BAJAK, Mateusz, SŁOWIK, Julia, ZAPASEK, Daniel, SZCZEPAŃSKI, Michał, MAMCZUR, Maciej, FERET, Dominik Maciej, INGLOT, Jadwiga, INGLOT, Julia, KULIGA, Marcin, SOWA, Damian and WIDAWSKA, Katarzyna. Contrast - induced nephropathy - prevention and treatment. Quality in Sport. 2024;34:56249 eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.34.56249
https://apcz.umk.pl/QS/article/view/56249

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assig589 ned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.11.2024. Revised: 20.11.2024. Accepted: 27.11.2024. Published: 27.11.2024.

Contrast - induced nephropathy - prevention and treatment

Mateusz Bajak
University Teaching Hospital them F. Chopin in Rzeszów, Poland
Fryderyka Szopena 2, 35-055 Rzeszów, Poland
https://orcid.org/0009-0006-8237-1295
mateuszbk88@gmail.com

Julia Słowik
University Teaching Hospital them F. Chopin in Rzeszów, Poland
Fryderyka Szopena 2, 35-055 Rzeszów, Poland
https://orcid.org/0009-0003-3821-5090
jj16@interia.eu

Daniel Zapasek
Medical Center in Łańcut, Poland
Ignacego Paderewskiego 5, 37-100 Łańcut, Poland
https://orcid.org/0009-0006-1383-1825
daniel.zapasek@interia.pl

Michał Szczepański
Medical Center in Łańcut, Poland
Ignacego Paderewskiego 5, 37-100 Łańcut, Poland
https://orcid.org/0009-0001-8586-3790
mszczepanski0202@gmail.com

Maciej Mamczur
Medical Center in Łańcut, Poland
Ignacego Paderewskiego 5, 37-100 Łańcut, Poland
https://orcid.org/0009-0000-2789-1235
maciej.mamczur@gmail.com

Dominik Maciej Feret
Independent Public Health Care Complex No. 1 in Rzeszów,
ul.Czackiego 3, 35-051 Rzeszów, Poland
https://orcid.org/0009-0004-3174-2784
feret.dominik@gmail.com

Jadwiga Inglot
Clinical Provincial Hospital No. 2 in Rzeszow, Poland
Lwowska 60, 35-301 Rzeszów, Poland
https://orcid.org/0000-0002-3071-4392
inglotjadzia@gmail.com

Julia Inglot
Clinical Provincial Hospital No. 2 in Rzeszów, Poland
Lwowska 60, 35-301 Rzeszów, Poland
https://orcid.org/0000-0002-6604-7229
inglotjulia@gmail.com

Marcin Kuliga
College of Medical Sciences, University of Rzeszów, Poland
al. Tadeusza Rejtana 16C, 35-310 Rzeszów
https://orcid.org/0009-0004-3452-7377
marcinkuliga@gmail.com

Damian Sowa
Clinical Provincial Hospital No. 2 in Rzeszow, Poland
Lwowska 60, 35-301 Rzeszów, Poland
https://orcid.org/0009-0003-0980-9324
damian_sowa@wp.pl

Katarzyna Widawska
Polish Red Cross Maritime Hospital in Gdynia, Poland
Powstania Styczniowego 1, 81-519 Gdynia, Poland
https://orcid.org/0009-0005-0146-2332
kasia.widawska@wp.pl

Abstract
Introduction and purpose: Contrast-induced nephropathy (CIN) is kidney damage that can occur after the administration of contrast agents used in medical imaging procedures like angiography and CT scans. The exact mechanism is not fully understood but is believed to involve direct toxic effects, changes in kidney blood flow, and inflammation. Diagnosis is based on increased serum creatinine levels after contrast exposure. CIN poses challenges due to the rising use of contrast imaging, an aging population, and the increasing prevalence of chronic conditions like diabetes and hypertension. The Aim of this article is to summarize information on how to prevent contrast-induced nephropathy. Review of medications and pre-procedural screening and monitoring helpful to lower risk of CIN.
State of knowledge: Contrast-induced nephropathy (CIN) is a form of kidney damage that may occur following the administration of contrast agents used in medical imaging procedures. The exact mechanism of contrast-induced nephropathy is not fully understood, but it is believed to involve a combination of factors, including the direct toxic effects of the contrast agent on kidney cells, changes in blood flow to the kidneys, and the body's inflammatory response, direct effect of oxygen free radicals. The diagnosis of CIN is typically based on an increase in serum creatinine levels within a certain time frame after the administration of the contrast agent. According to European guidelines, the definition of CIN is increased creatinine level in serum by 25% from baseline or creatinine total level in serum increased by 0.5 mg/dL (44 μmol/L) 48-72h after contrast media administration.
Material and methods. A review of the available literature of PubMed database from 1992 - 2024.

Keywords: contrast induced nephropathy; contrast agents; iodine contrast media; acute kidney disease; intervention radiology

Introduction

Contrast-induced nephropathy (CIN) is a form of kidney damage that may occur following the administration of contrast agents used in medical imaging procedures. These contrast agents, often containing iodine, are commonly used in diagnostic procedures such as angiography, computer tomography (CT) scans, and certain types of X-rays. While these imaging studies are valuable for diagnosing and monitoring various medical conditions, the contrast agents can have an impact on kidney function. Contrast-induced nephropathy (CIN) remains a challenge in clinical practice for several reasons: Increasing Use of Contrast Imaging. As medical imaging procedures, such as CT scans, angiography, and interventional radiology, become more prevalent, the total use of contrast agents has increased. [1,6] This exposes a

larger population to the potential risk of CIN. Aging Population: The global population is aging, and older individuals are more susceptible to kidney-related issues.
Aging kidneys may have reduced functional reserve, making them more vulnerable to the potential nephrotoxic effects of contrast agents. Growing Incidence of Chronic Conditions: Conditions such as diabetes and hypertension which are risk factors for CIN, are on the rise globally. [1,5,6] The increasing prevalence of these conditions contributes to a higher baseline risk for kidney-related complications. Preventing contrast-induced nephropathy (CIN) is a crucial aspect of patient care, especially in individuals at higher risk.

Prevention and treatment

Identifying High-Risk Patients: Practical and clinical way to estimate and predict risk of CIN. Authors gathered and analyzed professional medical materials to finally include 1404 patients who had procedures with administration of gadolinium-based contrast. 55 of these patients experienced CIN (3.92%) "The results showed that sex, systolic blood pressure, the absolute neutrophil count, albumin level, fasting blood glucose level, and furosemide use were the best predictors of CIN induced by gadolinium-based contrast agents."[1]

Hydration: Adequate hydration helps maintain optimal blood flow to the kidneys, reducing the concentration and potential toxicity of contrast agents [4]. Increased urine flow facilitated by hydration can help flush out the contrast agent more rapidly, minimizing its contact time with kidney tissues. Patients are often hydrated before contrast-enhanced imaging procedures. The timing and duration of pre-procedural hydration may vary but typically involve administering fluids before and after the contrast exposure. 0.9% NaCl is the most common choice for IV hydration in CIN prevention. However study based on group of 220 patients with risk factors(creatinine serum level >1.2mg/dL and/or diabetes mellitus type II, who received 0.9% NaCl (n = 113) or NaHCO3 (n = 107) before and after contrast dose, shows there were no significant differences between received fluids. "The mean creatinine value after the procedure was 1.26 mg/dL in the saline group and 1.22 mg/dL in the bicarbonate group (mean difference: 0.036; CI 95%: -0.16 to 0.23, $p = 0.865$)." [3] The volume of fluids administered is often individualized based on factors such as the patient's weight, renal function, and specific procedural considerations. According to this clinical trial where 264 patients with Chronic Kidney Disease and Congestive Heart Failure, undergoing coronary procedures, were divided into the two groups of 132 patients. Control group (standard hydration) vs Central Venous Pressure guided group "The total mean volume of isotonic saline administered in the CVP-guided hydration group was significantly higher than the control group (1,827 ± 497 ml vs. 1,202 ± 247 ml; $p < 0.001$). CIN occurred less frequently in the CVP-guided hydration group than the control group (15.9% vs. 29.5%)." [4]

Nicorandil: The use of nicorandil in the prevention of contrast-induced nephropathy (CIN) has been studied in some clinical trials. Nicorandil, with its vasodilatory and anti-ischemic properties, has been explored for its potential protective effects on renal function during procedures with contrast administration. In the context of CIN prevention, the vasodilatory effects of nicorandil are thought to improve renal blood flow and mitigate the potential

ischemic injury caused by contrast agents. Clinical trial, where 128 PCI scheduled patients were randomly divided to the two groups(each group of 64 patients) with inclusion criteria of minimum two risk factors of CIN:
Heart failure with ejection of left ventricle under 40%, hypertension, diabetes mellitus, elderly age at least 75 years, eGFR <60mL/min/1.73m2, or serum creatinine level >1.5ms/dL. [5] For Nicorandil group patients, authors used protocol with doses of 10 mg nicorandil, patients received the first dose of oral nicorandil 30 min before contrast procedures, and the same dose was continued for the next 3 days. Patients from this group also received standard intravenous hydration. Control group received the same standard intravenous hydration as nicorandil group patients. In the control group, CIN occurred in 14 patients (21.9%) and only 3 (4.7%) patients in the nicorandil group [5]. Similar conclusions were obtained by authors where group of 252 patients were allocated to the control group (n = 125) and nicorandil group (n = 127). Every group received the standard intravenous hydration, patients from the nicorandil group received 10 mg of oral nicorandil, first dose 2 days before and it was continued for next 2 days after coronary procedure. Incidence of CIN was significantly lower in the nicorandil group 8 patients vs 19 patients in the control group(6.30 vs. 15.20%).[7]

	Nicorandil Group	Control Group
Study 1	4.70%	21.90%
Study 2	6.30%	15.20%

Table 1. Incidence of CIN control group VS nicorandil group

Nebivolol is a beta-adrenergic receptor antagonist, commonly known as a beta-blocker. Nebivolol is unique among beta-blockers because it has vasodilatory effects. It can relax and widen blood vessels, leading to improved blood flow. This vasodilatory action is attributed to the stimulation of nitric oxide release in the blood vessels, which contributes to the widening of the vessels. Turkish study, where the aim was to compare two popular beta-blockers (metoprolol vs nebivolol) and their influence on the incidence of CIN in patients undergoing coronarography. [8] The results showed patients from the nebivolol group had a statistically lower incidence of CIN than patients from the metoprolol group (tab. 2)

Nebivolol group	Metoprolol group
24%	33%

Tab. 2 Incidence of CIN nebivolol group vs metoprolol group.

In different study where nebivolol was used[9], authors divided patients for 3 groups (N-Acetylcysteine + 0.9% Saline, Nebivolol + 0.9% Saline, and 0.9% Saline). Result of this study was statistically significant rises in mean creatinine levels on fifth day compared to base creatinine levels in two of three groups (NAC + 0.9% saline group and 0.9% saline group), only nebivolol + 0.9% saline group did not reach statistical significance on day 5. [9]

Statins are a class of medications commonly prescribed to lower cholesterol levels in the blood. Statins primarily target the enzyme HMG-CoA reductase, which plays a key role in cholesterol synthesis in the liver. Statins by inhibiting HMG-CoA reductase, reduce the production of cholesterol. Statins effectively lower low-density lipoprotein (LDL) cholesterol, often referred to as "bad" cholesterol. They may also have a modest effect on increasing high-density lipoprotein (HDL) cholesterol, often referred to as "good" cholesterol. Commonly prescribed statins include atorvastatin, simvastatin, rosuvastatin The role of statins, specifically in the prevention of CIN, has been a subject of research. Some studies and meta-analyses have suggested that statins may have renoprotective effects and could potentially reduce the risk of CIN. The mechanisms proposed for this protective effect include anti-inflammatory and antioxidant properties, improvement of endothelial function, and potential stabilization of atherosclerotic plaques. While some studies have reported a potential benefit of statins in reducing the incidence of CIN, the evidence is not consistent across all studies. There are conflicting results, and not all studies have demonstrated a clear protective effect. A study where authors were finding advantages from using atorvastatin before coronarography. Patients on chronic statin therapy were randomly divided into two groups. “We randomly assigned the population to the Atorvastatin Reloading group (AR group), by reloading patients with 80 mg of atorvastatin one day before and three days after the coronary procedure, and the Non-Reloading group (NR group), including patients who received their usual dose without a reloading dose. Atorvastatin Reloading group (AR group), by reloading patients with 80 mg of atorvastatin one day before and three days after the coronary procedure, and the Non-Reloading group (NR group), including patients who received their usual dose without a reloading dose.” [16] Results of this study did not show significant difference between both of groups Tab. 3

	Incidence of CIN
AR group	8.9%
NR group	11.1%

Tab. 3 Incidence of CIN AR group vs NR group.

N-acetylcysteine (NAC) is a medication and supplement that is often used for various medical purposes. It is a derivative of the amino acid cysteine and serves as a precursor to glutathione, a powerful antioxidant in the body. NAC has a range of applications, and its use has been studied in different medical contexts. NAC has been studied in the context of contrast-induced nephropathy (CIN) prevention. Some studies have suggested a potential protective effect.

Authors from this study,[17] compared incidence of CIN between groups of patients with mild to moderate kidney dysfunction who were undergoing coronarography/PCI. The study did not show a significant difference between the high-dose hydration vs standard protocol hydration. CIN was developed by 21 patients (9.5%). From the NAC + high-dose hydration group patients, only 2 of 80 (2.5% tab. 4) patients developed CIN, the groups without NAC administration, had significantly higher risk of developing CIN, in the high-dose hydration group CIN occurred in 13 of 80 patients (16.3% tab. 4), and 6 of 60 patients (10% tab. 4) in the control group (standard hydration protocol).

NAC + high-dose hydration	2.5%
high-dose hydration	16.3%
standard hydration protocol	10%

Table. 4 Incidence of CIN between all groups of patients

Similar results obtained by authors from this clinical trial in the emergency department, where 209 patients were divided into two groups (106 who received NAC and 103 in the control group) all received computed tomography enhanced by contrast. CIN rate was significantly lower in the NAC patients group (7.5%) than the control group (14.6%) [18]. However, there are other studies where authors did not obtain a positive effect of NAC in preventing CIN, results showed the effect of NAC as equal to placebo. [19, 20, 21, 23]

Iso- and low-osmolar contrast media

Contrast media, also known as contrast agents or contrast dyes, are substances used in medical imaging procedures to enhance the visibility of specific organs, tissues, or blood vessels. They help distinguish between different structures or highlight areas of interest in diagnostic imaging. Contrast media are commonly used in various medical imaging techniques, including: contrast-enhanced X-ray procedures, such as angiography, to visualize blood vessels and highlight structures like the gastrointestinal tract. Computed Tomography (CT): contrast agents are commonly used in CT scans to enhance the visibility of blood vessels and soft tissues. Iodine-based contrast agents, particularly, may pose a risk of contrast-induced nephropathy (CIN), especially in individuals with pre-existing kidney conditions. There are different types of iodine-based contrast agents, and they can be categorized based on their osmolality (a measure of the number of particles in a solution).

The main types includes:

High-Osmolality Contrast Media (HOCM): first generation of iodine-based contrast agents. They have a higher osmolality compared to blood plasma. Examples: Diatrizoate, Metrizoate.

Low-Osmolality Contrast Media (LOCM): Developed to reduce the side effects associated with high-osmolality contrast media. LOCM have a lower osmolality compared to blood plasma, making them better tolerated by patients. They are the most widely used iodine-based contrast agents today. Examples: Iohexol, Iopamidol, Iopromide.
Iso-Osmolality Contrast Media (IOCM): These have an osmolality similar to that of blood plasma, aiming to further reduce the risk of side effects. IOCM are considered to be well-tolerated and are often used in specific patient populations. Examples: Iodixanol.

Non-Ionic Contrast Media: Contrast agents are classified as either ionic or non-ionic based on the charge of the molecules. Non-ionic contrast media have molecules that do not dissociate into charged particles in solution, reducing the risk of adverse reactions. Both low-osmolality and iso-osmolality contrast media are often non-ionic. Examples: Iohexol, Iopamidol, Iodixanol.
The choice between high, low, or iso-osmolality contrast media, as well as ionic or non-ionic formulations, depends on factors such as the specific imaging procedure, the patient's medical history, and the risk of adverse reactions. In recent years, there has been a shift towards the use of low-osmolality and non-ionic contrast media due to their improved safety profile and better patient tolerance. There are a lot of studies and clinical trials, where authors wanted to state clearly which contrast media has the lowest chance to cause CIN in patients. In this clinical trial were considered differences between iso-osmolar and low-osmolar contrast media in diabetic patients. Iso-osmolar iodixanol was compared with low-osmolar contrast agents. The results showed Iodixanol had significantly lower risk of CIN only compared to iohexol. The rest LOCM media had similar risk to occur CIN as iodixanol. [26]

Conclusions

The article provides insights into contrast-induced nephropathy (CIN), a form of kidney damage that can occur following the administration of contrast agents in medical imaging procedures. CIN is kidney damage that may result from contrast agents containing iodine, commonly used in diagnostic procedures like angiography, CT scans, and certain X-rays. The exact mechanism of CIN involves factors such as the direct toxic effects of contrast agents, changes in kidney blood flow, and the body's inflammatory response. Diagnosis is based on an increase in serum creatinine levels within a specific time frame after contrast administration. The increasing use of contrast imaging procedures exposes a larger population to the potential risk of CIN. An aging population and the growing incidence of chronic conditions, such as diabetes and hypertension, contribute to a higher baseline risk for kidney-related complications. Hydration is a crucial preventive measure, with studies showing varying outcomes based on the type of fluids administered and individual patient factors. Medications like Nicorandil, Nebivolol, and Statins have been studied for their potential protective effects against CIN, with some trials reporting positive outcomes. Nebivolol, a beta-blocker with vasodilatory effects, demonstrated a lower incidence of CIN in comparison

to another beta-blocker (Metoprolol) in a specific study. Statins, commonly prescribed to lower cholesterol, have been investigated for their potential renoprotective effects, although results across studies are inconsistent. N-acetylcysteine (NAC) has been explored, with some studies reporting a lower incidence of CIN in patients who received NAC compared to those who did not. Studies comparing iso-osmolar and low-osmolar contrast media have shown varying results, with some suggesting lower CIN risk with iso-osmolar iodixanol. Randomized controlled trials comparing different contrast media found similar incidences of CIN between groups.

In summary, the article provides a comprehensive overview of CIN, its challenges, and preventive measures, emphasizing the importance of individualized approaches based on patient characteristics and procedural considerations.

Disclosure

Author's contribution

All authors contributed to the article.

:Conceptualization:M.B.;methodology:J.S.,D.Z.,;software:M.S.,M.M.;formalanalysis:D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;investigation;M.B.,J.S.,D.Z.,M.S.,M.M.,D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;resources:M.B,J.S.,D.Z.,M.S.,M.M.,D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;datacuration:M.B,J.S.,D.Z.,M.S.,M.M.,D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;writing-roughpreparation:M.B,J.S.,D.Z.,M.S.,M.M.,D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;writing–reviewandediting:M.B,J.S.,D.Z.,M.S.,M.M.,D.F.,J.I.,J.I.,M.K.,D.S.,K.W.;visualization:M.B.,J.S.,D.Z.,;supervision:J.I.,M.K.,D.S.,K.W.,;projectadministration:M.S.,M.M.,D.F.,J.I.

All authors have read and agreed with the published version of the manuscript.

Supplementary Materials: They have not been provided.

Funding statement: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest. All author shave read and agreed to the published version of the manuscript.

References

1. Zheng H, Wang G, Cao Q, Ren W, Xu L, Bu S. A risk prediction model for contrast-induced nephropathy associated with gadolinium-based contrast agents. *Ren Fail*. 2022;44(1):741-747. doi:10.1080/0886022X.2022.2069579

2. Nijssen EC, Rennenberg RJ, Nelemans PJ, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *Lancet*. 2017;389(10076):1312-1322. doi:10.1016/S0140-6736(17)30057-0
3. Nieto-Ríos JF, Salazar WAM, Sánchez OMS, et al.. Prevention of contrast induced nephropathy with sodium bicarbonate (the PROMEC study). *Braz J Nephrol*. 2014;36(3):360-366. doi:10.5935/0101-2800.20140051

4. Qian G, Fu Z, Guo J, Cao F, Chen Y. Prevention of Contrast-Induced Nephropathy by Central Venous Pressure-Guided Fluid Administration in Chronic Kidney Disease and Congestive Heart Failure Patients. *JACC Cardiovasc Interv*. 2016;9(1):89-96. doi:10.1016/j.jcin.2015.09.026
5. Iranirad L, Hejazi SF, Sadeghi MS, Jang SA. Efficacy of nicorandil treatment for prevention of contrast-induced nephropathy in high-risk patients undergoing cardiac catheterization: A prospective randomized controlled trial. *Cardiol J*. 2017;24(5):502-507. doi:10.5603/CJ.a2017.0028
6. Nawa T, Nishigaki K, Kinomura Y, et al. Continuous intravenous infusion of nicorandil for 4 hours before and 24 hours after percutaneous coronary intervention protects against contrast-induced nephropathy in patients with poor renal function. *Int J Cardiol*. 2015;195:228-234. doi:10.1016/j.ijcard.2015.05.078
7. Zeyuan Fan, Yang Li, Hanhua Ji, Xinwen Jian; Efficacy of Oral Nicorandil to Prevent Contrast-Induced Nephropathy in Patients with Chronic Renal Dysfunction Undergoing an Elective Coronary Procedure. *Kidney Blood Press Res* 16 December 2019; 44 (6): 1372–1382. doi:10.1159/000503160
8. Avci E, Yeşil M, Bayata S, Postaci N, Arikan E, Cirit M. The role of nebivolol in the prevention of contrast-induced nephropathy in patients with renal dysfunction. *Anadolu Kardiyol Derg*. 2011;11(7):613-617. doi:10.5152/akd.2011.164
9. Günebakmaz O, Kaya MG, Koc F, et al. Does nebivolol prevent contrast-induced nephropathy in humans?. *Clin Cardiol*. 2012;35(4):250-254. doi:10.1002/clc.21013
10. Lawlor DK, Moist L, DeRose G, et al. Prevention of contrast-induced nephropathy in vascular surgery patients. *Ann Vasc Surg*. 2007;21(5):593-597. doi:10.1016/j.avsg.2007.07.006
11. Nabi Z, Anjum N, Rashid RM, Zahideen ZU. Contrast Induced Nephropathy In High Risk Patients - Myth Or Reality. *J Ayub Med Coll Abbottabad*. 2021;33(4):568-571.
12. Zhang J, Guo Y, Jin Q, Bian L, Lin P. Meta-analysis of rosuvastatin efficacy in prevention of contrast-induced acute kidney injury. *Drug Des Devel Ther*. 2018;12:3685-3690. doi:10.2147/DDDT.S178020
13. Xie H, Ye Y, Shan G, et al. Effect of statins in preventing contrast-induced nephropathy: an updated meta-analysis. *Coron Artery Dis*. 2014;25(7):565-574. doi:10.1097/MCA.0000000000000148

14. Ozhan H, Erden I, Ordu S, et al. Efficacy of short-term high-dose atorvastatin for prevention of contrast-induced nephropathy in patients undergoing coronary angiography. *Angiology*. 2010;61(7):711-714. doi:10.1177/0003319710364216
15. Li Y, Liu Y, Fu L, Mei C, Dai B. Efficacy of short-term high-dose statin in preventing contrast-induced nephropathy: a meta-analysis of seven randomized controlled trials. *PLoS One*. 2012;7(4):e34450. doi:10.1371/journal.pone.0034450
16. Hammami R, Masmoudi O, Jdidi J, et al. Impact of atorvastatin reload on the prevention of contrast-induced nephropathy in patients on chronic statin therapy: A prospective randomized trial. *PLoS One*. 2023;18(5):e0270000. doi:10.1371/journal.pone.0270000
17. Koc F, Ozdemir K, Kaya MG, et al. Intravenous N-acetylcysteine plus high-dose hydration versus high-dose hydration and standard hydration for the prevention of contrast-induced nephropathy: CASIS--a multicenter prospective controlled trial. *Int J Cardiol*. 2012;155(3):418-423. doi:10.1016/j.ijcard.2010.10.041
18. Hsu TF, Huang MK, Yu SH, et al. N-acetylcysteine for the prevention of contrast-induced nephropathy in the emergency department. *Intern Med*. 2012;51(19):2709-2714. doi:10.2169/internalmedicine.51.7894
19. Aslanger E, Uslu B, Akdeniz C, Polat N, Cizgici Y, Oflaz H. Intrarenal application of N-acetylcysteine for the prevention of contrast medium-induced nephropathy in primary angioplasty. *Coron Artery Dis*. 2012;23(4):265-270. doi:10.1097/MCA.0b013e328351aacc
20. Rehman T, Fought J, Solomon R. N-acetylcysteine effect on serum creatinine and cystatin C levels in CKD patients. *Clin J Am Soc Nephrol*. 2008;3(6):1610-1614. doi:10.2215/CJN.01560408
21. Oldemeyer JB, Biddle WP, Wurdeman RL, Mooss AN, Cichowski E, Hilleman DE. Acetylcysteine in the prevention of contrast-induced nephropathy after coronary angiography. *Am Heart J*. 2003;146(6):E23. doi:10.1016/S0002-8703(03)00511-8
22. Yang K, Liu W, Ren W, Lv S. Different interventions in preventing contrast-induced nephropathy after percutaneous coronary intervention. *Int Urol Nephrol*. 2014;46(9):1801-1807. doi:10.1007/s11255-014-0765-3
23. Jaffery Z, Verma A, White CJ, et al. A randomized trial of intravenous n-acetylcysteine to prevent contrast induced nephropathy in acute coronary syndromes. *Catheter Cardiovasc Interv*. 2012;79(6):921-926. doi:10.1002/ccd.23157
24. Levin A, Pate GE, Shalansky S, et al. N-acetylcysteine reduces urinary albumin excretion following contrast administration: evidence of biological effect. *Nephrol Dial Transplant*. 2007;22(9):2520-2524. doi:10.1093/ndt/gfl707
25. Sun Z, Fu Q, Cao L, Jin W, Cheng L, Li Z. Intravenous N-acetylcysteine for prevention of contrast-induced nephropathy: a meta-analysis of randomized, controlled trials. *PLoS One*. 2013;8(1):e55124. doi:10.1371/journal.pone.0055124
26. Han XF, Zhang XX, Liu KM, Tan H, Zhang Q. Contrast-induced nephropathy in patients with diabetes mellitus between iso- and low-osmolar contrast media: A meta-analysis of full-text prospective, randomized controlled trials. *PLoS One*. 2018;13(3):e0194330. doi:10.1371/journal.pone.0194330
27. Mehran R, Nikolsky E, Kirtane AJ, et al. Ionic low-osmolar versus nonionic iso-osmolar contrast media to obviate worsening nephropathy after angioplasty in chronic renal failure

patients: the ICON (Ionic versus non-ionic Contrast to Obviate worsening Nephropathy after angioplasty in chronic renal failure patients) study. *JACC Cardiovasc Interv*. 2009;2(5):415-421. doi:10.1016/j.jcin.2009.03.007
28. Heinrich MC, Häberle L, Müller V, Bautz W, Uder M. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology*. 2009;250(1):68-86. doi:10.1148/radiol.2501080833
29. Serafin Z, Karolkiewicz M, Gruszka M, et al. High incidence of nephropathy in neurosurgical patients after intra-arterial administration of low-osmolar and iso-osmolar contrast media. *Acta Radiol*. 2011;52(4):422-429. doi:10.1258/ar.2011.100501
30. Barrett BJ, Parfrey PS, Vavasour HM, et al. Contrast nephropathy in patients with impaired renal function: high versus low osmolar media. *Kidney Int*. 1992;41(5):1274-1279. doi:10.1038/ki.1992.189
31. Nabi Z, Anjum N, Rashid RM, Zahideen ZU. Contrast Induced Nephropathy In High Risk Patients - Myth Or Reality. *J Ayub Med Coll Abbottabad*. 2021;33(4):568-571.