

Renal Insufficiency in Hospitalized Patients

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The medical consultant may be asked to evaluate a patient with renal insufficiency, either for acute renal failure (ARF) or for issues related to chronic renal insufficiency (CRI). Various etiologies for ARF exist in the hospitalized patient, with the major causes being acute tubular necrosis (ATN) and prerenal disease (due to sepsis, congestive heart failure, or true volume depletion).¹⁻³ For patients with CRI, management issues include prevention of contrast-induced nephropathy^{4,5}, control of blood pressure⁶, treatment of anemia⁶, and addressing problems with hemostasis⁷. This chapter addresses some of the more important considerations in evaluating patients with renal insufficiency. Another chapter specifically addresses the pre-operative evaluation of a patient with renal insufficiency.

Acute Renal Failure

Definition and Epidemiology

ARF is defined as a deterioration of renal function over a period of hours to days. There are other more specific definitions such as an increase of serum creatinine by more than 50% over the baseline value.⁸ ARF is estimated to occur in 2 to 5% of patients during hospitalization with higher rates in the intensive care units.⁹⁻¹² The mortality rate for patients with ARF is much higher than for other hospitalized patients, with a mortality rate of 35% (10 times higher than for patients without ARF) reported in one large study.¹¹ Considering the frequency and seriousness of ARF, it is essential that the medical consultant have familiarity with this entity. One of the consultant's key roles is to classify the cause of ARF into either prerenal, postrenal, or intrinsic renal.

Prerenal azotemia, due to decreased renal perfusion, can be due to multiple etiologies in the hospitalized patient. Although nonreplaced fluid deficits can be an etiology, prerenal azotemia is frequently due to decreased effective renal perfusion (such as from congestive heart failure or sepsis).^{1,13} Nonsteroidal anti-inflammatory drugs (NSAIDs) can contribute to prerenal azotemia by the inhibition of intrarenal vasodilatory prostaglandins. Patients at risk for NSAID-induced ARF include those with volume depletion, congestive heart failure, cirrhosis, atherosclerotic disease, systemic lupus erythematosus, nephrotic syndrome, and chronic renal insufficiency.¹³⁻¹⁵ Angiotensin-converting enzyme (ACE) inhibitors inhibit the ability of the glomerular efferent arteriole to vasoconstrict to

maintain glomerular filtration rate. Patients at risk for NSAID-induced ARF are also at risk for ACE inhibitor induced ARF.¹³ For patients undergoing surgery, note that anesthesia decreases effective blood volume and can contribute to decreased renal blood flow.⁸ If the various causes of prerenal azotemia go untreated, this process can progress to ischemic tubular necrosis.¹³

Postrenal ARF is due to obstruction of both urinary outflow tracts or one tract if there is a single functional kidney. Prostatic hypertrophy, retroperitoneal disorders, and malignancies of the genitourinary tract are common causes. Other causes include intratubular obstruction due to crystals, a neurogenic bladder, and colorectal carcinoma.⁸

Intrinsic renal diseases that can cause ARF can be classified according to the site of injury: tubules, interstitium, vessels, or glomerulus.⁸ ATN is the most common etiology for ARF in the hospitalized patient.¹³ Ischemia, such as due to hypotension and decreased renal blood flow, is the most common cause, followed by toxins, such as radiocontrast agents and aminoglycosides.⁸ Other less common causes for ARF include atheroembolic disease, allergic interstitial nephritis, and glomerulonephritis.¹

History and Physical Exam

The consultant needs to take a thorough history and do a complete chart review looking for factors that could contribute to ARF. Predisposing factors include diabetes mellitus, vascular disease, and hypertension. Consider a previous history of prostatic enlargement or kidney stones as a potential cause of obstructive uropathy. Note any family history of renal disease.

The patient's chart should be reviewed, looking for any drops in blood pressure, which could have caused transient renal ischemia and resultant ATN. If a trauma patient presents hypotensive and responds to volume resuscitation, renal ischemia could have already occurred, setting the stage for ATN. Review daily weights (if available) and evaluate oral and intravenous intake looking for evidence of volume depletion. Determine the urine output and classify the ARF as being oliguric (< 400 ml per day) or nonoliguric (> 400 ml per day).^{8,13} Patients who have nonoliguric ARF have a better prognosis.⁸

Thoroughly review medications paying particular attention to medications associated with renal insufficiency. Diuretics can contribute to volume depletion. NSAIDs and ACE inhibitors, as previously described, can contribute to prerenal

azotemia. Other medications that may be associated with renal insufficiency include cyclosporine (causes preglomerular vasoconstriction), aminoglycosides (direct tubular toxicity), and amphotericin B (direct tubular toxicity).^{8,13,15} Review the chart carefully checking for an exposure to radiographic contrast. This contrast exposure may have occurred with either computed tomography (CT) imaging or with angiographic studies. As with many toxic exposures, patients with underlying renal insufficiency are most likely to have a deterioration in renal function. Other risk factors include diabetes mellitus, multiple myeloma, and dehydration.¹⁵

During the physical examination, pay close attention to the patient's volume status. Check for orthostatic hypotension, dry mucous membranes, or other signs of hypovolemia. On the pulmonary and cardiovascular exam, look for evidence of congestive heart failure. On the abdominal exam, check for evidence of cirrhosis and for signs of bladder distention. Bladder catheterization can rule out urethral obstruction. Check the extremities for edema and for evidence of atheroembolism.

Laboratory studies

The urinalysis can provide clues to the possible etiology of ARF. Pigmented granular casts may be a sign of tubular ischemia. In the absence of red cells, heme-positive urine suggests the presence of myoglobin or hemoglobin, raising the possibility of rhabdomyolysis.⁸ Staining for urinary eosinophils can be helpful in diagnosing acute interstitial nephritis.^{8,16}

Serum chemistries are critical, with the serum sodium, potassium, bicarbonate, blood urea nitrogen (BUN), and creatinine providing essential information. Comparing the current serum creatinine to previous values can help determine whether the deterioration in renal function has been rapid or more chronic.¹⁷ Closely following the BUN and creatinine is key in monitoring the patient's status.

Urine indexes (urine osmolality, urinary sodium concentration, and fractional excretion of sodium) help to differentiate between prerenal azotemia and ATN because with tubular damage, there is loss of ability to concentrate urine. With tubular necrosis, the urine osmolality is < 350 mOsm per kilogram, the urinary sodium concentration is > 40 mmol per liter, and the fractional excretion of sodium is > 1.0 %. However, early in the course of some etiologies of tubular damage, the urinary sodium can be low.⁸

In most situations, a renal biopsy is not necessary in the evaluation of ARF. However, in certain

situations, if the evaluation suggests a primary renal disease other than ischemic or toxin-related ARF, a renal biopsy may be helpful.⁸

Radiographic studies

Rule out urinary obstruction since most cases can be corrected and a delay in therapy can lead to irreversible renal damage. Renal ultrasonography is the test of choice to exclude obstruction. CT without contrast can be performed if the ultrasound results are equivocal. Plain films, ultrasound, and CT will be adequate in over 80% of cases.¹⁹ Ultrasound can give false positive results if any visualization of collecting system is used as a criteria.^{18,20} The intravenous pyelogram (IVP) has a very low false positive rate but does require administration of contrast. Antegrade or retrograde pyelography can be performed when the history is highly suggestive (such as in a patient with a known pelvic malignancy) and the ultrasound and CT are negative.¹⁸

Therapy

The medical consultant needs to rapidly determine the cause of the deterioration in renal function, paying attention to any reversible causes. Identification and treatment of obstructive uropathy (such as by Foley catheter placement) is critical. Determination of the patient's volume status, as discussed above, will guide decisions regarding the administration of intravenous fluids. Prompt therapy for prerenal azotemia can prevent progression to ATN.¹³

Possible nephrotoxins should be discontinued. Other medications may need to be dose-adjusted for renal insufficiency. If metabolic acidosis is secondary to ARF, sodium bicarbonate may be indicated. Hyperkalemia may require treatment. Concentrate on preventing and treating infectious complications because the most common cause of death in ARF is sepsis.⁸

Low-dose dopamine has not been shown to alter the outcome of patients with ARF though some still advocate its use.^{2,8} Anaritide (atrial natriuretic peptide) has not been shown to improve dialysis-free survival in patients with ATN.^{21,22}

Mannitol, vigorous volume replacement, and sodium bicarbonate are recommended for the prevention and treatment of early myoglobinuric ARF (rhabdomyolysis).^{8,9} Mannitol or loop diuretics (such as furosemide), if administered early in the course of ischemic ARF, can convert oliguria to nonoliguria.⁸ However, it is not clear whether oliguric ARF patients with a loop diuretic-induced increase in urine output have a more favorable

prognosis than patients with ARF that are spontaneously nonoliguric.² Because of the generally low complication rate associated with loop diuretics, these agents are frequently administered to patients who continue to be oliguric despite exclusion of postrenal obstruction and the optimization of renal perfusion.² For the volume-overloaded patient, intravenous furosemide can be administered, and if an inadequate response occurs in one hour, the dose is doubled, repeating the process in an attempt to achieve adequate urine output. Furosemide can be administered every six hours or a continuous drip can be used.²³

The patient is evaluated for the need for dialysis. Patients potentially needing dialysis should be seen by a nephrologist. In the United States, most patients with ARF who require dialysis are treated with intermittent hemodialysis.¹³ Indications for acute dialysis include volume overload, hyperkalemia, metabolic acidosis, and symptoms and signs of severe uremia.⁸ However, considerable clinical judgment is required to determine the correct time to initiate hemodialysis.⁹ In critically ill patients, continuously administered venovenous and arteriovenous therapies offer better fluid and metabolic control.⁸

Management considerations in the patient with chronic renal disease

The medical consultant will need to make recommendations about the management of hospitalized patients with CRI. The goal is to prevent progression of the renal insufficiency and also to prevent complications caused by the patient's renal dysfunction.

Patients with CRI are at risk of ARF from contrast-induced nephropathy. Nonionic contrast agents appear to be less nephrotoxic than ionic contrast agents in patients with pre-existing renal insufficiency.^{2,24} Administration of intravenous fluids (0.45 percent saline) prior to, during, and after contrast is helpful, but neither furosemide nor mannitol are recommended.⁵ Recently, acetylcysteine administration has been shown to be helpful in prevention of radiographic contrast-induced nephropathy.⁴

Treatment of hypertension, with an ACE inhibitor if tolerated, helps to prevent progression of renal insufficiency.⁶ If an ACE inhibitor is not tolerated, angiotensin receptor blockers can be used. If necessary, diltiazem, verapamil, or a beta blocker may be added. Diuretic therapy is indicated in patients with volume overload.²⁵ The currently recommended target blood pressure is 130/85, and if proteinuria is over 3 grams per day, the goal is less

than 125/80.⁶ For patients treated with ACE inhibitors, monitor the serum creatinine and potassium to ensure that hyperkalemia and azotemia are not exacerbated.⁶

The nutritional status of a patient with CRI needs to be closely monitored. At a serum bicarbonate level of below 20 mEq/L, adverse effects on metabolic processes are noted. Oral vitamin supplements should be used that provide 1 mg/day of folic acid plus all other B vitamins and water-soluble vitamins. Calcium is used as a phosphate-binding agent to maintain the phosphorus in the range of 3.5 to 5.0.⁶

Patients with CRI have chronic anemia primarily due to deficient production of erythropoietin, with anemia beginning to develop when the serum creatinine climbs above 2 to 3 mg/dl.²⁵ Iron studies, B12 and folate levels, and checking for occult fecal blood are part of the evaluation of anemia. Endoscopic studies may be indicated. Therapy with iron, and in some cases parenteral iron dextran, may be needed. If the hemoglobin does not rise with conservative measures, erythropoietin is necessary.⁶

CRI can result in significant problems with hemostasis. In general, the more severe the uremia and the longer its duration, the greater is the risk of bleeding. The bleeding time is often prolonged. Dialysis does improve platelet function. Desmopressin (DDAVP) is beneficial in controlling bleeding associated with uremia. Cryoprecipitate can also be used to control bleeding, but there is the risk of viral transmission.⁷

In addition to the issues related to CRI addressed above, the medical consultant should recommend that a patient be referred to a nephrologist in certain circumstances. Consider specialist referral if the GFR is less than 30 ml/min (or serum creatinine above 3.0 mg/dl), if dialysis seems imminent within the next year, if the patient is a potential renal transplant recipient, and for certain issues related to CRI such as for management of anemia or provision of dialysis access.⁶

References

1. Rose BD. Diagnosis of acute tubular necrosis and prerenal disease. In: UpToDate, Rose BD (Ed), UpToDate, Wellesley, MA, 2001.
2. Nolan CR, Anderson RJ. Hospital-acquired acute renal failure. *J Am Soc Nephrol* 1998; 9: 710-718.
3. Liano F, Pascual J, and the Madrid Acute Renal Failure Study Group. Epidemiology of acute renal failure: A prospective, multicenter, community-based

study. *Kidney Int* 1996; 50: 811-818.

4. Tepel M, Van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000; 343: 180-184.

5. Solomon R, Werner C, Mann D, D'Elia, Silva P. Effects of saline, mannitol, and furosemide on acute decreases in renal function induced by radiocontrast agents. *N Engl J Med* 1994; 331: 1416-1420.

6. McCarthy JT. A practical approach to the management of patients with chronic renal failure. *Mayo Clin Proc* 1999; 74: 269-273.

7. Eberst ME, Berkowitz LR. Hemostasis in renal disease: Pathophysiology and management. *Am J Med* 1994; 96:168-179.

8. Thadhani R, Pascual M, Bonventre JV. Acute renal failure. *N Engl J Med* 1996; 334: 1448-1460.

9. DuBose TD, Warnock DG, Mehta RL, et al. Acute renal failure in the 21st century: Recommendations for management and outcomes assessment. *Am J Kidney Dis* 1997; 29: 793-799.

10. Brady HR, Singer GG. Acute renal failure. *Lancet* 1995; 346: 1533-1540.

11. Shusterman N, Strom BL, Murray TG, Morrison G, West SL, Maislin G. Risk factors and outcome of hospital-acquired acute renal failure. *Am J Med* 1987; 83: 65-71.

12. Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: A prospective study. *Am J Med* 1983; 74: 243-248.

13. Albright RC Jr. Acute renal failure: A practical update. *Mayo Clin Proc* 2001; 76: 67-74.

14. Sturmer T, Elseviers MM, De Broe ME. Nonsteroidal anti-inflammatory drugs and the kidney. *Curr Opin Nephrol Hypertens* 2001; 10: 161-163.

15. Cooper K, Bennett WM. Nephrotoxicity of common drugs used in clinical practice. *Arch Intern Med* 1987; 147: 1213-1218.

16. Rose BD, Appel GB. Drug-induced acute interstitial nephritis. In: UpToDate, Rose BD (Ed), UpToDate, Wellesley, MA, 2001.

17. Post TW, Rose BD. Approach to the patient with renal disease including acute renal failure. In: UpToDate, Rose BD (Ed), UpToDate. Wellesley, MA, 2001.

18. Rose BD. Diagnosis of urinary tract obstruction

and hydronephrosis. In: UpToDate, Rose BD (Ed), UpToDate, Wellesley, MA, 2001.

19. Webb JAW, Reznick RH, White FE, Cattell WR, Fry IK, Baker LRI. Can ultrasound and computed tomography replace high-dose urography in patients with impaired renal function? *Q J Med* 1984; 53: 411-425.

20. Webb JAW. Regular Review: Ultrasonography in the diagnosis of renal obstruction. *BMJ* 1990; 301: 944-946.

21. Lewis J, Salem MM, Chertow GM, et al. Atrial natriuretic factor in oliguric acute renal failure. *Am J Kidney Dis* 2000; 36: 767-774.

22. Allgren RL, Marbury TC, Rahman SN, et al. Anaritide in acute tubular necrosis. *N Eng J Med* 1997; 336: 828-834.

23. Agrawal M, Swartz R. Acute renal failure. *Am Fam Physician* 2000; 61: 2077-2088.

24. Rudnick MR, Goldfarb S, Wexler L, et al. Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: A randomized trial. *Kidney Int* 1995; 47: 254-261.

25. Post TW, Rose BD. Overview of the management of chronic renal failure - I. In: UpToDate, Rose, BD (Ed), UpToDate, Wellesley, MA, 2001.