BJA

British Journal of Anaesthesia, 117 (S2): ii63–ii73 (2016)

doi: 10.1093/bja/aew213
Special Issue

Contrast induced nephropathy in vascular surgery

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Abstract

Contrast induced nephropathy (CIN) is traditionally associated with outpatient imaging studies. More recently, patients afflicted with vascular pathologies are increasingly undergoing endovascular treatments that require the use of iodinated contrast media (CM) agents, thus placing them as risk of developing CIN. As perioperative physicians, anaesthetists should be aware of the risk factors and measures that might minimize acute kidney injury caused by CM. This review evaluates recent data regarding preventive measures against CIN and where possible, places the evidence in the context of the patient receiving endovascular surgical treatment. Measures including the use of peri-procedural hydration, N-acetylcysteine, statins, remote ischaemic preconditioning, renal vasodilators and renal replacement therapy and the use of alternatives to iodinated contrast agents are discussed. It should be noted that most of the available data regarding CIN are from non-surgical patients.

Key words: acute kidney injury; contrast media; endovascular procedures

Editor's key points

- A systematic review estimated the overall frequency of CIN in vascular surgery patients exposed to angiography to be 9.2%.
- Patients who develop CIN suffer an increased burden of in hospital and longer term morbidity.
- Maintaining adequate hydration remains a cornerstone of preventing CIN but evidence to support a particular hydration strategy is lacking.
- There is no evidence to support the routine use of NAC in prophylactic protocols for surgical patients at risk of CIN.

Despite efforts to prevent it, contrast induced nephropathy (CIN) remains a significant cause of iatrogenic acute kidney injury (AKI). With the increasing use of endovascular procedures requiring iodine containing contrast media (CM) in older patients and those with significant co-morbidities, the prevention of AKI is assuming greater importance. This narrative review will serve as an update to one previously published in this journal[1] and will concentrate on areas where there have been noteworthy changes, with a focus on patients undergoing vascular surgery where such data are available. Readers are referred to the previous review for more in depth discussion on the risk factors (Table 1),[2–4] the pathophysiology of CIN and renal handling of CM, the details of which remain largely unchanged, and will be mentioned only in brief here.

Definitions

The widely accepted definition for contrast induced nephropathy is a deterioration of renal function, indicated by either an increase in serum creatinine concentration of 25% from baseline, or an absolute increase of 26–44 μmol litre^{-1} (0.3–0.5 mg dl^{-1}) within 48–72 h of i.v. contrast administration.[5] In order to standardize the definition of acute kidney injury from different aetiologies, two groups, the Acute Dialysis Quality Initiative (ADQI) and Acute Kidney Injury Network (AKIN) have separately proposed a system of defining and staging AKI, regardless of the likely cause. These include the RIFLE (Risk, Injury, Failure, Loss, End-stage kidney disease) and the AKIN systems respectively, the latter being a modification of the former, which should theoretically improve sensitivity and specificity.[6]

Table 1 Risk factors for CIN

Pre-existing renal impairment[2–4]
Diabetes mellitus
Peri-procedural intravascular depletion
Congestive heart failure
Volume and type of contrast administered
Concomitant use of other nephrotoxic drugs

According to the AKIN criteria, stage 1 AKI may be diagnosed if one of the following occurs within 48 h:

- An absolute serum creatinine increase >26.4 μmol litre^{-1} (≥0.3 mg dl^{-1}).
- An increase in serum creatinine ≥50% (≥1.5-fold) above baseline.
- Urine output reduced to ≤0.5 ml kg^{-1} h^{-1} for at least 6 h.

These are not specific to suspected contrast-induced AKI and differ from the previously used definitions of CIN. These criteria may be seen more frequently in future studies of CIN, which will aid the comparison of different studies.

Incidence of CIN in patients with vascular disease

In the Manual on Contrast Media by the American College of Radiology,[7] the authors made a distinction in terminology between the diagnoses of post-contrast acute kidney injury and contrast induced nephropathy. In the latter CM is considered to be the cause of the renal injury. Be that as it may, very few studies have adequate controls to separate between the two entities and quoted incidences are likely to include a combination of both.[8] Furthermore, the reported incidences of CIN after cardiology and radiology procedures vary widely, owing to variation in the definitions used in earlier studies and the inclusion of patients with different numbers of known risk factors.[9] The aetiology of AKI in patients undergoing endovascular aneurysm repair (EVAR) in the perioperative period is multifactorial, with the kidneys being potentially subjected to a variety of haemodynamic, mechanical and pharmacological insults. Hence it is difficult to attribute AKI after EVAR solely to the adverse effects of CM and data are relatively scarce. An earlier study in patients undergoing EVAR showed that 24% of patients with baseline renal insufficiency had a creatinine increase postoperatively, with this being permanent in around two thirds of patients.[10] More recent data may be found in a multivariate analysis of the American College of Surgeons National Surgical Quality Improvement Program, where 13191 patients were identified as having undergone AAA repairs, 9877 of who had EVAR.[11] The investigators divided these patients as having moderate baseline renal impairment if their eGFR was between 30–60 ml min^{-1}, and severe impairment if their eGFR was <30 ml min^{-1}. Patients with moderate baseline renal impairment had an AKI rate of 1% and a dialysis rate of 1.1%. This compares with an AKI rate of 4.1 and 6.3% respectively in those with severely impaired baseline renal function. However, the definition of AKI used was a creatinine increase of 2 mg dl^{-1} (176 μmol litre^{-1}), a standard that is much higher than that used for the definition of CIN (0.5 mg dl^{-1} /44 μmol litre^{-1}). Interestingly, the odds of developing renal impairment were higher in the open repair group (OR=3, 95% CI 2.2–4.0). This was borne out in another systematic review of open vs EVAR in patients more than 80 yr old, where the relative risk for renal failure was close to three in the open procedure group.[12] Other studies investigating various preventative measures for AKI have shown incidences of CIN between 3–8% of vulnerable patients undergoing angiography in the vascular surgical setting.[13–15] In a systematic review by Zaraca and colleagues[16] the overall frequency of CIN from six eligible studies was 9.2% (79 out of 862 patients).

Clinical consequences of CIN

The sequelae of CIN are variable and difficult to quantify, as there is not a well-demarcated pathophysiological pathway to account for the morbidity and mortality in patients who develop CIN. For the most part, AKI associated with CIN is asymptomatic and transient; like other mild forms of AKI, it requires only observation and supportive management, and rarely requires renal replacement. However, observational studies consistently point to a greater chance of death in those who develop CIN, compared with those who do not, with the odds lasting beyond one yr after detection. Furthermore, data gleaned from randomized trials of therapeutic interventional measures also indicate an added morbidity attributable to the occurrence of CIN.[17] Earlier data indicated an in-hospital mortality rate of up to 30% and a two yr mortality rate of 80%.[2 18] In a prospective cohort analysis, the development of CIN after contrast-enhancing CT scan was shown to be associated with a similar risk of death in one yr as coronary artery disease, heart failure or advanced age.[19] In a prospective study of 9877 subjects with a median follow up of 42 months, the rate of CIN was 11% in those with chronic kidney disease (CKD) and 2% in those without CKD, calculated after adjusting for known confounders of death and excluding patients who had died in hospital (24), had surgery (2999), were on dialysis (250) and had incomplete laboratory data (2233). CIN was associated with long-term mortality for the entire cohort (HR=2.26, CI=1.62 to 2.29, P<0.0001). Subgroup analysis showed that patients with CKD also had a higher long-term mortality if they developed CIN (HR 2.62, CI=1.91 to3.57, P<0.0001) but CIN had no effect on mortality in patients without CKD (HR=1.23, CI 0.47=2.62, P=0.6).[20]

Pharmacology of iodinated contrast media (CM)

Commercially available CM are based on either one (monomers) or two (dimers) tri-iodinated benzene rings. They are further classified according to their ionization and osmolarity. CM vary in their chemical and physical properties but the imaging efficacy is solely based on their ability to attenuate x-rays, which is dependent on the number of iodine molecules present.[21] The ionic form affects the electrical potential of the cell membranes, which accounts for an increased toxicity.[22]

The improved safety profiles of the non-ionic low-osmolar or iso-osmolar CM (osmolality equal to that of blood) have resulted in universal uptake in clinical practice.[23–25] Osmolality was thought to play an important role in the pathogenesis of CIN, but the anticipated benefit of lower incidence of CIN by reducing osmolality has not been borne out in meta-analyses that compared the risks of CIN between high-osmolar and low-osmolar CM; and between low-osmolar and iso-osmolar CM regardless of the routes of administration.[25 26]

There has been a shift in thinking that suggests viscosity may be a particularly important contributing factor in the development of CIN, especially with low-osmolar CM having up to a 50-fold increase in viscosity.[27–29] The complex interaction of