Standards and Recommendations for the Provision of Renal Replacement Therapy on Intensive Care Units in the United Kingdom
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Ratified by ICS Council: January 2009
Review date January 2012
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<td>Activated clotting time</td>
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<td>Chronic kidney disease</td>
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<td>GFR</td>
<td>Glomerular filtration rate</td>
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<td>HCW(s)</td>
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<td>PS</td>
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<td>RRT</td>
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<td>Slow continuous ultrafiltration</td>
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1 Executive Summary

The purpose of this document is to summarise current options and best evidence available for provision of renal replacement therapy (RRT) in critically ill patients and to outline guidance on how these can be implemented in the safest and most effective manner. The document primarily describes standards for RRT in critically ill patients with acute kidney injury (AKI) and concomitant other organ (system) injury receiving Level 2 or Level 3 critical care. In certain circumstances, such as during the recovery phase from critical illness, these standards may be appropriate for patients receiving Level 1 care in a critical care setting. These standards are not intended for the patients with AKI or chronic renal insufficiency receiving Level 1 care in other clinical areas (e.g. nephrology wards).

Crucial to the care of the critically ill patients with impending AKI is the concept that in the early phase of a serious illness, renal impairment may be avoidable or reversible and hence concentrated efforts should be made to prevent the need for RRT. The extent to which such efforts should be pursued may be influenced by the stability of the patient’s condition, the presence of pre-existing renal impairment and the duration of the period for which renal compromise has been present.

In general, intermittent haemodialysis (IHD) is still the most frequently used method of renal support for majority of the patients with AKI, but for the critically ill patients with AKI continuous forms of renal replacement therapy are often used in the UK intensive care units (ICUs). Although both continuous renal replacement therapy (CRRT) and IHD may employ similar principles of clearance of uraemic toxins, there are important differences in the actual mode of solute removal and delivery of therapy.

In order to deliver optimum care with minimal treatment interruptions, health care workers (HCWs) on the ICU should have an understanding of the principles of CRRT. This includes the relevance of extracorporeal blood flow rates, ultrafiltrate production, anticoagulation and drug dosing principles. Good vascular access is important and it is essential that care of the access device is meticulous so as to preserve flows and reduce the risk of infection. HCWs should be familiar with the equipment available in their units and understand the operational characteristics. They should also be aware of all potential adverse effects of this invasive procedure in their patients. There are no nationally agreed standards for competencies in delivering CRRT in the critically ill. Although this document suggests a list of competencies, each unit is encouraged to develop competencies locally.

In creating this document, currently available standards and recommendations have been used from the following sources:

1. Acute Dialysis Quality Initiative (ADQI): http://www.adqi.net/

2. UK Renal Association: http://www.renal.org/guidelines/index.html

2 Introduction

Acute renal failure (now known as Acute Kidney Injury – AKI) with or without the need for renal replacement therapy (RRT) is a frequent problem on the ICU.

- The incidence of AKI in critical illness is 10-25% depending on the definition used and patient cohorts studied (1)
- The incidence of severe AKI needing RRT is 3-5% (2)
- Mortality in patients with AKI on the ICU is high at 23-80% and 57-80% if RRT is needed (1)
- The development of AKI is associated with a 2-10 fold increase in mortality, regardless of aetiology (3, 4, 5, 6)
- 15-32% of survivors remain RRT dependant at hospital discharge (7, 8)

There are many and often complex and co-existing causes for AKI in patients with established or developing critical illness. The crucial distinction for intensivists managing such patients is in appreciation of reversibility versus irreversibility of emerging AKI. Whereas most surviving patients developing AKI as part of their multiple organ dysfunction syndrome (MODS) will recover with normal renal function (reversible AKI), a small proportion of patients will not recover their kidney function either partly or fully (irreversible AKI); the latter will need ongoing care and management under nephrology services after discharge from ICU. Regardless of the underlying cause, if renal compromise cannot be rectified and if the patient’s primary condition is felt to have a reasonable prospect of eventual recovery, RRT is likely to be required. In most critically ill patients, RRT may have to be initiated usually without sufficient time for investigation and optimising procedures, for example if the patient’s condition is seriously compromised by severe complications such as hyperkalaemia, metabolic acidosis, severe sepsis and advanced MODS.

The effectiveness of RRT can be manipulated by modality choice, degree of solute clearance and dialysar/filter membrane characteristics. Good therapy is reliant on good vascular access and a properly functioning extracorporeal circuit. As RRT is not without complications, these should be prevented where possible or treated promptly by HCWs familiar with the therapy. Finally, RRT has an expanding role, and is used not just to treat the classical complications of renal failure, but is also used as adjunctive therapy in sepsis, to remove toxins, correct electrolytes and maintain fluid balance.
3 Initiation of renal replacement therapy

3.1 Indications for starting therapy

Classical ‘renal’ indications for starting renal replacement therapy (RRT) are:
- Rapidly rising serum urea and creatinine or the development of uraemic complications
- Hyperkalaemia unresponsive to medical management
- Severe metabolic acidosis
- Diuretic resistant pulmonary oedema
- Oliguria or anuria

‘Non renal’ indications for starting RRT are:
- Management of fluid balance e.g. in cardiac failure
- Clearing of ingested toxins
- Correction of electrolyte abnormalities
- Temperature control
- Removal of inflammatory mediators in sepsis

One large epidemiological study found that the main (but not the only) reasons for starting RRT were severe diuretic unresponsive oliguria/anuria followed by uncontrolled uraemia and fluid overload (9).

There are no universally accepted levels of urea, creatinine, potassium or pH or decreased level of glomerular filtration rate (GFR) at which to start the therapy. Urea and creatinine are easily measured but are not the only uraemic toxins and are affected by non-renal factors. Urea is affected by factors such as degree of catabolism, state of hydration and steroid use, and creatinine by age, race, sex, lean body weight and muscle mass. The search continues for biologic markers for AKI which may more accurately reflect GFR (e.g. cystatin C) but until they become universally available and applicable the rate of change of urea and creatinine rather than their absolute value is more informative (10).

Urine output may be more sensitive to changes in renal haemodynamics, but oliguric and non oliguric AKI can occur and urine volume may be influenced by diuretic use.

3.2 Timing of therapy

There is increasing evidence that early initiation of RRT is beneficial and may have survival or kidney function recovery advantages. In a retrospective study of post traumatic AKI there was a survival benefit if RRT was started when the urea was 15.2 mmol/L rather than 33.7 mmol/L (11). An early start of RRT is also suggested by more recent dose/outcome studies (12, 13) and data from the observational PICARD study (14) where a urea value of 27 mmol/L was used to demarcate early or late start. However, survival or renal recovery benefit by an early start of RRT is not supported by all studies (15).

In critically ill patients fluid balance problems may be another trigger for starting RRT (9). Two studies used oliguria within the first 8 hours post cardiothoracic surgery as a trigger for starting RRT (early start) rather than levels of urea, creatinine or potassium (late start) (16, 17). In both studies, RRT was started significantly earlier when oliguria, rather
than solute levels was used as a trigger, and an early start was associated with reduced hospital mortality. Despite their individual limitations, studies appear to support the early start of RRT. What is less clear is what constitutes ‘early’, as initiation of RRT may reflect factors other than the absolute levels of urea and creatinine or urine output.

3.3 Standard/recommendation

1. Conventional starting criteria for RRT should be used (Grade D).
2. Treatment should be started before complications develop (Grade E).
3. The rate of change of urea and creatinine is more significant than their absolute levels (Grade C), however in most cases RRT should be started before urea is 20 – 30 mmol/L. In many circumstances, starting RRT well before urea rises to these levels may well be justified.
4. Initiation of RRT on the basis of fluid balance, urine output, potassium level or degree of acidosis will be dependent on the patient’s clinical condition.

4 Intermittent versus continuous therapies

4.1 Current practice

- In the UK, Western Europe and Australia, continuous therapies are the predominant mode of delivery of RRT
- More than 10,000 patients are provided with RRT in UK ICUs annually
- About 90% of all ICUs in the UK provide RRT, most using CVVH or CVVHDF (18)
- Worldwide, 80% of patients who need RRT for AKI on the ICU are treated with continuous therapies, 16.9% of patients are treated with intermittent therapies and 3.2% receive either peritoneal dialysis or slow continuous ultrafiltration (19)

4.2 Advantages and disadvantages of different modalities of RRT

Patient and organisational factors influence the choice of intermittent or continuous therapy. In the critically ill, AKI often develops as part of MODS. Renal supportive therapy for AKI in these patients is thus delivered along with support of other failed organ systems. CRRT is a therapy that can be provided, in combination with other organ support, by an appropriately trained ICU nurse. Delivery of IHD requires the appropriate infrastructure to be in place; e.g. machines, water supply and staff trained to deliver intermittent therapy.

Critically ill patients are often haemodynamically unstable and tolerate sudden fluid shifts on IHD poorly resulting in repeated hypotensive episodes which may delay recovery of renal function (20). CRRT techniques are generally well tolerated by these haemodynamically vulnerable patients (21, 22). In one study, CVVH increased blood pressure and systemic vascular resistance as compared to IHD (23). There was a significant difference in temperature changes between the two groups and some of the haemodynamic stability seen in the CRRT group may have been related to its cooling effect. There was a better and more sustained resolution of acidosis with CVVH, but splanchnic oxygenation and mortality were the same for both groups. Continuous therapies have also been shown to be beneficial in patients with raised intracranial pressure and concomitant AKI (24, 25).
In the critically ill, supporting various failed organ systems involves significant, obligatory input of fluids, for example sedative drugs, inotropes, antibiotics and nutrition. This must continue even if the patient is oliguric or anuric. Any form of RRT must be able to remove large volumes of fluid and CRRT is well suited for the task although modern IHD machines can also remove significant quantities of fluid. CRRT, despite being a continuous therapy may not actually be delivered continuously; there are often significant periods of ‘filter down time’ due to filter clotting or transfer for procedures/imaging leading to inadequate delivery of therapy. To maintain the continuous nature of the extracorporeal circuit there is often a need for ‘continuous’ anticoagulation making invasive procedures difficult to organise. IHD allows flexibility for other therapies or procedures to take place and reduces the need for prolonged anticoagulation.

4.3 Impact of therapy on patient mortality
There are conflicting data concerning the effect of IHD versus CRRT on mortality, as often haemodynamically unstable patients are excluded from trials of IHD with clinicians preferring to use CRRT in such unstable patients. One randomised trial comparing IHD with CRRT found increased mortality in the CRRT limb (26), however despite randomisation sicker patients were assigned to the CRRT limb and were subjected to a lower efficiency CVVHDF/CAVHDF (ultrafiltrate produced - 800 ml/h). One meta-analysis concluded that mortality appeared lower for CRRT (27) but in contrast a further meta-analysis found no difference (28). Subsequent randomised trials have failed to conclusively support one therapy being superior to other in terms of patient mortality (22, 29, 30).

4.4 Impact of therapy on renal recovery
The effect on recovery of renal function has been studied. There is a possibility that CRRT leads to improved renal recovery for those who survive (31, 32); however when the competing risk of mortality is considered, it is difficult to draw conclusions (33, 34) and no robust evidence supports one therapy over the other (22, 29, 30).

4.5 Development of hybrid therapies
Given both intermittent and continuous therapies have their own potential benefits, hybrid therapies such as slow low efficiency daily dialysis (SLED(D)) have been developed as a ‘best of both worlds’. These therapies aim to provide haemodynamic stability over a time period short enough to avoid the complications of continuous anticoagulation, allowing time for therapeutic interventions/diagnostic imaging, but over a period long enough to gain good solute and fluid control. Slow low efficiency daily haemodiafiltration (SLEDD-f) can be used to combine the beneficial effects of diffusion with convection (35). There is little doubt that in terms of solute control they are comparable to other forms of RRT, but so far there is no evidence that hybrid therapies are superior to either CRRT or IHD. A need for a dialysis machine, water supply and trained nursing staff may also limit its widespread use.

4.6 Comparison with peritoneal dialysis
There are few data comparing peritoneal dialysis (PD) with CRRT. A randomised trial in patients with sepsis and AKI was stopped early because of the significant benefit on mortality of CRRT compared to PD (36). Although PD is not usually used in the critically ill, it may have a role in patients with problematic vascular access. Consultation with the local specialist renal services is recommended in such circumstances.
4.7 Standard/recommendation

1. There is insufficient evidence to recommend CRRT over IHD or vice versa in terms of patient mortality, but data tend to suggest a better renal outcome with CRRT.
2. Consensus favours CRRT for patients on the ICU with AKI (Grade E). In particular it appears appropriate to use CRRT in haemodynamically unstable patients and those with fluid balance issues.
3. CRRT also appears to offer particular benefit in patients with, or at risk of cerebral oedema (Grade C).
4. IHD is appropriate to use in haemodynamically stable patients during their recovery from a critical illness. Its use will be determined by local organisational factors.
5. PD should not be used routinely for critically ill patients with AKI on the ICU. (Grade C).

5 Dose of renal replacement therapy

5.1 Principles of solute removal

- Different methods of RRT are in part differentiated by the predominant method of solute removal, diffusion or convection (37, 38, 39)
- Diffusion is the movement of solutes down a concentration gradient across a semi permeable membrane
- With membranes with high hydraulic permeability (high permeability to water), plasma water moves across the membrane carrying solutes with it (solvent drag). This bulk-flow of solutes is termed convection or mass convective transfer. Water movement and therefore convection can be enhanced if pressure is applied across the membrane
- The predominant method of solute removal for each therapy is:
  - Intermittent haemodialysis (IHD) – diffusion
  - Continuous veno-venous haemofiltration (CVVH) - convection
  - Continuous veno-venous haemodialysis (CVVHD) - diffusion
  - Continuous veno-venous haemodiafiltration (CVVHDF) – diffusion and convection

5.2 Solute clearance during intermittent haemodialysis
Solute removal can be improved by maximising blood and dialysate flow rates, using haemodialysers of appropriate surface area and minimising access recirculation. Timing (for example daily or alternate day dialysis) and duration of therapy will also influence dose delivery. Combining diffusion and convection can increase solute clearance (13).

5.3 Solute clearance during continuous therapies
Small solute clearance (using urea as a surrogate) during convective therapies depends upon plasma water filtered i.e., ultrafiltrate production. For equal volumes of ultrafiltrate produced, it is better with CVVHDF compared to CVVH, however middle molecular weight molecules (MW > 500-1000Da) are generally better cleared by convection than
by diffusion (37, 38). Middle MW substances include endothelin, bradykinin, interleukin 1, interleukin 8, complement factors and beta-2 microglobulin. Pre-dilution affects solute clearance. There is a 15% reduction in urea clearance at ultrafiltration volumes of 2000 ml (37) but up to 34% for volumes of 4500 ml (38).

Solute clearance is also closely related to membrane characteristics such as pore size, charge and water permeability (flux) as well as circuit factors such as extracorporeal flow rates (40). Some mediators may also be removed by adsorption onto the filter, although to a variable degree (37, 38).

5.4 Relationship between dose and outcome

Studies in patients with end stage kidney disease (ESKD) requiring IHD have led to well defined targets for what constitutes adequate clearance (41). However in patients with AKI, what is adequate clearance and how this influences outcome is less clear.

There are several ways to determine the efficiency of any renal replacement therapy, one such method widely used in ESKD is Kt/V. This is the fractional clearance of a given solute (usually urea), which takes into consideration therapy duration (t) and the volume of distribution of the marker molecule in the body (V). Early work suggested that patients with AKI on the ICU with an intermediate severity of illness did better with a higher dose of dialysis, delivering a Kt/V of greater that 1.0 (42). A more recent study showed that a higher intensity of IHD improved outcome with a delivered Kt/V of 0.92 based on 6.2 treatments per week, with a mean of 3.3 hour sessions (43). The study excluded sicker patients who needed CRRT for haemodynamic reasons and there was concern about the degree of solute clearance in the control arm. This study did however lend weight to previous work that suggested that a higher dose of dialysis in AKI was associated with a better outcome.

Applying Kt/V or indeed other methods of solute clearance in critically ill patients with AKI is possible (44) but has limitations. (40, 45, 46, 47). In contrast to ESKD patients, critically ill patients are not in a metabolic steady state, are frequently catabolic and have labile, and often expanded fluid volumes. As the sieving coefficient of most small solutes (e.g. urea) is 1 in post dilution CVVH (37), ultrafiltration volume acts as a surrogate for clearance. This can be related to body weight giving a ‘dose’. Thus more recent studies have described dose of CRRT in terms of ml/kg/h of ultrafiltrate production (‘kg’ refers to of patient’s body weight).

This approach was used by Ronco et al in 2000 in a large prospective study using post dilution CVVH, comparing the effects of different doses of ultrafiltration (20, 35 and 45 ml/kg/h) on outcome (12). There was a survival benefit with 35 and 45 over 20 ml/kg/h but little difference between 35 and 45 ml/kg/h. The benefit of an increased dose was not supported by a subsequent study but prescribed doses were not standardised by weight and there were criticisms regarding study design (15). A more recent study using pre-dilution CRRT investigated the effect of adding a mean ‘diafiltration’ dose of 18 ml/kg/h to an ultrafiltration dose of 24 ml/kg/h producing a total ultrafiltrate of 42 ml/kg/h (13). It was found that survival was significantly higher in the group receiving 42 ml/kg/h of CVVHDF. From this study it cannot be inferred that CVVHDF is ‘better’ as the low dose group received a dose lower than that found to be beneficial by Ronco et al (12). Despite being underpowered, it did suggest that a higher level of solute clearance was beneficial.
From the limited studies conducted so far, no difference has been found between standard IHD and haemodiafiltration (48), or by using high flux dialysis to gain a degree of convective therapy (49). In other words, it is unclear whether the mode of solute removal (convection and/or diffusion) has an effect on patient outcome. So far, the studies on dose and outcome have been conflicting; problems often related to study design making comparisons difficult. When the 4 recent dose/outcome studies are pooled there is a very large effect on survival in favour of an augmented dose, with an odds ratio of 1.95 (50). What constitutes the ‘ideal dose’ has yet to be clarified, but 35 ml/kg/h of effluent production (ultrafiltrate, or 35 ml/kg/h ultrafiltrate plus dialysate in case of CVVHDF) has been recommended as a minimum dose. However, the recently concluded randomised controlled trial of American Acute Renal Failure Trials Network (ATN study, 51), did not find any difference in survival, rate of renal recovery or non-renal organ failure in ‘intensive’ versus ‘less-intensive’ renal support. This study used pre-dilution CVVHDF (with ultrafiltrate rates of 35 versus 20 ml/kg/h, the ultrafiltrate was a combination of effluent and dialysate in equal proportions) as the continuous RRT mode and as well as IHD and SLEDD in their patients. The Australian RENAL study (Randomised Evaluation of Normal vs. Augmented Level of renal replacement therapy in ICU) (52) will compare 40 ml/kg/h to 25 ml/kg/h of ultrafiltrate production in CVVHDF. This study is due to be concluded in 2008 and may support or refute the current recommendations.

5.5 Other factors affecting dose delivery
There may also be a discrepancy between prescribed dose of RRT and dose actually delivered to the patient. Technical problems such as poor blood flows and recirculation, reduced efficiency of the haemofilter over time or actual filter clotting leads to a reduction in dose delivered. With the move towards higher ultrafiltration rates, higher blood flows are needed to maintain a filtration fraction below 30% and avoid excessive haemoconcentration within the filter and thus filter clotting.

When considering CRRT, continuous may not indeed be continuous, and patients may receive inadequate solute control (53). One retrospective review found that only 68% of patients received their prescribed dose of CRRT (54) where as in the study by Ronco et al (12), over 85% of prescribed dose was delivered. Even with intermittent therapies, it has been found that the delivered dose may be up to 30% lower than the prescribed dose (45).

The most accurate way to assess adequacy of RRT is to formally measure solute clearance. As more information from dosing trials in critically ill patients becomes available, there may be a clearer understanding of the relationship between dose and outcome, which may necessitate stricter guidelines on formally measuring solute clearance.

It should be remembered that in critically ill patients, CRRT is more than just small solute removal. The removal of potassium, correction of acidosis or the removal of fluid may have just as much of an impact on patient outcome as solute clearance (39).

5.6 Standard/recommendation

1. For IHD a minimum Kt/V of 1.2 should be delivered 3 times a week in patients with kidney failure (Grade A). There is increasing evidence that an increase to
daily or near daily IHD may be more beneficial in critically ill patients with AKI but further information from trials is awaited.

2. The ideal dose for CRRT is not known; however 35 ml/kg/h of ultrafiltrate production is recommended as a minimum for CVVH (post-dilution) and CVVHDF (Grade C). Results from RENAL study (52) are awaited to increase our understanding. Besides, 35 ml/kg/h ensures that adequate dose of CRRT is delivered despite filter down times.

3. Pre-dilution CRRT reduces solute clearance and an increase of 15% for ultrafiltration rates of 2 L/h and up to 40% for rates of 4.5L/h or more should be considered.

4. There is no evidence to suggest that CVVH (convection) is superior to CVVHDF (convection plus diffusion) in terms of patient outcome or renal outcome (or vice versa). If adequate ultrafiltration rates cannot be achieved using CVVH due to machine limitations, then CVVHDF should be considered. A predominantly convective mode of clearance may be considered in severe sepsis (see section 12).

5. Assessment of solute clearance on CRRT/IHD should be as per local unit policy or by clinician direction. Urea and creatinine should be measured daily, but there is no recommendation as to the absolute level that should be achieved. A normal pH and potassium should be achieved and arterial blood gas samples should be analysed at a frequency dictated by the clinical state of the patient.

6. Efforts should be made to maintain effective therapy, with at least 85% of the prescribed dose being delivered. (Grade E).

6 Choice of replacement fluid

6.1 Composition of fluid
Replacement fluid consists of a balanced salt solution with a lactate or bicarbonate buffer. The individual components of filtration fluid vary but phosphate and potassium supplementation is often needed.

6.2 Choice of buffer
Some studies have shown better control of acidaemia with bicarbonate-based fluids (55) especially if there is concomitant liver dysfunction (56), but others have not (57, 58). The effect on cardiovascular status is mixed, with either improved cardiovascular stability with bicarbonate (55) or no difference (57, 58) when compared to lactate-buffered fluids. To date no studies have demonstrated a clear benefit on survival or renal outcome related to either buffer solutions (55, 57, 58). Bicarbonate may induce nitric oxide synthase activity, increase cyclo-oxygenase activity and increase p53 pro-apoptotic protein in the extracorporeal circuit (59), an undesirable side effect in the critically ill and could theoretically be harmful.

Many patients may show a rise in serum lactate when using a lactate based buffer (57) but for some this may be clinically significant with a worsening metabolic acidosis. Lactate intolerance is arbitrarily defined as a rise of > 5 mmol/L during CRRT with a
lactate buffer (60). Patients at high risk of lactate intolerance are patients with severe liver disease, those with profound hypoperfusion or pre-existing lactic acidosis at the start of RRT. The problem of bicarbonate stability in solution has been overcome by pre prepared bags of replacement fluid with a separate chamber containing the buffer and just prior to use the two compartments are mixed. Lactate-based fluids are stable with a long shelf life, are easier to use, as they do not need pre mixing and are generally cheaper.

Standard bicarbonate or lactate bags cannot be used if citrate anticoagulation is used; modified replacement and dialysate fluid should be used in such circumstances.

6.3 Pre dilution versus post dilution
Pre-dilution lowers the haematocrit of blood passing through it and has been used as an adjunct to anticoagulation (61). As discussed in the previous section, pre-dilution leads to a reduction in solute clearance.

6.4 Standard/recommendation

1. Bicarbonate-based fluids may have theoretical disadvantages but currently there are no data favouring either kind as replacement fluid (Grade C).

2. A rise of lactate of greater or equal to 5 mmol/L (from base-line) associated with a worsening metabolic acidosis suggests lactate-intolerance, under these circumstances the buffer should be changed to bicarbonate. Initial use of bicarbonate is recommended for patients with a severe pre-existing lactic acidosis pH <7.2 with associated lactate of ≥ 8 mmol/L or a lactate rise of ≥5 mmol/L with a drop in pH i.e., lactate intolerance or with severe liver dysfunction (Grade C).

7 Choice of dialysis/filter membrane

7.1 Choice of material
Dialysis membranes can be made of synthetic or cellulose fibres. Cellulose fibres are either unsubstituted (cuprophane) or substituted membranes (e.g. cellulose acetate). They are generally low flux, poor at removing middle MW molecules and predominately used in end ESKD. Synthetic fibres include polysulphone (PS), polyamide (PA), polyacrylonitrile (PAN) and polymethyl methacrylate (PMMA). They are high flux membranes, flux being a measure of ultrafiltration capacity and based on the membrane ultrafiltration coefficient. High flux membranes are highly water permeable therefore allowing convective therapy and the removal of middle MW molecules and are used in CVVH; CVVHDF etc. It should be noted that high permeability does not always equate to high urea clearance (efficiency).

Historically, data from the use of cellulose dialysis membranes in chronic haemodialysis showed that they caused complement and leukocyte activation as blood came into contact with the membrane surface. Leukocyte activation is associated with increased expression of adhesion molecules (62) leading to leukocyte retention in the lungs, renal parenchyma and other organs, thus resulting in further organ damage. Biocompatibility refers to this activation of inflammatory pathways, with more biocompatible membranes causing less activation. Synthetic membranes (e.g., PAN, PS etc) are more
biocompatible and they cause less leukocyte activation; however leukocyte activation is only reduced with these membranes but never completely abolished.

7.2 Effect on mortality and renal outcome
Studies on the effect of type of membrane on mortality show mixed results (63, 64, 65). Two meta-analyses failed to conclusively support one membrane over another in terms of patient or renal outcome (66, 67), however synthetic filters are better suited to CRRT with regard to fluid flux.

7.3 Effect of adsorption
A variable degree of adsorption occurs on to the membrane and it is thought that this may lead to the removal of some inflammatory mediators. PAN and PA membranes appear to have greater adsorptive properties than PS membranes (68) but membrane adsorption may or may not be clinically significant as membranes reach saturation relatively quickly (38).

7.4 Standard/recommendation

1. There is no conclusive evidence to suggest that modified cellulose membranes should be avoided, however until proven otherwise, biocompatible synthetic membranes are recommended over cellulose based membranes.

8 Choice of anticoagulation

8.1 The need for anticoagulation
As blood comes into contact with the extracorporeal circuit there is activation of coagulation cascade and therefore risk of clotting of the filter and the extracorporeal circuit. Partial filter clotting results in reduced filter performance, but complete clotting interrupts treatment with loss of the filter, circuit and blood contained in the circuit. AKI itself may be associated with a procoagulant state, but many filter clotting problems can also be traced back to factors such as poor vascular access, inadequate blood flow rates and excessive haemoconcentration during filtration. The use of anticoagulation is of particular importance in CRRT as by design it functions best when the circuit is kept patent and treatment is ‘continuous’.

Circuit failure can be minimised by meticulous care of access sites during RRT and when not in use. Each patient should be assessed for the most appropriate form of anticoagulation, if indeed any anticoagulation is needed. The risk of haemorrhage needs to be balanced against the disadvantages of the filter clotting, it being better to lose the filter rather than the patient.

8.2 No anticoagulation
Many critically ill patients may have an abnormal coagulation profile and/or thrombocytenia or have a very high risk of bleeding. This may obviate any need for ‘active’ anticoagulation for the extracorporeal circuit. Despite concerns about shorter circuit life, some workers have observed comparable filter life without anticoagulation in patients with high risk of bleeding when using pre-dilution therapy with adequate blood flow rates (69, 70).

8.3 Unfractionated heparin
In critically ill patients without coagulation impairment, some form of anticoagulation is generally required, and unfractionated heparin (UFH) is the commonest anticoagulant used for both CRRT and IHD. It is inexpensive and familiar to all clinicians and acts by a 1000-fold potentiation of antithrombin and inhibition of factors Xa and thrombin (IIa). A mixture of heparin molecules with different sizes (5-30 kDa), UFH is metabolised by the liver and metabolites are excreted by the kidneys, with a plasma half life varying from 30 minutes to 3 hours (71).

The effect of UFH in critically ill patients is often unpredictable as there may be a degree of heparin resistance due to low antithrombin levels and non-specific binding to certain drugs and acute phase proteins (72). The activated partial thromboplastin time (APTT) does not always accurately reflect the anticoagulation effect of UFH (72) and the activated clotting time (ACT) is imprecise in the lower range (73) and subject to operator/observer error. Finally it has been shown that there is no strong correlation between increasing APTT and prolonging filter life (69, 74).

8.4 Low molecular weight heparin
Low molecular weight heparins (LMWHs) may also be used. As a consequence of less protein-binding the pharmacokinetics of LMWHs are more predictable than UFH, which may be advantageous because of the low levels of albumin commonly associated with critical illness. With a more pronounced anti-Xa action LMWHs are only partially neutralised by protamine, as a result of which anticoagulation levels may last up to 4 hours. They are also not cleared by CVVH.

8.5 Unfractionated versus low molecular weight heparin
There is no definite evidence as to which type of heparin is superior in terms of efficacy and risk of side effects (71). LMWHs anticoagulation suffers from a lack of reliable predictors of bleeding and antithrombotic activity (75) and the daily cost of LMWHs including anti-Xa assays is higher (76). Both types of heparins are associated with the development of heparin induced thrombocytopenia (HIT) types I and II, but risk is greater with UFH than LWMH. The true incidence of HIT type II is unknown, but for patient receiving prophylactic UFH HIT type II occurs in 2.6% of cases compared with 0.2% of cases when LWMHs are used (77). In the intensive care setting HIT type II has been reported in around 1-5% of patients treated with heparin for more than 5 days (78). The development of HIT type II may be associated with repeated clotting of the extracorporeal circuit (78).

8.6 Regional heparinisation
Regional heparinisation can be considered in patients at risk of bleeding. UFH is infused pre filter and neutralised post filter with protamine. Although it has been shown to be effective, there is a risk of adverse effects from protamine, e.g., platelet dysfunction, activation of inflammatory mediators and systemic hypotension. As there are better alternatives, its use is not recommended (71).

8.7 Heparinoids
There is little experience of the use of heparinoids (e.g. danaparoid) in patients receiving CRRT and consequently no recommendations can currently be made regarding their use in RRT. Although used in cases of HIT cross reactivity is reported in some patients. If used, anti-Xa levels should be monitored regularly.
8.8 Prostaglandins
In patients at high risk of haemorrhage or requiring rapid reversal of anticoagulation, prostaglandin I2 (Prostacyclin) or prostaglandin E2 may be considered (79). Prostaglandins inhibit platelet reactivity and aggregation in a dose dependent manner, an effect that lasts for up to 2 hours after stopping infusion of prostaglandins. They act synergistically with heparins and so can be used either alone or in combination with low dose UFH or LMWHs to preserve circuit integrity with a lower risk of bleeding (71). Prostaglandins also have vasodilatory effects which last only for a few minutes (half life approximately 2 minutes). Prostacyclin may also reduce hypoxic pulmonary vasoconstriction in some patients and may thus occasionally cause serious hypoxemia.

8.9 Regional citrate anticoagulation
Regional citrate anticoagulation has been used successfully for some time in critically ill patients (80). Sodium citrate infused into the ‘arterial’ limb of the extracorporeal circuit to chelate calcium reduces ionised calcium thereby inhibiting clotting. A calcium infusion is required post filter to maintain normal systemic ionised calcium levels. Citrate is converted to citric acid, which is metabolised to bicarbonate by the hepatic, renal and muscle systems (each molecule of citric acid potentially yielding 3 molecules of bicarbonate), and as a consequence metabolic alkalosis may present a problem with citrate anticoagulation. Trisodium citrate solutions contain a substantial amount of sodium, increasing the risk of hypernatraemia. Calcium and magnesium may become depleted, as their citrate complexes are freely filterable. A variable amount of citrate may enter the circulation depending on filtration volumes and a severe acidosis may result, particularly if hepatic and muscular citrate metabolism is compromised (71).

Two small randomised studies have demonstrated longer circuit life and less bleeding with citrate anticoagulation when compared to UFH (81, 82). In recognition of the need for carers to be proficient in use of citrate anticoagulation a variety of ‘home made’ regimens have been proposed (71).

8.10 Others
Fondaparinux inhibits thrombin generation by antithrombin-dependent Xa inhibition. It is safe to use in cases of HIT, should be monitored through Anti-Xa levels, but there is limited experience of its use in CRRT. (71)

Recombiant hirudin and argatroban are direct thrombin inhibitors. Experience with these drugs is limited, but increasing and they may have pharmacological advantages (71).

Nefamostat mesilate, a synthetic serine protease inhibitor is only available in Japan. Its biological half-life is about 8 minutes and it prolongs thrombin time, PT and APTT. It has some severe side effects (agranulocytosis, hyperkalaemia, and anaphylaxis) (71). Currently it is not recommended for clinical practice in the UK. Pre-dilution may help to reduce haematocrit and help prevent premature clotting of the filter and therefore is often used as an adjunct to anticoagulation. However, because of reduced efficiency with pre-dilution, ultrafiltrate volumes will have to be increased appropriately.
Experience has shown that no anticoagulation is usually necessary for CRRT when patients are receiving activated protein C as part of their therapy; although substantial evidence to this effect is lacking in the literature.

8.11 Monitoring
If anticoagulation is used, close monitoring of anticoagulation process is mandatory but there is no consensus on the method or the frequency of testing (75, 83). It is suggested that during heparin anticoagulation, APTT and platelet counts be routinely measured (83) with other anticoagulation methods monitored accordingly (e.g. serum ionised calcium, sodium and acid-base status during citrate use).

8.12 Standard/recommendation

1. Consensus exists that anti coagulation free CRRT can be successfully achieved (Grade D). No anticoagulation is suggested when any of the following are present:
   a. INR > 2-2.5
   b. APTT > 60 seconds
   c. Thrombocytopenia e.g. platelet count < 60 x 103/mm3
   d. High risk of bleeding
   e. When patients are receiving activated protein C

2. In patients who have a normal coagulation profile, normal platelet count and who are not at risk of bleeding, UFH or LMWHs can be used (Grade C). UFH is inexpensive, familiar to all clinicians and has an antidote.

3. Suggested use of UFH:
   Optional loading dose of 2000-5000 IU depending on the clinical situation. Loading dose may be omitted in patients at increased risk of bleeding.
   Infusion of 5-10 IU/kg/h.
   APTT should be checked 6 hours after starting and then regularly until stable aiming for an APTT of 1-1.4 times normal (Grade E). A higher level of anticoagulation can be considered if clinically indicated.

4. The APTT does not always reflect the anticoagulation effect of UFH and there is no correlation between increasing APTT and filter life.

5. ACT is imprecise, especially at low doses of UFH and should be interpreted with caution. Its use in the critically ill to monitor coagulation is not recommended.

6. Reference should be made to individual drug guidelines when using LMWHs, but for prolonged use monitoring of anti-Xa levels is recommended (target 0.25-0.35 U/ml) (Grade E).

7. All patients being treated with UFH or LMWHs should have daily platelet counts performed. In the event of the development of heparin HIT, all heparins should be stopped and an alternative method of coagulation considered. (Grade C).
8. There is no evidence to suggest newer heparin alternative such as danaparoid, hirudin, fondaparinux or argatroban are better than UFH/LMWHs. There are still only limited safety data and therefore no recommendations can be made.

9. Regional citrate anticoagulation is an effective therapy, particularly if there is an increased risk of bleeding (Grade C). To avoid complications a strict protocol should be developed and adhered to.

10. Prostaglandins are also effective ‘anticoagulants’ if there is a high risk of bleeding. (Grade E). A low dose is generally used (2.5 – 10 ng/kg/min). They may be especially useful in complex situations e.g., AKI requiring RRT in a patient with recent subarachnoid haemorrhage.

11. Pre-dilution can be used as an adjunct to anticoagulation (Grade C), and is highly recommended if no anticoagulation is to be used. To preserve efficiency, ultrafiltrate volumes need to be increased accordingly.

9 Vascular access

9.1 Choice of catheter
The key to good RRT is good access as poor blood flows and recurrent filter clotting are seldom due to ineffective anticoagulation alone. Arterio-venous CRRT is very rarely used and so are arterial catheters, and as most units use double lumen venous catheters only these will be discussed.

Polyurethane catheters are often used for acute RRT as they are stiff enough to aid insertion, strong enough to avoid collapse at high negative pressures and become softer at body temperature (84). Debate continues over the use of antibiotic coated catheters (85). Catheters have either a double D (or D/O), coaxial or double O configuration. There is no evidence to suggest one is superior to another. The lumen should be large enough, generally greater than 11 French Gauge, to allow the blood flows needed.

The tip of the catheter should be correctly positioned so that it sits in the inferior vena cava (for femoral lines) or in the superior vena cava, 1-2 cm above the right atrium (for subclavian and jugular lines) (84, 86, 87). A catheter that is too short or incorrectly positioned leads to poor flow rates and increased recirculation.

Tunneled access catheters are associated with a lower rate of infection, and as they are often made of softer silicone the tip can be positioned in the right atrium to optimise blood flow. Given that ICU patients are often septic, coagulopathic and at high risk of secondary infections, tunneled lines are generally not appropriate. They may however be considered in situations when the patient is deemed ‘sepsis free’ and likely to need ongoing renal replacement therapy. They should be inserted by an appropriately trained operator, under strict asepsis, and after liaison with the accepting renal unit.

9.2 Site of placement
The site of access is often determined by other factors such as patient body habitus, clinical condition, presence of coagulopathy and the presence of other lines. Femoral catheters have been reported to carry an increased risk of infection but the data are conflicting and not enough to discourage the femoral route of insertion. Subclavian vein
access lines have been associated with subclavian stenosis (88) which may be clinically significant for patients who ultimately need long term vascular access for dialysis; hence this site should be avoided for insertion of temporary access line if at all possible.

9.3 Insertion
As with the insertion of any central venous line, insertion of access lines is associated with the risk of trauma to the vessel and local tissues, arterial puncture, haematoma formation and pneumothorax. A skilled operator should insert access lines using an aseptic technique. The use of a vessel ultrasound has been shown to reduce the risk of complications related to insertion (42, 83, 89).

9.4 Standard/recommendation

1. A polyurethane, > 11FG dual lumen venous catheter should be used (Grade D).
2. Right internal jugular lines are associated with the least recirculation (Grade C) however the site of insertion will be guided by patient factors. In patients with a high chance of remaining dialysis dependant, the subclavian route should be avoided if possible (grade C) as this site has a high rate of vessel stenosis. For subclavian and jugular lines the tip should sit in the superior vena cava, and for the femoral, the tip should sit in the inferior vena cava, this often necessitates the use of a line of 20-24cm in length.
3. A vessel ultrasound should be used for insertion (Grade B).
4. Tunneled access lines may be considered in patients who are deemed sepsis free and awaiting transfer to a renal unit for ongoing renal replacement therapy.
5. Each unit should develop guidelines for the insertion of lines, ongoing care of the lines and appropriate microbiological surveillance.

10 Drug dosing during renal replacement therapy

10.1 General principles
Drug kinetics are affected by mode of RRT (diffusive or convective therapy), timing of therapy (intermittent or continuous) and the patient’s residual GFR and urine production (if any). Drugs with a low MW are cleared equally by diffusion and convection; however as the molecular size of the drug increases, convection becomes better method of clearance.

As IHD is an intermittent process, drugs given pre-dialysis may be removed but those administered post-dialysis session will be retained. During CRRT, filterable drugs will be constantly removed, just like normal renal clearance albeit with reduced function. During CRRT water-soluble drugs are removed efficiently whereas protein-bound drugs may not be removed at all. Hypoalbuminaemia in critically ill patients may affect drug binding and thus elimination by CRRT with more of the drug being removed. There is some loss of nutrients, especially nitrogen, but this is rarely more than 10-15% of intake. Water soluble vitamins (e.g. folic acid) may be lost in significant amounts.

10.2 Dose adjustment
Special attention is required for drug dosing, particularly antibiotics in patients receiving RRT. Drug dosing is commonly extrapolated from experience and/or studies in patients with chronic kidney disease (CKD) and often based on creatinine clearance or GFR. Dosage based on such information is not appropriate for critically ill patients receiving
CRRT. Antibiotic ‘nomograms’ developed for CKD patients or those on IHD may result in serious under dosing in patients on CRRT. Similarly doses based on creatinine clearance are not generally appropriate, as although creatinine clearance in these patients is low, they are receiving continuous (or near-continuous) RRT (90). The best way to confirm appropriate drug dosage is by measuring drug levels wherever possible. Inotropes and vaso-active drugs are not removed to a very large extent, probably due to their low plasma level, and are easy to titrate in patients on CRRT. During CRRT, antibiotics may be eliminated by direct filtration (especially water soluble drugs) or may be bound to the filter membrane (e.g. aminoglycosides). The literature and evidence-base for different drug kinetics in CRRT continues to expand and should lead to improved guidance in the future.

### 10.3 Standard/recommendation

1. Drug dosing during CRRT should not be based on ‘nomograms’ prepared for chronic stable patients or patients on IHD.
2. Drug levels should be measured if possible. Clinicians should be careful not to under-dose these patients, particularly if using antibiotics to treat severe sepsis.
3. Access to a pharmacist with expertise in drug dosing during RRT is advisable but it is suggested that each unit has easily accessible or ‘bedside’ dosing guidelines for commonly prescribed drugs for patients who are on RRT.

### 11 Complications of renal replacement therapy

#### 11.1 General principles

RRT is an invasive procedure where the patient’s blood is circulated through an extracorporeal circuit and is therefore associated with complications that may hinder achievement of treatment goals or prove harmful to the patient. Inexperience or lack of familiarity with equipment leads to an increased risk of complications. Numerous complications can occur, many of which are common to both continuous and intermittent therapies.

#### 11.2 Specific problems

Large volumes of replacement fluid together with the passage of blood through the extracorporeal circuit may cause heat loss and the risk of clinically significant hypothermia. This cooling may be a desired effect in patients with marked pyrexia or may have beneficial effects on haemodynamic stability. It may however lead to patient discomfort and shivering, coagulopathy or most commonly, mask a fever. The temperature-reducing effect is sufficiently well recognised that many clinicians would regard normothermia in a patient receiving CRRT as an indicator of masked pyrexia. There may be the need for active re-warming measures applied to the circuit, patient or both.

Filter clotting results in loss of the filter and circuit. This leads to inadequate treatment, the associated blood loss may contribute to or exaggerate anaemia of critical illness (91) and it is a drain on financial and nursing resources. Adequate training in line placement, filter priming and troubleshooting the extra-corporeal circuit are important principles in reducing the complications. Adequate anticoagulation is important but if perceived to constitute a risk to the patient, CRRT can be carried out without it.
Vascular access patency or positioning problems can lead to flow restrictions, limiting filter and circuit duration if the access site is managed suboptimally or if inappropriate devices are used. Contamination may lead to infection of the vascular access catheter which may lead to systemic sepsis and compromise patient outcome. Femoral venous catheterisation may increase the risks of deep vein thrombosis and thromboembolism but this is not substantiated by current evidence. Subclavian venous catheterisation is associated with a risk of subclavian stenosis.

Historically fluid balance management was a major challenge in managing CRRT, but modern filtration pumps and automated fluid balance devices have significantly reduced this. Problems can nevertheless still occur because of incorrect treatment prescription.

Many patients on the ICU may be haemodynamically unstable before starting CRRT and a worsening of this haemodynamic instability can occur around the time of starting CRRT or during the procedure. This may be in part due to excessive fluid removal or fluid/osmotic shifts. The use of angiotensin converting enzyme inhibitors in patients using an AN69 membrane has been associated with anaphylactoid reactions (92).

11.3 Standard/recommendation

1. Clinicians should make all attempts to reduce the risk of complications associated with the therapy and should complications develop, treat them promptly.
2. Methods should be in place for either reducing extracorporeal circuit temperature loss for example specific circuit warmers or warming devices applied to the patient. 3. There should be regular microbiological surveillance.
3. Appropriate means of monitoring anticoagulation should be in place to avoid the risk of bleeding or other complications associated with choice of anticoagulant.
4. ACEIs should be omitted in patients if AN69 membranes are used for CRRT to avoid the risk of anaphylactoid reactions (Grade B).

12 Non-renal indications for RRT and allied modalities

12.1 Drug removal
CRRT may be useful in removing filterable drugs (93, 94) or toxins (95) from blood in cases of drug toxicity or self poisoning. Clearance rates on CRRT will be lower than with conventional haemodialysis, however if IHD is not available or in the setting of haemodynamic instability, CVVHDF or CVVH with higher extracorporeal flow rates can be used.

Haemolipodialysis and haemoperfusion, used for toxin removal with a variety of agents (e.g., toramyxin for adsorbing endotoxin) are modifications of CRRT.

12.2 Sepsis
A common ‘non-renal’ indication for CRRT is in the management of severe sepsis. It has been shown that many, if not all of the septic mediators can be removed by CVVH (96, 97, 98), however the benefit on clinical outcome is less clear. Inflammatory mediators have a high generation rate and therefore studies have concentrated on the use of ‘high dose’ or ‘high volume’ haemofiltration (HVHF) with rates of more than 35 ml/kg/h.
Filtration therapies coupled with adsorption and plasmapheresis have also been applied in sepsis and septic shock.

After encouraging animal studies came a series of observational, interventional and small scale randomised (but uncontrolled) studies showing beneficial cardio-vascular effects (99, 100, 101 102, 103, 104) and an improvement in predicted hospital (99, 103) and 28-day mortality (100, 101, 102, 103). Volumes of 40-85 ml/kg/h were applied either continuously (99, 101), or for short, ‘pulsed’ periods of 6-8 hours (100, 102, 104). High volume haemofiltration has also been used as ‘rescue therapy’ for patients with severe septic shock unresponsive to other treatments, with encouraging results. (100,102). Large scale randomised controlled trials using high volume haemofiltration, adsorptive therapies or plasmapheresis are needed to confirm these results and to determine the most appropriate prescription.

12.3 Temperature control
The thermolytic effect of CRRT can be used to reduce pyrexia and the associated hyperdynamic circulatory responses encountered in such patients. This may help improve cardiovascular stability by reducing requirements for vasopressor support.

12.4 Fluid balance
The mainstay of treatment in heart failure is pharmacological but ‘functional renal insufficiency’ due to a low cardiac output may lead to diuretic resistance. Ultrafiltration has been used as an adjunctive treatment in heart failure and has been shown to have beneficial effects beyond the acute period of fluid removal (105).

CRRT has also been used in acute respiratory distress syndrome and paediatric cardiac surgery as a method of efficient optimisation of fluid status.

12.5 Acute liver failure
The molecular adsorbing recirculating system (MARS, PROMETHEUS) used in severe acute liver failure as a bridge to liver transplantation was developed from CRRT technology. A full discussion of this therapy is beyond the scope of this document.

12.6 Standard/recommendation

1. Many non-renal indications of CRRT are emerging but there needs to be more evidence before routine use in other clinical situations is recommended.
2. CRRT can be used to remove drugs or toxins however IHD will provide higher clearance rates. If IHD cannot be used due to availability or haemodynamic instability, CVVHDF or CVVH with higher blood flow and ultrafiltration rates can be used.
3. The use of haemofiltration, therapeutic plasma exchange or absorptive therapies as adjunctive treatments in severe sepsis have biological rationale (Grade D). Ultrafiltrate volumes of < 2L/h in adults are unlikely to provide benefit (Grade C), 35 ml/kg/h of ultrafiltrate production appears to be the minimum effective dose (Grade C) but higher doses may be needed.
4. If RRT is needed for AKI in a patient who also has severe sepsis, 35 ml/kg/h should be the minimum (Grade C). Initial studies are promising but further studies are needed before HVHF can be recommended for widespread use in cases of severe septic shock.
5. CVVH is better than PD for the treatment of AKI in septic patients (Grade C), and consensus is that CRRT is better than IHD for haemodynamically unstable septic patients (Grade E).
6. Ultrafiltration, with or without haemofiltration can be used to manage fluid overload, in particular in patients with severe cardiac failure.

13 Competences for health care workers

13.1 Areas of competency

Patient safety is of paramount concern as the delivery of CRRT poses a risk to the patients and the staff if the process is not managed correctly. Nursing and medical staff should understand the principles of RRT in general and CRRT in particular. The details and depth of this knowledge will vary with each class of HCWs. There are as yet no published guidelines for competencies in HCWs who routinely care for patients receiving CRRT in ICU. Suggested areas for training are as follows:

- Indications for RRT
- Principles of CRRT: methods of solute removal, extracorporeal flow rates, therapy prescription and fluid balance
- Anticoagulation methods, associated risks and appropriate monitoring
- Vascular access: method of insertion, catheter care, potential complications and methods of reducing complications
- Delivery of therapy: initiation, maintenance and termination of therapy
- Complications associated with RRT

13.2 Assessment of competency

There is no consensus on the minimum frequency of CRRT delivery that is optimal to maintain adequate competencies among staff. In absence of any consensus, it is suggested that, in order to maintain competencies among staff in an ICU, at least 25 patients (one patient every fortnight on average) should receive CRRT in any one year.

There should be enough HCWs with experience and competency to oversee education and training of staff new to the techniques. Methods for assessment of newly trained personnel, as well as ongoing education and training programmes for safe delivery of CRRT should be developed. Mechanisms should be in place to replace experienced staff that leave or move on to other areas or institutions.

In the absence of national guidelines, individual ICUs are encouraged to produce local protocols that are suitable to their needs.

13.3 Standard/recommendation

1. HCWs should have a degree of knowledge appropriate for their level of training and responsibility.
2. Areas for training include the principles of renal replacement therapy, provision and monitoring of anticoagulation, placement and surveillance of vascular access and complications associated with therapy. Practical skills will involve priming of the dialysis machine/filters, initiation, maintenance and termination of therapy.
3. All staff should be updated as hardware and consumables are changed or updated.
4. Individual institutions should establish their own guidelines, with protocols and educational and training programmes developed to suit local needs.
14 Special considerations in paediatrics

This document does not refer to CRRT for AKI in critically ill children and European guidelines for the use of renal replacement therapy in children are published elsewhere (106). Most adult intensivists, unless also trained in paediatric intensive care, will have little experience of RRT in children. Critically ill children requiring RRT for AKI should be transferred to a paediatric ICU as soon as possible for investigation and management.

AKI is uncommon in childhood and traditionally children have been treated with peritoneal dialysis, however extracorporeal therapies are increasingly being used. The choice of RRT modality will depend on clinical circumstances, patient location and local expertise.

If for some reason a child with significant compromise as a result of AKI cannot be transferred to an appropriate paediatric ICU, it may occasionally be necessary to provide CRRT for them in a general ICU setting. The vascular access and RRT equipment used for adult patients can be used safely in older children and adolescents, but in infants and small children specialised equipment is essential. The smaller the child, the greater is the need to pay meticulous attention to fluid balance. It is strongly recommended that such interventions should only be undertaken with appropriate support from paediatric intensivists/nephrologists.

14.1 Standard/recommendation

1. All critically ill children requiring CRRT for AKI should have early transfer to a paediatric ICU unless paediatric nephrologists are available on site to provide/oversee the appropriate therapy.

15 Management of patients after intensive care

The majority of survivors will recover their renal function and, although close monitoring (including that of renal function) is essential, they can be stepped down to general, medical or surgical, high dependency units (HDUs). In selected cases, a referral to nephrologists before discharge from ICU may be appropriate. In a smaller proportion of patients, especially those with residual renal dysfunction, those with slow recovering renal function or those in whom renal function has not recovered at all nephrological referral well before discharge from ICU may be appropriate. Such patients should be cared for in nephrology step down areas (renal HDU) or other HDUs under nephrology supervision. The precise arrangements will vary from institution to institution and depend on local needs, access to nephrology services and available resources.

15.1 Standard/Recommendation

1. Survivors of AKI should be appropriately stepped down depending on the state of return of their renal function. Those requiring on-going renal support should be referred early to nephrologists.

16 Conclusion
16.1 Overview
Although AKI in the critically ill remains imprecisely defined and efforts are underway to develop a universal system of classification/definition based on measurement of creatinine and urine output. Multiple aetiological factors are responsible for causing AKI and the propensity of AKI developing increases when, in addition, one or more risk factors are present. Toxic (or drug induced) AKI is being increasingly recognised. There are no pharmacological agents that prevent or modify the course of AKI but adequate oxygenation, fluid resuscitation and optimising organ perfusion by correcting haemodynamic and/or cardiac output deficiencies are all important in preventing AKI. There are no established criteria for the point at which RRT should be initiated, but if renal impairment cannot be reversed reasonably early, RRT should be started earlier rather than later.

Although CRRT appears to be beneficial in terms of patient outcomes and renal function recovery (Grade C), there is no ‘Grade A’ evidence as to whether continuous therapies are superior to intermittent therapies. Most clinicians preferentially assign haemodynamically unstable patients to CRRT and it is the preferred modality of RRT in the critically ill in the UK. CRRT offers haemodynamic stability, is generally well tolerated and allows control of fluid balance as well as effective biochemical control; it has other advantages in the critically ill as well. As yet here are no clear benefits from predominately convective therapies over predominately diffusive therapies with many clinicians preferring to use a combination of both methods for solute removal. Further work is being done considering the benefits of high dose convective therapy in the subgroup of septic patients with AKI. We also await the results from further studies to answer the questions regarding optimal dose of therapy, and with that, the best method of assessing dose delivery.

Lactate-based replacement fluids are as effective as bicarbonate-based fluids except in conditions where liver function is compromised but there is little evidence that either kind of fluid has survival advantage. UFH is the most commonly used anticoagulant but LMWHs and prostacyclin are also effective. Citrate anticoagulation is gaining popularity in the UK but experience in its use is currently limited, and caution is required because of its high risk of metabolic complications. Drug dosages in patients receiving CRRT require special consideration as those extrapolated from regimens developed for patients with chronic renal failure or dialysis-dependent renal failure may result in serious under dosing.

Meticulous care of vascular access, care in circuit priming and optimal anticoagulation are essential to prevent circuit clotting and treatment interruptions. Institutions undertaking CRRT should develop competencies required in their HCWs based on local service provision, and have mechanisms in place for education, training and assessment.
References

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