Original Article

Incidence, outcome, and risk factors of contrast media extravasation injury during contrast-enhanced computed tomography scans: an observational cohort study

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Background: Contrast media (CM) is widely used in contrast-enhanced computed tomography (CECT) to enhance the visualization of abnormal structures. CM extravasation, a recognized complication, may cause mild swelling or severe injuries (e.g., ulceration, necrosis). Current research on severe extravasation is limited to case reports or lacks large-cohort analyses of risk factors. This study aimed to explore risk factors, validate incidence and outcomes, and compare patient/technique/CM-related factors between mild and severe CM extravasation injuries using large-scale clinical data to aid early recognition and prevention.

Methods: This is a retrospective cohort study. A total of 586,812 CM injections were performed during CECT scans at a single institution between November 2012 and December 2023. Among these, 709 cases (334 males, 375 females; age: 62.9±15.2 years) with CM extravasation injuries were included. Extravasation injuries were classified by severity. The frequency and clinical outcomes of different severities of injuries were investigated. Risk factors of serious injuries were evaluated using logistic regression with generalized estimating equation analyses.

Results: CM extravasation occurred in 0.12% (709/586,812) of cases. Of the 709 extravasation injuries, 672 (94.8%) were mild, 32 (4.5%) were moderate, and 5 (0.7%) were severe. Only 5 patients received consultations from dermatologists or burn specialists, and none required surgery. Multivariate analysis underscored the presence of diabetes mellitus [DM, odds ratio (OR) =8.04; P<0.01], injections in the dorsum of the hand (OR =4.86; P<0.01), without saline test (OR =2.58; P=0.02), and large-volume extravasation (OR =5.49; P<0.01) as potential risk factors of moderate or severe CM extravasation injury.

Conclusions: Most CM extravasation injuries are mild and without serious consequences. Multiple modifiable risk factors for serious CM extravasation injury have been identified that could mitigate the severity of the injury.

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Introduction

Contrast media (CM) is widely used in contrast-enhanced computed tomography (CECT) scans to improve the visualization of abnormal structures in various parts of the body (1). With the increasing availability of computed tomography (CT) equipment in healthcare, there were approximately 91.4 million CT scans conducted in the US in 2019; 48% of these recipients required the intravenous administration of CM (2). Characterized by its distinct physicochemical properties, including high concentration, osmotic pressure, and viscosity, CM typically requires intravenous injection into the human body at a rapid rate.

Multiple complications can occur after CM injection, of which extravasation is well-recognized, with an occurrence rate of 0.1–1.2% (3-8). Extravasation refers to the inadvertent administration of vesicant solutions or drugs into adjacent tissues (9,10). CM is categorized as a high-risk vesicant, with tissue toxicity primarily driven by its hyperosmolarity (11). Patients affected by CM extravasation typically experience mild swelling, which resolves within hours to days (12). However, in certain cases, extravasated CM can cause tissue injury, especially to the skin, leading to acute local inflammation peaking at 24–48 hours (6). In more serious cases, severe injuries such as skin ulceration, tissue necrosis, nerve damage, and compartment syndrome may occur, necessitating prompt surgical consultation for possible fasciotomy (13,14). Additionally, when CM extravasation occurs, it typically results in poor-quality CT images, which can adversely affect the patient's disease diagnosis and subsequent treatment plans. Therefore, CM extravasation injury is a non-negligible complication and warrants further investigation to minimize its clinical risks.

However, it remains difficult to minimize the occurrence of CM extravasation. Several non-modifiable factors increase the risk of CM extravasation, including female sex, age over 60 years, and patients in general wards or intensive care units (ICUs) (15-17). The multi-site quality improvement initiative by the American College of Radiology (ACR) (6) aimed to reduce the frequency of extravasation. However, it did not succeed across the participating sites, despite identifying risk factors and implementing proactive measures to mitigate the risk. Given the challenges in reducing the prevalence of CM extravasation, it is crucial to assess the risk factors associated with consequent serious extravasation injury (referred to as moderate or severe extravasation injury in this paper) to better address this complication.

A literature review revealed that existing research on serious CM extravasation injury predominantly focuses on case reports (18,19). Other original studies either lack grading criteria for the severity of CM extravasation injury or do not perform follow-up evaluations to assess severity. Although some effort has been made to explore the risk of extravasation injury, a comprehensive identification of patient-related, technique-related, and contrast-related risk factors has not yet been reliably achieved. Currently, there is a lack of comprehensive examination of independent risk factors of CM extravasation injury severity based on large cohort studies.

To address this research gap, we endeavored to investigate risk factors of CM extravasation injury based on large-scale clinical data. Additionally, we aimed to comprehensively explore the incidence and outcome of CM extravasation injury to confirm previous findings. We hypothesize that some patient-related, technique-related, and contrast-related factors may differ significantly between patients with mild injury and serious extravasation injury. The findings may assist radiology nurses in the early recognition and timely prevention of patients adversely affected by CM extravasation injury. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-2332/rc).

Methods

Design and participants

The study was a single-center, retrospective cohort study

conducted in a regional general hospital. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of The Second Affiliated Hospital, Zhejiang University (No. 2024-0635) and the requirement for individual consent for this retrospective analysis was waived. Based on our radiology system database, a total of 586,812 cases (adults over 18 years old) who underwent CECT scans at The Second Affiliated Hospital, Zhejiang University between November 2012 and December 2023 were initially identified for our study. Subsequent inclusion criteria were patients with extravasation/infiltration events during CECT. The exclusion criteria were as follows: (I) patients who died within 24 hours after CM injection and (II) patients who had saline infiltration before CM injection. Patients who encountered multiple episodes of extravasation were regarded as individual cases. Finally, out of 586,812 CECT scans, 709 cases with extravasation constituted the study population.

CM injection procedure

Nonionic CMs, including iodixanol, iopromide, iohexol, ioversol, and iopamidol, were utilized at our institution. All CMs were brought to room temperature before administration. We did not prewarm the CM to body temperature (37 ℃) because the clinical practices and guidelines we followed did not provide recommendations on the necessity of prewarming CM (20). In fact, recent research indicated that maintaining CM at room temperature is not inferior to warming it to body temperature (21). Warmed and room temperature CM have not been shown to differ in extravasation rate (22).

The majority of patients had intravenous catheters placed by radiology nurses, all of whom had received systematic training and comprehensive competency assessment in intravenous puncture techniques. A few patients had catheters inserted by nurses from other departments in response to emergencies. All catheters were placed within the preceding 24 hours. Catheters were preferentially placed in the antecubital fossa, followed by the forearm, and rarely in the upper arm, wrist, hand, and foot. Based on the patient's vascular conditions, an 18–22 G high pressure-resistant peripheral catheter (the maximum pressure allowed was 350 psi) was used. After successful catheter placement, the radiology nurse assessed patency by aspirating for blood return and manually flushing with 5 mL of normal saline.

During CT scans, saline testing was routinely performed prior to CM administration for all CMs except Optiray® 320 (Ioversol injection, Guerbet, Shanghai, China). The saline test, which involved injecting 20 mL of saline at the same rate as CM administration, was performed using an automatic power injector. This test was used to evaluate whether the intravenous access could withstand a high-flow-rate CM injection. There were two types of power injectors used: the MEDRAD® Stellant FLEX (Bayer, Leverkusen, Germany) and the OptiVantage® (Guerbet, China). The Optiray® prefilled syringe requires a dedicated OptiVantage® injector base, which precludes simultaneous loading of saline syringes in dual-headed power injectors, thereby preventing saline testing. In the event of saline infiltration, the CT nurse would access an alternative vein and document the incident. After completing a saline test, CMs were injected using automatic injectors and delivered through intravenous catheters.

When injecting CM, the nurse closely observed the patient's response and fluctuations in the pressure curve through the video system in the observation window. Patients were instructed to raise their hand or use the intercom to inform the medical staff if they felt any pain or discomfort during the high-pressure injection of CM. There were no extravasation detection accessories in use at our institution. During the injection and after the CT scan, the injection site was inspected to find any swelling or erythema.

Extravasation assessment procedure and data sources

Extravasation was identified by local symptoms in the affected extremity and by inadequate CM enhancement visible on CT images. Upon detection of extravasation, patients were assessed and treated by a radiology nurse. Outpatients were then monitored in the radiology department's injection room for 1 hour, whereas inpatients were returned to their original wards for continued observation. Patients with extravasated CM greater than 20 mL received additional assessment 4–6 hours after injury. For patients with serious CM extravasation injury involving prolonged non-healing or serious blistering, consultations from dermatologists or burn specialists will be obtained. Inpatients received daily ward visits from radiology nurses, whereas outpatients received daily telephone follow-ups. Follow-up continued until resolution of the swelling. Progress notes were made on the day of the extravasation and during each daily follow-up, with all relevant details

documented on a dedicated extravasation form.

Data collection and variables

We conducted a retrospective review to identify potential risk factors linked with the severity of CM extravasation injuries using data extracted from extravasation forms. One author extracted the data while another verified it for accuracy. Possible factors were classified into patient-related data, technique-related data, and contrast-related data.

Patient-related data included sex, age, body mass index (BMI), hospitalization status, and disease diagnosis. These details were further supplemented and verified by reviewing patients' medical records in the radiology system's database. The continuous BMI was categorized according to Chinese standards (23): (I) <18.5 kg/m^2, (II) 18.5–23.9 kg/m^2, (III) 24–27.9 kg/m^2, and (IV) ≥28 kg/m^2. Hospitalization status was classified into three groups: (I) outpatients, (II) inpatients, and (III) emergency patients. We identified common disease-related factors associated with CM extravasation injury, such as cancer, diabetes mellitus (DM), and hypertension, and excluded less frequent factors such as peripheral vascular disease, venous thrombosis, and transplantation from our analysis.

Technique-related data encompassed catheter size, injection side, injection site, saline test implementation, injection rate, peak injection pressure, and estimated extravasation volume (EEV). Catheter sizes ranged from 18 to 22 gauge. Injection sites were grouped into 6 regions, from distal to proximal: (I) foot; (II) hand; (III) wrist; (IV) forearm; (V) antecubital fossa; and (VI) upper arm. Saline testing was performed before CM administration for all CMs except Optiray® 320. EEV was estimated from the amount of CM entering the body in the CT images, the amount of CM remaining in the medicine bottle, and the extent of swelling at the injection site. It was an approximate value since it was difficult to calculate. EEV was classified into two categories according to the definition of large-volume extravasation: (I) EEV <50 mL and (II) EEV ≥50 mL.

Contrast-related data included the type of CM and its osmotic pressure. CM types were identified by generic names: (I) iodixanol; (II) iopromide; (III) iohexol; (IV) ioversol; and (V) iopamidol. The osmotic pressures were noted based on the CM used, whereas viscosity was excluded from our analysis due to its variability with room temperature changes.

Additionally, we collected data on the outcomes of CM extravasation, which included the range of swelling, symptoms and signs (e.g., redness, swelling, pain, blister, etc.), the duration of symptoms, the time to symptom relief, and the follow-up duration.

Severity assessment of extravasation injury

The severity of CM extravasation injury (mild, moderate, and severe) was assessed by 2 authors using the severity grading system proposed by Wang *et al.* (24). Mild extravasation injury occurred when there were no signs or symptoms or when there was only mild pain, swelling, and/or erythema. Moderate extravasation injury presented with initial symptoms such as moderate to severe erythema, blisters, significant pain, or swelling, typically resolving within 2 weeks. Severe extravasation injury resulted in lasting consequences, extending beyond 2 weeks, such as persistent pain, swelling, restricted movement of the affected limb, or necessitating surgical intervention.

Assessment of the large-volume extravasation

Large-volume extravasation was not only an important risk in extravasation injury but also a significant outcome of extravasation (25,26). In some previous studies, EEV greater than 100 mL was considered indicative of large-volume extravasation (15,24,27), whereas other standards, for example, 20 and 50 mL, have also been proposed (13,28). This discrepancy is possibly due to regional and demographic differences. Therefore, based on our local experience in clinical practice, we defined large-volume extravasation as EEV >50 mL.

Statistical analysis

All statistical analyses were performed using SPSS software (version 24.0, IBM Corp., Armonk, NY, USA). In the univariate analyses, CM extravasation injuries were divided into two groups (mild injuries and moderate or severe injuries) since there were relatively few serious injuries. The normality was assessed using the Shapiro-Wilk test. Continuous variables with normal and non-normal distributions were expressed as mean ± standard deviation or median (interquartile range), with *t*-test or non-parametric test performed for comparison between groups. Categorical variables were presented by frequency and percentage, with Chi-squared test used for the comparison. To adjust for the clustering effect in patients with multiple CM extravasation injuries, logistic regression analyses using generalized

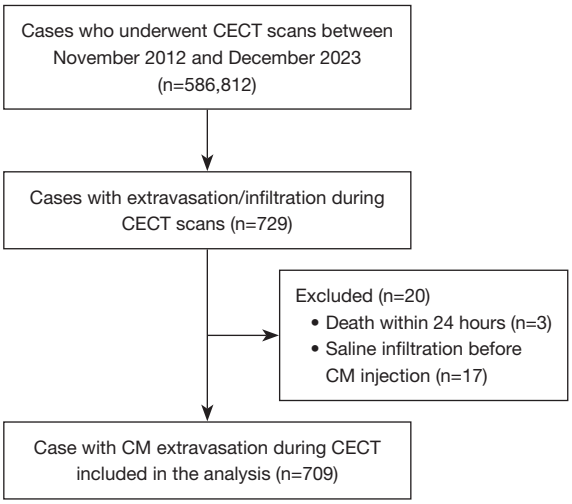

Figure 1 Flow chart of patient screening. CECT, contrast-enhanced computed tomography; CM, contrast media.

estimating equation analyses were performed to explore the risk factors of CM extravasation injury severity.

To adhere to the principle of at least 10 outcome events per variable in regression analysis (29), we restricted variable inclusion in the multivariable model to those with P<0.01 in univariate analyses. The variable BMI showed significance in the univariate logistic regression but was missing in 20% of cases; therefore, it was excluded from the multivariate logistic regression analysis. Significant variables retained in the final model included DM, injections in the dorsum of the hand, the absence of a saline test, and large-volume extravasation. The statistically significant difference was defined as a P value less than 0.05.

Results

The occurrence of CM extravasation injury

There were a total 586,812 intravenous injections of CM for CT during the study period. Of these, 729 cases with extravasation events were included in the study. Subsequently, 3 patients who died within 24 hours and 17 patients who experienced saline infiltration before CM injection were excluded from further analysis (*Figure 1*). Finally, 709 cases (334 males, 375 females; mean age: 62.9±15.2 years; age range, 19–95 years) constituted the study population. CM extravasation occurred in 0.12% (709/586,812) of cases. Among the 709 cases, 672 (94.8%), 32 (4.5%), and 5 (0.7%) had mild, moderate, and severe injuries, respectively. Comparison between patients with mild, moderate, and severe CM extravasation injury is summarized in *Tables 1*,*2*.

Management and outcome of CM extravasation injury

All patients with CM extravasation injury received conservative treatment, including elevating the affected limb and avoiding hot compression within 24 hours. Cold compression was permissible but not routinely recommended due to the risk of frostbite in elderly patients. Additionally, mucopolysaccharide polysulfate ointment (Hirudoid®, Mobilat Produktions GmbH, Bad Vilbel, Germany) was applied locally to promote the absorption of edema. In cases of serious injury, 0.05% dexamethasone was also applied. Based on the consultations with dermatologists or burn specialists, 3 severe and 2 moderate patients received additional treatment, including wound dressings and bandages, and none required surgery. Complications or sequelae were not observed during the follow-up.

Patients with CM extravasation had poor-quality CT images (*Figure 2*). In the 672 cases with mild CM extravasation injuries, initial symptoms, including insignificant swelling (n=672), redness (n=63), and pain (n=143), resolved within 1 week (mean recovery time, 2 days; range, 1–7 days). In the 32 patients with moderate CM extravasation injuries, symptoms including swelling (n=32), redness (n=8), pain (n=14), hardened mass (n=1), and blister (n=29) resolved within 2 weeks (mean recovery time, 5 days; range, 2–12 days). In the 5 patients with severe CM extravasation injuries, initial symptoms including swelling (n=5), redness (n=2), pain (n=4), and blister (n=5) resolved beyond 2 weeks (mean recovery time, 23 days; range, 17–30 days). *Figure 3* illustrates various manifestations in moderate-to-severe extravasation injuries. *Table 3* shows the characteristics of patients who experienced severe CM extravasation injury.

A total of 7 patients experienced multiple episodes of extravasation. A 67-year-old woman with a history of lung transplantation had 2 moderate CM extravasation injuries on CT pulmonary arteriography; 1 extravasation occurred in the left antecubital fossa with a 15 cm × 10 cm area of swelling and a small blister, and another extravasation happened in the right wrist with a 19 cm × 10 cm area of swelling and pale and tense skin. The other 6 patients encountered mild episodes. Among them, 1 patient experienced 3 episodes of extravasation within a year, 2 patients experienced 2 separate episodes of extravasation within a month, and the remaining 3 patients experienced 2

Table 1 Patient-related information among patients with mild and moderate or severe CM extravasation injuries

Variable	Mild injury (n=672)	Moderate or severe injury (n=37)	χ^2/Z	P valve
Sex			0.04†	0.85
Male	316 (47.0)	18 (48.6)		
Female	356 (53.0)	19 (51.4)		
Age quartiles (years)	64.5 (54.0–74.0)	63.0 (58.5–75.0)	0.60‡	0.55
18–54	173 (25.7)	6 (16.2)	4.51†	0.21
55–64	163 (24.3)	13 (35.1)		
65–74	182 (27.1)	7 (18.9)		
≥75	154 (22.9)	11 (29.7)		
BMI (kg/m^2)	22.6 (20.3–24.9)	25.8 (22.2–27.5)	1.61‡	0.11
<18.5	59 (8.8)	2 (5.4)	14.36§	<0.01**
18.5–23.9	295 (43.9)	10 (27.0)		
24–27.9	129 (19.2)	14 (37.8)		
≥28	50 (7.4)	7 (18.9)		
Missing	139 (20.7)	4 (10.8)		
Cancer	144 (21.4)	9 (24.3)	0.17†	0.68
Diabetes mellitus	13 (1.9)	5 (13.5)	–§	<0.01**
Hypertension	15 (2.2)	2 (5.4)	–§	0.22
Hospitalization status			1.36†	0.51
Outpatient	157 (23.4)	8 (21.6)		
Inpatient	337 (50.1)	16 (43.2)		
Emergency patient	178 (26.5)	13 (35.1)		

Data are presented as numbers with percentage (calculated by column) in parentheses or median with interquartile range. †, Pearson Chi-squared; ‡, Mann-Whitney *U* test; §, Fisher's exact test; **, P≤0.01. BMI, body mass index; CM, contrast media.

episodes of extravasation at longer intervals.

Potential risk factors of CM extravasation injury

Table 4 demonstrates the results of univariate and multivariate logistic regression analysis with a generalized estimating equation for the risk factors of CM extravasation injury severity. 18.5≤ BMI ≤23.9 kg/m^2 (P<0.01), 24≤ BMI ≤27.9 kg/m^2 (P=0.03) or BMI ≥28 kg/m^2 (P=0.04), DM (P<0.01), injections in the dorsum of the hand (P<0.01), without saline test (P<0.01), large-volume extravasation (P<0.01) were identified as significant variables in univariate analyses. Multivariate analyses showed that DM [odds ratio (OR) =8.04; P<0.01], injections in the dorsum of the hand (OR =4.86; P<0.01), without saline test (OR =2.58; P=0.02), and large-volume extravasation (OR =5.49; P<0.01) were potential independent risk factors of CM extravasation injury severity.

Discussion

Summary of results

This is a large retrospective single-institution study of 709 extravasations occurring after 586,812 intravenous CM injections during CECT scans. The incidence of CM extravasation was 0.12% (709/586,812). Most CM extravasation injuries are mild and without clinical complications or sequelae. In addition, we found that CM extravasation injury severity is positively associated with DM, injections in the dorsum of the hand, the absence of a

Table 2 Technique-related and contrast-related information among patients with mild and moderate or severe CM extravasation injuries

Variable	Mild injury (n=672)	Moderate or severe injury (n=37)	χ^2/Z	P valve
Catheter size (gauge)			2.95§	0.23
18 G	213 (31.7)	8 (21.6)		
20 G	304 (45.2)	22 (59.5)		
22 G	155 (23.1)	7 (18.9)		
Injection side			1.56§	0.38
Left	242 (36.0)	15 (40.5)		
Right	421 (62.6)	21 (56.8)		
Missing	9 (1.3)	1 (2.7)		
Injection site			13.97§	0.01**
Dorsum of the foot	1 (0.1)	0 (0.0)		
Dorsum of the hand	41 (6.1)	8 (21.6)		
Wrist	104 (15.5)	7 (18.9)		
Forearm	198 (29.5)	5 (13.5)		
Antecubital fossa	306 (45.5)	16 (43.2)		
Upper arm	22 (3.3)	1 (2.7)		
Contrast			4.14§	0.35
Iodixanol	7 (1.0)	0 (0.0)		
Iopromide	92 (13.7)	5 (13.5)		
Iohexol	163 (24.3)	5 (13.5)		
Ioversol	192 (28.6)	16 (43.2)		
Iopamidol	218 (32.4)	11 (29.7)		
Osmotic pressure (mOsm/kg H_2O)	710.0 (680.0–800.0)	710.0 (710.0–800.0)	–0.44‡	0.66
Without high-flow saline testing	116 (17.3)	14 (37.8)	9.92†	<0.01**
Injection rate (mL/s)	3.0 (2.5–4.5)	3.0 (2.5–4.0)	0.12‡	0.90
Peak pressure (psi)¶	150.0 (121.0–185.0)	158.0 (126.5–192.5)	1.00‡	0.32
EEV (mL)			27.58†	<0.01**
50	579 (86.2)	20 (54.1)		
≥50	93 (13.8)	17 (45.9)		

Data are presented as numbers with percentage (calculated by column) in parentheses or median with interquartile range. †, Pearson Chi-squared; ‡, Mann-Whitney U test; §, Fisher's exact test; ¶, 115 cases missing for this variable; **, P≤0.01. CM, contrast media; G, gauge; EEV, estimated extravasated volume.

saline test, and large-volume extravasation.

Incidence and outcome of CM extravasation injury

Our study revealed that the overall incidence of CM extravasation was 0.12% (709/586,812), which is consistent with reports from the ACR manual indicating an incidence range of 0.1% to 1.2% (6). Our results also confirm the predominance of mild injuries, the infrequency of moderate injuries, and the rarity of severe injuries among all CM extravasation injuries. This finding is also consistent with previous studies showing that the majority of CM

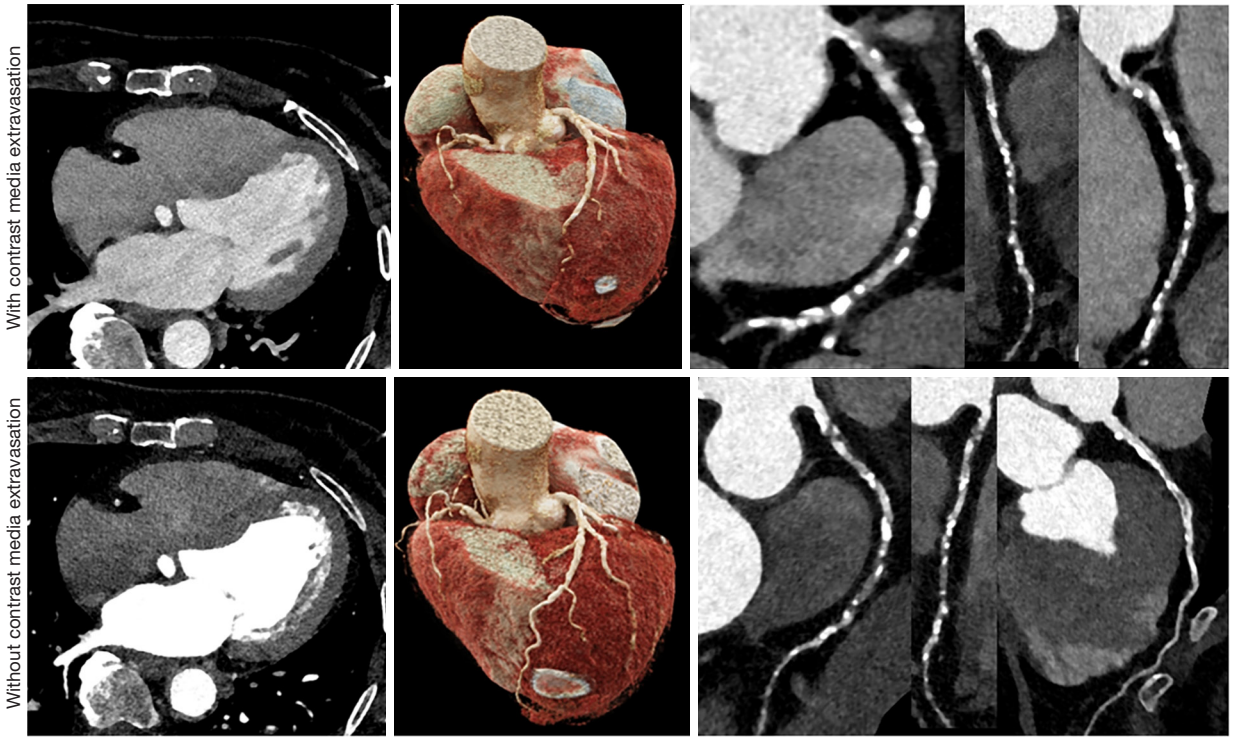

Figure 2 Comparison of CT enhancement in the same patient with and without CM extravasation. In this case, a patient undergoing CT examination experienced an episode of CM extravasation, resulting in low-quality CT images. CM was administered at a flow rate of 4 mL/s, with approximately 20 mL extravasated from a total of 45 mL. The images revealed suboptimal contrast in the distal coronary artery and a coarse vessel wall appearance, which complicates accurate assessment of stenosis. This demonstrates how CM extravasation compromises image quality and diagnostic accuracy, highlighting the need to investigate the common complication of CM extravasation. CM, contrast media; CT, computed tomography.

extravasation injuries are mild (15,24,27). In the single-center study by Wang *et al.*, among 442 adults with extravasation injuries, 9 (2.0%) were classified as moderate and 1 (0.2%) as severe (compartment syndrome) requiring fasciotomy (24). In a multi-center study by Dykes *et al.*, 729 (94.6%) were graded as mild, 36 (4.7%) as moderate, and 6 (0.8%) as severe, of which only 1 patient required surgery (27). In another single institutional study, all 321 extravasation injuries were deemed as mild (15). Our findings are in accordance with existing observations.

Risk factors of CM extravasation injury severity

Among patient-related factors, DM was the only significant factor associated with moderate or severe extravasation injuries, whereas sex, age, hypertension, cancer, and hospitalization status were not significantly related. A previous study has suggested that extravasation injury is more severe in patients with arterial insufficiency in the affected limb (6). In a retrospective study conducted by Upton *et al.* (30), vascular disease was observed in 22.6% (7/31) of patients with severe extravasation injuries. Diabetic peripheral neuropathy in DM patients may account for their insensitivity to extravasation, predisposing them to serious injury (30).

Although female sex, older age, and inpatient status were confirmed as factors increasing the rate of extravasation (15,31), these factors were not significantly associated with serious extravasation injury, consistent with the findings of Dykes *et al.* (27). It has been suggested that hypertension may not be a risk factor for serious extravasation injury (32). For cancer, however, a previous study has shown inconsistent results. Some researchers have suggested that chemotherapy drugs are to blame for serious extravasation injury in cancer patients (33). Meanwhile, a review by Silva *et al.* (34) of CM extravasation injury in cancer patients

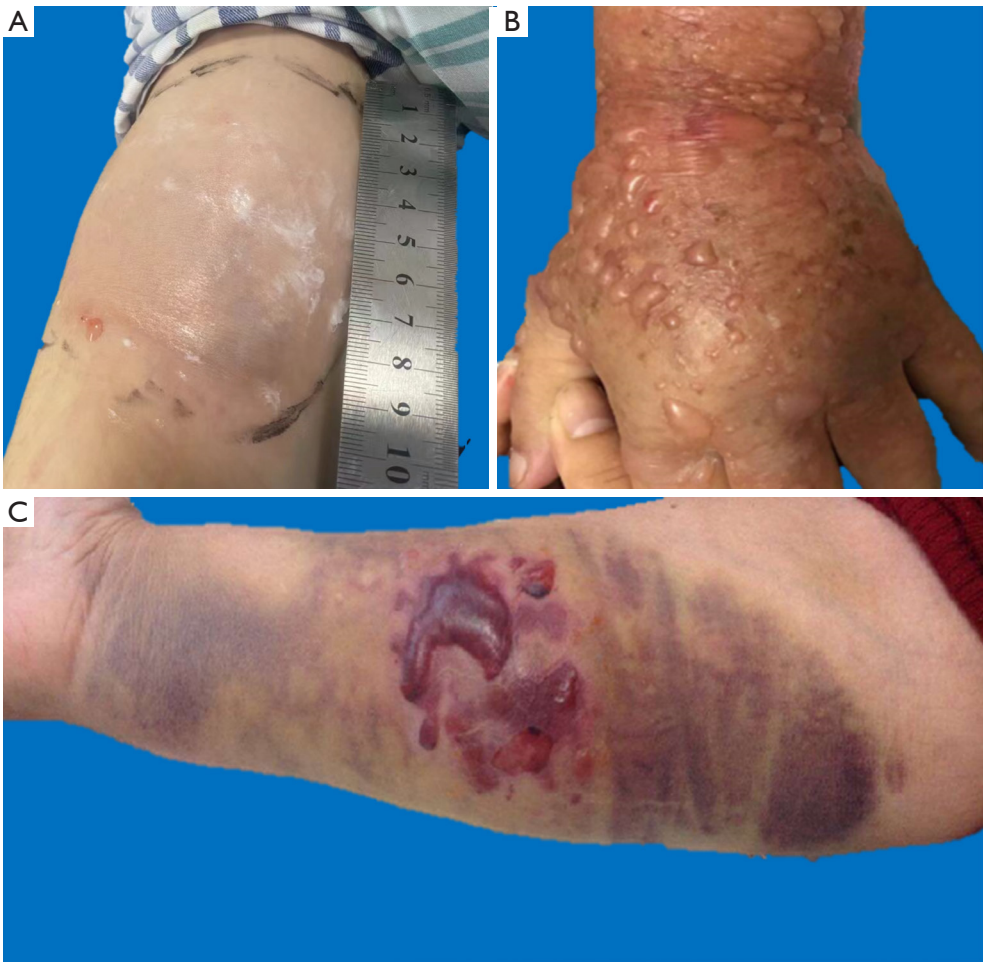

Figure 3 Various manifestations in moderate or severe extravasation injuries. (A) 10 cm × 5 cm area of swelling with a small blister. (B) Multiple blisters on the hand. (C) Integrated bleeding blisters with large ecchymosis. The images showed a clinical manifestation of serious extravasation injury, highlighting the importance of early recognition and timely prevention in patients at risk of serious injury.

showed that the chemotherapy status, radiotherapy experience, and clinical stage were not statistically significant for moderate injury. The effect of cancer on the severity of CM extravasation injury warrants further investigation.

Injection in the dorsum of the hand is also significantly associated with moderate or severe extravasation injury. This finding is consistent with Upton *et al.* (30), who found that extravasations in the dorsum of the hand accounted for 57.6% (19/33) of severe injuries. The penetration of extravasations into the dorsum of the hand results in the necrosis of the underlying dorsal intrinsic compartments (30). It can also be inferred from several case studies that patients with intravenous extravasation in the dorsum of the hand are at a greater risk of developing compartment syndrome (35,36). Researchers have postulated that extravasation injury is more likely to have adverse consequences when it occurs at injection sites with thin subcutaneous planes (37) or tight subfascial compartments (38), such as the dorsum of the hand. According to the ACR manual (6), low-risk intravenous sites are preferred when feasible. If low-risk sites are not feasible, higher-risk sites may be considered based on the risk–benefit analysis of administering CM for the examination indication.

In our study, we introduced a new variable: whether a saline test was performed, which might affect the severity of extravasation. This factor has not been extensively examined previously. Evidence suggests that performing a high-flow saline test may be beneficial in reducing the rate of

Table 3 Characteristics of the patients with severe contrast media extravasation injury

Characteristics	No. 1	No. 2	No. 3	No. 4	No. 5
Age (years)	75	63	85	71	63
Sex	M	F	M	M	F
Disease	Lung infection, hypertension, DM	Cerebellum hemorrhage	Rectal polyp	Heart valve disease, DM	Coronary heart disease
CM	Ioversol 320	Ioversol 320	Iopamidol 370	Iopamidol 370	Iopamidol 370
EEV (mL)	20	70	50	50	50
Injection site	Hand	Hand	Hand	Wrist	Forearm
Catheter	20 G	18 G	18 G	20 G	18 G
Flow rate (mL/s)	2	4	4	4	5
Peak pressure (psi)	100	176	180	181	125
Recovery time (days)	25	28	18	17	30

CM, contrast media; DM, diabetes mellitus; EEV, estimated extravasated volume; F, female; G, gauge; M, male.

extravasation (39,40). Wong *et al.* (41) reported a negative correlation between the volume of saline flush and the incidence of CM extravasation. Similarly, Karády *et al.* (42) observed significant differences in extravasation outcomes between patients who did and did not receive a saline pacer bolus. However, the effectiveness of high-flow saline flushes in mitigating the worsening of CM extravasation injury remains unconfirmed. The impact of saline testing on the severity of extravasation injuries merits further investigation.

Osmolality of nonionic CM did not show a significant association with extravasation injury in our study, whereas some researchers have found that nonionic CM with higher osmolality may increase the risk of more significant injury (28). The osmolality and ionicity of CM may influence the pathogenesis of extravasation injury (43). Higher osmolality causes cellular lysis (38) and local tissue toxicity (11,25). Non-ionic CM, despite its high osmolality, causes less necrosis, edema, and hemorrhage than ionic CM (44) and is better tolerated in humans (38). Thus, non-ionic low-osmolar CMs are preferred to lower the risk of serious extravasation injury (9).

We found a significant association between large-volume (>50 mL) extravasation and moderate or severe injury (P<0.001). Among the patients with large-volume extravasation, 15.5% (17/110) had moderate or severe extravasation injuries. Some 40.6% (13/32) of moderate injuries and all but one of the severe injuries occurred with large-volume extravasation. It is well-recognized that severe extravasation injury typically occurs with large-volume extravasation and unusually with small-volume extravasation (24,27). In Wang's study (24), one of 19 moderate or severe injuries resulted from an extravasation of less than 50 mL. Indeed, massive extravasation leads to a mechanical compression effect and the amount of extravasation is directly proportional to the damage caused (28).

Indications for clinical practice

There are three pathophysiological mechanisms that may produce tissue damage induced by CM extravasation (18,28): cytotoxicity, osmosis, and mechanical compression. Cytotoxicity is directly proportional to the osmolality of the CM (11). The hyperosmolar nature of CM can cause osmotic shifts resulting in swelling and increased risk of mechanical compression, including compartment syndrome (11). The underlying pathogenesis is intricate and involves multiple factors. By identifying the risk factors of CM extravasation injury and excluding unrelated ones (e.g., age, hospitalization status, cancer, hypertension, catheter size, injection rate, etc.), our results aid in the early recognition and timely prevention of serious extravasation injury. Wide dissemination of our findings could inform that caution in choosing the dorsum of the hand as an injection site, performing a saline test before CM administration, and preventing large-volume extravasation are critical to reducing serious extravasation injury. These findings also help radiology staff to take proactive measures and establish

Table 4 Univariate and multivariate logistic regression analysis with generalized estimating equation analyses for the risk factors of CM extravasation injury severity

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Sex (reference: male)				
Female	0.94 (0.48–1.85)	0.85		
Age (years)	1.18 (0.87–1.59)	0.29		
BMI (kg/m^2) (reference: BMI <18.5)				
18.5–23.9	0.35 (0.16–0.76)	<0.01**		
24–27.9	2.31 (1.11–4.80)	0.03*		
≥28	2.60 (1.07–6.33)	0.04*		
Cancer	1.18 (0.54–2.57)	0.68		
Diabetes mellitus	7.92 (2.65–23.66)	<0.01**	8.04 (2.93–22.04)	<0.01**
Hypertension	2.50 (0.55–11.40)	0.24		
Hospitalization status (reference: outpatients)				
Inpatients	0.76 (0.38–1.50)	0.42		
Emergency patients	1.50 (0.73–3.11)	0.27		
Catheter size (reference: 18 G)				
20 G	1.78 (0.92–3.42)	0.09		
22 G	0.78 (0.34–1.77)	0.55		
Injection side (reference: left)				
Right	0.80 (0.41–1.56)	0.52		
Injection site (reference: dorsum of the foot)				
Dorsum of the hand	4.25 (1.82–9.93)	<0.01**	4.86 (1.99–11.86)	<0.01**
Wrist	1.27 (0.56–2.91)	0.57		
Forearm	0.37 (0.14–0.98)	0.05		
Antecubital fossa	0.91 (0.48–1.75)	0.78		
Upper arm	0.82 (0.11–6.27)	0.85		
Contrast (reference: Iodixanol)				
Iopromide	0.99 (0.37–2.60)	0.98		
Iohexol	0.49 (0.19–1.28)	0.14		
Ioversol	1.91 (0.95–3.81)	0.07		
Iopamidol	0.88 (0.42–1.83)	0.73		
Without high-flow saline testing	2.92 (1.42–6.00)	<0.01**	2.58 (1.19–5.61)	0.02*
Osmotic pressure (mOsm/kg H_2O)	1.00 (1.00–1.00)	0.77		
Injection rate (mL/s)	1.01 (0.75–1.35)	0.95		
Peak pressure (psi)	1.00 (1.00–1.01)	0.18		
EEV (reference: EEV <50 mL)				
≥50	5.23 (2.61–10.48)	<0.01**	5.49 (2.59–11.63)	<0.01**

*, P≤0.05; **, P≤0.01. The variables with P<0.01 in univariate regression analyses were selected for multivariate regression analyses (except the BMI variable). BMI, body mass index; CI, confidence interval; CM, contrast media; EEV, estimated extravasated volume; G, gauge.

a specific practice protocol targeting modifiable risk factors related to extravasation injury to reduce adverse events in the radiology department.

Limitations and future directions

There are several limitations in our study. First, this was a single-center study; our results may not be generalizable to patients in other regions. Second, this was a retrospective cohort study; the results may be subject to bias, accuracy, and completeness of extravasation form. Third, even with well-defined criteria, the assessment of injury severity remained subjective. Nonetheless, the proportions of injury severities in our study aligned with those in prior research, indicating that our methodological approach was consistent with that of other researchers. Fourth, the paucity of serious extravasation events and the availability of other variables limit the exploration of additional potential risk factors (e.g., BMI, catheter-to-vein ratio, CM viscosity). Finally, there were no long-term follow-ups after the resolution of swelling. Patients with severe extravasation and multiple extravasations were not well-researched. It was unclear when to re-scan after extravasation. In the future, prospective multi-center studies involving more patients with CM extravasation injuries should employ a quantitative methodology to validate our findings and explore additional potential risk factors.

Conclusions

During CTCE, most CM extravasation injuries are mild and without long-term consequences. The presence of DM, injections in the dorsum of the hand, the absence of a saline test, and large-volume extravasation are identified as potential risk factors of serious CM extravasation injuries.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of The Second Affiliated Hospital, Zhejiang University (No. 2024-0635) and the requirement for individual consent for this retrospective analysis was waived.

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