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Allergic-like contrast reactions in the ED: Incidence, management, and impact on patient disposition

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ABSTRACT

Purpose: Determine the incidence, management, and impact on patient disposition of allergic-like contrast reactions (ALCR) to intravenous iodinated contrast in the emergency department (ED).

Methods: All ED patients who developed an ALCR following contrast-enhanced CT (CECT) from June 2011–December 2016 were retrospectively identified. Medical records were reviewed and reaction severity, management, and disposition were quantified using descriptive statistics. The total number of consecutive CECTs performed in the ED were available from June 2011–March 2016 and were used to derive ALCR incidence over that time period.

Results: A total of 90 patients developed an ALCR during the study period. An ALCR incidence of 0.2% was derived based on 74 ALCRs occurring out of 47,059 consecutive contrast injections in ED patients from June 2011–April 2016. Reaction severity was mild in 63/90 (70%) and moderate in 27/90 (30%) cases; no patient developed a severe reaction by American College of Radiology criteria. The most commonly administered treatments were diphenhydramine in 67/90 (74%), corticosteroid in 24/90 (27%), and epinephrine in 13/90 (14%); symptoms subsequently resolved in all cases. No patient required inpatient admission for contrast reaction alone, and 5 patients were sent to the ED observation unit for post-epinephrine monitoring and subsequently discharged.

Conclusion: ALCR among ED patients undergoing CECT are rare, generally of mild severity, respond well to pharmacologic management, and do not alter patient disposition in most cases. Familiarity with symptoms, management, and prevention strategies is increasingly relevant to the emergency physician given the ubiquity of CECT.

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1. Introduction

The utilization of computed tomography (CT) in the emergency department (ED) has grown tremendously over the past two decades owing to its wide availability and proven value as a clinical decision-making tool [1,2]. The addition of intravenous iodinated contrast improves soft tissue characterization and is indispensable when assessing vasculature, such as in the evaluation of suspected aortic dissection or pulmonary embolism. While the safety of iodinated contrast agents is well-established, a minority of patients experience adverse events such as allergic-like reactions, contrast-induced acute kidney injury, and contrast extravasation at the injection site [3,4].

Allergic-like contrast reactions (ALCR) are a well-characterized entity, with an estimated incidence of 0.1–0.7% when using low-osmolar contrast media [5–7]. ALCRs are classified by the American college of Radiology (ACR) as mild, moderate, or severe, with the latter generally accounting for only 2–3% of cases [8]. When reactions occur, appropriate management consists of focused patient assessment, prompt treatment corresponding to reaction severity, and preventative measures to mitigate the risk of future events [8].

The management of ALCRs in patients undergoing contrast-enhanced CT (CECT) in the ED poses a unique set of concerns. First, increasing pressure to streamline care in the ED given capacity limitations may complicate decisions regarding patient disposition following a reaction [9]. ALCRs can prolong length of stay (LOS) should they necessitate transfer to an ED observation unit (EDOU) or inpatient admission, thereby increasing resource utilization. Additionally, clarifying the presence of a known contrast allergy in patients presenting to an ED for the first time may be challenging given patient acuity and other

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factors that may limit the ability to screen for a history of ALCR. Finally, when an emergent indication for CECT exists in a patient with a known contrast allergy, lengthy premedication protocols that are easily implemented in outpatients may not be temporally feasible [8]. Given the growth of stand-alone urgent care and ED facilities where CECTs are performed in the absence of an on-site radiologist, emergency medicine (EM) physicians may be increasingly tasked as first responders in the setting of ALCRs [10].

Given the unique challenges that ALCRs may present in the ED setting, study of their incidence, treatment patterns, and impact on care is warranted. Therefore, this study aimed to determine the incidence, characteristics, management, and impact on patient disposition of ALCRs in ED patients at a large quaternary care center.

2. Methods

2.1. Human subjects compliance

This retrospective, Health Insurance Portability and Accountability Act–compliant study was approved by the Institutional Review Board with waiver of informed consent.

2.2. Study site

The study was performed at a 999-bed quaternary care academic center and Level 1 Trauma Center. Approximately 104,000 ED visits occur at the institution annually, and approximately 105,000 ED diagnostic imaging studies are performed and interpreted by the emergency radiology division annually. Radiology technologists, attending physicians, and trainees at our institution receive mandatory structured education regarding management of contrast reactions, including interactive lectures, online modules, and annual high-fidelity simulation sessions. In addition, these personnel are certified through the American Heart Association's Advanced Cardiac Life Support (ACLS) course.

2.3. Data collection

At our institution, all contrast reactions regardless of their severity are documented in the electronic medical record. An institutional database spanning June 2011 to December 2016 was queried to identify patients who developed a reaction following CECT in our ED. All patients with reactions categorized as “allergic-like” based on criteria outlined by the ACR were included, and any patients with symptoms indicating a “physiologic” reaction were excluded [8]. Allergic-like contrast reactions present in a similar manner to true allergic reactions seen with drugs or other allergens, with symptoms such as pruritis, urticaria, cutaneous or facial edema, sneezing/rhinorrhea, bronchospasm, hypotension, and others. Physiologic contrast reactions are distinct from allergic-like reactions and are thought to represent homeostatic alterations due to chemotoxicity or osmotoxicity of the contrast agent, manifesting with symptoms such as flushing, headache, vasovagal reactions, hypertensive urgency, nausea/vomiting, seizures, etc. Detailed classification criteria for allergic-like and physiologic reactions are contained within the ACR Manual on Contrast Media [8]. Inpatients being scanned in our ED and patients referred to our ED for management of a contrast reaction that occurred at another site were excluded. Demographic information including age and gender was collected from the database. Electronic medical records (EMRs) were reviewed to determine the presence of a known history of prior reaction, symptoms characterizing each reaction, time to onset of reaction, treatment provided, and patient disposition. Iopamidol (Isovue 370; Bracco Diagnostics Inc., Monroe Township, NJ) was the intravenous contrast agent administered in all patients imaged in the ED during the study period.

2.4. Outcome measures

The primary outcome measures were the incidence of contrast reactions and their severity. The number of CECT injections performed from April 2016 to December 2016 could not be obtained due to a change in our EMR system in April 2016, and therefore data from June 2011 to March 2016 was used to derive the incidence of reactions. Symptoms of ALCR were categorized into skin/mucosal, respiratory, and gastrointestinal. Reaction severity was categorized as mild, moderate, or severe based on criteria outlined in the ACR Manual on Contrast Media, Version 10.3 [8]. Patients reporting nonspecific dyspnea were classified as having moderate reactions according to previously described classification schemes [5].

Secondary outcome measures included management provided for contrast reactions and the influence of contrast reactions on patient disposition. Treatments included one or more of the following medications: intravenous (IV) or oral (PO) diphenhydramine, IV or PO corticosteroid, intramuscular epinephrine, albuterol nebulizer, and IV or PO histamine H2 antagonist. The analysis characterizing the impact of contrast reactions on disposition was limited to patients who were either discharged from the ED or admitted to the EDOU with the specific intent of monitoring for a rebound reaction. Patients admitted to the hospital or the EDOU for management of their presenting complaint were not included in this analysis, as their disposition was deemed to be unaffected by the contrast reaction.

2.5. Statistical analysis

Summary statistics were used to describe the outcome measures. Fischer's exact test was used to compare categorical variables and the Wilcoxon Rank-Sum test was used to compare nonparametric continuous variables, with the threshold for significance set at $p < 0.05$. JMP Pro 13 (SAS Institute Inc., Cary, NC) was used for all analyses.

3. Results

3.1. Patient population

A total of 97 patients were initially identified as having had a contrast reaction in our ED during the study period. Excluded patients consisted of 5 inpatients being imaged in the ED scanner, one patient who was referred to the ED for an ALCR that occurred at another imaging site, and one patient with a vasovagal reaction that was considered “physiologic”. The remaining 90 patients were included in our analysis. The mean age was 44 years (range 8–88 years), with 66% females. The incidence of ALCR derived over the period from June 2011 to March 2016 was 0.2%, based on 74 ALCRs out of 47,059 consecutive CECT injections. The most common types of CT exams obtained in patients developing ALCR were abdomen/pelvis CT (48%), pulmonary embolism CT (16%), head/neck CTA (12%), and coronary CTA (12%).

3.2. Characteristics of contrast reactions

Of all patients who developed reactions, 82/90 (91%) had skin/mucosal symptoms, 20/90 (22%) had respiratory symptoms, and 4/90 (4%) had gastrointestinal symptoms (Table 1). The most frequent specific symptoms from any category were urticaria (61%), sneezing/rhinorrhea (32%), and shortness of breath (16%). Based on symptoms, 70% of reactions were categorized as mild and 30% as moderate. None were categorized as severe according to strict interpretation of the current ACR guidelines [8]. Respiratory symptoms occurred in 70% of patients with moderate reactions and in 2% of patients with mild reactions. Data regarding time from contrast injection to onset of reaction were available in 76 patients, and reactions occurred within 5 min of injection in 62/76 (83%) cases (Table 2).

Table 1

Symptoms of contrast reactions by severity and organ system.

Symptom	Mild (n = 63)	Moderate (n = 27)	Total (n = 90)
Skin/Mucosal	61 (97%)	21 (78%)	82 (91%)
Urticaria	42 (67%)	13 (48%)	55 (61%)
Sneezing/rhinorrhea	21 (33%)	8 (30%)	29 (32%)
Throat itching	8 (13%)	5 (19%)	13 (14%)
Facial edema	2 (3%)	3 (11%)	5 (6%)
Facial erythema	1 (2%)	3 (11%)	4 (4%)
Respiratory	1 (2%)	19 (70%)	20 (22%)
Shortness of breath	1 (2%)	13 (48%)	14 (16%)
Throat tightness	0 (0%)	9 (33%)	9 (10%)
Wheezing	0 (0%)	5 (19%)	5 (6%)
Gastrointestinal	2 (3%)	2 (7%)	4 (4%)
Nausea/vomiting	2 (3%)	2 (7%)	4 (4%)

Three patients had a known history of prior mild ALCR. Two of them required CECT to evaluate for pulmonary embolism, and one had a clinical presentation suggestive of colitis for which contrast-enhanced abdominal CT was requested. All 3 patients were sent to the EDOU to undergo a 13-hour premedication protocol per departmental policy and ACR guidelines [8]. In all 3 patients, the breakthrough ALCRs were categorized as mild in severity and resulted in symptoms that were similar to those experienced during prior reactions. Two of these patients were subsequently admitted to the inpatient service on the basis of CTs that were positive for subsegmental pulmonary embolism and colitis, respectively. The third had a CT that was negative for findings that warranted additional acute care, prompting discharge.

3.3. Treatment of contrast reactions

Pharmacotherapy was administered for ALCR in 69/90 (77%) patients. The remainder were either given intravenous saline or simply observed. Treatments administered are illustrated in Fig. 1. The most commonly administered treatments were diphenhydramine in 67/90 (74%), corticosteroid in 24/90 (27%), and epinephrine in 13/90 (14%). Patients with moderate reactions were significantly more likely to receive epinephrine ($p < 0.001$), corticosteroid ($p < 0.001$), and albuterol nebulizer ($p = 0.003$) compared to patients with mild reactions. All patients reported resolution of reaction-related symptoms prior to leaving the ED.

3.4. Effect of contrast reactions on patient disposition

Of our cohort, 44/90 (49%) patients were either admitted to the inpatient ward or sent to the EDOU based on their presenting complaint and not as a result of their ALCR. Of the remaining subgroup of 46 patients, 41/46 (89%) were discharged and 5/46 (11%) were sent to the EDOU for monitoring of ALCR. In this subgroup, a larger proportion of patients with moderate reactions than with mild reactions were sent to the EDOU for monitoring (25% versus 3%, $p = 0.043$). Median time from contrast reaction to discharge was significantly longer in patients with moderate reactions than with mild reactions (4.3 versus 2.5 h, $p = 0.002$).

4. Discussion

CECT is an increasingly utilized component of the emergency physician's armamentarium for clinical decision-making and diagnostic evaluation [1]. While low-osmolar nonionic iodinated contrast agents

are safe and well-tolerated, ALCRs can occur and may have implications for patient care and clinical workflow in the emergency care setting. Our study underscores that these reactions are most often mild, respond well to medical management, and only infrequently alter patient disposition from the ED. Several important conclusions can be drawn from this study.

First, in a cohort of over 47,000 consecutive CECT exams in ED patients, the rate of ALCRs was found to be 0.2%. This findings is in line with other large cohorts comprising primarily non-ED patients [5–7]. Our finding that a majority (70%) of contrast reactions were mild is also concordant with the experience of others [5–7]. However, in contrast to prior studies where 2–3% of reactions were classified as severe, none of our patients experienced a severe reaction as strictly defined by the ACR guidelines. This discrepancy may stem in part from subjectivity in severity grading and evolution of the ACR guidelines over time. For example, while one large cohort classified moderate/severe bronchospasm as a severe reaction according to the ACR guidelines published at that time, the most recent guidelines require the presence of significant hypoxia which was not identified in any of our patients with bronchospasm [6,8,11].

Second, pharmacologic management sufficed in all patients, without the need for intubation or prolonged critical care. Management included diphenhydramine in 74% of cases, corticosteroid in 27% of cases, and intramuscular epinephrine in 14% of cases. Our higher rate of epinephrine administration compared to older studies suggests a lower threshold for use in our contemporary series, which could be due to ease of access to intramuscular epinephrine injections ("Epi-Pens") in our ED CT scanner rooms, variation in institutional practice, and/or possibly overutilization of epinephrine in our study [4,6,7]. Though we did not examine the appropriateness of epinephrine administration, other work has demonstrated that knowledge gaps regarding indications and dosing are common [12]. Contrast reaction simulation training is a potentially effective means of improving knowledge of ALCR management [13]. With the growth of stand-alone urgent care and ED facilities where CT scans are performed without a radiologist on site, EM physicians may be increasingly tasked with being first responders in the setting of contrast reactions [10]. Simulation training targeted toward EM physicians and personnel staffing these facilities could improve comfort and compliance with accepted management algorithms [14].

Third, ALCR infrequently altered patient disposition from the ED. Out of patients with ALCR who were not admitted or sent to the EDOU for a separate condition, 89% were discharged and the remainder were sent to the EDOU for post-epinephrine monitoring, with no patients requiring admission on the basis of an ALCR alone. While the increase in ED LOS resulting from ALCR could not be readily quantified given the presence of other parallel processes in the ED that may have affected LOS, patients with moderate reactions had a longer time from reaction to discharge than those with mild reactions. This is likely partially attributable to the increased proportion of moderate versus mild reactions sent to the EDOU for monitoring. The optimal monitoring strategy following a contrast reaction of any severity remains unclear, and the incidence of rebound reactions has not been well studied in contrast-mediated anaphylactoid reactions. Recommendations in the literature ranging from 6 to 24 h of observation following anaphylactic reactions of any etiology could be adapted to the management of moderate to severe contrast reactions [15–17]. We found that our EM physicians were generally comfortable with a 6 h observation period in cases where epinephrine was administered and a 1 to 2 h period in cases of mild reactions, with no patients developing a rebound reaction during these intervals or returning to our ED for recurrent symptoms. The impact of these observation periods on cost and ED resource utilization could be further studied by employing methods such as time-driven activity based costing, which may help elucidate the most cost-effective setting in which to monitor patients [18].

Three patients with a known history of prior contrast reaction underwent a 13 h premedication protocol prior to CECT and nonetheless developed a reaction, emphasizing that premedication does not eliminate the risk of ALCR. Prior work has also suggested that while

Table 2

Time to onset of reaction after contrast injection.

Time to onset	Mild (n = 51)	Moderate (n = 25)	Total (n = 76)
<2 min	35 (69%)	19 (76%)	54 (72%)
2–5 min	5 (10%)	3 (12%)	8 (11%)
>5–20 min	10 (20%)	3 (12%)	13 (17%)

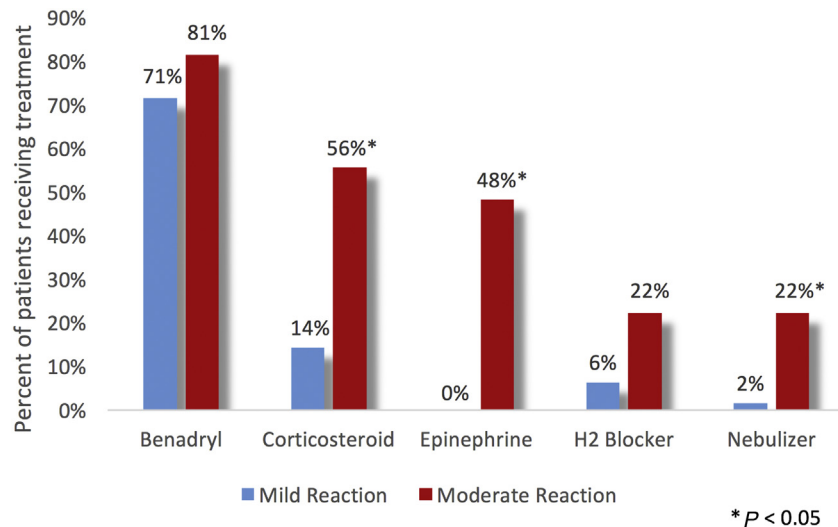


Fig. 1. Treatments administered by reaction severity.

premedication might mitigate the risk of a mild reaction, it may not confer significant protection against moderate or severe reactions [19,20]. EM physicians should be aware of the potential for repeat reaction when weighing the risks and benefits of CECT in patients with known contrast allergy, and contrast should generally be avoided in patients with a history of moderate or severe reactions, unless a compelling indication exists.

This retrospective study has several important limitations. The description of patient symptoms and classification of reaction severity relied on physician notes and incident reports. Direct quantification of the impact of ALCR on LOS was also precluded by the absence of comparison ED LOS metrics for patients who received CECT but did not develop a reaction. Additionally, the true incidence of ALCR over the entire study prior could not be obtained due to a change in our EMR system in April 2016, though the incidence derived from June 2011 through March 2016 represented a majority of the study period. Finally, the experience of a large quaternary care facility with an embedded ED imaging department that allows prompt attention by contrast simulation-trained technologist and physician responders may not be generalizable to other institutions.

In conclusion, contrast reactions among ED patients undergoing CECT are rare, generally of mild severity, respond well to prompt pharmacologic management, and do not alter patient disposition in most cases. The incidence of ALCR in the ED population does not appear to be significantly different from non-ED populations reported in prior studies. Familiarity with symptoms, management, and prevention strategies is vital to the emergency physician given the ubiquity of CECT in the modern clinical care paradigm. Further studies could quantify cost and resource utilization attributable to contrast reactions in the ED setting with the aim of refining care pathways.

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Conflict(s) of interest statements

Authors do not have any conflicts of interest.

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