ACUTE RENAL FAILURE

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Introduction

Acute renal failure (ARF) is seen commonly in the perioperative period and in the ICU.[1] It is associated with a high morbidity and mortality (oliguric 50-80% and non oliguric 10-40%).[2] It is therefore imperative to either prevent its occurrence or recognize its presence and treat it as soon and as efficiently as possible.

Definition of renal dysfunction and it's diagnosis[1,2]

Urinary output

Traditionally oliguria is defined as a urine output of less than 0.5 $mlkg^{-1}hr^{-1}$ or 400 $mlday^{-1}$. Anuria is defined as less than 50 ml per day (check that the Foley's catheter is not blocked). However, a reduction in the urine output need not necessarily mean renal failure. It may just be an external sign of an underlying process such as hypotension and hypovolemia which needs correction. Restoration of blood pressure and blood volume may increase the urine output showing that the kidney is in perfect condition.

Urinalysis. The presence of blood may suggest the presence of an embolic phenomenon and a large number of casts acute tubular necrosis. Also look for protein and myoglobin. However, 'dirty' results on urinalysis are common in critically ill patients.

Blood Urea Nitrogen (BUN) is the breakdown product of protein and in the presence of acute renal failure it typically rises by about 10 -15 $mgdl^{-1}day^{-1}$. However it must be remembered that the BUN level varies directly with protein intake and increases in the presence of gastrointestinal bleeding, sepsis and corticosteroid administration (and falls in starvation, malnutrition, muscle wasting and liver disease). Thus interpretation of BUN values must rely more on the change over time rather than on absolute values taking into account concomitant conditions such as those mentioned above as well as other measures of renal failure.

Creatinine is the breakdown product of muscle and its level rises by 1 to 2 $mgdl^{-1}day^{-1}$ in acute renal failure. Its absolute value and change over time is a much more reliable indicator of underlying renal function than the BUN levels. (Values higher than 2 $mgdl^{-1}day^{-1}$ may be seen in rhabdomyolysis)

Creatinine Clearance. Normal creatinine clearance is 120 $mlmin^{-1}$. A crude estimation of the creatinine clearance may be obtained by the following formula.

$$\text{CrCl (ml/min)} = \frac{(140\text{-age}) \times \text{weight(kg)}}{72 \times \text{serum Cr (mg/dl)}}$$

This equation is simply the ratio of the expected amount of muscle breakdown (taking age and weight into account) to the breakdown product present in the serum multiplied by a 'fudge factor' of 72. Women being smaller the resulting value is multiplied by 0.85 for females. However in acute renal failure with rapidly failing kidneys this formula may overestimate creatinine clearance and a more accurate estimation is required. This may be done by collecting urine over a period of time, usually 24 hours but in the ICU situation even 2 hours has been shown to yield accurate results and may be more practical ads well [3]. The following equation is then used

$$\text{CrCl (ml/min)} = \frac{\text{Urine [Cr](mg/dl)} \times \text{volume(ml/min}}{\text{Plasma [Cr] (mg/dl)}}$$

Urine sodium and osmolality. When perfusion of the kidneys is reduced, sodium reabsorption increases and excretion decreases and a urine sodium of less than 20 $meqL^{-1}$ results (urine osmolality >400 $mosmolkg^{-1}$). This may occur in hypovolemia due to dehydration or haemorrhage, or from decreased forward flow as is seen in patients with cardiac failure. Urinary sodium concentrations of less than 10 $meqL^{-1}$ may be seen in patients with hepatorenal syndrome or very severe hypo perfusion.

When there is an acute injury to the kidney, as in acute tubular necrosis, sodium reabsorption is impaired and there is an increase in sodium excretion resulting in urinary sodium levels of greater than 20 $meqL^{-1}$ or even greater than 40 $meqL^{-1}$ (urine osmolality <400 $mosmolkg^{-1}$).

Note that the above numbers are meaningless if diuretics have been given, Occasionally a combination of factors like hypovolemia in addition to chronic renal failure

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may make the interpretation of urinary sodium levels difficult. In these cases fractional excretion of sodium may help determine whether the cause is renal or prerenal.

Fractional Excretion of Sodium

$$Fe\ Na = \frac{Urine\ [Na] / plasma\ [Na]}{Urine\ [Cr] / plasma\ [Cr]} \times 100$$

A fractional excretion of sodium of less than 1% occurs in prerenal failure (hypovolemia and cardiac failure) and that of more than 2% in renal failure (e.g. acute tubular necrosis)

Abdominal ultrasound can help differentiate chronic causes (small kidneys hypertension and chronic renal failure, normal or large kidneys diabetes and amyloidosis) and obstructive causes (large dilated pelvis and ureters). It can also estimate renal perfusion using Doppler ultrasound.

Nuclear scans are useful in case of suspected embolus or vascular compromise.

Causes[1] (Table 1)

Pre renal

Hypoperfusion due to any cause makes the kidney concentrate urine, decreases the urine output and causes the BUN and creatinine to rise. The BUN level usually, but not always, rises out of proportion to the creatinine level and a ratio of 20:1 is achieved. Therefore prerenal failure is most often not a failure at all but a normal response on the part of the kidney to an inadequate perfusion. Common causes include hypovolemia, congestive cardiac failure and extreme vasodilation. Treating the precipitating cause may rapidly and completely reverse the rise in BUN and creatinine levels. Genuine renal injury may only occur if there is a superimposed insult like exposure to a nephrotoxic agent.

Table - 1[3] : Investigations to help differentiate pre renal and renal causes of renal failure

Investigation	Pre renal	Renal
Urinary sodium ($meqL^{-1}$)	< 20	> 40
Fractional excretion of sodium (%)	< 1	> 2
Urine osmolarity ($mosmL^{-1}$)	> 400	250 – 300
Urine creatinine/plasma creatinine	> 40	< 20
Urine/plasma osmolarity	> 1.5	< 1.1

Serum Potassium may be elevated

Renal or intrarenal renal failure classically falls into 3 categories: Tubular failure (including acute tubular necrosis), interstitial nephritis and glomerulonephritis and vasculitis. However, it is probably more helpful to classify intrarenal failure according to the causes of renal damage as enumerated in Table 2.

Post renal

This occurs when there is an obstruction to renal flow anywhere distal to the pelvis. Obstruction is always the most likely diagnosis when there is anuria.

For this to occur both ureters, or the urethra should be obstructed. It is commonly seen in patients with retroperitoneal or pelvic pathology and abdominal ultrasound is a good diagnostic tool. Do remember to check the patency of the Foleys catheter.

Table - 2[4] : Causes of oliguria

Pre renal	Renal	Post Renal
Hypovolemia	Hypoxia	Bladder neck obstruction
Hypotension	From pre renal causes	Blocked drainage system
Poor cardiac output	Renal vein thrombosis	Pelvis surgery
Pre existing renal damage	Nephrotoxins	Prostatic enlargement
Renal vascular disease	Aminoglycosides	Raised intra-abdominal pressure
Renal vasoconstriction	Amphotericin	Renal or ureteric
Sepsis	Chemotherapeutic agents	Calculi
	NSAIDS	Clots
	Contrast media (beware in diabetes and multiple myeloma)	Necrotic papillae
	Tissue injury	
	Haemoglobinuria	
	Myoglobinuria	
	Uric Acid (tumour lysis)	
	Inflammatory nephritides	
	Glomerulonephritis	
	Interstitial nephritis	
	Polyarteritis	
	Myeloma	

Perioperative considerations

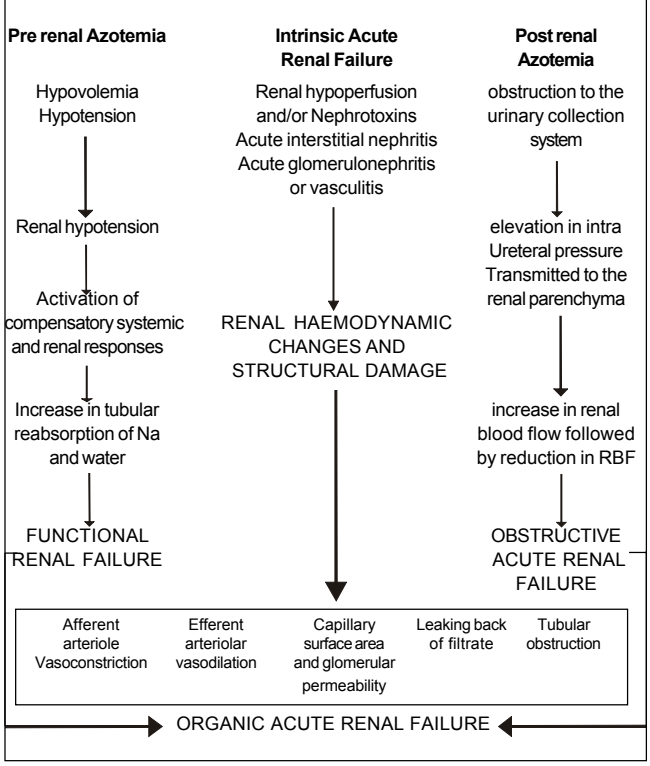
It is important to understand the *pathogenesis of renal failure*. Though the kidneys receive 25% of the cardiac output, they only get 10% of the total body oxygen uptake. Renal autoregulation does take care of the GFR over a wide range of blood pressures and glomerular ultra filtration is a balance between vasodilators and vasoconstrictors. However, of the blood that the kidneys receive the glomeruli receive 90-95% while the medulla only receives 5-10%. Oxygen extraction on the other hand is much greater in the medulla due to active water and salt

reabsorption. Thus the medulla is more prone to hypoxic damage.

The occurrence of perioperative renal failure depends upon the surgery, preoperative and intraoperative haemodynamics and renal conditions (diabetic patients have a 10 fold greater risk of renal deterioration in the presence of hypovolemia). All intravenous and volatile induction agents affect renal function by decreasing cardiac output and blood pressure. Extradural block (or high spinal) up to the level of T4 reduces sympathetic tone to the kidneys, resulting in a decrease in RBF and GFR. Mechanical ventilation with positive pressure also decreases renal blood flow. Major surgery with extensive third space losses can lead to hypovolemia and renal hypoperfusion.

Thus the progression of renal failure may take one of three paths as seen in Fig. 1. Exclusion of pre renal and post renal causes make intrinsic renal failure the most likely cause. This is often associated with an increased morbidity and mortality.

Fig - 1[4] : Pathogenesis of Acute Renal Failure



Risk factors for developing renal failure[2] The successful prevention of perioperative ARF depends on the identification of patients who are at risk for developing ARF as seen in Table 3.

Table - 3 : Risk Factors

Patient factors	Perioperative factors
Advanced age	Hemodynamic instability- hypotension
Major vascular surgery (AAA)	Hypovolemia (oliguria)
Atherosclerosis	Diuretic therapy
Coronary artery bypass and other cardiac surgery	Surgical oedema
Hypertension	Preoperative starvation
Congestive cardiac failure	Gastric aspiration/vomiting
Biliary surgery / jaundice	Peritonitis/ileus/obstruction
Chronic renal disease	Diarrhoea/bowel preparation
Cirrhosis liver	Prolonged tissue exposure
Diabetes mellitus	Blood loss
Myeloma	Hypoxia
Nephrotoxic drugs	Tissue damage and inflammation
Pre-eclampsia /eclampsiaSepsis	Ischaemia and reperfusion
	Major burns
	Polytrauma
	Muscle breakdown
	Pancreatitis
	Massive blood transfusions and Transfusion reactions

Physical examination and preparation for surgery

Check the adequacy of hydration, cardiac output and blood pressure. Also look at the daily intake and output charts.

Use a large bore cannula for intravenous fluid resuscitation and administer oxygen. Essential preliminary monitoring includes an electrocardiogram, noninvasive blood pressure monitoring and pulse oximetry. Invasive arterial monitoring and central venous pressure monitoring should be then considered. Echocardiography and pulmonary artery wedge pressure monitoring are helpful, if available.

Shift to the ICU for monitoring and preoperative stabilization if required.

Prevention of further deterioration of renal function and maintenance of adequate renal output (1-2 ml per kg – non oliguric renal failure) [2]

Preoperative rehydration is essential especially in those patients who are significantly dehydrated e.g. those with large bowel obstruction or sepsis. Aim to measure and maintain the CVP at 10-15 cms. H_2O. The response to a fluid bolus (250-500 ml of normal saline) over 10–15 minutes may help to differentiate between hypovolemia per se and acute tubular necrosis, while more invasive monitoring is got ready (CVP, Pulmonary artery catheterization and echocardiography may be required.) Some authors suggest that we aim to maintain a mean arterial blood pressure of at least 50 mmHg, which is the lower limit for renal autoregulation.[1] But most authors suggest maintaining a higher blood pressure – a mean

of >70 mmHg in normal patients and >85 mmHg in hypertensive patients[2] using ionotropes if necessary.

- If intra abdominal pressure is raised more than 20 mmHg (normal 0-17 mmHg) anuria can result from direct compression on the renal pelves.[5] This is seen in 30% of emergency laparotomies and is very common after massive intra abdominal bleeding such as leaking abdominal aortic aneurysms, intestinal distension, paralytic ileus and ascitis. Improvement in renal function only occurs after decompression. The probable mechanisms for a decrease in cardiac output and thus the GFR in these cases are as follows: reduced venous return, compression of the renal vein with reflex renal artery vasoconstriction, elevation of renal tubular pressure with a decrease in the filtration gradient and an increase in rennin, aldosterone and ADH production.

Intra abdominal pressure may be measured via the bladder. Instill 50 ml saline into the bladder via a Foley's catheter, clamp it off and measure the manometric pressure of the fluid within the bladder via a needle inserted into the catheter lumen

Raised intra abdominal pressure may also give rise to a false high CVP leading to under filling of the patient.

- On first recognition of deteriorating renal function immediately eliminate or appropriately reduce the dose of nephrotoxic drugs like gentamicin and vancomycin (measure levels where possible) and change amphotericin to fluconazole if possible.

Table - 4[5] : Nephrotoxins and nephrotoxic drugs, which could precipitate renal failure .

Nephrotoxic drugs	Nephrotoxins
Ace inhibitors	Haemoglobin
Aminoglycosides	Myoglobin
Amphotericin	Bilirubin
Aspirin	Uric acid
Cisplatin	
Cyclosporines	**Assoc. with crystal production**
Low molecular weight Dextrans	Acyclovir
Non steroidal anti inflammatory drugs	Methotrexate
	Indinivir
	Triamterene

- If the blood pressure is normal and hypovolemia is not an issue drastically cut down on the IV fluid therapy, thereby preventing a fluid overload.
- The use of dopamine and diuretics remains controversial (refer later)
- Reduce the administration of acid (commonly administered in the form of 0.9% sodium chloride solution which has a pH of 5), potassium, magnesium and phosphates in maintenance IV and enteral feeds.

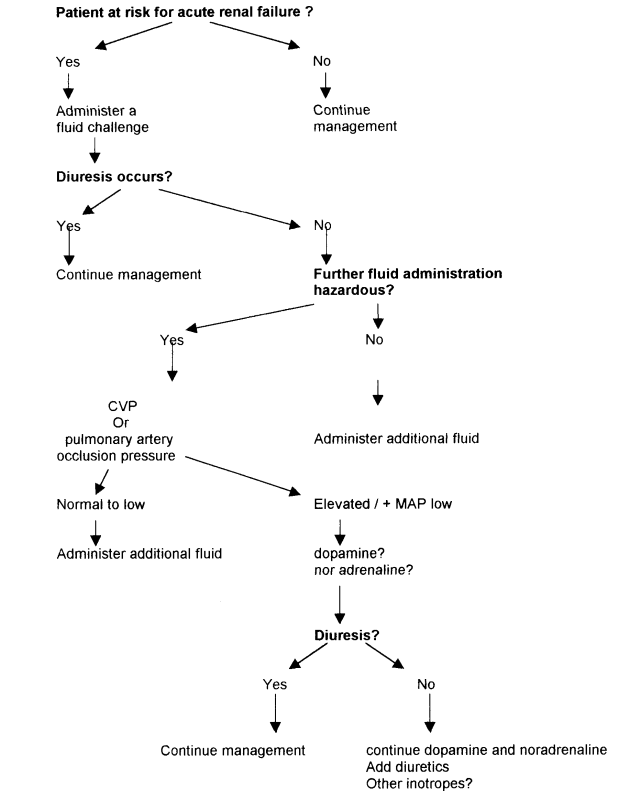


Fig. 2 : Treatment algorithm for management of acute oliguria during the perioperative period[4,7-14]

- Avoid NSAIDs in the post op period
- Start enteral feeds as early as possible and maximize enteral nutrition, as there is now evidence that outcomes are better in patients on enteral rather than parenteral nutrition.[1]

Other management issues

Use of diuretics

The rationale for their use rests on the assumption that they decrease oxygen consumption in the tubular cells by inhibiting trans cellular sodium transport and thus prevents ischemic cell injury. In addition, loop diuretics may vasodilate cortical vessels and improve oxygenation. Finally augmentation of tubular blood flow may reduce intratubular obstruction and back leak of filtrate thus rapidly accelerating resolution of ARF.[6] However, in patients with established ARF several studies have shown no benefit of loop diuretics.[7,8]

It is believed that the outcome of non-oliguric renal failure is better than oliguric renal failure. However, in a

recent retrospective survey of critically ill patients with ARF diuretic use was associated with an increased risk of death and non recovery of renal function.[9] The authors suggested that the adverse outcome was due to either direct deleterious effects of diuretics or indirect effects owing to a delay in the recognition of the severity of ARF and institution of dialysis support.[9,10] Other authors believe that diuretics may also prove harmful as frusemide can cause interstitial nephritis and hearing loss.[1]

Therefore, diuretics should be used cautiously in critically ill patients and no patient should be given furosemide unless they are adequately filled and the systemic arterial pressure is adequate as an already damaged kidney may be profoundly injured by a relatively mild decrease in perfusion pressure.[6] Frusemide has been given in a bolus of 20 – 40mg. In patients with established renal insufficiency (raised serum creatinine) and sustained oliguria this treatment should be withdrawn.[6] However, in responders 250 mg may be given as an infusion over an hour[2] as infusions are more effective and less toxic than bolus doses.[10] Mannitol 0.5 to 1gkg^{-1} may also be given[2]

Use of Dopamine

Low dose dopamine (1 to 3 ¼gkg^{-1} per min) increases diuresis and natriuresis in healthy experimental animals and humans. These effects are not seen uniformly in the critically ill.[11,12,13] However after extensively reviewing the data available the same authors came to the conclusion that the use of dopamine in renoprotective doses should be abandoned as there was no evidence supporting its effectiveness in preventing ARF and it should not be used as a panacea for oliguria. In addition, dopamine can precipitate serious cardiovascular and metabolic complications such as depression of the respiratory drive, triggering of tachyarrhythmias, causing myocardial ischemia, accelerating intestinal ischemia, depression of anterior pituitary hormones and decreased T-cell function[6,11,12,13]

Noradrenaline[14]

It markedly improves mean arterial pressure and glomerular filtration. This is especially seen in high output-low resistance septic shock. Urine flow reappears with restoration of systemic haemodynamics and renal function improves without the use of low dose dopamine or frusemide. This fact supports the hypothesis that renal ischaemia observed during hyperdynamic septic shock is not worsened by nor adrenaline infusion and even suggests that this drug may effectively optimize renal blood flow and renal vascular resistance.

Adrenaline In patients who fail to respond to fluid administration and other vasopressor adrenaline can increase arterial pressure primarily by increasing cardiac index and stroke volume. However, adrenaline has detrimental effects on splanchnic blood flow and causes transient decreases in pHi and increases the PCO_2.[14]

Dobutamine may be used to improve cardiac output. However, it causes peripheral vasodilatation and is usually used along with noradrenaline.

The use of *Fenoldopam* is also controversial

Calcium channel blockers.[5] During ischaemia, calcium channels open resulting in vasospasm. It is believed that calcium channel blockers exert direct vascular effect with preservation of renal autoregulation and enhanced recovery of RBF, GFR and natriuresis among other effects. However it must be remembered that calcium channel blockers in high doses may compromise the haemodynamic status in critically ill patients.

Specific pharmacological treatments[6] have been used in cases of acute renal failure associated with sepsis. Examples of these include Anti-TNF-± therapy, inhibition of platelet-activating factor, inhibition of nitric oxide synthase, endothelin antagonism, inhibition of arachidonic acid metabolism, natriuretic peptides, inhibition of leukocyte adhesion, inhibition of coagulation and growth factors – the details of whose use is beyond the scope of this article

Emergency management of raised serum potassium[2]

Treatment should be initiated if the serum potassium is > 6.5 mmol.L or ECG changes are present. Intervention is important as cardiac compromise may occur.

Table - 5 : Treatment of hyperkalemia.

Treatment	Mechanism of action	Onset of effect	Duration of action	Side effects
Calcium – IV Gluconate 5-10 ml of 10% solution- Chloride 3-5 ml of 10% solution	Directly antagonizes effects of potassium on the heart	Immediate	Brief	Avoid if being treated with digitalis
Insulin 15 U actrapid in 100ml 20% dextrose over 30 – 60 mins	Shifts potassium into cells	Prompt	4-6 hours	Hyperglycaemia, Hypoglycaemia
Beta agonist salbutamol 5 mg nebulized	Shifts potassium intracellularly	Prompt	Short	Requires nebuliser
Sodium bicarbonate 50-100 meq IV esp. if acidotic	Shifts potassium into cells	Prompt	short	Possible sodium overload
Ion exchange resin Calcium resonium 15G PO/30G PR 8 hrly	Removes potassium from the body	1-2 hours		Sodium overload
Dialysis or haemofiltration	Removes potassium from the body	Prompt		Requires vascular access

Other complications of renal failure include severe metabolic acidosis which is dealt with by dialysis

Dialysis

Dialysis may be emergent or elective. The indications for dialysis are volume overload, hyperkalemia, severe acidosis, and uremia (with a change in mentation, pericarditis, pleuritis or bleeding). Emergency dialysis is rarely required in hospitalized patients .In the ICU set up BUN and creatinine clearance is assessed daily and dialysis is usually started when the BUN level exceeds 100 $mgdl^{-1}$ or the creatinine clearance is less than15 $mlmin^{-1}$. (these figures are arbitrary and vary from center to center).

There are four contemporary modes of dialysis:

- Peritoneal Dialysis (PD, not usually considered in the post operative general surgical patient with abdominal pathology or respiratory compromise).
- Hemodialysis (HD, difficult to do especially in the hypotensive post operative or septic patient, requiring vasopressor support).
- Continuous Arterio Venous Hemofiltration (CAVH, relies on an adequate pressure head, has no external apparatus to control flow or provide warning and requires the insertion of a wide bore catheter into an artery which may result in bleeding, an aneurysm, thrombosis and clot formation).
- It has been largely replaced by Continuous Veno Venous Hemofiltration CVVH, is a slow method of solute and fluid removal, results in a largely haemodynamically stable milieu and can remove a large quantity of cytokines which may reduce the incidence or progression of multi-organ failure. The newer machines have improved safety features such as an air detector and a pressure monitor. They do however require one on one nursing and frequent, 4-6 hourly, potassium assessment. They are capable of removing upto 10 litres of fluid at one sitting and is often helpful in weaning from mechanical ventilation and shortening ICU stay.[1]

Prescribing common drugs in renal failure[1]

All medications prescribed for these patients should be reviewed and dose adjusted to accommodate the decreasing renal function and the effects of dialysis. Failure to do this may result in drug toxicity or further damage to the kidney.

Drugs most commonly used in the ICU, which will require adjustment, include penicillins, carbipenems, cephalosporins, vancomycin, aminoglycosides, amphotericin, digoxin, and some muscle relaxants. Anaesthetists should remember that though opioids and benzodiazepines are metabolized by the liver the excretion of their active metabolites are by the kidney and thus a reduction in dose is often necessary.

Summary

Acute renal failure is a common and in many cases it is a preventable and/or eminently treatable problem seen in the operation theaters and intensive care units and the physician treating the critically ill patient should be well versed in the diagnosis and management of renal failure.

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