Contrast Nephropathy

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Presentation Goals

- Understand pathogenesis of contrast induced nephropathy (CIN)
- Clinical presentation, diagnosis and risk of developing ESRD
- Assess risk factors for development of CIN
- Become acquainted with prevention of CIN
- Treatment of CIN
- Discussion of Cholesterol Atheroembolic Kidney Disease
Introduction

- Administration of radiocontrast media can lead to usually reversible ARF soon after the contrast agent is administered.

- Many important issues remain unresolved including pathogenesis of the disorder, efficacies of various prophylactic strategies and the relative nephrotoxicity of different iodinated radiocontrast agents.
Pathogenesis

- Some studies show evidence of ATN, mechanism poorly understood
- Renal vasoconstriction resulting in medullary hypoxemia, possibly mediated by alterations in nitric oxide, endothelin &/or adenosine
- Direct cytotoxic effects of contrast agents
- Recovery from CIN typically much faster than usually associated with ATN
Renal Vasoconstriction

- Mediated by contrast-induced release of endothelin and adenosine and by high osmolality of agent
- Reductions in medullary blood due to effects of viscosity
- Renal vasoconstriction and reduced medullary blood flow result in hypoxemic conditions facilitating renal injury
- Diabetes and heart failure associated w/ impaired nitric oxide generation, contributing to susceptibility to CIN
Tubular Injury

- Direct cytotoxic effects
- Generation of oxygen free radicals
- May act in concert with renal asoconstriction
Incidence

Incidence is negligible with normal renal function

- 4-11% with mild-moderate renal impairment (SCr 132 to 352umol/L)
- 9-38% with moderate renal impairment and DM
- 50% or more if SCr > 352-440umol/L
- Risk is increased with marked renal dysfunction, marked volume depletion, multiple contrast studies within a 72hr period
Percutaneous Coronary Intervention

- Review of 7500 PCI patients
- CIN occurrence in 3.3% overall
- 25% in individuals w/ SCr >177umol/L
- ARF assoc w/ significant increase in mortality in-hospital (22 v 1.4% without renal failure).

However these studies. However, these studies fail to establish cause of renal failure in the setting of PCI.
Dialysis

- Incidence of CIN requiring dialysis appears very low.
- Retrospective review of 58,000 coronary procedures: 10 and 49 patients required dialysis at one week and one month (i.e. <0.1%)
### Risk factors for contrast nephrotoxicity

<table>
<thead>
<tr>
<th>Factor</th>
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<tbody>
<tr>
<td>Pre-existing renal impairment (serum creatinine &gt;1.5 mg/dL)*</td>
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<tr>
<td>Diabetes*</td>
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<td>Age &gt; 75 years</td>
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<td>Fluid depletion</td>
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<td>Myeloma</td>
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<tr>
<td>Concurrent nephrotoxic drugs</td>
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<tr>
<td>Uricosuria</td>
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<td>Ionic contrast media</td>
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* The greatest risk is presented by the coincidence of diabetes and pre-existing renal impairment.
Radiocontrast Agents

- High osmolal, first generation contrast agents (osmolality 1400-1800 mosmol/kg) associated w/ higher risk of CIN
- Newer agents, iohexol (500-850 mosmol/kg) and iodixanol (290 mosmol/kg) appear to have less nephrotoxic properties
- Lower doses also associated with decreased incidence of CIN
Clinical Characteristics

- 12 to 24 hrs post contrast
- Typically nonoliguric in vast majority of patients
- Almost all cases, renal impairment is mild and transient, with recovery in 3 to 5 days
- Persistent renal failure has been primarily described in patients w/ preexisting advanced underlying disease, particularly diabetics.
- 2 year survival in group requiring dialysis is only 19%
Diagnosis

- Diagnosis based on characteristic rise in plasma creatinine 12 to 24 hours after contrast dose.
- Differential includes ischemic ATN, acute interstitial nephritis and renal atheroemboli.
- Particularly in angiography among those with diffuse atherosclerosis, contrast nephropathy must be distinguished from atheroemboli.
Treatment

- No specific treatment
- Maintain fluid and electrolyte balance
- Best treatment is prevention
Prevention

- Use ultrasonography, MRI or non-contrast CT in high risk patients, if clinically possible
- Lower doses of contrast, avoid repetitive studies
- Avoid volume depletion or NSAIDS
- Admin of IV saline or possibly Sodium Bicarb
- Administration of antioxidants, acetylcysteine
- Use of low or iso-osmololal contrast agents
Carbon Dioxide

- Alternative contrast agent
- No or little nephrotoxicity
- Satisfactory imaging, particularly with digital subtraction angiography
- Risk is neurotoxicity when injected close to cerebral circulation or if there is a right-to-left cardiac shunt
- Use should be limited to imaging below diaphragm
Hydration

- Prospective randomized trial, 1620 pts, isotonic vs one-half isotonic saline. Significant benefit to those given isotonic saline, 0.7 versus 2.0% incidence. Diabetics (0 versus 5.5%)

- 119 pts, bicarb or saline pre and post contrast, incidence was 1.7 versus 13.6% in favor of bicarb infusion.
Diuretics

- Diuretic administration associated with higher incidence of renal failure

- Dopamine, mannitol and atrial natriuretic peptide were associated with MUCH higher incidence of renal failure (75-83%) in diabetic subjects
Acetylcysteine

- Antioxidant and vasodilatory properties
- Great heterogeneity and conflicting results
- Overall direction of data is towards benefit
- Meta-analysis of 25 trials, 2195 patients, of oral acetylcysteine – non-significant 27% reduction in CIN (95% CI 0.52 to 1.0)
- Dosing: 600 – 1200mg po 12hourly, 24 hours before and after contrast administration.
Haemodialysis and Haemofiltration

- Contrast media is partially removed by HD and HF
- Studies to date have failed to demonstrate a benefit of prophylactic HD/HF
- May mask CIN by artificially lowering creatinine
Inhibition of Vasoconstriction

- 2005 meta-analysis of theophylline, 585 patients versus controls, showed theophylline may provide some benefit, albeit small.

- Prospective randomized trial (CONTRAST) assessed fenoldapam in 315 patients (one half diabetic) undergoing cardiovascular procedure with CKD. No reduction in incidence of CIN in group receiving fenoldapam versus placebo.
Emerging data from animal experiments, case reports and small series that gadolinium-based contrast media can be associated with nephrotoxicity.

Some have claimed that nephrotoxic profile of gadolinium is similar to diluted iodinated contrast media.

More importantly, among pts w/ mod to severe renal failure, potentially severe syndrome of nephrogenic systemic fibrosis.
Recommendations

- Avoid volume depletion
- Ultrasound, MRI w/o gadolinium, CT without radiocontrast agents
- Avoid use of high osmololalal agents
- Lower doses of contrast
- Isotonic volume expansion if possible
- Avoid concomitant use of NSAIDS, diuretics
- Acetylcysteine
<table>
<thead>
<tr>
<th>Renal failure, unknown cause</th>
<th>Ultrasound (US)</th>
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<tbody>
<tr>
<td>Hematuria</td>
<td>Intravenous urography (IVU)</td>
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<td></td>
<td>or US + plain radiograph of</td>
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<td></td>
<td>kidneys, ureter and bladder</td>
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<td>(KUB)</td>
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<td>Proteinuria/nephrotic syndrome</td>
<td>US</td>
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<td>Hypertension</td>
<td>CT angiography including</td>
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<td>with normal renal function</td>
<td>imaging of the adrenal</td>
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<td>glands</td>
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<td>with impaired renal function</td>
<td>MRA</td>
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<td>Renal artery stenosis</td>
<td>MRA</td>
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<td>with normal renal function</td>
<td>MRA</td>
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<tr>
<td>with impaired renal function</td>
<td>MRA</td>
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<tr>
<td>Renal infection</td>
<td>CT</td>
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<td>Hydronephrosis detected by US</td>
<td>IVU (if renal function is</td>
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<td>preserved) or ^99^Tc-DTPA</td>
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<td>renography</td>
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<td>Retroperitoneal fibrosis</td>
<td>CT</td>
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<td>Papillary necrosis</td>
<td>IVU</td>
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<td>Cortical necrosis</td>
<td>Contrast enhanced CT</td>
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<tr>
<td>Renal vein thrombosis</td>
<td>Contrast enhanced CT</td>
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<tr>
<td>Renal infarction</td>
<td>Contrast enhanced CT</td>
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<tr>
<td>Nephrocalcinosis</td>
<td>Noncontrast CT</td>
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MRA, magnetic resonance angiography; CT, computerized tomography.
Renal Atheroemboli

- Embolization of portions of atheroembolic plaques resulting in occlusion of multiple small arteries and tissue/organ ischemia.
- Atheroemboli (cholesterol crystals) usually affect older patients with diffuse erosive atherosclerosis.
Risk Factors

- Manipulation of aorta and other large arteries during arteriography, angioplasty or surgery.
- Some cases are spontaneous
Clinical Characteristics

- May be associated with embolization to other sites including blue toe syndrome, livedo reticularis and gastrointestinal manifestations
- 7.1% of 259 patients over age 60 w/ ARF undergoing biopsy had atheroembolic disease
- Progressive decline in renal function for three to eight weeks after procedure, starting one to two weeks after procedure
- Often has staggered course
- Rarely patients have stable renal impairment.
Diagnostic Findings

- Benign urine
- Rarely with proteinuria but may be nephrotic
- Rarely have haematuria and redcell casts
- Eosinophilia and hypocomplementemia
- Eosinophiluria may also be present
- Biopsy of a skin lesion or kidney may be necessary
Livedo Reticularis
Treatment and Prognosis

- No specific treatment
- Aggressively treat for secondary prevention of cardiovascular disease
- Poor overall prognosis
- Prospective study of 95 patients, end stage renal disease and death occurred in 24 and 38% of patients respectively