Numerous papers highlight the lack of a universal definition for ARF in ICU. One review of the subject found 26 different definitions of postoperative ARF in 26 studies. Even a consensus conference of intensivists and nephrologists on the subject in 2000 could not provide an adequate, universal definition. This makes it difficult to draw conclusions from the individual trials that are published.

- A specific definition of disease with tight exclusion criteria is essential in the design of clinical studies of a heterogeneous syndrome.

Particular issues around definition include:

- Biochemical:
  - What is the meaning of blood urea nitrogen if two-thirds of patients who develop ARF in ICUs have chronic renal dysfunction, and proteinuria (as a marker of glomerular filtration rate) is normal or low?
  - Any definition needs to take account of age, sex, race, and body size.
  - Serum creatinine is often not available, and albumin and bilirubin are often not measured.

- Functional:
  - Many patients who develop ARF in ICUs have chronic renal dysfunction due to factors such as age-related changes, long-standing hypertension, diabetes or renal vascular disease.
  - Chronic renal dysfunction is not difficult to diagnose, although the term ARF encompasses a broad range of definitions with no universally accepted definition.

- Pathological:
  - Pathological studies suggest persistent disease with tubular atrophy and interstitial fibrosis in many patients and a variable degree of inflammatory infiltrates in others.

- Clinical:
  - The combined published results for ARF, its incidence and outcome are:
    - Of ARF, mortality is 10-25%.
    - Many different disease processes can cause ARF, so one may not be comparing like with like.
    - Is it the incidence of ARF that varies or the incidence of the disease process in different centres?

- Pathogenesis:
  - Renal replacement therapy (RRT) is now a routine element of organ support in the intensive therapy unit (ITU). Yet despite great improvements in the recognition and management of ARF, including RRT, the mortality of patients who are admitted to (ITU with ARF) or who subsequently develop ARF, remains high at 20-80%.
  - If the cause of ARF has been removed and the patient has become physiologically stable slow recovery occurs over 4-6 days to 3-4 weeks in some cases; the urine output can be above normal for several days.

- Hemodynamic failure
  - Drug-induced renal failure
    - Drug-induced renal failure may improve rapidly on removal of the offending agent and according to a drug history it is important in all cases of renal failure.

- Renal replacement therapy
  - Renal replacement therapy (RRT) in a remote element of organ support in the intensive therapy unit (ITU). Yet despite great improvements in the recognition and management of ARF, including RRT, the mortality of patients who are admitted to (ITU with ARF) or who subsequently develop ARF, remains high at 20-80%.
  - If the cause of ARF has been removed and the patient has become physiologically stable slow recovery occurs over 4-6 days to 3-4 weeks in some cases; the urine output can be above normal for several days.

- Laboratory test failure
  - Acute tubular necrosis
    - The combined published results for ARF, its incidence and outcome are:
      - Of ARF, mortality is 10-25%.
      - Many different disease processes can cause ARF, so one may not be comparing like with like.
      - Is it the incidence of ARF that varies or the incidence of the disease process in different centres?

- General investigations include:
  - Examination of urinary sediment and exclusion of a urinary tract infection (most if not all patients).
  - Special investigations may include:
    - CK and myoglobin (for rhabdomyolysis)
    - Chest x-ray, blood film
    - Specific antibodies (anti-GBM, anti-dsDNA, anti-smooth muscle etc).

- General investigations:
  - Acute renal failure (ARF) is a common problem in intensive care. It is said to have an incidence of 10-25%. The diagnosis of ARF is not difficult, although the term ARF encompasses a broad range of definitions with no universally accepted definition.
  - The mortality of patients who are admitted to ITU with ARF, or who subsequently develop ARF, remains high at 20-80%.
  - If the cause of ARF has been removed and the patient has become physiologically stable slow recovery occurs over 4-6 days to 3-4 weeks in some cases; the urine output can be above normal for several days.

- Pre-replacement therapy failure
  - Renal replacement therapy (RRT) is now a routine element of organ support in the intensive therapy unit (ITU). Yet despite great improvements in the recognition and management of ARF, including RRT, the mortality of patients who are admitted to (ITU with ARF) or who subsequently develop ARF, remains high at 20-80%.
  - If the cause of ARF has been removed and the patient has become physiologically stable slow recovery occurs over 4-6 days to 3-4 weeks in some cases; the urine output can be above normal for several days.

- Pathophysiology
  - Renal blood flow is decreased by:
    - decreased cardiac output
    - hypovolemia
    - mixed intravascular pressure (decompensation should be considered when the intravascular pressure is greater than 25-30mmHg above the pulse)
    - In septic patients with hypodynamic circulations there may be adequate global blood flow to the kidney but intrarenal shunting away from the pelvis leading to malperfusion of the kidney.
    - Renal blood flow is decreased by:
      - Decreased cardiac output
      - Hypovolemia
      - Mixed intravascular pressure (decompensation should be considered when the intravascular pressure is greater than 25-30mmHg above the pulse)
      - In septic patients with hypodynamic circulations there may be adequate global blood flow to the kidney but intrarenal shunting away from the pelvis leading to malperfusion of the kidney.
      - Several mechanisms are involved in the development of renal injury in pre-replacement therapy failure:
        - Reduction in the order of the afferent arteriolar renal vasculature
        - Mitogen-activated protein kinases-induced renal injury