

Original Article

ความสอดคล้องของการรักษาเฉียบพลันตามแนวทางเวชปฏิบัติ ในผู้ป่วยภาวะภูมิไวเกินชนิดเกิดขึ้นทันทีต่อสารทึบรังสีชนิด ไม่แตกตัวเป็นไอออน

Guideline Concordance of Acute Management in Patients with Immediate Hypersensitivity Reactions to Non-ionic Contrast Media

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บทคัดย่อ

หลักการและเหตุผล: ปฏิกริยาภูมิไวเกินชนิดเกิดขึ้นทันทีต่อสารทึบรังสีชนิดไม่แตกตัวเป็นไอออนยังคงเกิดขึ้นอย่างต่อเนื่อง แม้ว่าสารทึบรังสีรุ่นใหม่จะมีข้อมูลความปลอดภัยที่ดีขึ้นก็ตาม แม้ที่ผ่านมาจะมีการศึกษาอย่างกว้างขวางเกี่ยวกับกลุ่มผู้ป่วยที่เกิดปฏิกิริยาเหล่านี้ แต่กลับมีการให้ความสนใจค่อนข้างน้อยว่าการรักษาที่ให้ในภายหลังนั้นสอดคล้องกับระดับความรุนแรงของปฏิกิริยาที่เกิดขึ้นจริงหรือไม่

รับต้นฉบับ

14 กรกฎาคม 2569

แก้ไขต้นฉบับ

21 กรกฎาคม 2569

รับต้นฉบับตีพิมพ์

25 กรกฎาคม 2569

วัตถุประสงค์: เพื่อประเมินความสอดคล้องของการรักษาเฉียบพลันกับความรุนแรงของปฏิกิริยาภูมิไวเกินชนิดเกิดขึ้นทันทีต่อสารทึบรังสีชนิดชนิดไม่แตกตัวเป็นไอออนและค้นหาปัจจัยที่สัมพันธ์กับการได้รับการรักษาที่สอดคล้องตามแนวทางเวชปฏิบัติ

วิธีการศึกษา: การศึกษาย้อนหลังเชิงวิเคราะห์ในโรงพยาบาลตติยภูมิแห่งหนึ่ง โดยใช้ฐานข้อมูลผู้ป่วยชุดเดียวกันกับงานวิจัยที่เคยรายงานไว้ก่อนหน้านี้ ผู้ป่วยที่มีปฏิกิริยาชนิดเกิดขึ้นทันทีที่ได้รับการบันทึกไว้จำนวน 412 ราย ถูกจำแนกตามระดับความรุนแรงและประเมินว่าการรักษาเฉียบพลันนั้นสอดคล้องกับการจัดการที่เหมาะสมตามระดับความรุนแรงหรือไม่ เนื่องจากไม่มีผู้ป่วยอาการรุนแรงรายใดได้รับการรักษาที่สอดคล้อง ส่งผลให้เกิดปัญหา complete separation คณะผู้วิจัยจึงใช้สถิติ Firth's penalized logistic regression สำหรับการวิเคราะห์ตัวแปรส่งผลหลายตัว

ผลการศึกษา: ผู้ป่วยมีอายุมัธยฐาน 60.0 ปี (พิสัยระหว่างควอไทล์ 52.0-67.0) และเป็นเพศหญิงร้อยละ 57.5 โดยภาพรวมพบผู้ป่วยได้รับการรักษาที่สอดคล้องตามแนวทาง 299 ราย (ร้อยละ 72.6) ความรุนแรงของปฏิกิริยามีความสัมพันธ์อย่างมากกับความสอดคล้องของการรักษา ($p < 0.001$) โดยกลุ่มอาการรุนแรงไม่มีผู้ป่วยรายใดจากทั้งหมด 15 รายได้รับการรักษาที่สอดคล้อง ภายหลังการปรับปัจจัยกวน พบว่าปฏิกิริยาระดับรุนแรงยังคงเป็นตัวพยากรณ์หลักของการรักษาที่ไม่สอดคล้อง (adjusted OR 0.01, 95% CI 0.0006-0.19; $p = 0.002$) ขณะที่อายุ เพศ โครงสร้างของสารทึบรังสี และโรคประจำตัว ไม่พบความสัมพันธ์อย่างมีนัยสำคัญ

สรุป: ถึงแม้อัตราความสอดคล้องโดยรวมต่อแนวทางเวชปฏิบัติจะอยู่ในระดับที่สมเหตุสมผล แต่ตัวเลขนี้ได้ปกปิดความล้มเหลวโดยสิ้นเชิงในการยกระดับการรักษาในกลุ่มอาการรุนแรง โดยไม่มีผู้ป่วยอาการรุนแรงรายใดเลยจากทั้งสิ้น 15 รายในกลุ่มศึกษานี้ที่ได้รับการรักษาด้วยยาอีพินเฟริน ช่องว่างนี้เป็นสิ่งที่ทางสถาบันต้องให้ความสนใจและแก้ไขโดยเร่งด่วน โดยเฉพาะอย่างยิ่งในเรื่องการเข้าถึงยาฉุกเฉินและความพร้อมของบุคลากรในหน่วยรังสีวิทยา

คำสำคัญ: ปฏิกิริยาภูมิไวเกินชนิดเกิดขึ้นทันที, สารทึบรังสีชนิดไม่แตกตัวเป็นไอออน, ความสอดคล้องตามแนวทางเวชปฏิบัติ, การจัดการภาวะเฉียบพลัน, อีพินเฟริน

Abstract

Background: Immediate hypersensitivity reactions (HSRs) to non-ionic contrast media (NICM) continue to occur despite the improved safety profile of modern agents. While much has been written about who develops these reactions, comparatively little attention has been paid to whether the treatment given afterward actually matches how severe the reaction is.

Objective: To evaluate concordance between acute treatment and reaction severity in patients with immediate HSRs to NICM, and to identify factors associated with receiving guideline-concordant treatment.

Methods: We conducted a retrospective cohort study at a tertiary care hospital, drawing on the same institutional database previously described in our earlier report. Four hundred and twelve patients with documented immediate reactions were classified by severity and by whether their acute treatment was concordant with severity-appropriate management. Because no severe case received concordant treatment—resulting in complete separation—we used Firth’s penalized logistic regression for the multivariable analysis.

Results: Median age was 60.0 years (IQR 52.0-67.0), and 57.5% of patients were female. Overall, 299 patients (72.6%) received concordant treatment. Severity was strongly associated with concordance ($p < 0.001$): none of the 15 patients with severe reactions received concordant management. After adjustment, severe reaction status remained the dominant predictor of non-concordance (adjusted OR 0.01, 95% CI 0.0006-0.19; $p = 0.002$), while age, sex, contrast agent structure, and comorbidities showed no significant association.

Conclusion: Although the overall rate of guideline concordance appeared reasonable, this figure concealed a complete failure of appropriate escalation in severe reactions—none of the fifteen severe cases in this cohort received epinephrine-based treatment. This gap warrants prompt institutional attention, particularly around emergency drug access and staff readiness in radiology settings.

Keywords: Immediate hypersensitivity reaction, Non-ionic contrast media, Guideline concordance, Acute management, Epinephrine

Introduction

Contrast-induced HSRs have been studied for decades, and the shift toward non-ionic agents has undeniably reduced both the frequency and severity of these events.^{1,2} Still, reactions happen—sometimes unpredictably, sometimes in patients with no prior history—and when they do, what happens in the next few minutes matters a great deal. A mild urticarial rash calls for a very different response than laryngeal edema

or hypotension, yet in the chaos of a busy imaging suite, that distinction is not always made correctly or acted upon in time.

Most of the existing literature on contrast reactions has focused on incidence, risk factors, and comparisons between different contrast agents.³⁻⁵ This is useful information, but it leaves an important question unanswered: once a reaction occurs, is the treatment actually delivered proportionate to its severity? Anecdotally, clinicians in our department have long suspected that treatment intensity does not always scale appropriately with reaction severity—particularly that epinephrine, despite being the recommended first-line drug for severe systemic reactions, may be used far less often than guidelines recommend.⁶⁻¹¹

This study builds directly on our previous work.¹² we examined the occurrence of HSRs across different NICM agents and described patient-level risk factors. That study answered a different question—essentially, who reacts and to what. The present study uses the same institutional cohort but asks a fundamentally different question: once a reaction has occurred, is the treatment given appropriate to how severe it is? We want to be explicit about this distinction from the outset, because readers familiar with our earlier work may reasonably wonder whether it represents overlapping publication. It does not. The outcome variable, the analytic approach, and the clinical question here are entirely separate from the earlier paper; only the source population is shared, which we believe is transparently disclosed and methodologically justified given that treatment concordance was never analyzed in the original study.

We hypothesized that treatment concordance would decline as reaction severity increased—the opposite of what would be clinically desirable—and that this pattern would be driven largely by underuse of epinephrine in severe cases. The objective of this study was therefore to determine the proportion of patients with immediate HSRs to NICM who received acute treatment concordant with their reaction severity, and to identify demographic, clinical, and pharmacological factors associated with receiving guideline-concordant treatment.

Methods

Study design

This was a retrospective cohort study, reported according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for cohort studies.¹³

Setting and data source

The study was conducted at Srinagarind Hospital, a tertiary care center in Khon Kaen, Thailand. Data were drawn from the same institutional registry used in our previously published,¹² covering the period from 1 January 2021 to 31 December 2023. Although the source population overlaps with the earlier report, the present analysis was conducted independently and addresses a different outcome: treatment concordance rather than reaction occurrence.

Participants

We included all patients who developed an immediate HSRs following administration of NICM during the study period and who had documented information on both reaction severity and acute treatment given. Immediate reactions were defined as those occurring within the timeframe conventionally recognized in radiology practice—typically within one hour of contrast administration. Four hundred and twelve patients met these criteria and form the analytic cohort for this study.

Severity classification

Reactions were classified as mild, moderate, or severe¹² based on the documented clinical features observed at the time of the event. This classification adhered to the categorization framework employed in institutional practice and aligned with widely accepted radiology contrast reaction guidelines,^{5,6,9} mild reactions were limited to localized cutaneous symptoms. Moderate reactions involved more diffuse urticaria or angioedema without hemodynamic compromise. Severe reactions included bronchospasm, hypotension, or clinical anaphylaxis.

Defining treatment concordance

This is arguably the most important methodological decision in the study, so we describe it in some detail. Rather than applying a single rigid definition across all patients, we tailored the concordance criteria to each severity tier, reflecting the reality that appropriate treatment differs by clinical scenario:

Mild reactions: Antihistamine monotherapy, with or without corticosteroid, was considered concordant, consistent with first-line management of isolated cutaneous symptoms.^{5,6,9,11}

Moderate reactions: We accepted antihistamine plus corticosteroid, antihistamine alone, or corticosteroid alone as concordant.^{9,11} This is a pragmatic choice—strict protocols might argue for combination therapy only—but we felt that penalizing monotherapy in this intermediate category would not reflect how these patients are actually and reasonably managed in practice.

Severe reactions: Only regimens including epinephrine were considered concordant. This reflects unambiguous guidance from anaphylaxis management literature; no substitute for epinephrine exists in this setting.^{7-9,11}

Patients with no documented active treatment were classified as non-concordant, since omission of treatment cannot be considered consistent with acute management recommendations regardless of severity tier.

Variables

We examined the following as candidate predictors of treatment concordance: age, sex, contrast agent structure (monomeric versus dimeric, i.e., iodixanol), and the presence of diabetes mellitus, hypertension, asthma, or heart disease.

Statistical analysis

Continuous variables are presented as median with interquartile range (IQR), given non-normal distribution on visual inspection and Shapiro-Wilk testing; categorical variables are presented as frequency and percentage. Comparisons between concordant and non-concordant groups were made using the Wilcoxon rank-sum test for age and chi-square or Fisher's exact test for categorical variables, as appropriate for expected cell counts. Because no patient with a severe reaction received concordant treatment, the severity variable produced complete separation in conventional logistic regression—the model simply cannot estimate a finite coefficient when one category has zero events in a cell. We addressed this using Firth's penalized likelihood logistic regression, which introduces a small-sample bias correction that yields finite, stable estimates even under separation. All candidate variables were entered simultaneously into the multivariable model. Results are reported as odds ratios (OR) with 95% confidence intervals (CI); a

two-sided p-value below 0.05 was considered statistically significant. Analyses were performed in Stata software (version 18.5; Stata Corp LLC, College Station, TX, USA).

Ethical considerations

This study was approved by Faculty of Medicine, Khon Kaen university Institutional Review Board (approval number HE681161). As a retrospective review of an existing de-identified dataset originally collected for the earlier institutional study, individual informed consent was waived in accordance with institutional policy.

STROBE statement and patient flow

This manuscript adheres to the STROBE¹³ guidelines for reporting cohort studies. Figure 1 presents the patient flow diagram from initial identification through final analytic cohort.

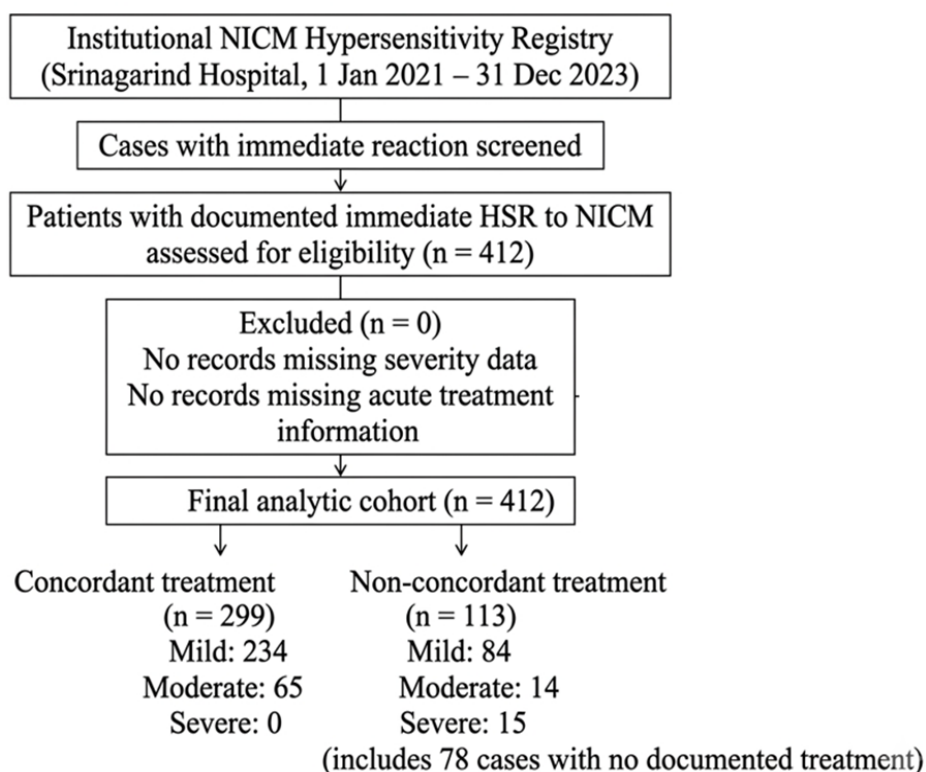


Figure 1 Flow diagram of patient selection. All 412 patients identified from the institutional NICM HSRs registry during the study period (1 January 2021 – 31 December 2023) had complete data on both reaction severity and acute treatment, and therefore all were included in the final analysis.

Results

Baseline characteristics

Four hundred and twelve patients were included. The median age was 60.0 years (IQR 52.0-67.0), and women made up just over half the cohort (57.5%). Most patients had received monomeric NICM (94.4%); only 23 patients (5.6%) had been given the dimeric agent iodixanol. Comorbidities were relatively uncommon in this population—hypertension and diabetes were each present in fewer than one in ten patients, and asthma and heart disease were similarly infrequent.

Table 1: Baseline characteristics of patients with immediate HSR to NICM, stratified by guideline-concordant acute treatment status (n=412)

Characteristics	Total (N=412)	Concordant (n=299)	Non-concordant (n=113)	Not evaluable (n=78)	p-value
Age (years), Median (IQR)	60.0 (52.0–67.0)	60.0 (52.0–67.0)	60.0 (52.0–67.0)		0.618 ¹
Sex, n (%)					0.823 ²
Female	237 (57.5)	173 (57.9)	64 (56.6)		
Male	175 (42.5)	126 (42.1)	49 (43.4)		
Contrast Media Structure, n (%)					0.739 ²
Monomeric NICM	389 (94.4)	283 (94.6)	106 (93.8)		
Dimeric NICM (Iodixanol)	23 (5.6)	16 (5.4)	7 (6.2)		
Underlying disease, n (%)					
Diabetes mellitus	26 (6.3)	18 (6.0)	8 (7.1)		0.693 ²
Hypertension	18 (4.4)	12 (4.0)	6 (5.3)		0.566 ²
Asthma	19 (4.6)	17 (5.7)	2 (1.8)		0.115 ³
Heart disease	34 (8.3)	23 (7.7)	11 (9.7)		0.502 ²
Severity of Reaction (ACR 2025), n (%)					<0.001 ³
Mild	318 (77.2)	234 (92.9)	22 (26.8)	62(79.5)	
Moderate	79 (19.2)	18 (7.1)	48 (58.5)	13(16.7)	
Severe	15 (3.6)	0 (0.0)	12 (14.6)	3(3.8)	

Note: Data are presented as n (%) for categorical variables and Median (IQR) for continuous variables. Percentages may not sum to 100% due to rounding.

Abbreviation: HSR = Hypersensitivity Reaction; NICM = Non-ionic Contrast Media; IQR = Interquartile Range; ACR = American College of Radiology (2025).

^a p-value calculated using the Two-sample Wilcoxon rank-sum (Mann–Whitney) test.

^b p-value calculated using the Pearson Chi-square test.

^c p-value calculated using Fisher's exact test.

Statistical significance was defined as p < 0.05.

Table 1 summarizes baseline characteristics stratified by concordance status. None of the demographic or comorbidity variables differed meaningfully between concordant and non-concordant groups. Severity, however, told a very different story: reactions classified as mild made up the overwhelming majority (92.9%) of the concordant group but only about a quarter (26.8%) of the non-concordant group. Every single severe reaction in the cohort fell into the non-concordant category.

Treatment patterns by severity as presented in Table 2 breaks down the actual treatment regimens received within each severity tier, together with the concordance classification applied to each. Among the 318 patients with mild reactions, 234 (73.6%) received concordant treatment—predominantly antihistamine monotherapy (194 patients). The remaining mild cases were split between inappropriate escalation (9 patients given epinephrine unnecessarily), corticosteroid monotherapy (13 patients), and, notably, 62 patients with no documented active treatment at all.

Among the 79 patients with moderate reactions, 65 (82.3%) fell into the concordant category under our pragmatic classification, spread across antihistamine-corticosteroid combinations and monotherapy regimens. Fourteen moderate cases were non-concordant, mostly due to absent documentation of any treatment (13 patients).

The severe category is where the numbers become genuinely concerning. Of 15 patients with severe reactions, none received epinephrine. Ten were treated with antihistamine and corticosteroid together, one with antihistamine alone, one with corticosteroid alone, and three had no treatment documented at all. Regardless of how the numbers are sliced, the concordance rate in this group is zero.

Table 2: Treatment regimens and concordance classification by severity (N=412)

Severity / Treatment Regimen	Total (N=412)	Concordant (n=299)	Non-concordant (n=113)	Statistical Interpretation & Guideline Logic
MILD SEVERITY (n=318)	318	234	84	Concordance Rate: 73.6% within Mild class
Antihistamine monotherapy	194	194	0	First-line recommended therapy per ACR 2025
Antihistamine + Corticosteroid	40	40	0	Acceptable combined relief (non-inferior concordance)
Corticosteroid monotherapy	13	0	13	Non-concordant: Delayed onset, insufficient acute coverage
Any epinephrine-containing regimen	9	0	9	Non-concordant: Over-treatment/ Inappropriate speed
No documented treatment (Omission)	62	0	62	Non-concordant: Insufficient monitoring/No acute intervention
MODERATE SEVERITY (n=79)	79	65	14	Concordance Rate: 82.3% within Moderate class
Antihistamine + Corticosteroid	18	18	0	Standard dual-pathway coverage per ACR criteria
Antihistamine monotherapy	40	40*	0	Acceptable acute symptomatic control
Corticosteroid monotherapy	7	7*	0	Acceptable anti-inflammatory control
Any epinephrine-containing regimen	1	0	1	Non-concordant: Lack of supportive dual block
No documented treatment (Omission)	13	0	13	Non-concordant: Absolute omission of moderate-level support
SEVERE SEVERITY (n=15)	15	0	15	Concordance Rate: 0.0% within Severe class (Critical Gap)

Severity / Treatment Regimen	Total (N=412)	Concordant (n=299)	Non-concordant (n=113)	Statistical Interpretation & Guideline Logic
Antihistamine + Corticosteroid	10	0	10	Non-concordant: Epinephrine omission in critical event
Antihistamine monotherapy	1	0	1	Non-concordant: Epinephrine omission in critical event
Corticosteroid monotherapy	1	0	1	Non-concordant: Epinephrine omission in critical event
No documented treatment (Omission)	3	0	3	Non-concordant: Absolute omission in anaphylactic setting

*Note: Under a pragmatic clinical audit framework, antihistamine or corticosteroid monotherapy in moderate reactions were accepted as partially concordant for symptomatic relief to reflect real-world clinical compromises.

Predictors of concordant treatment as showed in Table 3 presents the results of the Firth's penalized logistic regression. In the adjusted model, age showed essentially no association with concordance (OR 1.05 per 10-year increase, 95% CI 0.87-1.26, $p=0.635$), nor did sex (OR 0.92, 95% CI 0.57-1.47, $p=0.724$) or contrast agent structure (OR 0.97, 95% CI 0.35-2.67, $p=0.948$). None of the four comorbidities reached statistical significance, although asthma showed a suggestive—if imprecise—trend toward higher odds of concordant treatment (OR 4.09, 95% CI 0.75-22.27, $p=0.103$), perhaps reflecting heightened clinical vigilance when respiratory disease is already a known concern.

The one variable that mattered, unmistakably, was severity. Moderate reactions showed a non-significant trend toward greater concordance relative to mild reactions (adjusted OR 1.70, 95% CI 0.91-3.17, $p=0.094$). Severe reactions, by contrast, were associated with a near-total loss of concordant treatment (adjusted OR 0.01, 95% CI 0.0006-0.19, $p=0.002$)—a finding that should be read less as a precise point estimate and more as statistical confirmation of what Table 2 already shows plainly: nobody with a severe reaction received the treatment they needed.

Table 3 Multivariable Firth's Penalized Logistic Regression for predictors of guideline-concordant treatment (N=412)

Predictor Variables	Concordant (n=299)	Non-concordant (n=113)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI) [†]	p-value
Age (per 10-year increase)	60.0 [52–67]	60.0 [52–67]	1.04 (0.87–1.23)	0.684	1.05 (0.87–1.26)	0.635
Sex (Reference: Male)						
Female	173 (57.9)	64 (56.6)	0.95 (0.61–1.47)	0.818	0.92 (0.57–1.47)	0.724
NICM Structure (Ref: Monomeric)						
Dimeric NICM (Iodixanol)	16 (5.4)	7 (6.2)	0.83 (0.34–2.02)	0.675	0.97 (0.35–2.67)	0.948
Severity (Reference: Mild)						
Moderate	65 (21.7)	14 (12.4)	1.63 (0.87–3.03)	0.124	1.70 (0.91–3.17)	0.094
Severe	0 (0.0)	15 (13.3)	0.01 (0.0007–0.20)	0.002*	0.01 (0.0006–0.19)	0.002*
Underlying Diseases (Ref: No)						
Diabetes mellitus (DM)	18 (6.0)	8 (7.1)	0.82 (0.35–1.89)	0.636	0.90 (0.35–2.31)	0.830
Hypertension (HT)	12 (4.0)	6 (5.3)	0.72 (0.27–1.90)	0.507	0.74 (0.26–2.12)	0.574
Asthma	17 (5.7)	2 (1.8)	2.76 (0.72–10.59)	0.138	4.09 (0.75–22.27)	0.103
Heart disease	23 (7.7)	11 (9.7)	0.76 (0.36–1.59)	0.463	0.80 (0.35–1.80)	0.582

Note:^a Adjusted ORs were estimated using multivariable Firth's penalized logistic regression to account for complete separation in the severity variable and optimize model stability. *Statistically significant association ($p < 0.05$).

Discussion

The headline finding of this study is not subtle: patients with the most severe reactions were the least likely to receive appropriate treatment. Every other variable we examined—age, sex, contrast type, comorbid disease—washed out in the adjusted analysis. Only severity mattered, and it mattered in the wrong direction.

This is worth sitting with for a moment, because it runs counter to what one would hope to find. In an ideal system, severity and treatment intensity should move together—the sicker the patient, the more aggressive and appropriate the response. What we found instead was closer to the opposite: overall concordance looked reasonably good (72.6%), but that number was doing a lot of work to hide the fact that the sickest patients were uniformly undertreated.

Why might this happen? A few explanations seem plausible, though our retrospective design cannot definitively distinguish among them. One possibility is simple unfamiliarity—epinephrine is not an everyday drug for radiology staff the way antihistamines are, and hesitation to administer it, particularly in older patients or those with cardiac comorbidities, is a well-documented phenomenon even among physicians who know the guidelines.^{8-11,14} Another possibility is access: if epinephrine is not immediately available at the point of care, by the time it could be obtained, staff may have already moved to whatever was on hand—antihistamines, corticosteroids—even if these are not truly appropriate for the clinical picture. A third possibility, less charitable but worth considering, is under-recognition: some reactions labeled “severe” in retrospect may not have been immediately recognized as such in real time, delaying escalation until it was effectively too late to matter for treatment choice.

Our earlier study using this same patient population¹ examined at a different slice of this problem—essentially, which patients and which contrast agents were associated with reactions in the first place. That paper could not address whether treatment matched severity, because concordance was never part of its analytic framework. We think the present findings complement that work meaningfully: knowing who is at risk is one thing, but knowing whether the system responds appropriately once a reaction occurs is a separate and, arguably, more actionable question. Prevention strategies (informed by the earlier study) and response strategies (informed by this one) address different points along the same clinical pathway.

Methodologically, we want to highlight the use of Firth’s penalized logistic regression, since this may not be familiar to all readers. Standard logistic regression breaks down when one category of a predictor has zero events—here, zero concordant treatments among severe reactions—producing coefficients that mathematically run to infinity. Firth’s approach corrects for this using a penalty term added to the likelihood function, which pulls estimates back from infinity toward more plausible values while preserving the direction and approximate magnitude of the effect. This is exactly why we could still report an odds ratio for severe reactions (0.01) rather than simply noting that the model failed to converge. The specific point estimate should be interpreted with caution because, when every case in a category shares the same outcome, no amount of statistical sophistication turns that into a precise, generalizable number. Nevertheless, the practical message stands regardless of the exact OR: severe reactions in this cohort were essentially never treated according to guideline expectations.

It is also worth addressing the moderate-severity findings, which showed a non-significant trend toward higher odds of concordance compared with mild reactions (adjusted OR 1.70, $p=0.094$). We do not want to overstate this, given the wide confidence interval, but one plausible reading is that moderate reactions sit in a kind of clinical “sweet spot”—serious enough to prompt deliberate treatment decisions, but not so alarming that clinicians freeze or default to undertreatment. Mild reactions, by contrast, had a substantial proportion of undocumented or absent treatment (62 of 318 patients), which may reflect a different problem entirely: a tendency to under-document or simply observe patients whose symptoms resolve quickly, rather than any active clinical error. Whether that pattern reflects genuine under treatment or simply incomplete charting is something our data cannot resolve, and we flag it as a limitation below.

The comorbidity findings deserve brief comment as well. None reached statistical significance, though the asthma estimate (adjusted OR 4.09, 95% CI 0.75–22.27, $p=0.103$) is intriguing enough to mention without over interpreting. A wide confidence interval spanning from below 1 to above 20 tells us mainly that we do not have enough asthma patients in this cohort to say anything definitive—only nineteen in total. If anything, this points to a worthwhile question for future, larger studies: does a known respiratory comorbidity make clinicians more attentive to reaction severity, or does it simply co-occur

with reactions that happen to look more alarming for other reasons? We cannot distinguish between these possibilities here.

Taken together, our findings suggest that the problem in this cohort was not diffuse or evenly spread across the population—it was concentrated almost entirely in how severe reactions were handled. This has a practical upside: a concentrated problem is, in principle, easier to fix than a diffuse one. If the issue were spread thinly across every severity tier and patient subgroup, the intervention required would be broad, slow, and hard to evaluate. Because the failure here is narrow and specific—epinephrine is not being used when it should be—the corrective actions are correspondingly specific: ensuring epinephrine is physically stocked and immediately accessible in every room where contrast is administered, refreshing staff familiarity with recognition and treatment of anaphylactic-range reactions through periodic simulation drills, and possibly introducing a simple severity-triggered checklist that removes ambiguity about when escalation is required.

Strengths and limitations

This study has several strengths. It draws on a well-characterized institutional cohort with previously validated case ascertainment from our earlier publication, meaning the diagnostic accuracy of the reaction cases themselves is not a new source of uncertainty. The use of severity-stratified concordance definitions,^{8,9,11,14} rather than a single blanket standard applied uniformly, allowed us to reflect clinical nuance rather than imposing an artificial one-size-fits-all rule. And methodologically, the use of Firth's penalized regression allowed us to retain and quantify the severe-reaction effect rather than discarding it or reporting an uninformative “not estimable.”

That said, several limitations warrant discussion. First, this is a retrospective, single-center study, and documentation gaps are an inherent risk—some patients coded as receiving “no treatment” may have been treated without clear charting, which would bias our concordance estimates in an unpredictable direction. Second, our concordance framework, while clinically grounded, involved judgment calls, particularly the decision to accept monotherapy as concordant for moderate reactions; a stricter framework would likely show lower overall concordance in that tier, though it would not change the central

finding regarding severe reactions, since that classification allowed no ambiguity. Third, the small number of severe cases ($n=15$) limits the precision of our severity-specific estimates, even after applying Firth's correction; this finding should be replicated in a larger, ideally multicenter, sample before being treated as generalizable beyond our institution. Fourth, because this analysis reuses the cohort from our earlier publication, some process-level variables that would have been valuable here—such as the exact time elapsed between reaction onset and treatment administration, or which staff member made the treatment decision—were not collected in the original dataset and could not be reconstructed retrospectively. Future prospective work should capture these variables directly.

Despite these limitations, we believe the central finding is robust enough to act on: in this cohort, severe immediate HSRs to non-ionic contrast media were treated inconsistently with basic anaphylaxis management principles, and this was not explained by patient-level factors such as age, sex, comorbidity, contrast agent type, or underlying comorbidities. The problem, as far as we can tell, sits with system-level readiness, protocol familiarity, and the immediate physical availability of rescue medications in the radiology suite rather than patient-level complexity.

Conclusion

In this retrospective cohort of 412 patients with immediate hypersensitivity reactions to non-ionic contrast media, the overall rate of guideline-concordant acute treatment was 72.6%. However, this moderately acceptable figure obscured a critical clinical finding: a complete absence of concordant management among the fifteen patients with severe reactions, none of whom received life-saving epinephrine. Reaction severity was the only independent predictor of treatment concordance, whereas age, sex, contrast agent structure, and comorbid conditions showed no significant associations. Rather than pointing to a generalized clinical deficit, these findings reveal a highly specific, addressable gap in emergency response preparedness within the radiology setting. Closing this clinical safety gap requires a shift in institutional strategy. Instead of focusing solely on pre-reaction screening and risk factors, clinical leadership must implement robust post-reaction systems. This includes ensuring the immediate physical availability

of epinephrine in all imaging rooms, establishing standardized, severity-triggered checklists, and conducting regular, simulation-based emergency training for radiology staff.

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Conflict of interest

The authors declare that they have no conflicts of interest, financial or otherwise, related directly or indirectly to the work presented in this manuscript.

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Data availability statement

The de-identified dataset used in the current study is available from the corresponding author upon reasonable request, subject to approval by the Institutional Review Board of the Faculty of Medicine, Khon Kaen University.

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