

Contrast-Induced Nephropathy: a comprehensive review

Kamel Hassan Ghazal¹, Tamer Muhammed Moustafa Abdelghany¹, Khaled Muhammed Souliman Hamed², Ahmed Said Eldamahoury

¹Department of cardiology, Faculty of Medicine, Zagazig University.

²Department of cardiology, National Heart Institute.

Corresponding author: Khaled Muhammed Souliman Hamed

Email: khaledmuhammed178@gamil.com

ABSTRACT

Contrast-induced nephropathy (CIN) is defined as the impairment of renal function measured as either a 25% increase in serum creatinine (SCr) from baseline or a 0.5 mg/dL (44 μmol/L) increase in absolute SCr value within 48-72 hours after intravenous contrast administration. Although prophylactic hydration has been promising in decreasing the occurrence of CIN, other efforts such as diuretics, calcium channel blockers, theophylline, aminophylline, atrial natriuretic peptide, dopamine, and fenoldopam have been disappointing. The preventive effect of N-acetylcysteine on CIN has not been consistent in the literature. In a recent clinical trial, bicarbonate infusion was more effective than hydration in the prevention of CIN. Mechanical devices are in development to perfuse renal arteries with protective drugs during contrast exposure or for removal of contrast from coronary sinus during coronary angiography. In this article, we have reviewed available data in regards to CIN.

Introduction, incidence, and definition

Contrast-mediated imaging studies are an integral part of modern medical practice. Contrast agents are used in more than 10 million procedures annually in the world of the most important complications of contrast agents is kidney toxicity [1]. Contrast-induced nephropathy (CIN) is one of the leading causes of renal impairment in the world [2] and the third cause of hospital-acquired renal failure [3]. McCullough et al. [4] reported that CIN occurs in 14.5% of unselected patients undergoing coronary angiography. In another study involving 1144 patients, the incidence of contrast nephropathy in patients who underwent cardiac catheterization was approximately 0.7% and increased to 20% in patients with baseline creatinine between 1.5 and 2.0 mg/dl [5]. Patients with renal insufficiency have a higher risk of developing atherosclerosis and thus will be frequently referred for decreased renal angiography [6].

As such, in patients with cardiovascular diseases are accelerated due to various abnormalities in atherogenic factors [7]. The total incidence rate of CIN in another study was 29% [8]. On the other hand, Berg [9] estimated the chances of CIN in the general population undergoing coronary angiography to be less than 2%.

However, it could be as high as 80% in patients with diabetes and underlying kidney disease [10]. The impact of diabetes and existing renal insufficiency on the incidence of CIN has been studied by Parfrey et al.[2]. In a prospective study of patients with diabetes, renal insufficiency, and diabetes plus renal insufficiency, they determined that diabetic patients with normal renal function and nondiabetic patients with renal insufficiency are not at an increased risk of nephrotoxicity. However, the risk for diabetic patients with preexisting renal insufficiency was found to be higher than the control group (8.8% vs. 1.6%, respectively). Reduction in the incidence of CIN can lead to a decrease in the morbidity, mortality (up to 36%) and length of hospital stay [11]. In a recent meta-analysis, the incidence of CIN ranged from 2% to 26% in patients receiving N-acetylcysteine (NAC) plus sodium chloride and 11–45% in those patients administered sodium chloride hydration alone [12]. Although the use of low-osmolar contrast agents decreased the incidence of CIN, there is still a chance of CIN [13]. Different trials have used diverse definitions for CIN. These include a serum creatinine increase of more than 0.5 mg/dl [14] or more than 25% of the baseline level [15] at 120 h [16] after contrast exposure.

Pathophysiology

The pathophysiology of CIN is complex and poorly understood. Multiple mechanisms act in concert to induce CIN. Intrarenal vasoconstriction, generation of reactive oxygen species, and direct tubular damage are the predominant factors that lead to CIN. However, relative contribution of each mechanism alone is not known. Several groups have documented immediate vasoconstriction and reduction in renal blood flow occurring after administration of contrast medium. 6-12 Multiple studies in animal models have shown that intra-arterial infusion of ionic contrast medium caused transient initial increase in blood flow followed by an intense and prolonged constriction of renal vasculature [17]. Although the mechanism for this vasoconstriction is not completely known, these investigators demonstrated the importance of calcium influx in the vasoconstrictive phase following contrast exposure. 8 Recent information has demonstrated that the flow to the outer medulla is reduced by 40% following contrast material administration and is associated with a 60% reduction in oxygen delivery. These changes result in ischemic injury, which contributes to the histopathologic findings seen in CIN models [18]. Multiple agents are implicated in producing renal vasoconstriction. For instance, there is significant evidence for the role of endothelin in the pathogenesis of CIN. A seminal study demonstrated a significant elevation in plasma endothelin level within 5 min of contrast material administration [19]. Importantly, the study revealed that no significant change in plasma endothelin levels was detected until the volume of the contrast material exceeded 150 mL. Adenosine has also been found to induce local renal vasoconstriction.

In addition to the presence of vasoconstrictors, there is concomitant impairment of vasodilatation in patients with CIN. 10 Nitric oxide (NO) is a potent vasodilator produced from L-arginine in the presence of the enzyme NO synthase. High-osmolar contrast agents reduce NO production, and this reduction was proportional

to osmolality of the solution [20]. However, concerns regarding NO inhibition following contrast administration and its negative impact on renal function have been raised by Sancak et al. [21]. A compromised medullary blood supply brought on by contrast administration creates a mismatch between the metabolic demands of the thick ascending limbs of the loop of Henle and its own blood supply resulting in the production of superoxide (a potent reactive oxygen species) leading to oxidative tubular damage. Preexisting chronic renal failure, increased age, and diabetes decrease the ability to accommodate oxidative stress and lead to increased risk of CIN [21]. Contrast administration induces osmotic diuresis in euvolemic patients with normal kidney function. Exposure of renal tissue to high osmotic radiocontrast agents results in characteristic histopathologic changes called “osmotic nephrosis.” [22]. The most frequent histopathologic features of “osmotic nephrosis” include intense focal or diffuse proximal

Management of Contrast Nephropathy

To date, there is no definitive treatment of AKI following radiocontrast administration. However, prevention still remains the cornerstone of this entity and as such demands a careful analysis of the risk factors and implementation of preventive strategies noted below.

Maintenance of volume status

Avoidance of intravascular volume depletion is the single most important strategy to reduce the risk of contrast-induced renal injury. In this context, maintenance of adequate hydration is of paramount importance. Often patients are receiving NSAIDs. Such agents should be stopped 24–48 h before the procedure. Recommended regimens for volume replacement for hospitalized patients undergoing contrast administration include normal saline administered at 1 mL/kg/h for 6–12 h preprocedural, intraprocedural, and continued for 6–12 h post procedure [23]. In patients with compensated congestive heart failure, fluids should be administered based on physician discretion and with frequent lung examination. Normal saline produces better volume expansion and has been shown to have superiority over hypotonic solutions such as 0.45% saline [24]. While diuretics are not recommended, a recent study demonstrated that loop diuretics may decrease the incidence of CIN [25]. Conflicting data continue to surround the use of sodium bicarbonate versus normal saline. Thus far, the largest randomized clinical study failed to show any benefit of sodium bicarbonate over normal saline [26]. As such, normal saline is the best available solution to reduce the risk of contrast nephropathy. *N-acetylcysteine* the sulfhydryl group of *N-acetylcysteine* is an excellent antioxidant and scavenger of free oxygen radicals. However, it has failed to show conclusive evidence of protecting against the development of CIN [27].

Because of its low cost, lack of adverse effects, and potential beneficial effect, this agent is frequently a part of the protective strategies of multiple medical centers against contrast nephropathy. Nevertheless, based on the lack of conclusive evidence, we do not recommend this agent [28].

Prophylactic hemofiltration and hemodialysis

Clinicians often ask for dialysis therapy soon after the administration of contrast material. However, there is no conclusive evidence that prophylactic dialysis prevents renal injury due to contrast administration [29]. At present, we do not recommend prophylactic dialysis therapy. Dialysis itself is not devoid of complications and requires an invasive procedure of a large bore catheter insertion.

Risk Factors

For optimal management, it is critically important for providers to be able to stratify patients according to their risk for CIN. Preexisting CKD with concomitant diabetes mellitus poses the highest risk for CIN. Other factors that increase the risk for CIN include advanced age, cardiovascular disease, preprocedural hemodynamic instability, and concomitant use of certain drugs. Figure 1 summarizes some common risk factors [30]. A quick review of the risk factors could be very helpful in evaluating patients who would be at risk for the development of CIN.

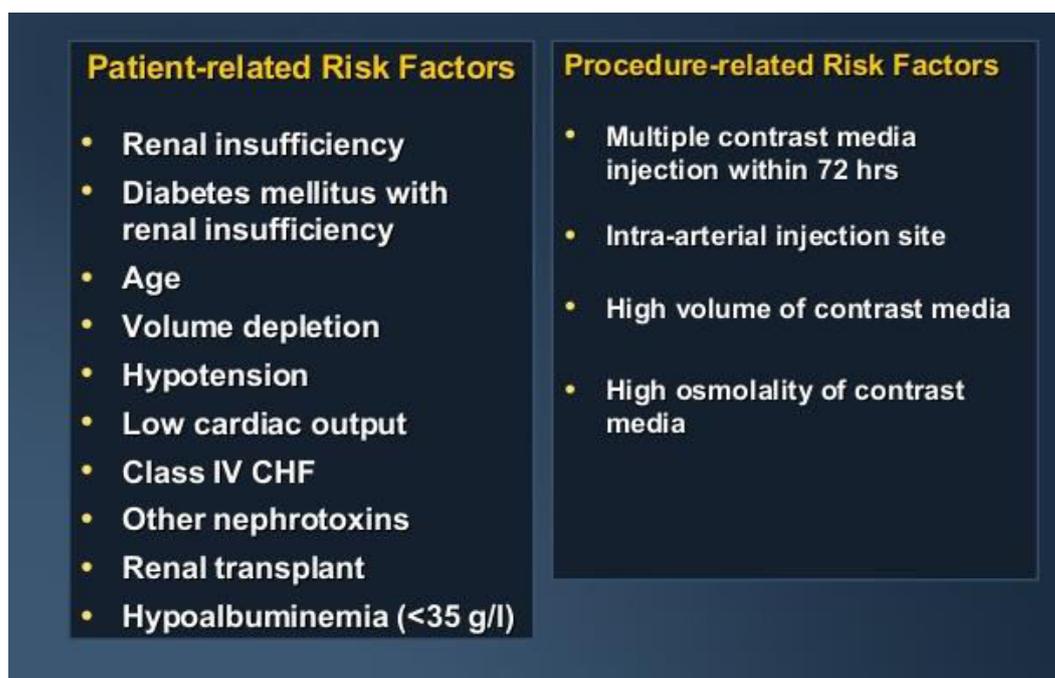


Figure 1: Risk Factors for CIN

Preexisting impairment of renal function

Preexisting CKD is of paramount importance and places patients at a high risk for the development of CIN. In a series of 1144 patients, Davidson et al [31], investigated patients undergoing cardiac catheterization and documented a low risk of CIN (increment of creatinine levels of at least 0.5 mg/dL) in patients with normal renal function compared to those with preexisting CKD (creatinine level exceeding 1.2 mg/dL). These investigators found that the risk for CIN increased significantly (20%) when serum creatinine exceeded 2.0 mg/dL.

Diabetes mellitus with preexisting chronic kidney disease

Diabetics with CKD are reported to have a four-fold increase in the risk for development of CIN when compared with patients without diabetic nephropathy.²⁰ Diabetes mellitus with associated renal insufficiency has been identified as an independent risk factor for contrast nephropathy, with as many as 56% of those who develop the condition progressing to irreversible renal failure. Diabetics with advanced CKD (serum creatinine >3.5 mg/dL) are at a particularly higher risk for the development of CIN [32].

Age

In many studies, higher prevalence of CIN was observed in patients with increased age, possibly reflecting the decline in renal function with age. Advanced age is associated with increased vascular stiffness with declined endothelial function resulting in reduced vasodilator responses as well as a reduced capacity for vascular repair with pluripotent stem cells. All these factors together increase the risk of CIN in the elderly patient and reduce the potential for prompt recovery [33].

Reduction of effective intravascular volume

Reduction of effective intravascular volume (due to congestive heart failure, liver cirrhosis, or abnormal fluid losses), prolonged hypotension (especially when induced by intensive antihypertensive treatment combined with angiotensin-converting enzyme (ACE) inhibitors, and diuretics, most notably furosemide), and dehydration have been reported as contributing to prerenal reduction in renal perfusion, thus enhancing the ischemic insult of contrast media [34].

Prevention

Although prophylactic hydration has been promising in decreasing the occurrence of CIN, other efforts such as diuretics [35], calcium channel blockers [36], theophylline [37], aminophylline [38], atrial natriuretic peptide [39], dopamine [40], and fenoldopam [41] have been disappointing in decreasing the incidence of CIN [42]. Because contrast agents preferentially reduce flow to the outer medulla, attempts to prevent CIN with vasodilators that do not augment medullary blood flow could worsen tissue hypoxia and thereby increase the incidence of contrast nephropathy [43].

Dopamine partially restored flow to the inner and outer cortex but had no effect on blood flow to the outer medulla [44]. However, CIN might result from hyperosmolar stress in the renal medulla, which is oxygen-deficient [45].

Volume and type of contrast

Existing evidence indicates that among patients with preexisting chronic kidney disease, the incidence of contrast nephropathy is not impacted by the volume of contrast. In a recent study to evaluate the role of volume of contrast in the development of nephropathy, Tardos et al. [46] reviewed 931 cases of coronary angiography and found 117 patients who had preexisting kidney disease (creatinine clearance ≤ 60 ml/min). They compared 22 patients who fulfilled the criteria for nephropathy with those without nephropathy and found that the volume of contrast was similar in both groups. Gadolinium-based media have been proposed as the

feasible alternatives to iodinated contrast for use in patients considered at high risk for nephropathy [47]. Kaufman et al. [48] have successfully used gadopentetate dimeglumine as contrast agent during peripheral vascular interventions in two patients, with no subsequent nephropathy.

Matchett et al. [49] used gadopentetate dimeglumine as contrast agent at digital subtraction angiography in one azotemic patient without complication. Rieger et al. [50] studied the effect of gadopentetate dimeglumine on renal function in 32 angiographic procedures among 29 patients with advanced renal insufficiency (59% diabetic). Only one patient who had undergone renal angioplasty and stenting developed worsening of renal function; this was attributed to possible cholesterol embolism. Using gadolinium dimeglumine to perform 34 digital subtraction angiographies in 31 patients with previous anaphylactic reaction to iodinated contrast agents, Hammer et al. [51] observed no side effects. Spinosa et al. [52] used gadodiamide as the angiographic contrast agent in diagnosis of renal artery stenosis in 25 procedures involving 24 patients with renal insufficiency. There was an increase in creatinine following two of the procedures. One of these patients had transplant rejection, and the other had evidence of cholesterol embolization. Gadodiamide appears to be a safe contrast in patients with renal insufficiency.

Ascorbic acid

Preliminary evidence supports a role for the prophylactic use of ascorbic acid in protecting against CIN. In a randomized, double-blind, placebo-controlled trial of ascorbic acid vs. placebo, Spargias et al. [53] evaluated the protective effect of ascorbic acid in 231 patients with a serum creatinine ≥ 1.2 mg/dl who underwent coronary angiography and/or intervention. A total of 7 g of ascorbic acid was administered in three doses (starting at least 2 h prior to the procedure, followed by two doses postprocedural).

CIN was noted to occur less commonly among the ascorbic acid group compared to the placebo group (9% vs. 20%, respectively; odds ratio: 0.38, 95% confidence interval: 0.17–0.85, $P=0.02$). The mean increase in serum creatinine was also significantly greater in the placebo group than in the ascorbic acid group.

Dialysis

Current evidence does not support the prophylactic use of dialysis for prevention of contrast nephropathy in patients with or without renal insufficiency [54]. However, Marenzi et al. [55] have successfully used hemofiltration in prevention of contrast nephropathy in 114 patients with chronic renal failure undergoing intravenous contrast studies. They compared 56 patients who only received hydration with 58 patients who received hemofiltration. Both interventions were initiated 4–8 h before the contrast exposure. The hemofiltration group demonstrated a benefit in all outcomes measured: incidence of nephropathy (5% vs. 50%), requirement of dialysis (3% vs. 25%), in-hospital mortality (2% vs. 14%), and 1-year mortality (10% vs. 30%). It is noteworthy that although very impressive, this is a preliminary study, and

further studies are required before hemofiltration can be incorporated as the standard of care in prevention of contrast nephropathy.

Future development

To decrease contrast exposure to the kidneys, there are investigational devices designed to infuse protective drugs into the renal arteries. One of the devices uses a bilateral catheter system to perfuse the renal bodies intra-arterially [56]. The long-term benefit of this device needs to be studied in future trials. A novel method for removing contrast from coronary sinus to decrease contrast exposure to the kidneys has been tested in animal models by Mogahed et al. [57] and could be a promising new development in the future.

Conclusion

CIN is a life-threatening condition in predisposed patients after iodine contrast exposure. Many medications for the prevention of CIN are tested in clinical trials with mixed results. Currently, intravenous hydration remains the gold standard for prevention of CIN. Most experts suggest the use of NAC in high-risk patients due to the lack of significant side effects. The use of sodium bicarbonate infusion is promising in the prevention of CIN but requires further studies before it is routinely used in clinical practice.

References:

- [1] **Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR.** Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;105(19):2259–64.
- [2] **Parfrey PS, Griffiths SM, Barrett BJ, Paul MD, Genge M, Withers J, Farid N, McManamon PJ.** Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. *N Engl J Med* 1989;320(3):143–9.
- [3] **Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT.** Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983;74(2):243–8.
- [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):368–75.
- [5] **Davidson CJ, Hlatky M, Morris KG, Pieper K, Skelton TN, Schwab SJ, Bashore TM.** Cardiovascular and renal toxicity of an anionic radiographic contrast agent after cardiac catheterization. A prospective trial. *Ann Intern Med* 1989;110(2):119–24.
- [6] **Foley RN, Parfrey PS, Sarnak MJ.** Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998;32(5):S112–9.
- [7] **McCullough PA.** Cardiorenal risk: an important clinical intersection. *Rev Cardiovasc Med* 2002;3(2):71–6.

- [8] **Tumlin JA, Wang A, Murray PT, Mathur VS.** Fenoldopam mesylate blocks reductions in renal plasma flow after radiocontrast dye infusion: a pilot trial in the prevention of contrast nephropathy. *Am Heart J* 2002;143(5):894–903
- [9] **Berg KJ.** Nephrotoxicity related to contrast media. *Scand J Urol Nephrol* 2000;34(5):317–22.
- [10] **Safirstein R, Andrade L, Vieira JM.** Acetylcysteine and nephrotoxic effects of radiographic contrast agents—a new use for an old drug. *N Engl J Med* 2000;343(3):210–2.
- [11] **Parfrey PS, Griffiths SM, Barrett BJ, Paul MD, Genge M, Withers J, Farid N, McManamon PJ.** Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. *N Engl J Med* 1989;320(3):143–9.
- [12] **Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W.** Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000;343(3):180–4.
- [13] **Birck R, Krzossok S, Markowitz F, Schnulle P, van der Woude FJ, Braun C.** Acetylcysteine for prevention of contrast nephropathy: metaanalysis. *Lancet* 2003;362(9384):598–603.
- [14] **Taliercio CP, Vlietstra RE, Ilstrup DM, Burnett JC, Menke KK, Stensrud SL, Holmes DR.** A randomized comparison of the nephrotoxicity of iopamidol and diatrizoate in high risk patients undergoing cardiac angiography. *J Am Coll Cardiol* 1991;17(2):384–90.
- [15] **Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H.** Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. *Arch Intern Med* 2002;162(3):329–36.
- [16] **Kay J, Chow WH, Chan TM, Lo SK, Kwok OH, Yip A, Fan K, Lee CH, Lam WF.** Acetylcysteine for prevention of acute deterioration of renal function following elective coronary angiography and intervention: a randomized controlled trial. *JAMA* 2003;289(5): 553–8.
- [17] **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):368–75.
- [18] **Solomon R.** Contrast-medium-induced acute renal failure. *Kidney Int* 1998;53(1):230–42.
- [19] **Schwab SJ, Hlatky MA, Pieper KS, Davidson CJ, Morris KG, Skelton TN, Bashore TM.** Contrast nephrotoxicity: a randomized controlled trial of a nonionic and an ionic radiographic contrast agent. *N Engl J Med* 1989;320(3):149–53.
- [20] **Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT.** Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983;74(2):243–8.

- [21] **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– 75.
- [22] **Davidson CJ, Hlatky M, Morris KG, Pieper K, Skelton TN, Schwab SJ, Bashore TM.** Cardiovascular and renal toxicity of an ionic radiographic contrast agent after cardiac catheterization. A prospective trial. *Ann Intern Med* 1989;110(2):119– 24.
- [23] **McCullough PA.** Cardiorenal risk: an important clinical intersection. *Rev Cardiovasc Med* 2002;3(2):71–6.
- [24] **Tumlin JA, Wang A, Murray PT, Mathur VS.** Fenoldopam mesylate blocks reductions in renal plasma flow after radiocontrast dye infusion: a pilot trial in the prevention of contrast nephropathy. *Am Heart J* 2002;143(5):894– 903.
- [25] **Durham JD, Caputo C, Dokko J, Zaharakis T, Pahlavan M, Keltz J, Dutka P, Marzo K, Maesaka JK, Fishbane S.** A randomized controlled trial of N-acetylcysteine to prevent contrast nephropathy in cardiac angiography. *Kidney Int* 2002;62(6):2202– 7.
- [26] **Briguori C, Manganelli F, Scarpato P, Elia PP, Golia B, Riviezzo G, Lepore S, Librera M, Villari B, Colombo A, Ricciardelli B.** Acetylcysteine and contrast agent-associated nephrotoxicity. *J Am Coll Cardiol* 2002;40(2):298 –303.
- [27] **Diaz-Sandoval LJ, Kosowsky BD, Losordo DW.** Acetylcysteine to prevent angiography-related renal tissue injury (the APART Trial). *Am J Cardiol* 2002;89(3):356–8.
- [28] **MacNeill BD, Harding SA, Bazari H, Patton KK, Colon-Hernandez P, DeJoseph D, Jang IK.** Prophylaxis of contrast-induced nephropathy in patients undergoing coronary angiography. *Catheter Cardiovasc Interv* 2003;60(4):458– 61.
- [29] **Bakris GL, Burnett JC.** A role of calcium in radiocontrast-induced reductions in renal hemodynamics. *Kidney Int* 1985;27(2):465– 8.
- [30] **Russo D, Minutolo R, Cianciaruso B, Memoli B, Conte G, DeNicola L.** Early effects of contrast media on renal hemodynamics and tubular function in chronic renal failure. *J Am Soc Nephrol* 1995;6(5):1451– 8.
- [31] **Flemming B, Seeliger E, Wronski T, Steer K, Arenz N, Persson PB.** Oxygen and renal hemodynamics in the conscious rat. *J Am Soc Nephrol* 2000;11(1):18– 24.
- [32] **Rudnick MR, Goldfarb S, Wexler L, Ludbrook PA, Murphy MJ, Halpern EF, Hill JA, Winniford M, Cohen MB, VanFossen DB.** Nephrotoxicity of ionic and

nonionic contrast media in 1196 patients: a randomized trial. The Iohexol Cooperative Study. *Kidney Int* 1995;47(1):254– 61.

[33] **Berns AS.** Nephrotoxicity of contrast media. *Kidney Int* 1989;36(4):730–40.

[34] **Tepe M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W.** Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000;343(3):180– 4

[35] **Gruberg L, Mintz GS, Mehran R, Gangas G, Lansky AJ, Kent KM, Pichard AD, Satler LF, Leon MB.** The prognostic implications of further renal function deterioration within 48 h of interventional coronary procedures in patients with pre-existent chronic renal insufficiency. *J Am Coll Cardiol* 2000;36(5):1542– 8.

[36]. **Aspelin P, Aubry P, Fransson SG.** Nephrotoxic effects in high-risk patients undergoing angiography. *N Engl J Med* 2003; 348:491-9.

[37] **Neumayer HH, Junge W, Kufner A, Wenning A.** Prevention of radiocontrast-media-induced nephrotoxicity by the calcium channel blocker nitrendipine: a prospective randomised clinical trial. *Nephrol Dial Transplant* 1989;4(12):1030– 6.

[38] **Erley CM, Duda SH, Schlepckow S, Koehler J, Huppert PE, Strohmaier WL, Bohle A, Risler T, Osswald H.** Adenosine antagonist theophylline prevents the reduction of glomerular filtration rate after contrast media application. *Kidney Int* 1994;45(5):1425– 31.

[39] **Shammas NW, Kapalis MJ, Harris M, McKinney D, Coyne EP.** Aminophylline does not protect against radiocontrast nephropathy in patients undergoing percutaneous angiographic procedures. *J Invasive Cardiol* 2001;13(11):738– 40.

[40] **Kurnik BR, Allgren RL, Genter FC, Solomon RJ, Bates ER, Weisberg LS.** Prospective study of atrial natriuretic peptide for the prevention of radiocontrast-induced nephropathy. *Am J Kid Dis* 1998;31(4):674– 80.

[41] **Kapoor A, Sinha N, Sharma RK, Shrivastava S, Radhakrishnan S, Goel PK, Bajaj R.** Use of dopamine in prevention of contrast induced acute renal failure—a randomised study. *Int J Cardiol* 1996;53(3):233– 6.

[42] **Stone GW, McCullough PA, Tumlin JA, Lepor NE, Madyoon H, Murray P, Wang A, Chu AA, Schaer GL, Stevens M, Wilensky RL, O'Neill WW, CONTRAST Investigators.** Fenoldopam mesylate for the prevention of contrast-induced nephropathy: a randomized controlled trial. *JAMA* 2003;290(17):2284– 91.

- [43] **Nygren A.** Contrast media and regional renal blood flow. A study of the effects of ionic and non-ionic monomeric and dimeric contrast media in the rat. *Acta Radiol Suppl* 1992;378(Pt 3):123– 35.
- [44] **Neiberger RE, Passmore JC.** Effects of dopamine on canine intrarenal blood flow distribution during hemorrhage. *Kidney Int* 1979;15(3): 219– 226.
- [45] **Tadros GM, Malik JA, Manske CL, Kasiske BL, Dickinson SE, Herzog CA, Wilson RF, Das G, Panetta CJ.** Iso-osmolar radio contrast iodixanol in patients with chronic kidney disease. *J Invasive Cardiol* 2005;17:211– 5.
- [46] **Kaufman JA, Geller SC, Waltman AC.** Renal insufficiency: gadopentetate dimeglumine as a radiographic contrast agent during peripheral vascular interventional procedures. *Radiology* 1996;198:579– 81.
- [47] **Matchett WJ, McFarland DR, Russell DK, Sailors DM, Moursi MM.** Azotemia: gadopentetate dimeglumine as contrast agent at digital subtraction angiography. *Radiology* 1996;201:569– 71.
- [48] **Rieger J, Sitter T, Toepfer M, Linsenmaier U, Pfeifer KJ, Schiffel H.** Gadolinium as an alternative contrast agent for diagnostic and interventional angiographic procedures in patients with impaired renal function. *Nephrol Dial Transplant* 2002;17:824– 8.
- [49] **Hammer FD, Gofette PP, Malaise J, Mathurin P.** Gadolinium dimeglumine: an alternative contrast agent for digital subtraction angiography. *Eur Radiol* 1999;9:128– 36.
- [50] **Spinosa DJ, Matsumoto AH, Angle JF, Hagspiel KD, McGraw JK, Ayers C.** Renal insufficiency: usefulness of gadodiamide-enhanced renal angiography to supplement CO₂-enhanced renal angiography for diagnosis and percutaneous treatment. *Radiology* 1999;210:663– 72.
- [51] **Spargias K, Alexopoulos E, Kyrzopoulos S, Iacovis P, Greenwood DC, Manginas A, Voudris V, Pavlides G, Buller CE, Kremastinos D, Cokkinos DV.** Ascorbic acid prevents contrast mediated nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. *Circulation* 2004;110(18):2837– 42.
- [52] **Vogt B, Ferrari P, Schonholzer C, Marti HP, Mohaupt M, Wiederkehr M, Cereghetti C, Serra A, Huynh-Do U, Uehlinger D, Frey FJ.** Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. *Am J Med* 2001;111:692–8.

[53] **Marenzi G, Marana I, Lauri G, Assanelli E, Grazi M, Campodonico J, Trabattori D, Fabbiochi F, Montorsi P, Bartorelli AL.** The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. *N Engl J Med* 2003;349(14):1333–40.

[54] **Minarsch L.** Renal protection in the cathlab: a novel therapeutic device for high-risk patients undergoing PCI. *Catheter Lab Dig* 2005;13(3):70 –1.

[56] **Movahed MR, Kassab G, Molloy SY.** Successful removal of iodine contrast from coronary sinus in swine during coronary angiography for prevention of contrast induced nephropathy. Annual Meeting American Society for Cardiac Angiography and Intervention [abstract]. *Catheter Cardiovasc Interv* 2004;62:97.

[57] **Vogt B, Ferrari P, Schonholzer C, Marti HP, Mohaupt M, Wiederkehr M, Cereghetti C, Serra A, Huynh-Do U, Uehlinger D, Frey FJ.** Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. *Am J Med* 2001;111:692–8.