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Renal Replacement Therapy in Acute Renal Failure

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Introduction

Acute renal failure (ARF) is defined as an abrupt decrease in renal function sufficient to result in retention of nitrogenous waste in the body. There is no consensus on the degree of rise of serum creatinine or blood urea nitrogen required to define acute renal failure, however commonly used definitions include doubling of serum creatinine from baseline, 30% rise in serum creatinine from baseline and need for renal replacement therapy or dialysis[1,2].

Serum Cystatin C appears to be a better marker than serum creatinine for detecting smaller increments in glomerular filtration rate however it has not been validated in acute renal failure in a prospective trial.[3]

The incidence of ARF varies depending on the setting. ARF occurs particularly in high incidence in seriously ill hospitalized patients. The overall mortality increases manifold in patients who develop ARF as compared to matched controls without ARF[4].

Etiology of acute renal failure

Traditionally ARF has been classified as

Pre renal (usually functional)

Renal (structural) and

Post renal: site of obstruction can vary from intra renal to urethral depending on the pathology.

Acute renal failure is a potentially reversible condition and the exact determination of etiology and treatment directed towards it improves the prognosis.

The role of good clinical examination followed by urine analysis, urine biochemistry, imaging studies and in select cases serologic tests and kidney biopsy to determine the etiology of acute renal failure cannot be overstated.

Clinical settings including multiple organ failure, older age, sepsis, postoperative status, trauma, burns, HIV infection, non-renal solid organ transplantation, heart failure, malignancy, liver diseases and rhabdomyolysis increase the chances of ARF and it is imperative to monitor renal function closely in these settings.

Complications of ARF

Determination of rate of occurrence of complications in patients with ARF is sometimes difficult. However the chances of cardiovascular complications including volume overload, congestive heart failure, cardiac tamponade, and hyperkalemia induced cardiac arrest are increased in ARF.[4,5,6]

Other complications of acute renal failure include respiratory failure, upper gastrointestinal bleeding, anorexia, vomiting, acute pancreatitis, anemia, coagulation abnormalities, neurological complications and sepsis.[4,7]

Conservative treatment of acute renal failure

The principles include

- Exclude reversible/ treatable causes of acute renal failure
- Maintain euvolemia
- Monitor drug dosages and modify drug dose/ dosing intervals according to renal function assessment.
- Maintain adequate nutrition
- Monitor and treat for clinical and biochemical complications
- Institute renal replacement therapy (RRT) when appropriate.

Renal replacement therapy in acute renal failure

The issues regarding renal replacement therapy in ARF are the source of much debate and investigation. The main questions that need to be answered include:

- When to start RRT
- Choice regarding modality of RRT
- Choice of dialyser membrane
- Dose of dialysis

When to start RRT?

Absolute indications for initiation of dialysis include persistent hyperkalemia, fluid overload resulting in pulmonary edema, ongoing marked acidemia, uremic pericarditis and encephalopathy. However a general trend towards earlier renal replacement therapy has occurred over the past decade based on recent studies.

In a prospective study of cardiac surgical patients, 61 patients were randomized to early or late dialysis. Early was defined as oliguria unresponsive to diuretics and late was defined as serum creatinine greater than 5 mg/dl and /or serum potassium greater than 5.5 meq/lt. It was found that the early group stayed less in ICU (7.9 versus 12 days) and had lower mortality (23 versus 55%).[8] In another retrospective trial of 100 trauma patients with ARF, It was found that a lower BUN at initiation of dialysis was associated with earlier commencement of dialysis and better survival[9]. The earliest data that indicated early dialysis to be superior was from Conger et al published in Journal of trauma in 1970. It was a randomized prospective trial that established that early and frequent dialysis leads to improvement in mortality and also decreases complications as sepsis and hemorrhage in addition to decreasing the hospital stay[10].

However there are some studies that have failed to establish the superiority of early dialysis. One study of critically ill 132 patients with ARF found an inverse relationship between serum creatinine at initiation of hemodialysis and increased mortality[11].

Some other clinical advantages of starting dialysis early include ease of optimizing fluid volume balance and nutritional status in ICU patients with ARF.

Choice regarding modality of RRT

Generally available modes of therapy include conventional intermittent hemodialysis (IHD), Slow low efficiency daily dialysis (SLEDD), Intermittent and continuous peritoneal dialysis (PD), Continuous arterio venous hemofiltration (CAVH), continuous arteriovenous hemodialysis (CAVHD), continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD) and continuous venovenous hemo dia filtration (CVVHDF)

There has been a trend for more use of continuous therapies and less of IHD. PD has fallen out of favor due to problems with peritonitis following peritoneal catheter insertion and the fact that relative efficiency of PD as compared to IHD as regards solute removal is only 10 to 20%.

Factors that are considered in choosing between different modalities include availability of necessary equipment, expertise demanded by the modality, cost, hemodynamic status, indication for therapy and the speed with which the indication needs to be corrected, availability of vascular access, issues regarding anticoagulation and associated clinical conditions of the patient.

The comparison of different modalities of RRT are shown in the Table 1.

Because of difficulties precisely matching seriously ill patients with ARF, a clear-cut consensus regarding CVVHD versus IHD as preferable mode of therapy has not evolved. It is likely that patients with ARF are best served by considering these modalities as complementary than competitive.

A randomized prospective trial of 166 patients by Mehta et al comparing CVVHD to IHD failed to show significant differences in mortality between the two groups[12]. Two systematic reviews by Tonelli et al and Kellum et al[13,14] failed to show any difference between intermittent and continuous therapies, however after adjusting for study quality and severity of illness Kellum et al found a decreased relative risk of death with continuous therapies.

The choice between CVVH and CVVHD, which are the commonly practiced continuous modalities, is an open question. CVVH works primarily by convection while CVVHD works primarily by diffusion. The proposed benefit of CVVH in cytokine removal and hence its superiority in treatment of sepsis has not been established beyond doubt. The counter argument that both good and bad cytokines are removed has not been refuted. CVVH is much more expensive due to the large amount of replacement fluid needed.

Differential methodologies, small numbers of patients, study flaws, lack of standardized approaches to timing and indication of dialytic intervention make comparisons difficult between therapies.

Newer modalities of dialysis that has emerged incorporating advantages of hemodynamic stability of CRRT coupled with high rates of solute and fluid removal of IHD is SLEDD (slow low efficiency daily dialysis). SLEDD offers better fluid control and more removal of solute than IHD and

Table 1 : Comparison of different RRT

Type of RRT	Advantages	Disadvantages
PD	Simple to perform Inexpensive No need of anticoagulant therapy Useful in remote areas	Technical problem due to paralytic ileus which is frequent Less efficient regarding solute removal High risk of infection
IHD	Simple to perform Inexpensive Efficient Can be performed without anticoagulation	Not suitable for hypotensive patients Risk of hemorrhage and hypotension
SLEDD	Simple to perform Less expensive Very efficient Better suited for hypotensive patients	Needs anticoagulation Dedicated ICU staff and technicians required
CAVHD	Simple to perform Requires no machine Efficient	Need arterial and venous catheter insertion Cannot be used in hypotension Risk of air embolism Rarely used in clinical practice today
CVVH	Efficient Enhanced removal of solute as it works by convection Claimed to be superior in septic patients	Needs dedicated machine and anticoagulation Expensive due to large amount of replacement fluid needed
CVVHD	Efficient Can be used with hypotension Less expensive than CVVH	Needs dedicated machine and anticoagulation Expensive than SLEDD and IHD

compares favorably with CRRT as regards patient outcomes[15,16]

Choice of dialyser membrane

The cellulosic membrane used in dialysis provides a trigger for complement activation via the alternative pathway, which leads to liberation of anaphylotoxins and activation of leucocytes. Meta analysis done by comparing different trials using cellulosic membranes versus biocompatible synthetic membranes have shown conflicting results. However, in a randomized trial of 72 patients Hakim et al compared treatment with cuprophane dialysis membranes to polymethyl methacrylate (PMMA), which has less effect on complement activation. The dialyser membranes chosen had similar clearance and ultra filtration characteristics. 57% of patients on PMMA survived as compared to 37% on cuprophane. Also with PMMA, the time to recovery was shortened.[17] This suggests that biocompatible membranes increase the likelihood of recovery from ARF and also improve survival of patients with ARF.

Dose of dialysis

How much dialysis should be provided to improve outcomes of ARF has been an area of debate. Schiffl et al[18] randomized 160 patients to daily HD versus alternate day HD. Patients perceived to require CRRT due to hemo dynamic instability were excluded. It was observed that daily HD improved patient survival (28% vs. 46%), decreased time to recovery from ARF (9 days vs. 16 days), and also significantly decreased complications as sepsis, respiratory failure, changes in mental status and gastrointestinal bleeding.

Ronco et al[19] studied 425 patients with ARF commencing CVVH, randomly assigning them to ultra filtration at 20 ml/hr/kg, 35 ml/hour/kg or 45 ml/hour/kg. He observed that survival was lowest in the group that received CVVH at 20 ml/hour/kg. However no statistically significant difference was observed between groups who received CVVH at 35 and 45 ml/hour/kg. With this evidence it is now accepted that renal and patient survival is improved by providing increased dose of dialysis.

Summary

ARF is a common problem particularly in tertiary care hospitals and intensive care units. It is important to diagnose ARF and a search for etiology should be instituted. ARF is a potentially curable condition hence urgency should be exercised in diagnosis and treatment.

Renal replacement therapy in ARF constitutes an important part of its management till renal recovery is established. Starting RRT early helps in improving patient and renal survival and also helps in avoiding complications of ARF and also helps optimizing fluid balance, better control of acidosis and allows better nutritional supplementation. There is no clear consensus on the choice of dialytic modality hence a complementary and not competitive usage of the different modalities is recommended till this debate is resolved.

The patient should be dialyzed with a synthetic biocompatible membrane and the dose of dialysis should be increased irrespective of which modality has been chosen as this has shown to decrease patient mortality. SLEDD is emerging as a good mix of intermittent and continuous therapies and has the potential to be the modality of choice in the future.

Future advances in RRT in management of ARF include the development of bio artificial kidney, which combines hemofiltration with a renal assist device containing human tubular epithelial cells and is currently in clinical trials. In bio artificial kidney an attempt is made at providing synthetic function in addition to the excretory function of the kidney.[20]

References

1. Bellomo R: Effects of different doses in continuous veno-venous haemofiltration on outcome of acute renal failure: A prospective randomized trial. *Lancet* 2000; 355:26.
2. Vincent, Jean Louis et al: Use of the SOFA score to assess

the incidence of organ dysfunction/failure in the intensive care units: Results of a multi center prospective study. *Critical care medicine*: 1998 Nov;26:1793 –1800.

3. Coll E, Botey A et al: Serum Cystatin C as a new marker for non-invasive estimation of Glomerular filtration rate and as a marker for early renal impairment. *Am J Kidney diseases* 2004; 36:29.
4. Levy EM et al: The effect of acute renal failure on mortality, a cohort analysis. *JAMA* 1996; 275:1489.
5. Hou SH et al: Hospital acquired renal insufficiency: a prospective study. *Am J Med* 1983; 74:243.
6. Baldwin JJ et al: Uremic pericarditis as a cause of cardiac tamponade. *Circulation* 1976; 53:896.
7. Fiaccadori E et al: Incidence, risk factors and prognosis of gastrointestinal hemorrhage complicating acute renal failure. *Kidney Int* 2001; 59:1510.
8. Demerkilic et al: Timing of replacement therapy for acute renal failure after cardiac surgery. *J card surg* 2004; 19:17.
9. Gettings LG et al: Outcome in posttraumatic acute renal failure when continuous renal replacement therapy is applied early versus late. *Intensive Care Med* 1999; 25: 805.
10. Conger JO et al: Journal of Trauma 1970; 15: 1056.
11. Chertow GM et al: Intensity of dialysis in established acute renal failure: *Seminars Dialysis* 1996; 7: 476.
12. Mehta RL et al: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. *Kidney Int* 2001; 60:1154.
13. Tonelli M et al: Acute renal failure in the intensive care unit: A systematic review of the impact of dialysis modality on mortality and renal recovery. *Am J Kidney Dis* 2002; 40: 875.
14. Kellum JA et al: Continuous versus intermittent renal replacement therapy: a Meta analysis. *Intensive Care Med* 2002; 28:29.
15. Vanholder R et al: What is the renal replacement therapy of first choice for intensive care patients? J Am Soc Nephrol 2001; 12(suppl 17): S 40.
16. Marshall MR et al: Sustained low efficiency daily dia filtration (SLEDD-f) for critically ill patients requiring renal replacement therapy: towards and adequate therapy. *Nephrol Dial Transplant* 2004; 19:877.
17. Hakim et al: Effect of the dialysis membrane in the treatment of patients with acute renal failure. *N Engl J Med* 1994; 331: 1338.
18. Schiffl et al: Daily haemodialysis and the outcome of acute renal failure. *N Engl J Med* 2002; 346: 305.
19. Ronco C et al: Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomized trial. *Lancet* 200; 356: 26.
20. Humes HD et al: Initial clinical results of the bioartificial kidney containing human cells in ICU patients with acute renal failure. *Kidney Int* 2004; 66(4): 1578.