Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy

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Literature review current through: Mar 2015. | **This topic last updated:** Dec 10, 2014.

INTRODUCTION — Contrast nephropathy is a generally reversible form of acute kidney injury (AKI) that occurs soon after the administration of radiocontrast media [1-11]. Important issues that remain unresolved include its pathogenesis and relative efficacies of various prophylactic strategies.

A review of the pathogenesis, clinical characteristics, and diagnosis of iodinated radiocontrast media-induced nephropathy is presented here. Preventive strategies for reducing the risk of contrast nephrotoxicity and a discussion of acute tubular necrosis (ATN), the most common cause of AKI developing in hospitalized patients, are presented separately. (See "Prevention of contrast-induced nephropathy" and "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury (acute renal failure)".)

PATHOGENESIS

Overview — The best data related to the pathogenesis of contrast nephropathy come from animal models. Studies show evidence of acute tubular necrosis (ATN), but the mechanism by which ATN occurs is not well understood [12-14]. The two major theories are that ATN is caused by renal vasoconstriction resulting in medullary hypoxia, possibly mediated by alterations in nitric oxide, endothelin, and/or adenosine, and that ATN is a direct result of the cytotoxic effects of the contrast agents [12-20].

However, unlike other types of ATN, contrast nephropathy is usually characterized by relatively rapid recovery of renal function. If ATN contributes to contrast nephropathy, it is not clear why recovery occurs relatively quickly (ie, within a few days), compared with a longer duration (ie, one to three weeks), as with ATN due to other causes. There are at least two possibilities to explain the short duration of ATN:

- The degree of tubular necrosis is much less severe than seen in other settings.
- The decline in glomerular filtration rate (GFR) is due to functional changes in tubule epithelial cells rather than necrosis per se. This phenomenon, which is similar to postischemic dysfunction in the "stunned" myocardium, may be at least in part due to redistribution of membrane transport proteins from the basolateral to the luminal membrane [21].

In addition, it is possible that prerenal factors or intratubular obstruction contribute to the pathogenesis. This possibility is suggested by the observation that the fractional sodium excretion (FENa) may be <1 percent in patients with contrast nephropathy, by contrast with that in patients with ischemic or toxin-induced ATN [22]. Since contrast nephropathy is almost always nonoliguric, however, the significance of a FENa <1 is unclear. (See 'Other laboratory manifestations' below and "Fractional excretion of sodium, urea, and other molecules in acute kidney injury (acute renal failure)", section on 'Fractional excretion of sodium in acute kidney injury'.)

Individual mechanisms are discussed below.

Renal vasoconstriction — Renal vasoconstriction is a common finding in contrast nephropathy and is mediated in part by vasoactive mediators such as endothelin and adenosine and possibly by direct contact with high osmolal contrast agent [17-20]. However, much of our understanding of the role of vasoactive mediators is derived from animal models. As a result, the magnitude of the contribution of individual mediators to human contrast nephropathy is not clear. Endothelin receptor antagonists failed to prevent contrast media-induced kidney injury in human studies, but the significance of this is not clear given the fact that nonselective antagonists were used [23].

(See "Prevention of contrast-induced nephropathy", section on 'Inhibition of renal vasoconstriction'.)

Although overall renal vasoconstriction (and reduced renal blood flow) do not appear to correlate well with a rise in the serum creatinine concentration [16], reductions in medullary blood flow may be important [14]. In a rat model, for example, the combined administration of iothalamate and inhibitors of endogenous vasodilators, such as nitric oxide and prostaglandins, causes marked ischemia and tubular necrosis in the medullary thick ascending limb of the loop of Henle [15].

In humans, reductions in renal blood flow of variable duration have been demonstrated following contrast administration:

- Renal blood flow determined by para-aminohippurate (PAH) clearance remained 30 percent below baseline up to two hours after the administration of contrast [19]. This effect was most pronounced following the administration of high-osmolal agents, but the low-osmolal agent, iopamidol, also significantly reduced blood flow [19].
- Renal blood flow remained 45 percent below baseline levels for at least four hours following contrast administration [24].

Further reduction in medullary blood flow may occur due to effects of viscosity. The renal medullary vascular bed, the vasa recta, is composed of long vessels of small diameter. Blood flow is facilitated by maintenance of low viscosity, which can be markedly altered by contrast media, especially iso-osmolal preparations [13]. Increased viscosity may also enhance tubular interstitial pressure, which further reduces medullary blood flow.

The outer medulla appears particularly susceptible to injury due to reductions in renal blood flow [14]. This increased susceptibility results from baseline borderline hypoxic conditions in the outer medulla, which are due in part to the high oxygen requirements for active sodium transport and countercurrent flow [25].

As will be described below, diabetes mellitus and heart failure increase the risk of contrast-induced kidney injury in humans. There is evidence that these disorders are associated with impaired nitric oxide generation, which could contribute to the susceptibility to contrast agents [15]. (See 'Epidemiology' below.)

Tubular injury — Tubular injury, due to direct cytotoxic effects or in association with the generation of oxygen free radicals, contributes to contrast nephropathy [12,13,26]. Some animal models suggest that decreased activity of protective antioxidant enzymes may explain the enhanced risk with hypovolemia [27,28]. Antioxidant activity may explain the apparent protective effect of acetylcysteine. (See "Prevention of contrast-induced nephropathy", section on 'Acetylcysteine'.)

Tubular injury may also be exacerbated by and act in concert with renal vasoconstriction [12,13]. In one study, for example, administration of a nonionic, low-osmolality contrast agent led to an 18 percent reduction in creatinine clearance and increased adenosine excretion [18]. Concurrent use of theophylline, an adenosine receptor antagonist, prevented the fall in creatinine clearance. In comparison, an ionic high-osmolality contrast agent produced a greater reduction in creatinine clearance (42 percent) that was only partially corrected by theophylline and that was associated with a more prolonged increase in adenosine excretion, suggesting concurrent tubular injury.

EPIDEMIOLOGY — The reported incidence of radiocontrast-induced nephropathy varies widely, depending on the presence or absence of risk factors (primary chronic kidney disease [CKD]), the amount and type of agent administered, and the exact radiologic procedure.

Adding to this uncertainty is the fact that reductions in renal function occur in hospitalized patients who do not receive iodinated contrast, and most studies do not reliably exclude other causes of acute kidney injury (AKI) unrelated to contrast media (eg, atheroemboli during angiography or changes in diuretic or renin-angiotensin system [RAS] inhibition in the immediate period postcontrast exposure). As an example, in one retrospective review of 32,161 patients who had serum creatinine measured on five consecutive days and who underwent a

computed tomography (CT) scan, but did not receive contrast material during the previous 10 days, more than half showed a change in creatinine of at least 25 percent, and more than two-fifths showed a change of at least 0.4 mg/dL [29]. This is an important point to remember when evaluating published reports, especially those that include patients of low risk for contrast nephropathy.

According to virtually all reports, among patients who have no risk factors, the risk of contrast nephropathy is negligible (ie, ≤1 percent) [1,2]. Among high-risk patients (especially those with diabetes and CKD), the reported risk following percutaneous angiography with or without intervention is 10 to 20 percent [30-34].

Risk factors for contrast nephropathy include the following [1-6,9,35-38]:

- CKD
- Diabetic nephropathy with renal insufficiency
- Advanced heart failure or other cause of reduced renal perfusion (such as hypovolemia or hemodynamic instability)
- High total dose of contrast agent
- First-generation hyperosmolal ionic contrast agents
- Percutaneous coronary interventions, which also promote the development of atheroemboli
- Multiple myeloma (especially with older contrast agents)

The contribution of individual factors to overall risk is discussed below.

Chronic kidney disease — The incidence of contrast nephropathy is higher among patients with CKD, and the magnitude of the risk is directly associated with the severity of renal dysfunction [1,2,4,6,35,39,40]. In one study of 7586 patients undergoing percutaneous interventions, the overall incidence of AKI (defined as a >0.5 mg/dL increase in the baseline serum creatinine) was 3.3 percent, but the incidence increased to 22 percent among patients with a serum creatinine of 2.0 to 2.9 (177 to 256 mmol/L) and to 31 percent for those with a baseline creatinine ≥3.0 mg/dL (265 mmol/L) [35].

Statistically, the increase in risk is likely continuous with the decline in glomerular filtration rate (GFR). However, the GFR at which a clinical significantly risk is incurred is not well defined. It is likely that nondiabetic patients with estimated GFR (eGFR) >45 mL/min have only a modest risk of contrast nephropathy, especially if contrast is administered intravenously.

Diabetic nephropathy with renal insufficiency — Among patients with CKD, diabetic patients are at higher risk for contrast nephropathy, compared with nondiabetic patients. In one prospective study that directly compared diabetic and nondiabetic patients who had a baseline serum creatinine greater than 1.69 mg/dL (150 mmol/L) and were undergoing CT scan with contrast, diabetic patients had a higher incidence of contrast nephropathy, compared with nondiabetic patients (8.8 versus 4.0 percent, respectively) [1]. Similarly, in an analysis of data from a randomized trial that included 250 patients with serum creatinine >1.5 mg/dL (133 mmol/L) who received iohexol during percutaneous coronary interventions, a much higher incidence was observed among diabetic patients, compared with nondiabetic patients (33 versus 12 percent, respectively) [2].

Among patients with normal kidney function, diabetes does not increase the risk of contrast nephropathy. As an example, in a randomized trial that included 341 patients with serum creatinine ≤1.5 mg/dL (133 mmol/L) who received iohexol during percutaneous interventions, there was no difference in the negligible incidence of contrast nephropathy between diabetic and nondiabetic patients [2].

Dose and type of contrast agent — Studies have demonstrated a dose-dependent risk of renal dysfunction, with lower doses of contrast being safer, but not free of risk [2,5,6,36,40]. Low dose has been variably defined in different studies, generally ranging from <30 to <125 mL [5,6,36,40]. As an example, in one study, low dose was defined by a formula as <5 mL/kg (to a maximum of 300 mL) divided by the serum creatinine concentration [40]. However, diabetic patients with a serum creatinine concentration >5 mg/dL (440 micromol/L) may be at risk from as little as 20 to 30 mL of contrast [40].

The type of administered contrast agent alters the risk. The use of first-generation hyperosmolal ionic contrast agents is associated with an enhanced risk of nephropathy (versus that observed with nonionic low-osmolal or iso-osmolal agents) [2]. This is particularly true if such agents are administered to high-risk patients without adequate additional preventive measures. The risk associated with specific agents is discussed elsewhere. (See "Prevention of contrast-induced nephropathy", section on 'Type of contrast agent'.)

Specific radiologic procedure — Most of the studies identifying risk factors for contrast nephropathy included patients undergoing percutaneous angiography, particularly coronary angiography. By contrast to that associated with angiography, the risk of contrast nephropathy associated with contrast CT scans is quite low, even among patients with CKD [41,42]:

- A single-center study compared the risk of AKI (defined as increase in serum creatine level ≥0.5 mg/dL [44 micromol/L] above baseline within 24 to 72 hours of receiving contrast) and risks of emergent dialysis or 30-day mortality between 10,673 mostly low-risk individuals who received contrast and an equal number of propensity-matched control individuals [42]. In this relatively low-risk population, there was no difference between groups in the risk of AKI (odds ratio [OR] 0.94, 95% CI 0.83-1.07), dialysis (OR 0.96, 95% CI 0.54-1.60) or 30-day mortality (hazard ratio [HR] 0.97, 95% CI 0.87-1.06).
- As another example, in a study of 421 patients with eGFR less than 60 mL/min per 1.73 m^2, only 3.5 percent had an increase in serum creatinine of greater than 0.5 mg/dL (44 micromol/L) within 48 to 96 hours postprocedure. Despite the absence of pre- and postprocedure intravenous fluid administration, <1 percent of outpatients who had a baseline eGFR between 45 and 60 mL/min per 1.73 m^2 had an increase in serum creatinine >0.5 mg/dL (44 micromol/L). Patients undergoing emergent CT (for diagnosis of ruptured aortic aneurysm or acute pulmonary embolus) were excluded from the study.

The incidence of AKI may be higher for patients who receive contrast for a nonelective contrast-enhanced CT. This was suggested by a prospective study of 633 outpatients who received intravenous contrast for contrast-enhanced CT in the emergency department of a single tertiary care center (2.4 percent of whom had a baseline eGFR <60 mL/min per 1.73 m^2) [43]. Seventy patients (11 percent) had an increase in serum creatinine >0.5 mg/dL (44 micromol/L) or >25 percent within two to seven days after contrast administration. Six patients (1 percent) developed severe kidney injury (defined as an increase in serum creatinine ≥3 mg/dL or the need for dialysis at 45 days); five required hemodialysis or died. A possible reason for the higher incidence of AKI in this study may be that patients identified through emergency department visits are more likely to have comorbidities that were not adjusted for, such as hypotension, hyperglycemia, or volume depletion.

Multiple myeloma — Patients with multiple myeloma are at increased risk from a contrast study, although the incidence of AKI appears to be less than 1.5 percent with the use of modern contrast agents, at least among patients who have no other risk factors. As an example, in a review of seven retrospective studies of myeloma patients receiving contrast media, 476 patients who had undergone 568 contrast media studies, the prevalence of AKI was 0.6 to 1.25 percent, which is low but likely higher than that among individuals who do not have multiple myeloma and have no other risk factors [44]. Volume depletion, which promotes the intratubular precipitation of filtered light chains, is usually present in those patients who develop contrast nephropathy [44]. In addition, a possible interaction between light chains and the contrast agent may play a contributory role, although this was more likely with older contrast agents no longer in use [44,45].

Other — Other risk factors that have been suggested by a few studies include hyperglycemia and the use of either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) [46,47].

Hyperglycemia may increase the risk for contrast nephropathy independent of a pre-existing diagnosis of diabetes mellitus. In a study of 6358 patients undergoing angiography following myocardial infarction, the adjusted risk of contrast nephropathy incrementally increased with higher glucose levels among patients without diabetes mellitus, with ORs of 1.31, 1.51, 1.58, and 2.14 for glucose groups of 110 to <140, 140 to <170, 170 to <200, and >200 mg/dL [46]. Although there was no increase in glucose-associated risk among patients with established diabetes

mellitus, the unadjusted risk for contrast nephropathy in patients with diabetes mellitus and a glucose of <140 mg/dL was approximately double that of nondiabetic patients in the same blood glucose categories. The presence or absence of CKD among individuals who developed contrast nephropathy was not reported in this study.

The effect of ACE inhibitors and/or ARBS on the incidence of contrast nephropathy is not clear. In a retrospective study of 5299 patients undergoing percutaneous interventions, compared with a propensity-matched cohort, ACE inhibitor or ARB users were more likely to develop AKI (OR 1.43, 95% CI 1.06-1.94) [47].

However, in a randomized trial of 220 patients with eGFR of 15 to 60 mL/min per 1.73 m^2, there was no difference in the incidence of contrast nephropathy between patients who were on ACE inhibitors and/or ARBs prior to angiography, and patients who had a similarly reduced eGFR but were not on ACE inhibitors and/or ARBS [48]. In addition, it is not clear whether holding or withdrawing an ACE inhibitor and/or ARB prior to angiography provides any benefit. Studies that have examined this issue and our approach to the use of ACE inhibitors and ARBs prior to contrast procedures are discussed elsewhere. (See "Prevention of contrast-induced nephropathy", section on 'Withholding ACE inhibitors and/or ARBs'.)

CLINICAL FEATURES

Creatinine increase — The onset of kidney injury is probably within minutes of exposure to contrast agents. However, clinical manifestations such as oliguria or an increase in the serum creatinine are generally observed within 24 to 48 hours after contrast exposure. Most patients are nonoliguric [4,49]. As an example, in a prospective study that compared nonionic and ionic contrast agents, among approximately 40 patients who developed contrast nephropathy, none were oliguric [4]. Thus, injury is usually manifested only by an increase in the serum creatinine.

In almost all cases, the increase in creatinine reflecting a decline in glomerular filtration rate (GFR) occurs within 24 to 48 hours of contrast administration and is mild. The creatinine usually starts to decline within three to seven days [8,49].

Other laboratory manifestations — As noted, the major laboratory manifestation is an increased serum creatinine. Other manifestations of acute kidney injury (AKI) may be present, including hyperkalemia, acidosis, and hyperphosphatemia. (See "Renal replacement therapy (dialysis) in acute kidney injury (acute renal failure) in adults: Indications, timing, and dialysis dose".)

The urinary sediment may show classic findings of acute tubular necrosis (ATN), including muddy brown granular and epithelial cell casts and free renal tubular epithelial cells. However, the absence of these urinary findings does not exclude the diagnosis, and their presence does not always establish the diagnosis of ATN. The sediment does not show evidence of glomerular disease (such as dysmorphic red blood cells [RBCs] or red blood casts) or interstitial nephritis (such as white cells or white cell casts). (See "Urinalysis in the diagnosis of kidney disease", section on 'Urine sediment' and "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury (acute renal failure)", section on 'Urinalysis'.)

Protein excretion on presentation is absent or mild. However, many of the commonly used iodinated radiocontrast agents induce false-positive results when either a dipstick or sulfosalicylic acid is used to detect proteinuria [50]. How this occurs is not clear, but protein excretion may be overestimated by as much as 1.5 to 2 g/L. Thus, the urine should not be tested for protein for at least 24 hours after a contrast study. If urine is tested and proteinuria is detected, the test should be repeated at least 48 hours after contrast exposure to exclude a false-positive result.

The fractional sodium excretion (FENa) is often <1 percent in patients with contrast nephropathy. In one study, among 12 patients with transient oliguric AKI, all 12 patients had FENa <1 percent [22]. In a larger, prospective study of 443 patients, despite the administration of sodium chloride prior to angiography, the mean FENa was 0.3 to 0.7 among patients who developed AKI [4]. The low FENa among such patients is in contrast to that in patients who develop AKI due to ischemic or toxin-induced ATN, which is usually >1 percent, but this may be explained by the fact that contrast nephropathy is usually nonoliguric, and ischemic ATN is usually oliguric. The use of the FENa in other forms of AKI is discussed elsewhere. (See "Fractional excretion of sodium, urea, and other molecules in

acute kidney injury (acute renal failure)", section on 'Fractional excretion of sodium in acute kidney injury'.)

Calculators for the FENa are available using either standard units (calculator 1) or SI units (calculator 2).

Radiographic manifestations — There are no characteristic radiographic features of contrast nephropathy. A prolonged nephrogram may be seen among patients with established contrast nephropathy who undergo an intravenous pyelogram (which is generally no longer performed in this setting) or a contrast-enhanced computed tomography (CT) scan.

DIAGNOSIS — The diagnosis of radiocontrast-induced nephropathy is based upon the clinical presentation, including the characteristic rise in serum creatinine concentration beginning with the first 24 to 48 hours after contrast exposure, and the exclusion of other causes of acute kidney injury (AKI). This typically requires a urinalysis and, occasionally, a renal ultrasound or biopsy.

The urinalysis provides important diagnostic information, usually by excluding other causes of AKI rather than by providing a conclusive, positive diagnosis of contrast nephropathy. As noted above, the presence of classic findings of contrast nephropathy include muddy brown granular and epithelial cell casts and free renal tubular epithelial cells (see 'Other laboratory manifestations' above). In the appropriate clinical setting, these findings strongly support the diagnosis of contrast nephropathy, although the absence of these urinary findings does not exclude the diagnosis. However, the absence of other findings such as white blood cells (WBCs), WBC casts, dysmorphic red blood cells (RBCs), or RBC casts generally excludes interstitial nephritis and glomerular diseases as causes of AKI. Conversely, the presence of WBCs, WBC casts, dysmorphic RBCs, or RBC casts suggests causes of AKI other than acute tubular necrosis (ATN), such as interstitial nephritis or glomerular lesions.

Although an ultrasound is usually obtained among all patients who present with an elevated creatinine, we generally do not obtain an ultrasound, at least initially, among patients who have a characteristic presentation of contrast nephropathy following contrast exposure. However, we do obtain an ultrasound to exclude other causes of AKI among patients who do not follow a classic clinical course of contrast nephropathy, or in whom the diagnosis of contrast nephropathy is questionable. (See "Diagnostic approach to the patient with acute kidney injury (acute renal failure) or chronic kidney disease".)

A renal biopsy is generally not helpful for the diagnosis of contrast nephropathy, since the lesions of ATN are focal and nonspecific and because AKI due to contrast nephropathy is generally short lived.

However, as with the ultrasound, a biopsy may rarely be required to exclude other causes of AKI among patients who do not follow a classic clinical course or in whom the diagnosis of contrast nephropathy is uncertain.

Differential diagnosis — The differential diagnosis includes, but is not limited to, ischemic ATN, acute interstitial nephritis, renal atheroemboli and prerenal changes caused by the addition of or dose adjustments in diuretics and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) in the postcontrast period. The former two require additional insults such as sepsis, hypotension, or medication exposure, which can be deduced by history. (See "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury (acute renal failure)" and "Clinical manifestations and diagnosis of acute interstitial nephritis".)

Among patients who develop AKI after angiography, contrast nephropathy must be distinguished from renal atheroemboli. The latter has one or more of the following distinguishing characteristics [8]:

- The presence of other embolic lesions (such as digital ischemia of the toes) or livedo reticularis
- Transient eosinophilia and hypocomplementemia
- Onset of kidney injury that may be delayed for days to weeks after the procedure
- Protracted course with frequently little or no recovery of renal function

A full discussion of this condition is provided separately. (See "Clinical presentation, evaluation, and treatment of renal atheroemboli" and "Embolism from atherosclerotic plaque: Atheroembolism (cholesterol crystal embolism)".)

PROGNOSIS AND MANAGEMENT — As noted above, the increase in creatinine reflecting a decline in glomerular filtration rate (GFR) is usually mild. In most cases, the creatinine usually starts to decline within three to seven days, and the patient returns to, or close to, baseline renal function [8,49]. As an example, among 21 patients with contrast nephropathy, 12 (57 percent) regained baseline renal function, and four additional patients (19 percent) had a partial recovery within five to seven days [49]. Only five patients had persistent renal dysfunction at the time of discharge.

Dialysis is rarely required for acute kidney injury (AKI) following contrast administration. In one study of over 1800 consecutive patients who underwent percutaneous interventions, the incidence of AKI that was severe enough to require dialysis was <1 percent [31]. The risk is higher among patients with severe, underlying chronic kidney disease (CKD) [2,8,34].

However, it is increasingly appreciated that residual renal dysfunction may persist even among patients in whom the creatinine returns to baseline. This is especially noted among patients with underlying CKD among whom an episode of AKI results in a persistent increase in the risk of progression of CKD. This issue is discussed separately. (See "Renal and patient outcomes after acute tubular necrosis", section on 'Degree of recovery'.)

Occasionally, patients will require dialysis in the acute setting. The indications for dialysis are the same as in other forms of AKI. (See "Renal replacement therapy (dialysis) in acute kidney injury (acute renal failure) in adults: Indications, timing, and dialysis dose".)

SUMMARY AND RECOMMENDATIONS

- Contrast nephropathy is a generally reversible type of acute kidney injury (AKI) that occurs soon after the administration of radiocontrast media. (See 'Introduction' above.)
- The pathogenesis is not completely understood. Based upon animal studies, contrast nephropathy is most likely due to acute tubular necrosis (ATN) related to vasoconstriction and cytotoxic effects from contrast, possibly with contributions from prerenal factors or intratubular obstruction. (See 'Pathogenesis' above.)
- The reported incidence of contrast-induced nephropathy varies widely, largely depending upon the presence or absence of risk factors, primarily including underlying chronic kidney disease (CKD). The risk is very small among patients with baseline normal renal function, even among diabetic patients. The risk increases with the severity of underlying renal dysfunction, especially among diabetic patients. The risk is also higher among patients with heart failure or hemodynamic instability. The risk increases as the volume of contrast agent increases, but there is no "safe" dose below which AKI does not occur. The risk varies with various types of contrast agents, particularly hyperosmolal ionic contrast agents. (See 'Epidemiology' above and "Prevention of contrast-induced nephropathy", section on 'Type of contrast agent'.)
- The clinical manifestations of contrast nephropathy are observed within the first 24 to 48 hours after the contrast study. Most patients are nonoliguric, and the only perceived abnormality is a mild increase in the serum creatinine, which starts to decline within three to seven days. The urinary sediment may show classic findings of ATN. Protein excretion is absent or mild. The fractional sodium excretion (FENa) is often <1 percent, which is in contrast to patients who develop AKI due to ischemic or toxin-induced ATN, but this may in part be explained by the fact that contrast nephropathy is usually nonoliguric, and ischemic ATN is usually oliguric. (See 'Clinical features' above.)
- The diagnosis is based upon the clinical presentation and the exclusion of other causes of AKI. A characteristic urinalysis supports the diagnosis, but does not provide a conclusive diagnosis of contrast nephropathy. The absence of other findings on urinalysis such as white blood cells (WBCs), WBC casts, dysmorphic red blood cells (RBCs), or RBC casts generally excludes other causes of AKI such as interstitial nephritis and glomerular diseases. Conversely, the presence of WBCs, WBC casts, dysmorphic RBCs, or RBC casts suggests other causes of AKI.
- We generally do not obtain an ultrasound, at least initially, among patients who have a characteristic

presentation of contrast nephropathy following contrast exposure. However, we do obtain an ultrasound to exclude other causes of AKI among patients who do not follow a classic clinical course of contrast nephropathy or in whom the diagnosis of contrast nephropathy is uncertain. (See 'Diagnosis' above.)

- A renal biopsy is generally not helpful for the diagnosis of contrast nephropathy, since the lesions of ATN are focal and nonspecific and because AKI due to contrast nephropathy is generally short lived. However, as with the ultrasound, a biopsy may rarely be required to exclude other causes of AKI among patients who do not follow a classic clinical course, or in whom the diagnosis of contrast nephropathy is uncertain. (See 'Diagnosis' above.)
- The differential diagnosis includes ischemic ATN, acute interstitial nephritis, and renal atheroemboli. The former two require additional insults such as sepsis or hypotension, or medication exposure, which may be excluded by history. Renal atheroemboli may be distinguished by the presence of other embolic lesions (as on the toes) or livedo reticularis, and transient eosinophilia and hypocomplementemia. In addition, the onset of kidney injury due to atheroemboli may be delayed for days to weeks after the procedure and has a protracted course, with frequently little or no recovery of renal function. (See 'Diagnosis' above.)

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Disclosures

Disclosures: **Michael R Rudnick, MD** Nothing to disclose. **Paul M Palevsky, MD** Grant/Research/Clinical Trial Support: Spectral Diagnostic injury). **Alice M Sheridan, MD** Nothing to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a m Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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