DEM Journal Club

Article Appraisal

Article: Risk of Acute Kidney Injury After Intravenous Contrast Media Administration, Hinson et al., Ann Emerg Med 2016

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Background and Study Objective(s):

Emergency physicians regularly order contrast-enhanced CT scans for diagnostic purposes. However, contrast media is cited as the third most common cause of iatrogenic acute kidney injury (AKI), as high as 14%. This claim is based on temporal association and the causal relationship is unclear. Most research has been done on older contrast media and/or have not used control populations. Newer low and iso-osmolar contrast media may hold less risk. The few available observational studies on contrast media and AKI have shown mixed results, but have been limited by selection bias. Randomized control trials have been considered unethical due to ongoing perception of risk and difficulty of methodological design. The dogma of intravenous (IV) contrast-induced acute kidney injury limits the use of contrast scans for patients with borderline kidney function and can often delay investigations, possibly contributing to patient morbidity and mortality, as well as hospital overcrowding. The study goal was to clarify the incidence of AKI independently associated with IV contrast media administration by conducting a large, well-controlled study in a modern setting.

Study Design:

Researchers conducted a single-center retrospective cohort in a large American urban academic center between 2009 and 2014. They studied three distinct populations: 1) Patients who received contrast CT scan; 2) Patients who received a non-contrast CT scan, and; 3) Patients who did not receive CT scans (used to control for bias associated with decision to obtain imaging). Inclusion criteria were: Age ≥18 and documented “before and after” serum creatinine measurements (either in ED or 8 h prior to CT and 48-72 h after either event). Exclusion criteria were: initial creatinine < 35 µmol/L; initial creatinine >354 µmol/L or ongoing dialysis; renal transplant, and; peri-event ED visit or CT scan (ED visit or CT scan 6 months before study start date or contrast enhanced CT within 72 h of ED departure). The authors obtained patient information from a chart review of an electronic medical record database, including: vital signs, medication administration, preexisting diagnoses, lab results, procedure codes and diagnostic codes. Their primary outcome was incidence of AKI, defined two ways: most commonly cited definition, and AKI Injury Network definition. This was defined by either an absolute rise in creatinine of 44 µmol/L or ≥25% from index measurement (common) or an absolute rise in Cr of 26 µmol/L or a 1.5-1.9 x from index measurement (AKI Network). The authors employed a test of proportions to compare AKI rates, and used multivariate logistic

regression and propensity score matching to control for systematic differences in baseline characteristics between groups. Results were presented as odds ratios (ORs).

Results:

There were 7201 contrast-enhanced CT scans and 5499 non-contrast CT scans for whom before-and-after serum creatinine values were available. These were matched with 5234 patients who did not receive a CT. Rates of AKI were the following: Contrast CT: 10.6% (common)/6.8% (AKI network); Non-contrast CT: 10.2% (common)/ 8.9% (AKI network); No CT: 10.9% (common)/ 8.1% (AKI network). With the common definition, OR was the same across all groups before and after propensity score matching. With AKI network definition, contrast media was associated with a decreased risk of AKI compared to all patients who did not receive contrast (OR 0.78, 95% CI 0.7-0.88) or to patients undergoing non-contrast CT (OR 0.75, 95% CI 0.66-0.85) but this disappeared after propensity score matching (OR=1.00 for both). Subgroup analysis failed to show any significant differences in initial GFR/creatinine and risk for AKI, albeit with only low patient numbers for patients with GFR<30 mL/min per 1.73m2. After multivariate logistic regression, there was no difference in chronic kidney disease at 6 months or initiation of dialysis. Instead, factors associated with increased AKI risk included: increased age, administration of nephrotoxins, pre-existing diagnosis of congestive heart failure or chronic kidney disease, and hypoalbuminemia. Administration of IV fluids was associated with a protective OR for AKI.

Validity of Results:

This study is concordant with previous controlled studies suggesting no risk of AKI after administration of IV contrast media. The precision of the result is excellent after propensity score matching, OR 1.00 (0.99-1.01) using common definition, and OR 1.00 (0.99-1.01) using AKI definition. The authors attempted to account for confounding variables using logistic regression and propensity score matching, but there may have been other factors that were not accounted for. Other variables may include presenting complaint (e.g., abdominal pain versus leg pain), weight (contrast protocols may not take weight into account) and specific dose of contrast (there may be a dose-response). Clinician gestalt and experience likely plays a very significant role and this is difficult to account for in the propensity score matching.

The study suggests that IV fluid administration may be nephroprotective and be responsible for some of the lack of observed effect. However, the AMACING trial (Lancet, 2017) was a prospective randomized control trial that showed patients at risk for contrast-induced AKI had no prophylactic benefit with IV hydration, adding to other literature that has failed to show a prophylactic benefit for N-acetyl cysteine or sodium bicarbonate. Although it is possible that the medical community has not tested the appropriate prophylactic strategy, it is also possible that the risk of AKI post contrast administration is related more to underlying cormorbid illness rather than the IV contrast itself.

Generalizability of Results:

This is a single-center study with a retrospective design. Their estimates for AKI rates are likely conservative for a general Emergency Department patient population; most patients studied were admitted to hospital and could represent a more co-morbid and acutely unwell population that would be expected to have a higher risk for AKI. The type of contrast media used in this study appear to be similar in osmolality and volume to that used in Vancouver General Hospital, Royal Columbian Hospital and Kelowna General Hospital. The results may not extrapolate to other interventional procedures that use contrast media (e.g., angiography), which use up to two times the contrast load of an enhanced CT scan.

The Bottom Line:

This is a well-conducted study and demonstrates that for patients with an initial creatinine less than 354 µmol/L, contrast media was not associated with increased risk of AKI. It seems that fear of triggering AKI with contrast is disproportionate to the data. The result confirms with what the majority of Emergency Physicians seem to believe in both Vancouver/Fraser and Kelowna sites, that is, the attributable risk in healthy patients of AKI to contrast media administration is exceedingly low and far lower than the risk of missing a diagnosis because of withholding contrast. This may even apply to patients thought to be “higher risk,” specifically those with elevated creatinine or GFR <30, although the number of patients in this subgroup was small.

Many physicians at both journal clubs felt that using a GFR cut-off of 30 before being concerned for AKI is reasonable. However, this will also require multidisciplinary buy-in, specifically from radiology. In Vancouver/Fraser, there seems to be mixed messages about whether radiology will be reluctant to perform contrast enhanced CT scans in “high risk” patients. In Kelowna, radiology has recently adopted a policy that they will perform contrast CT scans

without question if GFR>30, with a pre-scan 500 cc IV normal saline bolus in patients with GFR 15-30 and with a strong indication in GFR<15. This study might help springboard further discussion with our radiology colleagues to standardize protocols. Finally, it is often worth discussing the particular scan in a high-risk patient with radiology as modern CT scanners are often able to rule out many specific conditions without the use of contrast.