NEUROIMAGING CONSIDERATIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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CANON MEDICAL SYSTEMS

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Avicenna
empowering radiology with AI

UCI Health
Multifactorial Pathophysiology

Arnold et al. Journal of the Royal Society of Medicine Cardiovascular Disease (2016)
Imaging Findings Nonspecific

Vascular
- Infarcts
- Intracerebral hemorrhages
- Chronic microhemorrhages
- Posterior Reversible Encephalopathy Syndrome (PRES)

Degenerative / Toxic
- Uremic encephalopathy
- Dialysis disequilibrium syndrome
- Cerebral volume loss

Hemorrhagic Expansion & Conversion

- Hemorrhagic expansion in ICH
  - Mortality
  - Initial hematoma Volume
  - Hematoma Expansion (42% vs 15%)
    (Severe CKD vs Mild/Moderate CKD)

- Hemorrhagic Conversion in Infarcts
  - Increased risk for hemorrhagic conversion (OR = 1.95)
  - Secondary dysfunction of platelets (“uremic platelets”)

Kim et al. JKNS (2013)
Hemorrhagic Expansion

Challenges for Quantification

ABC/2 Formula for Intracerebral Hemorrhage Volume

Predicts volume of intracerebral hemorrhage from CT measurements.

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Hemorrhage Shape

- Round
- Ellipsoid
- Irregular
- Separated
- Multimodal

Hemorrhage Length

Unit: cm

Hemorrhage Width

Unit: cm

Number of CT Slices

Unit: cm

CT Slice Thickness

Unit: mm

Result:

Please fill out required fields.
Challenges for Quantification: Eccentric Shape

Quantification of a spontaneous ICH in a 44-year-old female. Segmented volume was 12 mL vs 22 mL by an ABC/2 calculation.

Challenges for Quantification: Head Tilt

58 year-old female with left basal ganglia hematoma. Routine follow-up head CT "marked interval expansion"
**Stroke Triage with Artificial Intelligence**

Leveraging deep learning for:

A. Automatic clearance for intracranial hemorrhages from CTs
   - 99.4% accuracy from a prospective study of 11,000 head CTs
B. Automatic ASPECTS scoring
C. Automatic Large Vessel Occlusion
D. Deep learning enabled quantification of infarcted tissue

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**Uremic Encephalopathy**

- **Clinical Presentation:** AMS, myoclonus, tremor, and seizures
- **Key Diagnostic Features:**
  - MRI:
    - Bilateral symmetrical swollen lentiform nuclei
    - Hyperintense T2/FLAIR signal rim delineating the boundaries of the putamen.
  - Lentiform fork sign:
    - Lateral arm: External capsule.
    - Handle: Fusion of external and internal capsules.
    - Medial arm: Splits in the internal and external medullary laminae
  - Restricted diffusion is not a classic findings

Central Pontine Myelinolysis

What is it:
- Acute demyelination in the pons, classically occurring in the setting of rapidly corrected hyponatremia.
- Direct osmotic changes and the uremia-related accumulation of metabolites in hemodialysis

Characteristic MR:
- Early restricted diffusion within the inferior pons
- Eventual high T2
- Trident shape

Other locations (extra-pontine):
- Basal ganglia
- External capsule
- Amygdala
- Cerebellum
Iodinated Contrast – Acute Kidney Injury

Questions
1. What is AKI and CIN?
2. Incidence?
3. Premedication?
4. Recommendations?

Definitions & Terminology

Post-Contrast Acute Kidney Injury (PC-AKI)
- Sudden deterioration in renal function within 48 hours following the IV administration of iodinated contrast.
- Correlative: Regardless of whether the contrast medium was the cause of the deterioration

Contrast-Induced Nephropathy (CIN)
- Causative: Sudden deterioration in renal function caused by IV administration of iodinated contrast.

Key Point #1: PC-AKI and CIN are NOT synonymous or interchangeable
What is the incidence of Contrast Induced Nephropathy (CIN)?

We don’t really know.
- Few studies have a control to allow the separation of CIN from PC-AKI
- Previous studies reporting PC-AKI observed clinically LIKELY includes a combination of
  - AKI related to contrast medium (CIN)
  - AKI unrelated to contrast medium

Contrast-Induced Nephropathy

Contrast required?

Newhouse et al. AJR 2008
**Pathogenesis & Diagnosis**

**Definition of Acute Kidney Injury (AKI)**
- Absolute serum Cr ≥0.3 mg/dL
- Percentage increase in serum Cr ≥ 50%
- Urine output reduced to ≤0.5 mL/kg/hour for at least 6 hours

**Pathogenesis**
- **PC-AKI**: Nephrotoxic event (*including CIN*) coincident with IV contrast
- **Contrast Induced Nephropathy (CIN)**:
  - Renal hemodynamic changes
  - Direct tubular toxicity
  - Osmotic / chemotoxic mechanisms

**Challenge**:
- Physiologic fluctuation in serum Cr will contribute to incidence of AKI
- Patients with higher serum Cr have a higher variance in daily serum Cr

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**What is the incidence of Contrast-Induced Nephropathy (CIN)?**

**The Route Matters**: Rate of CIN is higher in arterial injections compared to venous
- Injection is intra-arterial and supra-renal
- Catheter may dislodge emboli
- Dose to kidneys is more abrupt and concentrate

**Key Point #2:**
CIN data from angiography studies likely over-estimate the risk of CIN for patients undergoing IV contrast-enhanced studies

**Is CIN even real?**

At the current time, it is the position of ACR Committee on Drugs and Contrast Media that CIN is a real, albeit rare, entity. Published studies on CIN have been heavily contaminated by bias and conflation. Future investigations building on recent methodological advancements [3,4,7,9], are necessary to clarify the incidence and significance of this disease.
How about the more recent studies?

Contrast Induced Nephropathy (CIN) is real!

Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate.

Davenport MS\(^1\), Khalastchi S, Cohan RH, Dillman JR, Myles JD, Ellis JH.

Not so fast...


Intravenous contrast material-induced nephropathy: causal or coincident phenomenon?

McDonald RJ\(^1\), McDonald JS, Bida JP, Carter RE, Fleming CJ, Mirra S, Williamson EE, Karmes DF.

Any Agreement?

Recent studies shown that contrast-induced nephropathy is much less common than previously believed

- Stable baseline eGFR ≥45 mL / min/1.73m\(^2\), IV iodinated contrast are not an independent nephrotoxic risk factor
- Stable baseline eGFR 30-44 mL / min/1.73m\(^2\), IV iodinated contrast media are either not nephrotoxic or rarely so.
### What are the Risk Factors?

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<td>Severe Renal Insufficiency</td>
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What is the Risk Threshold for Renal Insufficiency

“There is no agreed-upon threshold of serum Cr elevation of eGFR declination beyond which the risk of CIN is considered so great that intravascular iodinated contrast medium should never be used”

But if you had to pick a number…?

- Very little evidence that IV iodinated contrast is an independent risk factor for AKI for eGFR $\geq 30$ mL / min/1.73m$^2$
- If a threshold for CIN risk is used at all, pick 30 mL / min/1.73m$^2$
Screening Recommendations

- Age > 60
- History of renal disease, including:
  - Dialysis
  - Kidney transplant
  - Single kidney
  - Renal cancer
  - Renal surgery
- History of hypertension requiring medical therapy
- History of diabetes mellitus
- Metformin or metformin-containing drug combinations

Reducing the Risk

- Contrast Medium Choice
  - Barrett and Carlise:
    - LOCM are less nephrotoxic than HOCM in patients with renal insufficiency
    - No difference in patients with normal renal function
  - Reference 78 (Meta-analysis of 25 trials)
    - No difference between LOCM and iso-osmality agent

- Volume Expansion
  - Major preventive action
  - Isotonic fluids preferred
  - Sodium Bicarbonate – no definitive evidence
  - N-acetylcysteine – no definitive evidence
Renal Safety of CTP in Acute Stroke

- Hopyan et al. 198 patients (2003-2007) in patients GFR > 30 mL/min
  - 0 patients developed CKD or required dialysis
  - 2.9% patients developed CIN

- Brinjikji et al meta analysis of 14 studies
  - No difference in risk of AKI between CTA/CTP (5727) and NCCT (981)
  - The overall rate of AKI in CTA/CTP patients was 3%
  - The overall rate of hemodialysis in the CTA/CTP group was 0.07%
  - There was no difference in AKI among CTA/CTP patients with and without chronic kidney disease (odds ratio=0.63)

Outline

- 01 – NEUROIMAGING FINDINGS
- 02 – IODINATED CONTRAST CONSIDERATIONS
- 03 – MISC. NEUROIMAGING CONSIDERATIONS
Metformin-Associated Lactic Acidosis

Incidence:
• Extremely rare (0 to 0.084 cases per 1,000 patient years)
• However, occurred because one or more patient-associated contraindications overlooked in almost all cases.
• There are no documented cases of metformin-associated lactic acidosis in properly selected patients.

FDA Warning
• The metformin package inserts approved by the FDA state that metformin should be withheld temporarily for patients undergoing radiological studies using IV iodinated contrast media.

Metformin

• Iodinated contrast is a potential concern for furthering renal damage in patients with acute kidney injury, and in patients with severe chronic kidney disease (stage IV or stage V).

• There have been no reports of lactic acidosis following intravenous iodinated contrast medium administration in patients properly selected for metformin administration.
Gadolinium – Nephrogenic Systemic Fibrosis

- Disease, primarily involving the skin and subcutaneous tissues
- Initial symptoms typically include skin thickening and/or pruritus
- Symptoms and signs may develop and progress rapidly

Contraindicated in CKD 4/5

UCI Health
Summary

1. Neuroimaging findings in CKD patients is nonspecific, but clinicians should be aware that patients with infarcts have higher rates of hemorrhagic conversion and patients with ICH have higher rates of hemorrhagic expansion.

2. Contrast-Induced Nephropathy incidence is significantly lower than previously thought.

3. Neurons over Nephrons when deciding whether to give contrast for CTA and CTP studies for patients with suspected strokes.

Thank you!