# Radiocontrast media (RCM) hypersensitivity and its evaluation

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Iodinated radiocontrast media (RCM) is one of the most widely used drug worldwide and major cause of drug hypersensitivity reactions in Korea.[1,2] RCM hypersensitivity can be divided into immediate reactions, which occur within 1 h after exposure, and delayed (non-immediate) reactions, which occur from 1 h to several days after exposure.[3] Symptoms of immediate reactions vary from simple cutaneous symptoms, such as itching and urticaria, to life-threatening anaphylactic shock. Fatal immediate reactions may occur in 1–3 individuals per 100,000 exposures.[4] For a long time before 2000s, immediate reactions to RCM was regarded as non-immunologic reaction, so-called anaphylactoid or pseudoallergic reaction, in which RCM directly stimulates basophil or mast cell.[4] However, there are growing evidences that a group of the reactions can be induced by specific immunologic mechanism such as IgE-mediated reactions recently.[5,6] RCM can be classified based on their ionicity and osmolarity. In the past when the high-osmolar ionic RCM were used, immediate adverse reactions were common because of their chemical toxicity.[1] In the 1970, the introduction of non-ionic low-osmolar RCM led to marked decrease in the incidence of these reactions.[1,3] However, RCM became more widely used in various radiologic tests and interventions. Repeated tests are commonly performed using RCM in the patients with cancers or cardiovascular diseases. Accordingly, clinical features of RCM hypersensitivity are also changing these days. Some patients experience hypersensitivity reaction to RCM which did not induce adverse reaction in the previous exposure. These suggest some immediate reactions of RCM hypersensitivity are immunologic reactions in which IgE-sensitization is involved.[6,7] Evidences of positive skin tests and positive basophil activation tests to RCM supports these pathogenic mechanism.[5,8]

The evaluation of patients with hypersensitivity reactions to RCM can be initiated during the acute phase of reactions. In immediate reactions, cutaneous symptoms such as pruritus, urticaria, angioedema, and flushing are common, but systemic reactions accompanied with respiratory or cardiovascular symptoms may

happen. Serum tryptase may help to identify the type of reactions in case of anaphylaxis. In delayed reactions, most of reactions are cutaneous reactions, but systemic involvement such as eosinophilia or renal and hepatic dysfunction can be also occurred.[7] Once the reaction has resolved, the patient should be assessed using available diagnostic methods for RCM hypersensitivity, including clinical history and skin tests and controlled challenge tests. The clinical history should be taken carefully, as with any adverse drug reaction. Details should include the RCM administered, the interval between administration of the ICM and the onset of symptoms, the types of symptoms and the treatment required to control symptoms. The history should also take account of previous exposure of RCM and presence of reactions in their prior exposures.[7]

Recently, skin tests for RCM receive spotlights in their roles in the diagnosis of RCM hypersensitivity.[5,9-11] Prick and intradermal skin tests can be performed in immediate reactions. The RCM generally are used undiluted for skin prick tests and diluted at 1:10 for the intradermal test. Skin testing should be performed with the RCM involved in the reaction if known. If the result is positive, or if the culprit RCM is unknown, skin testing can be performed with available panel of RCM.[7] The sensitivity of skin tests for immediate reactions varies from 4.2% to 73%.[7] However, it is more worthy to diagnose severe immediate reactions such anaphylaxis.[9,11] In the meta analysis, positive rate of skin tests were 17% (95% CI, 10–26%) in patients with all immediate reactions, and up to 52% (95% CI, 31–72%) when confined to severe immediate reactions.[11] Furthermore it was as high as 81.8% in patients with anaphylactic shock in another study.[9] However, it has no clinical utility in predicting future hypersensitivity reactions in patients with no previous exposure to RCM or no history of RCM hypersensitivity.[10] So far, their clinical value was only validated in the diagnosis of severe prior reaction to RCM. Thus, strategy to use RCM skin test with pharmacologic premedication is suggested for the selection of RCM, when re-exposure to RCM is needed.[12] Further studies are needed to clarify the role of RCM skin test for the prevention of reactions in patients with previous history of RCM hypersensitivity.

## References


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