RENAL REPLACEMENT THERAPY
FOR ACUTE POST OPERATIVE
RENAL FAILURE

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ACUTE KIDNEY INJURY

Acute kidney injury is the preferred nomenclature to replace acute renal failure. The spectrum of AKI is broad and includes different degrees of severity. The Acute Dialysis Quality Initiative group put forward the most recent proposal for a consensus definition for AKI. They suggested criteria for three grades of increasing severity (Risk of acute renal injury, injury to the kidney, failure of kidney function) and two outcome classes (Loss of kidney function and end stage kidney disease).

RIFLE criteria for the definition of acute kidney injury.

<table>
<thead>
<tr>
<th>RIFLE Category</th>
<th>GFR criteria</th>
<th>Urine Output Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>Decrease of GFR &gt;25%</td>
<td>Urine output &lt; 0.5 mL per kg per hr for 6 hrs</td>
</tr>
<tr>
<td>Injury</td>
<td>Decrease of GFR &gt;50%</td>
<td>Urine output &lt; 0.5 mL per kg per hr for 12 hrs</td>
</tr>
<tr>
<td>Failure</td>
<td>Decrease of GFR &gt;75% or Serum creatinine ≥4mg/dL</td>
<td>Urine output &lt;0.5 mL per kg per hr for 24 hrs or anuria for 12 hrs</td>
</tr>
<tr>
<td>Loss</td>
<td>Complete loss of renal function for &gt; 4 wks</td>
<td></td>
</tr>
<tr>
<td>End-stage kidney Disease</td>
<td>Need for RRT for &gt; 2 mos</td>
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</tbody>
</table>

UNDERLYING MECHANISMS OF ACUTE RENAL FAILURE

The final common pathway of all the renal insults is tubular cell death, by either apoptosis or necrosis. Pro-inflammatory mediators and renal tubular hypoxia are important processes in the development of peri-operative renal failure.

Hypoxia/hypotension

The kidney is said to live on the edge of hypoxia; with the inner medulla having a pO2 of only 2 kPa (15 mmHg). For this reason the kidney is especially vulnerable to the process of renal tubular hypoxia. The tone of renal blood vessels is controlled, by the balance between the vasoconstrictive action of endothelin-1 (ET-1) and the vasodilator action of nitric oxide (NO) produced by endothelial nitric oxide synthase (e-NOS). Hypoxia increases ET-1 expression and reduces e-NOS expression thus compounding ischaemic renal injury. In addition to this net vasoconstrictive effect, hypoxia increases levels of pro-inflammatory mediators within the kidney.

In addition to their direct effects, pro-inflammatory mediators also contribute to microcirculatory failure by further altering ET-1/ e-NOS balance such that vasoconstriction may be maintained for several hours after normoxia is restored. Renovascular autoregulation maintains near constant renal blood flow across a broad range of mean arterial pressures (MAP). In addition, if MAP falls below the lower limit of autoregulation, glomerular filtration rate (GFR) will fall in proportion to the fall in renal blood flow, resulting in less glomerular filtrate to be reabsorbed
by the tubules. This reduces the work of filtrate re-absorption and thus reduces tubular oxygen demand at a time when oxygen delivery is compromised.

Inflammatory mediators/cytokine balance
There is evidence that both locally produced and systemically detectable pro-inflammatory mediators contribute to renal failure. Tumour necrosis factor α (TNF-α) has been shown to cause direct damage to proximal tubular cells. Systemic levels of interleukin-8 (IL-8) have been found to correlate with increases in markers of subclinical tubular injury. The mechanism is thought to involve IL-8 mediated inflammatory infiltration of small renal vessels with a resultant reduction in oxygen delivery to vulnerable areas. In contrast, there is now evidence that the anti-inflammatory cytokine interleukin-10 (IL-10) has reno-protective properties.

Hence the balance of pro- and anti-inflammatory cytokines is important for the preservation of renal function. In addition preserved renal function is also a key component in the maintenance of normal cytokine balance. The clearance of pro-inflammatory cytokines from the circulation is heavily dependent on renal function and in health there is very little spill-over of pro-inflammatory cytokines into the systemic circulation. Hence the kidneys are integral to cytokine balance because they remove pro-inflammatory mediators while maintaining plasma concentrations of anti-inflammatory cytokines. Nonetheless this means that tubular filtrate is likely to have a cytokine balance weighted heavily in favour of pro-inflammatory cytokines, with all the attendant risks of direct pro-inflammatory damage. Recent reports suggest that the kidneys are able to increase production of urinary anti-inflammatory cytokines, IL-1ra, TNF-sr and transforming growth factor beta-1 (TGF-b1). Large increases in renal anti-inflammatory cytokine production have been demonstrated following cardiac surgery. Patients with pre-existing chronic renal dysfunction have been shown to have elevated baseline plasma concentrations of anti-inflammatory mediators such as IL-1ra and TNF-sr as well as granulocyte inhibitory protein (GIP). These may increase tolerance of the increase in inflammatory mediators provoked by major surgery. This interesting finding may help to account for the relatively low mortality rate among patients who develop worsening chronic renal failure in intensive care when compared with those who develop acute renal failure. Acute peri-operative renal dysfunction, in turn, may predispose to other organ dysfunction because of the role of the kidney in controlling the balance of pro- and anti-inflammatory cytokines.
AETIOLOGY OF POSTOPERATIVE RENAL DYSFUNCTION

Renal dysfunction in the surgical patient is usually multifactorial: the commonest cause is ATN as a result of hypoxic damage to nephrons in the medullary region of the kidney secondary to hypotension, hypovolaemia, and/or dehydration.

The time course of factors predisposing to renal dysfunction can be divided into pre- and intraoperative.

Risk factors for the development of perioperative renal failure

<table>
<thead>
<tr>
<th>PREOPERATIVE</th>
<th>INTRAOPERATIVE</th>
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<tbody>
<tr>
<td>Pre-existing renal insufficiency</td>
<td>hypovolaemia</td>
</tr>
<tr>
<td>Patient age over 65</td>
<td>Nephrotoxins/drugs</td>
</tr>
<tr>
<td>• Age-related decline in nephron mass</td>
<td>• Contrast media</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>• NSAIDS</td>
</tr>
<tr>
<td>• Episilon 4 allelic variant of the apoE gene</td>
<td>• Aminoglycosides</td>
</tr>
<tr>
<td>Nephrotoxins/drugs</td>
<td>• Enflurane-increased inorganic fluoride concentrations</td>
</tr>
<tr>
<td>Sepsis</td>
<td>• Bile pigments</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>• Long term ACEI therapy</td>
</tr>
<tr>
<td>Crush injury</td>
<td>Generalized embolism</td>
</tr>
<tr>
<td>Perioperative cardiac dysfunction</td>
<td>Surgical procedures</td>
</tr>
<tr>
<td></td>
<td>Cardiopulmonary bypass procedures</td>
</tr>
<tr>
<td></td>
<td>Bypass related</td>
</tr>
<tr>
<td></td>
<td>1. Contrast activation</td>
</tr>
<tr>
<td></td>
<td>2. Ischaemia</td>
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<tr>
<td></td>
<td>3. Endotoxin translocation from the gut to the kidney</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>• Surgery involving aortic cross clamp</td>
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<tr>
<td></td>
<td>• Liver transplant</td>
</tr>
<tr>
<td></td>
<td>• Kidney transplant</td>
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<tr>
<td></td>
<td>Increased intra-abdominal pressure</td>
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</table>

INCIDENCE

The incidence of peri-operative acute renal failure varies according to the aetiology, the definition and the type of surgery undergone. Its incidence ranges between 1 and 25%, with mortality rates varying between 40 and 90%.

In the cardiac surgical patient, postoperative ARF is associated with increased ICU stay and increased overall length of hospital stay. The development of postoperative renal dysfunction is also accompanied by a higher incidence of gastrointestinal bleeding, respiratory infections and sepsis.

Cardiopulmonary bypass

The incidence of renal dysfunction in patients undergoing CABG on CPB varies between 1 and 15%. This is associated with a mortality of up to 19%. The incidence of cases of ARF after CABG requiring dialysis is less than 2%; but in these cases, the mortality varies between 23 and 88%.
The ischaemic-reperfusion injury occurs post-CABG because of the combination of low cardiac output and hypovolaemia. Initially the duration of bypass was thought to be associated with the development of acute renal dysfunction and/or renal failure needing dialysis. The recent introduction of off-pump coronary artery surgery has shown no decrease in either of these two morbidities.

**Major surgery**

ARF is a common complication after major surgery. The incidence depends on comorbidity, preoperative kidney function, and the type and urgency of surgery. Intraoperative events can hinder kidney function; any of these factors, alone or in combination, may contribute to critical reductions in renal blood flow and ischaemia, impaired delivery of oxygen, and toxin- or inflammatory-mediated injury. Postoperative ARF is believed to be, in part, mediated by pro-inflammatory mechanisms such as increased adhesion of endothelial cells, tubular cell infiltration, generation of reactive oxygen species, pro-inflammatory cytokines and reperfusion injury.

**INDICATIONS FOR RRT IN ARF**

There is no consensus on exact indications for the initiation of RRT in ARF but general criteria have been proposed.

Proposed criteria for the initiation of renal replacement therapy.

- Anuria or oliguria (urine output <200 ml/12 hours)
- Hyperkalaemia (K > 6.5 mmol/l)
- Severe acidaemia (pH < 7.1)
- Azotaemia (urea > 30 mmol/l)
- Clinically significant organ oedema (particularly lung)
- Uraemic encephalopathy
- Uraemic pericarditis
- Uraemic neuropathy/myopathy
- Severe dysnatraemia ([Na] >160 or <115 mmol/l)
- Hyperthermia
- Drug overdose with a dialysable product

One criterion can be an indication for the initiation of RRT. Two or more criteria makes RRT mandatory. Multiple criteria can indicate an early initiation of RRT.
EVALUATION OF RENAL FUNCTION

Renal function is generally measured in terms of GFR, renal blood flow or tubular function. AKI is defined in terms of serum creatinine and changes in urine production. Many of the tests of renal function in current use are not sensitive enough to detect the earliest manifestations of acute peri-operative renal dysfunction.

**Urine output**

Urine output is often more sensitive to changes in renal haemodynamics than biochemical markers. Urine output alone is of limited value; patients are capable of developing severe ARF despite maintaining normal urine output (‘non-oliguric ARF’).

**Creatinine**

Serum creatinine varies with age, body habitus, sex, diet and hydration status. Changes in serum creatinine are not directly proportional to renal function and is not accurate in the acute setting but rather in a steady state which can take days to achieve. Serum creatinine concentration may be slow to rise because of the dilutional effect of intra-operative fluid administration. ‘Delta creatinine’ (the increase in creatinine concentration from preoperative baseline) continues to be used as a marker of postoperative renal dysfunction. It has been suggested that even small increases in serum creatinine concentration immediately after surgery correlate with later development of renal dysfunction and postoperative mortality.

**Creatinine Clearance**

This technique involves a 24 hour urinary collection. Only mean urinary creatinine concentration can be measured thus precluding any possibility of detecting acute changes occurring within that time. The repeatability of this test is quite poor, mainly due to errors in the collection of urine. There have been concerns regarding reliability of creatinine clearance measurement in chronically low GFR states.

**Glomerular Filtration Rate (GFR)**

**Equations For Estimating GFR**

The Cockcroft and Gault equation has, for many years, been used to estimate creatinine clearance and, in turn, GFR. In 1989 Kopple et al., as part of the Modification of Diet in Renal Disease (MDRD) study group, developed a predictive equation for estimating GFR (eGFR) based on plasma creatinine concentration and several clinical variables. MDRD eGFR correlated well with gold standard measures of GFR.

The MDRD equation performs well in populations with a low range of GFRs. Both MDRD and Cockcroft and Gault are superior to the 24 hour creatinine clearance measurement. MDRD equation is less useful in patients with chronic malnutrition. Both equations have lower precision in populations with high GFR.
**Other Tests**
Effective renal plasma flow (ERPF) and inulin clearance have also proved ineffective at detecting abnormalities occurring in the first 24 h after surgery.

**PREDICTORS OF ACUTE PERIOPERATIVE RENAL FAILURE**

**Clinical factors**

Studies by Zanardo et al and Brown et al have demonstrated risk factors for acute postoperative renal impairment in cardiac surgical patients. Kheterpal et al studied non-cardiac surgical patients and found several risk factors for post operative renal impairment.

<table>
<thead>
<tr>
<th>CARDIAC SURGERY</th>
<th>NON-CARDIAC SURGERY</th>
</tr>
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<tbody>
<tr>
<td>1. Advanced age</td>
<td>1. Age</td>
</tr>
<tr>
<td>2. Low cardiac output syndrome</td>
<td>2. Emergency surgery</td>
</tr>
<tr>
<td>3. Emergency operation</td>
<td>3. High risk surgery</td>
</tr>
<tr>
<td>4. Use of intra-aortic balloon</td>
<td>4. Peripheral vascular disease</td>
</tr>
<tr>
<td>pump</td>
<td>5. Liver disease</td>
</tr>
<tr>
<td>5. Low urinary output during CPB</td>
<td>6. Increased body mass index</td>
</tr>
<tr>
<td>6. Female gender</td>
<td>7. Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>7. Leucocyte count &gt; 12X10⁹/L</td>
<td>8. Intra-operative variables</td>
</tr>
<tr>
<td>8. Prior cardiac surgery</td>
<td>• Total vasopressor dose</td>
</tr>
<tr>
<td>9. Congestive cardiac failure</td>
<td>• Use of a vasopressor infusion</td>
</tr>
<tr>
<td>10. Peripheral vascular disease</td>
<td>• Use of a diuretic</td>
</tr>
<tr>
<td>11. Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>12. Hypertension</td>
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</tbody>
</table>

Despite these studies, perioperative renal failure is not entirely predictable on the basis of perioperative risk scores alone. Patients without risk factors may also go on to develop this complication. Hence there is a need for the identification of biological markers that could also help predict the likelihood of developing renal failure.

**Biological markers**

Urinary N-acetyl-beta-D-glucosaminidase (bNAG)/creatinine and a-1-microglobulin (a-1-m)/creatinine ratios are sensitive, early means of detecting tubular damage and dysfunction respectively. The problem with these markers is that changes in their measurement are often difficult to interpret outside of the research environment.
Postoperative increases in urinary pro-inflammatory mediators such as IL-18 and neutrophil gelatinase-associated lipocalin (NGAL) have been shown to correlate with both the development and duration of perioperative renal dysfunction.

NGAL is derived from neutrophils and is highly upregulated after AKI, with levels raised only a few hours after the injury. It functions as a marker of renal function across a wide variety of clinical settings.

Cystatin C, a protein produced by all nucleated cells, is freely filtered by the glomerulus, reabsorbed by the proximal tubule, and is not secreted by renal tubules. Immunosuppressants such as steroid therapy and hypothyroidism may affect levels of cystatin C independently from GFR.

IL8 is produced by caspase-1 and is involved in the pathogenesis of ARF. It has been found to be a predictor of AKI.

KIM-I is a transmembrane protein expressed in dedifferentiated proximal tubule epithelial cells after tubular injury. Studies have found that KIM-I is elevated 12 hours after ischaemic injury and that it can predict outcome in patients with ARF. These findings raise the possibility of early interventions aimed at restoring the microcirculation, which could possibly modify the severity of perioperative renal dysfunction or even prevent it. Nevertheless, to date, the field of prevention remains largely clinical.

**Usefulness of Biomarkers**

1. Early diagnosis of renal impairment
2. Monitoring of the trend of renal dysfunction
3. Predictor of mortality

**ROLE OF DIURETICS**

Several theoretical arguments support the use of mannitol and loop diuretics for the prevention and treatment of ARF. Both can induce a diuresis and potentially “wash out” obstructing cellular debris and casts.

Mannitol may preserve mitochondrial function by osmotically minimizing the degree of postischaemic swelling and by scavenging free radicals. Loop diuretics may improve medullary oxygenation by decreasing oxygen use in this portion by blocking active transport. Loop diuretics also act as renal vasodilators.

Several studies have however shown increased mortality or non-recovery in patients with ARF, receiving diuretics. They have shown that high doses of furosemide can induce high urine output and can convert oliguric renal failure to non-oliguric renal failure, without reducing the need for dialysis and mortality from ARF. In addition furosemide use has been associated with deafness and the aggregation of Tamm-Horsfall protein in the lumen of tubules, causing obstruction.
WHAT IS RENAL REPLACEMENT THERAPY?
Renal replacement therapy is a therapy which assumes part of the functions of the kidney ie. blood purification and water and electrolyte balance. This term therefore incorporates all forms of the artificial kidney. Renal replacement therapy may be divided into peritoneal and haemodialysis modes.

RENAL REPLACEMENT MODALITIES
The basic mechanisms for solute removal during RRT include diffusive or convective transport. There are two key principles that need to be understood in order to differentiate between the increasing numbers of techniques that are on offer. These are DIALYSIS, which should be strictly used when referring to diffusion, and ULTRAFILTRATION, which is convection. Diffusion is the movement of solutes along an electrochemical gradient, from a compartment in which they are in a high concentration to one in which they are in a lower concentration. During these types of dialysis, an electrolyte solution runs in a counter-current direction to the patient’s blood flowing on the opposite side of a semipermeable filter. Small molecules in the blood, such as urea, move along the concentration gradient into the dialysate fluid. Larger molecules are poorly removed by this process. The rate of diffusion of a given solute depends on its charge and molecular weight (diffusion coefficient), the surface area, membrane porosity, thickness and amount of protein binding, the blood flow rate and dialysate flow rate (which generates the concentration gradient) and the temperature of the system.

Conversely with ULTRAFILTRATION, solute is carried in solution across a semi permeable membrane in response to a transmembrane driving pressure (also called solvent drag). This is a more effective method for removal of fluid and middle-sized molecules. The rate of ultrafiltration simply depends on the hydraulic permeability coefficient, transmembrane pressure and the surface area of the membrane. Some techniques incorporate both mechanisms.

RRT may be further subdivided into intermittent and continuous techniques dependant on the expected time frame which is required in achieving the desired end-points of the treatment. The modalities that need to be considered are Intermittent Haemodialysis (IHD) and CRRT which also includes Peritoneal Dialysis (PD). Peritoneal dialysis relies on diffusion, but it is quite inefficient owing to slow peritoneal blood flow. Slow, low efficiency daily dialysis is a technique that uses extended haemodialysis treatment sessions with gradual fluid removal.
PHYSIOLOGY OF RRT

**Fluid removal**
Safe prescription of fluid loss during RRT requires intimate knowledge of the patients underlying condition, understanding the process of ultrafiltration and close monitoring of the patient’s cardiovascular response to fluid removal.
In order to preserve tissue perfusion in patients with AKI, it is important to optimize fluid balance by removing patient’s excess water without compromising the effective circulating fluid volume. It is still a matter of controversy which clinical parameter or currently available monitorization should be utilized in order to uniformly define the concept of “volume overload.”
In patients who are clinically fluid overloaded, however, it is extremely important to accurately evaluate the amount of fluid to remove.

**TIMING OF RRT**
In general, RRT should be initiated early for ARF and before the development of complications. The timing of implementation of RRT may have an effect on outcome. A retrospective study showed an improved survival with earlier start of RRT in posttraumatic ARF.

**WHAT ARE THE DIFFERENCES BETWEEN THE TYPES OF RRT?**

**Continuous Renal Replacement Therapies**
(CRRT) CRRT provides a slow continuous ultrafiltration over a prolonged period of time, and is therefore generally better tolerated than shorter and intense IHD treatments. There has been a slow acceptance of CRRT for the management of ARF in intensive care and renal units due to initial troubles with low blood flow and coagulation. The application of blood pumps and the substitution from arteriovenous to venovenous circuitry led to the birth of current CRRT practice. In recent years there have been tremendous advancements in CRRT technology. There are numerous continuous techniques using extracorporeal circuits which carry the patient’s blood through a filter where varying degrees of dialysis and ultrafiltration may occur. The blood flow rates are lower than in IHD. These methods are described with reference to the patient’s vascular access (arterial and venous access catheters or just venous access) as well as the predominant technique taking place (i.e. haemodialysis (CAVHD or CVVHD—mainly diffusive), haemofiltration (CAVH or CVVH mainly convective) or haemodiafiltration when both are occurring (CAVHDF or CVVHDF). Arterial access is rarely required with the advent of more sophisticated machines where mechanical pump systems have replaced the need for an arterial driving pressure in the circuits. Slow Continuous Ultrafiltration (SCUF) refers to a seldom used method of slow fluid removal only (e.g. 100–300 ml/h), whereby solvent drag and clearance are not significant.
PD utilizes the peritoneal epithelial lining as a natural semi-permeable membrane. Blood flow is rich to this area and dialysate is inserted via a catheter through the abdominal wall. This technique is most often used by patients with chronic renal failure in the community who have an individualized regimen of dialysate dwell times and exchange frequencies. Fluid removal is determined by the concentration of glucose in the dialysate fluid, with fluid shifts generated by osmotic pressure differences between the dialysate and patients blood. After a period of equilibration, the dialysate fluid is removed. The process may be continuous or intermittent and is used mainly for home dialysis.

**Disadvantages Of Peritoneal Dialysis**

Solute and volume clearance may be inefficient in haemodynamically unstable patients with dubious intestinal blood flow.

Reduced diaphragm excursion associated with rise in intra-abdominal volume caused by the dialysate.

Contraindicated in patients with intra-abdominal pathologies and is associated with significant risk of peritonitis from dialysate peritoneal fluid leak (into the abdominal wall or chest cavity).

There is a strong biological rationale for the efficient removal of uraemic toxins in ARF. The accumulation of toxins may have detrimental effects and blood purification treatments should look beyond simple urea and electrolyte clearance. CRRT provides various options to increase ultrafiltration volume (dialytic dose) which has been demonstrated to improve haemodynamics and survival.

**Intermittent Haemodialysis**

IHD is primarily a diffusive technique, hence is best for removal of small solute molecules. A hydrostatic pressure is generated to drive the patient’s blood through a circuit and filter, and therefore fluid removal by ultrafiltration also occurs. To enable rapid corrections to volume and electrolyte status, high blood flow rates (e.g. 300 ml/min) and dialysate flow rates (e.g. 600 ml/min) are required. IHD is the standard procedure used in CRF patients that can also be applied in ARF. It requires specialized nursing staff. Standard treatments usually last 3–4 hours and are applied on indication only or on a daily or alternate daily basis. Hence this method must extract in a few hours, the equivalent of 2 days of administered fluids plus excess body water which may be present in the anuric patient. Although its intermittent nature can theoretically limit its applicability, it continues to be widely used.

**Slow, Low- Efficiency Daily Dialysis (SLEDD)**

This technique has the combined advantages of all available therapies and is very much like prolonged nocturnal IHD, using the same machines and dialysates. The main difference is that longer sessions (usually 8-12hours) enable slower blood and dialysate flow rates (100ml/min). As with IHD this technique is excellent for solute clearance but fluid may also be removed. It allows for less work in night shifts and allows for patient mobilization during the off-treatment periods.
## COMPARING TREATMENTS

**Advantages and disadvantages of intermittent versus continuous renal replacement therapy**

<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorter sessions and lower risk of systemic bleeding/filter clotting</td>
<td>More difficult haemodynamic control with risk of tissue ischaemia-reperfusion injury</td>
</tr>
<tr>
<td>More time available for diagnostic and therapeutic interventions</td>
<td>Availability of dialysis staff</td>
</tr>
<tr>
<td>Superior solute clearance (more suitable for severe hyperkalaemia)</td>
<td>Inadequate dialysis dose</td>
</tr>
<tr>
<td>Better haemodynamic stability</td>
<td>Inadequate fluid control</td>
</tr>
<tr>
<td>Better fluid control</td>
<td>Risk of central pontine demyelination from rapid correction of hyponatraemia</td>
</tr>
<tr>
<td>High level of biocompatibility</td>
<td>Risk of cerebral oedema from over rapid solute clearance. Not suitable for patients with intracranial hypertension.</td>
</tr>
<tr>
<td>Superior biochemical control (better control of metabolic acidosis and serum electrolyte levels)</td>
<td>No removal of cytokines</td>
</tr>
<tr>
<td>Better pulmonary gas exchange</td>
<td>Risk of protein starvation and highly negative nitrogen balance</td>
</tr>
<tr>
<td>Improved nutritional support (neutral nitrogen balance)</td>
<td>Higher risk of systemic bleeding (bleeding complications of up to 26%)</td>
</tr>
<tr>
<td>Suitable for patients with intracranial hypertension</td>
<td>Greater vascular access problems</td>
</tr>
<tr>
<td>(avoidance of dangerous swings in intracerebral water)</td>
<td>More filter problems</td>
</tr>
<tr>
<td>Lower cost</td>
<td>More immobilization of patient</td>
</tr>
<tr>
<td>Fewer cardiac arrhythmias</td>
<td>Greater cost</td>
</tr>
<tr>
<td>Shorter stay in ICU</td>
<td>Risk of hypophosphataemia due to high phosphate clearance</td>
</tr>
<tr>
<td>More rapid removal of dialyzable toxins</td>
<td>Specialized training required</td>
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</tbody>
</table>

## COMPARING OUTCOMES

**IHD vs. CRRT**

To date there is no definitive evidence that CRRT can improve mortality when compared to IHD in patients with ARF. However there is some evidence of better recovery of renal function using CRRT compared to IHD. Meta-analyses of all trials have conflicting conclusions being in favour or showing no advantage of CRRT.
TREATMENT ISSUES IN ARF

The target of any RRT should be to mimic the functions and physiology of the native organ: ensure qualitative and quantitative blood purification, restore and maintain homeostasis, avoid complications and provide good clinical tolerance that may favour organ recovery. The therapy should also consume minimal resources, labour and costs, providing optimal survival rates with minimal complications. The two classic options include intermittent haemodialysis (IHD) and continuous renal replacement therapy (CRRT). There is much controversy over the preferred modality for the treatment of ARF and at present there is no convincing data that one modality has advantages over the other. The choice of therapy seems dependent on the institutions experience, on geography and whether an intensivist or nephrologist writes and controls the prescription.

TREATMENT DOSE

The “dose” of dialysis is a measurement of the effectiveness of solute clearance, and the subject of much confusion. The dialytic dose has been demonstrated to affect outcome in ARF. Whether IHD or CRRT is used the patient must receive an adequate treatment dose. The “dose” is defined differently for IHD and CRRT. In IHD, the dose is assessed as either the urea reduction ratio (URR) which is the percentage reduction in [urea] post dialysis, compared with pre-dialysis session, or the kt/V. The kt/V refers to the blood water urea clearance, where k represents the rate of urea clearance by the dialyser in millilitres per minute, t the duration in minutes of the treatment session, and V the volume of distribution of urea in the patient in millilitres.

Dose is assessed in CRRT by the ultrafiltration rate. In a randomized trial of ICU patients with oliguric acute renal failure, ultrafiltration rates of 20, 35 and 45 ml/kg/h with CVVH were compared. It was shown that 35 and 45 ml/kg/h were of equal utility but both doses were superior to 20 ml/kg/h with respect to survival 15 days after CRRT was ceased.

MEMBRANES

Artificial kidney membranes have the potential to activate inflammatory cascades and affect cell function (bio-compatibility). The selection of a membrane has to take into account the indication for RRT (small, middle or large solute removal) and the biocompatibility issue. Large-pore or high-flux membranes can remove larger molecules up to 30 000 Da, including drugs such as vancomycin and inflammatory mediators such as TNF. There are insufficient data to support the choice of a specific membrane in ARF patients. High-volume haemofiltration and general CRRT treatments mostly use synthetic membranes with larger solute removal (high flux). IHD and SLEDD treatments often utilize larger surface area filters to maximize small solute clearance. Although the role of special sorbent cartridges and membrane adsorption in eliminating a broader range of accumulated renal toxins is still under investigation, this approach seems to provide enhanced efficiency for a wide spectrum of molecules.
ARE ALL DIALYSIS FLUIDS EQUAL?
The major difference between dialysates is the buffer base. This may be acetate, lactate or bicarbonate. There is substantial loss of endogenous bicarbonate during RRT which must be replaced. Acetate is converted to bicarbonate by the liver and skeletal muscle. Lactate is converted to bicarbonate by the liver.

A prospective cohort study of critically ill patients subjected to CVVHDF with any of the 3 buffers, found that those who received lactate or bicarbonate had significantly higher serum bicarbonate and arterial pH with superior haemodynamics than those treated with acetate.

Bicarbonate containing fluids are more expensive with a shorter shelf life.

ANTICOAGULATION

Blood flowing through an extracorporeal circuit activates the coagulation cascade. In order to prevent clotting of the filter anticoagulation often needs to be given. A baseline assessment of the patient’s coagulation status, including medical problems (eg. liver dysfunction, procoagulant disorders) and medications (eg. drugs with antiplatelet properties, consideration of heparin-induced thrombocytopaenia and thrombosis if heparin has been recently administered). The circuit has many design features to help prevent clotting. Despite all of these features and the relative hypothermia resulting from extracorporeal circulation, many patients still require anticoagulant drugs. There is no strong evidence to favour aspirin, although it is commonly used. Most centres prime the circuit with unfractionated heparin and a systemic bolus dose of around 5000 units, followed by an infusion of heparin. The selection of dose (either low, medium or full systemic heparinization with unfractionated heparin, or low molecular weight heparin) depends on the patient’s individual bleeding risk.

Patients that bleed on low dose heparin may require regional anticoagulation. Regional heparinization can be achieved with pre-filter heparin being neutralized by the infusion of post-filter protamine. Citrate is an alternative to heparin, causing anticoagulation through chelation of calcium ions. Calcium is infused post-filter to prevent hypocalcaemia. There is a risk of metabolic alkalosis as citrate is converted to bicarbonate by the liver.

In the setting of HITTS, anticoagulation can be achieved with heparinoids, the recombinant hirudin molecules or prostacyclin. Prostacyclin is however expensive and can cause bleeding, vasodilation and hypotension.

CONCLUSION

Our efficiency and comfort in the management of acute renal failure patients requiring RRT demands understanding of the principles involved, and is facilitated by practice guidelines. Despite our best efforts, ARF is a serious condition that carries a considerable mortality.
REFERENCES

4. Dosing Patterns for Continuous Renal Replacement Therapy at A Large Academic Medical Center in the United States. R. Venkataraman et al; Journal of Critical Care; 2002; 17(4); 246-250
6. Peri-operative renal protection. Jones et al; Best Practice & Research Clinical Anaesthesiology; 2008; 22(1); 193–208
8. Renal failure and its treatment. Murphy et al; anaesthesia and intensive care medicine; 2006; 7:7; 247-252
10. Renal protection. Sadovnikoff et al; Bailliere’s Clinical Anaesthesiology; 2000; 14(1); 161-171
11. Renal protection strategies in the perioperative period. Jarnberg et al; Best Practice & Research Clinical Anaesthesiology; 2004; 18(4); 645-660
12. Renal replacement therapy in acute renal failure. Ronco et al; Best Practice & Research Clinical Anaesthesiology; 2004; 18(1); 145-157
13. So you need to start renal replacement therapy on your ICU patient? Current Anaesthesia & Critical Care; 2005; 16; 321–329
15. The management of acute renal failure. Slack et al; Medicine; 2007; 35:8; 434-437
16. Loop diuretics for patients with acute renal failure. Lameire et al; JAMA; 2002; 288(20); 2599-2601
17. Diuretics, mortality, and non-recovery of renal function in acute renal failure. Mehta et al; JAMA; 2002; 288(20); 2547-2552
18. Acute kidney injury in the intensive care unit according to RIFLE. Ostermann et al; Crit care Med; 2007; 35(8); 1837-1842
19. Renal replacement therapies: physiological review. Ronco et al; intensive care med; 2008; 34; 2139-2146
20. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the second international consensus conference of the acute dialysis quality initiative (ADQI) group. Critical care;2004; 8(4); R204-R211
21. Peri-operative acute renal failure. Mahon et al; current opinion in anaesthesiology; 2006; 19; 332-338