European Society of Urogenital Radiology guidelines on contrast media application

Henrik S. Thomsen

Purpose of review

The present review covers the European Society of Urogenital Radiology guidelines for safe use of contrast media of importance for referring urologists.

Recent findings

During the recent years contrast medium-induced nephropathy has become a hot topic. It is of importance to reduce its incidence. First of all, the patients at risk should be identified prior to the administration of a contrast medium, so that appropriate measures can be taken. Before intravenous administration of an iodinated agent but not before gadolinium-based and ultrasound agents, all patients should be questioned about the potential renal dysfunction at the time of referral, and only those who answer affirmative to at least one question should have their serum creatinine level determined. Before intraarterial injection, the serum creatinine should always be measured. In case of an abnormal level, another imaging procedure should be considered. If impossible, hydration should be instituted and administration of nephrotoxic drugs should be stopped. After administration, delayed reactions such as nephrogenic systemic fibrosis, thyreotoxicosis, skin rash, etc. may be seen. Interaction with isotope studies and biochemical analysis occurs too.

Summary

The awareness regarding the potential adverse reactions due to contrast media and the necessary precautions to be taken are of utmost importance both for radiologists and referring physicians. This is the only way to reduce their incidence.

Keywords

contrast media, contrast medium-induced nephropathy, delayed adverse reactions

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Department of Diagnostic Radiology, Copenhagen University Hospital at Herlev, Herlev, Denmark

Correspondence to Professor Henrik S. Thomsen MD, Department of Diagnostic Radiology, Copenhagen University Hospital at Herlev, Herlev Ringvej 75, DK-2730 Herlev, Denmark,
Tel: +45 44 88 32 12; fax: +45 44 91 04 80; e-mail: heth@herlevhosp.kbhamt.dk

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Abbreviations

CMIN	contrast medium-induced nephropathy
CMSC	Contrast Media Safety Committee
CT	computed tomography
ESUR	European Society of Urogenital Radiology
GFR	glomerular filtration rate
MDRD	Modification of Diet in Renal Disease
MR	magnetic resonance
MRI	magnetic resonance imaging
SCr	serum creatinine

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Introduction

Most work-up of the signs and symptoms of urologic disease requires the use of contrast media with renal stone/flank pain as the major exception. An ideal contrast medium should be totally inert, causing no interactions with the organism at any level. Furthermore, it should be excreted rapidly and completely. In reality, a contrast agent is not totally inert, but the modern agents are close to that state. Since 1996, the Contrast Media Safety Committee (CMSC) of the European Society of Urogenital Radiology (ESUR) has released 19 guidelines regarding safety in relation to the use of radiographic, ultrasonographic, as well as magnetic resonance agents [1,2••]. The guidelines have been received well by the radiological community not only in Europe but also all over the world, and these are now standards for good practice at many institutions. The present paper focuses on the portions of the work that are of special interest to an urologist.

Contrast medium application in patients with elevated creatinine levels

All extracellular contrast media are excreted from the body through glomerular filtration. During their passage through the kidney, contrast agents may induce a temporary or permanent decrease in renal function, particularly when the function is abnormal [serum creatinine (SCr) > 132 μmol/l (1.5 mg/dl)] [3••]. As a matter of fact, contrast medium-induced nephropathy (CMIN) is considered an important cause of hospital-acquired renal failure [4,5]. Prevention of this complication is important to avoid substantial morbidity and even mortality that can be sometimes associated with CMIN. Even a small decrease in renal function may greatly exacerbate morbidity that is caused by the coexisting conditions [6,7].

Sepsis, bleeding, coma, and respiratory failure are frequently observed in patients with acute renal failure. CMIN may occur both after the administration of gadolinium-based [for magnetic resonance imaging (MRI)] and iodine-based agents (for radiography) [3••,8•,9].

Identifying the high-risk patients at the time of referral

The patients at the highest risk of developing CMIN are those with pre-existing renal impairment [>132 μmol/l (1.5 mg/dl)], particularly when reduction in renal function is secondary to diabetic nephropathy [10,11•]. Without renal impairment, diabetes mellitus is not a risk factor *per se* [11•,12]. It is crucial to identify patients who are at increased risk of developing CMIN at the time of referral. Given the relatively low incidence of CMIN, it would be impractical and expensive to routinely measure the SCr levels for all patients scheduled for diagnostic procedures with parenteral contrast administration.

Iodine-based contrast media

The ESUR recommends that all patients scheduled for intraarterial application of an iodinated contrast medium should have their SCr levels determined before the examination and all patients referred for contrast-enhanced diagnostic examinations, in which the contrast medium is given intravenously, should be asked about a history of renal disease, diabetes, proteinuria, renal surgery, hypertension, and/or gout [2••,3••,13•]. Given the identification of left ventricular function as a predictor of CMIN in several retrospective analyses, Pannu *et al.* [14••] believe that a history of congestive heart failure should also be sought. The patients with chronic heart failure, however, underwent intraarterial injection. The patients for whom determination of the SCr is recommended, the measurement should take place within 7 days prior to the scheduled examination and the department of radiology should be informed no later than 24 h before the scheduled examination so that the necessary precautions can be taken [start of hydration prior to the examination, doing ultrasound, and MRI instead of computed tomography (CT), etc] [2••,3••,13•].

In the emergency room, the SCr measurement may cause unacceptable delays in diagnostic imaging. Therefore, the patients who require urgent procedures before renal function can be measured should also be considered at high risk if possible.

The use of SCr level has been questioned, as SCr is not an ideal marker of renal function. The SCr level depends on muscle mass and is not usually raised until the glomerular filtration rate (GFR) has fallen by at least 50%. Endogenous SCr clearance as a measure of GFR is also inaccurate, especially when renal function is low because of a compensatory increase in tubular secretion, limiting its validity as a glomerular filtration marker [3••,13•,15•]. Radionuclide techniques are preferable; however, each of these tests is labor intensive and impossible to perform in all patients undergoing contrast-enhanced imaging. Alternatively, renal function can be estimated by using specially derived predictive equations. The most accurate results are obtained with the Cockroft–Gault equation, whereas the most precise formula is the Modification of Diet in Renal Disease (MDRD) study equation [13•,16••,17]. Unfortunately, the predictive capabilities of these formulae are suboptimal for ideal patient care. The Cockroft–Gault formula progressively overestimates the GFR as it reaches the lower levels, whereas the MDRD formula yields an estimate corrected to a body surface area of 1.73 m^2, which is not appropriate in judging the impact of drug exposure on an individual. On the contrary, these methods, which are readily available for use on hand-held electronic devices if the calculation is not automatically provided by the local laboratory in their reports, are far superior for assessing renal function compared with a simple SCr measurement. Despite the inaccuracies of the SCr measurements, it is an adequate measure for identifying the patients who are at risk of CMIN as patients with normal SCr [<132 μmol/l (1.5 mg/dl)] are at almost no risk [11•,15•,18]. The degree of renal insufficiency present before the administration of CM determines the severity of CMIN to a great extent, and the patients with a GFR below 30 ml/min/1.73 m^2 are particularly at risk [15•,19].

Gadolinium-based contrast media

The fact that CMIN is only rarely seen after the intravenous administration of magnetic resonance (MR) approved doses (0.1–0.3 mmol/l) has led to the erroneous inference that gadolinium-based CM are not at all nephrotoxic. The doses commonly used for CT examinations and angiography are, however, higher than those used for MRI, but they still do not provide equal radiographic attenuation compared with iodine [8•,11•,20]. At radiographic doses, gadolinium-based agents are probably at least as nephrotoxic, if not more, as the iodinated agents. Regarding MRI, the incidence is not so high that it could be recommended that the SCr level is determined before MRI with gadolinium-based agents (see also Delayed reactions).

Increased serum creatinine and metformin

Iodinated contrast media should be used with care in patients receiving metformin. Contrast media can induce a reduction in renal function, leading to the retention of metformin that may induce lactic acidosis, as there is a very rapid onset of renal injury after the administration of the agent [21,22]. The complication is almost always observed in noninsulin-dependent diabetic patients with abnormal renal function before the injection of the contrast medium. The CMSC recommends that in the patients with abnormal SCr levels, the intake of metformin is stopped 48 h prior to contrast administration

[21,22]. SCr should always be monitored to check that it is within the normal range before the administration of metformin is resumed.

The patients with increased serum creatinine levels

That the department of radiology is informed at least 24 h before the examination is scheduled is extremely important, so that adequate precautions can be taken [3••,13•]. Over the years, several measures have been recommended to reduce the incidence of CMIN [3••,14••,16••,17,23••,24,25••,26,27••,28•,29]: volume expansion, hydration with intravenous administration of normal saline solution (NaCl 0.9%) or half-strength saline solution (NaCl 0.45%), infusion of sodium bicarbonate instead of normal saline, infusion of mannitol, pharmacological manipulation (administration of atrial natriuretic peptide, loop diuretics, calcium antagonists, theophylline, dopamine, dopamine-1 receptor antagonist fenoldopam, acetylcysteine), use of low-osmolar nonionic contrast media instead of high-osmolar ionic contrast media, use of isoosmolar contrast media instead of low-osmolar contrast media, gadolinium-based agents instead of iodine-based agents for radiography and CT, hemodialysis immediately after contrast administration, hemofiltration during and after contrast administration, injection of a small volume of contrast medium, and avoiding short intervals (less than 48 h) between procedures requiring intravascular administration of contrast agents.

Of all the above-mentioned measures, extracellular volume expansion and the use of low-osmolar contrast media have been found systematically to be consistently effective [3••,9,16••,23••,29,30,31•,32,33]. Volume expansion can be achieved with an intravenous injection of at least 100 ml/h of 0.9% saline solution starting 4 h before contrast administration and continuing for 24 h afterward [1,2••,3••]. In the areas with hot climate, more fluid should be given. This regime is suitable for patients who are not at risk of congestive heart failure and are not allowed to drink or eat before undergoing an interventional or surgical procedure. If there is no contraindication to oral administration, free fluid intake should be encouraged. The CMSC recommends at least 500 ml of water or soft drinks before the procedure and 2500 ml for 24 h after the procedure. Recently, it has been suggested that sodium bicarbonate offers better protection than normal saline solution [34], but the experience is still limited. High quantity of sodium bicarbonate, as proposed in some guidelines, may cause alkalosis [35••]. Concurrent administration of nephrotoxic drugs such as gentamicin and nonsteroid anti-inflammatory drugs should also be avoided. Mannitol and furosemide enhance the risk of nephrotoxicity [36].

Over the years, various regimes of pharmacologic manipulation have been suggested in order to reduce the frequency of CMIN. The regimes have included calcium channel blockers that prevent the influx of calcium ions through voltage-operated channels and thereby cause a vasorelaxant effect in all vascular beds including the kidney, selective dopamine-1 receptor agonist (fenoldopam) that, in contrast to dopamine, increases both the cortical and medullary blood flow, endothelin antagonists that play an important role in renal vasculature, non-selective adenosine receptor antagonist, theophylline, which also causes vascular dilatation, and acetylcysteine, which is an antioxidant and a scavenger of oxygen free radicals. Administration of these drugs has been shown to be both effective in preventing CMIN in some studies and without any effect on others. Even the results of several metaanalyses have been conflicting [37••]. Therefore, at present, the CMSC does not recommend any pharmacologic manipulation for routine use in the prevention of CMIN.

High osmolar ionic media should not be used in patients at a risk of developing CMIN. At present, it is unclear whether there is a difference in the nephrotoxic potential between all the low-osmolar nonionic monomeric agents and the isoosmolar nonionic dimeric agent; there seems to be a difference between various low-osmolar nonionic agents [25••,27••,38]. It is, however, clear that all contrast agents can cause nephropathy in the patients with risk factors.

Guidelines

A recent review of various guidelines published over the last 7 years has observed inconsistency regarding the advice on the prophylactic use of drugs and the isoosmolar dimer to reduce the incidence of CMIN [35••]. Consistency was found in relation to the importance of hydration, cessation of intake of nephrotoxic drugs, and the administration of the lowest possible dose of CM. As a matter of fact, no new consensus has been observed in the comparison to the ESUR guidelines on nephrotoxicity that were published in 1999 [9].

Dialysis and contrast media

Dialysis has been used in the prevention of CMIN [39,40•,41]. Hemodialysis and peritoneal dialysis safely remove both iodinated-based and gadolinium-based contrast media from the body. The effectiveness of hemodialysis depends on various factors including blood and dialysate flow rate, permeability of dialysis membrane, duration of hemodialysis and molecular size, protein binding, hydrophilicity, and electrical charge of the agent. Generally, several hemodialysis sessions are needed to remove all contrast agents, whereas it takes 3 weeks for continuous ambulatory dialysis to remove the agent completely. Hemodialysis does not protect the poorly functioning kidneys against CMIN [42,43]. In addition, hemodialysis may cause deterioration of renal function through the activation of inflammatory reactions with the

release of vasoactive substances that may induce acute hypotension. The CMSC concluded that there is no need to schedule the dialysis in relation to the time of the injection of a contrast medium or schedule the injection of the agent in relation to the dialysis program [1,2••,39,40•].

Hemofiltration, which is a continuous form of renal replacement therapy, requires intravenous infusion of large volume of isotonic replacement fluid (1000 ml/h). This is exactly matched with the rate of ultrafiltrate production, so that no net fluid loss or overload occurs. A single study [44] has shown that in patients with chronic renal failure who are undergoing coronary interventions, hemofiltration given in intensive care unit (ICU) setting appears to be effective in reducing the incidence of CMIN as well as the rate of in-hospital morbidity and mortality. The procedure, however, is very expensive and requires intensive treatment setting. Further studies are strongly warranted before this expensive method can be recommended for routine use.

Delayed reactions

Late adverse reactions to contrast media are defined as reactions occurring 1 h to 1 week after the administration. Very late reactions are those occurring more than 1 week after the administration.

Iodine-based contrast media

Late adverse reactions to intravascular-iodinated contrast media have received increasing interest over the past decade, but their prevalence remains uncertain and their pathophysiology is not fully understood [45]. The reactions include symptoms such as nausea, vomiting, headache, itching, skin rash, musculoskeletal pain, and fever. A significant proportion of these reactions is unrelated to the agent. Allergy-like skin reactions, however, are well documented side-effects of contrast media with an incidence of approximately 2%. Late reactions appear to be commoner after nonionic dimers than after monomers. The majority of late skin reactions after the contrast medium exposure are probably the T-cell-mediated allergic reactions. Patients at an increased risk of late skin reactions are those with a history of previous contrast medium reaction and those on interleukin-2 treatment. Most skin reactions are self-limiting and resolve within a week. Management is symptomatic and similar to the management of other drug-induced skin reactions. The CMSC does not recommend prophylaxis in general, but patients who have had a previous serious late adverse reaction can be given oral steroids [2••,46,47•]. One should tell the patients, who have had a previous contrast medium reaction or are on interleukin-2 treatment, that a late skin reaction is possible and they should contact a doctor if they have a problem [45,46,47•].

Excess free iodide in the blood (ingested or injected) may cause thyrotoxicosis in patients with Graves' disease and those with multinodular goiter with thyroid autonomy, especially elderly patients and patients living in the areas of dietry iodine deficiency [48,49•]. Radiographic water-soluble contrast medium solutions contain small amounts of free iodide and may be of significance for patients at risk. It is contraindicated to administer iodinated agent to the patients with manifest hyperthyroidism. Patients with Graves' disease and those with multinodular goiter and thyroid autonomy, especially if they are elderly and/or live in the areas of dietary iodine deficiency, are at risk of developing thyrotoxicosis. Prophylaxis, however, is generally not necessary. Patients who are at risk should be closely monitored by endocrinologists after the injection of iodinated contrast medium. In selected high-risk patients, prophylactic treatment may be given by an endocrinologist; this is more relevant in the areas of dietary iodine deficiency [1,2••,48,49•]. Intravenous cholangiographic contrast agents should not be given to the patients at risk. Free iodide may also interfere with the nuclear medicine diagnostic procedures and treatment for up to 2 months.

Gadolinium-based contrast media

One of the extracellular gadolinium-based contrast agents [gadodiamide (Omniscan, GE Healthcare Diagnostics, Amersham, United Kingdom)] may trigger the development of nephrogenic systemic fibrosis up to 3 months after administration [50••]. The molecular structure of chelate (DTPA-BMA) binding gadolinium is linear. Gadodiamide formulation differs from most of the other nontissue-specific extracellular MRI agents by having an excess chelate (12 mg/ml) and being less stable than the other agents approved for clinical use in Europe. Whether the excess of chelate could have an impact on the nephrogenic systemic fibrosis (NSF) development is not known. Alternatively, NSF could be a toxic reaction to the free gadolinium liberated from gadodiamide. Free gadolinium is highly toxic, particularly in its ionic form (Gd^{3+}) [51]. In patients with normal renal function, gadodiamide leaves two to four times more gadolinium in the bone than does gadoteriodol [52]. Gadodiamide should not be administered to the patients with reduced kidney function or to those on dialysis. Whether other gadolinium-based agents can also trigger the development of nephrogenic systemic fibrosis remains unknown.

Miscellaneous

Contrast agents can also cause reactions other than the classical renal and nonrenal adverse reactions, as well as interaction with laboratory examinations.

Catecholamine-producing tumors and contrast media

Phaeochromocytomas are relatively rare tumors that secrete catecholamines adrenaline and noradrenalin (epinephrine and norepinephrine). Secretion of catecholamines by

phaeochromocytomas and paragangliomas may be continuous or intermittent. Typical clinical presentations include hypertension resistance to conventional treatment and intermittent crises: attacks of hypertension, headache, sweating, anxiety and pallor, or flushing. Crises occur when catecholamines are released from the tumor and may be spontaneous or precipitated by drugs including contrast media or by physical compression of the tumor. When a contrast agent is needed for tumor localization in the patients with a catecholamine-producing tumor detected biochemically, the CMSC recommends that before the administration of intravenous contrast medium, α-adrenergic and β-adrenergic blockade with orally administered drugs is done under the supervision of the referring physician [2••,53•]. Further α-adrenergic blockade with intravenous phenoxybenzamine is not necessary. Before the intraarterial administration of iodinated contrast medium, α-adrenergic and β-adrenergic blockade with orally administered drugs and α-blockade with intravenous phenoxybenzamine are recommended under the supervision of a referring physician. No special preparation is recommended in the patients undergoing enhanced imaging for a characterization of incidentally detected adrenal mass. A nonionic agent should always be used [2••,53•].

Interaction

The interactions between drugs and contrast agents are generally subdivided into (a) drugs that will be retained in the body because of reduction in renal function induced by the contrast medium, (b) drugs that enhance the renal effects of the contrast medium, (c) drugs that enhance allergic-like reactions to the contrast medium, (d) drugs that interfere with the hematological effects of the contrast medium, (e) contrast medium and neuroleptic drugs, (f) drugs that enhance the effects of the contrast medium on the heart, (g) the effects of contrast agents on isotope studies, (h) mixing contrast media with other drugs, and (i) the effects of contrast agents on biochemical assays [2••,54,55•].

The CMSC recommends that one should be aware of the patient's drug history and should keep proper records of the contrast injection (time, dose, and name). The patients taking drugs such as metformin cyclosporine, cisplatin, aminoglycosides, nonsteroid anti-inflammatory drugs, β-blocker, interleukin-2, and hydralazine should be given special attention before the injection of the contrast agent. One should never mix contrast media with other drugs in tubes or syringes. The CMSC recommends that no biochemical analyses on blood or urine collected are made within 24 h of iodine-based and gadolinium-based contrast medium injections [2••]. Measurements of clotting time and other coagulation factors can be falsely increased after the intravascular administration of iodinated contrast agents, which may also interfere with the determination of bilirubin, copper, iron, phosphate, and proteins in the blood. Caution should be exercised when using colorimetric assays for the angiotensin-converting enzyme, calcium, iron, magnesium, total iron-binding capacity, and zinc in serum samples of the patients who have recently received gadolinium-based agents. The contrast agent in urine interferes with some of the protein assay techniques, leading to false-positive results. The contrast medium injection should be avoided for at least 24 h before the isotope study of the bone and before labeling red blood cells for isotope studies.

Contrast media for ultrasonography

In-vitro and animal studies have shown adverse effects of ultrasound contrast media related to the properties of the particles and the interaction between microbubbles and ultrasound beam energy causing bubble destruction. Clinical studies [56,57•], however, have not shown such adverse events and indicate that ultrasound contrast media are generally safe. Most adverse events seen clinically are nonspecific and unrelated to the constituents of the various products. Adverse reactions are usually minor (e.g., headache, nausea, altered taste, and sensation of heat) and self-resolving. These symptoms may not be related to the ultrasound contrast materials, as they have also been observed in placebo-controlled groups. Intolerance to some components, however, may occur. It is contraindicated to use ultrasonographic contrast medium in patients with severe heart disease (e.g., class III/IV). Generalized allergy-like or hypersensitivity reactions occur only rarely. Any rare adverse reactions should be treated symptomatically. The use of ultrasound contrast medium should always be clinically justified. It is important that the exposure time to ultrasound and the acoustic output shown be kept at the lowest level consistent with the obtained diagnostic information.

Conclusion

The current contrast agents are not totally inert drugs. They can cause adverse reactions, which most frequently are minor, but severe acute and delayed reactions can occur, particularly in high-risk groups. It is of utmost importance that both radiologists and referring physicians are aware of the potential adverse reactions due to contrast media and the necessary precautions to be taken. This is the only way to reduce their incidence, but it is not done everywhere [58••].

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1 Thomsen HS, Morcos SK. ESUR guidelines on contrast media. Abdom Imag 2006; 31:131–140.

2 Thomsen HS, Morcos SK, Almén T, *et al.* Guidelines on contrast media. In: •• Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 145–159.
ESUR guidelines produced during the last years are gathered.

3 Thomsen HS. Reducing the risk of contrast media induced nephrotoxicity. In: •• Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 35–46.
A review of the existing clinical evidence regarding the incidence of contrast medium-induced nephropathy.

4 Hou SH, Bushinsky DA, Wish JB, *et al.* Hospital acquired renal insufficiency: a prospective study. Am J Med 1993; 74:243–248.

5 Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis 2002; 39:930–936.

6 Gruberg L, Mintz GS, Mehran R, *et al.* The prognostic implications of further renal function deterioration with 48 h of interventional coronary procedures in patients with preexistent chronic renal insufficiency. J Am Coll Cardiol 2000; 36:1542–1548.

7 McCullough PA, Wolyn R, Rocher LL, *et al.* Acute renal failure after coronary intervention: incidence, risk factors and relationship to mortality. Am J Med 1997; 103:368–375.

8 Thomsen HS. Gadolinium contrast media for radiographic examinations. In: • Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 115–120.
A review of risks of replacing iodine-based contrast media with gadolinium-based contrast media for radiography. There is no evidence that gadolinium-based contrast media are less nephrotoxic than iodine-based contrast media in equimolar doses.

9 Morcos SK, Thomsen HS, Webb JAW, *et al.* Contrast media induced nephrotoxicity: a consensus report. Eur Radiol 1999; 9:1602–1613.

10 Rudnik MR, Goldfarb S, Wexler L, *et al.* Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: a randomized trial. Kidney Int 1995; 47:254–261.

11 Briguori C, Colombo A, Airoldi F, *et al.* Gadolinium-based contrast agents and • nephrotoxicity in patients undergoing coronary artery procedures. Catheter Cardiovasc Interv 2006; 67:175–180.
Prospective study showing that gadolinium-based contrast media are at least as nephrotoxic as iodine-based contrast media when used for coronary angiography.

12 Parfrey PS, Griffiths SM, Barrett BJ, *et al.* Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective, controlled study. N Engl J Med 1989; 320:143–149.

13 Thomsen HS, Morcos SK, Members of Contrast Media Safety Committee of • European Society of Urogenital Radiology (ESUR). In which patients should serum creatinine be measured before iodinated contrast medium administration? Eur Radiol 2005; 15: 749–754.
The paper introduces a guideline for identifying patients with reduced renal function among the patients referred for contrast-enhanced imaging without measuring serum creatinine levels in all patients.

14 Pannu N, Wiebe N, Tonelli M for the Alberta Kidney Disease Network. •• Prophylaxis strategies for contrast-induced nephropathy. JAMA 2006; 295:2765–2779.
Although several risk factors for contrast medium-induced nephropathy have been identified, the paper documents that the development of a 100% effective prophylaxis strategy for contrast medium-induced nephropathy has been limited by the poor understanding of the pathophysiology and clinical significance of this condition.

15 Finn WF. The clinical and renal consequences of contrast-induced nephro- • pathy. Nephrol Dial Transplant 2006; 21 (Suppl 1):i2–i10.
A review documenting that contrast medium-induced nephropathy should not be viewed as a treatable and acceptable complication of contrast produced, and education is of importance.

16 Barrett BJ, Parfrey PS. Preventing nephropathy induced by contrast medium. •• N Engl J Med 2006; 354:379–386.
A review of several aspects of contrast medium-induced nephropathy. It stresses that the value of possible preventive strategies including *N*-acetylcysteine, vasodilators, and isoosmolar contrast media in reducing the risk of contrast medium-induced nephropathy and associated morbidity also remains uncertain.

17 Lameire NH. Contrast-induced nephropathy – prevention and risk reduction. Nephrol Dial Transplant 2006; 21 (Suppl 1):i11–i23.

18 Stacul F. Reducing the risks for contrast-induced nephropathy. Cardiovasc Interv Radiol 2005; 28 (Suppl 2):S12–S18.

19 McCullough PA, Sandberg KR. Epidemiology of contrast-induced nephropathy. Rev Cardiovasc Med 2003; 4 (Suppl 5):S3–S9.

20 Thomsen HS, Almén T, Morcos SK, *et al.* Gadolinium-containing contrast media for radiographic examination: a position paper. Eur Radiol 2002; 12:2600–2605.

21 Thomsen HS, Morcos SK, and Members of the Contrast Media Safety Committee of the European Society of Urogenital Radiology (ESUR). Contrast media and metformin. Guidelines to diminish the risk of lactic acidosis in noninsulin dependent diabetics after administration of contrast media. Eur Radiol 1999; 9:738–740.

22 Thomsen HS. Noninsulin dependent diabetes and contrast media. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 35–46.

23 Tepel M, Aspelin P, Lameire N. Contrast-induced nephropathy: a clinical and •• evidence-based approach. Circulation 2006; 113:1799–1806.
The differences in physicochemical properties between various iodine-based agents and their relationship to contrast medium-induced nephropathy are discussed.

24 Sanaei-Ardekani M, Movahed MR, Movafagh S, Ghahramani N. Contrast-induced nephropathy: a review. Cardiovasc Revasc Med 2005; 6:82–88.

25 Solomon R, DuMouchel W. Contrast media and nephropathy. Findings from •• systematic analysis and Food and Drug Administration reports of adverse effects. Invest Radiol 2006; 41:651–660.
The authors' report is based on a review of the literature and Food and Drug Administration (FDA) reports on adverse effects that there might be a difference between at least iohexol and iopamidol in nephrotoxic potential.

26 Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. CMJ 2005; 172:1461–1471.

27 Solomon R, Biguori C, Bettmann M. Selection of contrast media. Kidney Int •• 2006; 69:S39–S45.
The aspects of importance with regard to contrast medium-induced nephropathy are addressed: the route of administration, the volume of contrast medium, the manner of X-ray attenuation, and the specific chemical structure of contrast media.

28 Bagshaw SM, Culleton BF. Contrast-induced nephropathy: epidemiology and • prevention. Minerva Cardioangiol 2006; 54:109–129.
A review covering most aspects of contrast medium-induced nephropathy. It includes 183 references.

29 Coyle LC, Rodriquez RE. Acetylcysteine in diabetes (AID): a randomized study of acetylcysteine for the prevention of contrast nephropathy in diabetics. Am Heart J 2006; 151:1032.e9–1032e.12.

30 Weisbord SD, Palevsky PM. Radiocontrast-induced acute renal failure. J Intensive Care Med 2005; 20:63–75.

31 Mueller C. Prevention of contrast-induced nephropathy with volume supple- • mentation. Kidney Int 2006; 69:S16–S19.
A review of various hydration protocols.

32 Kotlyar E, Keogh AM, Thavapalachandran S, *et al.* Prehydration alone is sufficient to prevent contrast-induced nephropathy after day-only angiography procedures–: a randomized controlled trial. Heart Lung Circ 2005; 14:245–251.

33 Trivedi HS, Moore H, Nasr S, *et al.* A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity. Nephron Clin Pract 2003; 93:c29–c34.

34 Merten GJ, Burgess WP, Gray LV, *et al.* Prevention of contrast-induced nephropathy with sodium bicarbonate. A randomized controlled trial. JAMA 2004; 291:2328–2334.

35 Thomsen HS, Morcos SK. Contrast-medium-induced nephropathy: is there a •• new consensus? A review of published guidelines. Eur Radiol 2006; 16: 1835–1840.
An analysis of various proposed guidelines for reducing the risk of contrast medium-induced nephropathy published in this century.

36 Solomon R, Werner C, Mann D, *et al.* Effects of saline, mannitol and furosemide on acute decreases in renal function induced by radiocontrast agents. N Engl J Med 1994; 331:1416–1420.

37 Bagshaw SM, McAlister FA, Manns BJ, *et al.* Acetylcysteine in the prevention •• of contrast-induced nephropathy. A case study of the pitfalls in the evolution of evidence. Arch Intern Med 2006; 166:161–166.
The article demonstrates that despite 34 empirical studies of the role of acetylcysteine for prevention of contrast medium-induced nephropathy, the evidence is still lacking.

38 Bettmann MA. Contrast medium-induced nephropathy: critical review of the existing clinical evidence. Nephrol Dial Transplant 2005; 20 (Suppl 1): i12–i17.

39 Morcos SK, Thomsen HS, Webb JAW, *et al.* Dialysis and contrast media. Eur Radiol 2002; 12:3026–3030.

40 Morcos SK. Dialysis and contrast media. In: Thomsen HS, editor. • Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 47–52.
A review of the role of dialysis in reducing the risk of contrast medium-induced nephropathy.

41 Deray G. Dialysis and iodinated contrast media. Kidney Int 2006; 69:S25–S29.

42 Vogt B, Ferrari P, Schonholzer C, *et al.* Preemptive haemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. Am J Med 2001; 111:692–698.

43 Frank H, Werner D, Lorusso V, *et al.* Simultaneous hemodialysis during coronary angiography fails to prevent radiocontrast-induced nephropathy in chronic renal failure. Clin Nephrol 2003; 60:176–182.

44 Marenzi G, Marana I, Lauri G, *et al.* The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. N Engl J Med 2003; 349:1333–1340.

45 Brockow K, Christiansen C, Kanny G, *et al.* Management of hypersensitivity reactions to iodinated contrast media. Allergy 2005; 60:150–158.

46 Webb JAW, Stacul F, Thomsen HS, *et al.* Late adverse reactions to intravascular iodinated contrast media. Eur Radiol 2003; 13:181–184.

47 • Stacul F. Late adverse reactions to intravascular iodinated contrast media. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 27–32.
A review dealing with the occurrence of delayed reaction to contrast medium.

48 Molen Avd, Thomsen HS, Morcos SK, *et al.* Effect of iodinated contrast media on thyroid function in adults. Eur Radiol 2004; 14:902–906.

49 • Molen Avd. Effects of iodinated contrast media on thyroid function. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 75–82.
The article manifests that thyreotoxicosis is a contraindication to administration of iodine-based contrast media and in selected high-risk groups thyreotoxicosis may occur as a late reaction after administration of contrast media.

50 •• Marckmann P, Skov L, Rossen K, *et al.* Nephrogenic systemic fibrosis: suspected etiological role of gadodiamide used for contrast-enhanced magnetic resonance imaging. J Am Soc Nephrol 2006; 17:2359–2362.
The authors report that gadodiamide may be one etiologic factor for the development of nephrogenic systemic fibrosis.

51 Behra-Miellet J, Gressier B, Brunet C, *et al.* Free gadolinium and gadodiamide, a gadolinium chelate used in magnetic resonance imaging: evaluation of their in vitro effects on human neutrophil viability. Methods Find Exp Clin Pharmacol 1996; 18:437–442.

52 White GW, Gibby WA, Tweedle MF. Comparison of Gd(DTPA-BMA) (Omniscan) versus Gd(HP-DO3A) (ProHance) relative to gadolinium retention in human bone tissue by inductively coupled plasma mass spectroscopy. Invest Radiol 2006; 41:272–278.

53 • Webb JAW. Phaechromocytoma. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 89–92.
A review of the current knowledge regarding phaechromocytoma and administration of contrast media in order to avoid hypertensive crises.

54 Morcos SK, Thomsen HS, Exley CM, *et al.* Contrast media: interaction with other drugs and clinical tests. Eur Radiol 2005; 15:1463–1468.

55 • Morcos SK. Interactions with other drugs and clinical tests. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 93–98.
An update on interactions between contrast media and (a) other drugs, (b) biochemical analysis, and (c) isotope studies.

56 Jakobsen JA, Oyen R, Thomsen HS, *et al.* Safety of ultrasound contrast agents. Eur Radiol 2005; 15:941–945.

57 • Oyen R. Safety of ultrasound contrast agents. In: Thomsen HS, editor. Contrast media: safety issues and ESUR guidelines. Heidelberg: Springer; 2006. pp. 131–136.
An update on the safety of ultrasound contrast media.

58 •• Elicker BM, Cypel YS, Weinreb JC. IV contrast administration for CT: a survey of practices for the screening and prevention of contrast nephropathy. Am J Roentgenol 2006; 186:1651–1658.
A survey of practices for the screening and prevention of contrast medium-induced nephropathy. There is still a lack of knowledge among radiologists. There are wide variations in practice patterns, and some patterns even conflict with the recommendations in the literature.