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Adverse reactions to iodinated contrast media in patients with a history of allergies

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OBJECTIVE: To investigate the prevalence, patterns and influence factors for iodinated contrast media (ICM)-related adverse reaction (AR) in patients with a history of allergies.

METHODS: Patients with a history of allergies who underwent contrast-enhanced CT between January 2014 and December 2020 were enrolled. ICM-related AR and patient information were retrospectively analyzed. χ^2 and Student *t* test were used to compare between different groups, and logistic regression analyses were adopted to investigate influence factors for AR.

RESULTS: 325243 patients performed contrast-enhanced CT examinations. 713 cases with ICM allergy history and 27045 cases with non-ICM allergies history were included. The overall AR incidence was 0.66% (184/27758) and severe AR occurred in 0.05% (14 of 27758). 90.22% (166/184) of AR occurred within 20 minutes after injection. 2 severe AR occurred more than 30 minutes in patients with non-ICM allergies history. Compared with other ICMs, iodixanol was associated with higher incidence of AR in patients with ICM allergy history (10.71%; 12 of 112) and non-ICM allergies history (1.1%; 46 of 4172). Iohexol was associated with lower incidence of AR in patients with non-ICM allergies history (0.24%; 17 of 7134). Age ≥70 years (OR, 0.2; $P<0.001$) and hypertension (OR, 0.6; $P=0.025$) were protective factors for ICM-related AR in patients with non-ICM allergies history.

CONCLUSIONS: In patients with a history of allergies, most AR occurred within 20 minutes after injection. The AR incidence was associated with ICM generics. Age ≥70 years and hypertension were protective factors for ICM-related AR in patients with non-ICM allergies history.

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Introduction

The use of iodinated contrast media (ICM) has significantly increased with the growth of contrast-enhanced CT (CECT) examinations. More than 1 billion ICMs have been adopted worldwide so far.[1] The occurrence of ICM-related adverse reaction (AR) is growing with the rapidly growing use of ICM.[2] Although most events are mild with the application of non-ionic ICM, AR can still be fatal in some rare instances.[3,4] Studies demonstrated that the incidence of deaths because of AR was about 0.001‰–0.03‰.[2,5] Previous studies showed that there was about fivefold increased risk of recurring AR if using the same class of ICM in patients with ICM allergy history. And there was about two- to threefold increased risk of developing an ICM-related AR in patients with non-ICM allergies history.[6] So it is urgently needed to comprehensively identify prevalence, patterns and influence factors associated with AR in patients with a history of allergies. It would be helpful to radiologists to better make assessment procedures and take more effective precautions when receiving a CECT examination. Although some relevant underlying diseases and uncertain risk factors had been defined by previous studies,[7–14] most of them chose the general population as the study subject and did not focus on a patient population who had a history of allergies. The risk evaluation of CECT examination for this special population lacks sufficient clinical evidence. Therefore, detailed investigation of the incidence of AR and its patterns and influence factors in patients with a history of allergies is very necessary.

We hypothesized that this large-scale study could provide references to the safe usage of ICM in patients with a history of allergies. The purpose of this study was twofold. First, we aimed to identify the prevalence and patterns of AR. Second, we tried to identify influence factors for the occurrence of ICM-related AR.

Methods

Study participants

This study was ratified by the Institutional Ethical Committee in the hospital (ratification number: 2022(80)). The written informed consent was waived because it was a retrospective study. Inclusion criteria: (a) Patients ≥18 years and received CECT examination from January 2014 to December 2020 in our hospital; (b) Patients who experienced allergies (ICM allergy or non-ICM allergies) in the past. The ICM allergy history only contained mild (711 patients) and moderate (2 patients) allergies history in this investigation. Patients with severe ICM allergy history did not receive CECT examination and were advised to consider a substitute test in our hospital. Exclusion criteria: Patients with incomplete clinical AR data records. Considering different risk levels of ICM allergy and non-ICM allergies for AR, study subjects contained two categories: patients with ICM and non-ICM allergies history. The types of non-ICM allergies contained drugs, foods, pollinosis, specific allergies, others and unknown allergies. Patients with non-ICM allergies history all previously performed CECT examination and did not have an ICM-related AR.

ICM used

Nonionic ICM was intravenously injected through a high-pressure injector (Ulrich Medical® Inc.). In this study, the ICMs used included 9 brands of contrast media: Ultravist 370 (Bayer Healthcare), Visipaque 270 (GE Healthcare), Optiray 320 (Jiangsu Hengrui Medicine Co., Ltd), Optiray 350 (Guerbet), Ousu 350 (Yangtze River Pharmaceutical Co., Ltd), Iopamiro 350 (Bracco), Xenetix 350 (Guerbet), Omnipaque 350 (GE Healthcare) and Visipaque 320 (Jiangsu Hengrui Medicine Co., Ltd). As for generic profiles, five nonionic low-osmolar ICMs were used. It included iopamidol (13.72%), iobitridol (6.65%), iopromide (15.23%), iohexol (26.39%) and ioversol (22.58%). One nonionic iso-osmolar ICM was used, iodixanol (15.43%). According to our institutional protocol (Supplementary Table 1), the ICM injection rates and doses were determined on the basis of CT examination purpose and patient weight. All of the ICMs was warmed to 37∘C before injection. We supplied all healthcare by specially trained nurses. When patients waiting for the examination they sufficiently explained the necessity, safety profiles, probable normal and systemic responses after injection of ICM in order to reduce the anxiety of patients.

Evaluation content and quality control

An informed consent form about ICM usage was signed for all patients before the examination. The ICM usage evaluation form was filled out. It mainly contained patients' basic information and underlying diseases, risk factors, history of ICM usage and reactions, non-ICM allergic history, examination positions, ICM names, injection doses and rates. Patients were required to wait in the radiology department for 30 minutes after examination. After leaving the radiology department, the patients were instructed to tell nearby medical personnel if they had any abnormalities, and if they had left the hospital, they were required to contact the radiology department or emergency department. AR was defined and the severity was classified according to the 2021 American College of Radiology guideline. The criteria in the guideline were as follows: (1) mild AR (self-limited symptoms and signs without evidence of progression): limited scratchy and itchy throat, nasal congestion, rhinorrhea, sneezing, conjunctivitis, limited urticaria and pruritis, cutaneous edema; (2) moderate AR (more pronounced symptoms and signs which commonly require medical management): diffuse pruritis and urticaria, diffuse erythema and stable vital signs, facial edema without dyspnea, throat hoarseness or tightness without dyspnea, bronchospasm and wheezing, mild or no hypoxia; (3) severe AR (life-threatening symptoms and signs which can cause permanent morbidity even death if not managed properly): diffuse facial edema or edema with dyspnea, diffuse erythema with hypotension, laryngeal edema with hypoxia and/or stridor, wheezing and bronchospasm with significant

hypoxia, anaphylactic shock (hypotension + tachycardia).[6] Considering there can be overlap between allergic-like reactions and physiologic reactions in clinical practice and it is difficult to distinguish them. So gastrointestinal symptoms containing nausea and/or vomiting and flushing were also monitored except for allergic-like reactions. Physiological reactions such as angialgia and heat sensation were excluded. The AR record form was filled out in detail for patients who developed AR. It included the onset time, signs and symptoms, treatment, remission time and outcomes of AR. Patients with both ICM allergy history and non-ICM allergies history did not undergo any type of premedication before administration of ICM in this investigation. Standardized electronic documents were adopted to record and save data. To ensure the data completeness and accuracy, two radiology nurses checked the raw data blind-to-blind. They all had over eight years of work experience.[7]

Management strategy for AR

The basic principles of the management for AR were as follows: (1) mild AR: the contrast media injection was stopped and no other special management was needed. Patients could generally recover spontaneously. Besides, symptomatic management could be adopted and the conditions were closely monitored; (2) moderate AR: aggressive management was adopted. Clinicians in the first-aid department were asked for help for the patients who needed drug therapy. Then the patients were quickly transferred to the inpatient department or the first-aid department for further observation and management; (3) severe AR: immediate management was adopted. The clinicians from the first-aid department and other related departments performed treatments in cooperation. Heart, lung and brain resuscitations were performed immediately if cardiorespiratory arrest occurred. In the radiology department, basic life support and advanced life support were adopted. And the patients were transferred to the intensive care unit or the first-aid department when the disease had been stabilized.[8]

Statistical methods

Statistical analysis was performed using SPSS18.0 (IBM, Chicago, USA). Continuous variables were described by mean values and standard deviation. Counting data was presented in terms of frequencies and percentages (%). The Student t test for continuous variables and the χ^2 test for categorical variables were used to compare groups with and without AR. Logistic regression analyses with a forward stepwise (Likelihood Ratio) method were performed to identify influence factors for ICM-related AR. Candidate variables with a P value < 0.2 on univariate analysis were included in the multivariable model. $P<0.05$ was considered statistically significant.

Results

Baseline information and overall incidence and severity of AR

325243 patients were performed CECT examinations. 27758 patients who have a history of allergies (mean age, 59.1 years ± 13.7; 13343 women [48%]) were included, containing ICM allergy and non-ICM allergies history, 713 patients and 27045 patients, respectively (Fig 1). The overall incidence of AR was 0.66% (184/27758). As for severity, 80.43% of AR were classified as mild and the overall incidence was 0.53% (148 of 27758); 11.96% as moderate AR (0.08%; 22 of 27758); 7.61% as severe AR (0.05%; 14 of 27758). In patients with ICM allergy history, no severe AR was found. The incidence of AR was different according to ICM products (P=0.042) (Table 1). In patients with non-ICM allergies history, 9.93% was classified as severe AR and the incidence was

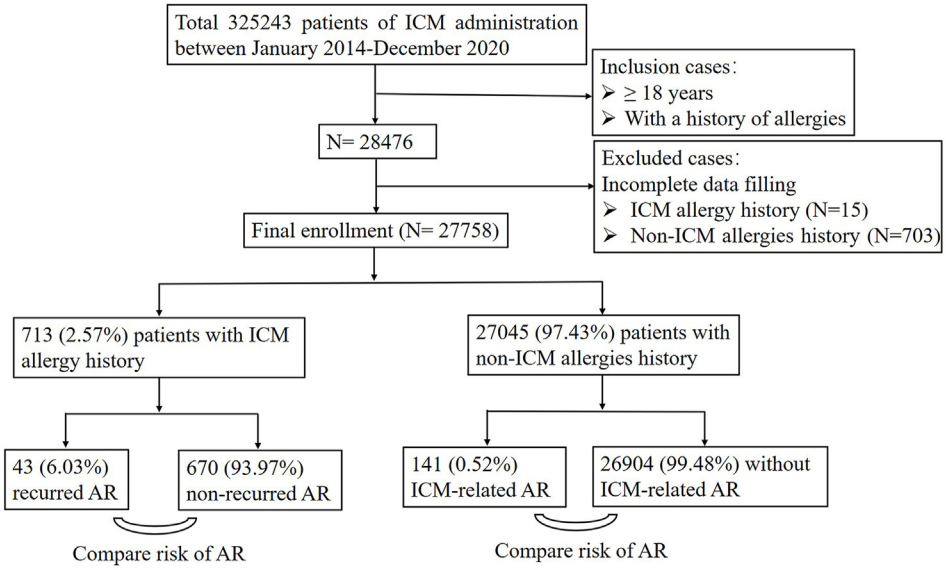

Figure 1 The diagram showed the study population. AR=adverse reaction, ICM = iodinated contrast media.

Table 1
The prevalence and severity of AR according to the ICM generic in patients with ICM and non-ICM allergies history.

Generic and products*	ICM usage	AR (%)	Mild (%)	Moderate (%)	Severe (%)
ICM allergy history					
Iopamidol					
Iopamidol 350 (ICM1)	106	4 (3.77)	4 (3.77)	0 (0)	0 (0)
Iobitridol					
Iobitridol 350 (ICM2)	41	1 (2.44)	1 (2.44)	0 (0)	0 (0)
Iopromide					
Iopromide 370 (ICM3)	111	8 (7.21)	8 (7.21)	0 (0)	0 (0)
Iohexol					
Iohexol 350 (ICM4)	191	13 (6.81)	9 (4.71)	4 (2.09)	0 (0)
Ioversol					
Ioversol 320 (ICM5)	136	3 (2.21)	3 (2.21)	0 (0)	0 (0)
Ioversol 350 (ICM6)	16	2 (12.5)	2 (12.5)	0 (0)	0 (0)
Iodixanol					
Iodixanol 270 (ICM7)	91	8 (8.79)	7 (7.69)	1 (1.10)	0 (0)
Iodixanol 320 (ICM8)	21	4 (19.05)	4 (19.05)	0 (0)	0 (0)
Total	713	43 (6.03)	38 (5.33)	5 (0.70)	0 (0)
Non-ICM allergies history					
Iopamidol					
Iopamidol 350 (ICM1)	3703	12 (0.32)	12 (0.32)	0 (0)	0 (0)
Iobitridol					
Iobitridol 350 (ICM2)	1804	6 (0.33)	6 (0.33)	0 (0)	0 (0)
Iopromide					
Iopromide 370 (ICM3)	4116	32 (0.78)	28 (0.68)	2 (0.05)	2 (0.05)
Iohexol					
Iohexol 350 (ICM4)	7134	17 (0.24)	15 (0.21)	1 (0.01)	1 (0.01)
Ioversol					
Ioversol 320 (ICM5)	5635	26 (0.46)	21 (0.37)	5 (0.09)	0 (0)
Ioversol 350 (ICM6)	481	2 (0.42)	2 (0.42)	0 (0)	0 (0)
Iodixanol					
Iodixanol 270 (ICM7)	3259	41 (1.26)	21 (0.64)	9 (0.28)	11 (0.33)
Iodixanol 320 (ICM8)	913	5 (0.55)	5 (0.55)	0 (0)	0 (0)
Total	27045	141 (0.52)	110 (0.41)	17 (0.06)	14 (0.05)

Note.-Data are patient numbers, with percentages in parentheses. AR=adverse reaction, ICM = iodinated contrast media. * Product names were anonymized.

0.05% (14 of 27045). The incidence of AR was also different according to ICM products ($P<0.001$) (Table 1).

The incidence and severity of AR according to ICM generics and concentration

In patients with ICM allergy history, when we analyzed the recurrence rate of AR according to ICM generics by comparing the recurrence rate of AR for each with the combined recurrence rate of AR for the others, iodixanol (10.71%; 12 of 112) was found to be associated with higher recurrence rate of AR ($P=0.023$). There was no difference in the recurrence rate of AR for iopamidol (3.77%; 4 of 106), iopromide (7.21%; 8 of 111), iobitridol (2.44%; 1 of 41), iohexol (6.81%; 13 of 191) and ioversol (3.29%; 5 of 152) ($P=0.403$, $P=0.571$, $P=0.511$, $P=0.599$ and $P=0.109$,

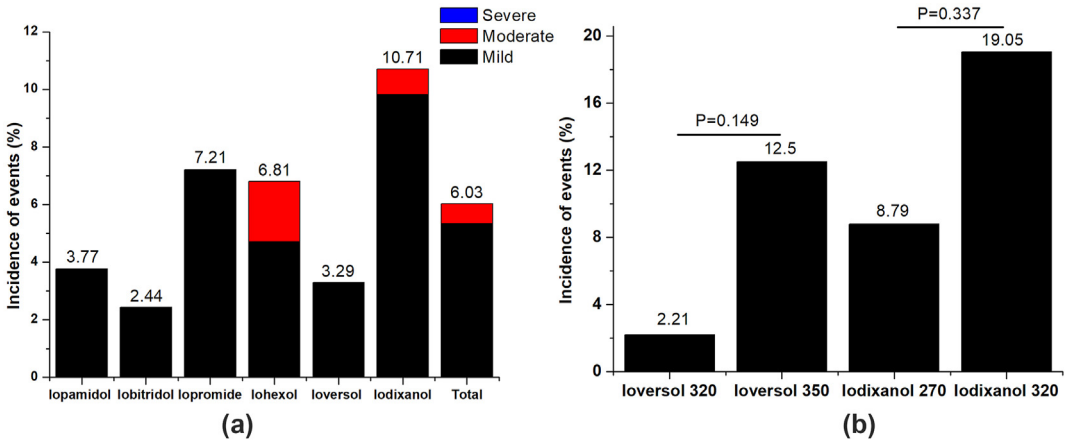

Figure 2 (a) The graph showed incidence and severity of adverse reaction according to the ICM generics for patients with ICM allergy history; (b) The graph showed comparison of incidence of adverse reaction according to ICM concentration for patients with ICM allergy history. ICM = iodinated contrast media.

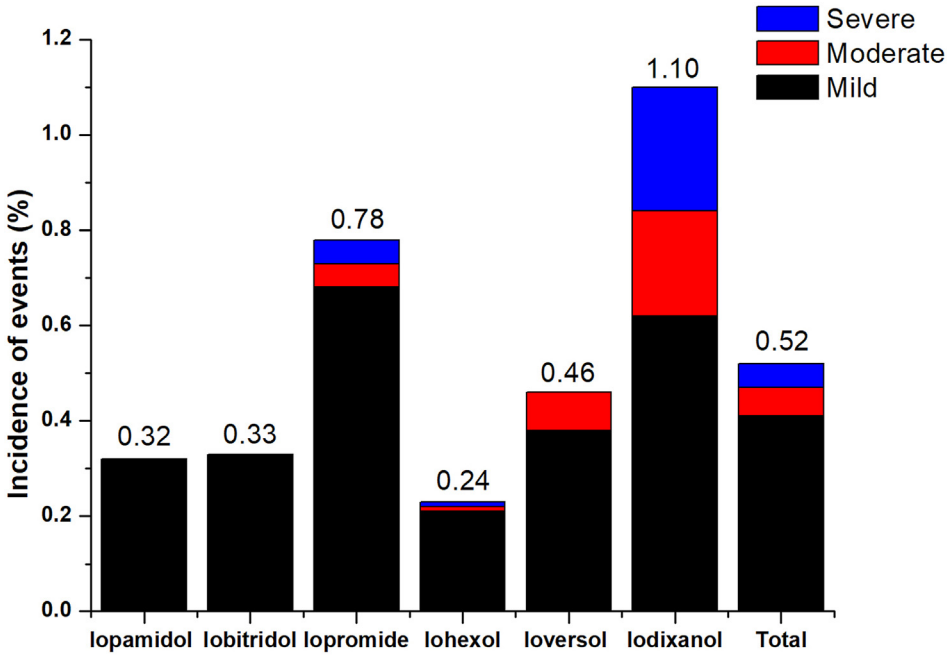

Figure 3 The graph showed incidence and severity of adverse reaction according to the ICM generics for patients with non-ICM allergies history. ICM = iodinated contrast media.

respectively) (Fig 2A). Regarding ICM concentration, there was no difference in the recurrence rate of AR between ioversol 320 (320 mg/ml) and ioversol 350 (350 mg/ml), iodixanol 270 (270 mg/ml) and iodixanol 320 (320 mg/ml) (P=0.149, P=0.337) (Fig 2B).

In patients with non-ICM allergies history, when we analyzed the incidence of AR according to ICM generics by comparing the incidence of AR for each with the combined incidence of AR for the others, iodixanol (1.1%; 46 of 4172) and iopromide (0.78%; 32 of 4116) was found to be associated with higher incidence of AR (P=0.013 and P<0.001); iohexol (0.24%; 17 of 7134) was found to be associated with lower incidence of AR (P<0.001). There was no difference in the incidence of AR for iopamidol (0.32%; 12 of 3703), iobitridol (0.33%; 6 of 1804) and ioversol (0.46%; 28 of 6116) (P=0.073, P=0.249 and P=0.433, respectively) (Fig 3). The incidence of severe AR was 0.33% (11/3259) when iodixanol 270 was used, which was higher than other ICMs (P=0.008) (Table 1). Regarding ICM concentration, there was no difference in the incidence of AR between ioversol 320 (320 mg/ml) and ioversol 350 (350 mg/ml), iodixanol 270 (270 mg/ml) and iodixanol 320 (320 mg/ml) (P>0.99, P=0.069) (Fig 4).

The incidence and severity of AR in different onset time

In patients with ICM allergy history, 81.40% (35/43) of AR occurred within 5 minutes of ICM injection, 93.02% (40/43) occurred within 20 minutes and 6.98% (3/43) occurred more than 30 minutes after injection. No case occurred within 20–30 minutes. 4 cases of moderate AR occurred within 5 minutes and 1 case of moderate AR occurred more than 30 minutes after injection (Table 2).

In patients with non-ICM allergies history, 72.34% (102/141) of AR occurred within 5 minutes of ICM injection, 89.36% (126/141) occurred within 20 minutes, 10.64% (15/141) occurred more than 30 minutes after injection. No case occurred within 20–30 minutes. 85.71% (12/14) severe AR and 64.71% (11/17) moderate AR occurred within 20 minutes, 14.29% (2/14) severe AR and 35.29% (6/17) moderate AR occurred more than 30 minutes after injection (Table 2). The incidence of severe AR differed according to the different onset times (P=0.017). The incidence of severe AR was highest within 6–20 minutes of ICM injection.

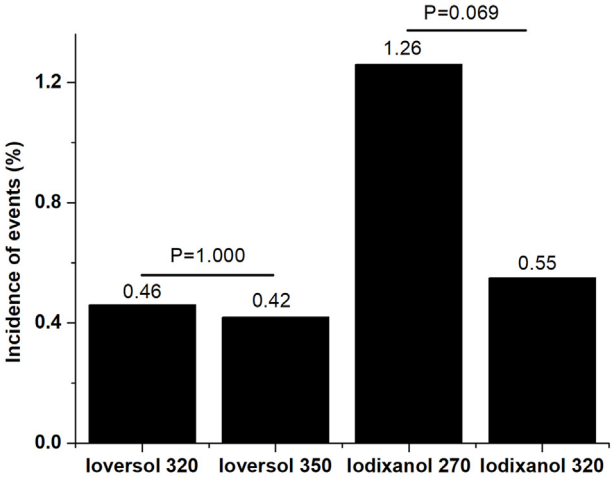

Figure 4 The graph showed comparison of incidence of adverse reaction according to ICM concentration for patients with non-ICM allergies history. ICM = iodinated contrast media.

Table 2
The prevalence and severity of AR in different onset time in patients with ICM and non-ICM allergies history.

Occurrence time	AR	Mild (%)	Moderate (%)	Severe (%)
ICM allergy history				
≤5 min	35	31 (88.57)	4 (11.43)	0 (0)
6–20 min	5	5 (100)	0 (0)	0 (0)
21–30 min	0	0 (0)	0 (0)	0 (0)
>30 min	3	2 (66.67)	1 (0)	0 (0)
Total	43	38 (88.37)	5 (11.63)	0 (0)
Non-ICM allergies history				
≤5 min	102	85 (83.33)	11 (10.78)	6 (5.88)
6–20 min	24	18 (75)	0 (0)	6 (25)
21–30 min	0	0 (0)	0 (0)	0 (0)
>30 min	15	7 (46.67)	6 (40)	2 (13.33)
Total	141	110 (78.01)	17 (12.06)	14 (9.93)

Note.-Data are patient numbers, with percentages in parentheses. AR=adverse reaction, ICM = iodinated contrast media.

Influence factors for ICM-related AR in patients with a history of allergies

In patients with ICM allergy history, 43 patients (mean age, 52.6 years ± 12.4; 14 women [33%]) experienced recurrent AR. The univariate and multivariable regression analysis results demonstrated that all of the factors in the table had no influence on AR recurrence ($P>0.05$) (Table 3).

In patients with non-ICM allergies history, 141 (mean age, 52.6 years ± 13.0; 74 women [52%]) patients experienced ICM-related AR. The age of patients with ICM-related AR was lower than that of patients without AR (59.30 years ± 13.6) ($P<0.001$). The univariate and multivariable regression analysis results demonstrated that age ≥70 years (OR, 0.2; 95% CI: 0.1, 0.4; $P<0.001$) and hypertension (OR, 0.6; 95% CI: 0.4, 0.9; $P=0.025$) were protective factors for ICM-related AR in patients with non-ICM allergies history. ICM genetics was an influence factor for ICM-related AR. The other factors in table had no influence on ICM-related AR occurrence ($P>0.05$) (Table 4).

Discussion

In this study, the prevalence, patterns and influence factors for ICM-related AR were investigated in patients with a history of allergies. The overall AR incidence was 0.66% and severe AR occurred in 0.05%. Most of AR occurred within 20 minutes and moderate or severe AR could occur more than 30 minutes after injection. The AR incidence differed according to ICM generics. Age ≥70 years and hypertension were associated with lower incidence of ICM-related AR in patients with non-ICM allergies history.

In this study, most (88.37% and 78.01%) of AR was mild in patients with ICM and non-ICM allergies history. The overall AR incidence was lower than previous research in patients with ICM allergy history.[9,16–18] The incidence of severe AR was also lower than previous research in patients both with

Table 3
Univariable and multivariate regression analysis to identify influence factors for recurrent AR in patients with ICM allergy history.

Characteristic	With recurrent	Without recurrent	Univariable		Multivariable	
	AR (n=43)	AR (n=670)	Or (95% CI)	*P*	Or (95% CI)	*P*
Age(y)	52.6 ± 12.4	56.1 ± 13.3	…	0.090		
Age≥70 years	2 (4.65)	111 (16.57)	0.2(0.1, 1.0)	0.063	0.3(0.1, 1.1)	0.067
Sex				0.127		
Men	29 (67.44)	372 (55.52)	…	…		
Women	14 (32.56)	298 (44.48)	…	…		
Examination sites				0.854		
Abdominal	16 (37.21)	240 (35.82)	…	…		
Non-abdominal	27 (62.79)	430 (64.18)	…	…		
Patient source				0.547		
Inpatients	24 (55.81)	405 (60.45)	…	…		
Outpatients	19 (44.19)	265 (39.54)	…	…		
Underlying diseases						
Hypertension	7 (16.28)	155 (23.13)	0.6(0.3, 1.5)	0.298		
Coronary heart disease	0	60 (8.96)	…	0.042	…	0.997
Tumor radio-chemotherapy	4 (9.30)	73 (10.90)	0.8(0.3, 2.4)	0.942		
β blockers	1 (2.33)	62 (9.25)	0.2(0.1, 1.7)	0.202		
Diabetes	2 (4.65)	27 (4.03)	1.2(0.3, 5.0)	>0.99		
ICM injection dose≥100 mL	2 (4.65)	86 (12.84)	0.3(0.1, 1.4)	0.179		
ICM injection rate≥5mL/s	9 (20.93)	220 (32.84)	0.5(0.3, 1.1)	0.105		
ICM genetics				0.042		
Iopamidol 350	4 (9.30)	102 (15.22)	…	…		
Iobitridol 350	1 (2.33)	40 (5.97)	…	…		
Iopromide 370	8 (18.60)	103 (15.37)	…	…		
Iohexol 350	13 (30.23)	178 (26.57)	…	…		
Ioversol 320	3 (6.98)	133 (19,85)	…	…		
Ioversol 350	2 (4.65)	14 (2.09)	…	…		
Iodixanol 270	8 (18.60)	83 (12.39)	…	…		
Iodixanol 320	4 (9.30)	17 (2.54)	…	…		

Note.-Data are patient numbers, with percentages in parentheses in patients with or without recurrent AR. AR=adverse reaction, CI = confidence interval, ICM = iodinated contrast media, OR= odds ratio.

Table 4
Univariable and multivariate regression analysis to identify influence factors for ICM-related AR in patients with non-ICM allergies history.

Characteristic	With ICM-related	Without ICM-related	Univariable		Multivariable	
	AR (n=141)	AR (n=26904)	Or (95% CI)	*P*	Or (95% CI)	*P*
Age(y) *	52.6 ± 13.0	59.30 ± 13.6	…	<0.001		
Age≥70 years*	9 (6.38)	6343 (23.58)	0.2(0.1, 0.4)	<0.001	0.2(0.1, 0.4)	<0.001
Sex				0.306		
Men	67 (47.52)	13947 (51.84)	…	…		
Women	74 (52.48)	12957 (48.16)	…	…		
Examination sites				0.922		
Abdominal	50 (35.46)	9434 (35.07)	…	…		
Non-abdominal	91 (64.54)	17470 (64.93)	…	…		
Patient source				0.345		
Inpatients	78 (55.32)	15938 (59.24)	…	…		
Outpatients	63 (44.68)	10966 (40.76)	…	…		
Underlying diseases						
Asthma	3 (2.13)	210 (0.78)	2.8(0.9, 8.7)	0.184		
Hypertension	29 (20.57)	7938 (29.50)	0.6(0.4, 0.9)	0.020	0.6(0.4, 1.0)	0.025
Coronary heart disease	9 (6.38)	2591 (9.63)	0.6(0.3, 1.3)	0.192		
Heart insufficiency	1 (0.71)	58 (0.22)	3.3(0.5, 24.0)	0.728		
Tumor radio-chemotherapy	5 (3.55)	1193 (4.43)	0.8(0.3, 1.9)	0.609		
β blockers	13 (9.22)	2181 (8.11)	1.2(0.7, 2.0)	0.629		
Diabetes	8 (5.67)	1382 (5.14)	1.1(0.5, 2.3)	0.773		
ICM injection dose≥100 mL	12 (8.51)	2701 (10.04)	0.8(0.5, 1.5)	0.547		
ICM injection rate≥5 mL/s	52 (36.88)	9859 (36.65)	1.0(0.7, 1.4)	0.954		
ICM genetics				<0.001	0.9(0.8, 1.0)	<0.001
Iopamidol 350	12 (8.51)	3691 (13.72)	…	…		
Iobitridol 350	6 (4.26)	1798 (6.68)	…	…		
Iopromide 370	32 (22.70)	4084 (15.18)	…	…		
Iohexol 350	17 (12.06)	7117 (26.45)	…	…		
Ioversol 320	26 (18.44)	5609 (20.85)	…	…		
Ioversol 350	2 (1.42)	479 (1.78)	…	…		
Iodixanol 270	41 (29.08)	3218 (11.96)	…	…		
Iodixanol 320	5 (3.55)	908 (3.37)	…	…		

Note.-Data are patient numbers, with percentages in parentheses in patients with or without ICM-related AR. AR=adverse reaction, CI = confidence interval, ICM = iodinated contrast media, OR= odds ratio.

ICM and non-ICM allergies history.[9] The reason might be that whole-process standardized management was performed before, during and after the CECT examination.[8,19] Recurrent severe AR was not found in patients with ICM allergy history. The reason might be patients with only mild and moderate ICM allergies history were enrolled in this investigation and patients with severe ICM allergy history were not performed CECT examination.

European Society of Urogenital Radiology guideline on Contrast Agents v10.0 clarified that non-ionic low-osmolar and iso-osmolar ICM had no difference in the incidence of acute reactions.[20] However, iodixanol, as the only iso-osmolar ICM, was found to be associated with higher incidence of ICM-related AR in patients both with ICM and non-ICM allergies history in this study. The probable reason might be as follows: first, we took patients with a history of allergies as study subjects, which was different from previous research; second, we observed all of the AR after ICM injection not only acute reactions. Iohexol was found to be associated with lower incidence of ICM-related AR in patients with non-ICM allergies history, which was consistent with previous reports that take the general population as the study subject.[2]

In this study, 81.40% and 72.34% of AR occurred within 5 minutes of ICM injection in patients with ICM and non-ICM allergies history, which was slightly higher than previous report (about 70%).[9] 93.02% and 89.36% of AR occurred within 20 minutes. No AR occurred within 20–30 minutes in patients with ICM and non-ICM allergies history. Therefore, within 20 minutes of ICM injection was critical to observation of AR in patients with a history of allergies. Patients waiting in a CT room for 20 minutes might be more appropriate after ICM injection. However, 1 case (0.14%, 1/713) moderate AR occurred more than 30 min after injection in patients with ICM allergy history. 2 cases (2/14) severe AR and 6 cases (6/17) moderate AR occurred more than 30 min after injection in patients with non-ICM allergies history. It suggested that it was still very necessary to instruct patients to contact the emergency department or CT room if they observed any abnormalities after leaving CT room.

Previous studies showed that unstable asthma,[9,10,21] heat disease[7] and β blockers[15] were associated with a higher risk of ICM-related AR. But our study showed hypertension, coronary heart disease and β blockers were not influence factors for AR recurrence in patients with ICM allergy history. The reason might be previous studies take the general population as study subject, different from this study. Considering the sample size of patients with asthma was quite small (three cases), we did not explore whether

asthma was an influence factor for AR recurrence in patients with ICM allergy history.

A previous study that took the general population as study subject showed that the incidence of AR in the elderly was lower than middle-aged patients.[3] In this study we found the age of patients with AR was lower than that patients without AR and age ≥70 years was a protective factor for ICM-related AR in patients with non-ICM allergies history, consistent with previous report. The reason might be associated with the decreased immune activity in old patients. Also, our results demonstrated that hypertension was a protective factor for ICM-related AR in patients with non-ICM allergies history. Considering most of the patients with hypertension had got drugs treatment before ICM injection, we conclude the reason might be associated with hypotensive drugs, which need further study.

There were some limitations in this study. Firstly, it was a single-center study and had a limitation in generalizability. Further study is needed, including more institutions and larger sample size. Secondly, this was a retrospective study. However, we recorded and monitored the AR data real time to minimize probable bias. Thirdly, we only recorded non-ICM allergies history of patients, and we did not classify them according to the severity of allergy.

In this study, we identified the prevalence, patterns and influence factors for ICM-related AR in patients both with ICM and non-ICM allergies history. We found most of AR was mild and occurred within 20 minutes of ICM injection. Some moderate and severe AR could occur more than 30 min after injection. The incidence of AR was associated with ICM generics. Age ≥70 years and hypertension were protective factors for ICM-related AR in patients with non-ICM allergies history. These could provide references to safe usage of ICM in patients with a history of allergies.

Conflicts of interest

The authors declare that there is no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2024.106771.

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