THIS WEEK:

• Contrast Nephropathy
• Next Week’s Case
• Joke of the Week

**CONTRAST NEPHROPATHY**

Thanks to Hicham C. Hassan, the Renal Registrar at Liverpool hospital for his update on contrast induced nephropathy at Grand Rounds. Here is the summary of his presentation.

**Definition**

• Acute renal impairment following IV contrast in the absence of other causes
• An increase in serum creatinine >44 mmol/l
• A 25% or greater relative increase from baseline 48–72 h after administration of contrast.
• Terms include contrast nephropathy contrast-induced, acute kidney injury (AKI), contrast induced nephropathy (CIN)

**Pathogenesis**

• Multiple theories with conflicting evidence
• Thought to be either due to/ combination of:
  - Acute Tubular Necrosis
  - Renal vasoconstriction
  - Pre-renal Failure
  - Direct cytotoxic effect of contrast
  - Free radical formation
  - Hyperosmolality of contrast

**What are the Risk Factors?**

<table>
<thead>
<tr>
<th>Patient-related factors</th>
<th>Procedure-related factors</th>
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<tr>
<td>Underlying renal insufficiency</td>
<td>Volume of contrast used</td>
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<tr>
<td>Diabetes mellitus</td>
<td>Hyper-osmolar contrast media</td>
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<tr>
<td>Intravascular volume depletion</td>
<td>Intra-arterial contrast administration</td>
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<tr>
<td>Congestive heart failure</td>
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*Amplifies risk in the setting of renal insufficiency.*

Using these factors, scoring systems have been developed to predict a post–percutaneous coronary intervention range of CI-AKI from a rate of 7% for those at lowest risk to a rate of >50% for those with the highest risk score.
Clinical Characteristics

• Begins 12-24hrs after contrast administered
• In most cases, it is nonoliguric
• Mild and transient with recovery beginning in 3-5 days.
• Usually reversible with renal function normalizing by day 14.
• Consider in the differential diagnosis:
  - Acute tubular necrosis
  - Acute Interstitial nephritis
  - Atheroemboli (especially in PCI)

Things To Do

• Avoid when possible
  - Do they really need the scan?
  - Ultrasound or CT with no contrast an option?
  - VQ scan instead of CTPA
  - MRI instead of CT Brain Angiography
• Optimise condition prior to scan:
  - Delay till condition improved
  - Cease nephrotoxins (NSAID’s, Gentamicin, ACE, ARB’s) - increased odds ratio by 6 if not ceased 48 hrs pre-contrast.
  - Correct dehydration
  - Avoid repeated or closely spaced scans < 48 hrs apart
  - Lower doses of contrast

Pre-Hydration

• Most guidelines emphasise pre-hydration. Animal studies convincingly show that being volume depleted is harmful.
• Patients given oral fluid rehydration do worse than those given intravenous saline (34.6% vs. 3.7%)
• Isotonic saline (0.9% NaCl) reduces risk when compared to half-normal saline (0.45% NaCl) – 0.7% vs. 2.0% (p < 0.04)
• Salt loading has the same efficacy as intravenous saline (1g/10kg/day)

Bicarbonate

• Used for volume expansion & urinary alkalinisation (antioxidant properties on tubules)
  - “Over the past 5 years, 10 clinical trials comparing the development of CIAKI following the administration of either isotonic bicarbonate or isotonic saline have been published in the peer-reviewed literature, 6 demonstrating a lower incidence of CIAKI with bicarbonate administration, whereas 4 showed no significant benefit. The disparate results of these 10 clinical trials led to a proliferation of systematic reviews and meta-analyses comparing the effectiveness of bicarbonate and saline, 11 of which have now been published. Among the most recent, Zoungas et al. pooled the results of 23 published and unpublished trials that contained data on over 3500 patients. They found an overall relative risk of CIAKI of 0.62 (95% CI 0.45–0.86) with bicarbonate therapy as compared with saline. However, the strength of this finding must be tempered by evidence of both study heterogeneity and publication bias. When they limited the analysis to only published studies they observed an even lower relative risk of CIAKI with bicarbonate (RR 0.43, 95% CI 0.25–0.75), whereas analyses of the unpublished trials failed to demonstrate such a benefit (RR 0.78, 95% CI 0.52–1.17). As a result, the authors concluded that the effectiveness of IV isotonic bicarbonate compared with saline remains uncertain. In an even more recent meta-analysis, Kunadian et al. included data from 7 published trials and documented a lower risk of CIAKI with IV isotonic bicarbonate compared with IV isotonic saline (OR 0.33, 95% CI 0.16–0.69)” (either equivalent or better outcomes with sodium bicarbonate). “However, once again these results need to be regarded with caution
as the investigators also identified significant heterogeneity and evidence of publication bias

- Conclusion: “At this time, data on the comparative effectiveness of bicarbonate and saline for the prevention of CIAKI are insufficient to warrant a recommendation for the routine use of a specific isotonic intravenous fluid”.

• Likewise the International society of Nephrology recommends an isotonic solution of either normal saline or bicarbonate, although there is “a possible but inconsistent benefit of bicarbonate solutions based on overall moderate-quality evidence”.

• Up-To-Date concludes for those at risk of contrast nephropathy. “If there are no contraindications to volume expansion, we recommend isotonic intravenous fluids prior to and continued for several hours after contrast administration (Grade 1B). The optimal type of fluid and timing of administration are not well established. We suggest isotonic bicarbonate rather than isotonic saline (Grade 2B).
  - A suggested regimen is a bolus of 3 mL/kg of isotonic bicarbonate for one hour prior to the procedure, and continued at a rate of 1 mL/kg per hour for six hours after the procedure- longer if dry or more impaired renal function. This solution can be prepared by adding 150 meq of sodium bicarbonate (three 50 mL ampoules of 1 meq/mL sodium bicarbonate) to 850 mL of 5% dextrose.
  - Adverse effects – fluid overload / hypokalaemia.

**Prophylactic Dialysis Pre-Contrast.**

• No benefit
• Harmful, especially in more severe CRF
  - Hydration + N-Acetylcysteine (NAC) – CIN 4.3% (OR 0.5)
  - Hydration alone – CIN 7.2% (OR 1)
  - Hydration + Dialysis – CIN 16.4% (OR 2.5)

**Dialysis Post-Contrast.**

• Retrospective analysis of 58,000 patients
  - < 0.1% (n=59) required dialysis
• General incidence 0.4%-0.8%
• Patients who require dialysis are those who were going to end up on dialysis either way.

**N-Acetylcysteine.**

• Oral - inexpensive with no toxicity (smells terrible).
• Usual dose is 600 mg BD, better outcomes with higher doses (1200 mg BD)
• Usually given for 24 hours before and after procedure.
• In PCI studies – CIN in 5% given 1600mgBD, 15% usual dose, 30% placebo.
• Intravenous NAC - The current evidence does not support the routine use of IV NAC to prevent contrast nephropathy in patients with renal impairment. Administration also comes with a reasonable risk of anaphylactoid reaction (14.6% in one trial).

**Other Therapies.**

• Forced diuresis does not work- in fact it increases the risk of CIN.
  - Fluids – 11% risk of CIN
  - Mannitol – 28% risk of CIN
  - Frusemide – 40% risk of CIN
• Dopamine - no improvement.
• Inhibitors of Vasoconstriction (calcium channel blockers, theophylline, aminophylline, nifedipine, captopril, prostaglandin, low dose dopamine) - Not really found to be beneficial in studies and most were underpowered.
• Theophylline – High quality studies showed no difference while meta-analysis may show lower creatinine peaks yet but not rates of developing CIN. No difference in need to dialyse and mortality.
• Ascorbic Acid - received 3g IV or oral 0.5g every 12 hrs for 2 days pre-procedure (5g total) / No significance in creatinine increase or incidence of CIN.
**Other Therapies.**

- Statin (high or low dose) – jury awaiting further trials – insufficient evidence to support routine use.

**Take Home Points.**

- Stratify risk of complications (CIN)
- Don’t do the scan with IV contrast if alternative possible (or delay till improved)
- Avoid repeated scans
- Stop toxins – NSAID, ACE/ARB
- Pre-hydrate with isotonic solution IV (saline or bicarbonate)
- Can give oral NAC 600mg or 1200 mg BD 2 day’s pre and post scan.

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**NEXT WEEK’S CASE**

30 year old, right-handed man presented with pain in the dorso-ulnar aspect of the wrist (base of 4th and 5th MC bases and dorsoulnar carpal bones) after punching a wall. Swelling and pain in the above mentioned area. X-rays seen below – reported as normal. (Lateral film was not helpful). What do you do next (other than lecturing him about walls)?
JOKE / QUOTE OF THE WEEK

The past reflects current times. You may have seen the section in the SMH where they have snippets from an old SMH to reflect the news of the day. The other day they had a clip from 1822 which sounds very much like 2012 in South West Sydney...

“Mary Goodall - 51, a married woman who was cohabiting in the Prospect district with one Stephen Hunter, became intoxicated and also fell under a carriage. Her body stopped the wheel’s progress and it did not pass over her, but she was thought badly injured and transported to the Sign of the Ship Inn on Parramatta Rd. There she was attended by the landlady, and a man, apparently her husband, who said there was nothing wrong with her except she was drunk. She was rather worse than that and died four hours later. The Gazette said, “Such is one of the awful ends consequent on drunkenness and adultery!”