ORIGINAL ARTICLE

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Clinical outcomes and management of contrast hypersensitivity in patients requiring repeated computed tomography imaging

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ABSTRACT

Introduction: In collaboration with the Department of Rheumatology, Allergy and Immunology, our study aims to review the outcomes of and propose an improved workflow for the management of patients with prior hypersensitivity reactions to iodinated contrast media (ICM).

Method: Outpatients coming for contrast-enhanced computed tomography (CECT) were stratified into 3 categories (definite, unconfirmed and inaccurate) based on likelihood of their contrast hypersensitivity label. Patients could be offered a different ICM, receive the same ICM, or be referred to an allergist for further evaluation. There were 4 outcomes: (1) alternative ICM tolerated; (2) same ICM tolerated again; (3) patient developed a hypersensitivity reaction to either alternative or original ICM; and (4) CECT was deferred until assessment by an allergist. Comparison was made pre- and post-intervention to see if patient outcomes were improved.

Results: There were 132 patients who made a total of 154 visits (90.3% had documented contrast hypersensitivity). Post-intervention, the number of visits postponed for premedication decreased (81.0% to 34.7%). There was a reduction in hypersensitivity reactions (from 42.9% to 14.3%). Of the 12 patients assessed by the allergist, 6 could continue using the same or alternative ICM, 4 were advised to abstain from further contrast administration and 2 were pending testing with a third agent.

Conclusion: Active intervention by the radiologist can decrease the number of postponed, converted or cancelled CECT studies as well as reduce the number of adverse allergic-like events. Direct collaboration between radiologist and allergist for specific cases may be helpful in patients who will likely need future/repeated CECTs.

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Keywords: Corticosteroid, hypersensitivity, ICM, iodinated contrast media, premedication, skin testing

INTRODUCTION

Allergic and non-allergic hypersensitivity reactions to iodinated contrast media (ICM) are increasingly recognised, particularly the latter where there is greater clarity on pathomechanisms.[1] There is limited evidence for the use of corticosteroids as premedication to prevent the occurrence of contrast-related reactions. At our institution, a dose of 30mg oral prednisolone daily for 3 days prior to a contrast-enhanced computed tomography (CECT) is recommended for patients assessed to have reactions to contrast, or whose reactions were reported to be non-severe. When this regimen was incomplete or omitted, subsequent management was left to the discretion of the attending radiologist, with variable clinical decisions. These included postponing for prednisolone premedication, switching to an alternative low osmolar ICM, opting for an unenhanced CT or different modality of imaging, or even cancelling the scan altogether.[1,2] Furthermore, even with premedication, the decision to proceed with contrast and choice of ICM were variable depending on the perceived severity of adverse reaction by the radiologist on duty that day. These variations in management led to different patient outcomes and

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CLINICAL IMPACT

What is New

- This pilot study in the Singapore setting highlights how direct collaboration between the radiologist and allergist can ultimately improve patient outcome and quality of care by accurate allergy reporting.

Clinical Implications

- Corticosteroid premedication to prevent hypersensitivity reaction to iodinated contrast media (ICM) is controversial.
- Direct collaboration between the radiologist and allergist is useful for prompt patient management and accurate allergy reporting.
- Careful analysis of patient records and timely usage of alternative ICM can prevent unnecessary postponements, or change of imaging technique or modality, ultimately improving patient outcome and quality of care.

inconsistent quality of care. Contributing to this would be the accuracy, or even lack thereof, in allergy information pertaining to the index contrast reaction contained in the patients' Critical Medical Information Store (CMIS), which is a nationwide integrated medical information repository that allows the sharing of drug allergies and other significant medical alerts with institutions' electronic medical records.

Beginning December 2019, we emphasised a more streamlined practice by proactively reviewing CMIS allergy records on the day of scan to determine if an alternative ICM could be administered. We also started collaboration with our institution's Department of Rheumatology, Allergy and Immunology (RAI) for direct referral of patients with contrast reactions to confirm or refute, and expediently update the patient's drug allergy status in CMIS.

Our study aims to review if these 2 interventions are superior to other alternatives—including postponing for premedication, converting to an unenhanced CT, and employing different mode(s) of imaging—which are listed as equivalent management pathways for such patients. We believe that by inculcating this in the department's clinical practice, there would be resultant time and cost savings to our patients without compromising on their safety.

METHOD

We reviewed all outpatients, who presented to the Department of Radiology at Tan Tock Seng Hospital, Singapore for a CECT from 1 January 2018 to 31 December 2020, with a record of contrast hypersensitivity regardless of whether they had completed a prescribed course of prednisolone premedication. Inclusion criteria were patients (1) with a reported contrast hypersensitivity in CMIS; (2) with documented contrast hypersensitivity in the clinical records but not in CMIS; and (3) who self-reported a reaction to contrast. Exclusion criteria were patients without known contrast hypersensitivity, and who developed a de novo reaction following their current CECT.

Before intervention, management has been varied and included postponing for premedication before re-attending (only to be given the same rather than an alternative contrast), administering a single dose of intravenous hydrocortisone on site before scanning (which occurred on one occasion), opting for an unenhanced CT or different modality of imaging, or even cancelling the scan altogether (Table 1). Few underwent their CECT on the same day. Two specific interventions were introduced on 1 December 2019 to improve the management of these patients.

Firstly, we encouraged the radiologist to stratify patients according to the risk of developing a contrast hypersensitivity reaction by studying each patient's contrast reaction history. This includes evaluating credibility of the CMIS record (such as when it was made in relation to contrast administration and whether it was a retrospective entry by a secondary observer), attempt to grade the severity of the index reaction, as well as to check if the patient had received the ICM he/she was reported to be allergic to without complications in the interim. Severity was graded according to the American College of Radiology (ACR) into mild (e.g. self-limiting urticaria and sneezing), moderate (e.g. diffuse urticaria, facial swelling, and wheezing that may progress and usually requires medical management) and severe (e.g. frank anaphylactic shock that usually requires urgent critical care).[3]

Patients were stratified into 3 categories. Category 1 comprised patients with a definite contrast hypersensitivity, where there were objective signs and symptoms of a hypersensitivity reaction following administration of an ICM at least once. Category 2 comprised patients who received the same ICM recurrently throughout time with inconsistent symptoms at each exposure (thus, the probability of a hypersensitivity reaction was unconfirmed). Category 3 consisted of patients

Table 1. Options available within Tan Tock Seng Hospital for managing patients with contrast hypersensitivity requiring contrast-enhanced computed tomography pre-intervention and rationale for change in practice post-intervention

Pre-intervention	Post-intervention
30mg oral prednisolone daily for 3 days before receiving iodinated contrast media	Discourage, as evidence is not strong, and there are potential risks in patients with diabetes, tuberculosis or chronic hepatitis[5,8]
Postponing for prednisolone before re-attending	Discourage, as it causes a time delay
Administer a single dose of intravenous hydrocortisone before imaging at 4 hours later	This is feasible for CECT required urgently, but not recommended for elective outpatients[5,8]
Perform unenhanced computed tomography	Discourage, as it may be sub-optimal
Utilise a different modality of imaging	Discourage, as it may be sub-optimal, can be expensive and also adds to time delay
Cancelling the scan altogether	Discourage, as it does not solve the clinical query
Perform CECT using the same or alternative ICM	The usage of alternative ICM has not been emphasised sufficiently in our institution and can be better guided by correct interpretation of the patient's contrast history Develop direct referral route from radiologists to allergist to perform objective testing for contrast hypersensitivity (new initiative)

CECT: contrast-enhanced computed tomography; ICM: iodinated contrast media
Superscript numbers: Refer to REFERENCES

who had a reaction to ICM but tolerated the same ICM again (CMIS record inaccurate, or delabelling was not performed). Category 1 patients may attempt using an alternative ICM, and if this was tolerated, the patient's CMIS record was supplemented with the caveat that the patient was able to tolerate the alternative contrast (Outcome 1) and could circumvent premedication for future attendances. Categories 2 and 3 patients could proceed with CECT using an alternative ICM (if previous index reaction was graded as moderate), or even the same ICM (mild index reaction), which if tolerated may suggest that the CMIS record could be wrong and be delabelled (Outcome 2). Any of these patients could still develop a hypersensitivity reaction to the given ICM (Outcome 3). However, if contrast administration was considered high risk (severe index reaction) and/or the patient was not keen on proceeding, ICM was avoided altogether by way of an unenhanced CT, a different imaging modality (e.g. ultrasound, MRI or PET-CT), or all radiological evaluation was withheld until assessment by the allergist (Outcome 4). Fig. 1 illustrates this workflow.

Stratification serves 2 purposes: to guide the choice of ICM in premedicated patients; and to allow some who were not/partially premedicated to proceed on the same day, usually with a change of ICM, rather than take premedication and return at a later date. The latter group usually comprised patients who had been warned by their referring clinicians on the importance of completing the premedication. Patients who proceeded on the same day were counselled for the risk of contrast allergy and were assured that they would be observed for 1 hour to ensure that no untoward reaction occurred.[4] If the trial of the same or alternate contrast was tolerated, and the CMIS amended/delabelled, they could avoid premedication for subsequent presentations.

Secondly, we offered all patients, particularly those with severe reactions whom we deemed too risky to administer ICM, direct referral to an allergist (which was a new initiative) to objectively determine their contrast hypersensitivity status.

Clinical data were collected from the patient's hospital records and department file of problematic contrast allergy patients (containing positive reaction, postponed, cancelled and referred cases) during CECT. These included variables such as demographics, the ICM which was used, description of reaction (e.g. urticaria and maculopapular exanthem), and the final diagnosis from the allergists after their outpatient review. Data in the post-intervention period were compared to that of pre-intervention in the preceding year. All data were anonymised and tabulated in a password-protected Microsoft Excel 2018 (Microsoft Corp, Redmond, US) file. Associations between continuous data were assessed using t-tests while categorical variables were tested using Pearson's chi-square test. Statistical significance was declared if the *P* value was less than 0.05. All statistical analyses were done using SPSS Statistics version 26.0 (IBM Corp, Armonk, US). This retrospective study was approved by our Institutional Review Board (DRSB reference: 2021/00054).

RESULTS

Demographics

There were 132 patients who made a total of 154 visits to the Department of Radiology (Table 2). Each visit was for a new CT imaging request and did not include

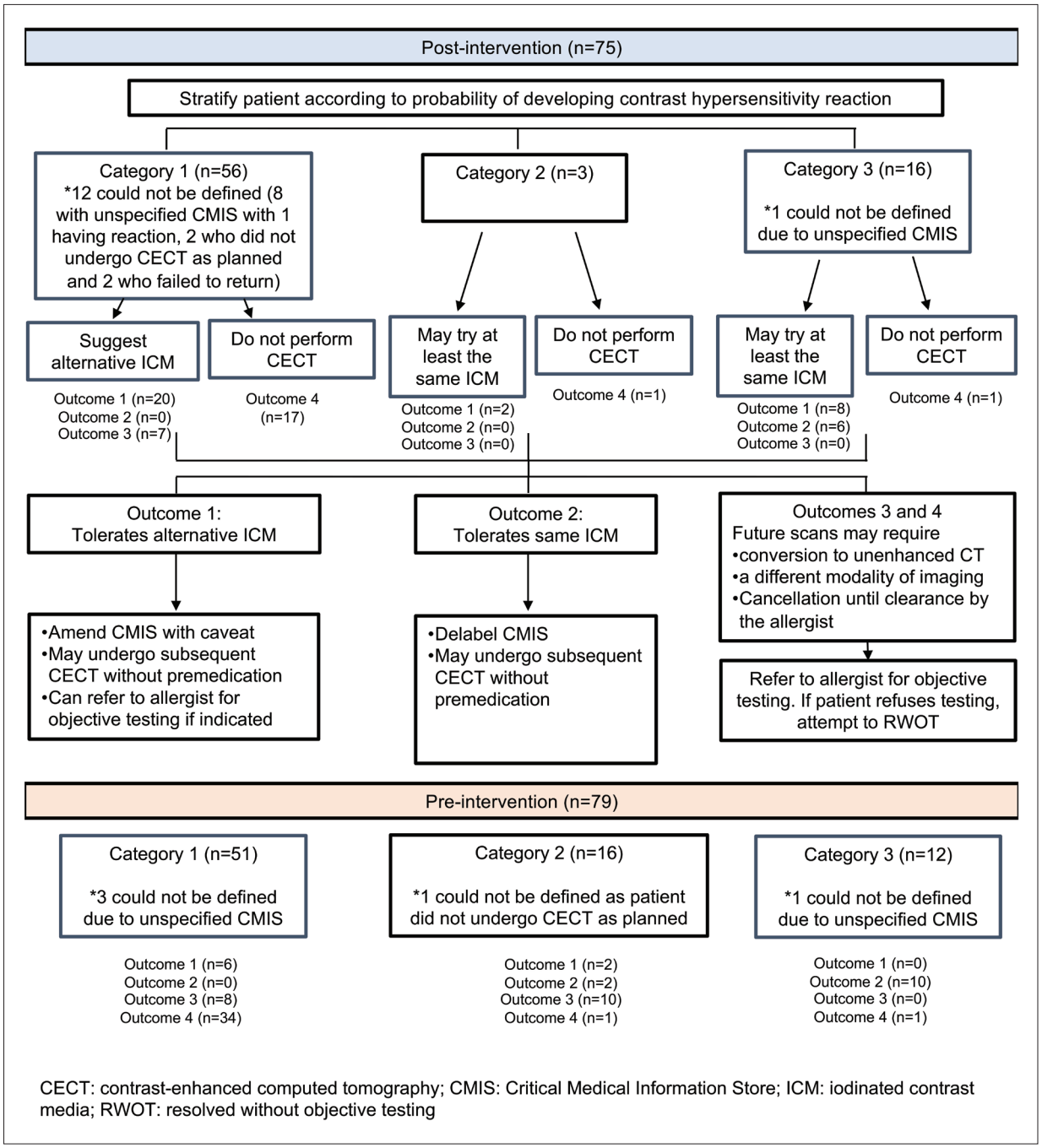


Fig. 1. Post-intervention workflow depicting categories and number of patients based on probability of hypersensitivity, decision on proceeding with contrast-enhanced computed tomography, choice of iodinated contrast media (ICM), and management depending on presence/absence of a reaction. The approximate pre-intervention categories and numbers are shown below for comparison, given that stratification of patients and use of alternative ICM had not yet been widely implemented.

the repeat attendance for patients postponed for prednisolone premedication. In the post-intervention period, there were 64 new patients, in addition to 8 regulars who had also attended pre-intervention. Throughout our study duration, 6 visited thrice, 10 visited twice and 116 presented once.

CMIS documentation

The CMIS reported 139 visits (90.3%) that showed contrast hypersensitivity. Of these, the proportions allergic to iohexol was (n=102, 73.4%), iodixanol (n=3, 2.2%), iopromide (n=2, 1.4%), iodine (n=1, 0.7%), iodamide (n=1, 0.7%), 2 contrast agents (n=4, 2.9%) and

Table 2. Patient demographics

	Pre-intervention (n=68)	Post-intervention (n=72)
Age, median (SD), years	60.7 (10.7)	66.3 (11.7)
Sex, no. (%)		
Male	28 (41.2)	28 (38.9)
Female	40 (58.8)	44 (61.1)
Ethnicity, no. (%)		
Chinese	56 (82.4)	61 (84.7)
Malay	4 (5.9)	4 (5.6)
Indian	5 (7.4)	4 (5.6)
Others	3 (4.4)	3 (4.2)
Total no. of visits	79	75

SD: standard deviation

not specified (n=26, 18.7%). The remaining 15 visits (9.7%) did not have a formal CMIS record, but indicated hypersensitivity to contrast documented in the clinical notes or were reported by patient to the radiologist, of which only 1 could be attributed to iohexol.

Management of patients pre- and post-intervention

Fig. 1 reveals 2 findings. First is found in Category 1, where a large proportion had Outcome 4 pre-intervention (i.e. CECT was not performed) when compared to Outcome 1 post-intervention (i.e. successful completion of CECT using an alternative ICM). Second is a reduction in patients with Outcome 3 (i.e. a hypersensitivity reaction to the ICM used), which showed 18 before intervention and 7 after intervention.

Table 3 presents the comparative management before and after intervention. Pre-intervention, there was a relatively higher (about 4-fold) proportion of visits postponed for premedication (n=34, 81.0%) compared to those that continued with CECT (n=8, 19.0%). When the CECT was eventually done, the same ICM patient documented as being allergic to was used in 18/42 (42.9%) of visits. Allergic reaction was observed in 11/34 (32.4%) of postponed visits and 7/8 (87.5%) of visits where patients continued with CECT. Post-intervention, the proportion of visits postponed for premedication decreased (n=26, 34.7%), with an increase in those who continued with CECT (n=30, 40.0%). Also, fewer used the same ICM 8/56 (14.3%). Hypersensitivity reactions were observed in 4/26 (15.4%) of postponed visits and 4/30 (13.3%) of continued cases.

Postponing a patient for premedication or changing the scanning modality entailed a time delay. There were 48 visits pre-intervention that were postponed (including one that had to be aborted again despite being postponed for a different scanning modality) and 26 visits post-intervention that were postponed (due to 2 patients failing to return). Median time of delay was 4 days and 5 days, respectively. Although there was no significant difference with regards to the time delay pre- and post-intervention, there was a significant decrease in proportion of cases being delayed (P=0.038).There was a decrease in adverse drug

Table 3. Comparative management before and after intervention. Visits requiring contrast were stratified by whether they used the same or different type of iodinated contrast media (ICM), with presence of hypersensitivity reaction shown within parentheses

	Pre-intervention (n=79 visits)				Post-intervention (n=75 visits)			
	Total	Same ICM	Different ICM	Others[a]	Total	Same ICM	Different ICM	Others[a]
Postponed with pre-medications	34	14 (5)	10 (5)	10[b] (1)	26	3 (0)	16 (3)	7[c] (1)
Continued with CECT	8	4 (4)	3 (2)	1 (1)	30	5 (2)	16 (2)	9 (0)
Converted to NCCT	18	-	-	-	15	-	-	-
Changed modality	15	-	-	-	2	-	-	-
Cancelled	4	-	-	-	2	-	-	-

CECT: contrast-enhanced computed tomography; CMIS: Critical Medical Information Store; ICM: iodinated contrast media; NCCT: non-contrast-enhanced computed tomography

[a] Others include patients without a formal CMIS or CMIS with unspecified contrast agent, in whom administration of ICM could neither be defined as being the same nor different.

[b] Includes 1 with failure to cannulate resulting in NCCT being performed.

[c] Includes 2 patients who ended up having NCCT (one from deteriorating renal function and another who declined after further consideration) and 2 who failed to return.

events from 18/42 cases pre-intervention to 8/56 post-intervention (P=0.005). Of the 26 encountered events during our study, 23 were managed conservatively or had antihistamine administered orally, and discharged well. Three (1 pre- and 2 post-intervention) had to be referred to the Emergency Department. No admissions were necessary, and no deaths occurred.

Evaluation by the Department of RAI

Table 4 presents cases referred to allergist and proportion of those who refused, waited for or completed testing, as well as those resolved by radiologist. Table 5 summarises the allergy testing of the 12 patients seen by allergist and recommendations for subsequent management.

If the patient could tolerate the alternative or same ICM, and henceforth was able to continue with subsequent CECT scans, the clinical issue of contrast administration was considered "resolved" (Outcomes 1 and 2). Despite the practical usefulness of this assumption, objective testing for confirmation may be justified in the case of regular patients who may benefit from reverting to iohexol, which is the department's default and cheaper ICM. Outcomes 3 and 4 were regarded as "unresolved" because the drug allergy label remained, which would lead to further time delay or increased healthcare costs with multiple attendances.

Table 4. Cases referred to allergist and proportion of those who refused, waited for or completed testing, as well as those resolved by radiologist

Refused referral to allergist, did not attend clinic appointment and declined to undergo testing	**22**
Overlooked	**15**
Awaiting clinic appointment	**13**
Seen by allergist and resolved without objective testing	**7**
Category 1 Outcome 1[a]	4
Category 1 Outcome 3	1
Category 3 Outcome 2	2
Seen by allergist requiring/completed testing	**12**
Category 1 Outcome 1[a]	1
Category 1 Outcome 3[a]	5
Category 1 Outcome 4	4
Category 1 Outcome undefined	1
Category 3 Outcome 1	1
Seen by radiologist and resolved without objective testing	**6**
Category 1 Outcome 1[a]	4
Category 3 Outcome 1	1
Category 3 Outcome 2	1
Total	**75**

[a] Best attempt was made to define an Outcome in patients with unspecified contrast agent in the Critical Medical Information Store by incorporating information from patient's recollection and available documentation.

To date, 12 patients have been assessed by the allergist. Eleven belonged to Category 1 (91.7%), and with Outcomes 3 or 4 (75.0%). Definitive assessment allowed 4 to revert to using iohexol, 2 to continue with iodixanol as alternative, and 4 to abstain from further ICM use. Another 2 had testing with iopromide deferred as they had no upcoming CECT scheduled. Despite offering objective testing to all patients, slightly more than a third refused referral, did not attend their clinic appointment, or declined to undergo testing. Judgement based only on contrast history allowed 13 patients to be resolved without objective testing by the allergist and radiologist.

DISCUSSION

The prevalence of hypersensitivity reactions to monomeric ionic contrast media is estimated to vary from 3.8% to 12.7%.[5] These reactions are classified into immediate and non-immediate. Immediate reactions are further categorised into immunoglobulin E (IgE)-mediated and non-IgE-mediated, the latter due to effect of the contrast media on mast cell membranes leading to mediator release, or by direct complement activation. Among the guidelines, the European Society of Urogenital Radiology (ESUR) has come out strongest by stating that this prophylaxis is generally not recommended due to lack of evidence, and many recommend a change in contrast media instead.[3,6-11] Studies have shown that switching contrast media has a greater effect than only administering premedication alone, but combining premedication with a change in agent appears to have the greatest effect.[12,13] Referral for allergy testing has been suggested among other recommendations but not emphasised strongly enough.[3,10] ESUR advocates it for moderate to severe reactions while the Royal Australian and New Zealand College of Radiologists proposes it for cases of anaphylaxis.[9,11] At our institution, patients with prior reaction to ICM are still premedicated with prednisolone prior to contrast-enhanced CT scan. However occasionally, such patients miss premedication or are incompletely premedicated, for various reasons.

Streamlining the department workflow and its benefits

In the pre-intervention period, management of outpatients who arrived for CECT in the Department of Radiology was not consistent. Many cases were postponed for prednisolone premedication. Even when contrast was administered, a high proportion received the same ICM that they had reported reactions to. This is despite literature stating that a prior reaction to the same class of contrast medium is deemed to be the greatest risk factor for predicting future adverse events, with a 5- to 10-fold

Table 5. Summary of allergy testing on the 12 patients seen by the allergist and recommendations for subsequent management

Patient	SPT and IDT to iohexol	DPT to iohexol	SPT and IDT to iodixanol	DPT to iodixanol	SPT and IDT to iopromide	DPT to iopromide	Test outcome
1	Negative	Not done	Negative	No immediate or delayed reaction	Not done	Not done	CMIS allergy to iohexol (Category 1 Outcome 4). DPT performed for iodixanol confirming that it was safe to use.
2	Negative	Not done	Negative	Delayed reaction	Not done	Not done	CMIS allergy to iohexol (Category 1 Outcome 4). Positive DPT to iodixanol confirming that it was unsafe. Patient not planned for further CECT hence iopromide testing was deferred.
3	Negative	No immediate or delayed reaction	Negative	Not done	Not done	Not done	CMIS allergy to iohexol (Category 1 Outcome 4). DPT performed for iohexol confirming that it was safe to use.
4	Negative	No immediate or delayed reaction	Negative	Not done	Not done	Not done	CMIS allergy to unspecified ICM (Category 1 Outcome 4). DPT performed for iohexol confirming that it was safe to use.
5	Negative	Not done	Negative	Delayed reaction	Not done	Not done	Allergy to iohexol (Category 1 Outcome 3[a]). Positive DPT to iodixanol confirming that it was unsafe. Patient not planned for further CECT hence iopromide testing was deferred.
6	Not done	Not done	Not done	Not done	Negative SPT Positive IDT	Not done	CMIS allergy to iohexol (Category 1 Outcome 3). Strong clinical history suggestive of reactions to both iohexol and iodixanol. Positive IDT to iopromide; allergist recommendation to avoid as well.
7	Positive IDT	Not done	Positive IDT	Not done	Negative SPT Positive IDT	Not done	CMIS allergy to iohexol and iodixanol (Category 1 Outcome 3). Positive IDT to iopromide; allergist recommendation to avoid as well.
8	Negative	Not done	Negative	Not done	Not done	Not done	CMIS allergy to iohexol (Category 3 Outcome 1). Assessment by allergist; recommended using iodixanol for future scans.
9	Negative	Not done	Negative	Immediate reaction	Negative SPT Positive IDT	Not done	Allergy to iohexol (Category 1 Outcome 3[a]). Positive DPT to iodixanol and positive IDT to iopromide confirming that both were unsafe.
10	Negative SPT Positive IDT	Not done	Not done	Not done	Negative SPT Positive IDT	Not done	CMIS allergy to iohexol (Category 1 Outcome 3). Strong clinical history of reactions to both iohexol and iodixanol. Positive IDT to iopromide; allergist recommendation to avoid as well.
11	Negative	No immediate or delayed reaction	Negative	Not done	Not done	Not done	Allergy to iohexol (Category 1 Outcome 1[a]). DPT performed for iohexol confirming that it was safe to use.
12	Not done	No immediate or delayed reaction	Not done	Not done	Not done	Not done	CMIS allergy to unspecified ICM (Category 1 Outcome undefined). DPT performed for iohexol confirming that it was safe to use.

CMIS: Critical Medical Information Store; DPT: drug provocation test; IDT: intra-dermal test; ICM: iodinated contrast media; SPT: skin-prick test

[a] Best attempt was made to define an Outcome in patients with unspecified contrast agent in CMIS by incorporating information from patient's recollection and available documentation.

increased risk.[3,9] In our study, the number of patients who continued with CECT increased from 8 pre-intervention to 30 in the post-intervention phase. A higher proportion received a different type of ICM while exhibiting a significant reduction in reaction rates. Radiologists have a proactive role in elucidating the contrast allergy history of patients and advocating a change of ICM, especially when the initial CMIS record appears increasingly doubtful. In so doing, more patients were able to have their CT done on the same day with a concomitant reduction in number of adverse drug events. Nevertheless, we still counselled these patients and monitored them for up to an hour post-scan. Although a few developed contrast reactions, these were mild, and the majority were discharged well. None required a hospital admission, and no deaths were encountered.

Pre-intervention, there were also patients with a CMIS record who underwent an unenhanced CT or a different imaging modality. It may be sub-optimal (in the case of an unenhanced CT) or a delay awaiting another appointment while incurring a higher expense (should more sophisticated modes of imaging be necessary). The latter 2 factors would be compounded, especially for patients requiring regular imaging. Our intervention approximately halved the numbers of patients facing this predicament and freed up time slots that could be better utilised for other patients. Even if the time delay was not significant, any rescheduling necessitates patients and their caregivers taking another day off to return for that appointment and runs the risk of them forgetting to re-attend, possibly contributing to delay in treatment.

Collaboration with the Department of RAI

Radiology guidelines have not strongly advocated allergy testing. ACR guidelines state that pretesting with intradermal skin testing with contrast media is not useful in minimising reaction risk while ESUR recommends referral for skin testing 1 to 6 months after occurrence of a contrast media adverse reaction.[3,11] Current literature recommends the use of skin testing for ICM immediate hypersensitivity reactions to prevent recurrence of adverse reactions; allow patients to benefit from ICM reuse that are sometimes essential; and identify safe alternatives for future radiologic investigations.[5,14] Complete evaluation includes skin-prick test and intra-dermal testing to check for IgE-mediated reactions followed by drug provocation testing when skin testing is negative.[5] Our allergists adopted this approach in assessing patients with ICM reactions, where either the initial reaction was disproved, or an alternative ICM was identified via negative skin testing and drug provocation test. Given that there is high cross-reactivity (up to 17.6%) between iohexol and iodixanol, iopromide—which has lower cross-reactivity to both—was introduced as a third option in our institution in mid-2020.[15] Studies estimate the negative predictive value of skin testing in ICM reactions to be 93.1–94.8% for immediate hypersensitivity reactions and 68.4–86.1% for non-immediate hypersensitivity reactions.[15,16]

A direct referral process from radiologist to an allergist, as well as a structured approach to allergy testing to ICM, is a new initiative in Singapore practice. We believe it is useful for 2 reasons: the radiologist is the best witness of the extent and severity of de novo contrast reactions; and this averts an overlooked referral by the time a patient sees the primary doctor in the clinic, where discussions are likely to focus on the disease at hand rather than the adverse drug event. Through this direct referral process, more patients with contrast hypersensitivity reactions are expected to be evaluated, making decision for subsequent administration of contrast clearer.

Maintaining accurate drug allergy documentation

A study by Deng et al. analysing the records of 2.7 million patients showed that most contrast allergy records were ambiguous (69.1%), rather than imaging modality-specific contrast (19.4%) or specific contrast agents (11.5%).[17] In our study, our patients had higher rates of their contrast reactions reported in CMIS (this may be due to the ease of reporting via an electronic platform, as well as lower threshold of reporting by cautious clinicians); our experience also mirrors that of Deng et al., where the same percentage had their contrast agent unspecified in CMIS. We found that non-specific, misleading or incomplete information of these entries were often unhelpful and contributed to unnecessary avoidance of CECT or use of premedication. Once objective testing had taken place, the patient's allergy records were promptly updated, where the contrast was delabelled if tolerated again, or a caveat inserted into the records clarifying that the patient could tolerate an alternative ICM. This will make subsequent decisions regarding contrast administration easier and safer.

This workflow has become the standard of care in our institution, with soft copies uploaded in the electronic Department Handbook and hard copies placed in the CT scan room. Regular reminders, audit and feedback are required to ensure sustenance of this workflow and maintenance of accuracy in the CMIS reporting. The initial future challenge would be to educate other clinicians of this practice and negating the illusion that steroid or hydrocortisone are sufficient to protect against

contrast allergy. Another would be to convince patients in this quandary to accept allergy testing, as the current sentiment is that apart from those with malignancy requiring regular scans, the others tended to decline testing. The final one would be to make this service more available, hence shortening the waiting time.

Limitations

As this was a retrospective study, the pre-intervention categories had to be approximated to allow comparison with post-intervention outcomes. Prospective studies would be required to confirm the true impact of these interventions. Given that this was a new initiative, the number of patients seen in the allergy clinic was small. Our study also involved only outpatients, which is a relative limitation. These patients may have a healthier premorbid condition and thus, more able to furnish a history of contrast reactions. On the other hand, they are the ones where postponement leads to inconvenience of a repeat visit, in contrast to inpatients who are already warded and may receive hydrocortisone while waiting.

CONCLUSION

In patients who have previous possible or confirmed contrast allergies, active intervention by the radiologist can decrease the number of postponed, converted or cancelled CECT studies. This approach will reduce the number of adverse allergic-like events should decision be made to proceed with CECT. Direct collaboration between the Departments of Radiology and RAI for specific cases may be especially helpful in patients who will likely need future/repeated CECTs. Hence, we propose our post-intervention workflow as depicted in Fig. 1.

REFERENCES

1. Jimenez-Rodriguez TW, Garcia-Neuer M, Alenazy LA, et al. Anaphylaxis in the 21st century: phenotypes, endotypes, and biomarkers. J Asthma Allergy 2018;11:121-42.
2. Wu YW, Leow KS, Zhu Y, et al. Prevention and Management of Adverse Reactions Induced by Iodinated Contrast Media. Ann Acad Med Singap 2016;45:157-64.
3. ACR Committee on Drugs and Contrast Media. ACR Manual on Contrast Media, 2022. http://www.acr.org/-/media/ACR/files/clinical-resources/contrast_media.pdf. Accessed 28 January 2022.
4. Cheng DWL, Chiew JL, Wong PMP, et al. Asthma, drug allergies and iodinated contrast media: A retrospective evaluation and proposed CT workflow. Ann Acad Med Singap 2021;50:441-3.
5. Sánchez-Borges M, Aberer W, Brockow K, et al. Controversies in Drug Allergy: Radiographic Contrast Media. J Allergy Clin Immunol Pract 2019;7:61-5.
6. Kolbe AB, Hartman RP, Hoskin TL, et al. Premedication of patients for prior urticarial reaction to iodinated contrast medium. Abdom Imaging 2014;39:432-7.
7. Madowitz JS, Schweiger MJ. Severe anaphylactoid reaction to radiographic contrast media. Recurrences despites premedication with diphenhydramine and prednisone. JAMA 1979;24:2813-5.
8. Davenport MS, Cohan RH. The Evidence for and Against Corticosteroid Prophylaxis in At-Risk Patients. Radiol Clin North Am 2017;55:413-21.
9. The Royal Australian and New Zealand College of Radiologists. RANZCR Iodinated Contrast Media Guidelines, 2018. https://www.ranzcr.com/college/document-library/ranzcr-iodinated-contrast-guidelines. Accessed 27 May 2022.
10. The Royal College of Radiologists. Standards for intravascular contrast administration to adult patients, 3rd Ed. London: The Royal College of Radiologists, 2015. https://www.rcr.ac.uk/sites/default/files/Intravasc_contrast_web.pdf. Accessed 27 May 2022.
11. European Society of Urogenital Radiology. ESUR Guidelines on Contrast Agents v.10.0, March 2018. https://www.esur.org/wp-content/uploads/2022/03/ESUR-Guidelines-10_0-Final-Version.pdf. Accessed 30 January 2022.
12. Abe S, Fukuda H, Tobe K, et al. Protective effect against repeat adverse reactions to iodinated contrast medium: Premedication vs. changing the contrast medium. Eur Radiol 2015;26:2148-54.
13. Park HJ, Park JW, Yang MS, et al. Re-exposure to low osmolar iodinated contrast media in patients with prior moderate-to-severe hypersensitivity reactions: A multicentre retrospective cohort study. Eur Radiol 2017;27:2886-93.
14. Zaiem A, Ben Hammamia S, Ben Salem F, et al. Skin tests for the exploration of hypersensitivity reactions associated with iodinated contrast media. Curr Drug Saf 2022;17:169-75.
15. Yoon SH, Lee SY, Kang HR, et al. Skin tests in patients with hypersensitivity reaction to iodinated contrast media: a meta-analysis. Allergy 2015;70:625-37.
16. Schrijvers R, Breynaert C, Ahmedali Y, et al. Skin Testing for Suspected Iodinated Contrast Media Hypersensitivity. J Allergy Clin Immunol Pract 2018;6:1246-54.
17. Deng F, Li MD, Wong A, et al. Quality of Documentation of Contrast Agent Allergies in Electronic Health Records. J Am Coll Radiol 2019;16:1027-35.