

# CLINICAL INQUIRIES

From the Family Practice Inquiries Network

## What interventions reduce the risk of contrast nephropathy for high-risk patients?

### ■ Evidence-Based Answer

Several interventions may reduce the risk of contrast nephropathy for high-risk patients; however, most evidence uses surrogate markers for clinically relevant outcomes. Because dehydration is a risk factor for developing contrast nephropathy, periprocedural hydration is routinely recommended (strength of recommendation [SOR]: C, expert opinion). Single studies have suggested that isotonic saline is associated with less risk than half-normal saline, and hydration with fluids containing sodium bicarbonate is more efficacious than those containing isotonic saline (SOR: B, single randomized controlled trial [RCT]).

Oral acetylcysteine lowers the risk of post-contrast elevations in creatinine if taken more than 24 hours before contrast administration (SOR: A, RCTs). Acetylcysteine's low cost and favorable side effect profile make it an appealing option. Hypo-osmolar contrast media are less likely to induce contrast nephropathy than hyper-osmolar media (SOR: A, RCTs). Finally, hemofiltration might be considered for patients with extremely high risk of developing contrast nephropathy (SOR: B, single RCT).

### ■ Evidence Summary

Intravascular administration of radiocontrast is frequently associated with acute reductions in renal function, particularly for patients with risk factors (TABLE 1). Most studies have used operational definitions of contrast nephropathy based on predefined elevations in serum creatinine from baseline, the great majority of which are transient and clinically insignificant. It is unclear if interventions that reduce the rate of mild creatinine elevations (TABLE 2) also reduce the risk of clinically

relevant adverse outcomes.

A single RCT showed decreased risk of contrast nephropathy for patients pretreated with intravenous fluids containing sodium bicarbonate compared with those pretreated with a sodium chloride solution (number needed to treat [NNT]=8.4).<sup>2</sup> Another RCT showed that periprocedural hydration with isotonic saline is superior to half-normal saline in preventing contrast nephropathy (NNT=77).<sup>3</sup> Several studies have demonstrated decreased risk of contrast nephropathy

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## What are Clinical Inquiries?

**Clinical Inquiries** answer recent questions from the practices of family physicians. Practicing family physicians choose the most relevant questions submitted through a web-based voting system operated by the Family Physicians Inquiries Network (FPIN; online at [www.fpin.org](http://www.fpin.org)).

FPIN is national, not-for-profit consortium of family medicine departments, community residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists. Once questions are selected, FPIN editors then organize teams of clinicians and librarians to answer them based on systematic review of the world literature. Answers are developed through an explicit, systematic method:

- FPIN librarians and editors identify questions recently answered in best evidence sources (e.g. Cochrane Reviews, Clinical Evidence, the US Preventive Services Task Force, Evidence Based Guidelines, a published systematic review).
- FPIN librarians then conduct systematic and standardized literature searches of best evidence sources, Medline, and other databases in collaboration with an FPIN clinician or clinicians. If a best evidence source has been identified, the search begins from the date of the search conducted for that source. Otherwise, the searches are comprehensive.
- FPIN clinician authors then choose the highest quality original research sources, and critically appraise the research and integrate the findings in the Evidence Based Answer and Evidence Summary section of Clinical Inquiries. Authoritative sources are also quoted in the "Recommendations from Others" section of the Clinical Inquiry.
- Each Clinical Inquiry is reviewed by 4 or more peers or editors before publication in *JFP*.
- FPIN medical librarians are accountable for the thoroughness of the literature search, for recording the databases searched, search hedges used and the search terms. The details of each search is available to any interested reader (contact [managingeditor@fpin.org](mailto:managingeditor@fpin.org)).
- Finally, a practicing family physician or other clinician writes an accompanying commentary to provide a clinical perspective.

TABLE 1

**Risk factors for the development of contrast nephropathy**

Advanced age
Diabetes mellitus
Chronic renal insufficiency
Congestive heart failure
Acute myocardial infarction
Cardiogenic shock
Renal transplant
Hemodynamic instability
Dehydration
Low serum albumin
Angiotensin-converting enzyme use
Nonsteroidal anti-inflammatory drug use
Furosemide use
Higher volume of contrast media

Source: Nikolsky et al, *Rev Cardiovasc Med* 2003.<sup>1</sup>

thy for high-risk patients when low-osmolality contrast media are used rather than high-osmolality contrast media (NNT=27).<sup>4</sup> A single study suggested that iso-osmolar contrast media generate less contrast induced nephropathy than low-osmolar contrast media.<sup>5</sup> Because the primary outcome in these studies was a change in serum creatinine, the NNTs listed above may not predict clinical outcomes.

Periprocedural administration of acetylcysteine reduces the risk of contrast nephropathy in high-risk patients (odds ratio=0.56; 95% confidence interval, 0.37–0.84). Oral acetylcysteine is effective if intervention is begun 24 hours before contrast administration.<sup>6</sup> Preliminary evidence shows that intravenous administration of acetylcysteine immediately before contrast administration lowers the risk of contrast nephropathy.<sup>7</sup> Oral acetylcysteine is low in cost and has no known side effects.

A single RCT suggests that hemofiltration initiated 4 to 6 hours before contrast administration reduces the incidence of contrast nephropathy among high-risk patients.<sup>8</sup> The study was unusual

in that patients in the intervention group experienced statistically significant reductions in several clinically relevant outcomes, including in-hospital mortality and cumulative 1-year mortality (in-hospital mortality, NNT=8.3; cumulative 1-year mortality, NNT=5). Hemofiltration is expensive and is not available in many institutions.

**Recommendations from Others**

The American College of Radiology recommends using low-osmolality contrast media for patients with renal insufficiency, particularly those with diabetes.<sup>9</sup> Clinical Evidence found support for the use of low-osmolality contrast media, periprocedural hydration, and acetylcysteine as interventions to reduce the risk of contrast nephropathy.<sup>10</sup>

**Paul D. Grossman, MD,**  
Del Norte Community Health Center, Crescent City, Calif;  
**Martha Burroughs, MLS,**  
University of Colorado Health Sciences Center, Denver

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TABLE 2

## Interventions to reduce risk of contrast nephropathy

INTERVENTION	SOR	PROTOCOLS
Acetylcysteine (oral)	A	Acetylcysteine 600 mg PO twice daily is generally given for 2 days beginning on the day prior to the procedure. <sup>6</sup>
Hypo-osmolar contrast media	A	A variety of protocols have been demonstrated to be effective. <sup>4</sup>
Acetylcysteine (IV)	B	150 mg/kg of acetylcysteine was given in 500 mL of normal saline over 30 min immediately before contrast followed by 50 mg/kg of acetylcysteine in 500 mL of normal saline over 4 h. <sup>7</sup>
Iso-osmolar contrast media	B	Varying volumes of iodixanol, an iso-osmolar contrast medium, were used rather than iohexol, a low osmolar contrast medium. <sup>5</sup>
Sodium bicarbonate	B	Patients were given 4.23% dextrose in H <sub>2</sub> O with 154 mEq of sodium bicarbonate added per liter. Fluids were begun 1 hour prior to contrast administration running at 3 mL/kg/hr for 1 hour and then at 1 mL/kg/hr until 6 hours after contrast administration. <sup>2</sup>
Isotonic saline	B	0.9% sodium chloride was run at 1 mL/kg/hr beginning at 8 a.m. on the morning of the procedure or as early as possible prior to emergency procedures. The infusion was discontinued at 8 a.m. on the morning following the procedure. <sup>3</sup>
Hemofiltration	B	Hemofiltration was started 4 to 6 hours before the procedure. It was resumed after the procedure was completed and continued for 18 to 24 hours. <sup>8</sup>

SOR, strength of recommendation. (For more on evidence ratings, see "Evidence-based medicine terms" on page 381.)

### ■ Clinical Commentary

#### Avoid radiocontrast agents when possible; consider hydration and acetylcysteine

The best prevention of contrast nephropathy is to avoid radiocontrast agents whenever possible. Ultrasound, MRI, or CT scanning without radiocontrast can often provide adequate information. However, when contrast agents must be used for high-risk patients, lower doses and iso-osmolal nonionic agents should be considered, and serial studies should be spaced out.

Adequate hydration and avoidance of drugs with renal effects, including nonsteroidal anti-inflammatory drugs, diuretics, and angiotensin-converting enzyme inhibitors, can decrease the risk of contrast nephropathy for patients requiring a contrast study. Patients can be hydrated and their medicines held starting the day before

the procedure. For patients with any risk factors for contrast nephropathy, acetylcysteine should also be administered. Sodium bicarbonate can also lower the risk of nephropathy by administering it at the time of the procedure.

Contrast nephropathy has often been defined as an immediate increase in creatinine greater than 25%. The clinical significance of small transient elevations in creatinine is unclear. Furthermore, the wide variability reported in the incidence of contrast nephropathy results from differences in the presence of risk factors. Therefore, it is important to assess each patient's risk individually and undertake additional preventive measures accordingly.

**Richard A. Guthmann, MD,**  
Illinois Masonic Family Practice Residency,  
University of Illinois at Chicago