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Clinical characteristics and management of iodine contrast media-related anaphylactic shock during cardiac catheterization

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ABSTRACT

Objective: This study aimed to investigate the clinical characteristics and impact of intra-aortic balloon pump (IABP) implantation on the prognosis of patients with anaphylactic shock (AS) during cardiac catheterization.

Methods: We analyzed the medical records of 34 patients who had AS caused by iodine contrast media (ICM) between January 2009 and December 2019. Clinical features and treatments were analyzed, and patients were categorized into survival and dead groups. In addition, the patients were further divided into IABP and non-IABP (NIABP) groups to assess the impact on AS according to whether a IABP was used or not.

Results: Of the 417,938 patients in whom ICM was used, 34 with AS were monitored. The prevalence of AS was 0.008%. Among the 34 patients, 6 (0.001%) died from fatal anaphylactic reactions accompanying shock, 26 (76.5%) had hypotension as the first presentation of AS in the survival and dead groups (78.6% and 66.7%, respectively), and 5 (14.7%) had unconsciousness at the initial onset of AS. The subgroup analysis revealed a higher mortality in the IABP group than in the NIABP (4/9, 44.4% vs. 2/25, 8%; $P = 0.031$).

Conclusions: The present study suggests a low prevalence of ICM-related AS. Hypotension was more frequent in AS related to ICM, and unconsciousness at the initial onset of AS implied a poor prognosis. The use of an IABP did not improve the outcome of the patients with AS. IABP implantation should not be used as a routine treatment for patients with AS.

Keywords: Coronary angiography, Contrast media, Anaphylactic shock, Intra-aortic balloon pumping

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INTRODUCTION

Iodine contrast media (ICM)-related anaphylactic shock (AS) is the most serious adverse reaction that occurs in imaging examinations. It is a serious allergic reaction, setting in rapidly, which may lead to life-threatening cardiovascular collapse and cardiac arrest, and prompt recognition and treatment are required. Therefore, information on clinical features and management strategy associated with ICM-related anaphylaxis accompanying shock is of importance. Although the newer low-osmolality, nonionic contrast media have less adverse reactions, the risk of fatal reactions was reported to be similar for ionic and non-ionic contrast media and was estimated to range from 1 in 100 000 examinations.[1] The Chinese population is becoming aged, and with the increased risk factors of arteriosclerosis, the number of patients with cardiovascular diseases is increasing. As a result, utilization of ICM imaging examination to evaluate patients has grown tremendously in the past 3 decades. Inevitably, the adverse events caused by ICM are also increasing. Two more recent large series studies demonstrated incidence rates of allergy-type reactions of 0.6% and 0.2% rate, and 0.01 and 0.002% of the total number of nonionic ICM injections were classified as severe reactions.[2,3] However, epidemiological data about allergic reactions, especially AS, in the Chinese population are scarce. The previous studies demonstrated clearly that introduction of low osmolar nonionic ICM caused an overall reduction in the number of contrast reactions, but no definite reduction in the incidence of fatal reactions, which are extremely rare, was observed. Therefore, the present study aimed to investigate the prevalence, clinical characteristics, and impact of intra-aortic balloon pumping (IABP) on the prognosis of patients with AS during cardiac catheterization to examine the treatment regimen of AS associated with ICM.

PATIENTS AND METHODS

Design and setting

This study protocol was approved by the institutional review board (IRB). Patient informed consent was exempted by the IRB because of the retrospective nature of the study. All involved personal information was removed, and numbers not associated with personal identity of the patients were used. The research personnel only used the personal password to access the data.

Selection of patients

Patients who underwent cardiac catheterization were screened. Pregnant and lactating women were excluded. Hypotension was considered as a systolic blood pressure of $<$90 mmHg or $>$30% decrease from an individual's baseline.[4] Hypotension unrelated with underlying diseases or other drugs with or without other allergic reactions was considered a manifestation of AS during cardiac catheterization. Subjects with AS were enrolled. We extracted from our electronic medical database all the cases of ICM-related AS on the basis of the Anatomical Therapeutic Chemical code of the causative agents that were collected from January 2009 to December 2019. The subjects with AS were divided into survival and non-survival groups. Whether an IABP was inserted or not was determined by the interventional cardiologist during cardiac catheterization, depending on the physician's judgment of the patient's condition. Moreover, on the basis of whether an IABP was applied or not, the patients were further divided into IABP and non-IABP (NIABP) groups for the subgroup analysis.

Data collection

Demographic data, including age, sex, medical history (including comorbidities and history of allergy), current medicine, lifestyle habits, height (cm), and weight (kg), were recorded. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). The number of contrast exposures, laboratory test results, and underlying diseases based on the *International Statistical Classification of Disease and Related Health Problems, 10th Revision*, codes were collected from the patients' electronic medical records. Coronary arterial disease (CAD) severity was calculated using the SYNTAX II score, which was calculated by an intervention cardiologist that was blinded to the patients' survival status.

Definitions of the risk factors

Hypertension was defined as resting systolic and diastolic blood pressures were $>$140 and/or

>90 mmHg, respectively, measured with an appropriate cuff size on 2 different days, and/or as current use of antihypertensive medications. Hyperlipidemia was defined as current use of cholesterol-lowering medications and/or levels of total cholesterol of >200 mg/dL, triglycerides of >150 mg/dL, and low-density lipoprotein cholesterol of >130 mg/dL in a plasma sample drawn after an overnight fast. Diabetes mellitus was confirmed if a patient had a history of fasting blood glucose level of >125 mg/dL or use of insulin and/or oral antidiabetic agents. Smokers were defined as subjects with a current smoking habit or with a severe history of smoking.

Skin tests with iodinated contrast agents

Skin tests with ICM were performed before coronary angiography (CAG). Skin prick and intradermal tests with 5 different non-ionic contrast agents (ioversol, iohexol, iopromide, iodixanol, and iopamidol) used in our hospital were performed on the volar part of the forearm. Undiluted and 1:10 diluted solutions were used for the skin prick and intradermal tests, respectively, with the method described in a previous study.[5]

Statistical analyses

Continuous variables with normal distributions are expressed as mean ± SD, and continuous variables without normal distributions are expressed as median (interquartile range), whereas categorical variables are reported as absolute numbers and percentages. The two-independent-samples *t*-test was used for the normally distributed variables, and the Mann-Whitney *U* test was used for the continuous variables without normal distributions. The chi-square or Fisher exact test was used to compare the categorical variables across the two groups. Statistical analyses were performed with the computer software SPSS version 18 for Windows (SPSS, Chicago, IL). A *P* value of <0.05 was considered statistically significant.

RESULTS

The total number of cases of non-ionic iodine contrast agent use during the study period was 417 938, of which 34 nonduplicate cases of ICM with anaphylactic shock were monitored during the study period (Fig. 1). The incidence rate of contrast-related AS was 0.008%. Six patients died from AS. The mortality rate was 0.001% in our study. As the total frequency of ICM use increased over the study period, the incidence of ICM-related AS also showed an increasing tendency with the exception of years 2014 and 2016 (Fig. 2). Of the patients who died, 3 received iopromide (50%), 1 received an iodixanol injection, another received ioversol, and the remaining patient received iopamiro. Ten patients in the survival group received iopromide (35.7%). No significant differences were between the groups ($P = 0.653$). The results of the skin tests showed that only 1 patient among those with AS was allergic to contrast media. The patients' baseline characteristics are summarized in Table 1. The mean age of the patients was 59.1 ± 10.9 years, and 82.4% (28/34) of the patients were male. The mean ages of the patients in the survival and non-survival groups were similar (58.8 ± 11.5 years and 60.5 ± 8.5 years, respectively). No significant differences in sex, comorbidities, allergic tendencies, left ventricular ejection fraction (LVEF), and smoking history were found between the groups.

Table 2 shows a comparison of the procedural characteristics, medications, and incidence of acute ICM-related AS between the survival and non-survival groups. The prevalence rates of single-, two-, and three-vessel diseases between the two groups had no significant difference. CAD severity, assessed using the SYNTAX II score, was higher in the non-survival group, but the difference was not significant. The contrast dose, onset of

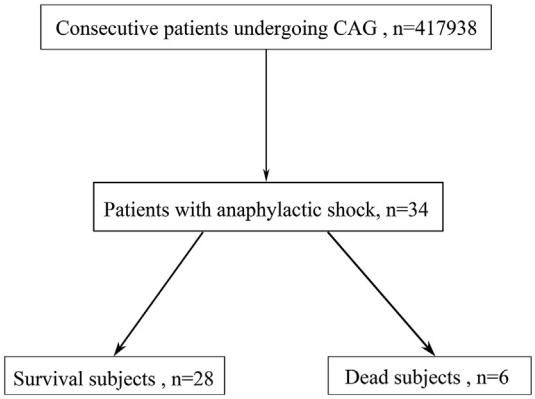

Fig. 1 Flow diagram of the study. CAG, coronary angiography.

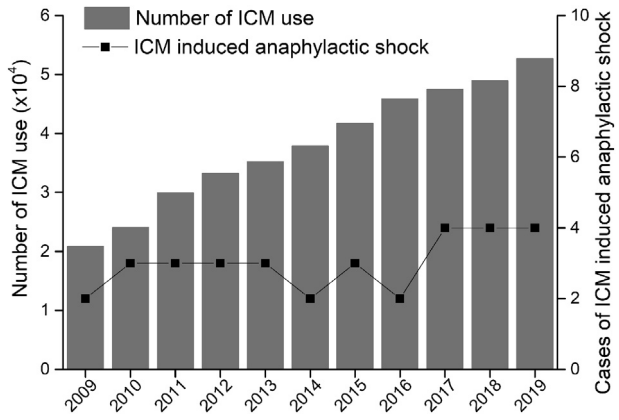

Fig. 2 Anaphylactic shock and total number of ICM use every year.

adverse drug reactions (ADRs), and rescue medication in the non-survival group were similar to those in the survival group. The application of intra-aortic balloon pumps was more frequent in the non-survival than in the survival group ($P = 0.031$). The most common symptom of ICM-related AS was reduced blood pressure without rash. Furthermore, unconsciousness at the onset of AS was more common in the non-survival group (3/6, 50%), with a significant difference from that in the survival group ($P = 0.029$).

Table 3 demonstrates the anthropometric and clinical characteristics of the patients with or without IABP. No significant differences in age, sex, comorbidities, allergic tendencies, LVEF, estimated glomerular filtration rate, and smoking history were observed between the groups. Table 4 shows that the contrast dose and rescue medication had no significant differences between the subgroups divided according to IABP use. Although the difference was not significant, the IABP group had a higher SYNTAX II score than the NIABP group. Unexpectedly, IABP implantation did not improve the outcome of the patients with ICM-related AS compared with no IABP ($P = 0.031$).

Variables	Survival group (n = 28)	Dead group (n = 6)	P
Age, year	58.8 ± 11.5	60.5 ± 8.5	0.739
Male sex	24 (85.7%)	4 (66.7%)	0.281
BMI (kg/m^2)	25.8 ± 2.5	24.4 ± 3.7	0.246
Hypertension	21 (75.0%)	4 (66.7%)	0.644
Hypercholesterolaemia	21 (75.0%)	5 (83.3%)	1.000
Diabetes mellitus	8 (27.6%)	3 (50.0%)	0.352
Smoking history	12 (42.9%)	4 (66.7%)	0.387
Prior MI	12 (42.9%)	1 (16.7%)	0.370
Pre-existing renal disease	1 (3.6%)	1 (16.7%)	0.326
Prior contrast	18 (64.3%)	6 (100%)	0.148
Times of prior contrast	0.9 ± 0.8	1.5 ± 0.5	0.640
Allergic tendencies	10 (35.7%)	0 (0.0%)	0.148
Asthma	0 (0.0%)	0 (0.0%)	1.000
LVEF (%)	60 ± 7	55 ± 10	0.123
NTpro-BNP(pg/ml)	180.1 (132.3–550.3)	652.0 (303.0–1352.3)	0.145
eGFR (ml/min/1.73 m^2)	84 ± 24	71 ± 35	0.304

Table 1. Anthropometric and clinical characteristics of the study subjects with anaphylactic shock. *Data are presented as the means ± SD, Median or as numbers and percentages. BMI, Body mass index; MI, myocardial infarction; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate*

Variables	Survival group (n = 28)	Dead group (n = 6)	P
Contrast dose, mL	13.3 ± 6.9	12.8 ± 7.2	0.885
Time of ADR, min	10.4 ± 6.5	10.2 ± 6.4	0.929
First appearance of ADR			
BP reduction	22 (78.6%)	4 (66.7%)	0.609
Urticaria	4 (14.3%)	1 (16.7%)	1.000
Unconsciousness	2 (7.1%)	3 (50.0%)	0.029
SYNTAX II score	24.2 ± 11.2	32.9 ± 10.1	0.090
Medication			
Epinephrine	28 (100%)	6 (100%)	1.000
H1-receptor blocker	5 (17.9%)	2 (33.3%)	0.580
Norepinephrine	6 (21.4%)	3 (50%)	0.306
Dopamine	26 (92.9%)	5 (83.3%)	0.453
Corticosteroids			
Dexamethasone	23 (82.1%)	5 (83.3%)	1.000
Hydrocortisone	2 (7.1%)	1 (16.7%)	0.453
Methylprednisolone	15 (53.6%)	3 (50.0%)	1.000
IABP	5 (17.9%)	4 (66.7%)	0.031

Table 2. Procedural characteristics, medication and acute adverse drug reactions. *Data are presented as the means ± SD or as numbers and percentages. BP, blood pressure; ADR, adverse drug reaction; IABP, Intra-aortic balloon pump*

DISCUSSION

In the present study, we investigated the prevalence, clinical characteristics, and management of ICM-related AS during cardiac catheterization. We found that few patients (0.008%) had AS, hypotension was more frequent in AS related to ICM, and unconsciousness implied a poor prognosis. The treatment of AS was challenging. Use of an IABP cannot improve the outcome of ICM-related AS. To the best of our knowledge, this is the first report regarding the use and impact of IABP on the mortality of patients with ICM-related AS.

Nowadays, with the rapid development of the economy and improvement of people's living standard in China, an increasing number of patients with suspected CAD undergo CAG. As a result, the incidence of ADRs caused by ICM is increasing rapidly. Mild acute general adverse reactions include nausea, vomiting, mild urticaria, pallor, and pain in the injected extremity. Moderate adverse reactions include severe vomiting, extensive urticaria, laryngeal edema, dyspnea, and rigors. Severe reactions include pulmonary edema, cardiac arrhythmias, cardiac arrest, circulatory collapse, and unconsciousness.[6] Mild reactions are self-limiting and generally do not require specific treatments. However, moderate and severe reactions represent serious degrees of reactions that need immediate management. In this present study, we focused on AS, which is the most severe form of ICM-related adverse reaction. According to a previous study, the incidence of anaphylaxis is known to range from 4 to 50 per 100,000 person-years.[7] Our outcome, which is 8/100 000, is consistent with this report. In our data, the frequency of AS showed an increasing tendency, with the exception of years 2014 and 2016, when the total frequency of ICM use increased. The reasons for the changes in AS frequency in 2014 and 2016 were unknown. This may be because some cases were not recorded in the electronic medical records. Pradubpongsa et al[8] and Cochran et al[9] reported low mortality rates ranging from 1 to 3 per 100 000 administrations for both ionic and nonionic ICM. Similarly, the rate of mortality related with ICM was 0.001% in our study. Of the 6 patients who died, 3 received iopromide, 1 received an iodixanol injection,

Variables	IABP group (n = 9)	NIABP group (n = 25)	P
Age, year	61.8 ± 11.2	58.2 ± 10.9	0.403
Male sex	8 (88.9%)	20 (80.0%)	1.000
BMI (kg/m^2)	25.7 ± 3.8	25.5 ± 2.4	0.855
Hypertension	6 (66.7%)	18 (72.0%)	1.000
Hypercholesterolaemia	7 (77.8%)	19 (76.0%)	1.000
Diabetes mellitus	4 (44.4%)	7 (28.0%)	0.425
Smoking history	5 (55.6%)	11 (45.8%)	0.708
Prior MI	4 (44.4%)	9 (36.0%)	0.704
Pre-existing renal disease	1 (11.1%)	1 (4.0%)	0.465
Prior contrast	8 (88.9%)	16 (64.0%)	0.225
Allergic tendencies	2 (22.2%)	8 (32.0%)	0.692
Asthma	0 (0.0%)	0 (0.0%)	1.000
LVEF (%)	55 ± 9	60 ± 7	0.079
NTpro-BNP(pg/ml)	636.0 (160.5–2056.5)	184.1.0 (126.2–516.6)	0.120
eGFR (ml/min/1.73 m^2)	76 ± 35	83 ± 23	0.475

Table 3. Anthropometric and clinical characteristics of the participants with or without IABP. *Data are presented as the means ± SD, Median or as numbers and percentages. BMI, Body mass index; MI, myocardial infarction; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; IABP, Intra-aortic balloon pump*

another patient received ioversol, and the remaining patient received iopamiro. No evidence indicated that AS was associated with different contrast agents.

Until now, the clinical characteristics and risk factors for the development and progress of AS are not well understood. A previous study verified that 94%–100% of all cases of severe and fatal reactions to

Variables	IABP group (n = 9)	NIABP group (n = 25)	P
Contrast dose, mL	13.3 ± 5.5	13.3 ± 7.3	0.949
Time of ADR, min	11.1 ± 4.3	10.1 ± 7.0	0.695
SYNTAX II score	31.6 ± 12.1	23.6 ± 10.6	0.071
Medication			
Epinephrine	9 (100%)	25 (100%)	1.000
H1-receptor blocker	1 (11.1%)	6 (24.0%)	0.644
Norepinephrine	2 (22.2%)	7 (28.0%)	1.000
Dopamine	7 (77.8%)	24 (96.0%)	0.164
Corticosteroids			
Dexamethasone	8 (88.9%)	20 (80.0%)	1.000
Hydrocortisone	1 (11.1%)	2 (8.0%)	1.000
Methylprednisolone	5 (55.6%)	13 (52.0%)	1.000
Survival rate	5 (55.6%)	23 (92.0%)	0.031

Table 4. The comparison of survival rate between patients with or without IABP. *Data are presented as the means ± SD or as numbers and percentages. BP, blood pressure; ADR, adverse drug reaction; IABP, Intra-aortic balloon pump; NIABP, non intra-aortic balloon I pump- «*

intravascular contrast media occurred within 20 min after contrast injection.[10] Our data indicated that most cases (31/34, 91.2%) occurred within 20 min in the course of CAG. The mean onset time was similar between the non-survival and survival groups. Moreover, the most common symptom is reduced systemic blood pressure at the onset of AS in both groups. When hypotension occurs as a sudden-onset adverse reaction either with or without other symptoms, clinicians must pay special attention to a subsequent possible cardiovascular collapse, which is the pivotal cause of mortality in AS. Unconsciousness at the onset of AS occurred in 3 patients (1 in the survival group and 2 in the non-survival group), with a significant difference between the groups ($P = 0.029$). This suggests that the clinical manifestations of AS are not always the result of hypotension but are present prior to the onset of hypotension. This finding was supported by the work of Park and colleague.[11] Hence, clinicians should suspect an impending shock if the patient complains of multiple-organ symptoms, particularly neurological manifestations. The several known risk factors of severe ICM-related adverse reactions include a previous history of ICM hypersensitivity, asthma, allergies requiring medical treatment, use of beta-adrenergic blockers, female sex, Indian and Mediterranean ethnicities, and malignant tumors.[12] In our study, one patient with a history of ICM use had an ICM-related anaphylaxis, although he received pretreatment with corticosteroids and antihistamines. Premedication with corticosteroids prior to contrast administration is effective in reducing the risk of mild or moderate reactions. However, severe, even life-threatening, reactions may still occur in patients who receive premedication.[13] Two subjects had malignant lung tumors. We could not confirm the association of pulmonary tumor with AS because of the limited AS samples. In addition, 10 patients (10/34, 35.7%) in the survival group had a history of allergic reactions. All the subjects who died had been exposed to ICM. This emphasizes that the absence of allergic reactions to previous contrast agents does not mean that patients are safe when they are re-exposed to ICM. Age has been widely discussed for its significance in ADR prediction. Kopp et al[14] and Vogl et al[15] found that ages 18–30 years were related with a higher incidence of ADRs. Another study conducted by Lasser et al[16] showed that patients aged between 20 and 50 years had a higher probability of ADR occurrence, while patients either <20 or >50 years old had a reduced probability of ADR occurrence. A recent registration research implied that patients between the ages of 50 and 69 years had a reduced risk of ADR.[17] Nevertheless, in our study, we found that most subjects with AS were >50 and $<$ 69 years old (21/34, 61.8%). This can reasonably explain why older patients are more at risk when they are allergic because they have organic lesions in their cardiovascular system. When allergies occur, their cardiovascular system is susceptible to attack or harm by anaphylaxis. The exact mechanism of the acute cardiac dysfunction related with ICM is unclear. Bhaskaran and colleague found that acute coronary syndrome caused by radioiodine contrast may be associated with Kounis syndrome and highlight the role of plaque rupture and vasospasm.[18]

Acute severe life-threatening or fatal reactions to ICM are often unpredictable, and prompt recognition and immediate intervention are required. Important first-line management includes the use of adrenaline, administration of intravascular fluids, establishment of an adequate airway, and oxygen supplementation. Although dispute exists regarding its intravenous use for anaphylactoid reactions,[19,20] intravenous administration of epinephrine is considered a fast response in the catheterization laboratory, where hemodynamic and electrocardiographic monitoring are performed. Intravenous injection of high-dose corticosteroids may have an immediate stabilizing effect on the cell membrane and could be used as the second-line therapy. Standard doses can be effective in reducing delayed recurrent symptoms, which can be observed for as long as 48 h after an initial reaction.[21] No significant difference in the use of corticosteroids, including dexamethasone, hydrocortisone,. and methylprednisolone, was found between the survival and non-survival groups in the present study. To our knowledge, results of the use and impact of IABP on mortality have not been reported in patients with ICM-related AS, even in a small patient group, except for a few cases. Alam et al reported a case of ICM-related AS that was unresponsive to the conventional medical therapy, but insertion of an IABP prevented death.[22] Another similar case report by Sugiura and colleague described the combined use of

extracorporeal membrane oxygenation and hemodialysis and IABP to treat contrast-mediated anaphylaxis.[23] However, according to our data, the concomitant diseases, cardiac function, and renal function were similar at baseline between the groups. However, the mortality was higher in the patients than in those without IABP implantation. The exact reason is unclear. The SYNTAX II score in the IABP group was higher than that in the NIABP group. A potential explanation was that patients with severe coronary lesions are more prone to hemodynamic instability during allergic reactions and have an increased the risk of death. The use of an IABP did not improve the outcome of the patients with AS. This provides a reminder that IABP should not be used as a routine treatment in patients with AS. However, these results must be interpreted with caution. The SYNTAX II score in the IABP group was higher than that in the IABP group, but no statistical difference was found.

Limitations

This study had some limitations that should be addressed. First, it was a retrospective and non-randomized controlled study. Nonetheless, our study is valuable because it analyzed a large number of patients. Second, it included a relatively small number of patients. A multivariate logistic regression model was not performed to investigate the predictors of death related with ICM. However, a large-scale clinical trial is difficult to conduct owing to the low incidence of AS. Third, serum samples were not collected during AS. Thus, we failed to analyze the pathophysiology of AS to elucidate the precise pathogenesis.

CONCLUSIONS

The present study data suggest a relative low prevalence of ICM-related AS. Hypotension was more frequent in AS related to ICM, and unconsciousness implied a poor prognosis. The employment of IABP did not improve the outcome of the patients with AS. IABP should not be used as a routine treatment in patients with AS. The rescue strategy of fatal anaphylactic episodes is challenging. An anaphylactoid reaction must be considered in any patient with hypotension during catheterization. Prompt recognition of acute contrast adverse reactions will facilitate treatment and may improve patient outcomes.

Abbreviations

AS: anaphylactic shock; IABP: intra-aortic balloon pump; ICM: iodine contrast media; IRB: institutional review board; BMI: body mass index; CAD: coronary arterial disease; LDL-C: low-density lipoprotein cholesterol; CAG: coronary angiography; ADR: adverse drug reaction; eGFR: estimated glomerular filtration rate

Financial support

Not applicable.

Consent for publication

All authors have participated in the work and have reviewed and agree with the content of the article, and agree to submit to World Allergy Organization Journal.

Availability of data and materials

All authors agree to share their raw data, any digital study materials, and analysis code as appropriate.

Ethics approval

This study protocol was approved by the institutional review board (IRB) of Fuwai Hospital. Informed consents of patients were exempted from IRB due to the study collecting the data retrospectively, and all involved personal information was removed, and use of some numbers was not associated with personal identity.

Author contributions

FH H and ZW H conceived the study and designed the trial. HL Z, ML, and YW supervised the conduct of the trial and data collection. WX Y and SB Q provided advice on study design and analyzed the data. ZW H drafted the manuscript, and all authors contributed substantially to its revision. FH H takes responsibility for the paper as a whole.

Declaration of competing interest

The authors report no conflicts of interest.

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REFERENCES

1. Caro JJ, Trindade E, McGregor M. The risks of death and of severe nonfatal reactions with high- vs low-osmolality contrast media: a meta-analysis. *Am J Roentgenol*. 1991;156:825–832.
2. Wang CL, Cohan RH, Ellis JH, Caoili EM, Wang G, Francis IR. Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. *Am J Roentgenol*. 2008;191:409–415.
3. Hunt CH, Hartman RP, Hesley GK. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. *Am J Roentgenol*. 2009;193:1124–1127.
4. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report–second national institute of allergy and infectious disease food allergy and anaphylaxis network symposium. *J Allergy Clin Immunol*. 2006;117:391–397.
5. Caimmi S, Benyahia B, Suau D, et al. Clinical value of negative skin tests to iodinated contrast media. *Clin Exp Allergy*. 2010;40:805–810.
6. Simons FE. Anaphylaxis: recent advances in assessment and treatment. *J Allergy Clin Immunol*. 2009;124:625–636.
7. Lee JK, Vadas P. Anaphylaxis: mechanisms and management. *Clin Exp Allergy*. 2011;41:923–938.
8. Cochran ST. Anaphylactoid reactions to radiocontrast media. *Curr Allergy Asthma Rep*. 2005;5:28–31.
9. Pradubpongsa P, Dhana N, Jongjarearnprasert K, Janpanich S, Thongngarm T. Adverse reactions to iodinated contrast media: prevalence, risk factors and outcome-the results of a 3-year period. *Asian Pac J Allergy Immunol*. 2013;31:299–306.
10. Thomsen HS. European Society of Urogenital Radiology (ESUR) guidelines on the safe use of iodinated contrast media. *Eur J Radiol*. 2006;60:307–313.
11. Park HJ, Kim SH. Factors associated with shock in anaphylaxis. *Am J Emerg Med*. 2012;30:1674–1678.
12. Morcos SK. Review article: acute serious and fatal reactions to contrast media: our current understanding. *Br J Radiol*. 2005;78:686–693.
13. Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K. Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology*. 1990;175:621–628.
14. Vogl TJ, Honold E, Wolf M, Mohajeri H, Hammerstingl R. Safety of iobitridol in the general population and at-risk patients. *Eur Radiol*. 2006;16:1288–1297.
15. Kopp AF, Mortele KJ, Cho YD, Palkowitsch P, Bettmann MA, Claussen CD. Prevalence of acute reactions to iopromide: postmarketing surveillance study of 74,717 patients. *Acta Radiol*. 2008;49:902–911.
16. Lasser EC, Berry CC, Mishkin MM, Williamson B, Zheutlin N, Silverman JM. Pretreatment with corticosteroids to prevent adverse reactions to nonionic contrast media. *AJR Am J Roentgenol*. 1994;162:523–526.
17. He Y, Huang Y, Yang J, et al. Novel risk model for predicting acute adverse drug reactions following cardiac catheterization from TRUST study (The Safety and toleRability of UltraviSt in Patients Undergoing Cardiac CaTheterization). *J Thorac Dis*. 2019;11:1611–1620.
18. Bhaskaran A, Deshmukh T, Sivagangabalan G. Intraprocedure type II Kounis syndrome secondary to radioiodine contrast during coronary angiography. *Can J Cardiol*. 2018;34:1688.e1–1688. e3.
19. Barach EM, Norvak RM, Tennyson GL, Tomlanovick MC. Epinephrine for treatment of anaphylactic shock. *J Am Med Assoc*. 1984;251:2118–2122.
20. Hughes G, Fitzharris P. Managing acute anaphylaxis, new guidelines emphasize importance of intramuscular adrenaline. *BMJ*. 1999;319:1–2.
21. Thomsen HS, Morcos SK. Contrast media safety committee of European society of urogenital radiology. Management of acute adverse reactions to contrast media. *Eur Radiol*. 2004;14:476–481.
22. Alam R, Anantharaman R. Use of IABP in contrast media-induced anaphylactic shock: the ultimate lifesaver. *BMJ Case Rep*. 2013;2013, bcr2013008838.
23. Sugiura A, Nakayama T, Takahara M, Sugimoto K, Hattori N, Abe R. Combined use of ECMO and hemodialysis in the case of contrast-induced biphasic anaphylactic shock. *Am J Emerg Med*. 2016;34:1919.e1-2.