current KDIGO recommendation.[58–61]

Conditions associated with extremely high catabolism should be treated with CRRT, IHD, or PIRRT rather than PD.[47,48,62]

In children, the choice of the initial RRT modality is predominantly based on patient age, underlying illness and clinical status, expertise and experience with the modality, and cost of therapy. Although recent CRRT technology has been developed for neonates and small infants,[63] CRRT is rarely available in developing regions with limited resources. Instead, PD is the first choice in most countries. It is relatively inexpensive and easy to initiate and monitor, especially in infants and in children younger than 3 years old. Stylet-based rigid catheters are still commonly used for the first session of PD, although the use of soft catheters has increased. Older children, especially those with severe metabolic complications or fluid overload, are best managed by IHD.

Recommendations for Clinical Practice

All RRT modalities have particular advantages and offer clinicians options to manage patients and optimize care. Based on the existing evidence, the choice of RRT modality should be based on the clinical status of the

patient (hemodynamic stability, catabolic state, need for removal of large amounts of fluid, presence of life-threatening complications, or acute brain injury), availability of modalities, clinical experience, and financial cost of therapy (Figure 3). For young children (younger than 5 years), PD is often the first choice because of its availability and the ease of initiation. Transition of modality should be considered when the option exists, and adequate infrastructure and trained personnel are available.

Research Recommendations

- **To assess the safety of different RRT modalities in developing countries.**
- **To perform cost-effectiveness studies of acute RRT.**

Q3c: What Is the Most Appropriate Prescription for Acute RRT?

Peritoneal Dialysis: Access.

Consensus Statements.

3c.1. We recommend that flexible PD catheters should be used for acute PD where resources and expertise exist. We suggest that alternatives such as rigid stylet catheters be used if flexible catheters are unavailable.

3c.2. We recommend that healthcare professionals receive training to insert these catheters to ensure timely dialysis in the emergency setting.

3c.3. We recommend the use of prophylactic antibiotics before PD catheter insertion.

Context. It should be recognized that the volumes of fluid used in acute PD are significantly greater than those in the chronic setting. Thus, flow rates need to be high, and the catheters need to tolerate them. Time spent filling and draining is effectively lost dwell time. As such, time for effective clearance can be seriously influenced by the performance of the catheter, especially if cycle time is short. For this reason, flexible PD catheters (e.g., Tenckhoff catheters) have an advantage because they have a larger lumen and side holes compared with rigid catheters.

Nonflexible catheters are still frequently used and can be life-saving. The rigid stylet catheter, which is introduced with the aid of a trocar through a skin incision sub-umbilically, is the most widely used nontunneled catheter. However, it has major drawbacks. First, it is produced from rigid nylon, and injury to the visceral organs may occur during insertion or later. Second, it may become obstructed with fibrin and therefore needs to be flushed regularly. The break in the sterile circuit necessary to perform regular flushes may explain the higher rates of peritonitis.[64]

Knowledge of the key aspects related to PD has improved significantly because of initiatives like the Saving Young Lives Campaign and industry-sponsored training sessions, but the task of teaching and training is enormous. The ISPD guidelines strongly recommend that flexible PD catheters are

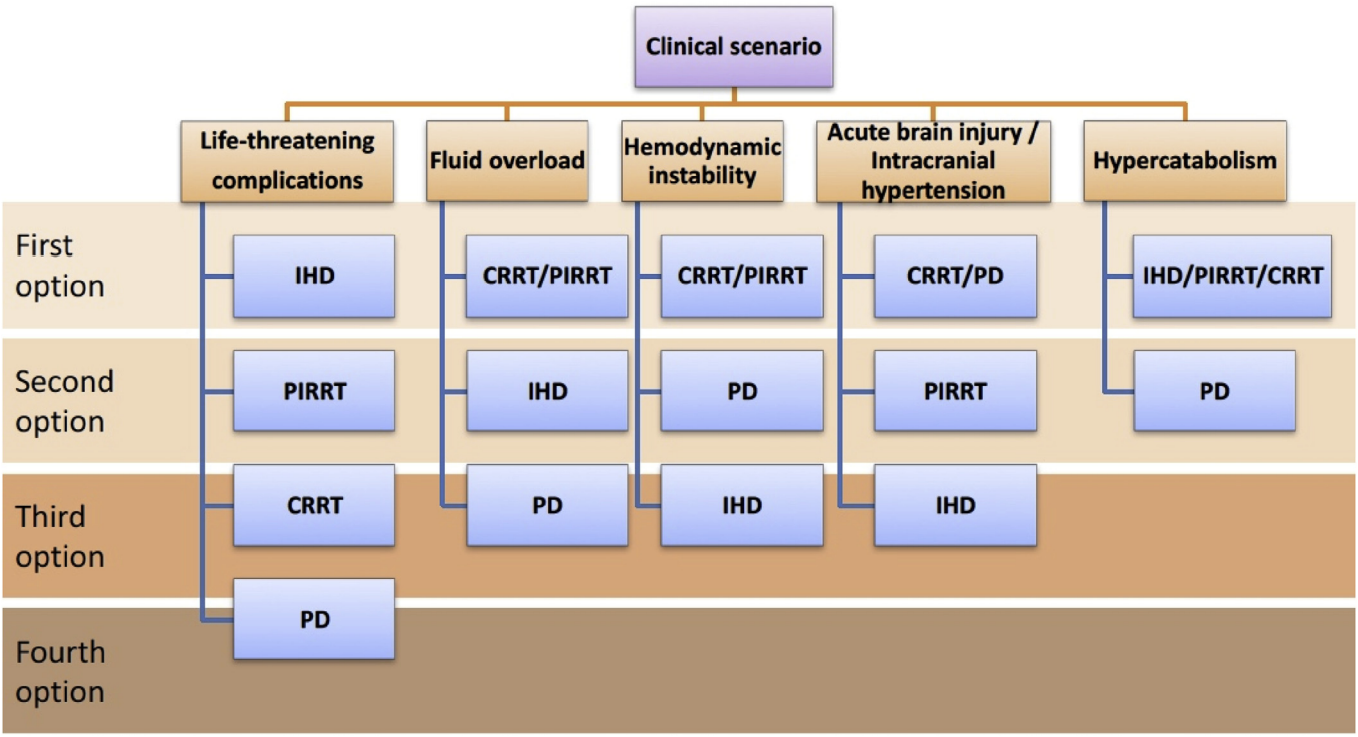

Figure 3. Clinical scenarios for choosing renal replacement therapy techniques. CRRT, continuous renal replacement therapy; IHD, intermittent hemodialysis; PD, peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy.

inserted by nephrologists at the bedside to avoid delays in initiating treatment.[55] In the early stages of PD, there is a risk of leakage of peritoneal fluid. To prevent this, the most important step is to keep the patient at bed rest while the abdomen is full. Tunneled catheters inserted by the Seldinger technique have been shown to have a lower risk of leaking compared with surgically placed catheters.[64] Videos demonstrating different techniques of catheter placement are available.[65,66]

Peritoneal Dialysis: Fluid Delivery.

Consensus Statements.

3c.4. We recommend that, when possible, a closed system be used (Y connection).

3c.5. We suggest that automatic and manual PD should be considered as equivalent.

Context. The technique of fluid delivery in acute PD can increase the risk of peritonitis because there are significantly more connections and disconnections compared with the 3 to 4 exchanges in chronic continuous ambulatory PD. In low-resource environments, makeshift and proprietary circuits are used, with each bag of dialysate being attached using a spike. By gravity, the fluid flows into the peritoneal cavity through a 3-way tap. Drainage into a bag or bucket also occurs through gravity. Although this is an effective and inexpensive system, there is a risk of contamination every time the bag is spiked. In addition, the open drainage system risks retrograde travel of bacteria into the peritoneum. Disconnecting systems with a Y-set and double bag, as used in chronic PD, are associated with lower peritonitis rates.[48,67–70] There is no reason to suspect this would not also apply to acute PD.

Automated cycler PD uses a mechanized device to deliver and drain the dialysate. It can be set up by a trained staff member once per day, which reduces the risk of complications, including contamination. Nursing time is also reduced because all cycles occur automatically. There are conflicting reports related to the incidence of peritonitis with cyclers, but there appears to be no difference compared with the manual system used in chronic PD. Cyclers also offer tidal PD in which a small volume of fluid is left in the abdomen at all times, which may reduce mechanical complications and discomfort. Tidal PD also has the theoretical benefit of increased solute clearance because fluid continuously dwells in the peritoneal space, including during the fill and drain portion of the cycle. Automated cyclers have been used extensively for PD in AKI, but they may prove to be too expensive in low-resource settings.

Peritoneal Dialysis: Solutions.

Consensus Statements.

3c.6. We suggest that patients with shock or liver failure should be treated with bicarbonate-containing solutions. When these solutions are not available, the use of lactate-containing solutions is an alternative.

3c.7. We suggest that commercially prepared solutions should be used. However, when resources do not permit this, custom-prepared fluids may be life-saving.

3c.8. Once serum potassium level falls to <4 mmol/L, potassium should be added to dialysate using a sterile technique.

Context. The ISPD guidelines recommend the use of commercially produced PD solutions.[55] Although dialysate solutions are manufactured in a number of developing countries, their availability continues to be difficult in many regions of the world. Because they are too heavy to be delivered by air, they often need to pass through several countries before they reach their destination. As a result, a number of PD units produce their own solutions using a mixture of modified Ringer's lactate and glucose, both of which are readily available in most hospitals. The potential risks are contamination and infection.

There has been much interest in the composition of dialysate or replacement fluid used for RRT in critically ill patients, in particular because patients with shock or liver failure may not be able to convert lactate to bicarbonate. In RCTs that compare lactate-based replacement fluids versus bicarbonate-based replacement fluids for CRRT, patients randomized to bicarbonate-buffered solutions had more rapid correction of acidosis and less cardiovascular instability.[71] In PD, the evidence is limited to 1 small RCT that also showed that acidosis in patients with shock or liver failure was corrected significantly faster if bicarbonate-containing solutions were used rather than lactate-based fluids.[72] The ISPD guidelines advocate bicarbonate-containing solutions for those with shock or liver failure, but not for other patient groups.[55]

Standard PD solutions do not contain any potassium. As a result, a significant number of chronic PD patients develop hypokalemia (potassium <3.5 mmol/L) or require potassium supplementation, especially because hypokalemia is a risk factor for peritonitis and death in chronic PD patients.[73,74] In acute PD, potassium loss can be particularly high because each 2-L exchange has the potential to remove up to 2 times the serum potassium concentration. Such rapid potassium loss can be prevented or corrected by adding potassium to the dialysis solution (4 mmol/L).[75]

Ponce *et al*. and Gabriel *et al*.[75–78] demonstrated that control of serum potassium was obtained after a 1-day session of high-volume PD. In case serum potassium fell to <4 mmol/L, potassium 3.5 to 5 mmol/L was added to the dialysis solutions.

Strict adherence to an aseptic technique and attention to detail are important when adding fluids or drugs to the dialysis solution.[53] The process should be undertaken in a clean environment using a minimum number of punctures and involve the least number of steps to reduce the risk of infection and error. The fluids should be used immediately.

Peritoneal Dialysis: Prescription.

Consensus Statements.

3c.9. We recommend continuous PD until metabolic and fluid control are achieved.

3c.10. We suggest targeting a minimal weekly Kt/V urea of 2.1 in noncritically ill patients.

3c.11. We suggest targeting a weekly Kt/V urea of 3.5 in critically ill patients.

3c.12. We suggest prescribing 1 to 2 L of dialysate per cycle and 24 to 36 L per session with 1 session lasting 24 hours. For a 70-kg patient, the minimal volume prescribed would be 24 L per session.

3c.13. To correct fluid overload, we suggest raising the concentration of dextrose and/or shortening the cycle duration. When the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance.

3c.14. We suggest measuring effluent concentrations to determine delivered Kt/V urea at least once a week.

Context. PD has been shown to provide comparable outcomes to IHD in appropriately selected patients, but several areas of uncertainty remain. The dose and/or efficacy of PD can be assessed by measuring urea clearance over time as Kt/V urea where: K = volume of dialysate drained multiplied by dialysate/plasma urea concentration; t = duration of dialysis; and V = volume of distribution of urea (total body water ~ 0.5 [female] or 0.6 [male] multiplied by body weight).

The most appropriate dose of PD for patients with AKI is unknown, mainly due to a limited number of trials, the existence of methodological flaws in some studies, and the fact that the doses of dialysis used varied widely. In the most thorough study by Ponce *et al*., acute PD using a cuffed catheter (36–44 L per session, 18 to 22 cycles, 2 L per cycle, weekly delivered Kt/V urea of 3.6) was compared with daily HD.[77] Clinical outcomes were comparable. Other studies have also shown good outcomes with much lower doses (16–24 L per session, 8–16 cycles, 1–2 L per cycle).[77,78] However, because these studies were nonrandomized, the problem of a positive reporting bias needs to be kept in mind. Ponce *et al*. followed up their initial report with a study that compared high volume with lower volume acute PD and showed no clinical benefit with higher volumes; the lower dose group achieved a weekly Kt/V urea of 3.43 and did as well as the higher dose group with a Kt/V of 4.13.[77]

By inference from data from extracorporeal blood therapies, it has been suggested that a targeted PD dose of a weekly Kt/V urea of 2.1 may represent a reasonable goal as the minimum dose, but the optimal dose for an individual patient remains unknown.[62,79–81] It is certainly possible that higher small-solute clearance is necessary for patients with more complex catabolic illnesses.[62] It also remains uncertain whether removal of small molecules (e.g., urea, creatinine) or larger molecules (e.g., cytokines, soluble receptors) is more important. According to the ISPD Guideline PD for AKI, a weekly Kt/V urea target of 3.5 provides outcomes comparable to that of daily HD.[55] Higher doses are not associated with better outcomes. For noncritically ill AKI patients, a weekly Kt/V target of 2.1 may be acceptable, but this suggestion is not evidence-based.[81]

Much attention has focused on solute clearances, but there is increasing evidence that fluid overload is also harmful and should be avoided or corrected. In principle, regular assessment of volume status and the prescription of clear ultrafiltration and fluid balance targets are necessary for all patients receiving RRT, including PD. Relatively large amounts of fluid can be removed by PD (i.e., up to 1 L in 4 hours when using a 4.25% PD solution). Although this may cause hyperglycemia, the risks of hypertonic solutions are negligible in the short term.

For children treated with PD, not enough information is available regarding dosing. However, it has been suggested that the Kt/V target should exceed that of the adult standards because daily protein intake per kilogram is higher in children.[82] Exchange volumes of 20 to 30 ml/kg have been traditionally applied. In infants, the peritoneal surface area per unit body weight is twice that of adults, whereas the relationship between body surface area and peritoneal membrane surface area is constant and age-independent. Therefore, an exchange volume of 1,100 ml/m^2 of body surface area (equivalent to 2000 ml/1.73 m^2) might be a better suggestion.[83] If possible, intra-abdominal pressure should be measured to detect the fill volume limit, which has been reported up to 1400 ml/m^2, leading to an intra-abdominal pressure of 18 cm H_2O.[84]

Recommendations for Clinical Practice

- **During the initial 24 hours of acute PD, the duration of the cycle time needs to be determined based on the clinical circumstances. Short cycle times (every 1–2 hours) may be necessary in the first 24 to 48 hours to correct hyperkalemia, fluid overload, and/or metabolic acidosis. Thereafter, the cycle time may be increased to 4 to 6 hours depending on the clinical circumstances.**
- **To treat or avoid fluid overload, ultrafiltration can be increased by raising the concentration of dextrose and/or shortening the cycle duration. When the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance.**

Research Recommendations

- **To focus on comparing higher intensity PD versus lower intensity PD in lower demand/capacity settings.**
- **To perform risk−benefit analyses of more frequent versus less frequent monitoring.**
- **To identify clinical parameters to guide ultrafiltration.**
- **To identify the most appropriate fluid delivery method and solutions for acute PD.**

Extracorporeal Renal Replacement Therapies.

Consensus Statements.

3c.15. We recommend ultrasound guidance for vascular catheter placement. If not available, blinded puncture is acceptable.

3c.16. We recommend using either the right jugular or right femoral site as the first option for vascular access in non-obese patients.

3c.17. We suggest using bicarbonate-based solutions.

3c.18. We recommend implementing water quality measurements and providing adequate equipment, including either commercially available fluids or reverse osmosis.

3c.19. For IHD or PIRRT, we suggest a minimum urea reduction ratio of 60% or Kt/V urea of 1.2 per treatment.

3c.20. For CRRT, we recommend using citrate for anticoagulation. If not available, CRRT can be delivered without anticoagulation in patients at high risk of bleeding or heparin for low-risk patients.

3c.21. For CRRT, we suggest delivering a minimum effluent volume of 20 to 25 ml/kg per hour; however, the dose should be dynamic and adapted to the metabolic demands placed on the patient.

Context. Good vascular access is essential for adequate delivery of extracorporeal RRT. Ultrasound guidance for catheter placement has reduced the risk of catheter placement failure (RR: 0.12; 95% CI: 0.04–0.37; $P < 0.001$) and arterial puncture (RR: 0.22; 95% CI: 0.06–0.81; $P = 0.02$), as well as the number of attempts.[85] However, even in nonlimited resource settings, ultrasound machines may not always be available.

An evaluation of sites for acute temporal catheter placement showed that circuit life was comparable between jugular and femoral access (17.1 hours vs. 20.2 hours, respectively).[86] A RCT that included 750 patients showed a higher incidence of hematomas with jugular access (3.6% vs. 1.1%; $P = 0.03$).[87] There was no difference in catheter-related bloodstream infection (2.3 per 1000 catheter-days vs. 1.5 per 1000 catheter-days; $P = 0.42$), but there was a trend to higher colonization in patients with a body mass index >28.4 kg/m^2 who were randomized to femoral access. Choosing the right length of catheter is also important because it influences blood flow, recirculation, filter survival, and ultimately, the dose of RRT.[88,89] Tunneled catheters are associated with a reduced infection risk, but they require special training. Switching to tunneled catheters should be considered when prolonged RRT is anticipated.

For catheter care, 2 meta-analyses suggested that low-dose citrate lock solutions might help to reduce the risk of catheter malfunction and catheter-related bacteremia.[90] Due to the potential of systemic exposure, neither antibiotic nor high-dose heparin (5000 U) are recommended as locking solutions.[91–93] Chlorhexidine-impregnated dressing seems to reduce catheter-related bacteremia, but if not available, standard polyurethane dressing is recommended over using the gauze and tape approach, no dressing, or any highly adhesive strategies.[94,95]

In 2015, a Cochrane systematic review assessed the composition of dialysate and replacement solutions and compared bicarbonate-buffered solutions versus lactate-buffered solutions for CRRT.[96] Analysis of 4 clinical trials that included 171 patients revealed no significant differences in mortality and acid-base or electrolyte parameters, except for higher serum lactate levels in the lactate group. Only 1 study reported fewer cardiovascular events and fewer hypotensive events in the bicarbonate group,[71] whereas a different study found a higher mean arterial pressure using bicarbonate.[97] Therefore, we consider bicarbonate-based fluids to be the first option; if not available, lactate solutions are acceptable for extracorporeal RRT, as long it is recognized that they may cause a rise in serum lactate in patients with liver failure.

Anticoagulation is a potential limitation of extracorporeal RRT. Regional anticoagulation with citrate has emerged as an effective method to maintain circuit patency.[16] A recent meta-analysis that included 14 RCTs and 1134 patients showed significantly longer

circuit life with citrate, with a mean difference of 15.69 hours (range: 9.3–22.08 hours) and a significantly lower bleeding risk (RR: 0.31; 95% CI: 0.19–0.51) compared with heparin.[98] A systematic review of observational studies in children found a circuit survival of almost 70% at 60 hours and a decreased risk of bleeding with citrate.[99] However, metabolic alkalosis was common, affecting 20% to 100% of patients. Citrate accumulation was reported in only 1 study and reported in 20% of children.[99] If citrate is not available, extracorporeal RRT without anticoagulation is feasible in patients at high risk of bleeding, especially when using IHD. For PIRRT, filter loss due to clotting has been reported in approximately 25% of sessions beyond 6 hours.[100] Other methods of keeping the circuit patent include using predilution fluid and keeping a filtration fraction of <20%.[101,102] Finally, based on a meta-analysis, filter life may be better with hemodiafiltration compared with hemofiltration.[103]

Increasing the dose of extracorporeal RRT in AKI patients has not been associated with improved survival.[104,105] A study that compared daily versus alternate day intermittent RRT showed a reduction in mortality with daily treatment together with better control of uremia, fewer hypotensive episodes, and more rapid resolution of AKI.[106] Although these results have not been replicated, it seems reasonable that more frequent intermittent support would allow better control of fluid balance, regardless of small-solute clearance. With regards to CRRT, high volume hemofiltration (>50 ml/kg per hour) has not been associated with a survival benefit but with a higher risk of inadvertent nutrient and antibiotic loss.[104,107] No study has demonstrated a substantial benefit with CRRT doses in the range of 20 to 50 ml/kg per hour, but not enough information is available to recommend a dose <20 ml/kg per hour.[108] Although Jiang *et al*. randomized patients with pancreatitis to 1000 ml/h (approximately equivalent to 14 ml/kg per hour) and reported a higher mortality in the lower dose group,[109] a retrospective analysis by Uchino *et al*. found no difference in mortality between patients who received 14.3 ml/kg per hour versus 20 to 25 ml/kg per hour.[110] Based on the existing data and in support of the KDIGO recommendations,[16] the ADQI consensus recommendation suggests a target dose between 20 and 25 ml/kg per hour, recognizing that the dose may need to be increased or reduced to meet changes in demand or capacity.[3] Importantly, reuse of filters confers a risk of reduced dose delivery, but variations exist due to different reuse techniques.[111,112]

No evidence-based recommendations can be made for children receiving CRRT. Doses between 2000 and 3000 ml/h per 1.73 m^2 have been used.[113,114]

Research Recommendations

- **To design a RCT comparing a low dose versus a standard dose of extracorporeal RRT in low-income countries.**
- **To evaluate different ways of dosing beyond classical small-solute clearance.**
- **To conduct an RCT to evaluate citrate dosing for specific populations (pediatrics, patients with liver failure, and patients with hypoperfusion).**
- **To test surrogate outcomes for different prescriptions based on filtration fraction.**
- **To compare different dose regimens for extracorporeal RRT in children.**

Q3d. How Should RRT Be Monitored?

Consensus Statements.

3d.1. We recommend that standardized protocols for prescribing and delivering RRT are developed, adopted, and continuously reviewed.

3d.2. We recommend the standardized documentation of RRT treatments received by the patient.

3d.3. We suggest that patient-related parameters such as hemodynamics, volume status, temperature, and nutrition be monitored during RRT.

3d.4. We suggest monitoring of delivered dose of RRT at least once a week.

3d.5. We suggest reassessing the delivered RRT dose when significant changes in prescription or in the clinical status of patients occur.

Context. Recent reports indicate that the care received by patients with AKI and RRT for AKI is suboptimal even in developed countries, which may be due to variations in the practices of RRT worldwide and a general lack of consensus.[33,115,116] Standardized protocols of RRT help to improve the delivery, quality, and safety of RRT. Centers that provide RRT for AKI patients should develop protocols for the initiation, monitoring, and termination of RRT according to their local needs based on the patient case mix, economics, and resource availability. In developing countries, protocols for RRT should also take into consideration the availability of resources and equipment, as well as financial costs. Protocols should be reviewed periodically to identify any deficiencies and improve clinical care. Clear roles and lines of responsibility should be set. The documentation should be standardized and include patient specific information and data related to the machine, extracorporeal circuit, fluids used, anticoagulation, and complications and interventions performed during dialysis.

Hypotension is a common complication of RRT and may contribute to morbidity and delay in recovery from AKI. Akhoundi *et al*. reported that 43% of

patients on CRRT developed hypotension within 1 hour of initiation.[117] The Acute Renal Failure Trial Network (ATN) study compared high intensive RRT versus less intensive RRT in critically ill patients with AKI and reported significantly more hypotension in the high intensity group (14.4% vs. 10%; $P = 0.02$).[104] Gaudry *et al*. compared early and late initiation of RRT and reported serious cardiac arrhythmias in 3.2% and moderately serious arrhythmias in 15.7% of patients.[17]

Fluid overload is common in critically ill patients, especially in those with AKI who receive RRT. The importance of monitoring fluid balance has been recognized, especially because fluid overload of >10% of body weight and prolonged duration of fluid accumulation has been found to be associated with an increased risk of complications and mortality.[118–121] A recent multicenter study also showed that the speed of fluid accumulation was independently associated with ICU mortality.[121] Rate of fluid removal during RRT depends on the degree of fluid overload and hemodynamic stability. Several methods have been proposed to guide fluid removal, including chest radiography, measurement of natriuretic peptides, bioimpedance analysis, thoracic ultrasound, and ultrasonic measurement of the vena cava. Other factors should also be monitored during RRT, including body temperature and nutritional values.

The dose of RRT delivered to the patient needs to be monitored, especially because it is often 15% to 30% lower than the prescription.[122–124] Hence, it is recommended to prescribe a dose that is 25% higher than the required dose of 20 ml/kg per minute.[16] The discrepancy between prescribed and delivered solute clearance is due to 2 main reasons: (i) down time effect, in which CRRT is provided for <24 h/d; and (ii) progressive reduction in efficiency of the filter over time due to clogging of the hollow fibers. The down time effect is common and usually due to circuit clotting, poor vascular access, and patient-related factors, such as need for investigations and procedures.[125] Monitoring of the down time effect and periodic measurement of solute clearance should be part of routine monitoring in CRRT.

We recommend that the delivered dose of RRT should be measured at least once a week and every time after significant changes in prescriptions or in the clinical status of patients have occurred, to ensure that the changing demands are met by the therapy. Several methods have been proposed to measure solute clearance during CRRT. Claure-de Granado *et al*. determined solute clearance from the blood-side and dialysate-side kinetics.[126] They recommended using dialysate-side measurements in CRRT (in milliliters per minute) and blood-side kinetics for clearance measurement in IHD and hybrid therapies in Kt/V urea or equivalent renal urea clearance. Clearance of middle molecules is not generally measured.

Consensus Statement.

3d.6. We suggest that the frequency of blood tests should be based on the clinical state of the patient.

Context. Electrolyte and acid-base abnormalities are common in patients with AKI. IHD allows more rapid correction of life-threatening abnormalities, whereas CRRT takes longer.[127] Hypophosphatemia and hypokalaemia are commonly observed on CRRT. The renal replacement therapy study RENAL reported a 59.5% incidence of hypophosphatemia in patients who underwent CRRT.[105] Hypocalemia was observed in 22% to 63% of patients on CRRT, commonly in the context of citrate-based anticoagulation.[117] The frequency of laboratory tests depends mainly on the condition of the patient, but other factors (e.g., availability and cost) play an important role. More serious derangements require more frequent monitoring.

Monitoring of anticoagulation is important during RRT. However, the relationship between heparin dose, activated prothrombin time (APTT), filter survival, and bleeding complications is not straightforward.[128] Hence, monitoring of APTT during heparin anticoagulation during RRT should be individualized. Routine monitoring of APTT is not essential during IHD and PIRRT when heparin anticoagulation is used, but measurement of APTT should be considered in case of premature filter clotting or bleeding complications. When using heparin anticoagulation for CRRT, APTT may be measured at 6- to 8-hour intervals during the first 24 hours and subsequently at least twice daily. Monitoring of citrate anticoagulation in CRRT is more complex and requires more frequent monitoring of serum electrolytes, ionized calcium and serum calcium, and arterial blood gases.[129] We suggest that ionized calcium be measured at 6- to 8-hour intervals, and the total calcium to ionized calcium ratio and ABG be measured at least once a day to monitor efficacy and safety of citrate-based therapy.

Consensus Statement.

3d.7. For patients who receive RRT, we suggest monitoring of drug levels when possible and to adjust drug doses accordingly.

Context. Appropriate delivery of drugs, especially antibiotics, is crucial. There is a large gap in our understanding of the pharmacokinetics and pharmacodynamics of many drugs in patients with AKI and multiorgan failure. As a result, data to guide drug dosing in patients who receive RRT are limited, and patients are at risk of both drug underdosing and overdosing.[130] The removal of drugs during RRT depends on several factors,

such as blood concentration, sieving coefficient, degree of protein binding, dialysis dose, and duration. Therapeutic drug monitoring by prospective measurement of serum drug concentrations should be used whenever possible, but the necessary laboratory assays are rarely available and generally expensive.

Guidance for drug dosing during RRT is available (e.g., *British National Formulary*, *Martindale: The Complete Drug Reference*, and *American Hospital Drug Information*). However, they vary in the source of information and recommendations.[131] Table 3 lists the recommended doses of common drugs during RRT, as compiled from several sources.[132–134]

Consensus Statement.

3d.8. We suggest implementing an infection control plan.

Context. Dialysis catheter-related infections can contribute significantly to morbidity and cost of hospitalization. Hoste *et al*. reported an 8.8% incidence of bloodstream infection in patients who received acute RRT compared with 3.5% observed in non-AKI patients in the same unit.[135] Sixteen percent of bloodstream infections in the dialysis population were related to the dialysis catheter. The risk is higher with femoral vein catheters.[87] To reduce the risk, infection control protocols, education of staff with periodic reinforcement, periodic review of infection rates, and regular feedback are advised.[136] Dialysis catheters should be removed as soon as dialysis is no longer necessary or when infections are suspected or proven.[137]

The role of antimicrobial catheter lock solutions is controversial. A recent meta-analysis that included 23 studies concluded that their use reduced the risk of catheter-related bloodstream (CRBS) infections by 69%.[138] However, several guidelines do not recommend routine use of antimicrobial catheter lock solutions because of the potential risk of fungal infections, antimicrobial resistance, and systemic toxicity.[16,139,140] We suggest considering the use of antimicrobial catheter lock solutions in specific patient groups, that is, in ICU patients with an increased risk of CRBS infections, patients in whom CRBS infections are likely to have devastating consequences, and in those with a previous CRBS infection. The choice of antimicrobial lock depends on the local prevalence of bacterial isolates in the hospital. Citrate-based catheter lock solutions are effective in preventing CRBS infections, but may increase the risk of thrombotic complications.[141]

The risk of acute peritonitis related to acute PD is relatively high in developing countries. Ponce *et al*. reported peritonitis in patients who underwent high volume PD for AKI; 18 of 204 patients (12%) had peritonitis, of whom 8 (61%) underwent catheter removal.[47] There is a risk of hospital-acquired bacterial peritonitis

Table 3. Recommendations for dose adjustment of common drugs during renal replacement therapy

Antimicrobial drug	Normal dose	IHD or PIRRT	CRRT	PD
Acyclovir (IV)	5–10 mg/kg q8h	5–10 mg/kg q48h, dose after dialysis	5–7.5 mg q24h	2.5–5 mg/kg q24h
Amikacin (IV)[a]	7.5 mg/kg q12h	7.5 mg/kg q48–72h, additional dose of 3.5 mg/kg after each HD	7.5 mg/kg q24–48h	15–20 mg/L/d
Amphotericin (IV)	0.5–1.5 mg/kg/d	Normal dose	Normal dose	Normal dose
Amoxicillin (IV)	1–2 g q6h	1–2 g q12h, dose after dialysis	1–2 g q8h	250 mg q12h
Cefazolin (IV)	1–2 g q8h	1–2 g q12–24h, 0.5–1 gm after dialysis	1–2 g q12h	0.5 gm q12h
Ceftazidime (IV)	1–2 g q8h	1 g q24h, and 1 g post-HD	1–2 g q12h	0.5 gm q12h
Cetrioxone (IV)	1–2 g q24h	Normal dose, post-HD	0.75 g q12h	Normal dose
Cefotoxime (IV)	1–2 g q6–8h	1–2 g q12–24h, and 1 g post-HD	1 g q24h	1 g q12h
Cefoperazone (IV)	1–2 g q12h	Normal dose and 1 g post-HD	Normal dose	Normal dose
Colistin (IV)	2.5 mg/kg q12h	1.5 mg/kg q36h	2.5 mg/kg q48h	1.5 mg/kg q36h
Ciprofloxacin (IV)	200–400 mg q12h	200 mg q24h	200 mg q12h	200 mg q24h
Fluconozole (IV)	200–800 mg q24h	100–400 mg q24h, 200 mg after dialysis	200–800 mg q24h	100–400 mg q24h
Gancyclovir (IV)	5 mg/kg q12h	2.5 mg/kg q24h, dose after dialysis	2.5 mg/kg q24h	2.5 mg/kg q24h
Gentamicin (IV)[a]	1.7 mg/kg q8h	1.7 mg/kg q24h, half the dose post-HD	1–2.5 mg/kg q24–48h	3–4 mg/L/d
Imipenem/cilastatin (IV)	250–500 mg q6h	250 mg q12h, dose after dialysis	250–500 mg q8–12h	250 mg q12h
Levofloxacin (IV)	500–750 mg q24h	500 mg q48h	250–750 mg q24h	250 mg q24h
Meropenem (IV)	1 g q8h	0.5–1 g q24h, dose after dialysis	0.5–1 g q12h	0.5–1 g q24h
Penicillin G (IV)	1–2 million U q4h	1–2 million U q8h, dose post-HD	1–2 million U q6h	1–2 million U q8h
Piperacillin/tazobactam (IV)	3.375 g q6h	3.375 g q12h, dose post-HD	3.375 g q8h	3.375 g q12h
Valacyclovir (PO)	1 g q8h	0.5 g q24h, dose post-HD	1 g q12–24h	0.5 g q24h
Voriconozole (IV)	200 mg q12h	Normal dose	Normal dose	Normal dose
Vancomycin (IV)[a]	1 g q12h	1 g q48–72h	1 g q48–72h	1 g q48h

CRRT, continuous renal replacement therapy; HD, hemodialysis; IHD, intermittent hemodialysis; PD, peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy; PO, oral; q, every.
[a]Monitoring of serum drug levels and dose adjustment accordingly is recommended.

in children if the stylet catheter is used beyond 36 to 48 hours, which may limit the duration of PD.

Patients initiated on RRT should be screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). We suggest that dialyzers not be reused if patients are seropositive for HBV, HCV, or HIV. Standard disinfection procedures for the dialysis machines should be carried out after each therapy, irrespective of the infectious status of the patient. It may not be practical to use dedicated machines for patients who are seropositive for HBV, HCV, or HIV, but in units where segregation of machines for seropositive long-term dialysis patients is practiced, the same policy should apply to patients with AKI.

Research Recommendations

- **To study the impact of frequent laboratory tests versus infrequent laboratory tests on the rate of complications and therapeutic goals in a randomized fashion.**
- **To compare online monitoring of solute clearance by analyzing ionic changes and actual measurement of small-solute clearance.**
- **To develop models to predict the risk of circuit clotting based on pressure changes within the extracorporeal circuit.**
- **To study the impact of ultrafiltration rates based on hemodynamic parameters, such as mean arterial pressure, and other technologies, such as bioimpedance on renal recovery, hospital stay, time on mechanical ventilation, and hospital mortality.**
- **To study quality control initiatives to reduce the risk of bacterial infections during PD and IHD.**

Q4: When Should RRT Be Transitioned or Stopped?

Consensus Statements

4.1. We recommend the transition of RRT should depend on patient-related factors, such as physiological status, degree of discrepancy between demand and capacity, chances of renal recovery, and technical considerations (e.g., equipment availability and cost).

4.2. When the demand-to-capacity ratio increases and the hemodynamic condition of the patient worsens, escalation of RRT should be considered.

4.3. When the demand-to-capacity ratio improves, de-escalation of RRT to a therapy that places less strain on resources and cost should be considered.

Context

The transition from one initial RRT modality to another modality later in the course of AKI is common in clinical practice. The main reasons for switching are changes in the clinical condition of the patient or adverse events. In an RCT that compared CRRT and IHD, 20% of patients switched from initial CRRT to IHD, and 18% transitioned from initial IHD to CRRT.[30] Higher rates were reported in a different RCT, in which 20% of the patients assigned to IHD group switched to CRRT, and 46% of the patients who were randomized to CRRT later changed to IHD.[31] The transition from IHD to CRRT occurred earlier (mean time: 4.4 ±12 days) compared with the switch from CRRT to IHD (mean time: 6.2 ± 5.6 days). In the recent early versus late initiation of RRT in critically ill patients with AKI (ELAIN) study, 26% of patients switched from CRRT to SLED, 2% transitioned from CRRT to IHD, and 6% changed from CRRT to IHD and SLED.[18]

Transition from hybrid therapy to CRRT has also been reported. Fieghen *et al*. analyzed the data of 158 critically ill patients whose initial RRT modality was CRRT, and 74 patients who were initiated on SLED.[38] Within 3 days of RRT initiation, 15% of patients who were initially started on SLED were changed to CRRT and 15% switched from IHD to SLED. Using data from 146 critically ill patients on RRT, Khanal *et al*. reported that 81% received PIRRT as the initial mode of RRT, of whom 21.2% also had exposure to CRRT.[142] Annigeri *et al*. reported transition from PIRRT to CRRT within 24 hours of RRT initiation due to hemodynamic intolerance in 5% of patients.[143] Ponce *et al*. had the largest experience using acute PD and recently reported that 51 of 301 patients (16.9%) were transferred from initial acute PD to IHD.[48]

Based on the existing data, we propose a schema to guide the appropriate transition of RRT (Table 4 and Figure 4). If the demand-to-capacity balance worsens or side effects related to a particular RRT modality occur, it is reasonable to consider escalation of RRT. Similarly, if the demand-to-capacity ratio improves, it is prudent to consider de-escalating to a RRT modality that places less strain on cost and resources.

Consensus Statement

4.4. RRT should be discontinued if kidney function has recovered sufficiently to reduce the demand-to-capacity imbalance (current and expected) to acceptable levels or the overall goals of treatment have changed.

Context

Discontinuation of RRT may be considered when there is sufficient improvement in renal function to meet the metabolic and fluid demands, or there is an improvement in the demand-to-capacity balance that favors weaning patients from RRT. When only fluid demand exists, it is reasonable to consider a trial of diuretics at a higher dose, in view of the reduced GFR.[144]

Table 4. Factors that influence the transition of modality of renal replacement therapy in acute kidney injury

Patient-related factors:
1. Change in the physiologic status of the patient
2. Change in the metabolic demand and capacity ratio (azotemia, acidosis, and electrolyte and divalent ion balance and fluid balance)
3. To facilitate mobility of patient
4. To facilitate better renal recovery
Factors related to technology, technical capacity, and availability:
1. Availability of technology
2. Availability for human resources and expertise to provide therapy
3. Backup technical support
4. Technical failure and complications related to technology
Factors related to cost and resource constraints:
1. Cost of therapy
2. Resource allocation issues

Common triggers that prompt a trial of RRT discontinuation are a decline in serum creatinine while on a constant dose of RRT and a progressive increase in urine output.[145,146] In a large multicenter observational study, Uchino *et al*. showed that a spontaneous urine output of >400 ml/d was associated with a 80.9% chance of successful transition off RRT.[145] In patients who received diuretics, a urine output >2330 ml/d had a positive predictive value of 87.9% for transition off RRT. In a recent analysis of 67 patients, Aniort *et al*. concluded that daily urine urea excretion was superior to urine output in predicting successful weaning from IHD.[147]

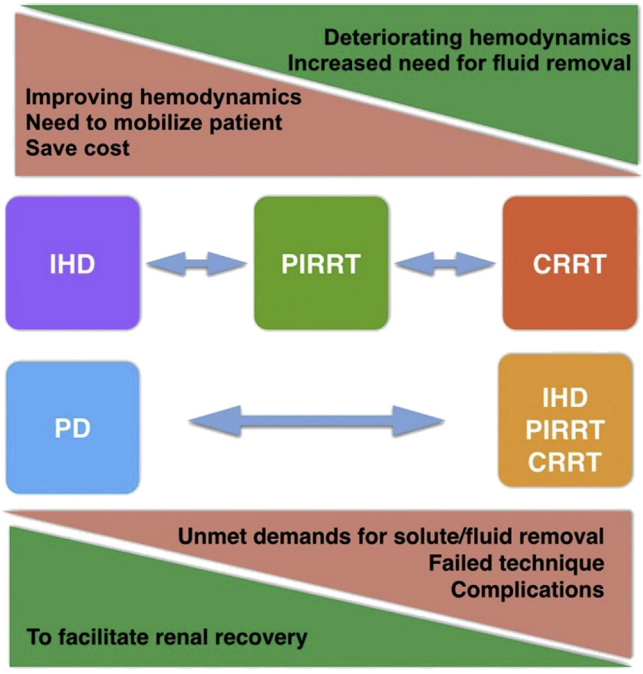

Figure 4. Schematic representation of proposed guide for consideration of transition of renal replacement therapy modality in acute kidney injury. CRRT, continuous renal replacement therapy; IHD, intermittent hemodialysis; PD, peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy.

Consensus Statement

4.5. We suggest considering discontinuation of RRT after a time trial of 48 hours in cases of deteriorating or non-improving clinical status.

Context

As stated previously (see section Q2), if a time trial of RRT was implemented following a shared decision process, lack of clinical improvement and worsening multiple organ failure after 48 hours could prompt the decision to discontinue RRT. Ferreira *et al*. showed that a rise in the sequential organ failure assessment score by 30% was associated with a mortality risk of >50%.[148] When the goal of therapy is palliation, it is also rational to discontinue RRT.

Research Recommendations

- **To prospectively study the common reasons for transition of RRT modality to determine clinical practice patterns across the world.**
- **To evaluate a strategy of using CRRT as the initial modality followed by a rapid switch to hybrid therapy after 36 to 72 hours. This has the advantage of offering the most tolerated modality when the demand is maximum and switching to a less expensive modality as soon as the clinical situation allows.**
- **To evaluate a strategy of using PD as the primary RRT with supplementary hybrid therapy as directed by the demand-to-capacity balance instead of switching from PD to IHD. Such a strategy may save costs and improve the chances of renal recovery.**

Summary

Providing RRT for patients with AKI in developing countries is challenging due to limited resources, cost constraints, and sociocultural aspects. Our consensus recommendations provide minimum requirements for use of RRT in resource-limited countries. Future research should focus on the innovations in RRT to provide optimum care and maximum outcomes in these settings.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

RA, AT, AVR, DP, RC, and RM all participated in the consensus-building process and drafting of this paper. MO, RM, RC, and AB provided a critical review of this paper.

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