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An Overview about Contrast Induced Nephropathy in Elderly Patients

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Abstract:Background: A rise in blood creatinine or a decrease in urine volume are symptoms of (AKI), which is a sudden and frequently reversible loss of kidney function. Kidney Disease Improving Global Outcomes (KDIGO) provided an updated definition, which is currently the most widely used. According to KDIGO, CI-AKI is defined as a creatinine level increase of ≥ 0.3 mg/dl (26.5 µmol/l) above baseline value within 48 h of contrast media exposure, or an increase of at least 1.5 times the baseline value within 7 days. Contrast induced nephropathy (CIN) is defined as acute renal impairment after exposure to iodinated contrast media (CM). In the modern era with the advancement of the diagnostic modalities, increase in number of percutaneous coronary and peripheral artery interventions and frequent use of contrast media, CIN has emerged as a common cause of acute renal failure. Mostly, it results in transient renal impairment; however in patients with multiple comorbidities it can be associated with high morbidity and mortality. It is therefore imperative to identify patients at risk to decrease its occurrence and diagnose it early in course to avoid short and long term clinical adverse effects. It presents a challenging situation that is often encountered by practitioners in varied specialties including emergency medicine, nephrology, cardiology, radiology and intensive care unit (ICU). Currently, contrast-associated acute **kidney** injury (CA-AKI) is a common cause of hospital-acquired AKI in the older patients

Keywords: Contrast Induced Nephropathy, Elderly patients

Introduction

A rise in blood creatinine or a decrease in urine volume are symptoms of (AKI), which is a sudden and frequently reversible loss of kidney function. Serum creatinine levels that rise by at least 0.3 mg/dl in less than 48 hours, levels that rise by at least 1.5 times the baseline value in less than 7 days, or urine output that is less than 0.5 ml/kg/h for six hours are all considered signs of AKI. Atherosclerotic renal disease is more likely to require long-term renal replacement treatment and is highly related with inferior outcomes following immediate (PCI) for acute coronary syndrome **(1).**

The most precise marker for mortality and serious adverse cardiovascular events is an increase in blood creatinine of 0.3 mg/dL 48 hours after PCI. Contrast-associated AKI (CA-AKI) can be brought on by kidney injury, lipid embolism, renal medulla ischemia, and vasoconstriction. Some biomarkers, such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury marker 1 (KIM-1), liver fatty acid-binding protein (L-FABP), and interleukin 18 (IL-18), are employed for early detection of contrast-induced AKI (CI-AKI), as serum creatinine is a delayed sign. An increase in creatinine level of ≥ 0.5 mg/dl (44 μmol/l), or ≥ 25% from baseline, within 2–5 days of contrast exposure had been the universal definition of CI-AKI for a longtime **(2).**
Kidney Disease Improving Global Outcomes (KDIGO) provided an updated definition, which is currently the most widely used. According to KDIGO, CI-AKI is defined as a creatinine level increase of ≥ 0.3 mg/dl (26.5 μmol/l) above baseline value within 48 h of contrast media exposure, or an increase of at least 1.5 times the baseline value within 7 days**.** However, it is important to note that although serum creatinine level is associated with moderate sensitivity, its specificity is low as it is directly affected by fluid shifts and administered drugs **(2).**
Contrast induced nephropathy (CIN) is defined as acute renal impairment after exposure to iodinated contrast media (CM). In the modern era with the advancement of the diagnostic modalities, increase in number of percutaneous coronary and peripheral artery interventions and frequent use of contrast media, CIN has emerged as a common cause of acute renal failure. Mostly, it results in transient renal impairment; however in patients with multiple comorbidities it can be associated with high morbidity and mortality. It is therefore imperative to identify patients at risk to decrease its occurrence and diagnose it early in course to avoid short and long term clinical adverse effects. It presents a challenging situation that is often encountered by practitioners in varied specialties including emergency medicine, nephrology, cardiology, radiology and intensive care unit (ICU) (**3**).

Epidemiology
CIN remains an important cause of in-hospital AKI, accounting for approximately 11% of the total cases of AKI. CIN occur following exposure to iodinated contrast during coronary or peripheral angiography or diagnostic imaging, however recent data shows contrast exposure associated with modern radiographic procedure is not associated with significant increase in CIN incidence (**4**).
In general population without any risk factor, incidence of CIN is very low; however risk increases as comorbidities increases. Critically ill patients with baseline renal impairment are particularly susceptible and contrast enhanced computed tomography (CECT) might account for 18% of AKI cases in this population. The incidence of CIN can reach 20–25% in patients who receive coronaray angiography and/or PCI, and even 40% in high-risk groups (**5**).
Reported incidence of CIN varies with the procedure and is reported to be 11% after outpatient CECT, 4% following intravenous pyelography, 9% after peripheral arteriography (4),< 3% following percutaneous trans-luminal coronary angioplasty (PTCA) in patient with normal renal function and as high as 40% in patient with underlying renal impairment (**6**).

The underlying pathophysiology
The exact pathophysiology of CIN is not fully understood. Direct cytotoxicity, altered intrarenal hemodynamics, and Reactive Oxygen Species. (ROS) generation have been proposed as the main pathophysiologic mechanisms of CIN **(7).**
Iodinated CM has direct cytotoxic effect on endothelial cells and renal tubular epithelial cells, induces vasoconstriction causing hypoxia in the outer medulla, and enhances the generation of reactive oxygen species. These changes influence one another and ultimately lead to kidney injury. Hydration is the mainstay of CIN preventive strategies and can reduce harmful effect of CM in all three aspects **(7).**
Other previously reported preventive measures and pharmaceutical agents are presented with regard to each pathogenic process. These pharmaceutical agents have been studied in in vitro and in vivo experiments to

reduce oxidative stress, that is, to reverse each pathogenic pathway. However, because Nuclear factor erythtoid 2_related factor 2 (Nrf2) expression increases during CM-induced oxidative stress as a cytoprotective response, Nrf2 activation is preventive against CIN. The preventive role of these agents on CIN is controversial **(7).**

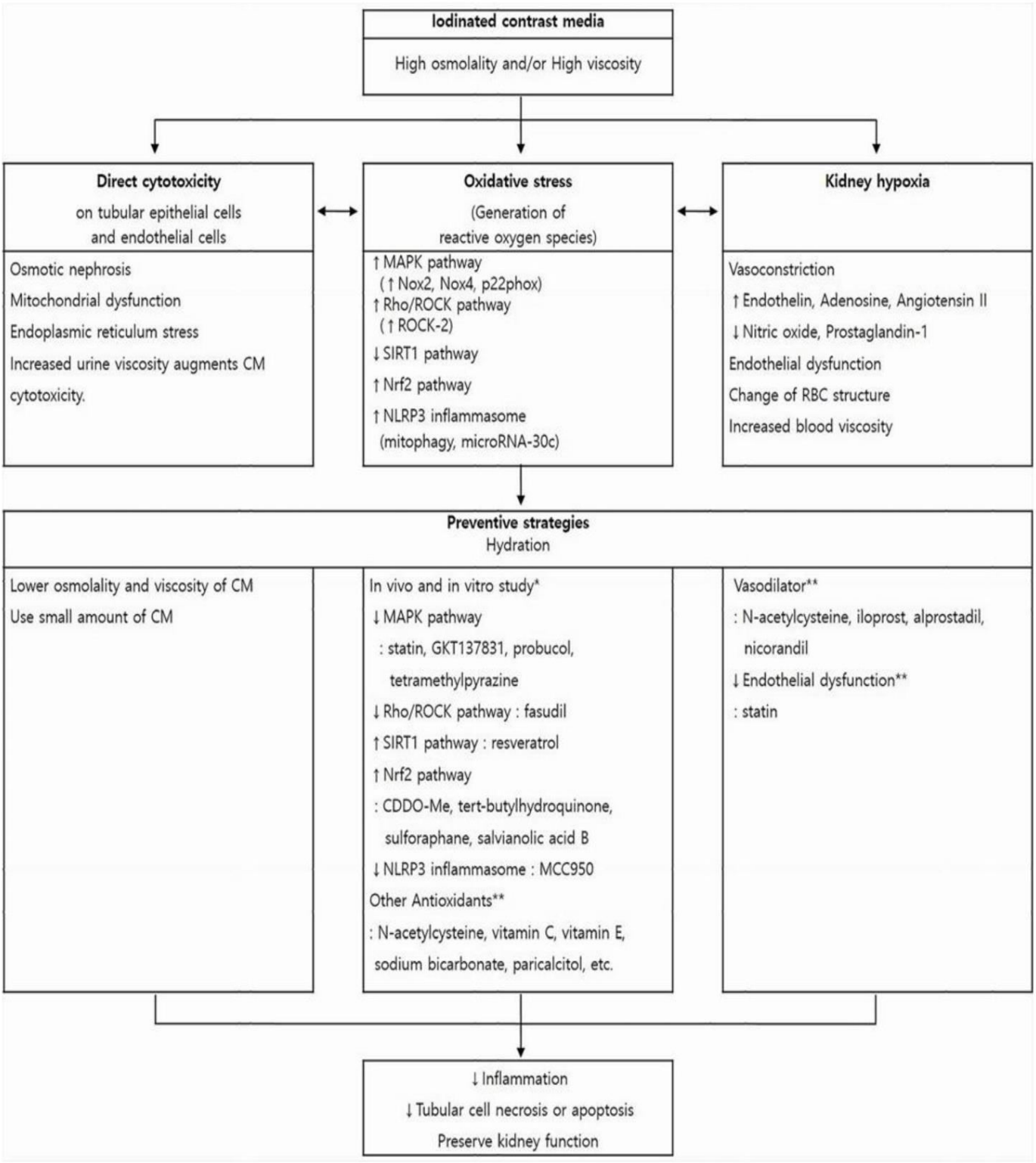

Fig (1): mechanisms influence and aggravate one another, creating a vicious cycle that ultimately leads to inflammation, tubular cell apoptosis, and impaired kidney function **(7).**

CM induced vacuolization in kidney tubular cells by pinocytosis (osmotic nephrosis), mitochondrial dysfunction that led to ROS generation and apoptosis, and endoplasmic reticulum stress that activated intrinsic apoptotic pathways **(8).**

CM has a direct cytotoxic effect on kidney tubular epithelial cells and vascular endothelial cells **(8).**

Loss of the tubular brush border and cell membrane integrity and sloughing of the tubular epithelial cells into the lumen were caused by the direct cytotoxicity of CM **(2).**

CM administration induces transient vasodilation followed by vasoconstriction that can be sustained for several hours in the kidney vasculature as a result of alterations in kidney vasomodulators such as endothelin, adenosine, and nitric oxide **(8).**

Vasoconstriction of afferent arterioles reduces GFR and kidney blood flow, causing kidney parenchymal hypoxia. The kidney outer medulla is in a relative hypoxic situation because of tubular ion transport in the basal state and the low partial pressure of oxygen with limited blood flow caused by the unique anatomy of the kidney vasculature. Hence, the thick ascending limbs of the loop of Henle (TAL) and segments of the proximal kidney tubules in the outer medulla are particularly susceptible to hypoxic injury **(9).**

The high osmolality and viscosity of CM causes osmotic diuresis, an increase in tubular pressure, and decrease in tubular and blood flow rates, all of which lead to an increase in tubular oxygen demand and a decrease in kidney blood supply. Furthermore, CM induces direct vasoconstriction of the vasa recta through endothelial dysfunction and changes in red blood cell structure and function, both of which worsen kidney medullary hypoxia. This mismatch between the metabolic demands of the TAL and the kidney medullary blood supply leads to oxidative stress. Tubular transport is associated with ROS production and the dense mitochondrial population in the proximal tubule and TAL is the major source of ROS **(7) .**

Moreover, CM retention in the tubular lumen caused by the decreased tubular flow rate augments its cytotoxic impact. Ischemic and cytotoxic tubular cell damage again induces tubuloglomerular feedback, which enhances vasoconstriction of the afferent arteriole and produces further decreases in kidney blood flow and GFR **(10) .**

Associated risk factor

Because no definite treatment to ameliorate CIN has been established, the importance of preventive measures has been highlighted, and identifying patients at high risk for CIN is the first step in prevention. A variety of risk factors has been reported and can be divided into patient-related and procedure-related risk factors, like Impaired kidney function, diabetes, advanced age, and preexisting intravascular volume depletion before CM administration are frequently reported patient-related risk factors **(11) .**

Risk factors for contrast-induced nephropathy (CIN) can be divided into patient-related and procedure-related risk factors. Some patient-related risk factors such as volume depletion and using nephrotoxic medications are modifiable. With regard to procedure-related risk factors, the risk of CIN varies according to type, volume, and route of CM administration. Atheroembolism related to catheter manipulation and repeated CM administration also poses an increased risk of CIN. CM, contrast media **(11).**

The reported incidence of CIN in non-elderly population undergoing elective percutaneous coronary intervention (PCI) is relatively low. However, elderly patients with ST-segment elevation myocardial infarction (STEMI) undergoing emergency PCI are at increasing risk of CIN. The occurrence and progression of CIN are influenced by individual risk profiles, especially in patients with advanced age, delayed reperfusion, and hemodynamic instability. There are several patient- and procedure-related risk factors associated with the development of CI-AKI. They include baseline kidney disease, advanced age, diabetes mellitus, anemia, and patient status on presentation (i.e., cardiogenic shock, congestive heart failure, acute coronary syndrome, ST-segment elevation, etc.) **(11).**

Advanced CKD, with an estimated glomerular filtration rate (eGFR) of less than 30 ml/min/1.73 m2, is the strongest patient-related risk factor contributing up to a threefold increase in risk of CIAKI Indeed, the lower the renal function the higher the risk of kidney injury **(12).**

Table 1: Risk factors predisposing the development of contrast-induced nephropathy **(11) .**

Patient-Related	**Procedure-Related**
* Anemia *Hyperuricemia *Nephrotoxic medications: Diuretics,Nonsteroidalantiinflammatorydrugsaminoglycosides,amphotericinB,antiviral drugs such as acyclovir, cyclosporine A, cisplatin *Impaired renal function *Diabetes mellitus *Effective intravascular volume depletion:dehydration, blood loss, congestive heart failure, liver cirrhosis, nephrosis *Advanced age *Female gender *Cardiovascular disease including hypertension *Malignancy *Inflammation	Route of CM administration: intra-arterial vs. intravenous administration Type of procedure: catheter-based procedure Type of CM Volume of CM Repeated CM administration within 24–72 h

Several risk factors have been reported to be associated with the development of CIN, including female gender, older age, congestive heart failure, diabetes mellitus, increased basal creatinine levels, lower total bilirubin levels, anemia, the volume of contrast media, and use of Impact of CI-AKI on outcomesnephrotoxic medication **(13).**

Strategies to prevent CI-AKI

prevention is the best management strategy for CIN and can be divided into patient-, procedure-, and pathophysiology-related methods .All patients receiving intravascular CM should be evaluated for the risk of CIN, and clinicians should adopt interventions for modifiable risk factors such as dehydration and consider discontinuing nephrotoxic medications before CM administration **(14).**

Since Mehranfirst developed a risk scoring system, which involves eight clinical and procedural variables, to predict CIN after PCI, several simpler risk assessment models have been proposed. The ACEF (age, creatinine, and ejection fraction) score was originally developed in 2009 to assess the mortality risk in patients undergoing elective cardiac operations, but that simple risk scoring system has subsequently been validated in other clinical conditions, including CIN after CAG or PCI. It is now the basis for comparison, along with Mehran's score system, for new CIN risk scoring systems **(15).**

Table 2: Strategies to reduce the development of contrast-induced nephropathy **(14).**

Patient-related	*Risk stratification of individual patients *Evaluate and correct patient's volume status *Correct modifiable factors including cessation of nephrotoxic drugs
Procedure-related	*Use low-osmolar or iso-osmolar contrast media *Minimize the volume of contrast media * limit maximum contrast volume * consider the interval of contrast administration
Pathophysiology-related	*Hydration *Pharmaceutical agents targeting pathogenic process including oxidative stress

When clinically feasible, it is recommended to withhold nonessential nephrotoxic medications before CM administration **(16).**

Renin–angiotensin–aldosterone system (RAAS) blockers (angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB)) are generally used in patients with cardiovascular disease, CKD, and diabetes. Because RAAS blockade can change renal hemodynamics and induce AKI, the effect of ACEI/ARBs on the incidence of CIN is of great concern **(17).**

The overall estimate demonstrated significantly increased risk of CIN in the ACEI/ARB group compared to the control group in a recent meta-analysis by Wang et al. that included 12 studies with 14 trials, containing 4864 patients (2484 treated with RAAS blockers and 2380 in the control group), the pooled relative risk of CIN incidence in the RAAS blocker group was 1.22 (95% CI 0.81–1.84) **(18).**

However, an increased risk of CIN in the RAAS blocker group was observed among older people, non-Asians, chronic users, and studies with larger sample sizes **(18).**

It remains inconclusive whether ACEI/ARBs increase or decrease the incidence of CIN and, currently, withholding RAAS blockers before CM administration is not recommended in guidelines **(19).**

In diabetic patients, metformin is widely prescribed as the first-line therapy. Metformin is mainly excreted by the kidneys and confers an increased risk of lactic acidosis when CIN occurs, although it does not increase the risk of CIN. However, as the reported incidence of metformin-associated lactic acidosis has been very low (<10 cases per 100,000 patient-years) **(20).**

The Contrast Media Safety Committee (CMSC) recommends to stop taking metformin at the time of CM administration in (1) patients with eGFR < 30 mL/min/1.73 m2 receiving IV CM or IA CM with second pass renal exposure, (2) patients receiving IA CM with first pass renal exposure, and (3) patients with AKI. They also recommend to measure eGFR within 48 h and restart metformin if renal function has not changed significantly **(21).**

Minimizing the total volume of CM and using the least nephrotoxic CM should be applied in all cases. There have been efforts to reduce the contrast volume (iodine dose) as low as reasonably achievable during both CAG and CECT **(22).**

Clinicians should also consider the interval of CM administration when repeated procedures are needed because multiple doses of CM within a short period of time (24–72 h) increase the risk of CIN **(21).**

In addition to modifying patient-related risk factors and properly choosing the type and volume of CM, intravenous fluid hydration is the mainstay of CIN preventive strategies. Hydration is theoretically reasonable because it can correct or improve the patient's volume status, dilute CM concentration, and increase kidney blood flow and tubular urine flow, which can subsequently reduce CM retention and toxic effects in the tubular lumen. Guidelines recommend intravascular volume expansion as CIN prophylaxis, but there is no consensus on the optimal hydration regime **(7).**

To achieve optimal hydration status without increasing the risk of pulmonary edema, two tailored hydration regimens have been proposed and widely investigated: (1) left ventricular end-diastolic pressure (LVEDP)-guided hydration and (2) urine flow rate (UFR)-guided hydration using the RenalGuard system **(23).**

All patients received a bolus infusion of normal saline (3 mL/kg) for 1 h prior to the procedure. During and for 4 h after the procedure, the LVEDP-guided group received normal saline at a rate of 1.5 to 5 mL/kg/h, depending on the LVEDP, and the control group received 1.5 mL/kg/h of normal saline. The total hydration volume was higher in the LVEDP-guided group (mean volume, 1727 mL vs. 812 mL, $p < 0.001$), and significantly fewer cases of CIN occurred in that group (6.7% vs. 16.3%, $p = 0.005$). Noticeably, the odds of CIN decreased by 9% for every additional 100 mL of normal saline administered (OR 0.91, 95% CI 0.89–0.94, $p = 0.01$). The reported rate of shortness of breath was 1.5% and similar in the two groups. The 6-month composite outcome that considered all-cause mortality, myocardial infarction, and renal replacement therapy (RRT) was better in the LVEDP-guided group than in the control group **(23).**

Theoretically, a high UFR will rapidly remove CM from the kidney, reducing its toxicity within the nephron. For UFR-guided hydration, a bolus of normal saline hydration plus IV furosemide (0.25 mg/kg) was initially administered to achieve UFR ≥300 mL/h, followed by urine output-matched hydration using the RenalGuard system to maintain that high UFR during and after contrast exposure **(24).**

Contrast Induced Nephropathy in Elderly Patients

Currently, contrast-associated acute kidney injury (CA-AKI) is a common cause of hospital-acquired AKI in the older patients **(2).**

With longer average life expectancy, the number of older patients receiving coronary angiography and/or percutaneous coronary intervention (PCI) has increased. With the further acceleration of population aging, an increasing number of elderly patients worldwide are undergoing procedures using contrast agents. Currently, contrast-induced nephropathy (CIN) has been the common cause of hospital-acquired acute kidney injury in the elderly patients **(25).**

The increasing aging process means that more elderly patients are undergoing PCI. The reduction of nephrons, insufficient renal function reserve, and more comorbidity in elderly patients make the elderly more sensitive to CI-AKI, with a higher probability of CI-AKI and a worse prognosis than the general population **(26).**

The probability of CI-AKI in elderly patients after PCI is significantly increased, and the reason may be the substantial loss of nephrons at the same time, with the increase of age, vascular stiffness increases, and vascular endothelial function decreases in elderly patients, which reduces the possibility of rapid recovery of postoperative creatinine and increases the risk of CI-AKI in elderly patients **(27).**

The lack of sufficient functional reserve makes the older kidney more vulnerable to acute stress and more likely to develop clinically relevant acute kidney injury **(28).**

Due to no effective treatment measures available for CI-AKI in clinical work, it is of great value to accurately identify high-risk elderly patients **(29).**

Once CIN occurs, the complications such as renal insufficiency, diabetes, heart failure, and hypertension would significantly increase the incidence and mortality of renal and cardiovascular adverse events, severely affecting the survival and prognosis of elderly patients **(25).**

Studies have shown that the incidence of CIN in elderly patients with coronary heart disease receiving PCI was as high as 19.51% **(30).**

Iodinated CM remains the sole agent for diagnostic and interventional vascular procedures. Since there is no effective therapy available to treat established CIN, it is imperative to maintain adequate volume expansion in the periprocedure period, minimize the volume of CM used, and avoid the use of nephrotoxic medications whenever possible.

References:

1. Carande EJ, Brown K, Jackson D, et al. (2022). Acute kidney injury following percutaneous coronary intervention for acute coronary syndrome: incidence, aetiology, risk factors and outcomes. Angiology;73(2):139-45.
2. Mehran, R., Dangas, G. D., & Weisbord, S. D. (2019). Contrast-associated acute kidney injury. New England Journal of Medicine, 380(22), 2146-2155.
3. Sonali G, Pradeep G, Nishant G, Harpreet S, Vivek K (2018). Contrast-Induced Nephropathy: Current practice. J Urol Neph St 1(1)- 2018. JUNS. MS.ID.000103.
4. Hinson JS, Ehmann MR, Fine DM, Fishman EK, Toerper MF et al. (2017). Risk of acute kidney injury after intravenous contrast media administration. Ann Emerg Med 69(5): 577-586.
5. Barbieri, L., Verdoia, M., Nardin, M., et al., (2017). Gender difference in the risk of contrast-induced nephropathy in patients undergoing coronary angiography or percutaneous coronary intervention. Angiology, 68(6), pp.542-546.
6. Chong E, Shen L, Poh K, et al., (2012). Risk scoring system for prediction of contrast induced nephropathy in patients with pre-existing renal impairment undergoing percutaneous coronary intervention. Singapore Med J 53(3): 164-169.
7. Mamoulakis, C., Tsarouhas, K., Fragkiadoulaki, I., Heretis, I., Wilks, M.F., Spandidos, D.A., Tsitsimpikou, C. and Tsatsakis, A., 2017. Contrast-induced nephropathy: Basic concepts, pathophysiological implications and prevention strategies. Pharmacology & therapeutics, 180, pp.99-112.
8. Ward, D.B. and Valentovic, M.A., 2019. Contrast induced acute kidney injury and direct cytotoxicity of iodinated radiocontrast media on renal proximal tubule cells. Journal of Pharmacology and Experimental Therapeutics, 370(2), pp.160-171.
9. Heyman, S.N., Khamaisi, M., Zorbavel, D., Rosen, S. and Abassi, Z., 2019, November. Role of hypoxia in renal failure caused by nephrotoxins and hypertonic solutions. In Seminars in nephrology (Vol. 39, No. 6, pp. 530-542). WB Saunders.
10. Liu, Z. B., Fu, X. H., Wei, G., & Gao, J. L. (2014). Cytochrome c release in acute myocardial infarction predicts poor prognosis and myocardial reperfusion on contrast-enhanced magnetic resonance imaging. Coronary Artery Disease, 25(1), 66-72.
11. Boccalandro, F., Shreyder, K., Harmon, L., et al., (2021). Five-Year Follow-Up of Patients With Radio-Contrast-Induced Acute Renal Injury: Can Intravenous Sodium Bicarbonate Improve Long-Term Outcomes?. Cardiovascular Revascularization Medicine, 31, pp.61-68.
12. McCullough, P.A., Adam, A., Becker, C.R., Davidson, C., Lameire, N., Stacul, F., Tumlin, J. and Panel, C.C.W., 2006. Risk prediction of contrast-induced nephropathy. The American journal of cardiology, 98(6), pp.27-36.
13. Shacham, Y., Gal-Oz, A., Leshem-Rubinow, E., Arbel, Y., Flint, N., Keren, G., Roth, A. and Steinvil, A., 2015. Association of admission hemoglobin levels and acute kidney injury among myocardial infarction patients treated with primary percutaneous intervention. Canadian Journal of Cardiology, 31(1), pp.50-55.
14. Yao, Z.F., Shen, H., Tang, M.N., Yan, Y. and Ge, J.B., 2021. A novel risk assessment model of contrast-induced nephropathy after percutaneous coronary intervention in patients with diabetes. Basic & clinical pharmacology & toxicology, 128(2), pp.305-314.
15. Ni, Z., Liang, Y., Xie, N., Liu, J., Sun, G., Chen, S., Ye, J., He, Y., Guo, W., Tan, N. and Chen, J., 2019. Simple pre-procedure risk stratification tool for contrast-induced nephropathy. Journal of Thoracic Disease, 11(4), p.1597.
16. Davenport, M.S., (2020) .Use of intravenous iodinated contrast media in patients with kidney disease: consensus statements from the, American College of Radiology and the National Kidney Foundation Radiology 294 (2020) 660–668.
17. Motes, A.T., Ratanasrimetha, P., Wongsaengsak, S., Vorakunthada, Y., Mingbunjerdsuk, T., Pena, C. and Nugent, K., 2021. Impact of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers on Renal Function in Chronic Kidney Disease Patients Undergoing Coronary Angiography. Cureus, 13(1).
18. Wang JJ, Zhang JM, She LP. Meta-analysis of the risk factors of contrast-induced nephropathy for patients after coronary angiography and interventional therapy. Chin Clin Nurs. 2021;13:498-504.
19. Isaka, Y., Hayashi, H., Aonuma, K., Horio, M., Terada, Y., Doi, K., Fujigaki, Y., Yasuda, H., Sato, T., Fujikura, T. and Kuwatsuru, R., 2020. Japanese Society of Nephrology, Japan Radiological Society, and Japanese Circulation Society Joint Working Group. Guideline on the use of iodinated contrast media in patients with kidney disease 2018. Clin Exp Nephrol, 24(1), pp.1-44
20. DeFronzo, R., Fleming, G.A., Chen, K. et al., (2016). Metformin-associated lactic acidosis: Current perspectives on causes and risk. Metabolism, 65(2), pp.20-29.
21. van der Molen, A.J., Reimer, P., Dekkers, I.A., Bongartz, G., Bellin, M.F., Bertolotto, M., Clement, O., Heinz-Peer, G., Stacul, F., Webb, J.A. and Thomsen, H.S., 2018. Post-contrast acute kidney injury. Part 2: risk stratification, role of hydration and other prophylactic measures, patients taking metformin and chronic dialysis patients:

Recommendations for updated ESUR Contrast Medium Safety Committee guidelines. European radiology, 28, pp.2856-2869.
22. Gurm, H.S., Seth, M., Dixon, S.R., Michael Grossman, P., Sukul, D., Lalonde, T., Cannon, L., West, D., Madder, R.D. and Adam Lauver, D., 2019. Contemporary use of and outcomes associated with ultra-low contrast volume in patients undergoing percutaneous coronary interventions. Catheterization and Cardiovascular Interventions, 93(2), pp.222-230.
23. Cho, E. and Ko, G.J., 2022. The pathophysiology and the management of radiocontrast-induced nephropathy. Diagnostics, 12(1), p.180.
24. Briguori, C., D'Amore, C., De Micco, F., et al., (2020). Renal insufficiency following contrast media administration trial III: Urine flow rate-guided versus left-ventricular end-diastolic pressure-guided hydration in high-risk patients for contrast-induced acute kidney injury. Rationale and design. Catheterization and Cardiovascular Interventions, 95(5), pp.895-903.
25. Rear, R., Bell, R.M. and Hausenloy, D.J., 2016. Contrast-induced nephropathy following angiography and cardiac interventions. Heart, 102(8), pp.638-648.
26. Denic, A., Lieske, J.C., Chakkera, H.A., et al., (2017). The substantial loss of nephrons in healthy human kidneys with aging. Journal of the American Society of Nephrology, 28(1), pp.313-320.
27. Stojanović, S.D., Fiedler, J., Bauersachs, J., Thum, T. and Sedding, D.G., 2020. Senescence-induced inflammation: an important player and key therapeutic target in atherosclerosis. European Heart Journal, 41(31), pp.2983-2996.
28. Grams, M. E., Sang, Y., Ballew, S. H., Gansevoort, R. T., Kimm, H., Kovesdy, C. P., ... & Woodward, M. (2015). A meta-analysis of the association of estimated GFR, albuminuria, age, race, and sex with acute kidney injury. American Journal of Kidney Diseases, 66(4), 591-601.
29. Chandiramani, R., Cao, D., Nicolas, J. et al., (2020). Contrast-induced acute kidney injury. Cardiovascular intervention and therapeutics, 35, pp.209-217.
30. Kumar, B.V. and Mohan, T., 2017. Retrospective comparison of estimated GFR using 2006 MDRD, 2009 CKD-EPI and Cockcroft-Gault with 24 hour urine creatinine clearance. Journal of clinical and diagnostic research: JCDR, 11(5), p.BC09.