Kidney Biopsy

When prerenal AKI, ATN, and obstructive uropathy are unlikely, percutaneous kidney biopsy is sometimes required to determine the cause of AKI and to direct appropriate therapy. Reasonable criteria to support use of kidney biopsy include absence of an obvious cause of AKI such as hypotension or nephrotoxin exposure and prolonged oliguria, usually for more than 2 to 3 weeks. Other potential indications include evaluation for myeloma-related kidney disease in an elderly patient with unexplained AKI; extrarenal manifestations of systemic diseases such as systemic lupus erythematosus, rheumatoid arthritis, or vasculitis; and determination of whether AIN is present in patients receiving a potential culprit drug.

Kidney tissue should be thoroughly examined with the use of light microscopy, immunofluorescence staining, and electron microscopy to facilitate an accurate diagnosis. This ensures a diagnosis of the cause of AKI in most patients. However, kidney biopsy should be employed judiciously to avoid complications such as traumatic renal arteriovenous malformation, severe bleeding requiring transfusion or embolization, other organ injury (liver, spleen, bowel), and nephrectomy for intractable bleeding.

Future Tests for AKI

The limitations of currently available tests to estimate GFR and kidney injury have led to proteomics-based studies to identify novel biomarkers of AKI. The hope is that novel biomarkers will improve the diagnosis and prognosis of AKI. For example, early AKI diagnosis would permit implementation of appropriate preventive strategies and treatment regimens to abrogate permanent loss of kidney function. In patients who develop AKI, biomarker concentrations demonstrate changes earlier than serum creatinine concentrations and appear to distinguish between prerenal AKI, ATN, and other glomerular disorders, which may allow directed interventions and avoidance of potentially harmful therapies. One such example is aggressive intravenous fluid therapy in patients with ATN, which risks volume overload and other end-organ consequences. Finally, biomarkers may allow clinicians to better predict outcomes such as worsening kidney function, RRT requirement, and mortality in patients with hospital-acquired AKI.

CLINICAL PRESENTATION, DIFFERENTIAL DIAGNOSIS, AND MANAGEMENT OF AKI

Prerenal AKI

Prerenal AKI is primarily the result of inadequate blood flow to the kidneys. Renal blood flow approximates more than 1 L/minute, which is necessary to maintain GFR, preserve oxygen delivery, and sustain ion transport and other energy-requiring processes. Therefore, normal kidney function depends on adequate perfusion; a significant reduction in renal perfusion diminishes filtration pressure and lowers GFR.

Volume Depletion

Both "true" and "effective" hypovolemia activate several neurohormonal vasoconstrictor systems as mechanisms to protect circulatory stability. The substances released include catecholamines from the sympathetic nervous system, endothelin from the vasculature, angiotensin II from the renin-angiotensin system (RAS), and vasopressin. They raise BP through arterial and venous constriction but also can constrict afferent arterioles and reduce GFR, especially when systemic BP is inadequate to maintain renal perfusion pressure.

Structural lesions in the renal arterial and arteriolar tree can also reduce perfusion and promote prerenal AKI. Kidney adaptive responses are stimulated to counterbalance diminished renal perfusion in these circumstances. These adaptive processes include the myogenic reflex, which is activated by low distending pressures sensed in the renal baroreceptors and causes afferent arteriolar vasodilatation. Prostaglandins (e.g., PGE_2, PGI_2), nitric oxide, and products from the kallikrein-kinin system modify the effects of these vasoconstrictors on the afferent arteriole. Importantly, disturbance of the balance between afferent vasodilatation and efferent vasoconstriction can disrupt intrarenal hemodynamics and precipitate AKI.

Medications

The balance of vasoconstricting and vasodilating processes may be altered by medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and selective cyclooxygenase 2 (COX2) inhibitors. These drugs act to cause prerenal AKI through inhibition of vasodilatory prostaglandins in patients who require prostaglandin effects to maintain renal perfusion. Despite its vasoconstrictor properties, angiotensin II acutely preserves glomerular filtration pressure and GFR in states of reduced renal perfusion by constricting the efferent arteriole more than the afferent arteriole. This salutary effect in part explains the GFR reduction that occurs when a patient who is dependent on angiotensin II to constrict the efferent arteriole is treated with an ACE inhibitor or an angiotensin II receptor blocker (ARB).

Cardiorenal Syndrome

The cardiorenal syndrome (CRS) is an umbrella term that encompasses a number of coexistent cardiac or kidney derangements. Although there are five subtypes of CRS, hospital-acquired AKI due to CRS is most often of the type 1 variety. Reduced cardiac output, arterial underfilling, elevated atrial pressures, and venous congestion, independently or in combination, can impair the renal circulation and reduce GFR, thereby causing a form of prerenal AKI. These processes stimulate neurohumoral adaptations such as activation of the sympathetic nervous system and RAS and increases in vasopressin and endothelin-1, in an attempt to preserve perfusion to vital organs. However, these adaptations enhance salt and water retention and systemic vasoconstriction, which ultimately promote or exacerbate prerenal AKI by two mechanisms: (1) They increase cardiac afterload and further reduce cardiac output and renal perfusion, and (2) they increase central venous pressure, renal venous pressure, and/or intra-abdominal pressure, ultimately lowering GFR.

AKI in patients with heart failure is often caused by CRS type 1, but certainly these patients can also suffer true prerenal AKI from overzealous diuresis or from ischemic or nephrotoxic ATN. Prerenal AKI from true volume depletion is responsive