

Acute Adverse Reactions to Nonionic Iodinated Contrast Media for CT: Prospective Randomized Evaluation of the Effects of Dehydration, Oral Rehydration, and Patient Risk Factors

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OBJECTIVE. The objective of our study was to determine the effects of dehydration and oral rehydration on the incidence of acute adverse reactions to iodinated contrast media administered during abdominal and pelvic CT in outpatients.

SUBJECTS AND METHODS. For our prospective randomized study performed at a single institution, adult outpatients undergoing contrast-enhanced abdominal CT were randomly divided into a rehydration group ($n = 2244$ patients [1379 men and 865 women]; mean age, 65.2 years; age range, 18–90 years) and a control group ($n = 3715$ [2112 male patients and 1603 female patients]; mean age, 65.8 years; age range, 17–96 years), which included an age- and sex-matched subgroup (adjusted control group, $n = 2244$). The rehydration group received an oral rehydration solution (500 mL of liquid in which osmotic pressure is adjusted to enhance gastrointestinal absorption) before abdominal and pelvic CT. Patients were also divided into subclinically dehydrated ($n = 997$) and hydrated ($n = 4962$) groups according to their answers to a questionnaire that they completed before the CT examination. The patients were interviewed about contrast-induced adverse reactions before they left the CT room, and the reactions were categorized as allergiclike or physiologic. The incidence of reactions was compared between the rehydration and control groups and between the subclinical dehydration and hydrated groups. The rehydration and control groups were compared with an unpaired t test or a chi-square or Fisher test.

RESULTS. The overall incidence of an acute adverse reaction was 4.3% (254/5959); the acute adverse reactions included 136 allergiclike and 118 physiologic reactions. Fourteen allergiclike and nine physiologic reactions were moderate grade, and none was severe. There was no significant difference between the rehydration group and adjusted control group in the overall incidence of adverse reactions (99/2244 [4.4%] vs 100/2244 [4.5%], respectively; $p = 0.9422$) or between the subclinically dehydrated group and hydrated group in the incidence of allergiclike reactions (25/997 [2.5%] vs 111/4962 [2.2%], $p = 0.6062$) and physiologic reactions (22/997 [2.2%] vs 96/4962 [1.9%], $p = 0.5793$). Younger age was a risk factor for both allergiclike and physiologic reactions ($p \leq 0.0019$).

CONCLUSION. Dehydration and oral rehydration did not affect the incidence of acute adverse reactions to iodinated contrast material for abdominal and pelvic CT in our randomized prospective trial.

Nonionic iodine contrast media are widely used in contrast-enhanced CT and are generally considered safe. Contrast-induced adverse events are uncommon [1]; when they occur, they are typically mild to moderate in severity and are usually not life-threatening [2]. These acute adverse reactions are of concern clinically [3–6] because they are unpredictable and uncomfortable for patients [7].

The American College of Radiology (ACR) guidelines [8] classify acute adverse reactions as allergiclike or physiologic and

organize them according to severity as follows: mild, moderate, or severe. The symptoms of allergiclike reactions resemble those of true allergic reactions and include skin and respiratory tract symptoms. Because an antigen-antibody response is not always identifiable, these reactions are considered allergiclike reactions instead of an allergic or anaphylactic reaction [9]. The exact cause of allergiclike reactions is unclear, although multiple vasoactive substances or mediators, including histamine, may contribute [10–12]. The second reaction type, physiologic reac-

tions, includes cardiovascular effects; physiologic reactions are especially problematic in patients with underlying cardiac disease [13]. These vasovagal reactions are characterized by hypotension with bradycardia [10] and gastrointestinal signs (e.g., nausea and vomiting) [14]. Symptoms including flushing, warmth, chills, headache, dizziness, anxiety, and altered taste may also occur [8, 14]. The exact cause of physiologic reactions is also unclear but may be related to direct chemotoxicity [15] or osmotoxicity [16] by specific molecules.

Identification of the factors affecting the prevalence of acute adverse reactions is difficult. A previous allergiclike reaction is the only confirmed risk factor, to our knowledge, for a recurrent allergiclike reaction [1, 17, 18]. Other suspected risk factors include atopy, asthma, young age [19], and female sex [19]. The risk may also increase with increased contrast dose and concentration [10] and with the administration of high-osmolality contrast material, which shifts fluid from the intracellular compartment to the extracellular compartment, resulting in cell dehydration [16].

Interestingly, outpatients reportedly have a higher incidence of acute adverse reactions than hospitalized patients [6]. In outpatients, hydration can vary according to their preparation for CT by the institution. There

is no consensus about the appropriate fluid intake before CT. Some institutions recommend that patients avoid drinking for 4–6 hours before CT, whereas others encourage patients to drink well until CT to remain hydrated. Our institution lies between them: We permit patients to drink water until CT, but we do not specifically recommend it.

The use of IV iodine contrast medium is believed to be one of the risk factors for contrast-induced nephropathy (CIN) [20]. The dehydration status of the patients probably has some role in CIN [21], and the current ACR guidelines [8] recommend providing adequate hydration before CT for patients at high risk of CIN. However, it is not well known whether or not dehydration also can affect the incidence of acute adverse reactions.

Oral rehydration was recently proposed as an alternative to IV hydration in dehydrated patients [22, 23]. Oral rehydration is reportedly as effective as IV hydration in preventing CIN [24–27], is well tolerated, and is inexpensive [28]. An oral rehydration solution—a liquid in which osmotic pressure is adjusted to enhance gastrointestinal absorption—is absorbed systemically within 30 minutes, which allows the patient to be rehydrated immediately before CT [29]. Hence, the purpose of our study was to investigate the effects of dehydration and rehydration

on the prevalence of acute adverse reactions to iodinated contrast media administered to outpatients for abdominal and pelvic CT.

Subjects and Methods

Our institutional review board approved this prospective single-center randomized trial. Informed consent was obtained from all patients enrolled in our study.

Sample Size Estimation

The sample size needed to detect a difference in the rates of an acute adverse reaction between the rehydration and control groups was estimated. The rate of all acute adverse reactions was assumed to be 3% [1]. The suggested difference between the two groups was set at 0.15%. Using these parameters, we calculated a sample size of 2048 patients per group with an alpha of 0.05 and a statistical power of 0.8.

Patients

Patients visiting our radiology department for contrast-enhanced abdominal and pelvic CT were recruited and divided into a rehydration group and a control group. Patients in the rehydration group were given an oral rehydration liquid before CT; the liquid is a commercially available oral rehydration solution (OS-1, Otsuka Pharmaceutical) in which the osmotic pressure has been adjusted to enhance gastrointestinal absorption. All patients

TABLE 1: Subject Characteristics and Incidence of Subclinical Dehydration

Characteristic	Oral Rehydration Group (n = 2244)	Nonadjusted Control Group (n = 3715)	p	Adjusted Control Group ^a (n = 2244)	p
Age (y), mean (SD)	65.2 (18.1)	65.8 (17.0)	0.1731	65.2 (12.8)	0.8985
Female	865 (38.5)	1603 (43.1)	0.0005	865 (38.5)	1.0000
Body weight (kg), mean (SD)	58.8 (11.2)	57.3 (11.2)	<0.0001	58.7 (11.4)	0.7035
Asthma	72 (3.2)	132 (3.6)	0.4784	84 (3.7)	0.3281
Allergy to iodine contrast agent	2 (0.1)	12 (0.3)	0.0521	7 (0.3)	0.0860
Other allergy	336 (15.0)	548 (14.8)	0.8152	319 (14.2)	0.4723
No previous experience of contrast injection	269 (12.0)	427 (11.5)	0.5654	264 (11.8)	0.8175
Subclinical dehydration	359 (16.0)	638 (17.2)	0.2389	389 (17.3)	0.2295
Contrast material ^b			<0.0001		1.0000
Iohexol	861 (38.4)	1252 (33.7)		861 (38.4)	
Iopamidol	649 (28.9)	1053 (28.3)		649 (28.9)	
Iomeprol	514 (22.9)	896 (24.1)		514 (22.9)	
Ioversol	220 (9.8)	514 (13.8)		220 (9.8)	
Iodine dose, mean (SD)					
Total iodine dose (mg I/kg)	583.9 (45.0)	583.3 (44.6)	0.6612	583.4 (44.5)	0.7328
Injection rate (mg I/s)	1031 (279)	1003 (279)	<0.0001	1045 (271)	0.0849

Note—Data presented as the raw numbers of patients with rate (% of patients) in parentheses unless indicated otherwise.

^aSubjects in the adjusted control group were matched to those in the rehydration group according to age, sex, body weight, and contrast material.

^bIodine concentrations were 300 mg I/mL for iohexol, 370 mg I/mL for iopamidol, 350 mg I/mL for iomeprol, and 320 mg I/mL for ioversol.

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completed an enrollment form before CT. The inclusion criteria were as follows: outpatients presenting for contrast-enhanced abdominal CT, age of 16 years old or older, and the ability to complete and submit an enrollment form before CT.

According to departmental protocol, we avoided administering iodine contrast media to patients who had previously experienced a significant contrast-related adverse reaction. If contrast-enhanced CT was clinically indicated despite this history, then premedication including IV hydration was administered as appropriate, but these patients were excluded from our study. Patients with a prior mild adverse reaction to contrast media, as determined by the attending radiologist, did not receive premedication and were included.

A total of 8653 patients were eligible for enrollment between February 2012 and March 2013 (Fig. 1). If multiple contrast-enhanced CT examinations of the same patient were performed during the study period, then only the first CT examination was included. A total of 1011 patients ($n = 470$, rehydration group; $n = 541$, control group) declined to enroll in the study, and 134 patients ($n = 70$, oral rehydration group; $n = 64$, control group) were excluded because the enrollment form that they submitted was incomplete. Patients unable to consume a sufficient volume of the oral rehydration solution (< 200 mL) were also excluded.

Finally, 5959 patients were enrolled: 2244 patients in the oral rehydration group and 3715 in the control group. The male-female ratio, body weight, contrast material, and injection rate differed significantly between the two groups (Table 1). Therefore, we randomly selected an adjusted control group matched to the rehydration group according to age, male-female ratio, body weight, and contrast material ($n = 2244$) (Table 1).

The following information was determined from the enrollment form: age, sex, body weight, asthma history, allergy to iodine contrast agent, any other allergy, history of IV injection of iodine contrast agent, food and fluid consumption on the day of the CT examination, and the presence of diarrhea, vomiting, or fever. Patients meeting the following criteria were considered subclinically dehydrated: no food or fluid consumption within 6 hours before CT, diarrhea or vomiting within 24 hours of CT, or a fever of $\geq 38^{\circ}\text{C}$.

Contrast-Enhanced CT

Our study did not require a specific contrast medium formulation. One of the following four contrast media formulations, all of which were considered appropriate for patients, was selected by the attending radiologist according to the requirements of the specific CT examination: iohexol (Omnipaque, 300 mg I/mL, Daiichi-Sankyo Health-

care), iopamidol (Iopamiron, 370 mg I/mL, Bayer HealthCare), iomeprol (Iomeron, 350 mg I/mL, Esai Company), or ioversol (Optiray, 320 mg I/mL, Fuji Pharmacy). Most patients received 600 mg I/kg of contrast agent, which is the standard iodine dose at our institution: 79.5% (1785/2244) of the rehydration group, 79.3% (2947/3715) of the control group, and 80.7% (1811/2244) of the adjusted control group. The amount of contrast agent and the iodine dose administered were not specified by the study protocol and varied according to the demands of the examination. The median contrast dose was 600 mg I/kg. The contrast dose ranged from 171 to 1039 mg I/kg in the rehydration group, from 171 to 948 mg I/kg in the control group, and from 212 to 948 mg I/kg in the adjusted control group.

Acute Adverse Reactions

All adverse events after contrast administration were recorded by a nurse or CT technologist. Patients were interviewed after the CT examinations by a nurse or CT technologist about any potential symptoms after contrast administration. The patients were instructed to remain in the hospital for at least 30 minutes after the CT examination and to report any adverse reactions. Objective symptoms such as sneezing or vomiting were also recorded.

A single radiologist with 13 years of experience classified the adverse events as allergiclike reac-

TABLE 2: Incidence of Various Adverse Reactions After Contrast-Enhanced CT in Patients With and Without Oral Rehydration

Parameter	Total	Oral Rehydration Group	Nonadjusted Control Group	p^a	Adjusted Control Group	p^a
All subjects	5959	2244	3715		2244	
Any adverse reaction	254 (4.3)	99 (4.4)	155 (4.2)	0.6575	100 (4.5)	0.9422
Moderate-grade adverse reaction	23 (0.4)	13 (0.6)	10 (0.3)	0.0616	7 (0.3)	0.1787
Any allergiclike reaction	136 (2.3)	52 (2.3)	84 (2.3)	0.8881	53 (2.4)	0.9213
Rash	16 (0.3)	8 (0.4)	8 (0.2)	0.4460	6 (0.3)	0.7889
Itching	68 (1.1)	27 (1.2)	41 (1.1)	0.7258	27 (1.2)	1.0000
Sneezing	61 (1.0)	23 (1.0)	38 (1.0)	0.9938	21 (0.9)	0.7619
Throat-related reaction	8 (0.1)	2 (0.1)	6 (0.2)	0.7081	3 (0.1)	1.0000
Any physiologic reaction	118 (2.0)	47 (2.1)	71 (1.9)	0.6226	47 (2.1)	1.0000
Nausea or vomiting	93 (1.6)	37 (1.6)	56 (1.5)	0.6695	37 (1.6)	1.0000
Vasovagal reaction	6 (0.1)	0 (0.0)	6 (0.2)	0.1380	4 (0.2)	0.1334
Others	25 (0.4)	10 (0.4)	15 (0.4)	0.8086	12 (0.5)	0.6691
Subpopulation with subclinical dehydration	997	359	638		389	
Any adverse reaction	47 (4.7)	16 (4.5)	31 (4.9)	0.7737	16 (4.1)	0.8165
Moderate-grade adverse reaction	3 (0.3)	2 (0.6)	1 (0.2)	0.6131	0 (0.0)	0.4440
Allergiclike reaction	25 (2.5)	8 (2.2)	17 (2.7)	0.6724	10 (2.6)	0.7602
Physiologic reaction	22 (2.2)	8 (2.2)	14 (2.2)	0.9720	6 (1.5)	0.6733

Note—Data are presented as the raw numbers of patients with the rate (% of patients) in parentheses.

^aYates correction was performed if a single value was < 5 or if the sum of two values was < 10 .

TABLE 3: Incidence of Adverse Reactions After Contrast-Enhanced CT in Hydrated Patients and in Subclinically Dehydrated Patients

Parameter	Subclinically Dehydrated Group	Hydrated Group	<i>p</i>
All subjects	997	4962	
Any adverse reaction	47 (4.7)	207 (4.2)	0.4450
Moderate-grade adverse reaction	3 (0.3)	20 (0.4)	0.6240
Allergiclike reaction	25 (2.5)	111 (2.2)	0.6062
Physiologic reaction	22 (2.2)	96 (1.9)	0.5793
Oral rehydration group	359	1885	
Any adverse reaction	16 (4.5)	83 (4.4)	0.9639
Moderate-grade adverse reaction	2 (0.6)	11 (0.6)	0.9515
Allergiclike reaction	8 (2.2)	44 (2.3)	0.9023
Physiologic reaction	8 (2.2)	39 (2.1)	0.8479
Adjusted control group	389	1855	
Any adverse reaction	16 (4.1)	84 (4.5)	0.7155
Moderate-grade adverse reaction	0 (0.0)	7 (0.4)	0.1023
Allergiclike reaction	10 (2.6)	43 (2.3)	0.7679
Physiologic reaction	6 (1.5)	41 (2.2)	0.3850

Note—Data are presented as the raw numbers of patients with the rate (% of patients) in parentheses.

tions or as physiologic reactions and classified the severity of the reactions as mild, moderate, or severe according to the *ACR Manual on Contrast Media*, 10th edition [8]. The severity assessment was modified from the reference guidelines for simplicity as follows: Erythema and urticaria were

not distinguished as diffuse or limited but were instead graded as moderate if either was prominent and was accompanied by itching; obvious vomiting was graded as moderate; and nausea without vomiting was graded as mild. In addition, limited and protracted categories of erythema and urti-

caria were not distinguished. The medical records of patients who experienced a moderate or severe adverse reaction were reviewed, and any medical treatment of the reaction was recorded. Extravasation of the contrast agent was not considered an adverse reaction [30]. Also, isolated effects on the extremities (e.g., coolness, warmth, or local pain) at the injection site [31] were not considered an adverse reaction.

Statistical Analysis

The baseline patient characteristics, contrast agents, and incidence of adverse reactions were compared between the rehydration and control groups. Categorical data were compared using the chi-square test or the Fisher exact test as appropriate. The unpaired *t* test was used to compare numeric data. Trends in the incidence of adverse reactions according to patient age were analyzed using the Cochran-Armitage test, and age groups were designated as follows: < 40 years (*n* = 238 patients), 40–59 years (*n* = 1384), 60–74 years (*n* = 2811), and ≥ 75 years (*n* = 1526).

A subanalysis was performed to determine any effect of rehydration and the associated risk level. Another subanalysis was performed in the rehydration and adjusted control groups to identify potential risk factors for acute adverse reactions by comparing patients who did and those who did not experience an acute adverse reaction. Factors differing significantly between the two groups were further assessed by multivariate logistic regression analysis.

TABLE 4: Risk Factors for an Allergiclike Reaction After Contrast-Enhanced CT

Risk Factor	Univariate Analysis			Multivariate Analysis	
	Reaction	No Reaction	<i>p</i>	Odds Ratio (95% CI)	<i>p</i>
No. of subjects	105	4383			
Age (y), mean (SD)	62.1 (13.9)	65.3 (15.7)	0.0216	0.98 (0.97–0.99)	0.0019
Female patients	28 (26.7)	1702 (38.8)	0.0114	0.65 (0.44–0.94)	0.0218
Asthma	5 (4.8)	151 (3.4)	0.4666		
Allergy to iodine contrast agent	1 (1.0)	8 (0.2)	0.2036		
Other allergy	18 (17.1)	637 (14.5)	0.4641		
No history of contrast injection	17 (16.2)	516 (11.8)	0.1667		
Subclinical dehydration	18 (17.1)	730 (16.7)	0.8946		
Contrast agent			0.0254		
Iohexol	34 (32.4)	1688 (38.5)		Control	
Iopamidol	26 (24.8)	1272 (29.0)		0.96 (0.60–1.54)	0.8728
Iomeprol	37 (35.2)	991 (22.6)		1.90 (1.26–2.90)	0.0023
Ioversol	8 (7.6)	432 (9.9)		0.87 (0.42–1.65)	0.6766
Total iodine dose (mg I/kg), mean (SD)	576.8 (42.4)	583.8 (44.7)	0.0953		
Injection rate (mg I/s), mean (SD)	1091 (305)	1037 (274)	0.0766		
Oral rehydration	52 (49.5)	2192 (50.0)	0.9213		

Note—Data are presented as the raw numbers of patients with the rate (% of patients) in parentheses unless otherwise indicated.

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JMP software (version 11.1, SAS Institute) was used for all statistical analyses. A two-tailed p value of < 0.05 was considered significant.

Results

Baseline Patient Characteristics and Incidence of Subclinical Dehydration

The baseline characteristics of the patients and contrast-enhanced CT examinations are summarized in Table 1. No statistically significant differences were observed in any factor between the rehydration and adjusted control groups. Subclinical dehydration was observed in 997 patients matching one of the following three criteria: did not eat or drink anything within 6 hours before CT ($n = 822$ patients), had diarrhea ($n = 168$) or vomited ($n = 4$) on the day of CT, or had a fever of $\geq 38^\circ\text{C}$ ($n = 3$). There were 359 patients in the rehydration group, 638 in the control group, and 389 in the adjusted control group.

Incidence of Acute Adverse Reactions in the Rehydration and Control Groups

The overall incidence of an acute adverse reaction was 4.3% (254/5959), including 136 allergiclike reactions and 118 physiologic reactions. Twenty-three reactions (14 allergiclike and 9 physiologic) were graded moderate as follows: nausea accompanied by vomiting ($n = 8$), throat tightness without dyspnea ($n = 3$), prominent erythema or urti-

caria with itching ($n = 11$), and vasovagal reaction requiring and responding to treatment ($n = 1$). IV hydration was performed in five patients and observation only without further treatment in 14 patients; corticosteroid administration was performed in the remaining four patients to prevent further progression of the reactions. None of the subjects experienced a severe-grade reaction.

None of the incidence rates differed significantly between the rehydration group (99/2244 [4.4%]) and the nonadjusted control group (155/3715 [4.2%], $p = 0.6575$) or the adjusted control group (100/2244 [4.5%], $p = 0.9422$) (Table 2). As age increased, there was a significant decreasing trend in the incidence of adverse reactions overall ($p < 0.0001$), moderate-grade reactions ($p = 0.0001$), allergiclike reactions ($p = 0.0277$), and physiologic reactions ($p < 0.0001$) (Fig. 2).

In subjects with subclinical dehydration, there was no significant reduction in the incidence of adverse reactions. The incidences of adverse reactions in the rehydration group and adjusted control group were 4.5% (16/359) and 4.1% (16/389), respectively (Table 2).

Incidence of Acute Adverse Reactions in Patients With and Those Without Subclinical Dehydration

The incidence did not differ significantly in subclinically dehydrated patients and hy-

drated patients for adverse reactions overall (47/997 [4.7%] vs 207/4962 [4.2%], respectively; $p = 0.4450$), an allergiclike reaction (25/997 [2.5%] vs 111/4962 [2.2%], $p = 0.6062$), or a physiologic reaction (22/997 [2.2%] vs 96/4962 [1.9%], $p = 0.5793$) (Table 3).

Risk Factors for Acute Adverse Reactions

In the subanalysis performed to identify the risk factors for an allergiclike reaction, age, sex, and contrast medium formulation were selected as potential risks. A multivariate logistic analysis revealed that lower age (odds ratio [OR] = 0.98 per 1-year increase in age, $p = 0.0019$), male sex (OR = 0.65 for women compared with men, $p = 0.0218$), and iomeprol formulation (OR = 1.90 compared with iohexol, $p = 0.0023$) were independently associated with the incidence of an allergiclike adverse reaction (Table 4 and Fig. 3).

Age and a history of an allergy other than asthma or of an iodine contrast allergy were selected as potential risk factors for a physiologic reaction by univariate analysis. Only younger age was independently associated with the incidence of a physiologic reaction (OR = 0.97 per 1-year increase in age, $p < 0.0001$) (Table 5).

Discussion

In our study, we prospectively evaluated the contrast-enhanced abdominal CT scans

TABLE 5: Risk Factors for a Physiologic Reaction After Contrast-Enhanced CT

Risk Factor	Univariate Analysis			Multivariate Analysis	
	Reaction	No Reaction	p	Odds Ratio (95% CI)	p
No. of subjects	94	4394			
Age (y), mean (SD)	60.0 (14.6)	65.4 (15.7)	< 0.0001	0.97 (0.96–0.98)	< 0.0001
Female patients	45 (47.9)	1685 (38.3)	0.0605		
Asthma	6 (6.4)	150 (3.4)	0.1199		
Allergy to iodine contrast agent	0 (0.0)	9 (0.2)	0.5369		
Other allergy	23 (24.5)	632 (14.4)	0.0109	1.36 (0.86–2.10)	0.1768
No history of contrast injection	13 (13.8)	520 (11.8)	0.5540		
Subclinical dehydration	14 (14.9)	734 (16.7)	0.6411		
Contrast agent			0.0613		
Iohexol	28 (29.8)	1694 (38.6)			
Iopamidol	33 (35.1)	1265 (28.8)			
Iomeprol	28 (29.8)	1000 (22.8)			
Ioversol	5 (5.3)	435 (9.9)			
Total iodine dose (mg I/kg), mean (SD)	587.9 (29.8)	583.6 (45.0)	0.1678		
Injection rate (mg I/s), mean (SD)	1042 (327)	1039 (274)	0.9276		
Oral rehydration	47 (50.0)	2197 (50.0)	1.0000		

Note—Data are presented as the raw numbers of patients with the rate (% of patients) in parentheses unless otherwise indicated.

of 5959 outpatients and observed 254 (4.3%) acute adverse reactions, including 23 (0.4%) moderate-grade reactions. The incidence of allergiclike reactions and the incidence of physiologic reactions were nearly identical. Subclinical dehydration, as determined by patient self-reporting, was not a risk factor for an acute adverse reaction. In addition, oral rehydration did not reduce the incidence of acute adverse reactions. The independent risk factors for an allergiclike reaction were younger age, male sex, and the contrast medium formulation, whereas the only risk factor for a physiologic reaction was younger age.

The reported incidence of an acute adverse reaction varies from 0.15% [31] to 3.1% [1]. The rate of adverse reactions in our study is higher than the rates in previous reports. This difference can be explained by the protocol of our study. We interviewed all patients to detect any possible adverse reaction, which likely encouraged patients to report mild adverse reactions that medical personnel would be unable to recognize otherwise. As a result, the frequency of mild adverse reactions was increased. When only the moderate-grade reactions are counted, however, the incident rate in our study is consistent with the rate in a prospective study (moderate or severe adverse reaction, 0.65%) [19].

In general, fluid intake is recommended to prevent CIN [21]. However, on the basis of our results, there is no reason to promote fluid intake to prevent acute adverse reactions. Fluid intake does not help patients feel comfortable with the IV contrast injection. On the other hand, fluid intake immediately before CT did not increase the prevalence of adverse reactions. Thus, there is also no reason, to our knowledge, to advise patients to avoid fluid consumption before contrast-enhanced CT.

Determining the common risk factors for an acute adverse reaction is difficult. A previous allergiclike reaction to iodine contrast medium is the most substantial risk factor for a recurrent allergiclike adverse event [1, 17, 18]. Other risks are less clear [8] but may include an allergy other than an allergy to contrast media [1, 17], asthma [1, 10], youth [1, 19], female sex [17, 19], nonwhite race [17], and β -blocker use [32]. Of the risks suggested in previous studies, younger age (range, 17 to < 40 years) was a clear risk factor in our results. In addition, men were more likely to experience an allergiclike reaction in all age groups, which contradicts a previous report [19]. The cause of this discrepancy is unclear,

but race, contrast medium formulation, or the interview method may be responsible.

Interestingly, the contrast medium composition was a risk factor for an allergiclike reaction. However, all of the contrast agents used in our study were in the same category: monomer-type, nonionic, low-osmolality iodinated contrast media. The mechanism underlying this result is unclear, but selection bias may be responsible. In our study, the choice of contrast medium was not prescribed in the protocol but was determined by a radiologist for each patient. The subanalysis results, which contradict those of previous studies, require a randomized trial designed specifically to evaluate differences according to contrast formulation.

Our study has several limitations. We included only acute adverse reactions observed within 30 minutes after contrast-enhanced CT. An additional study is required to determine the effects of dehydration and rehydration on the incidence of late adverse reactions [33]. In addition, other contrast agent injection-related events, such as contrast extravasation, were not evaluated [34]. The relatively small sample size in our study compared with those in previous reports is another potential limitation. The sample was estimated to reveal any difference in the prevalence between the rehydration and control groups and is adequate for this purpose. However, the subanalysis may have been affected by the small sample size. In particular, the risk factor analysis should be performed using a larger sample to ensure that a sufficient number of severe adverse reactions (prevalence rate, $\approx 0.001\%$ [2, 6, 14]) are available. It can be also a limitation that we excluded patients who had a history of a severe adverse reaction. These patients might potentially benefit the most from rehydration. However, it was not feasible to include these patients. A single-institution study design in one country was also a limitation. A multiinstitutional study involving multiple countries is necessary to generalize our results.

In conclusion, in our randomized prospective study, neither dehydration nor oral rehydration affected the prevalence of acute adverse reactions to iodinated contrast media administered during abdominal and pelvic CT.

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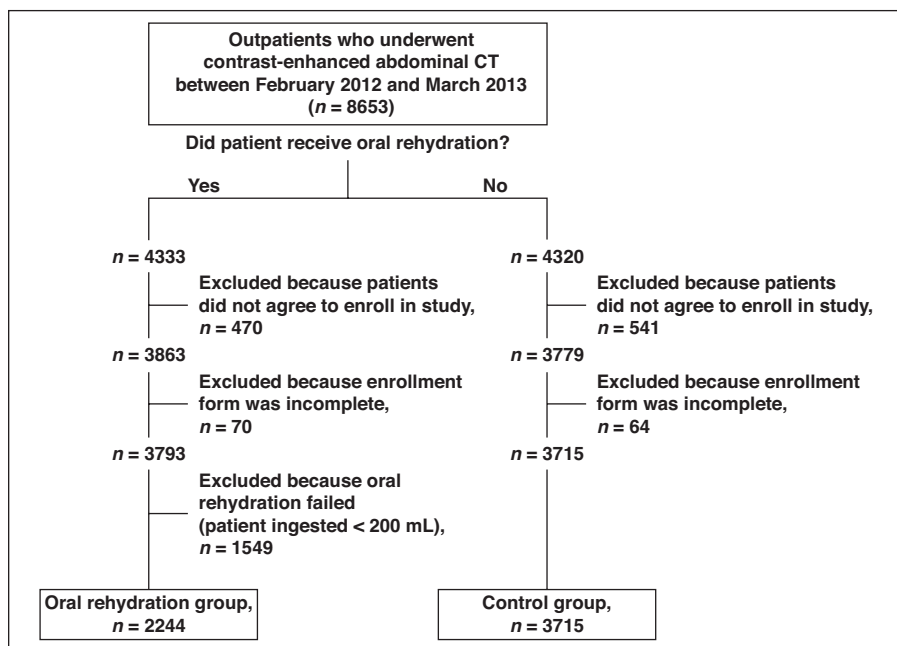


Fig. 1—Flowchart summarizes subject recruitment and group allocation.

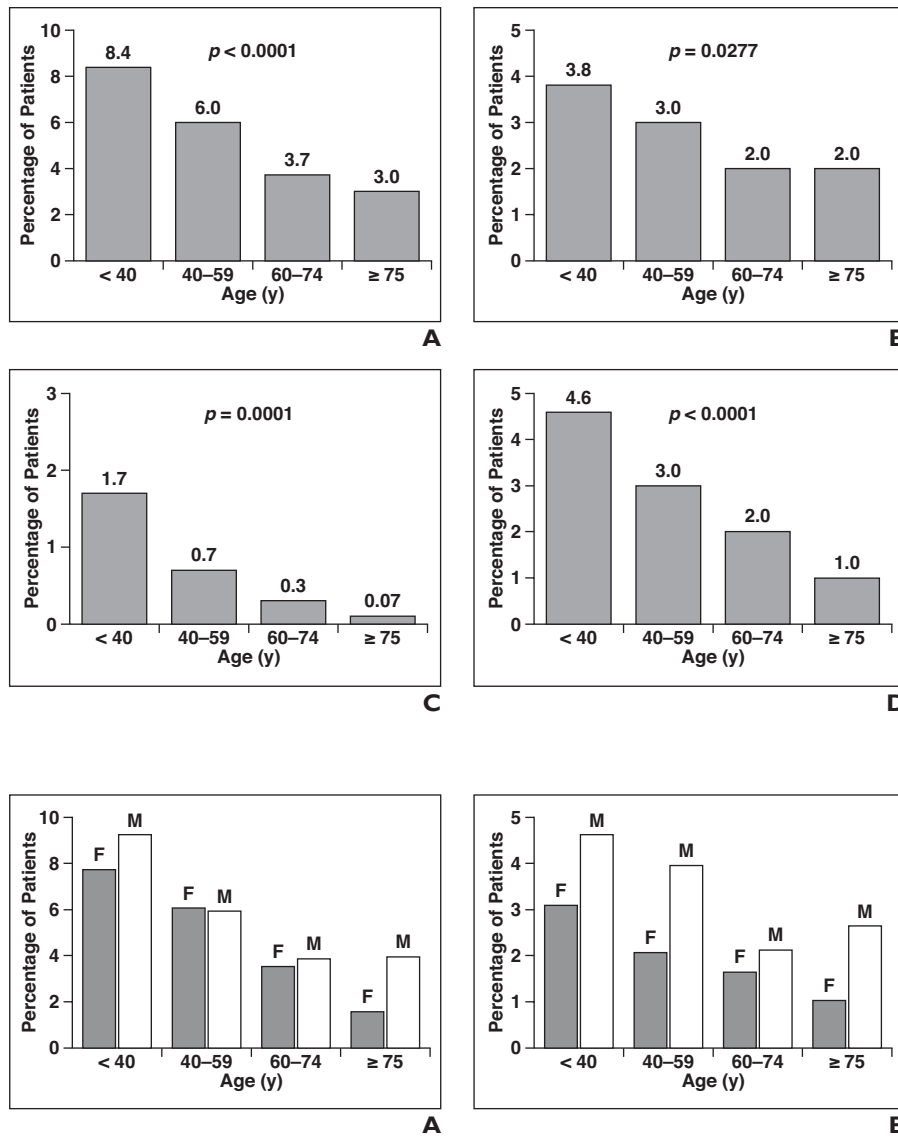


Fig. 2—Bar graphs show incidence of various acute adverse reactions according to patient age. Incidence of adverse reaction decreased with increased age for all reaction types ($p < 0.0277$). Number of patients in each age group was as follows: < 40 years ($n = 238$), 40–59 years ($n = 1384$), 60–74 years ($n = 2811$), and ≥ 75 years ($n = 1526$).
A, Any adverse reaction.
B, Allergiclike reaction.
C, Moderate-grade adverse reaction.
D, Physiologic reaction.

Fig. 3—Bar graphs show incidence of various acute adverse reactions in male patients (M) and female patients (F) according to age.
A, Any adverse reaction.
B, Allergiclike reaction. Allergiclike reactions occurred more frequently in male patients than in female patients.
C, Physiologic reaction.