Contrast-induced nephropathy: focused on risk factors

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Abstract
Contrast-induced nephropathy (CIN) refers to an abrupt deterioration in renal function associated with the use of iodinated contrast media. Today, contrast media is commonly used in both diagnostic and therapeutic procedures; the use of contrast media will likely increase in the future. To prevent CIN, the at-risk patients and contrast agents must first be identified. Traditional risk factors are chronic kidney disease (CKD), diabetes mellitus, advanced age, congestive heart failure and anemia. Prominent risks factors are CKD and diabetes mellitus, particularly the combination of the two. Contrast agent dose should be as low as possible and iso-osmolar agents should be used for high-risk patients. Current intravenous periprocedural volume expansion has a strong consensus for prevention of CIN in at-risk patients.

Keywords: Contrast-induced nephropathy (CIN), Risk factors, Iodinated contrast agent.

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Introduction
Contrast media-induced nephropathy (CIN) is mostly commonly defined by the increase in serum creatinine (SCr) by >25% or 0.5 mg/dL within 48-72 hours with an absence of an alternative etiology following intravascular administration of iodinated contrast media (1). After the procedure, SCr levels begin to rise within the first 24 hours and generally peak between 3-5 days, returning to baseline levels within 10-14 days (2-4). In particular, cardiac procedures such as coronary angiography, angioplasty, invasive radiologic procedures and computed tomography using iodinated contrast media are common causes of CIN.

CIN is associated with increased morbidity, mortality, longer hospitalization, incremental costs and progression of chronic kidney disease (CKD) (5,6). CIN is the third most common cause of acute kidney injury originating in the hospital (7). Incidence of CIN in the general population is estimated to be less than 2%. However, in high-risk patients (those with increased age, CKD, diabetes mellitus, congestive heart failure, and anemia), CIN incidences as high as 50% have been reported (8).

The incidence of CIN will continue to increase as life expectancy and prevalence of principal risk factors for CIN is increasing worldwide. The administration of iodinated contrast media for imaging and invasive procedures is also increasing.

Who are at high-risk group for CIN?

Which patients have more risk?

Many risk factors have been identified for CIN. However, the most important risk is CKD, particularly in combination with diabetes mellitus. In prospective studies investigating imaging for diagnosis or intervention in patients with peripheral vascular disease, elevation of SCr occurred in 2%, 10.4%, and 62% of studies in patients with baseline SCr levels of ≤1.2 mg/dl, 1.3 to 1.9 mg/dl, and ≥2.0 mg/dl, respectively (9). Other traditional risk factors are advanced age, congestive heart failure, volume depletion, myocardial infarction, and anemia. Several various agents, including antibiotics, furosemide and non-steroidal anti-inflammatory drugs have also been identified as risk factors for CIN (4,10,11). In addition to the traditional risk factors, prediabetes, hyperuricemia, hypertriglyceridemia and impaired fasting glucose before the procedure and the use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are also important (Table 1) (12).

How can we predict the risk of CIN?

Baseline renal function is the most important predictor of CIN; therefore, determination of renal function is the first step in predicting CIN. Although SCr is commonly used as an indicator of renal function, glomerular filtration rate (GFR) provides the
best indication of renal function. Measurement of GFR by radionuclide agent or other biochemical substance clearance over a 24-hour urine collection is impractical and time-consuming. However, estimated (eGFR) calculation is often used in most clinical settings. The Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) equation are suitable for eGFR (13,14). Furthermore, Cystatin C can be used as an indicator of renal function and a predictor of CIN (15). In recent years, novel biomarkers have been identified to determine renal function and predict CIN. These markers include neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18, and glutathione-S-transferase (16). The European Society of Urogenital Radiology (ESUR) guidelines on contrast media recommend that eGFR is measured in selected high-risk patients (1). Several risk scores have been identified to determine high-risk patients; the most popular of these is Mehran’s model. This score takes into account congestive heart failure, hypotension, intra-aortic balloon pump, age >75 years, anemia, diabetes mellitus, contrast volume, and estimated glomerular filtration rate (eGFR) (17).

Which contrast medias have greater risk?

Iodinated contrast media may be classified according to their osmolarity, their ionicity (ionic or nonionic) and according to their chemical structure (monomer or dimer). Significant differences have been observed between contrast medias groups in terms of CIN. There is fair and adequate evidence that low osmolar contrast medias (LOCM) have a lower risk of CIN than the conventional high osmolar contrast media (HOCM) (18,19). A meta-analysis including 24 trials suggested that the mean change in Scr was less with LOCM than with HOCM (20). Nevertheless, studies of iso-osmolar contrast media (IOCM) and LOCM offer conflicting data. A meta-analysis including 16 trials and 2,763 subjects suggested that ioxilan (IOCM) compared with LOCM is not associated with less CIN overall (21). Another meta-analysis including 16 randomized, controlled trials and 2,727 subjects suggested that IOCM ioxilan was associated with fewer increases in Scr and lower incidences of CIN than LOCM, especially in patients with CKD and CKD plus DM (22). Finally, a recent meta-analysis including 36 trials and 7,166 subjects found that ioxilan did not lead to a statistically significant reduction in CIN (22).

Contrast media volume and dose are important factors in terms of CIN incidence. A recently study showed that in patients with CKD undergoing coronary angiography, the use of ultralow volumes (<50 ml) of contrast media was associated with a significant reduction in CIN and that each 20 ml increase in the amount of contrast media led to a two-fold increase in risk (23). A meta-analysis showed an intimate relationship between the dose of iodine and the occurrence of CIN (24). The recommended maximum dose of contrast media can be calculated based on body weight and Scr (25). Generally, volume should be limited to no more than 100 ml, particularly in patients with eGFR <60 ml/min per 1.73 m2.

Table 1: Risk factors for contrast-induced nephropathy

| Chronic kidney disease (particularly in combination with diabetes mellitus) |
| Advanced age |
| Diabetes mellitus |
| Prediabetes |
| Impaired fasting glucose |
| Congestive heart failure |
| Myocardial infarction |
| Hypertension |
| Hyperuricemia |
| Hypertriglyceridemia |
| Volume depletion |
| Anemia |
| Use of intra-aortic balloon pump |
| Drugs |
| Antibiotics |
| Furosemide |
| Angiotensin-converting enzyme inhibitors |
| Angiotensin II receptor blockers |
| Non-steroidal anti-inflammatory drugs |
| Contrast medias |
| High osmolar contrast media |
| Contrast media volume (> 100 mL) |

Conclusion

Definition of CIN, risk factors, prevention methods and treatment were reviewed in the current publication. CIN is a preventable iatrogenic disorder, resulting from exposure to contrast media. An aging population, increase in the number of patients with diabetes mellitus and chronic renal failure and an increase in the number of procedures that require contrast media has led to an increase in the incidence of CIN. Risk can be reduced by identification of high-risk patients and through several strategies for the protection. The amount of contrast media should be as low as possible and low-osmolar or iso-osmolar contrast media should be used to prevent CIN in high-risk patients. The literature supports periprocedural hydration with intravenous administration of isotonic solutions.
saline but there is a lack of evidence to support the routine use of NAC and other pharmaceutical interventions in high risk patient.

References


