International Journal of Renal Diseases and Therapy

Contrast-induced Acute Kidney Injury: A Contemporary Review

Anton A. Khilchuk[1]
Sergey V. Vlasenko[1,2]
Sergey G. Scherbak[2]
Andrey M. Sarana[2]

[1]Department of Interventional Radiology, City Hospital, St. Petersburg, Russian Federation
[2]Medical Faculty, St. Petersburg State University, St. Petersburg, Russian Federation

Abstract

Clinically significant contrast-induced acute kidney injury (CIAKI) is a severe complication of interventional contrast-based procedures of all kinds. It involves high morbidity, mortality, social and financial losses. Acute renal damage after coronary angiography or percutaneous coronary intervention may occur in 1-2% of cases in the general population or 50+% of cases with high CIAKI exposure. It is essential to detect high-risk patients with renal damage as a major and frequent CIAKI predisposing factor. There are novel biomarkers with rapid or nearly instant response to acute subclinical contrast-induced renal damage, which are highly valuable in CIAKI diagnosis and for this reason desire deeper clinical research. Despite a number of controversies, prophylactic and therapeutic measures are practically the same in a vast majority of guidelines. An intravenous 0.9% NaCl solution remains the only proven measure in CIAKI prophylaxis and treatment, while the use of other pharmacological approaches still needs more relevant prospective clinical research. The aim of this paper was to review contemporary evidence-based CIAKI data.

Keywords

Nephropathy, Renal injury, Contrast media, Renal injury biomarkers

Introduction

Contrast-induced nephropathy (CIN), or contrast-induced acute kidney injury (CIAKI), is acute damage to the renal parenchyma, caused by the intravascular administration of iodinated contrast media (CM) without other alternative reasons [1]. CIAKI was first described by clinicians in a 1950s case history, clinically proceeding as a lethal acute renal failure after intravenous pyelography in myeloma patients [2,3]. The incidence of CIAKI may be as low as 2% in patients without risk factors, but in those with risk factors, such as diabetes, the rate rises to 9%, and even as high as 90% in patients with diabetic nephropathy or preexisting chronic kidney disease [4,5]. Therefore, the number and the type of preexisting risk factors directly influence the incidence of renal insufficiency. Incidence rates are also procedure dependent, with reports in the literature ranging from 1.6-2.3% for diagnostic interventions to 14.5% overall in patients undergoing coronary intervention [4,5]. Renal damage after coronary angiography or percutaneous coronary intervention may develop in 1-2% of cases in the general population and almost 50% of patients with high CIAKI exposure [1,6]. A major CIAKI factor is existing nephropathy, especially in diabetic patients [5,7].

Every year, the growing number of patients receiving percutaneous cardiac care increases CM consumption and consequently CIAKI incidence. CIAKI entails an increased frequency and number of cardiovascular complications, extended admission, need for substitutive renal therapy, and fivefold increase in hospital mortality [8]. CIAKI's fully iatrogenic and predictable nature makes this disease available for a comprehensive study with focus on its pathophysiology, risk stratification, prophylaxis and treatment.

CI-AKI meets one of the following criteria of acute kidney injury, regardless of etiology [9]:

- Serum creatinine (SC) increase by 26.5 mcmol/l within 48 h;
- SC increase by 1.5+ times above its known or estimated level in previous 7 days;
- Lower diuresis (oliguria <0.5 ml/kg/h) for 6 h (cannot be regarded as a reliable diagnostic criterion, since it rarely develops after CM administration for a variety of reasons).

The key factor in diagnosing and determining nephropathy severity is relative or absolute SC growth in the first 48-72 h after CM injection.

The downside of this definition is hyposensitivity to small oscillations of plasma creatinine, related to renal parenchyma damage, and the absent functional estimation of renal function condition [10-12].

Article Information

DOI: 10.31021/ijrdt.20181102
Article Type: Review
Journal Type: Open Access
Volume: 1 **Issue:** 1
Manuscript ID: IJRDT-1-102
Publisher: Boffin Access Limited

Received Date: April 15, 2018
Accepted Date: May 17, 2018
Published Date: May 19, 2018

*Corresponding author:

Anton Khilchuk
Department of Interventional Radiology
City Hospital No.40,, 197706
9 Borisova str., Sestroretsk
St. Petersburg, Russian Federation
Tel: +7-931-210-46-45
E-mail: anton.khilchuk@gmail.com

Citation: Khilchuk AA, Vlasenko SV, Scherbak SG, Sarana AM. Contrast-induced Acute Kidney Injury: A Contemporary Review. Int J Ren Dis Ther. 2018 May;1(1):102.

Under recommendations by Kidney Disease: Improving Global Outcomes (KDIGO), CIAKI is classified into 3 groups [13] (Table 1).

The problem of using SC as a renal damage biomarker is that SC increase after CM injection characterizes a preexisting decrease in glomerular filtration rate (GFR), not cellular damage. Creatinine increase is only observed 48-72 h after CM injection and has no clinical value during preexisting AKI [14]. However, a study by Ribichini et al. [15] has proved that SC increase by 5% 12 h after CM injection is an AKI marker with 75% sensitivity and 72% specificity. In addition, such SC growth dynamics may be used to estimate a 30-day nephropathy prognosis [15].

However, clinical practice and most studies on CI nephropathy prefer the first definition as a simpler one with superior correlation with clinical outcomes [1,7,16-21].

Based on the fast or nearly instant response by some biomarkers to subclinical AKI, measuring their urine or plasma concentration is now a promising research trend. Significant AKI biomarkers include neutrophil gelatinase-associated lipocalin (NGAL), Cystatin C, Kidney Injury Molecule-1 (KIM-1), and interleukins-6, 8, 18 (IL-6,8,18).

1. Urine or plasma NGAL. Used both for early detection (within 4 h) and prognosis of AKI progression [22-26].
2. Plasma Cystatin C. The plasma level of this biomarker accurately reflects renal function change – 10% increase within 24 h highly likely eliminates AKI presence after CM injection [27-31].
3. Kidney Injury Molecule-1, a Type I transmembrane protein normally absent in the urine, is a sensitive and specific AKI biomarker, under some studies [29,32-36].
4. Measuring concentrations of IL-6,8,18 released by glomerular mesangial cells in response to CIAKI can help detect CIAKI shortly (within 24 h) after contrast X-ray [37-40].

Despite reliable correlation between changes in these markers' concentrations and AKI presence, their routine use is not yet included in current guidelines on CIAKI prophylaxis and treatment for lack of major multicenter studies [6,7,18,41-45] and evidence of the relevant novel biomarker response in contrast-induced acute kidney injury.

Contrast Media

As to CI nephropathy, radiopaque iodinated substances as the prime AKI cause, widely used in modern interventional radiology, cannot escape consideration. The first CM works were published in 1896 by E. Haschek and O. Lindenthal [46]. At that time, bismuth, plumbic and barium salts were used in stump vessel angiography but were unsafe for lifetime diagnostics. In the early 1920s, Osborne et al. [47] found that a syphilis patient's urine, after long-term treatment with iodinated drugs, acquires radiopaque properties. This observation led the researchers to the first successful pyelogram taken at Mayo Clinic in 1923. Intravascular iodinated CM were introduced into clinical practice by urologist Moses Swick [48] in 1928, thus initiating long-term experiments with structural CM modification so as to reduce their toxicity and increase efficiency.

In present-day interventional radiology, iodinated CM remains frontline therapy, despite the significant nephrotoxic effect, due to almost totally absent alternatives.

CM's damaging effect on the renal parenchyma is conditioned by 2 main mechanisms (Figure 1):

1. CM's direct cytotoxic effect on the glomerular endothelium with a developing vasoconstriction of afferent arterioles and the tubular epithelium.
2. CM's indirect effects on blood and urine viscosity, followed by increased intratubular pressure and reduced GFR [49-52]. (Figure 1)

CM's ability to damage, renal tissue results from such factors as ion composition, osmolality, and viscosity (Table 2). Low- or

CIAKI Stage	SC	Diuresis
1	1.5-1.9x up or ≥26.5 mcmol/l (0.3 mg/dL) above baseline	<0.5 ml/kg/h for 6-12 h
2	2.0-2.9x upt	<0.5 ml/kg/h >12 h
3	3x up above baseline or ≥353.6 mcmol/l (4.0 mg/dL) above baseline or need for substitutive therapy or GFR reduction <35 ml/min/1.73 m^2	<0.3 ml/kg/h >24 h or anuria ≥12 h

Table 1: CIAKI severity under KDIGO Clinical Practice Guidelines for Acute Kidney Injury, 2012

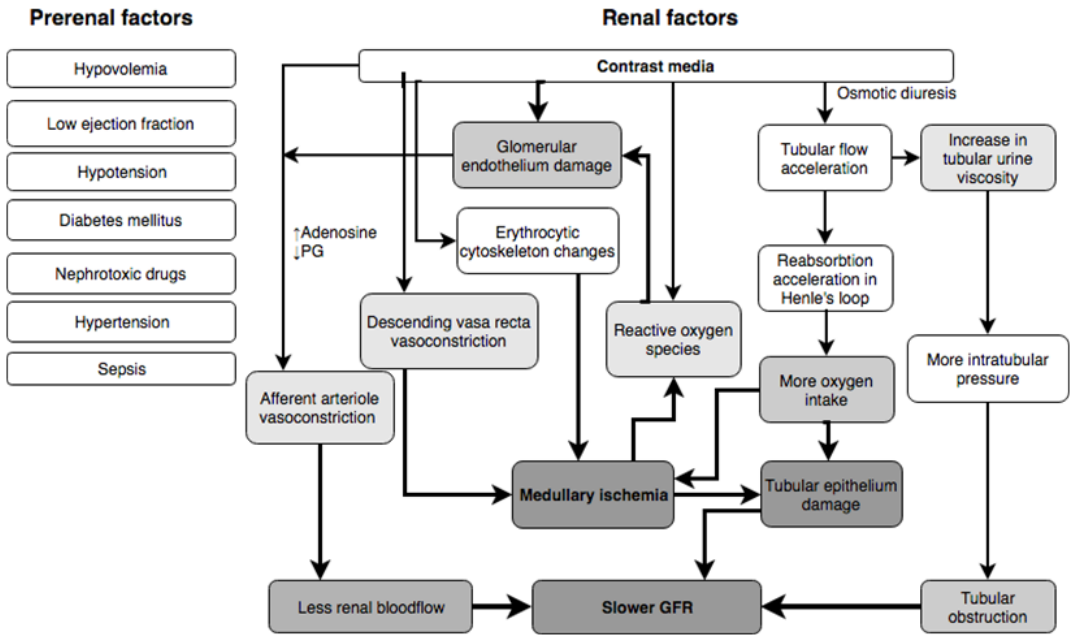

Figure 1: CIAKI pathophysiology
PG: Prostaglandins

isosmolar CM are recognized standards in interventional cardiology, which is confirmed by a number of studies, while ionic CM is used rarely nowadays due to frank nephrotoxicity [17,49,53].

A NEPHRIC study comparing use of isosmolar Iodixanol to low-osmolarIohexol in cohorts of high-risk nephropathy, diabetic patients with initial nephropathy showed ninefold lower CIAKI risk in the Iodixanol cohort [41]. A RECOVER study also showed a lower CIAKI incidence in the cohort administered with isosmolar Iodixanol versus low-osmolar Ioxaglate [54].

Although apparent benefit from using Iodixanol is not confirmed by the majority of clinical studies, the use of low- or isosmolar CM is most encouraged in clinical practice, especially in high-risk patients with strict contraindications against using high-osmolar CM.

CM injection amount is an independent CIAKI risk factor and even in small doses (30 ml) may trigger adverse effects in high-risk patients. Therefore, contrast-using procedures should be done on the "as low as possible" (ALAP) principle, using the precise CM amount to achieve satisfactory image quality. For example, diagnostic coronary angiography requires optimal CM amount at <30 ml, with minimum of 100 ml for percutaneous coronary intervention (PCI) [8,55]. The maximum allowable contrast dose (MACD) is calculated by the formula "5 ml CM x body weight [kg]/initial plasma creatinine [mg/DL]"[56] and must not exceed allowable values.

Speaking about iodinated CM alternatives, first of all we should mention a gadolinium CM, usage of which did not show superiority to iodinated media in patients with moderate renal function impairment [57,58]. According to some researchers, gadolinium CM rises the incidence of nephrogenic systemic sclerosis (also known as nephrogenic fibrosing dermopathy) – serious invalidizing skin and internal organs sclerosis [59,60], however a series of multiple studies showed no evidence of that statement [61,62].

A promising yet controversial iodinated CM, alternative carbon dioxide is contraindicated in intra-arterial injection above the diaphragm (coronary and brachiocephalic arteries, thoracic aorta). CO_2 is currently used only in diagnostic endovascular procedures below the diaphragm (abdominal aorta, lower limb vessels) through an introduction system (CO_2mmander) and portable tanks with carbon dioxide [63-65]. (Table 2)

Risk Factors

The patient's CIAKI risk during contrast X-ray must be measured before preoperative assessment and selecting the CM type.

There are several proved CIAKI risk factors:

1. Initial nephropathy is the strongest CIN predictor, as proved by most studies [6,7,18,41-45]. Specifically, patients with very low creatinine clearance before the procedure (<40 ml/min) are 10 times more likely to suffer from CIAKI versus the cohort with a normal renal function [45].
2. The presence of diabetes mellitus with diabetic nephropathy predisposes to developing adverse renal complications during CM injection, while diabetes mellitus with a normal renal function hardly affects CIAKI development [9,45,66]. Other major CIAKI risk factors are in the Table 3.

Risk Assessment

Given that patients with chronic kidney disease (CKD) and GFR<60 ml/min/1.73 m^2 are predisposed to a high CIN risk, all CM procedure candidates must have their GFR measured. Since CIAKI results from many factors, isolated GFR measurement does not reliably identify nephropathy risk, so risk assessment systems are developed based on the cumulative effect of many factors [67-69]. Clinical practice prefers several systems for measuring perceived CIAKI risk.

As calculated by Maioli et al. [44] risk stratification should factor in 7 basic parameters (Table 4) [70]. Availability of each parameter is assessed in points resulting in patient distribution into low, medium, high and very high-risk cohorts. CM injection in previous 72 h, low LVEF, difference between SC before the procedure and initial creatinine, higher initial creatinine, diabetes mellitus, 73+ age, and lower GFR are factored in. (Table 4)

Mehran et al. [68] developed a calculation system with 8 variables (Table 5). In addition to patient distribution into low, medium, high and very high-risk cohorts, dialysis probability and death risk are also estimated. Points are awarded for hypotension, CKD, IABP, CHF, diabetes mellitus, 75+ age, anemia, and administered CM amount.

The most up-to-date, though uncommon, system in clinical

	Blood plasma	Isosmolar CM (Iodixanol)	Low-osmolar CM (Iohexol)	High-osmolar CM (Diatrizoate)
Osmolality, mosm/kg H_2O	290	290	890	2,100
Viscosity, mPa.s	3-4	8.8	6.8	4.1
Ion composition		Nonionic	Nonionic	Ionic
Molecular composition		Dimer	Monomer	Monomer
CIAKI exposure	-	Low	Low	High

Table 2: CM comparison
CM : Contrast Media; CIAKI: Contrast-induced Acute Kidney Injury

	Non-modifiable	Modifiable
Patient factors	Age Female Diabetes mellitus Hypertension Renal damage CHF Myeloma Albuminuria	Anemia Hypovolemia Nephrotoxic drugs Hypoalbuminemia Higher glucose level Higher low-density lipoprotein level
Procedure factors	Manipulation urgency	Periprocedural hypotension Intra-arterial injection Large CM amount High-osmolar ionic CM Intraoperative hemorrhage IABP

Table 3: CIAKI risk factors
CHF: Chronic Heart Failure; IABP: Intra-Aortic Balloon Pump

practice is the one by Tziakas et al. [18] (Table 6), using 5 variables, including the presence of previously detected CKD, permanent metformin introduction, previously done PCI, obliterating atherosclerosis of peripheral arteries and intraoperative injected CM amount. The score is distributed among 3 CIAKI exposure cohorts: low, medium and high-risk. (Table 6)

Having assessed perceived CIAKI exposure, it is necessary to start preparing the patient for the procedure, based on the standardized prophylaxis and treatment protocol (Figure 2) [71].

Prophylaxis

CIAKI prophylaxis should begin with the cancellation of the patient's nephrotoxic drugsamong non-steroidal anti-inflammatory, antifungal, antiviral, antitumoral ones, immunosuppressants and antibiotics, especially aminoglycosides, 24 h before the study. In diabetic patients, metformin introduction must be canceled 48 h before and limited 48 h after CM injection. ACE inhibitors and angiotensin receptor blockers, due to possible harm and inadequate data on their positive effects on renal hemodynamics and GFR, should be excluded from therapy 1 day before the study, although, under the KDIGO consensus, this allegation has not been fully proved [13,72].

To date, intravenous loading with a 0.9% NaCl solution is the only proved efficient CIAKI prophylactic measure [9,41,42,45,73-76]. Despite the aforesaid superiority of using intravenous sodium bicarbonate, its role in nephropathy prophylaxis is comparable to 0.9% NaCl, based on the findings of some randomized studies [66,73,75,77]. Although one study did show the benefits of high sodium bicarbonate concentrations (833 mEq/L) [78], clinical guidelines for nephropathy prophylaxis have not supported this fact.

N-acetylcysteine (NAC) was widely used in CIAKI prophylaxis in high-risk patients, based on some positive observations, in a dose of 600 mg twice a day, 2 days before the planned study [79]. Subsequent studies (~40 clinical trials and 13 meta-analyses) using both high oral NAC doses and intravenous drug injection showed contradictory

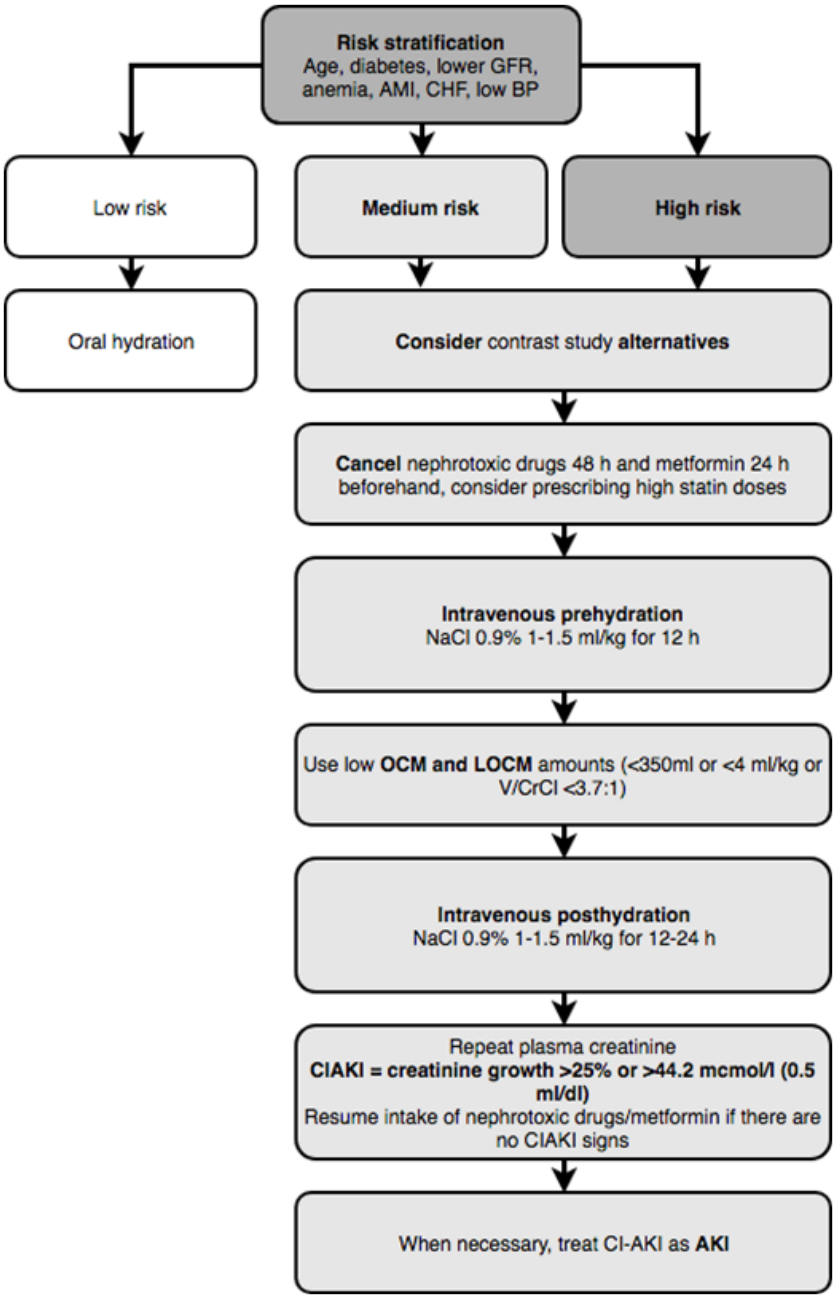

Figure 2: Algorithm of prophylaxis and treatment of patients with different CIAKI exposure [71]
AMI: Acute Myocardial Infarction; BP - Blood Pressure; Nacl: Sodium Chloride; IOCM: Isosmolar Contrast Media; LOCM: Low-Osmolar Contrast Media; V/Crcl - Ratio of Injected CM to Creatinine Clearance

Risk factor				Score
CM injection in previous 72 h				3
LVEF <45%				2
Preprocedural SC >initial SC				2
Initial SC >132.6 mcmol/l (1.5 mg/dL)				2
Diabetes mellitus				2
GFR<44 ml/min				2
Age >73				1
Result	**0-3**	**4-6**	**7-8**	**>9**
CIAKI risk	Low 1.1%	Medium 7.5%	High 22.3%	Very high 52.1%

Table 4. CIAKI risk stratification [70]
CM: Contrast Media; LVEF: Left Ventricular Ejection Fraction; SC: Serum Creatinine; GFR: Glomerular Filtration Rate; CIAKI: Contrast- Induced Acute Kidney Injury

Risk factor				Score
Hypotension (SBP<80 mmHg or >1 h of inotropic support)				5
IABP				5
CHF (NYHA III/IV or recent pulmonary edema)				5
Age >75				4
Diabetes mellitus				3
Anemia (M: HCT <0.39, F: HCT <0.36)				3
GRF <20 ml/min				6
GRF <20-40 ml/min				4
GFR <40-60 ml/min				2
CM amount				1 point per 100 ml
Result	**0-3**	**4-6**	**7-8**	**>9**
CIAKI risk	Low 7.5%	Medium 14%	High 26.1%	Very high 57.3%
Dialysis risk	0.04%	0.12%	1.09%	12.6%

Table 5: CIAKI exposure stratification [68]
SBP: Systolic Blood Pressure; IABP: Intraaortic Balloon Pump; CHF: Congestive Heart Failure; NYHA: New York Heart Association; HCT: Hematocrit; GFR: Glomerular Filtration Rate;CM: Contrast Media; CIAKI: Contrast-Induced Acute Kidney Injury.

Risk factor			Score
CKD			2
Metformin administration			2
Previously performed PCI			1
Presence of obliterating atherosclerosis of peripheral arteries			2
CM amount ≥300 ml			1
Result	**0-1**	**2-3**	**>4**
CIAKI risk	Low 3-11%	Medium 11-27%	High 27-83%

Table 6: CIAKI exposure stratification [18]
CKD: Chronic Kidney Disease; PCI: Percutaneous Coronary Intervention; CM: Contrast Media; CIAKI: Contrast-induced Acute Kidney Injury

results. NAC use causes no side effects (except for anaphylactoid reactions to high intravenous and oral doses) and is generally not contraindicated in CIAKI prophylaxis [42,45,80].

The most recent, major and well-designed PRESERVE (Prevention of Serious Adverse Events Following Angiography) study comparingintravenous 1.26% sodium bicarbonate, intravenous 0.9% sodium chloride and 5 days, oral acetylcysteine and oral placebo showed no benefit of intravenous sodium bicarbonate over intravenous sodium chloride or of oral acetylcysteine over placebofor the prevention of death, need for dialysis, or persistent decline in kidney function at 90 days or for the prevention of CIAKI [81].

Atrial natriuretic peptide, dopamine, fenoldopam as well as theophylline and ascorbic acid have not demonstrated positive effects in CIAKI prophylaxis, whereas forced diuresis with mannitol or furosemide is contraindicated due to its damaging action [42,45].

Using prostaglandin E1 and statins has shown clinical benefits, but insufficient observation still prevents their adoption. Targeted therapy with the infusion system Benefit™ for selective fenoldopam delivery and using the RenalGuard™ infusion system demonstrated a lower CIAKI incidence only in few minor clinical trials [82-84].

Patients already under hemodialysis do not require volume support before a contrast study, and dialysis after the procedure is necessary only with frank liquid overload. As to hemofiltration, benefits in high-risk cohorts were not confirmed, despite some authors' successful use in very high-risk patients with Stage 5 CKD before and after the radiographic contrast study [19,21,85,86].

Safe CM reinjection time is not exactly defined, but, according to the average renal function recovery time with CIAKI (3 weeks), this period is recommended for a repeated contrast study.

For high-risk patients, daily SC control for 5 days is indicated, and in case of oliguria, patient treatment is the same as with other AKI reasons including monitoring of acid-base, electrolyte and fluid

balances. Severe cases may require temporary hemodialysis and permanent one in exceedingly rare cases [87,88].

Conclusion

Clinically significant CIAKI is a major complication of endovascular radiographic procedures, associated with high morbidity, mortality rates, and consequent socioeconomic losses. Despite few guideline differences, there are several strict positions in CIAKI prophylaxis and treatment. Early detection of high CIAKI exposure in patients is crucial for timely initiation of preventive measures and reducing likelihood of renal parenchyma damage and further nephropathy. In interventional cardiologists' and radiologists' practice, preference must be given to using only low-and isosmolar CM as less as possible. Based on the rapid or nearly instant reaction of some biomarkers to subclinical AKI, measuring their urine or plasma concentration is now a promising research trend, although their routine usage is not yet featured in current guidelines for CIAKI prophylaxis and treatment. Intravenous loading with a 0.9% sodium chloride solution is the only proven efficient CIAKI prophylactic measure, whereas other pharmacological support is either damaging or requires further research and more prospective studies.

References

1. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006 Apr; 69(100):S11–S15.
2. Bartels ED, Brun GC, Gammeltoft A, Gjørup PA. Acute anuria following intravenous pyelography in a patient with myelomatosis. Acta Med Scand. 1954;150(4):297–302.
3. Killmann SA, Gjorup S, Thaysen JH. Fatal acute renal failure following intravenous pyelography in a patient with multiple myeloma. Acta Med Scand. 1957 Jul;158:(1):43–46.
4. McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med. 1997;103(5):368-375.
5. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis. 2002;39(5):930–936.
6. Finn WF. The clinical and renal consequences of contrast-induced nephropathy. Nephrol Dial Transplant. 2006 Jun;21(6):i2-10.
7. Caixeta A, Nikolsky E, Mehran R. Prevention and treatment of contrast-associated nephropathy in interventional cardiology. Curr Cardiol Re. 2009 11(5):377–383.
8. McCullough PA, Choi JP, Feghali GA, Schussler JM, Stoler RM, et al. Contrast-Induced Acute Kidney Injury J. Am. Coll. Cardiol. Elsevier, 2016 Sep;68(13):1465–1473.
9. Morcos S.K, Thomsn HS, Webb JA. Contrast-media-induced nephrotoxicity: a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). Eur Radiol. 1999;9(8):1602–1613.
10. Solomon RJ, Mehran R, Natarajan MK, Doucet S, Katholi RE, et al. Contrast-induced nephropathy and long-term adverse events: Cause and effect? Clin J Am Soc. Nephrol. 2009 Jul;4(7):1162–1169.
11. Weisbord SD, Chen H, Stone RA, Kip KE, Fine MJ, et al. Associations of Increases in Serum Creatinine with Mortality and Length of Hospital Stay after Coronary Angiography. J Am Soc Nephrol. 2006 Oct 17(10):2871–2877.
12. Kellum JA, Mehta RL, Levin A, Molitoris BA, Warnock DG, et al. Development of a clinical research agenda for acute kidney injury using an international, interdisciplinary, three-step modified Delphi process Clin J Am Soc Nephrol. 2008 May;3(3):887–894.
13. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury Nephron Clin Pract. 2012;120(4):179–184.
14. Waikar SS, Bonventre JV. Creatinine kinetics and the definition of acute kidney injury. J Am Soc Nephrol. 2009 Mar;20(3):672–679.
15. Ribichini F, Graziani M, Gambaro G, Pasoli P, Pighi M, et al. Early creatinine shifts predict contrast-induced nephropathy and persistent renal damage after angiography Am J Med Elsevier Inc. 2010 Aug;3(8):755–763.
16. Mehran R, Nikolsky E, Kirtane AJ, Caixeta A, Wong SC, et al. Ionic Low-Osmolar Versus Nonionic Iso-Osmolar Contrast Media to Obviate Worsening Nephropathy After Angioplasty in Chronic Renal Failure Patients. JACC Cardiovasc Interv. 2009 May;2(5):415–421.
17. Pandya B, Chalhoub JM, Parikh V, Gaddam S, Spagnola J, et al. Contrast media use in patients with chronic kidney disease undergoing coronary angiography: A systematic review and meta-analysis of randomized trials. Int J Cardiol. 2017 Feb;228(6):137–144.
18. Tziakas D, Chalikias G, Stakos D, Apostolakis S, Adina T, et al. Development of an easily applicable risk score model for contrast-induced nephropathy prediction after percutaneous coronary intervention: A novel approach tailored to current practice. Int J Cardiol. 2013 Feb;163(1):46–55.
19. Choi MJ, Yoon JW, Han SJ, Choi HH, Song YR, et al. The prevention of contrast-induced nephropathy by simultaneous hemofiltration during coronary angiographic procedures: A comparison with periprocedural hemofiltration. Int J Cardiol. 2014 ;176(3):941–945.
20. Parfrey. The clinical epidemiology of contrast-induced nephropathy. Cardiovasc Interv Radiol. 2005;28 Suppl 2:S3-11.
21. Chang CF, Lin CC. Current concepts of contrast-induced nephropathy: A brief review. J Chin Med Assoc. 2013 Dec;6(12):673–681.
22. Filiopoulos V, Biblaki D, Vlassopoulos D. Neutrophil gelatinase-associated lipocalin (NGAL): a promising biomarker of contrast-induced nephropathy after computed tomography. Ren Fail. 2014 Jul;36(6):979–986.
23. Ribitsch W, Schilcher G, Quehenberger F, Pilz S, Portugaller RH ,et al. Neutrophil gelatinase-associated lipocalin (NGAL): fails as an early predictor of contrast induced nephropathy in chronic kidney disease (ANTI-CI-AKI study). Sci Rep. 2017 Jan; 7:41300.
24. Schilcher G, Ribitsch W, Otto R, Portugaller RH, Quehenberger F, et al. Early detection and intervention using neutrophil gelatinase-associated lipocalin (NGAL): may improve renal outcome of acute contrast media induced nephropathy: A randomized controlled trial in patients undergoing intra-arterial angiography. BMC Nephrol. 2011 Aug 12:39.
25. Filiopoulos V, Biblaki D, Lazarou D,Chrisis D, Fatourou M, et al. Plasma neutrophil gelatinase-associated lipocalin (NGAL): as an early predictive marker of contrast-induced nephropathy in hospitalized patients undergoing computed tomography. Clin Kidney J. 2013 6(6):578–583.
26. You W, Qi CL, Ye F, Huang SL, Xie DJ, et al. [The value of urinary neutrophil gelatinase-associated lipocalin for early diagnosis of contrast-induced nephropathy]. Europe PMC. 2016 Dec;44(12):1024–1029.
27. Bachorzewska-Gajewska H, Malyszko J, Sitniewska E, Malyszko JS, Pawlak K, et al. Could Neutrophil-Gelatinase-Associated Lipocalin and Cystatin C Predict the Development of Contrast-Induced Nephropathy after Percutaneous Coronary Interventions in Patients with Stable Angina and Normal Serum Creatinine Values? Kidney Blood Press Res. 2007;30(6):408–415.
28. Ribichini F, Gambaro G, Graziani MS, Pighi M, Pesarini G, et al. Comparison of serum creatinine and cystatin C for early diagnosis of contrast-induced nephropathy after coronary angiography and interventions Clin Chem. 2012 Feb;58(2):458–464.
29. Malyszko J, Bachorzewska-Gajewska H, Poniatowski B, Malyszko JS, Dobrzycki S, et al. Urinary and Serum Biomarkers after Cardiac Catheterization in Diabetic Patients with Stable Angina and without Severe Chronic Kidney Disease Ren. Fail. 2009;31(10):910–919.
30. Ashalatha VL, Bitla AR, Kumar VS, Rajasekhar D, Suchitra MM, et al. Biomarker response to contrast administration in diabetic and nondiabetic patients following coronary angiography. Indian J Nephrol. 2017 Jan-Feb;27(1):20–27.
31. Duan SB, Liu GL, Yu ZQ, Pan P. Urinary KIM-1, IL-18 and Cys-c as early predictive biomarkers in gadolinium-based contrast-induced nephropathy in the elderly patients Clin Nephrol. 2013;80(11):349–354.

32. El-Ashmawy NE, El-Zamarany EA, KhedrNF, Abd El-Fattah AI, Eltoukhy SA, et al. Kidney injury molecule-1 (Kim-1):: an early biomarker for nephropathy in type II diabetic patients. Int J Diabetes Dev Ctries. 2015 Nov;35:431–438.
33. Han WK, Bailly V, Abichandani R, Thadhani R, Bonventre JV. Kidney Injury Molecule-1 (KIM-1): A novel biomarker for human renal proximal tubule injury. Kidney Int. 2002 Jul;62(1):237–244.
34. Bonventre JV. Kidney Injury Molecule-1 (KIM-1): A specific and sensitive biomarker of kidney injury Scand. J Clin Lab Invest. 2008;68(sup241):78–83.
35. van Timmeren MM, van den Heuvel MC, Bailly V, Bakker SJ, van Goor H, et al. Tubular kidney injury molecule-1 (KIM-1): in human renal disease. J Pathol. 2007 Jun;212(2):209–217.
36. Zhao X, Jiang C, Olufade R, Liu D, Emmett N, et al. Kidney Injury Molecule-1 Enhances Endocytosis of Albumin in Renal Proximal Tubular Cells. J Cell Physiol. 2016 231(4):896–907.
37. Pianta TJ, et al. Monitoring Treatment of Acute Kidney Injury with Damage Biomarkers Toxicol Lett. 2017 Feb;268:63-70.
38. Guan X, Chen QJ, Zuo XC, Guo R, Peng XD, et al. Contrast Media-Induced Renal Inflammation Is Mediated Through HMGB1 and Its Receptors in Human Tubular Cells. DNA Cell Biol. 2017 Jan;36(1):67–76.
39. Lichosik M, Jung A, Jobs K, Mierzejewska A, Zdanowski R, et al. Interleukin 18 and neutrophil-gelatinase associated lipocalin in assessment of the risk of contrast-induced nephropathy in children. Cent Eur J Immunol. 2015;40(4):447–453.
40. Mawad H, Laurin LP, Naud JF, Leblond FA, Henley N, et al. Changes in urinary and serum levels of novel biomarkers after administration of gadolinium-based contrast agents. Biomark Insights. 2016 Jun;11:91–94.
41. Aspelin P, Aubry P, Fransson SG, Strasser R, Willenbrock R, et al. Nephrotoxic Effects in High-Risk Patients Undergoing Angiography N Engl J Med. 2003;348(6):491-499.
42. Bagshaw SM, Culleton BF. Contrast-induced nephropathy: Epidemiology and prevention Minerva Cardioangiologica. 2006 Feb;54(1):109–129.
43. McCullough PA, Sandberg KR. Epidemiology of contrast-induced nephropathy. Rev Cardiovasc Med. 2003;4 Suppl 5:S3-S9.
44. Sarabu N, Rahman M. Nephrology Update: Acute Kidney Injury. FP Essent. 2016 May;444:11–17.
45. Sudarsky D, Nikolsky E. Contrast-induced nephropathy in interventional cardiology. Int J Nephrol Renovasc Dis. 2011 4:85–99.
46. Haschek ELO. A contribution to the practical use of photography according to Roentgen. Wien Chir Wochenschr. 1896. (9):63.
47. Osborne ED, Sutherland CG, Scholl AJ Jr, Rowntree LG, et al. Landmark article Feb 10, 1923: Roentgenography of urinary tract during excretion of sodium iodid. By Earl D. Osborne, Charles G. Sutherland, Albert J. Scholl, Jr. and Leonard G. Rowntree. JAMA. 1983 Nov;250(20):2848–2853.
48. Loughlin K.R, Hawtrey CE. Moses Swick, the father of intravenous urography. Urology. 2003 Aug;62(2):385–389.
49. Sendeski MM. Pathophysiology of renal tissue damage by iodinated contrast media. Clin Ex Pharmacol Physiol. 2011 38(5):292–299.
50. Sendeski MM, Persson AB, Liu ZZ, Busch JF, Weikert S, et al. Iodinated contrast media cause endothelial damage leading to vasoconstriction of human and rat vasa recta AJP Ren. Am J Physiol Renal Physiol. 2012 Dec;303(12)1592–1598.
51. McCullough PA, Adam A, Becker CR, Davidson C, Lameire N ,et al. Risk Prediction of Contrast-Induced Nephropathy Am J Cardiol. 2006;98(6):27–36.
52. Brezis MRS. Hypoxia of the Renal Medulla — Its Implications for Disease .N Engl J Med. 1995 Mar;332(10):647–655.
53. Cooper MW, Reed PJ. Comparison of ionic and non-ionic contrast agents in cardiac catheterization: the effects of ventriculography and coronary arteriography on hemodynamics, electrocardiography, and serum creatinine. Cathet Cardiovasc Diagn. 1991;22(4):267–277.
54. Jo SH, Youn TJ, Koo BK, Park JS, Kang HJ, et al. Renal toxicity evaluation and comparison between visipaque (iodixanol): and hexabrix (ioxaglate): in patients with renal insufficiency undergoing coronary angiography: the RECOVER study: a randomized controlled trial. J Am Coll Cardiol. 2006 Sep;48(5):924–930.
55. McCullough PA. Contrast-Induced Acute Kidney Injury. J Am Coll Cardiol. 2008 Apr;51(15):1419–1428.
56. Cigarroa RG, Lange RA, Williams RH, Hillis LD. Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. Am J Med. 1989 Jun;86(6 Pt 1):649–652.
57. Michaely HJ, Aschauer M, Deutschmann H, Bongartz G, Gutberlet M, et al. Gadobutrol in Renally Impaired Patients. Invest Radiol. 2017;52(1):55–60.
58. Cubero-Gómez JM, Guerrero Márquez FJ, Diaz-de la-Llera L, Fernández-Quero M, Guisado-Rasco A, et al. Severe thrombocytopenia induced by iodinated contrast after coronary angiography: The use of gadolinium contrast and intravascular ultrasound as an alternative to guide percutaneous coronary intervention. Rev Port Cardiol. 2017 Jan;36(1):61.e1-61.e4.
59. He A, Kwatra SG, Zampella JG, Loss MJ. Nephrogenic systemic fibrosis: fibrotic plaques and contracture following exposure to gadolinium-based contrast media. BMJ Case Rep. 2016 Apr;2016.
60. Ozawa Y, Hayashi S, Hamasaki Y, Hatamochi A, et al. Effects of Gadodiamide on cell proliferation and collagen production in cultured human dermal fibroblasts. Arch Dermatol Res. 2016 Dec;308(10):695-701.
61. Bryant BJ, Im K, Broome DR. Evaluation of the incidence of nephrogenic systemic fibrosis in patients with moderate renal insufficiency administered gadobenate dimeglumine for MRI. Clin Radiol. 2009; 64(7):706-713.
62. Soulez G, Bloomgarden DC, Rofsky NM, Smith MP, Abujudeh HH, et al. Prospective Cohort Study of Nephrogenic Systemic Fibrosis in Patients With Stage 3–5 Chronic Kidney Disease Undergoing MRI With Injected Gadobenate Dimeglumine or Gadoteridol. AJR Am J Roentgenol. 2015 Sep;205(3):469-478.
63. Caridi JG. Vascular Imaging with Carbon Dioxide: Confidence in a Safe, Efficacious, User-Friendly System. Semin Intervent Radiol. 2015; 32(4):339-342.
64. Renton M, Hameed MA, Dasgupta I, Hoey ET, Freedman J, et al. The use of carbon dioxide angiography for renal sympathetic denervation: a technical report. Br J Radiol. 2016 Dec;89(1068):2016031.
65. de Almeida Mendes C, de Arruda Martins A, Teivelis MP, Kuzniec S, Varella AY, et al. Carbon Dioxide as Contrast Medium to Guide Endovascular Aortic Aneurysm Repair. Ann Vasc Surg. 2017 Feb;39:67-73.
66. Hörl WH. Contrast induced nephropathy Wien Klin Wochenschr. 2009; 121(1-2):15-32.
67. Victor SM, Gnanaraj A, S V, Deshmukh R, Kandasamy M, et al. Risk scoring system to predict contrast induced nephropathy following percutaneous coronary intervention Indian Heart J. 2014; 66(5):517-524.
68. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: Development and initial validation. J Am Coll Cardiol. 2004 Oct;44(7):1393-1399.
69. Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, et al. Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. Am J Cardiol. 2004 Jun;93(12):1515-1519.
70. Maioli M, Toso A, Gallopin M, Leoncini M, Tedeschi D, et al. Preprocedural score for risk of contrast-induced nephropathy in elective coronary angiography and intervention. J Cardiovasc Med (Hagerstown). 2010 Jun;11(6):444-449.
71. Rear R, Bell RM, Hausenloy DJ.. Contrast-induced nephropathy following angiography and cardiac interventions. Heart. 2016 Apr;102(8):638-648.
72. Kalyesubula R, Bagasha P, Perazella MA.. ACE-I/ARB therapy prior to contrast exposure: What should the clinician do? Biomed Res Int. 2014;2014:423848.

73. Brar SS, Shen AY, Jorgensen MB, Kotlewski A, Aharonian VJ, et al. Sodium Bicarbonate vs Sodium Chloride for the Prevention of Contrast Undergoing Coronary Angiography. JAMA. 2008 Sep;300(9):1038-1046.
74. Busch SV, Jensen SE, Rosenberg J, Gögenur I. Prevention of contrast-induced nephropathy in STEMI patients undergoing primary percutaneous coronary intervention: A systematic review. J Interv Cardiol. 2013 Feb;26(1):97-105.
75. Maioli M, Toso A, Leoncini M, Gallopin M, Tedeschi D, et al. Sodium Bicarbonate Versus Saline for the Prevention of Contrast-Induced Nephropathy in Patients With Renal Dysfunction Undergoing Coronary Angiography or Intervention. J Am Coll Cardiol. 2008 Aug;52(8):599-604.
76. Wu YW, Leow KS, Zhu Y, Tan CH.. Prevention and Management of Adverse Reactions Induced by Iodinated Contrast Media. Ann Acad Med Singapore. 2016 Apr;45(4):157-164.
77. Dong Y, Zhang B, Liang L, Lian Z, Liu J, et al. How Strong Is the Evidence for Sodium Bicarbonate to Prevent Contrast-Induced Acute Kidney Injury After Coronary Angiography and Percutaneous Coronary Intervention?. Medicine (Baltimore). 2016 Feb;95(7):e2715.
78. Tamai N, Ito S, Nakasuka K, Morimoto K, Miyata K, et al. Sodium bicarbonate for the prevention of contrast-induced nephropathy: the efficacy of high concentration solution. J Invasive Cardiol. 2012 Sep;24(9):439-342.
79. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, et al. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. N Engl J Med. 2000 Jul;343(3):180-184.
80. Wang N, Qian P, Kumar S, Yan TD, Phan K. The effect of N-acetylcysteine on the incidence of contrast-induced kidney injury: A systematic review and trial sequential analysis. Int J Cardiol. 2016 Apr;209:319-327.
81. Weisbord SD, Martin G, Hani Jneid, Santiago G, Alan C, Soe-Soe T, et al. Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine. N Engl J Med. 2017;378(7):603-614.
82. Briguori C, Visconti G, Donahue M, De Micco F, Focaccio A, et al. RenalGuard system in high-risk patients for contrast-induced acute kidney injury. Am Heart J. 2016 Mar;173:67-76.
83. Weisz G, Filby SJ, Cohen MG, Allie DE, Weinstock BS, et al. Safety and Performance of Targeted Renal Therapy: The Be-RITe! Registry. J Endovasc Ther. 2009 Feb;16(1):1-12.
84. Andreucci M, Faga T, Pisani A, Sabbatini M, Michael A. Acute kidney injury by radiographic contrast media: Pathogenesis and prevention. BioMed Res Int. 2014.
85. Rey JR, Iglesias D, López De Sá E, Armada E, Moreno R, Salvador O, et al. Prevention of contrast-induced nephropathy with haemofiltration in high-risk patients after percutaneous coronary intervention. Acute Card Care. 2011 Sep;13(3):164-169.
86. Spini V, Cecchi E, Chiostri M, Landi D, Romano SM, et al. Effects of two different treatments with continuous renal replacement therapy in patients with chronic renal dysfunction submitted to coronary invasive procedures. J Invasive Cardiol. 2013;25(2):80-84.
87. Rudnick MR, Berns JS, Cohen RM, Goldfarb S. Contrast media-associated nephrotoxicity. Semin Nephrol. 1997 Jan;17(1):15-26.
88. Brady HR, Singer GG. Acute Renal Failure. Lancet. 1995 Dec;346(8989):1533-1540.