

Whole-Process Pharmaceutical Care for Iodine Contrast Media

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*Clinical Professional Committee on Rational Drug Use of the China Medical
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ABSTRACT OBJECTIVE To explore a whole-process pharmaceutical care model for iodine contrast media and promote its rational clinical use. **METHODS** The Clinical Professional Committee on Rational Drug Use of the China Medical Education Association and the Expert Committee on Drug Evaluation and Clinical Research of the Guangdong Pharmaceutical Association organized domestic experts to form a working group to establish a consensus on whole-process pharmaceutical care for iodine contrast media. The group conducted a systematic literature review, evidence-based analyses, and discussions on key topics, including the development process, indications, contraindications, adverse reactions, interactions, use in special populations, and pharmaceutical care procedures. Based on these evaluations, this expert consensus was ultimately formed. **RESULTS** The consensus on whole-process pharmaceutical care for iodine contrast media encompasses patient evaluation, renal function assessment, considerations for combined drug use, hydration regimens prior to examination, monitoring for iodine contrast media extravasation and acute adverse reactions during examination, and observation and follow-up after examination. Specific work in each stage is elaborated in a pharmaceutical care flowchart. Additionally, a medication monitoring record form was created to document the pharmaceutical care process. **CONCLUSIONS** This consensus establishes a whole-process pharmaceutical care system for iodine contrast media, offering clinical physicians and nursing staff scientific evidence on the safe and effective use of these agents and serving as a practical reference for pharmacists in providing related pharmaceutical care.

KEYWORDS

iodine contrast media; rational drug use; adverse reactions; pharmaceutical care; whole-process; consensus

Iodine, with a relative atomic mass of 127, is heavier than most atoms in the human body and possesses strong X-ray absorption properties. Upon administration, it generates density differences within the examined area, thereby enhancing image contrast to facilitate the visualization of cavity morphology. Iodine is characterized by its stable structure and low biological toxicity. A class of iodine-containing contrast agents, formed by the complexation of iodine atoms with various compounds, is

referred to as iodine contrast media (ICM). ICM is widely utilized in clinical settings for computed tomography (CT) angiographic enhancement, CT perfusion, as well as imaging of body cavities, joints, and the spinal cord.

With ongoing advancements in CT scanning technology, the clinical application of ICM has grown significantly. However, the use of ICM may be associated with adverse reactions, such as extravasation, acute adverse reactions, and, in certain cases, post-contrast acute kidney injury (PC-AKI). Additionally, ICM may interact with other medications that patients are already using, and its administration in specific populations, such as those with renal insufficiency, pregnant or lactating women, children, and elderly individuals, requires special considerations and heightened clinical vigilance. Despite these requirements, a systematic and comprehensive pharmaceutical care consensus for conducting pharmaceutical monitoring has yet to be established to ensure the safety of patients administered ICM, which is a class of special drugs. Therefore, this consensus, based on the elaboration of the rational clinical use and safety management of commonly used ICM, summarizes the content and processes of a whole-process pharmaceutical care for ICM. It also encompasses pharmaceutical monitoring for patients who are administered ICM before, during, and after the examination procedure. This consensus aims to provide a basis for the rational use of ICM, thereby facilitating the standardization and homogenization of the management and application of these agents.

1. Consensus Working Group and Preparation Process

The consensus working group comprised an expert panel and a writing team. The expert panel included experts in pharmacy and medicine with associate senior or higher titles from the Clinical Professional Committee on Rational Drug Use of the China Medical Education Association and the Expert Committee on Drug Evaluation and Clinical Research of the Guangdong Pharmaceutical Association. This panel was tasked with identifying clinical issues and reviewing the recommendations set forth in the consensus. The writing team, led by two leaders and supported by three deputy leaders, coordinated the entire consensus preparation process. In addition to supervising the consensus workflow, they participated in the identification of key clinical issues and contributed to the initial draft review. The core writers, experienced pharmacists with expertise in rational drug use and evidence-based pharmacy practices, were responsible for systematically collecting and analyzing existing clinical evidence to support the expert panel. They compiled these findings into comprehensive reports and drafted the initial version of the consensus.

The preparation framework and specific clinical issues were established through expert discussions. Utilizing this predetermined framework and clinical issues, the core writers conducted an extensive literature retrieval in both Chinese and English databases and then drafted the initial version of the consensus based on the collected evidence. Chinese literature was sourced from Chinese Medical Journal Full-text Database, China National Knowledge Infrastructure (CNKI) and Wanfang Data, while English literature was obtained from PubMed and the Cochrane Library. The writing team and the writers held three rounds of discussion meetings with the expert panel regarding the initial version of the consensus, and completed the revision and finalization of the consensus according to the opinions from these expert discussions.

2. Overview of ICM

2.1 Development History

The development of ICM has progressed from ionic to non-ionic formulations. In the 1950s, the introduction of acetrizic acid signified the transition of ICM to the ionic phase. Due to their high osmolality, ionic ICMs were linked to various vascular-related adverse reactions. In the 1970s, Torsten Almén identified high osmolality as the primary cause of patient discomfort and introduced the concept of non-ionic ICM. Non-ionic ICM, unlike their ionic counterparts, do not ionize and therefore do not elevate plasma osmolality, resulting in a significantly reduced incidence of adverse reactions [1].

Based on their osmolality, ICM can be classified as high osmolality, low osmolality, and iso-osmolality. High-osmolar ICM has an osmotic concentration over five times that of blood (approximately 290 mmol/L), while iso-osmolar ICM has an osmotic concentration like that of blood. ICM can be categorized into monomeric and dimeric forms based on their chemical structure. Dimeric ICM contains twice the iodine content per molecule compared to monomeric ICM; at equivalent iodine levels, dimeric ICM has a lower molecule count and osmotic concentration but a higher viscosity [2].

The main factors affecting the application of ICM include iodine content, osmolality, and viscosity. Generally, high iodine content can enhance imaging quality, but often increases solution osmolality and viscosity. The use of ICM with high osmolality and high viscosity can elevate the risk of renal injury in patients [2]. The classification and physicochemical properties of commonly used ICM are presented in Table 1.

Table 1 The classification and physicochemical properties of commonly used ICMs

Category	Generic Name	Molecular Weight	Iodine Concentration (mg/mL)	Osmolarity (mmol/L)	Viscosity at 37°C (mPa·s)
Ionic Monomer	Diatrizoate	809	306	1530	5.0
Ionic low osmolality Dimer	Ioxipric Acid	1270	320	600	7.5
	Iohexol	821	300	672	6.3
Non-ionic low osmolality Monomer	Iopamidol	777	350	844	10.4
			300	616	4.7
	Iomeprol	778	370	796	9.4
			300	520	4.8
	Iopromide	791	350	620	7.5
			400	726	13.9
			300	607	4.7
			370	774	10.0
Ioversol	807	320	710	5.8	
		350	790	9.0	
Iobitridol	835	300	695	6.0	
		350	915	10.0	
Non-ionic Isosmolar Dimer	Iodixanol	1550	270	290	5.8
			320	290	11.4

2.2 Pharmacokinetics

The pharmacokinetics of intravenously administered ICM adheres to a two-compartment model, characterized by a rapid peak plasma concentration after injection and rapid distribution across various organs. As indicated in the package inserts, ICM rarely bind to plasma proteins and remains in plasma in their unaltered form. The distribution and elimination pharmacokinetic parameters (clearance, the half-life, and steady-state volume of distribution) are generally consistent among different ICMs. Under standard dosing with intravenous administration, the elimination half-lives of various ICMs show minimal variation. Currently, no studies report ICM metabolism in vivo. Regarding elimination, all ICM are excreted unchanged via the kidneys.

3. Clinical Rational Use of ICM

3.1 Indications and Contraindications of ICM

Currently, all ICM are approved for intravascular administration in CT angiographic enhancement, with certain agents, such as iohexol, iopamidol, and iopromide also suitable for extravascular CT angiography. Prior to ICM administration, it is essential to thoroughly review the indications and contraindications detailed in each ICM's package insert (Table 2). Appropriate ICM selection should be based on the examination type, target site, and patient weight, as per package insert guidance. Regarding contraindications, patients with known allergies to ICM or its excipients should not receive these agents. Patients with severe thyroid diseases should consider the use of ICM after a comprehensive evaluation. Additionally, the underlying medical conditions at the imaging site of the patient may potentially influence the utilization of ICM.

Table 2 The indications and contraindications of different ICMs

Generic Name	Indications	Contraindications
Iohexol	(1) Intravenous angiography: urinary tract, lower extremity veins, digital subtraction angiography (DSA), CT enhancement; (2) Arterial angiography: aorta, selective cerebral arteries, lower extremity arteries, etc.; cardiovascular, left ventricle and aortic root, selective coronary arteries, DSA; (3) Myelography; (4) Body cavity angiography: joint cavity, uterine tubal, salivary duct, gastrointestinal tract (oral), CT enhancement	(1) Prohibited in patients with severe thyrotoxicosis; (2) Prohibited in patients with a history of severe reactions to iohexol injection

Iopamidol	(1) Nervous system angiography: spinal nerve roots, cerebral cisterns and ventricles; (2) Vascular angiography: cerebral vessels, coronary arteries, thoracic aorta, abdominal aorta, cardiovascular, selective visceral arteries, peripheral arteries and veins; (3) DSA: cerebral arteries, peripheral arteries, abdominal arteries; (4) Intravenous urography; (5) Body cavity angiography: joints, fistulas	(1) Should not be used in patients known to be allergic to iopamidol or any of its excipients; (2) When pregnancy is suspected or confirmed, and during acute inflammation of female genital organs, radiological examination of female genital organs is prohibited; (3) Contraindicated for intrathecal injection of corticosteroids and iopamidol simultaneously; (4) To avoid drug overdose, when technical errors occur, myelography should not be repeated immediately
Iomeprol	(1) Intravenous urography (adults and children); (2) Peripheral venography, CT (brain and trunk), venous and arterial DSA, cavernous body angiography, conventional angiography, cardiovascular angiography (adults and children); (3) Myelography; (4) Body cavity angiography: endoscopic retrograde cannulation of the pancreatic duct (ERCP), etc.	(1) Contraindicated in patients known to be allergic to iomeprol or any of its excipients; (2) Radiological examination of the female genital organs is prohibited during pregnancy or acute inflammation; (3) Contraindicated for intrathecal injection of corticosteroids and iomeprol simultaneously; (4) To avoid drug overdose, when technical errors occur, myelography should not be repeated immediately
Ioversol	(1) Cardiovascular system angiography, head and body CT enhancement scans, intravenous urography for adults and children; (2) Peripheral and visceral arterial angiography for adults	(1) Patients with known or suspected hypersensitivity to ioversol should not be used; (2) Patients with impaired liver or renal function should not be used
Iopromide	(1) CT enhancement; (2) DSA; (3) Intravenous urography; (4) Arterial angiography; (5) Venous angiography; (6) Body cavity angiography, but not for subarachnoid, ventricular or cerebral cisternal angiography	(1) Contraindicated in patients with allergy to ICM and obvious hyperthyroidism; (2) Uterine tubal angiography is contraindicated in pregnancy and acute pelvic inflammatory disease; (3) ERCP is contraindicated in acute pancreatitis; (4) Contraindicated for intrathecal injection
Iobitridol	(1) Intravenous urography; (2) Arterial angiography; (3) Head and whole-body CT; (4) DSA	(1) Contraindicated in patients with allergy to iobitridol or any excipients, with a history of severe immediate-type allergic reactions or delayed-type skin reactions; (2) Contraindicated in patients with obvious thyrotoxicosis; (3) Uterine tubal angiography is contraindicated during pregnancy
Iodixanol	(1) Cardiovascular and cerebrovascular angiography (routine angiography and arterial DSA) for adults; (2) Peripheral arterial angiography (routine angiography and arterial DSA), abdominal angiography (routine angiography and arterial DSA); (3) Intravenous urography, CT enhancement examination	(1) Contraindicated in patients with definite manifestations of thyrotoxicosis; (2) Contraindicated in patients with hypersensitivity to active substances or excipients in this product; (3) Contraindicated for intrathecal injection

3.2 Precautions

3.2.1 Preparation-Related Precautions

Rubber bottle stoppers should be punctured only once to prevent many particles from the rubber stopper falling into the solution. It is advisable to use a long cannula needle.

for puncturing the rubber bottle stopper and withdrawing the ICM. The needle of the syringe should not exceed 18G (preferably with a specialized cannula needle with a small hole on the side). It is recommended to draw ICM directly from the original container, and any opened sterile ICM should be used within four hours [2, 3].

3.2.2 Maximum Allowable Daily Dose for Patients

The maximum allowable daily dose of ICM can be calculated using the Cigarroa formula [4]: $5 \text{ mL} \times \text{body weight (kg)} / \text{serum creatinine (mg/dL)}$, with an upper limit of 300 mL per day. Large-volume ICM (500 mL) is now widely recommended, as studies suggest that it reduces contrast medium waste, alleviates patient economic burden, and decreases healthcare costs compared to smaller-volume ICM (50 or 100 mL) [5].

3.2.3 Fasting Requirements

Current evidence does not support fasting before intravascular ICM administration, as fasting does not reduce the risk of nausea, vomiting, or aspiration pneumonia. Furthermore, fasting may limit the timing of examinations, increase hypoglycemia risk in diabetic patients, and lead to other discomforts. For extravascular administration, fasting requirements vary by route; for instance, fasting is recommended before gastrointestinal administration but is not necessary before cavity or spinal cord administration [2, 3].

3.3 Special Populations

ICM use in specific populations, including elderly individuals, children, and pregnant or lactating women, requires clinical consideration. Additionally, patients with certain conditions, such as hyperthyroidism, multiple myeloma, and paraproteinemia, should exercise caution when using ICM [2]. Table 3 outlining precautions for ICM use in special populations is provided.

Table 3 Precautions for the Use of ICM in Special Populations

Special Populations	Precautions
Elderly	For individuals aged 65 and above, relevant tests for cardiac and renal function should be completed before the examination to fully assess the risk of PC-AKI (Contrast-induced Acute Kidney Injury). Adequate hydration therapy should be provided under the condition of good cardiac function. While ensuring image quality, the dosage of ICM (Iodinated Contrast Media) should be minimized, and its use should be closely monitored.

Children	It is recommended to use the revised Bedside Schwartz formula [estimated glomerular filtration rate (eGFR) = $36.5 \times \text{height (cm)} / \text{serum creatinine } (\mu\text{mol/L})$] to assess renal function. The preventive regimen is the same as for adults. Infants (<1 year old), especially newborns, are prone to electrolyte imbalances and hemodynamic changes. Therefore, attention should be paid to the dosage of ICM, technical operations during the examination, and the patient's condition. For patients who cannot cooperate with the examination, sedatives can be administered as prescribed. Psychological care should be strengthened to eliminate their fear.
Pregnant Women	Pregnant women should use ICM cautiously. If ICM is necessary for disease diagnosis, patients should be advised to check their thyroid function after the birth of the fetus.
Lactating Women	The proportion of ICM that can enter breast milk is less than 1%, and therapeutic doses of ICM are unlikely to cause harm to the breastfed infant. However, for safety reasons, it is recommended to stop breastfeeding for at least 24 hours after using ICM.
Hyperthyroidism	These patients can choose ICM without contraindications for hyperthyroidism to avoid off-label drug use. Patients with hyperthyroidism may experience thyroid toxicity after using ICM, but this complication is rare. Therefore, it is not recommended to restrict the use of ICM based solely on the patient's history of hyperthyroidism. There are two special situations that may affect the use of ICM: (1) In patients with acute thyroid storm, exposure to ICM may exacerbate thyroid toxicity, so such patients should avoid using ICM. (2) In patients considering radioactive iodine therapy or undergoing thyroid radioactive iodine imaging, administering ICM may interfere with treatment. If ICM is used in these patients, a washout period is recommended to minimize this interaction. The washout period for patients with hyperthyroidism is up to 3 to 4 weeks.
Multiple Myeloma and Paraproteinemia	ICM may increase the risk of renal injury in these patients. Therefore, adequate hydration is recommended before the examination.
Sickle Cell Trait/Disease	ICM can trigger episodes in homozygous sickle cell disease patients. Therefore, adequate hydration is recommended before the examination.
Myasthenia Gravis	ICM may exacerbate the symptoms of myasthenia gravis patients, and close monitoring is required.
Pheochromocytoma	Intravascular administration of ICM in these patients may cause severe hypertensive crisis, and close monitoring is required.

3.4 Drug Interactions

ICM is predominantly excreted unchanged via the kidneys. Concurrent use of drugs that are either renally excreted or possess nephrotoxic properties may elevate the risk of PC-AKI. Although metformin itself does not directly increase PC-AKI risk, it can lead to lactic acidosis when used with ICM. Current guidelines and package inserts offer differing recommendations on metformin management around ICM use, including whether to discontinue it, how to stop it, and when to resume it post-discontinuation. It is recommended to follow the requirements in the respective package insert when deciding on the discontinuation of metformin ^[4]. Furthermore, medications such as beta-blockers, interleukin-2, and sedative-hypnotics may elevate the risk of ICM-induced adverse reactions, and patients should be closely monitored when these drugs

are used concomitantly. Table 4 summarizing ICM drug interactions and corresponding recommendations is provided.

Table 4 Drug Interactions and/or Recommendations for ICM

Concurrently Used Drugs	Possible Drug Interactions and/or Recommendations
Metformin	<p>Guidelines from the Canadian Association of Radiologists recommend^[6]: (1) For patients with an eGFR ≥ 30 mL/(min\cdot1.73 m²), metformin does not need to be discontinued before or after ICM injection, and renal function does not need to be reviewed afterwards. (2) For patients with an eGFR <30 mL/ (min\cdot1.73 m²), acute kidney injury (AKI), or those undergoing aortic catheter examinations that may lead to renal artery embolism, metformin should be temporarily discontinued during or before the procedure and held for at least 48 hours post-procedure. Metformin may be resumed when renal function is unchanged compared to before the imaging examination.</p> <p>According to the drug insert:(1) The metformin inserts approved by the National Medical Products Administration mentions that intravascular administration of ICM can cause AKI, with a risk of metformin accumulation and lactic acidosis. Diabetic patients scheduled for ICM should discontinue metformin before or during the examination and may resume it only after at least 48 hours and when renal function has stabilized upon re-examination. (2) The Iodixanol insert mentions that for patients with normal renal function, metformin must be discontinued before ICM injection and cannot be resumed within 48 hours or until renal function indicators return to normal. For patients with abnormal renal function, metformin must be discontinued, and the ICM examination should be postponed until 48 hours after discontinuation. Metformin can only be resumed when renal function is stable. For emergency patients with abnormal or unknown renal function, doctors must assess the benefits and risks of using ICM and take preventive measures, such as discontinuing metformin, adequately hydrating the patient, monitoring renal function, and closely observing symptoms of lactic acidosis.</p>
β -blockers	<p>β-blockers can lower the threshold for adverse reactions to ICM, enhance the intensity of ICM responses, and reduce the responsiveness of adrenaline in treating anaphylactoid reactions.</p>
Interleukin-2	<p>Patients using this drug have a higher frequency of ICM anaphylactoid reactions, mainly manifesting as delayed reactions such as cold-like symptoms and skin reactions.</p>
Sedatives, hypnotics, and antidepressants	<p>Sedatives, hypnotics, and antidepressants can lower the seizure threshold, thereby increasing the risk of ICM-related adverse reactions. It is recommended to discontinue these drugs before ICM administration and only resume them 24 hours after the examination.</p>
Diuretics	<p>Discontinuation of diuretics before ICM is not recommended^[6]. Although the use of diuretics has been considered a risk factor for PC-AKI, this causality is not yet clear. However, for certain patients, discontinuing diuretics may lead to fluid overload, which not only increases the risk of pulmonary edema and others but may also impair renal function^[7].</p>
ACE inhibitors or ARBs	<p>It is not advisable to discontinue angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) before administering ICM. According to a meta-analysis, the cessation of ACEI/ARB prior to coronary angiography does not decrease the risk of AKI^[8].</p>

Cisplatin and bisphosphonates	Considering the nephrotoxicity of cisplatin and bisphosphonates, it is recommended to check patients' renal function before using ICM. If necessary, cisplatin and ICM should be used with an interval of 5 to 7 days, and zoledronic acid and ICM should be used with an interval of 14 days ^[9] .
Other nephrotoxic drugs (e.g., renal function. If the potential risk of discontinuing a certain nephrotoxic drug outweighs the risk of PC-aminoglycosides, cyclosporine, etc.)	For patients with an eGFR <30 mL/ (min·1.73 m ²), it is recommended to discontinue nephrotoxic drugs 24 to 48 hours before ICM examination and within 48 hours after the examination, and to monitor patients' renal function. If the potential risk of discontinuing a certain nephrotoxic drug outweighs the risk of PC-aminoglycosides, AKI, individualization should be considered based on the patient's condition, where necessary drugs may be retained and hydration conditions may be relaxed ^[6] .

4. Major Adverse Reactions of ICM

Acute adverse reactions to ICM can be categorized as allergic-like reactions, which are non-dose-dependent, and physiologic reactions, which are dose-dependent, based on their underlying pathogenesis. Allergic-like reactions exhibit no correlation with the dosage, mode of injection, or speed of ICM administration. Clinically, allergic-like reactions to ICM manifest similarly to true allergic reactions seen with other drugs and allergens, though an antigen-antibody response cannot be always identified in patients with allergic-like reactions. In contrast, physiologic reactions to ICM are frequently dose- and concentration-dependent and are influenced by the injection mode, injection speed, and the physicochemical properties of ICM. These reactions often affect specific organs or systems, with the kidneys, cardiovascular system, and nervous system being the most affected.

Adverse reactions to ICM can be further classified by severity into mild, moderate, or severe, and by the timing of their onset following ICM exposure: acute adverse reactions occurring within 1-hour post-injection, delayed adverse reactions manifesting between 1 hour and 1-week post-injection, and late adverse reactions emerging beyond 1-week post-injection. Acute adverse reactions encompass a full range of severities, whereas delayed and late adverse reactions are generally mild to moderate in intensity, though they may carry potential risks for the development of PC-AKI and hyperthyroidism^[2, 3].

PC-AKI remains a crucial concern for clinicians and researchers in the application of ICM. In addition to renal adverse reactions, ICM extravasation during administration is also a common adverse reaction. Acute adverse reactions to ICM are more prevalent and may lead to more serious clinical consequences. Therefore, this section will focus on the management strategies for ICM extravasation, acute adverse reactions, and PC-AKI to promote patient safety following ICM administration.

4.1 ICM Extravasation

Extravasation refers to a phenomenon in which intravenous ICM leaks into surrounding soft tissues (typically the skin and subcutaneous tissues), potentially causing limb injury and pain to patients. While most extravasations are mild, severe injuries after extravasation may result in local tissue swelling, even skin ulceration, tissue necrosis, or compartment syndrome. Most patients with ICM extravasation recover without obvious sequelae^[10]. Currently, there is no known effective treatment for ICM

extravasation. Elevation of the affected extremity above the level of the heart to decrease capillary hydrostatic pressure and thereby promote resorption of extravasated fluid is recommended^[11]. Patients with ICM extravasation should be observed for 2-4 hours and can leave only after medical staff confirm that no new complications or severe injuries have developed. Management recommendations based on the severity of extravasation are as follows.

(1) Mild Extravasation

Patients with mild extravasation generally experience minor injuries that require minimal intervention. If significant pain occurs, elevate the affected limb, apply a cold compress, and monitor the patient’s condition. If symptoms persist, consult a clinician for potential medication.

(2) Moderate to Severe Extravasation

In cases of moderate to severe extravasation, X-ray computed tomography can assist in evaluating the extent and severity of the injury. For suspected severe complications, such as neurovascular injury, compartment syndrome, or tissue necrosis, immediate medical attention is required. Management includes elevating the affected limb, applying local cold compresses, and administering topical agents (e.g., 50% magnesium sulfate, hirudoid cream, or 0.05% dexamethasone). Continuous monitoring of the extravasation site is essential, with symptomatic treatment as needed. Consult a clinician promptly if additional medication or intervention is necessary^[12].

4.2 Acute Adverse Reactions to ICM

4.2.1 Preventive Strategies for Acute Adverse Reactions to ICM

Routine allergy testing for ICM is not generally recommended unless specifically indicated by the product package insert. This recommendation stems from the potential for anaphylactoid reactions in patients who test negative, as well as the possibility that patients with positive test results may not necessarily experience reactions. Moreover, the allergy test itself carries a risk of inducing severe adverse reactions^[2, 13].

For patients at high-risk, particularly those with a prior allergic-like reaction to the same class of ICM-premedication may be considered if feasible, with specific recommended premedication regimens outlined in Table 5. Evidence suggests that premedication is most beneficial for patients with a history of mild allergic-like reactions. However, it has not been demonstrated that premedication alleviates symptom severity or reduces mortality in patients with moderate or severe allergic-like reactions^[14].

Table 5 Recommended Premedication Regimens for Acute Adverse Reactions to ICM in High-Risk Populations

Category	Specific Content
Elective Premedication Regimen (Oral premedication)	(1) Prednisone-based: 50 mg prednisone by mouth at 13 hours, 7 hours, and 1 hour before ICM administration, plus 50 mg diphenhydramine intravenously, intramuscularly, or by mouth 1 hour before ICM administration. (2) Methylprednisolone-based: 32 mg methylprednisolone by mouth 12 hours and 2 hours before ICM administration. optionally combined with an anti-histamine (e.g., 50 mg diphenhydramine). If a patient is allergic to diphenhydramine, an

	alternate anti-histamine without cross-reactivity may be considered, or the anti-histamine portion of the regimen may be dropped.
Accelerated Premedication Regimen (Intravenous Premedication)	(1) Methylprednisolone sodium succinate 40 mg IV or hydrocortisone sodium succinate 200 mg IV immediately, and then every 4 hours until ICM administration, plus diphenhydramine 50 mg IV 1 hour before ICM administration. This regimen usually is 4-5 hours in duration. (2) Dexamethasone sodium 7.5 mg IV immediately, and then every 4 hours until ICM administration, plus diphenhydramine 50 mg IV 1 hour before ICM administration. This regimen may be useful in patients with an allergy to methylprednisolone and is also usually 4-5 hours in duration. Dexamethasone exhibits a slow onset and a long time to reach peak effect (12 to 24 hours), requiring metabolism within the body to exert its therapeutic effect, and is not the preferred drug for treating allergic-like reactions.

4.2.2 Management of Acute Adverse Reactions to ICM

Most adverse reactions to non-ionic ICMs are mild and non-life-threatening, often necessitating only observational monitoring, reassurance, and/or symptomatic treatment. In cases of moderate adverse reactions, active symptomatic management coupled with close monitoring of vital signs is recommended until the reaction is fully resolved. Severe, potentially life-threatening reactions to ICMs are rare and largely unpredictable, with nearly all these severe reactions occurring within 20 minutes post-administration [2]. For these severe cases, rapid clinical identification and emergency intervention are essential. According to the “ACR Manual on Contrast Media” [2], specific management strategies for ICM-related acute adverse reactions affecting various organ systems are outlined in Table 6.

Table 6 Common Acute Adverse Reactions to ICM Across Different Systems and Their Treatment

Categories of Acute Adverse Reactions	Subtype	Treatment Strategy	Dosing
Cardiovascular abnormality.	Simple hypotension	Elevate legs at least 60 degrees; O ₂ by mask (6-10 L/min); preserve IV access; IV fluids; monitor vitals; pulse oximeter. If no response, IV fluids and Epinephrine (IM) as doctor's orders.	IV fluids with 0.9% normal saline or Lactated Ringer's; IM 0.5 mL of 1 mg/mL epinephrine, repeatable.
	Hypotension with bradycardia (pulse <60 bpm)	In addition to above measures for simple, if heart rate drops below 50 bpm, Atropine (IV)	administer into a running IV infusion of fluids; 0.6–1.0 mg Atropine, can repeat up to 3 mg total
	Hypotension with tachycardia (pulse >100 bpm)	In addition to above measures for simple hypotension, if hypotension persists, Epinephrine (IV or IM)	IV fluids with 0.9% normal saline or Lactated Ringer's; IM 0.3 mL of 1.0 mg/mL or IV 1 mL of 0.1 mg/mL Epinephrine; can repeat every few minutes as needed up to 1 mg total

	Hypertensive Crisis (diastolic BP > 120 mmHg; systolic > 200 mmHg; symptoms of end organ compromise) (1 mmHg = 0.133 kPa)	(1) Preserve IV access; Monitor vitals; Pulse oximeter; O ₂ by mask (6-10 L/min). (2) Labetalol (IV), or if labetalol not available, Nitroglycerin tablet (SL) and Furosemide (IV). (3) Call emergency response team.	(1) Labetalol: 20 mg IV; administer slowly, over 2 min; can double the dose every 10 min (e.g., 40 mg 10 min later, then 80 mg 10 min after that). (2) Nitroglycerin Tablet: 0.4 mg, can repeat every 5-10 min. (3) Furosemide: 20-40 mg IV; administer slowly over 2 min
Skin Abnormalities	Urticaria	Mild (fewer than 20 wheals, intermittent itching): observe closely, use anti-histamines if symptoms are prominent. Moderate (20-50 wheals, persistent itching): monitor vital; preserve IV access; consider anti-histamines. Severe (more than 50 wheals or large areas of wheals, persistent severe itching): monitor vital; preserve IV access; anti-histamines	Diphenhydramine: 25-50 mg PO or Fexofenadine: 180mg PO Diphenhydramine: 25-50 mg PO or Fexofenadine: 180mg PO; or if ineffective, Diphenhydramine: 25-50 mg IM or IV (administer IV dose slowly over 1-2 min) Diphenhydramine: 25-50 mg IM or IV (administer IV dose slowly over 1-2 min)
	Pruritus, Skin Rash, Facial Flushing	Observe closely, monitor vital, ensure the patient's clinical stability; if necessary, undress the patient to examine for rashes or erythema, preserve IV access, use medications as doctor's orders.	Diphenhydramine: 25-50 mg PO or Fexofenadine: 180mg PO
	Warmth or Tingling at Injection Site	Stop ICM injection; check the puncture site for extravasation; re-establish IV access, using ultrasound guidance if necessary; apply medication topically as doctor's orders.	Topical administration of mucopolysaccharide polysulfate cream.
Gastrointestinal Abnormalities	Nausea, Vomiting	transient reactions, observe closely; if persistent or progressive, use anti-emetics as doctor's orders.	None
	Abdominal Pain	Mild or transient, provide oxygen, rest in a supine position; if moderate, severe, or persistent, use medications as doctor's orders.	Epinephrine 0.5 mg IM or Dexamethasone 5 mg IV or administration of antispasmodic and analgesic medications.
Respiratory Abnormalities	Bronchospasm	All forms: Preserve IV access, monitor vital, pulse oximeter, O ₂ by mask (6-10 L/min). Mild: (1) β 2-agonist inhaler (salbutamol inhaler); (2) consider calling emergency response team based upon the completeness of the response to the β 2-agonist inhaler Moderate: (1) β 2-agonist inhaler (salbutamol inhaler); (2) consider adding epinephrine (IM or IV); (3) consider calling emergency response team based on efficacy.	Selected based on severity. β 2-agonist inhaler (salbutamol inhaler): 2 puffs (90 μ g/puff), can repeat up to 3 times. (1) β 2-agonist inhaler (salbutamol inhaler): 2 puffs, (90 μ g/puff), can repeat up to 3 times. (2) IM 0.3 mL of 1.0 mg/mL or IV 1 mL of 0.1 mg/mL Epinephrine; can repeat every few minutes as needed up to 1 mg total

	Severe: (1) Epinephrine (IV or IM); and (2) β 2-agonist inhaler (salbutamol inhaler); (3) Call emergency response team.	(1) IM 0.3 mL of 1.0 mg/mL or IV 1 mL of 0.1 mg/mL Epinephrine; can repeat every few minutes as needed up to 1 mg total (2) β 2-agonist inhaler (salbutamol inhaler): 2 puffs, (90 μ g/puff); can repeat up to 3 times.
Laryngeal Edema	(1) Preserve IV access, monitor vital; pulse oximeter; O ₂ by mask (6-10 L/min); (2) Epinephrine (IM or IV); (3) Consider calling emergency response team based on efficacy.	IM 0.3 mL of 1.0 mg/mL or IV 1 mL of 0.1 mg/mL Epinephrine; can repeat every few minutes as needed up to 1 mg total
pulmonary edema	(1) Preserve IV access, monitor vital, pulse oximeter, O ₂ by mask (6-10 L/min) and elevate head of bed, if possible; (2) Furosemide (IV); (3) Call emergency response team.	Furosemide: 20-40 mg IV; administer slowly over 2 min

BP: blood pressure; IM: intramuscular; IV: intravenous; PO: per os

4.3 PC-AKI

4.3.1 Concept of PC-AKI

With the in-depth research on the relationship between ICM and AKI, the term "contrast-induced nephropathy (CIN)" is less commonly used. To better clarify this relationship, the American College of Radiology and the European Society of Urogenital Radiology have introduced terms such as PC-AKI and contrast-induced acute kidney injury (CI-AKI) [2]. PC-AKI refers to AKI occurring within 48 hours after the administration of contrast medium. When a causal link between ICM and AKI is established, the term CI-AKI is recommended. This consensus uses the term PC-AKI for description.

PC-AKI can be diagnosed if any of the following criteria are met within 48 hours after intravascular ICM administration:

- (1) An absolute increase in serum creatinine ≥ 0.3 mg/dL (≥ 26.52 μ mol/L);
- (2) A percentage increase in serum creatinine $\geq 50\%$ (≥ 1.5 times baseline);
- (3) A reduction in urine output to ≤ 0.5 mL/(kg·h) for a minimum of 6 hours [2].

Since a subset of patients may experience PC-AKI beyond 48 hours, with cases reported up to one-week post-administration, it is advisable to reassess renal function 1-2 weeks after ICM administration.

Previously, CI-AKI was considered a common complication, ranking as the third most common cause of AKI, following only hypovolemia and major surgery [6]. However, current evidence suggests that CI-AKI incidence is low [15-17]. Patients at higher risk include those with chronic kidney disease (CKD) with an eGFR ≤ 30 mL/(min·1.73m²), AKI, and/or those receiving high doses of intra-arterial contrast medium [6].

4.3.2 Mechanism and Major Risk Factors for PC-AKI

The mechanism of PC-AKI remains unclear, possibly involving direct damage to renal tubular epithelial cells by ICM and ischemic injury caused by reduced perfusion [9]. The primary risk factors for the occurrence of PC-AKI involve factors related to the patient as well as the characteristics of the ICM. Among patient-related factors, renal

impairment is an independent risk factor for PC-AKI [6, 9]. Clinicians should carefully assess ICM suitability based on the patient's degree of renal impairment. Table 7 provides details on patient-related risk factors contributing to PC-AKI and recommended management. When deciding to use ICM for examinations, it is essential to consider the type of ICM, dosage, administration method, and the interval between repeat administrations to reduce the risk of PC-AKI. For ICM-related risk factors leading to PC-AKI and recommended management, please refer to Table 8.

Table 7 Patient-Related Risk Factors for PC-AKI and Recommended Management

Patient-Related Risk Factors	Recommended Handling Opinions
CKD	(1) Patients with $eGFR > 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ can undergo the examination directly. (2) For patients with $eGFR \leq 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ or suspected AKI: if the clinician clearly states that the diagnosis is necessary, or if the situation is urgent (e.g., stroke, pulmonary embolism, other high-risk conditions), or if there is no alternative to CT enhancement scanning, the radiologist can decide whether to use ICM; in cases of uncertainty, the radiologist should contact the clinician to discuss the importance of the examination and assess the patient's benefits and risks. (3) Dialysis patients: ICM can be used in patients undergoing peritoneal dialysis or hemodialysis, without considering residual urine volume or altering the dialysis protocol.
AKI	While AKI patients might exhibit a higher susceptibility to PC-AKI than non-AKI patients, the current lack of high-quality evidence substantiates this claim. Clinicians are recommended to carefully consider the risks and benefits associated with the development of PC-AKI and the possibility of delayed or missed diagnosis resulting from the avoidance of ICM utilization.

4.3.3 Prevention of PC-AKI

Hydration therapy is widely regarded as one of the most effective, convenient, and economical methods for PC-AKI prevention. By increasing renal blood flow and perfusion, hydration helps reduce the renal toxicity of iodinated contrast media. Research indicates that for patients with $eGFR > 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$, intravenous hydration does not confer significant benefits compared to no hydration. However, in high-risk patients with an $eGFR \leq 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$, hydration may be considered based on individual clinical assessments [17].

Intravenous hydration is commonly used in clinical practice, although low-quality evidence suggests that oral hydration may offer similar efficacy. A frequently used hydration protocol involves the intravenous infusion of 0.9% sodium chloride solution over 1 to 4 hours before the examination, followed by continuous infusion for 3 to 12 hours post-examination. The typical fluid volume administered is a fixed infusion of 500 mL before and after ICM use, or an adjusted infusion protocol based on patient weight [$1 \text{ to } 3 \text{ mL}/(\text{kg} \cdot \text{h})$] [18]. A prolonged hydration protocol (approximately 12 hours) is more effective in reducing the risk of PC-AKI compared to a short-term hydration regimen. However, implementing a prolonged hydration protocol is challenging for outpatient patients [19].

Table 8 ICM-Related Risk Factors for PC-AKI and Recommended Management

ICM-Related Risk Factors	Recommended Handling Opinions
Type of ICM	Ionic hyperosmolar ICM increases the risk of PC-AKI. It is recommended to use iso-osmolality contrast media (IOCM) or low osmolality contrast media (LOCM).
ICM Dosage	Reducing the dosage of ICM is one of the measures to decrease the risk of PC-AKI. It is recommended to moderately decrease the ICM dosage while maintaining image quality. However, care should be taken to avoid significantly reducing the ICM dosage, which may result in degraded image quality that fails to meet diagnostic requirements.
ICM Administration Route	(1) Intravenous Administration: ICM reaches the renal artery after being diluted by the right heart, pulmonary circulation, or capillary bed. (2) Arterial Administration (Secondary Renal Exposure): ICM reaches the right heart, pulmonary artery, or arteries such as the carotid, coronary, lower abdominal aorta, or femoral artery via a catheter. In these cases, ICM is diluted to some extent before reaching the renal artery, and the risk of PC-AKI is comparable to intravenous administration. (3) Arterial Administration (Primary Renal Exposure): ICM is directly injected into the left heart, thoracic aorta, abdominal aorta above the kidney level, or renal artery via a catheter. ICM reaches the renal artery in a relatively undiluted form, resulting in a higher concentration of ICM exposure to the kidneys and a higher risk of PC-AKI compared to intravenous administration.
Interval Between Repeated ICM Administrations	(1) For patients with $eGFR > 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ receiving intravenous administration and without AKI, current evidence does not support restricting the repeated use of ICM. (2) For patients with $eGFR \leq 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$, arterial administration, or AKI, the risk of PC-AKI is high. It is recommended that these patients avoid repeated ICM administration within 48 hours. (3) In life-threatening conditions where clinical judgment necessitates repeated administration of ICM, physicians should conduct a comprehensive evaluation based on the individual patient's condition and closely monitor them.

5. Pharmaceutical Care Content and Process for ICM

Comprehensive pharmaceutical care for patients undergoing imaging with ICM includes pharmaceutical monitoring before, during, and after the examination. Please refer to Figure 1 for the pharmaceutical service workflow and Figure 2 for medication monitoring records.

5.1 Pre-Examination

(1) Review the patient's allergy, medical, and medication history to identify any contraindications for ICM use. For patients with a history of allergic reactions to similar ICM, consider premedication.

(2) Assess the patient's renal function to determine eligibility for ICM administration.

(3) Conduct a thorough review of the patient's concurrent medications, status as a member of a special population, and hydration protocols.

(4) Verify the specific type and dose of ICM intended for the patient.

(5) Provide the patient with verbal education on the purpose, use, and potential adverse effects of ICM.

5.2 During Examination

During and after the injection of ICM, closely monitor the patient for the occurrence of

any acute adverse reactions. If any reactions occur, classify them as mild, moderate, or severe based on whether the event is an allergic-like reaction or a physiological reaction, and take appropriate management measures.

5.3 post-examination

(1) To facilitate the early detection and management of acute adverse reactions to ICM, patients are advised to remain in the medical facility for observation for at least 30 minutes post-injection. Response measures for managing acute adverse reactions are outlined in Table 6.

(2) Monitor the patient's renal function to evaluate the potential occurrence of PC-AKI.

(3) Follow up with the patient to assess for any delayed or late-onset adverse reactions.

6. Conclusion

Iodinated contrast media (ICM) are widely utilized in various healthcare facilities. Improper utilization may lead to adverse drug reactions and escalate healthcare expenses. To promote the rational use of ICM, the consensus working group conducted multiple rounds of expert discussions and literature analysis to formulate recommendations on the clinically sound utilization of ICM. Furthermore, the group has developed a comprehensive pharmaceutical care workflow for ICM and a medication monitoring record based on clinical practices to guide healthcare practices. The publication of this consensus provides a scientific foundation for clinicians and nursing staff to use these agents safely and effectively. It also serves as a reference for pharmacists in delivering tailored pharmaceutical care to patients receiving ICM.

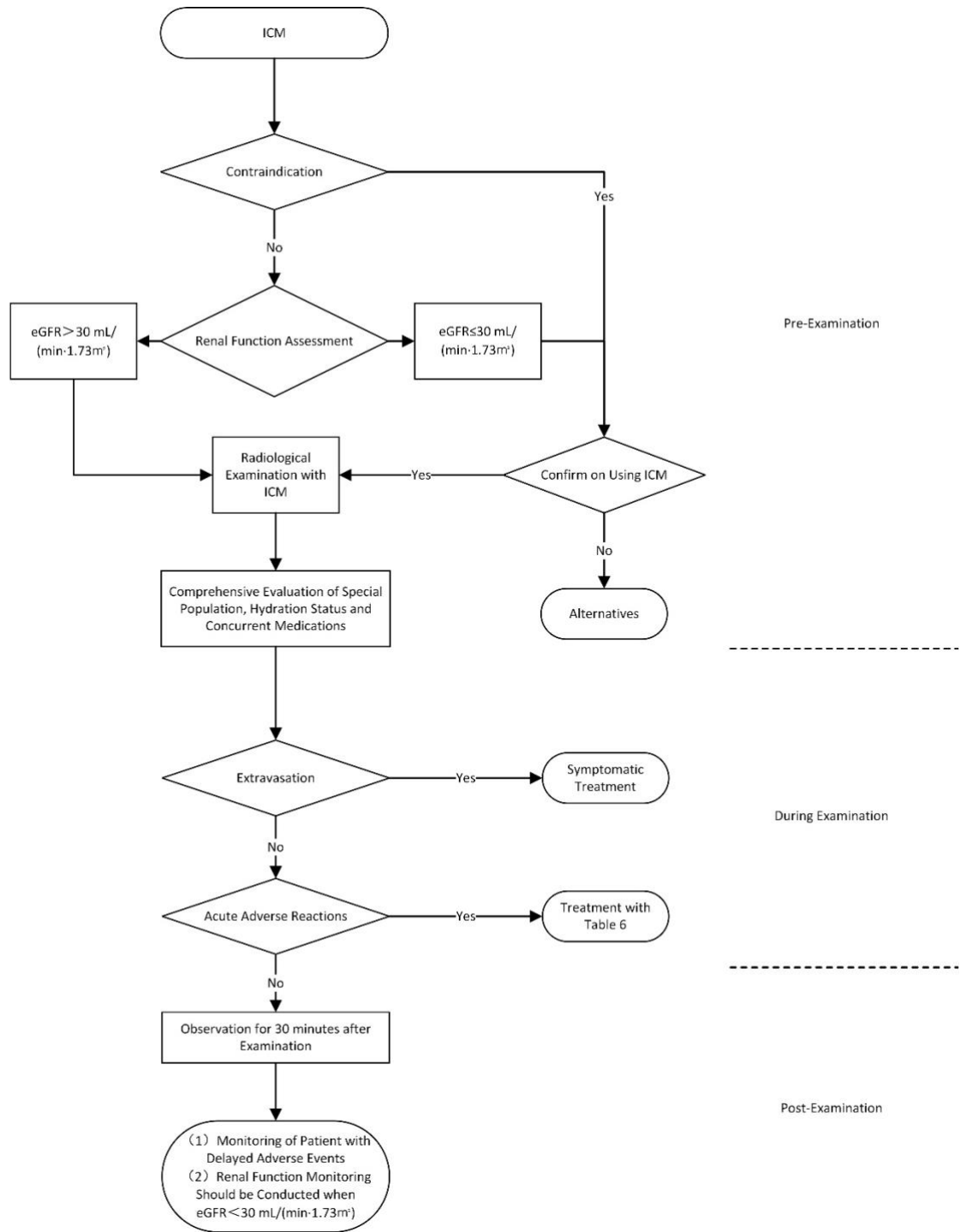


Figure 1 The pharmaceutical service workflow of ICM

Iodinated Contrast Media Medication Monitoring Record Form						
Name:		ID:	Gender:	Age (years):	Height (cm):	Weight (kg):
Diagnosis:			Contact Information:		Record Date:	
Pre-Examination						
Examination Site:				ICM Name:		
Route of Administration: <input type="checkbox"/> Intravenous <input type="checkbox"/> Arterial <input type="checkbox"/> Gastrointestinal <input type="checkbox"/> Intracavitary <input type="checkbox"/> Other						
Any contraindications for the use of ICM (Table 2): <input type="checkbox"/> No <input type="checkbox"/> Yes Details:			Previous Adverse Reactions to ICM: <input type="checkbox"/> No <input type="checkbox"/> Yes Details:			
			Premedication Regimens: <input type="checkbox"/> No <input type="checkbox"/> Yes Specific Regimen:			
Patient Type		Outpatient: Previous Renal Disease/Transplant/Visits to Nephrology/Urology <input type="checkbox"/> No (Use appropriate ICM based on patient condition) <input type="checkbox"/> Yes (Renal Function Assessment)				
		Emergency or Inpatient: Acute/Critical Illness <input type="checkbox"/> Not(Renal Function Assessment) <input type="checkbox"/> Yes (Use appropriate ICM based on patient condition)				
Renal Function Assessment		Serum Creatinine ($\mu\text{mol/L}$): eGFR [$\text{mL}/(\text{min}\cdot 1.73 \text{ m}^2)$]: <input type="checkbox"/> eGFR > 30 $\text{mL}/(\text{min}\cdot 1.73 \text{ m}^2)$ or No AKI: Use appropriate ICM based on patient condition <input type="checkbox"/> eGFR < 30 $\text{mL}/(\text{min}\cdot 1.73 \text{ m}^2)$ or AKI: Physician to assess the need for hydration based on patient condition				
Concurrent Medications		<input type="checkbox"/> Metformin <input type="checkbox"/> Do Not Discontinue <input type="checkbox"/> Discontinue until at least 48 hours post-examination, resume after renal function normalization <input type="checkbox"/> Beta-blockers/Interleukin-2 Monitor for potential adverse reactions <input type="checkbox"/> Sedatives and Antidepressants Discontinue until 24 hours after examination <input type="checkbox"/> Cisplatin Recommend interval of 5-7 days between ICM use <input type="checkbox"/> Bisphosphonates Recommend interval of 14 days between ICM use <input type="checkbox"/> Other Nephrotoxic Drugs or patients with eGFR < 30 $\text{mL}/(\text{min}\cdot 1.73 \text{ m}^2)$, discontinue 24-48 hours pre- and 48 hours post-examination, monitor renal function. If potential risks of discontinuation outweigh risks of PC-AKI, retain essential medications and relax hydration criteria.				
Special Populations		<input type="checkbox"/> No <input type="checkbox"/> Elderly (≥ 65 years) Hydration therapy under adequate cardiac function <input type="checkbox"/> Pediatric Use revised Bedside Schwartz formula [$\text{eGFR} = 36.5 \times \text{Height (cm)} / \text{Serum Creatinine } (\mu\text{mol/L})$] for renal function assessment, same prevention regimen as adults <input type="checkbox"/> Pregnant Weigh risks and benefits, if necessary, recommend thyroid function test after birth <input type="checkbox"/> Lactating Recommend discontinuing breastfeeding for at least 24 hours after ICM use <input type="checkbox"/> Hyperthyroidism Prefer ICM without hyperthyroidism contraindications <input type="checkbox"/> Multiple Myeloma/Paraproteinemia/Sickle Cell Disease Recommend adequate hydration <input type="checkbox"/> Other				

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Reference:

1. Mao YJ, Li YM, Zeng XH. Nursing practice manual for intravenous injection of iodine contrast agent. Shanghai: Shanghai Scientific & Technical Publishers, 2020:12-16.
2. ACR Committee on Drugs and Contrast Media. ACR manual on contrast media. 2021 edition. Washington: American college of radiology, 2021:5-55.
3. Radiology European Society of Urogenital. ESUR guidelines on contrast agents. Vienna: ESUR Guidelines on Contrast Agents, 2018:6-30.
4. Chinese Society of Clinical Pharmacy, Hospital Pharmacy Committee of the Chinese Pharmaceutical Association, Nephrology Branch of the Chinese Medical Association. Expert consensus on prevention and treatment of iodine contrast media-induced acute kidney injury. *Chin J Nephrol*, 2022, 38(3): 265-288. <https://doi.org/10.3760/cma.j.cn441217-20210909-00041>
5. Wei Y, He Z, Zhang C et al. Cost-Minimization Analysis of Multidose and Single-Dose Packaging of Contrast Media for Contrast-Enhanced CT: Results From Real-World Data in China. *AJR American journal of roentgenology*. 2020;215(1):5-14. <https://doi.org/10.2214/ajr.19.22006>.
6. Macdonald DB, Hurrell CD, Costa AF et al. Canadian Association of Radiologists Guidance on Contrast-Associated Acute Kidney Injury. *Canadian journal of kidney health and disease*. 2022;9:20543581221097455. <https://doi.org/10.1177/20543581221097455>.
7. Perner A, Prowle J, Joannidis M et al. Fluid management in acute kidney injury. *Intensive care medicine*. 2017;43(6):807-15. <https://doi.org/10.1007/s00134-017-4817-x>.
8. Whiting P, Morden A, Tomlinson LA et al. What are the risks and benefits of temporarily discontinuing medications to prevent acute kidney injury? A systematic review and meta-analysis. *BMJ open*. 2017;7(4):e012674. <https://doi.org/10.1136/bmjopen-2016-012674>.
9. Orlacchio A, Guastoni C, Beretta GD et al. SIRM-SIN-AIOM: appropriateness criteria for evaluation and prevention of renal damage in the patient undergoing contrast medium examinations-consensus statements from Italian College of Radiology (SIRM), Italian College of Nephrology (SIN) and Italian Association of Medical Oncology (AIOM). *La Radiologia medica*. 2022;127(5):534-42. <https://doi.org/10.1007/s11547-022-01483-8>.
10. Hwang EJ, Shin CI, Choi YH et al. Frequency, outcome, and risk factors of contrast media extravasation in 142,651 intravenous contrast-enhanced CT scans. *European radiology*. 2018;28(12):5368-75. <https://doi.org/10.1007/s00330-018-5507-y>.
11. Plumb AA, Murphy G. The use of central venous catheters for intravenous contrast injection for CT examinations. *The British journal of radiology*. 2011;84(999):197-203. <https://doi.org/10.1259/bjr/26062221>.
12. Contrast Media Safety Committee of the Radiology Branch of the Chinese Medical Association. Guide to the use of iodine contrast agents: 2nd edition. *Natl Med J China*, 2014, 94(43): 3363-3369.

- <https://doi.org/10.3760/cma.j.issn.1005-1201.2013.10.001>
13. Yamaguchi K, Katayama H, Takashima T et al. Prediction of severe adverse reactions to ionic and nonionic contrast media in Japan: evaluation of pretesting. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology*.1991;178(2):363-7.<https://doi.org/10.1148/radiology.178.2.1987594>.
 14. Lasser EC, Berry CC, Mishkin MM et al. Pretreatment with corticosteroids to prevent adverse reactions to nonionic contrast media. *AJR American journal of roentgenology*. 1994;162(3):523-6. <https://doi.org/10.2214/ajr.162.3.8109489>.
 15. Davenport MS, Khalatbari S, Cohan RH et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. *Radiology*. 2013;268(3):719-28. <https://doi.org/10.1148/radiol.13122276>.
 16. McDonald RJ, McDonald JS, Bida JP et al. Intravenous Contrast Material-induced Nephropathy: Causal or Coincident Phenomenon? *Radiology*. 2016;278(1):306. <https://doi.org/10.1148/radiol.2015154044>.
 17. McDonald JS, McDonald RJ, Carter RE et al. Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline-estimated glomerular filtration rate. *Radiology*. 2014;271(1):65-73. <https://doi.org/10.1148/radiol.13130775>.
 18. Quality Control and Safety Management Committee of the Radiology Branch of the Chinese Medical Association. Expert consensus of iodinated contrast agent use in patients with renal diseases. *Chin J Radiol*, 2021, 55(6): 580-590. <https://doi.org/10.3760/cma.j.cn112149-20201111-01226>
 19. Hiremath S, Akbari A, Shabana W et al. Prevention of contrast-induced acute kidney injury: is simple oral hydration similar to intravenous? A systematic review of the evidence. *PLoS One*. 2013;8(3):e60009. <https://doi.org/10.1371/journal.pone.0060009>.