Intravascular Iodinated Contrast Media Administration in Adults: A Patient Safety Approach

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Date of Approval: 01/29/2015
Revisions approved 03/01/2017

Key words: contrast induced nephropathy, contrast extravasation, contrast allergy, contrast media documentation

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Introduction

The Indianapolis Coalition for Patient Safety, Inc. (ICPS) provides a forum for Indianapolis-area hospitals to share information about best practices and work together to solve patient safety issues. A free standing non-profit, ICPS is comprised of chief executive, medical, nursing, quality/safety and pharmacy leaders from the six major health-systems located in Indianapolis: Community Health Network, Eskenazi Health, Franciscan Health Indianapolis, Indiana University Health, Richard L. Roudebush VA Medical Center, and St. Vincent. While competitors in the market-place, hospital leaders have come together to promote patient safety. Coalition hospitals pool their expert resources to accelerate patient safety improvements through community-wide efforts.

The ICPS has historically achieved accelerated outcomes by sharing resources, performance targets, accountability, and learning. Using subject matter experts from Coalition hospitals, Coalition-wide multidisciplinary teams are formed. ICPS members undertake projects that focus on patient-centered strategies to improve safety.

In 2013, The ICPS Contrast Media Usage and Exposure Workgroup was formed to review, define, assess and implement best practices regarding the use of intravascular iodinated contrast media (CM) in diagnostic and interventional procedures with respect to the associated risk of contrast media-induced nephropathy (CIN) and other adverse events. The interdisciplinary workgroup consisted of radiologists, cardiologists, nephrologists, nurses, technologists, pharmacists and patient safety experts. The workgroup met regularly to review published best practices and current practices within each member health-system. The workgroup focused on opportunities to improve patient safety within represent health-systems and emphasized consensus-based recommendations aimed at reducing intra-institutional variability. Based on current literature, best practices, and professional experience, the workgroup created these recommendations for safe use of intravenous iodinated contrast media. These recommendations do not replace sound clinical judgment or other published guidelines.

Early in the process the group identified discordance among the best practice statements published by national organizations of the represented specialties (cardiology, nephrology, radiology.) The workgroup also identified discordance between the national best practice statements and subsequently published literature. As a result, where discordance existed, the workgroup ultimately constructed a summative consensus statement describing the current evidence-supported, best-practices based on a systematic review for CM usage and exposure, specific to the risks related to intravascular contrast media administration including: patient screening and risk-stratification, preventive measures, electronic health record enhancements aimed at improving patient safety, and other adverse events. We employed the search phrase described in Table 1 to identify the body of CIN literature which was the major focus of this effort.

Table 1. Basic search phrase for CIN in OVID	
1	acute kidney injury.mp. or exp Acute Kidney Injury/
2	acute renal failure.mp.
3	exp Kidney Diseases/
4	kidney diseas$.mp.
5	exp Nephritis/ or nephritis.mp
6	(nephropa$ or nephrotox$).mp.
7	1 or 2 or 3 or 4 or 5 or 6
8	acute kidney failure.mp.
9	exp Kidney/in, de, pd, to, ae [Injuries, Drug Effects, Parmacology, Toxicity, Adverse Effects]
10	(ARF or AKF).mp.
11	((impair$ or damag$ or acute$) adj2 (renal$ or kidney$)).mp.
12	(acute kidney insuffici$ or acute renal insufficie$).mp.
13	7 or 8 or 9 or 10 or 11 or 12
14	contrast associated nephropathy.mp.
15	contrast associated nephro$.mp.
16	contrast nephropa$.mp.
17	radiocontrast nephropathy.mp.
18	contrast nephroto$.mp.
19	radiocontrast nephrotox$.mp.
20	radiocontrast induced nephropathy.mp.
21	((nephropa$ or nephrotox) and (contrast or media)).mp.
22	CIN.mp.
23	(kidney$ or renal$ or contrast$).mp. and 22
24	14 or 15 or 16 or 17 or 18 or 19 or 20 or 23
25	21 or 24
26	13 or 22 or 23 or 25

List of Abbreviations

ACR = American College of Radiology
ACC = American College of Cardiology
ACEi = angiotensin converting enzyme inhibitors
AHA = American Heart Association
ASN = American Society of Nephrology
ARB = angiotensin receptor blockers
CT = Computed Tomography
CIN = contrast media-induced nephropathy
CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration
CM = iodinated, intravascular contrast media
CPOE = computerized physician order entry
eGFR = estimated glomerular filtration rate
EHR = electronic health record
eMAR = electronic medication administration record
ICPS = Indiana Coalition for Patient Safety
IV = intravenous
LOCM = low-osmolar contrast media
MDRD = Modification of Diet Renal Disease
MRI = magnetic resonance imaging
NAC = n-acetylcysteine
NSAID = non-steroidal anti-inflammatory drugs
NKDEP = National Kidney Disease Education Program
NKF = National Kidney Foundation
STEMI = ST-elevation myocardial infarction
SCAI = Society for Cardiovascular Angiography and Interventions

Summary of Recommendations

I. Screening

1. Risk Factor Screening

Consensus Statement I-1 (page 18-19)

A. The workgroup recommends screening procedures that identify patients with the following independent risk factors for contrast induced nephropathy (CIN): chronic kidney disease (CKD), diabetes mellitus, age ≥75 years, and congestive heart failure.

B. The work group recommends using a minimum threshold for estimated glomerular filtrate rate (eGFR) of <40 ml/min/1.73m^2 to define renal insufficiency/CKD. The workgroup also recognizes that data support a widened threshold of <60 ml/min/1.73m^2.

C. For patients with risk factors, who do receive iodinated, intravascular contrast media (CM), the workgroup recommends a follow-up evaluation and screening for CIN within 72 hours in the inpatient setting and within 7 days in the ambulatory setting.

2. Renal Function Screening

Consensus Statements I-2 and I-3 (page 15-16)

A. The workgroup recommends using eGFR to identify renal insufficiency/CKD. The Modification of Diet in Renal Disease (MDRD) study equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), and the Cockcroft-Gault equation are all acceptable methods to determine eGFR rate using measured serum creatinine.

B. The workgroup supports a screening serum creatinine to assess eGFR within 30 days prior to exposure to CM in the ambulatory setting and within 48 hours in the inpatient setting.

C. The workgroup supports assessment of eGFR in patients with a history of renal dysfunction.

D. While less clearly supported by current literature, eGFR screening appears reasonable in the patients with the following conditions: age ≥ 60 years, hypertension and/or prior kidney surgery.

E. The workgroup also recommends referral of patients at increased risk of CIN for follow-up assessment of eGFR within 72 hours in inpatients and within 1 week in outpatients following CM administration.

3. Emergency Exception

Consensus Statement I-4 (page 16)

A. For specific emergent indications, pre-procedural screening and lengthy treatment measures, including serum creatinine screening for assessment of eGFR, may delay access to emergent diagnostic and interventional procedures and are of limited benefit. Examples include: 1) ST elevation myocardial infarction (STEMI) requiring emergent cardiac catheterization; 2) emergent evaluation for thrombolysis for acute cerebral vascular accident (“stroke one” or “code stroke”); 3) acute vascular complications requiring emergent intervention such as aortic dissection, aortic aneurysm rupture, acute limb ischemia, and mesenteric ischemia; and 4) indications for potentially life or limb threatening conditions.

II. Prevention

1. Peri-procedural Hydration

Consensus Statement II-1 (page 17-18)

A. Peri-procedural intravenous hydration with normal saline and, if appropriate, post-procedural oral hydration, is recommended for patients at increased risk of CIN. Please refer to consensus statement II-01 for hydration recommendations.

2. N-Acetylcysteine (NAC)

Consensus Statement II-2 (page 19)

A. There are insufficient data to support the use of NAC to prevent CIN in patients at risk, including patients who are volume-sensitive.

3. Sodium Bicarbonate

Consensus Statement II-3 (page 19-20)

A. There are insufficient data to support the use of sodium bicarbonate to prevent CIN in patients at risk, including patients who are volume-sensitive.

4. Post-procedural Dialysis

Consensus Statement II-4 (page 20)

A. Post-procedural dialysis for the prevention of CIN in patients with CKD is of limited effectiveness and is potentially harmful.

5. Iso-osmolar Contrast Media

Consensus Statement II-5 (page 20-21)

A. There are insufficient data to support the use of iso-osmolar CM as an alternative to contemporary low-osmolar, non-ionic agents to prevent CIN in patients at risk, including patients who are volume-sensitive.

6. Cessation of Concurrent Medications

Consensus Statements II-6 and II-7 (pages 21-23)

A. There are insufficient data to recommended cessation or restriction of the medications reviewed by the workgroup (detailed in consensus statement II-6) prior to or following CM exposure.

B. The workgroup recommends selective discontinuation of metformin for a minimum of 48 hours after CM administration for patients with the following conditions: CKD, liver disease, alcohol abuse, cardiac failure, myocardial or peripheral muscle ischemia, and/or sepsis or severe infection. In patients at increased risk of acute kidney injury, discontinuation of metformin is recommended along with an assessment of renal function and ongoing risk for progressive renal dysfunction, prior to resuming metformin use.

7. Minimizing Contrast Media Exposure

Consensus Statement II-8 (page 23)

A. The workgroup recommends recurring institution and site-level reviews of imaging and interventional protocols for adherence to the ACR Appropriateness Criteria® and the ACCF/AHA Guidelines with specific attention to the inclusion of protocols that reduce or eliminate CM exposure in patients at increased risk of CIN.

B. The workgroup supports institutional efforts to identify and evaluate emerging imaging or interventional techniques that avoid or limit CM exposure in patients at increased risk of CIN.

C. The work group supports the referral of selected patients at increased risk of CIN to institutions or sites where appropriate non-CM or reduced-CM alternatives are performed with demonstrated reliability.

III. Electronic Health Record (EHR) Recommendations

1. Reporting Contrast Media Administration

Consensus Statement III-1 (page 24)

A. The workgroup recommends recording of CM administration, including date, time, type/concentration, volume, and route of administration, in a central location in the EHR that is accessible to all departments within the health system.
B. The workgroup recommends the development of interfaces with the central EHR and existing setting-specific electronic systems. These interfaces should allow for an automatic entry into the central EHR and should minimize additional re-entry by end users. (Regulatory processes reviewed in consensus statement III-1).

2. Computer Order Entry

Consensus Statement III-2 (page 24-25)

A. When the use of CM is planned for non-emergent cardiovascular, interventional radiology or other interventional procedures, the pre- procedural patient evaluation should include specific screening for risk factors for CIN (consensus statements I-1, I-2, I-3 and I-4) and for exposures to CM within 1 week (consensus statement III-1). In cases where the interventionalist is not directly assessing these factors, institutions should identify specific processes for communicating the presence of one or more CIN risk-factors to the interventionalist performing the procedure.
B. For diagnostic radiology imaging studies, institutions should develop targeted, automatic alerts that can be integrated in CPOE systems. Such alerts should be generated based on information available in the EHR (e.g. problem lists, medication records, etc.). The alert should provide the following information to the ordering/referring provider: 1) That the patient is at increased risk of CIN; and 2) Real-time contact information for the appropriate diagnostic radiologist(s). Institutions should also have a process for ensuring that contact information is correct, up-to-date, and includes backup contacts.
C. The workgroup recommends that each CPOE order structure for diagnostic radiology imaging studies should prompt the ordering/referring provider to describe the specific clinical indications and/or clinical concern(s) for the study. General procedural or diagnostic code categories do not meet this recommendation.

IV. Management of Intravenous Contrast Media Extravasation and Allergic Reactions

1. Extravasation

Consensus Statement IV-1 (page 26)

A. Identification – Patients may complain of swelling, tightness, stinging or burning at the extravasation site. Additionally the site may appear edematous, erythematous, and be tender to palpation.

B. For management the workgroup recommends elevating the affected extremity above the level of the heart, application of cold compresses, and frequent clinical assessments for several hours after an extravasation. The workgroup does not recommend aspiration of the extravasated contrast media and does not recommend local injection of corticosteroids or hyaluronidase based on a lack of evidence of efficacy

2. Allergic Reactions

Consensus Statement IV-2 (page 26-27)

A. For classification of reactions, the workgroup recommends appropriate assessment of contrast reactions as treatments and level of care are determined based on the classification of the reaction. Unlike most medication allergy classifications, both moderate and severe contrast allergic reactions may require intervention. Refer to Table 2 for descriptions of allergic reaction presentations. Delayed adverse reactions most commonly present as urticarial, a persistent rash, or generalized exanthematous pustulosis. Non-cutanous reactions include nausea, vomiting, fever, drowsiness, and headache. Severe delayed reactions are rare.

Table 2: Contrast Allergic Reaction Presentations

	Mild	**Moderate**	**Severe**
Allergic-Like*	• Limited: urticaria, pruritus, cutaneous edema, itchy/scratchy throat • Nasal congestion • Sneezing, conjunctivitis, rhinorrhea	• Diffuse: urticaria, pruritus, erythema • Facial edema without dyspnea • Throat tightness or hoarseness without dyspnea • Wheezing, bronchospasm with mild to no hypoxia	• Diffuse edema or facial edema with dyspnea • Diffuse erythema with hypotension • Laryngeal edema with stridor and/or hypoxia • Wheezing, bronchospasm • Significant hypoxia • Anaphylactic shock
Physiologic	• Limited nausea and vomiting • Transient flushing, warmth, chills • Headache • Dizziness • Anxiety • Altered taste • Mild Hypertension • Vasovagal reaction that resolves spontaneously	• Stable vital signs • Protracted N/V • Hypertensive urgency • Isolated chest pain • Vasovagal reaction that is responsive to treatment	• Vasovagal reaction resistant to treatment • Arrhythmia • Convulsions/seizures • Hypertensive emergency

*Adapted from American College of Radiology Contrast Media Guidelines

*The term allergic-like is used as these reactions are often not true allergies (i.e. not immune mediated)

B. Because mild reactions are usually self-limiting, the workgroup does not have specific recommendations for routine treatment of mild reactions. The workgroup recommends continued evaluation of the patient for potential progression. Delayed reactions are also typically self-limiting. The workgroup recommends verbal and written patient education about the possibility of delayed reactions and when to seek medical attention. For management of moderate or severe CM allergic reactions, the workgroup recommends that treatment should be targeted based on the specific reaction a patient is experiencing according to Table 3. The following additional reactions may occur and the team should be prepared to treat them: arrhythmia, hypertensive crisis, hypoglycemia, pulmonary edema, seizures. the workgroup recommends that the patient should be monitored for a minimum of 4 hours if any medication was given to treat a moderate or severe reaction. The workgroup recommends that prior to discharge the patient should be provided with a verbal and written emergency plan in the event of a reaction recurrence. Finally, the allergy and a description of the severity of the reaction should be documented in the EHR.

Table 3: Treatment of Moderate or Severe Contrast Allergic Reactions

Reaction	**Treatment**[a]
If any of the following: • Diffuse urticaria, pruritus, erythema • Hypotension	Administer all of the following: • Diphenhydramine 25 to 50 mg IV once • Supplemental oxygen • 0.9% normal saline IV bolus
If mild bronchospasm	Administer the above therapies AND **Add** albuterol 0.083% solution 1 ampule via nebulizer q2h prn bronchospasm
If any of the following: • Moderate to severe bronchospasm • Laryngeal edema • Hypotension that is profound or unresponsive to fluids	Administer the above therapies AND **Add** epinephrine 0.2 mg IM once. May repeat every 5-15 minutes for persistent severe symptoms **Add** famotidine 20 mg IV once or equivalent

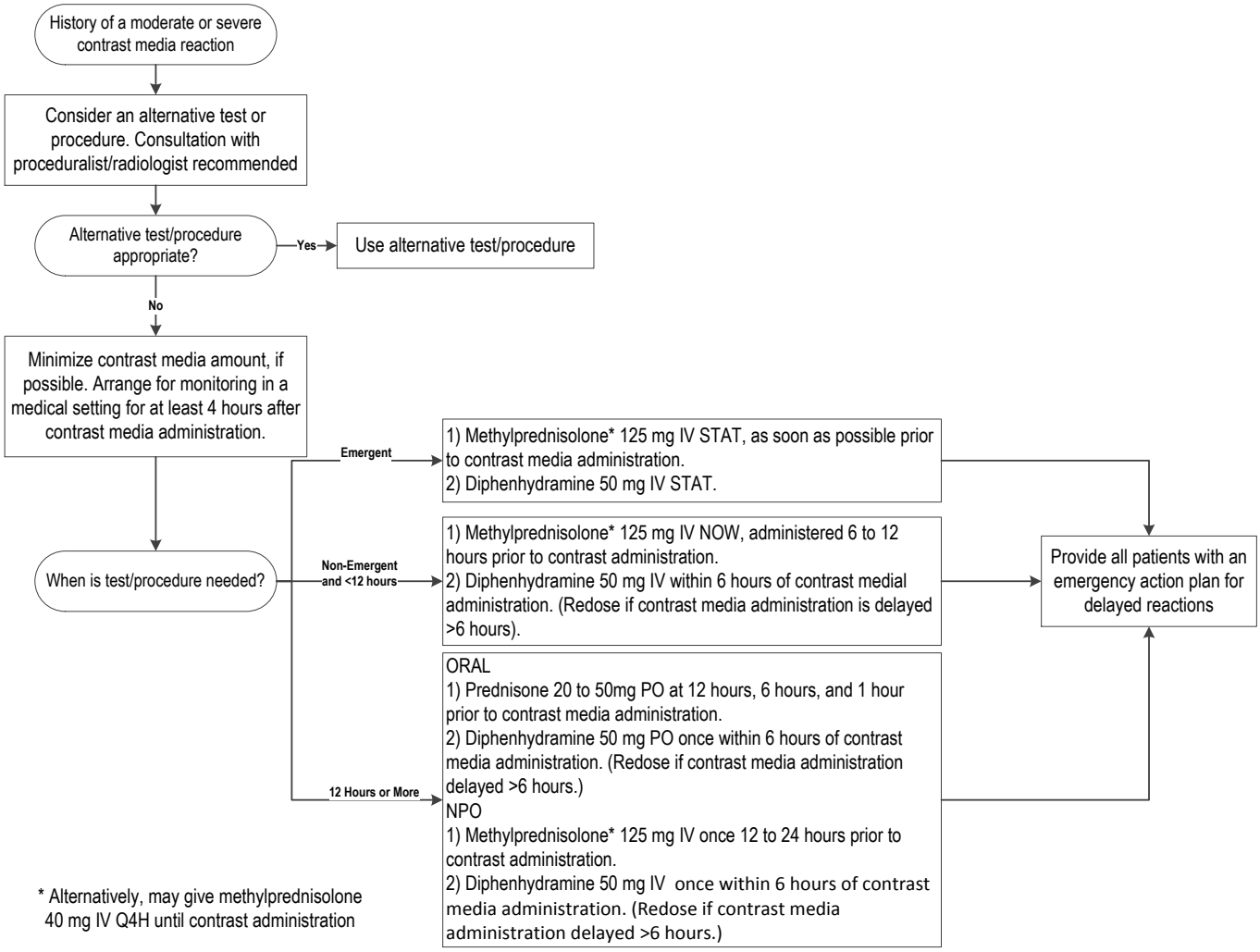
[a]The workgroup recommends that these medications be available as either a physical kit or a virtual kit in an automated dispensing cabinet.

3. Management of Patients with a History of a Moderate or Severe Contrast Allergy

Consensus Statement IV-3 (page 27-28)

A. The workgroup recommends that a patient with a history of a moderate or severe contrast allergy should be managed according to Figure 1.

Figure 1: Management of Patients with a History of Moderate or Severe Contrast Allergy



Consensus Statements

Note: Consensus statements focus on contrast media-induced nephropathy (CIN) in adults from intravascular, iodinated contrast media (CM) administration and do not address the following: 1) risks associated with iodinated, oral CM or CM administered by other routes; 2) risks associated with other agents, including the risk of nephrogenic systemic fibrosis from gadolinium; OR 3) risks specific to the pediatric population.

I. Screening

I-1 Risk Factors

A myriad of CIN risk factors exist in the literature today, some more widely studied than others. While there are over 200 risk factors for CIN identified in published literature, [1-43] the most widely accepted include CKD (identified by an eGFR min threshold < 40 ml/min/1.73m^2 [minimum standard] with data supporting a widened threshold of <60 ml/min/1.73m^2), diabetes mellitus, congestive heart failure and advanced age (≥ 75 years). Of these, CKD and diabetes mellitus are more consistently recognized as risk factors for CIN. [29,33,37,38,41,43] Data also demonstrates that congestive heart failure and advanced age (≥ 75 years) are also independently associated with an increased risk of CIN. [33,37,39,42,43] These data are summarized in Table 4. Several conditions limit the accuracy of CIN risk factors in the current literature: 1) highly variable definitions within the related literature for CIN as an outcome; 2) the definitions and thresholds defining specific risk factors vary widely among studies; and 3) data outside cardiac catheterization populations are limited. Furthermore, many studies designed to evaluate associated risk of CIN in the presence of particular risk factors are performed in patient populations that are already defined by CKD. [33-35] As a result, it is not possible to extend the comparisons made in this summary beyond a general description of current literature and local practices.

Conclusion

CKD (identified by an eGFR min threshold < 40 ml/min/1.73m^2 [minimum standard] with data supporting a widened threshold of <60 ml/min/1.73m^2), diabetes mellitus, age ≥75 years, and congestive heart failure are the most well recognized and literature supported, independent risk-factors associated with an increased risk of CIN. While not specifically addressed, other additional risk factors identified by the current literature may be important in certain situations or populations.

Table 4. Measures of Association for CIN Risk Factors

Risk Factor	Reference	Odds Ratio	95% Confidence Interval
Renal Insufficiency Chronic Kidney disease	Nikolsky E et al.[33]	1.51[a]	1.11 to 2.07
	Rihal CS et al.[38]	7.37[b]	4.78 to 11.39
	Rihal CS et al.[38]	12.82[c]	8.01 to 20.54
	Mehran R et al.[37]	1.19[d]	1.10 to 1.30
	Mehran R et al.[37]	2.05[e]	1.57 to 2.66
Diabetes Mellitus	Nikolsky E et al.[33]	1.84	1.36 to 2.47
	Rihal CS et al.[38]	1.61	1.21 to 2.16
	McCullough PA et al.[41]	5.47	1.40 to 21.32
	Mehran R et al.[37]	1.60	1.34 to 1.91
	Bartholomew BA et al.[43]	3.10	2.30 to 4.20
Congestive Heart Failure	Nikolsky E et al. [33]	2.21	1.34 to 3.64
	Rihal CS et al.[38]	1.53	1.12 to 2.10
	Manske CL et al.[42]	10.0	1.0 to 69.4
	Mehran R et al. [37]	2.70	2.02 to 2.60
	Bartholomew BA et al.[43]	2.20	1.60 to 2.90
Age ≥ 75 years	Mehran R et al.[37]	2.20	1.78 to 2.71
	Marenzi G et al.[39]	5.28	1.98 to 14.05

[a] Baseline creatinine> 1.5 mg/dL or GFR < 60 mL/min/1.73 m^2 [b] Baseline Cr 2.0-2.9 mg/dL (GFR data not available)
[c] Baseline Cr ≥ 3.0 mg/dL (GFR data not available)
[d] GFR < 60 mL/min/1.73 m^2
[e] Baseline Cr > 1.5 mg/dL

I-2 Estimated Glomerular Filtration Rate (eGFR)

Conclusion
The American College of Cardiology (ACC), the American College of Radiology (ACR), the National Kidney Disease Education Program (NKDEP), the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) all recommend estimating glomerular filtration rate from serum creatinine. While all equations have limitations, the Modification in Renal Disease (MDRD) study equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), and the Cockcroft-Gault equation are all acceptable methods to estimated glomerular filtration rate using measured serum creatinine.[8] All of these equations use measured serum creatinine in combination with sex, weight, or race to estimate glomerular filtration rate. As a result, these equations improve upon the limitations of measured serum creatinine alone.

I-3 Selective Assessment of Renal Function

Compulsory creatinine screening and assessment of eGFR to risk-stratify patients for CIN is not cost-effective and often time prohibitive, particularly with urgent or emergent procedures.[44] The ACR recommends selective serum creatinine screening prior to routine intravascular studies for patients age >60 years or with a history of any of the following renal disease: dialysis dependence, kidney transplant, single kidney, renal cancer, renal surgery, hypertension requiring medical therapy, or a history of diabetes mellitus.[45] This guideline also recommend serum creatinine screening for patients using metformin, but acknowledge that this recommendation is not aimed at assessing the risk of CIN, but rather the risk of lactic acidosis.[45] Additionally, the ACR guideline

classifies serum creatinine screening performed within 30 days is prudent, but acknowledges the lack of evidence to support a specific time-frame and supports more timely screening in hospitalized patients.[45] Finally, the guideline also acknowledges the potential need for exceptions to screening for emergent studies and procedures, but does not further specify recommendations for creatinine screening in these situations.[45] The ACC and the American Heart Association (AHA) guidelines are less specific with recommendations for peri-procedural creatinine screening, instead recommending the assessment of multiple risk-factors for CIN.[46]

To improve selective screening with serum creatinine, three studies define screening criteria aimed at identifying patients at risk of CKD.[44,47,48] In all three studies, the primary outcome assessed was the identification of an elevated serum creatinine. The largest of these studies includes retrospective data from 2,555 consecutive patients undergoing computed tomography (CT) studies with serum creatinine measurements performed within 3 days prior to CM exposure. In 94% of these cases the patient had a history of CKD and 18% had a history of diabetes mellitus (insulin dependent diabetes mellitus or non-insulin dependent diabetes mellitus). Concurrent chemotherapy and the presence of a solitary kidney were also studied as risk-factors for renal insufficiency/CKD, with these factors identifying <1% of cases of renal insufficiency/CKD in the absence of either prior CKD or diabetes mellitus. Assessment of all four risk-factors would have identified 99% of patients with CKD.[44] Choyke et al. studied the accuracy of a patient questionnaire administered to 633 consecutive patients undergoing CT. Patients were asked to give a history of any of the following: chronic kidney disease proteinuria, hypertension, diabetes mellitus, gout, or kidney surgery. The use of this questionnaire identified 70% of patients with CKD and decreased the need for serum creatinine testing by 67%.[47] These studies are both cited as acceptable means of selecting patients for serum creatinine screening by the ACR guideline.[45] Finally, Olsen et al. measured the prevalence of CKD in 640 patients undergoing iv pyelogram or contrast-enhanced CT of the brain or abdomen.[48] Combined, the following risk-factors identified 98% of cases of CKD: age >60 years, diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, and/or liver disease.[48] Importantly, all three studies defined renal insufficiency or CKD using a serum creatinine threshold (1.5 to 1.8 mg/dL). However, current published evidence supports the use of eGFR rather than an absolute serum creatinine threshold.[8] Moreover, the primary outcome of these studies was limited to the identification of chronic renal dysfunction and none of these studies directly measured the outcome of CIN.

Conclusion

Serum creatinine screening is most strongly supported in patients with a history of renal dysfunction and/or diabetes mellitus (both insulin dependent and non-insulin dependent diabetes mellitus). While less clearly supported by current literature, serum creatinine screening (and assessment of eGFR) in patients with the following conditions appears reasonable: age ≥ 60 years, hypertension, congestive heart failure or prior kidney surgery. While there are no data establishing a specific time frame, consensus supports the use of serum creatinine measurements within 30 days in the ambulatory setting and within 48 hours in the inpatient setting.

I-4 Emergency Exception

Conclusion

National guidelines support emergency exceptions screening for CIN, including serum creatinine screening, and pre-exposure treatment. [8,45,46] The following emergent indications for contrast-enhanced diagnostic imaging and interventional procedures were identified: 1) ST elevation myocardial infarction (STEMI) requiring emergent cardiac catheterization; 2) emergent evaluation for thrombolysis for acute cerebral vascular accident (“stroke one” or “code stroke”); 3) acute vascular complications requiring emergent intervention such as aortic dissection, aortic aneurysm rupture, acute limb ischemia, and mesenteric ischemia; and 4) indications for potentially life or limb threatening conditions. In these situations, screening and treatment measures, including serum creatinine screening, for CIN that may delay access to emergent diagnostic and interventional procedures are of limited benefit.

II. Prevention

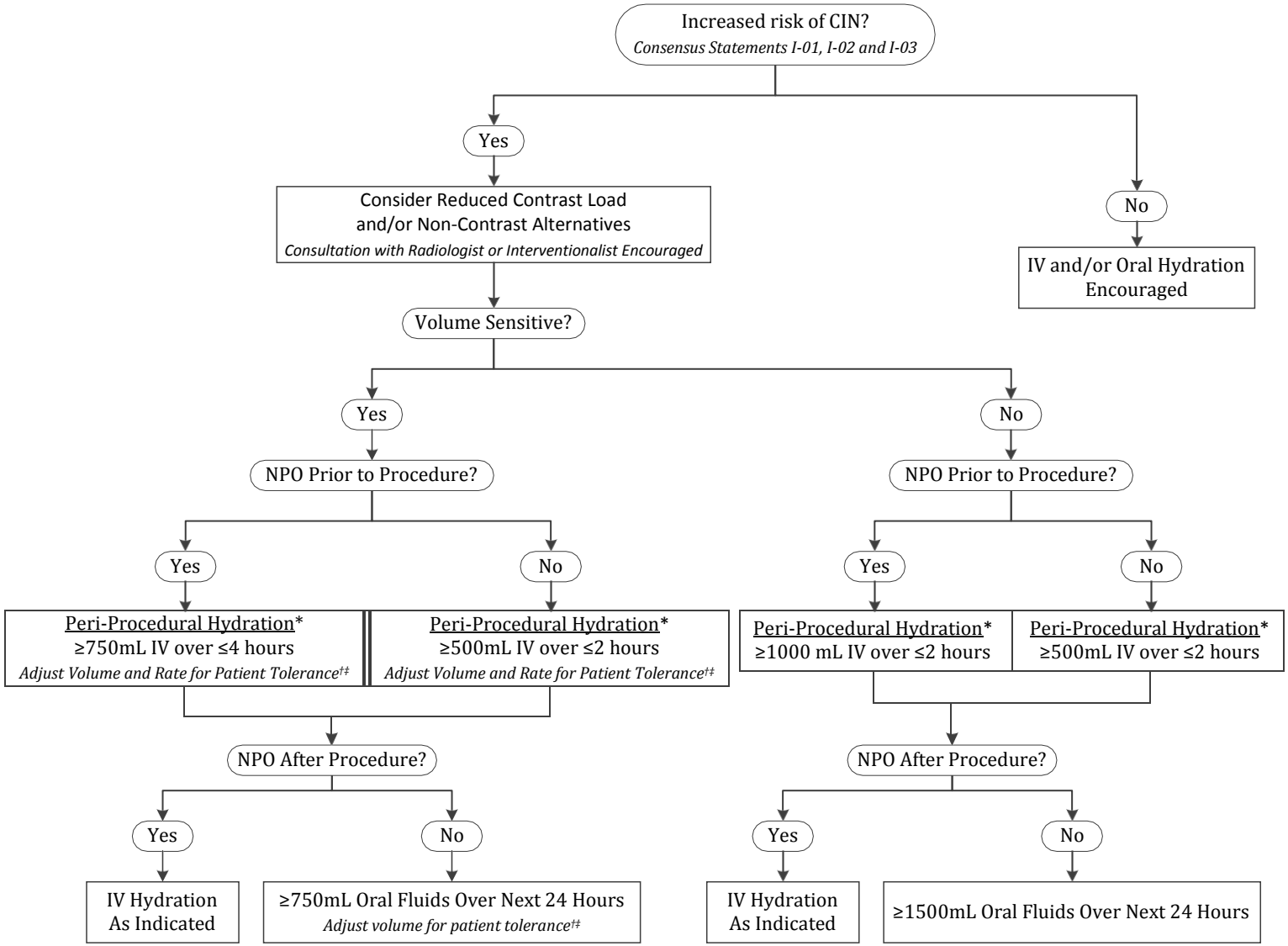
II-1 Peri-Procedural Hydration

Conventional hydration protocols have recommended intravenous (IV) hydration prior to CM exposure with the aim of decreasing the risk subsequent risk of CIN. These are designed to induce a state of mild hypervolemia, thereby increasing renal filtration, in patients presumed to be euvolemic at the onset. Recent studies suggest oral hydration may be as efficacious as IV hydration. In an early study, oral hydration was shown to be as effective as IV hydration in preventing CIN in patients undergoing cardiac catheterization.[49] Multiple subsequent studies have demonstrated oral hydration is as effective as IV hydration in patients undergoing cardiac procedures with moderate-severe baseline renal dysfunction[50-52] as well as patients with normal to mildly impaired baseline renal function, including two randomized trials.[53-55] Conversely, Trivedi et al[56] demonstrated IV hydration is more effective than oral hydration in patients undergoing cardiac catheterization in a prospective, randomized controlled trial where the study instructed patients in the oral intake arm to "increase fluid intake" unmonitored and without a protocol. The potential safety of oral versus IV hydration is of particular concern in volume sensitive patients. However, only two studies have specifically addressed this question. Lee et al[57] demonstrated a non-significant trend of increased pulmonary edema and pleural effusions in patients undergoing IV fluid replacement. Agoulvant et al[53] observed no IV hydration-induced pulmonary edema in patients with impaired left ventricular function. With all of these studies, the volume and time of administration and follow-up vary widely, and data comparing IV to oral fluid administration are particularly limiting in settings where hydration administered over several hours is impractical. There are no studies demonstrating the effectiveness of oral hydration initiated after CM exposure, nor are there studies evaluating an additive benefit of oral hydration as an adjuvant to IV hydration. Finally, there are no studies demonstrating the effectiveness of either oral or IV fluid administration in hypovolemic patients or patients exposed to CM following any period of fluid restriction. Outside of CIN, oral hydration has been shown to be as beneficial as IV hydration in fluid replacement therapy in patients with dengue hemorrhagic fever[57] and dehydration.[58] Transient hydronephrosis has also been observed ultrasonically following rapid oral fluid administration. Studies of oral hydration were conducted in the setting of causes of extreme hypovolemia and dehydration. Close monitoring of adequate intake and active patient instruction occurred. There are no studies demonstrating the effectiveness of simplified instructions allowing ad lib oral fluid intake. Notably, there are no studies demonstrating either increased CM retention with hypovolemic states nor data directly demonstrating volume- induced changes renal CM elimination.[59]

<u>Conclusion</u>

Sufficient data exist to support protocol-driven oral hydration initiated 12 to 24 hours prior to CM exposure. Although oral hydration may offer additional safety for volume-sensitive patients, data are not sufficient to demonstrate the efficacy of oral hydration alone or as an adjuvant to IV hydration in these populations specifically. All data are limited to patients whose exposure to iodinated CM occurs in the setting of cardiac catheterization. There are no data specifically examining oral hydration following single-bolus IV administration, which may have some differential effect. Similarly, oral hydration initiated immediately prior to or after CM exposure or in hypovolemic patients has not been studied.

Figure 2. Recommended peri-procedural hydration guideline



*Initiation of intravenous hydration with normal saline is recommended prior to, but may be completed after CM administration.
†This guideline is intended as a recommendation only and should be adjusted as clinically indicated. Consultation with the referring or treating provider is recommended.
‡Consider holding loop diuretics starting 12 hours prior to CM administration, in volume-sensitive patients on chronic loop diuretic therapy who are unable to tolerate IV hydration.

II-2 N-Acetylcysteine

Prophylactic use of IV and oral N-acetylcysteine (NAC) for the prevention of CIN has been examined for over ten years, yet evidence examining efficacy remains inconclusive. The first trial, published in 2000[60], demonstrated a 90% reduction in the incidence of CIN with prophylactic NAC treatment. Subsequent studies have demonstrated mixed results. Eight randomized controlled trials were reviewed to examine the efficacy of prophylactic NAC in patients undergoing cardiac angiography, angioplasty, or intra-operative CM exposure: seven concluded prophylactic NAC has no additional benefit compared the placebo or normal saline hydration groups[61-66] and one concluded IV NAC reduces the rate of CIN in a dose-dependent manner[67]. A single randomized controlled trial, published in abstract format, studied IV NAC administered as a 6 hour infusion initiated 1 hour prior to CT, did not demonstrate a benefit to NAC administration in addition to IV hydration.[68] Eight meta-analyses were also examined: five concluded prophylactic NAC is beneficial in reducing CIN[69-73] and three concluded the effect of NAC is inconclusive[74-76]. However, all meta- analyses reporting benefit and all but one reporting inconclusive findings[77] were significantly limited by significant statistical heterogeneity. There are no published data demonstrating the benefit of NAC as an alternative to hydration in volume-sensitive patient populations.

Conclusion

The prophylactic administration of IV or oral NAC is of limited effectiveness compared to hydration alone in the prevention of CIN. This recommendation is based on both the preponderance and strength of evidence evaluated in patients undergoing cardiac catheterization. There are insufficient data to support a recommendation for or against the use of NAC as an alternative to hydration, for patients exposed to CM outside of cardiac catheterization, or as a substitute for use in volume-sensitive patients.

II-3 Sodium Bicarbonate

Multiple meta-analyses were reviewed to examine the effect of prophylactic administration of sodium bicarbonate in the prevention of CIN. These meta-analyses analyzed between four[78] and eighteen[79] controlled trials. Overall, the majority of meta-analyses concluded that there is some benefit to an infusion of sodium bicarbonate in decreasing the incidence of CIN, although with small effect size. Notably, some controlled trials included in these meta-analyses combined administration of sodium bicarbonate with NAC in the treatment arm, complicating the ability to draw conclusions on the effect of sodium bicarbonate alone in the prevention of CIN. However, all meta-analyses[78-86] were limited by significant statistical and population heterogeneity. Only two analyses addressed statistical and population heterogeneity.[79,86] Hoste et al[79] demonstrated borderline effect size and significance of sodium bicarbonate in the prevention of CIN in patients undergoing cardiac procedures. However, the benefit of sodium bicarbonate was eliminated when cardiac and non-cardiac procedures were combined. Brar et al[86] separated their analysis into large ($n \geq 290$) and small ($n \leq 290$) trials. In doing so, statistical heterogeneity was minimized in the large trial analysis resulting in no observed benefit to sodium bicarbonate.

Data supporting the use of sodium bicarbonate in preference to saline hydration in volume-sensitive populations are extremely limited. We were only able to identify a single randomized controlled trial (n=72), which did not demonstrate any difference in the incidence of CIN or in complications from hypervolemia among patients receiving sodium bicarbonate compared to those hydrated with IV saline alone.[87]

Conclusion

The benefit of sodium bicarbonate in preventing CIN demonstrated in several meta-analyses is limited by statistical and population heterogeneity. In a meta-analysis supported by large prospective studies, where statistical heterogeneity is addressed, the benefit if sodium bicarbonate is no longer observed.[9] There may be some benefit, although with a small effect size, specifically in patients undergoing cardiac catheterization, but this benefit is no longer observed when data are

combined with patients exposed to CM outside of cardiac catheterization.[2]

II-4 Post-Procedural Dialysis

Many *in vitro* and *in vivo* studies have demonstrated the efficient removal of intravascular CM via hemodialysis, yet evidence suggests hemodialysis does not significantly reduce the incidence of CIN. Three reviews, one meta-analysis, and eight prospective studies were evaluated to determine the effect of hemodialysis on the incidence of CIN after CM administration, largely in the setting of cardiac procedures. All three reviews[88-90] concluded hemodialysis does not significantly reduce the incidence of CIN. The one meta-analysis[91] reviewed also concluded hemodialysis does not significantly reduce CIN (no statistical heterogeneity for hemodialysis). Seven of the prospective studies[92-98] demonstrated hemodialysis does not significantly reduce the incidence of CIN after CM administration in patients with chronic kidney disease. Vogt et al[93] suggests hemodialysis may even be harmful. Only one of the prospective studies[99] demonstrated a significant reduction in the incidence of CIN following post-exposure hemodialysis. There are no definitive data to support alterations in either the timing of regularly scheduled dialysis with respect to CM exposure or the timing of CM exposure with respect to regularly scheduled dialysis. Studies were limited by significant heterogeneity with respect to populations studied, the hemodialysis protocol utilized, and the concurrent use of adjuvant prophylactic therapies such as saline hydration and NAC.

Conclusion

Post-exposure hemodialysis for the prevention of CIN in patients with chronic kidney disease is of limited effectiveness. This recommendation is based on a preponderance of published studies demonstrating a lack of effectiveness and one study demonstrating the potential for harm. These studies are limited by significant heterogeneity.

II-5 Iso-Osmolar Contrast Media

Currently, the only commercially available non-ionic, iso-osmolar, iodinated CM is iodixanol (Visipaque). The osmolarity of this agent is 290 mOsm/kg compared to 470 to 670 mOsm/kg for low-osmolar agents. A second agent, iotrolan (Isovist) has an osmolarlity of 320 mOsm/kg, but is less well studied and is a more expensive agent than even iodixanol. Studies have compared the incidence of CIN following iodixanol to that associated with the administration of the following non-ionic, low-osmolar CM (LOCM) agents: ioxaglate (Hexabrix), iopamidol (Isovue), iohexol (Omnipaque), iomeprol (Iomeron), and iopromide (Ultravist). Early studies demonstrated inconclusive outcomes when comparing iodixanol to LOCM. [100-102] The results of subsequent randomized controlled trials are variable. The NEPHRIC trial demonstrated a significant reduction in CIN in 129 patients with both chronic renal disease and diabetes undergoing cardiac catheterization randomized to iodixanol versus iohexanol (serum creatinine increase ≥ 0.5 mg/dL, 3% with iodixanol versus 26% with iohexanol, $p<0.05$).[103] In a larger study of 414 patients with CKD, the CARE trial compared iodixanol to iopamidol. The rates of post-cardiac catheterization CIN were not statistically distinguishable: serum creatinine increase ≥ 0.5 mg/dL, 6.7% for iodixanol and 4.4% for iopamidol, $p = 0.39$; serum creatinine increase ≥ 2 5 % from baseline, 12.4% for iodixanol and 9.4% for iopamidol, $p = 0.44$.[104] We also reviewed the results of 5 smaller randomized controlled trials comparing LOCM agents in patients undergoing contrast-enhanced CT and/or cardiac catheterization procedures: two studies concluded iodixanol was significantly less nephrotoxic than ioxaglate[105] and to iopromide[106], two studies concluded iodixanol was not associated with a statistically significant reduction in the incidence of CIN compared to LOCM agents tested individually [107,108], and one study concluded the incidence of CIN was significantly higher with iodixanol than with iomeprol[109]. Three of four meta-analyses concluded that iodixanol does not significantly reduce the incidence of CIN when compared to LOCMs (pooled result) in patients with CKD.[110-112] However, these three studies do report a modest, but statistically significant reduction in CIN with iodixanol compared to iohexol, but not with other agents. [110-112] One meta-analysis concluded iodixanol significantly reduces the incidence of CIN in patients with chronic kidney disease and diabetes mellitus when compared to other LOCM agents.[113] Notably, the

manufacturer of iodixanol sponsored this study and supplied the data. Aspelin et al. demonstrated that despite a 20% difference in cost, the use of iodixanol was cost- effective compared to iohexanol.[114] However, when the same cost-benefit analysis methods were applied using data from the CARE trial, the use of iopamidol had a comparatively larger cost-benefit compared to iodixanol, even among high-risk patients.[115]

While not directly affecting the issue of CIN, there are some experts who recommend stocking iso-osmolar agents, in addition to LOCM agents specifically for oral or bronchial administration, because of a potential for decreased risk with aspiration. There are data demonstrating increased safety with the use of LOCM for off-label oral administration compared to high-osmolar agents and barium. [116] The safety of iotrolan, but not iodixanol, with bronchial introduction has been studied and appears to be similar to that of LOCM agents.[117] There are no published data demonstrating an advantage with respect to the risk of aspiration of an iso-osmolar agent compared to other LOCM.

Conclusion

Published data does not demonstrated a consistent therapeutic benefit or a cost-effectiveness benefit supporting the use of iso-osmolar CM agents as an alternative to contemporary low-osmolar CM agents for the prevention of CIN.

II-6 Cessation of Concurrent Medications

The development of CIN as an outcome of CM exposure combined with the use of certain renal or nephrotoxic medications deserves attention. Potentially nephrotoxic medications of concern include, but are not limited to: diuretics, nephrotoxic antibiotics (gentamicin and tobramycin), non-steroidal anti-inflammatory drugs (NSAID), antihypertensive agents (angiotensin converting enzyme inhibitors [ACEi] and angiotensin receptor blockers [ARB]), chemotherapeutic agents, and specifically, tenofovir, colchicine, and amphotericin B. Limited evidence regarding these medications and their effects on the development of CIN exists in the medical literature. Neither the ACR nor the ACC/AHA have published recommendations for either discontinuation or dose modification of these medications.[45,46]

Furosemide (Lasix), torsemide (Demadex), bumetanide (Bumex), spironolactone (Aldactone), and acetazolamide (Diamox) are diuretics that were included in our literature search. Effects of these medications on the development of CIN are largely ambiguous. Four randomized controlled trials[50,118-120] evaluating furosemide and CM concluded that furosemide did not effectively reduce the incidence of CIN. Two trials concluded furosemide effectively prevents the development of CIN if high urine output is achieved through matched hydration.[121,122] Contrarily, three of the four studies further concluded that furosemide has the potential to increase the risk of developing CIN after CM exposure.[118-120] Of note, mannitol was included in three of the studies addressing furosemide.[118,119,122] The observed effects of mannitol were the same as furosemide in the respective studies. Only one study was identified for acetazolamide and suggested the risk of CIN development is reduced with acetazolamide.[123] No studies were identified for the other diuretics included in the literature search.

Of the antihypertensive agents, benzapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, moexepril, perindopril, quinapril, ramipril, trandolapril, azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan were included in our literature search. Only one study was identified for these medications, and it addressed the effect of captopril on the development of CIN.[124] The study concluded captopril reduces the risk of developing CIN after CM exposure in the diabetic population.[124] No studies were identified for the other antihypertensive medications.

No studies were identified for any of the other medications or classes of drugs: NSAIDs (ibuprofen, naproxen, toradol, celecoxib, and indomethacin), chemotherapeutic agents (cisplatin, carboplatin, bendamustin, cyclophosphamide, streptazocin, mitomycin C, bleomycin, methotrexate, vincristine,

vinblastine, topotecan, interleukin 2 and interferon), tenofovir, colchicine, and amphotericin B.

Conclusion
There is little evidence in current medical literature to support a recommendation guiding the use of the medications reviewed by this committee with intravascular iodinated CM exposure. Though multiple studies addressing the effect of furosemide and other loop diuretics on the development of CIN exist, conflicting conclusions prohibit the development of a specific guideline recommending that patients either continue or discontinue furosemide prior to CM exposure. However, in patient on chronic furosemide, who are unable to tolerate intravenous hydration, withholding loop diuretics 12 hours prior to CM administration should be considered.

II-7 Metformin

It is well-recognized that metformin use, alone or as part of combination therapy, does not increase the risk of CIN. However, current package inserts approve by the US Food and Drug administration recommend temporarily discontinuing the use of metformin after the administration of intravascular CM. (http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020357s031,021202s016lbl.pdf, accessed 08/12/13) This recommendation is based on the potential for patient to develop lactic acidosis as a result of developing CIN and subsequently decreased lactic acid metabolism. The occurrence of lactic acidosis resulting from metformin use in the setting of CIN is extremely rare. In fact, there are no published accounts of CIN-related, metformin-induced lactic acidosis with contemporary nonionic, low-osmolar agents. In fact, nearly all cases of non-CIN related metformin-induced lactic acidosis have occurred in patients with co-morbid conditions that result in either increased production or decreased metabolism of lactic acid: liver disease, advanced kidney disease, and conditions associate with regional or global hypoperfusion and/or shock including cardiac failure, sepsis, hemorrhage, vascular occlusion, etc.). These conditions are independent contraindications to metformin use. (http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020357s031,021202s016lbl.pdf, accessed 08/12/13) Over the past decade, the prevalence of metformin use has increased significantly, as has the use of metformin in general, and for treatment of conditions outside of type 2 diabetes mellitus.[125,126]

The ACR recommends the discontinuation of metformin only in patients with known renal dysfunction and those with: liver disease, alcohol abuse, cardiac failure, myocardial or peripheral muscle ischemia, and/or sepsis or severe infection. Furthermore, the ACR guideline recommends that metformin can be resumed after 48 hours in patients without known renal dysfunction (at the time of CM administration) and have not had the intercurrent development of risk factors for acute kidney injury. In patients with known renal dysfunction, the guideline recommends "cautious follow-up until safe restitution of metformin can be assured." Discontinuation of metformin is not recommended in patients without these conditions.[45]

The ACC and the Society for Cardiovascular Angiography and Interventions (SCAI) recommend discontinuation of metformin on the day of the CM administration for routine, non-emergent percutaneous coronary angiography procedures and 48 hours after CM administration for all procedures, with resumption of metformin only after documentation of stable renal function.[127] This recommendation may reflect the increased prevalence of conditions that increase the risk of acute kidney injury or that disrupt lactic acid metabolism in this population. However, the strength of this recommendation remains controversial, with some studies demonstrating improved outcomes with continued metformin administration after coronary angiography.[128]

Conclusion
Metformin use does not increase the risk of CIN. Rarely, the risk of lactic acidosis may be increased in patients that develop CIN while taking metformin. For percutaneous coronary angiography, national guidelines currently recommend the discontinuation of metformin starting the day of the

non-emergent procedures continuing for at least 48 hours after all procedures. Reassessment of renal function is currently recommended prior to resuming metformin use. However, in some select cases, continued metformin use may be indicated. For radiologic studies and procedures involving CM administration, national guidelines recommend the discontinuation of metformin for a minimum of 48 hours after CM administration in patients with known chronic kidney disease or those with liver disease, alcohol abuse, cardiac failure, myocardial or peripheral muscle ischemia, and/or sepsis or severe infection. In patients with conditions that may result in acute kidney injury, assessment of renal function and risk of progressive renal dysfunction are also recommended prior to resuming metformin use.

II-8 Minimizing Contrast Media Exposure

CT imaging without CM or alternative imaging modalities such as ultrasound or magnetic resonance imaging (MRI) are recommended for an increasingly wider spectrum of clinical indications. (American College of Radiology. ACR Appropriateness Criteria®. Available at www.acr.org/ac Accessed 3/26/2014) Similarly, national guidelines recommend approaches to conserve CM exposure for diagnostic and therapeutic peripheral vascular and cardiovascular procedures for patients at increased risk of CIN. [129-131] Given the current state of available technologies and expertise currently available across healthcare institutions represented within the Contrast Media Workgroup, both the ACR Appropriateness Criteria® and the ACCF/AHA Guidelines represent potential opportunities to create a guideline to limit unnecessary CM exposure that can be reliably applied across institutions in the Indianapolis region.

However, CM remains integral to the diagnosis and management for many clinical indications for which there are currently no viable alternatives. Moreover, communication between the referring physician and the radiologist, cardiologist or other interventionalist is critical to identifying specific cases where reduced-CM or non-CM alternatives are appropriate.

Recent advances in contrast-enhanced CT imaging have resulted in methods to reduce CM dose for specific imaging indications. Such protocols are particularly valuable in cases where alternatives to contrast-enhanced CT imaging are not viable, especially in patients at increased risk of CIN. The workgroup has reviewed the experience of local institutions with reduced dose CT imaging protocols that leverage high resolution CT scanners and with software that allows for adjusted CM dosing. Notably, not all institutions or affiliated sites (e.g. outpatient, free-standing imaging centers) are able to offer reduced-CM protocols because of equipment or other technologic restrictions. Furthermore, the reliability and reproducibility of these methods appear to vary significantly from institution to institution and even site to site. In some cases, inconsistent image quality resulting in the need for repeat imaging, may conversely result in increased patient exposure to CM. At this time, the workgroup was unable to identify specific reduced-CM protocols that can be reliably applied on a regional basis. However, as these techniques undergo further development, the workgroup anticipates that regional institutions will be able to adopt reduced-CM protocols with increasing frequency in the near future.

Conclusions

1) The workgroup recommends recurring institution and site-level reviews of imaging and interventional protocols for adherence to the ACR Appropriateness Criteria® and ACCF/AHA Guidelines, with specific attention to the inclusion of protocols that reduce or eliminate CM exposure in patients at increased risk of CIN.
2) The workgroup supports institutional efforts to identify and evaluate emerging imaging or interventional techniques that avoid or limit CM exposure in patients at increased risk of CIN.
3) The work group supports the referral of selected patients at increased risk of CIN requiring CM to institutions or sites where appropriate non-CM or reduced-CM alternatives are performed with demonstrated reliability.

III. Electronic Health Record (EHR)

III-1 Reporting Contrast Media Administration

Creating the ability within an EHR to easily query recent exposure, prior to the administration of additional CM, provides a safer framework when ordering CM, potentially avoiding excess exposure and allowing providers to make more fully informed decisions. The ability to query CM administration in a central, single location within the EHR presents unique challenges because CM is administered in multiple settings (operating rooms, cardiac catheterization suites, interventional radiology, diagnostic radiology, etc.). Additionally, each of these settings has varying methods of recording CM administration, including separate electronic record systems. It is the consensus of the workgroup that referring providers and the radiologist, cardiologist or other interventionalist be made aware of exposures to CM within one week from any setting within an institution (including associated outpatient locations), before additional exposures for non-emergent indications.

The workgroup does recognize that the introduction of additional steps that require multiple and repetitive entries into various systems is likely to introduce unintended opportunities for error, have poor compliance and may interfere with the high throughput required to provide diagnostic and interventional procedures within our medical community. The workgroup has reviewed the EHR systems, including engagement of EHR system managers and technologists, for the represented intuitions. We recommend the development of interfaces linking the central EHR and existing setting-specific electronic systems. These interfaces should allow for an automatic entry of contrast administration events into a single location in the central EHR, minimizing additional re-entry by end users.

Importantly in cooperation with the ICPS Medication Safety Workgroup, this workgroup reviewed many regulatory issues including the need for a separate provider order, pharmacy reconciliation and technologist administration of CM. Individual institutions represented within the workgroup have successfully initiated documentation of CM administration in the electronic medication administration record (eMAR). These institutions have established CM administration protocols that function in lieu of case-by-case, provider-initiated medication orders ("er protocol" orders). These protocols specify the administration of CM by the appropriate providers, nurses, and/or technologists for diagnostic imaging and interventional procedures in a range of inpatient and outpatient settings, and have created processes for post-hoc pharmacy review and reconciliation ("auto-verification"). In the case of CM, the ICPS Medication Safety Workgroup supports these processes, which are compliant with external regulatory requirements.

<u>Conclusion</u>

1) The workgroup recommends recording of intravascular CM administration, including date, type/concentration, volume, route of administration, and location, within the EHR.
2) The workgroup recommends the development of interfaces with the central EHR and existing setting-specific electronic systems. These interfaces should allow for shared information by an automatic entry into the central EHR and should minimize need for additional re-entry by end users.

III-2 Computerized Physician Order Entry (CPOE)

The Contrast Media Workgroup has determined that communication barriers contribute to missed opportunities to limit or avoid intravascular CM exposures in patients at increased risk of CIN. The workgroup also recognizes that the nature of cardiovascular, interventional radiology and other interventional procedures is more conducive to direct patient evaluation and identification of patients at increased risk. However, in the diagnostic radiology setting, opportunities for direct patient evaluation and risk assessment are significantly limited and rely heavily on information

from referring providers. At the same time, the pool of referring providers is extremely large and heterogeneous with respect to knowledge of CIN risk, preventive therapies and/or the selection of alternative or adapted imaging strategies. Notably, the overwhelming majority of patient exposures to intravascular CM agents occur in the diagnostic radiology setting, underscoring the importance of improving opportunities for direct communication between referring physicians and radiologists.

The introduction of EHR and computer physician order-entry (CPOE) systems has also impacted communication with diagnostic radiologists. Traditionally, written orders for diagnostic imaging tests were structured around clinical indications that were closely matched to imaging protocols that were regularly reviewed at the institutional level and identified when CM was needed. Recurring review of institutional imaging protocols also allowed for adaptations to these protocols in response to national guidelines and technologic advances. Now, current systems often require referring providers to request the administration of CM without additional guidance. Moreover, the use of provider-defined order templates (e.g. "favorites") and the use of limited menus of diagnostic or procedural codes also limit the opportunity to communicate patient-specific information. Expanding patient volumes, throughput demand, and variability in referring sources also contribute to communication barriers, underscoring the need for specific, targeted actions to improve communication. The workgroup also identified significant opportunities to leverage the EHR and CPOE systems available at regional institutions represented by the workgroup.

Conclusion

1) When the use of intravascular iodinated CM is planned for non-emergent cardiovascular, interventional radiology or other interventional procedures, the pre-procedural patient evaluation should include specific screening for risk factors for CIN (consensus statements I-01, I-02, I-03 and I-04) and for exposure to CM exposure within 1 week (consensus statement III-01). In cases where the interventionalist is not directly assessing these factors, institutions should identify specific processes for communicating the presence of one or more CIN risk-factors to the interventionalist performing the procedure.
2) For diagnostic radiology imaging studies, institutions should develop targeted, automatic alerts that can be integrated in CPOE systems. Such alerts should be generated based on information available in the EHR (e.g. problem lists, medication records, etc.). The alert should provide the following information to the ordering/referring provider: 1) that the patient is at increased risk of CIN; and 2) Real-time contact information for the appropriate diagnostic radiologist(s). Institutions should also have a process for ensuring that contact information is correct, up-to-date, and includes backup contacts.
3) The workgroup recommends that each CPOE order structure for diagnostic radiology imaging studies should prompt the ordering/referring provider to describe the specific clinical indications and/or clinical concern(s) for the study. General procedural or diagnostic code categories do not meet this recommendation.

IV. Management of Intravenous Contrast Media Extravasation and Allergic Reactions[132]

IV-1 Extravasation

Patients may complain of swelling, tightness, stinging or burning at the extravasation site. Additionally the site may appear edematous, erythematous, and be tender to palpation. For management, the workgroup recommends elevating the affected extremity above the level of the heart, application of cold compresses, and frequent clinical assessments for several hours after an extravasation. The workgroup does not recommend aspiration of the extravasated contrast media and does not recommend local injection of corticosteroids or hyaluronidase based on a lack of evidence of efficacy. Finally, the extravasation event and any treatments should be documented in the EHR.

IV-2 Allergic Reactions

For classification of reactions, the workgroup recommends appropriate assessment of contrast reactions as treatments and level of care are determined based on the classification of the reaction. Unlike most medication allergy classifications, both moderate and severe contrast allergic reactions may require intervention. Refer to Table 1 for descriptions of allergic reaction presentations. Delayed adverse reactions most commonly present as urticarial, a persistent rash, or generalized exanthematous pustulosis. Non-cutanous reactions include nausea, vomiting, fever, drowsiness, and headache. Severe delayed reactions are rare.

Table 2: Contrast Allergic Reaction Presentations

	Mild	Moderate	Severe
Allergic-Like*	• Limited: urticaria, pruritus, cutaneous edema, itchy/scratchy throat • Nasal congestion • Sneezing, conjunctivitis, rhinorrhea	• Diffuse: urticaria, pruritus, erythema • Facial edema without dyspnea • Throat tightness or hoarseness without dyspnea • Wheezing, bronchospasm with mild to no hypoxia	• Diffuse edema or facial edema with dyspnea • Diffuse erythema with hypotension • Laryngeal edema with stridor and/or hypoxia • Wheezing, bronchospasm • Significant hypoxia • Anaphylactic shock
Physiologic	• Limited nausea and vomiting • Transient flushing, warmth, chills • Headache • Dizziness • Anxiety • Altered taste • Mild Hypertension • Vasovagal reaction that resolves spontaneously	• Stable vital signs • Protracted N/V • Hypertensive urgency • Isolated chest pain • Vasovagal reaction that is responsive to treatment	• Vasovagal reaction resistant to treatment • Arrhythmia • Convulsions/seizures • Hypertensive emergency

*Adapted from American College of Radiology Contrast Media Guidelines[132]

*The term allergic-like is used as these reactions are often not true allergies (i.e. not immune mediated)

Because mild reactions are usually self-limiting, the workgroup does not have specific recommendations for routine treatment of mild reactions. The workgroup recommends continued evaluation of the patient for potential progression. Delayed reactions are also typically self-limiting. The workgroup recommends verbal and written patient education about the possibility of delayed reactions and when to seek medical attention. For management of moderate or severe CM allergic reactions, the workgroup recommends that treatment should be targeted based on the specific reaction a patient is experiencing according to Table 3. The following additional reactions may occur and the team should be prepared to treat them: arrhythmia, hypertensive crisis, hypoglycemia, pulmonary edema, seizures. the workgroup recommends that the patient should be monitored for a minimum of 4 hours if any medication was given to treat a moderate or severe reaction. The workgroup recommends that prior to discharge the patient should be provided with a verbal and written emergency plan in the event of a reaction recurrence. Finally, the allergy and a description of the severity of the reaction should be documented in the EHR.

Table 3: Treatment of Moderate or Severe Contrast Allergic Reactions

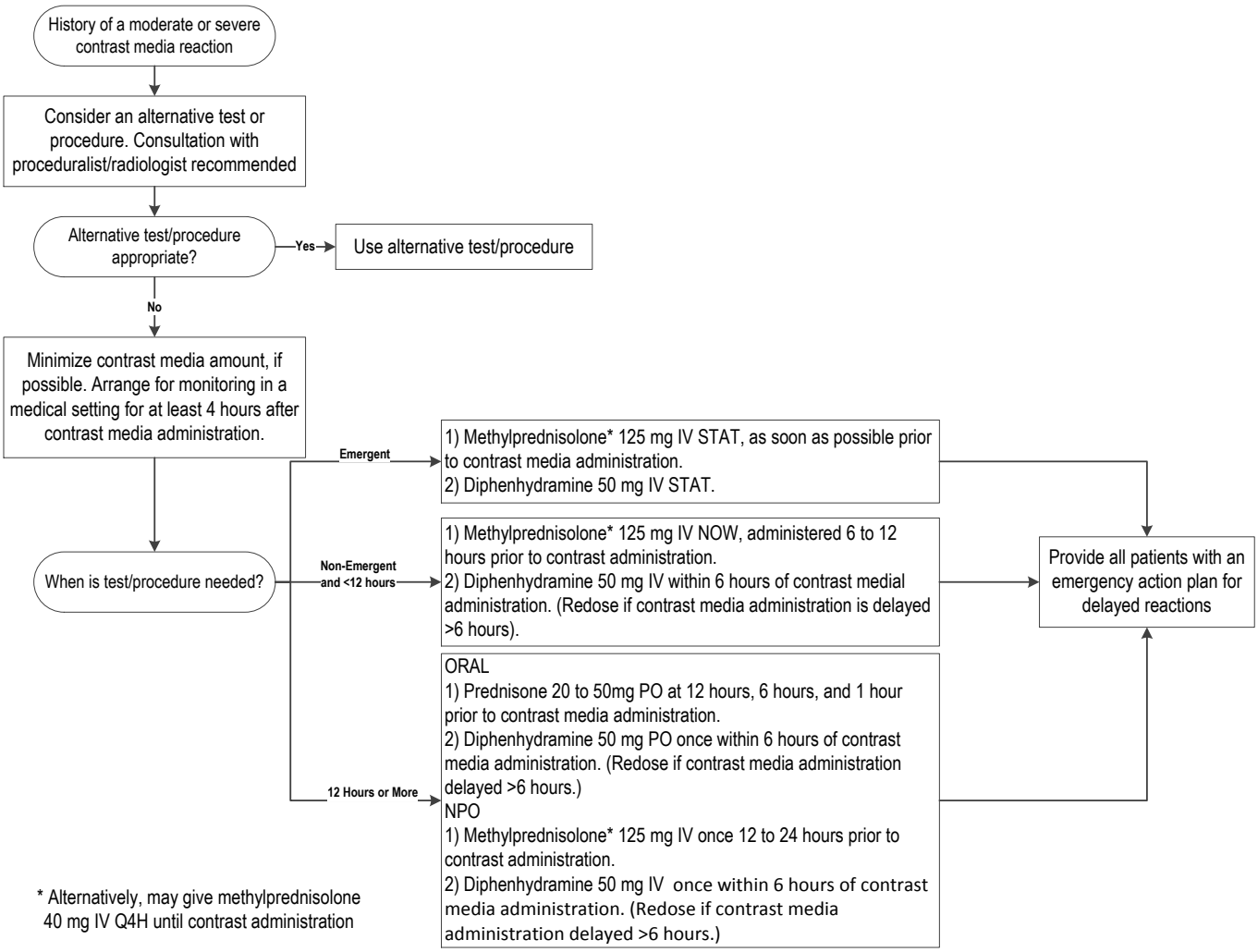
Reaction	Treatment[a]
If any of the following: • Diffuse urticaria, pruritus, erythema • Hypotension	Administer all of the following: • Diphenhydramine 25 to 50 mg IV once • Supplemental oxygen • 0.9% normal saline IV bolus
If mild bronchospasm	Administer the above therapies AND **Add** albuterol 0.083% solution 1 ampule via nebulizer q2h prn bronchospasm
If any of the following: • Moderate to severe bronchospasm • Laryngeal edema • Hypotension that is profound or unresponsive to fluids	Administer the above therapies AND **Add** epinephrine 0.2 mg IM once. May repeat every 5-15 minutes for persistent severe symptoms **Add** famotidine 20 mg IV once or equivalent

[a]The workgroup recommends that these medications be available as either a physical kit or a virtual kit in an automated dispensing cabinet.

IV-3 Management of Patients with a History of a Moderate or Severe Contrast Allergy

The workgroup recommends that a patient with a history of a moderate or severe contrast allergy should be managed according to Figure 1

Figure 1: Management of Patients with a History of Moderate or Severe Contrast Allergy[a]



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