

# Nonrenal Complications of Contrast Media



Damien Marycz, MD, Khaled M. Ziada, MD\*

## KEYWORDS

• Contrast media • Anaphylactoid reactions • Preoperative treatment • Chemotoxicity

## KEY POINTS

- Chemotoxic reactions to contrast media are mostly related to ionicity and osmolality; these have become less significant with the nonionic iso-osmolar agents more commonly used today.
- Anaphylactoid reactions to contrast media are secondary to release of histamine and other vasoactive substances, but cannot be considered typical of true anaphylactic reactions, which are mediated by immunoglobulin E antibodies.
- Patients who have had a previous anaphylactoid reaction to contrast or those with atopic conditions are at increased risk for adverse reactions to contrast, and should be targeted for preventive treatment before repeat exposure.
- A history of seafood or shellfish allergy is not associated with an increased risk for anaphylactoid reactions to contrast media.
- Appropriate medical pretreatment to avoid anaphylactoid reactions must include prednisone, with at least 1 dose administered more than 12 hours before contrast injection.
- Patients undergoing immunotherapy treatment with recombinant interleukin 2 have been shown to have an increased risk for the development of delayed adverse reactions to contrast media.

Injection of contrast media is the foundation of invasive and interventional cardiovascular practice. Iodine-based contrast was first safely used in the 1920s for urologic procedures and examinations. Initially these agents were poorly tolerated owing to the side effects of nausea, vomiting, and hypotension related to the very high ionic and osmolar concentrations. In the 1950s, the triiodobenzoic acid derivatives were developed (sodium and meglumine salts of triiodinated benzoic acid derivatives), which contained lower ionic concentrations and had lower osmolality than the contrast agents originally used. These newer agents, with their lower ionic and osmolar concentration, were more hydrophilic and better tolerated by patients because of their less chemotoxic profiles.<sup>1</sup>

Despite the high safety profile of iodinated contrast agents, their use can be associated with side effects and complications. Contrast-induced nephropathy is one of the major concerns associated with the use of these agents in the catheterization laboratory and radiology suites (see later discussion). This article is dedicated to the discussion of all nonrenal side effects and complications related to the use of contrast agents in the catheterization laboratory.

There are 2 major classes of side effects and complications related to contrast media: chemotoxicity and anaphylactoid reactions. Chemotoxicity is related to the physical and chemical properties of the agent used, whereas anaphylactoid reactions are probably related to the iodine content

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The authors have nothing to disclose.

Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, 900 South Limestone Street, 326 Wethington Building, Lexington, KY 40536-0200, USA

\* Corresponding author.

E-mail address: [khaled.ziada@uky.edu](mailto:khaled.ziada@uky.edu)

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(Fig. 1). The various reactions, their clinical presentations, and management strategies are discussed in detail.

## CHEMOTOXIC REACTIONS

Chemotoxic reactions are related to the chemical properties, dose, and rate of infusion of the contrast agent used. The typical minor chemotoxic reactions of contrast media include nausea, flushing, warmth, and pain at the injection site. The major chemotoxic reactions include hypotension, dysrhythmias, depressed myocardial contractility, and myocardial ischemia. The ionic concentration, osmolality, viscosity, and calcium-binding properties of these contrast agents are responsible for most types of reactions.

These reactions were more frequent and more severe in the earlier days of angiography, when contrast media were ionic and had high osmolality (up to 1400 mOsm/kg). As significant volumes of such agents are injected in the intravascular space, a dramatic increase in intravascular osmolality ensues, which in turn leads to fluid shift from the intracellular to the extracellular spaces. The intravascular volume increase manifests as an elevation of the left ventricular end-diastolic pressure, pulmonary edema, and cellular dysfunction.<sup>2</sup> Electrophysiologic effects of ionic contrast media included decreased rate of depolarization of the sinoatrial node, PR-interval prolongation, and, occasionally, heart block or even ventricular fibrillation. The electrophysiologic effects are thought to be caused by transient hypocalcemia via binding of calcium from the radiopaque anion in addition to calcium-sequestering agents (such as

sodium citrate and sodium ethylenediaminetetraacetic acid) often used in ionic contrast agents of high osmolality.<sup>3,4</sup> The use of ionic high-osmolar contrast agents was also known to produce a transient depression in myocardial performance and was responsible for the hypotension seen with the use of these agents. This decrease in blood pressure can further lead to myocardial ischemia and circulatory collapse in patients with severe coronary ischemia, decompensated heart failure, or critical aortic stenosis.

Modifications to the ionic structure and iodine content of contrast media in the 1980s led to the development of ionic low-osmolar contrast media, nonionic low-osmolar contrast media, and nonionic iso-osmolar contrast media. By virtue of their lower osmolality and low ionic concentrations, these contrast agents are better tolerated by patients and produce fewer major side effects in comparison with ionic high-osmolar contrast agents.

## ACUTE AND EARLY ANAPHYLACTOID REACTIONS

Anaphylactoid reactions to contrast media are typically divided into 2 classes related to the onset of the reaction in relation to the time of contrast exposure: acute or early reactions occur within 1 hour of delivery, and delayed reactions occur within 1 hour to 7 days after exposure (see Fig. 1).<sup>5</sup>

### Manifestations and Incidence

The acute reactions are typically characterized as being allergic-like reactions or physiologic reactions to the chemical properties of the contrast media. The severity of these reactions can range

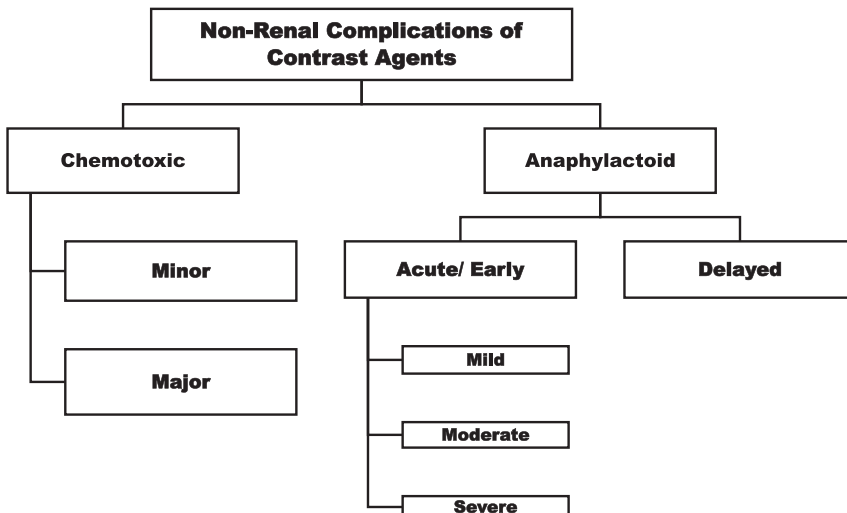


Fig. 1. Types of complications associated with use of contrast agents.

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