Acute Kidney Injury post cardiac surgery
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AKI

• WHO

• WHAT

• WHY?
  - Cost
  - Morbidity
  - Mortality
Causes:

- Prerenal (pre-renal azotemia)
  - decrease blood flow to kidney
  - low blood pressure
  - heart failure
  - renal ischemia ... hypovolemia, low C.O.

- Intrinsic
  - ATN, AIN ..damage to structure of kidney

- Post Renal
  - obstruction... BPH, stones, malignancy
Renal Medulla

• The part most sensitive to poor oxygen delivery, suffers from a hypoxic injury if renal perfusion is compromised.

• Many preoperative patients are exposed to medications and nephrotoxins

Kramer, 2015
Highest Risk to develop AKI

• Pre-existing renal disease  
  - Age
  - Female gender
  - Hypertension
  - CHF
  - WBC count over 12,000
  - PVD
  - IABP
  - REDO CABG

  Rosner, 2006

• Those patients with “normal or near-normal”
  - Age
  - Female gender
  - Hypertension
  - CHF
  - WBC count over 12,000
  - PVD
  - IABP
  - REDO CABG

  Brown, 2007
Additional risks associated with AKI

**Patient Related**
- Increased age
- Female
- Pre-op renal dysfunction
- Obesity  BMI>40
- IDDM
- CHF
- PVD
- COPD
- HTN
- IABP (shock)
- Emergency surgery
- Contrast dye
- NSAIDS

**Procedure related**
- Length of CPB
- Cross clamp time
- OFF pump vs ON pump
- Hemodilution
Those most vulnerable to AKI

- Patients with poor renal reserve
- Patients with renovascular disease
- Recently diuresed
- Fasting for a procedure
- Impaired LV function with poor Cardiac Output

Kramer, 2015
AKI

• WHO

• WHAT

• WHY?
  - Cost
  - Morbidity
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Definitions: What is “captured’ by the STS database

- RIFLE (2004)
  - Renal Risk Injury
  - Failure
  - Loss of Renal Function
  - End-Stage Renal Disease

STS – Definition of Failure as above:
“Increase in the serum creatinine x3, or serum creatinine level \( \geq 4 \text{ mg/dl} \) with at least a 0.5 mg/dl rise, or GFR decrease by 75 percent; or urine output of \(<0.3 \text{ mL/kg per hour} \) for 24 hours, or anuria for 12 hours”

STS database for ETCVSG 3226 pts. 2.13%
Definitions:

- **KDIGO (2012)**
  Kidney Disease: Improving Global Outcomes

- Increase SCr ≥ 0.3 mg/dl within 48 hours

- Increase SCr ≥ 1.5 times baseline within prior 7 days

- Urine volume < 0.5 ml/kg/hr for 6 hours
AKI

- WHO
- WHAT

**NOW WHY?**
- Cost
- Morbidity
- Mortality
## 2014 STS CABG only

<table>
<thead>
<tr>
<th>Percent Incidence</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 30 day Operative Mortality</td>
<td>• 2.1%</td>
</tr>
<tr>
<td>• Deep Sternal Wound</td>
<td>• 9.0%</td>
</tr>
<tr>
<td>• Leg Wound</td>
<td>• Unknown</td>
</tr>
<tr>
<td>• Permanent Stroke</td>
<td>• 14%</td>
</tr>
<tr>
<td>• MI New Q wave</td>
<td>• 5%</td>
</tr>
<tr>
<td>• Atrial Fibrillation</td>
<td>• 6%</td>
</tr>
</tbody>
</table>

* Multiple authors
Risk of End Stage Renal Disease

- 29,300 patients post CABG
- AKI gave a 3 fold increased risk of ESRD
- 15% Mortality

mean follow up 4.3 ± 2.4 years

Ryden, 2014
Predicting Acute Kidney Injury

- Systematic review of 7 articles
- 3-30% depending on the definition used
- 1-5% required Dialysis
  - 60% Mortality vs 2.8%

- **AKI** => (non-dialysis) 4 fold increase short and long term mortality
  - 3 fold increase risk mortality (up to 0.5mg/dl)
  - 18 fold increase risk mortality (> 0.5 mg/dl)

- Increased ICU LOS

Huen, 2012
Survival by duration of AKI. The proportion of patients surviving form the time of cardiac surgery is plotted by the categories for the duration of AKI: no AKI (gray line), AKI for 1–2, 3–6, and ≥7 days (black lines; \( p < .0001 \) by log-rank test) (2). Reprinted from Ann Thorac Surg 2010;90:1142–9 with permission from Elsevier Brown, 2010
• Preoperative Variables - Arora, et al.
  – Increasing age
  – Nonwhite race
  – Combined valve surgery and CABG
  – ASA risk score 4/5
  – DM
  – CHF
  – Neurologic Disease at baseline
  – ACEI / ARB
• Intra and post op factors
  – Hypotension during surgery
  – Use of vasopressors
  – Post operative hypotension

Arora, 2008
Timing of Cardiac cath to surgery

- Institutional policy of limiting surgery on the same day as angiography
- Reduction of AKI 30 to 42% from two date related studies
- 4,400 patients

- Preoperative cardiac cath within 24 hours of valve surgery
- Increased Acute Renal Failure more than FIVE fold

Ranucci, 2013
Hennesey, 2010
CPB

• Promote microemboli consisting of
  – Fibrin
  – Activated leukocytes and
  – Aggregated platelets

• Resulting microvascular plugging with leukocytes and activated platelets may be pivotal in the pathogenesis of postoperative AKI
• Platelet Activation well recognized

• Several studies its role in bleeding, postoperative procoagulable state, and resultant macrothrombotic complications
  – Perioperative stroke
  – Myocardial infarction
Platelet counts and AKI

• CPB is associated with platelet activation
• Platelets are recognized as important effectors of ischemia and end organ inflammatory injury

Hypothesis:

• Whether postoperative nadir platelet counts are associated with AKI and associated mortality

Kertai, 2016
Kidney Disease: Improving Global Outcomes (KDIGO)

- Rise in SCr of 0.3 mg/dl using a rolling 48 hour window across a 10 day period, or greater than 50% rise in the same 10 day period
Results

• N = 4,217 pt.
• AKI was 54% overall
  – 87% Where Stage I Meeting the criteria but not Stage II or Stage III
  – 9.5% Stage II 2.0-2.9-fold in SCr (100-200% rise)
  – 3.4% Stage III > 3.0-fold rise (>200 % rise)

Kertai, 2016
Postoperative nadir Platelet counts

< 74,000  lowest 10\textsuperscript{th} percentile
- N = 428
- 51% Stage I
- 13% Stage II
- 7% Stage III

> 74,000  90\textsuperscript{th} percentile
- N = 3,781
- 46 % Stage I
- 4 % Stage II
- 1 % Stage III

Similar and statistically significant difference with patients diagnosed with HIT both included and excluded. N = 13 patients with HIT
## Cost and Outcomes

<table>
<thead>
<tr>
<th></th>
<th>AKI patients (n=258)</th>
<th>Matched Controls (n = 258)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total post op costs</td>
<td>$ 37,674</td>
<td>$ 18,463</td>
</tr>
<tr>
<td>ICU costs</td>
<td>$ 25,949</td>
<td>$ 13,836</td>
</tr>
<tr>
<td>Total post op LOS</td>
<td>11.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Total ICU LOS</td>
<td>3.2</td>
<td>1.4</td>
</tr>
<tr>
<td>RRT (%)</td>
<td>3.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>11.2</td>
<td>2.3</td>
</tr>
</tbody>
</table>

All are statistically different (p<0.001)

Dasta, 2008
## Effects of RRT on costs and outcomes

<table>
<thead>
<tr>
<th>Total Post operative cost</th>
<th>cases with RRT (n=27) $74,040</th>
<th>cases w/o RRT (n=231) $34,953</th>
<th>Controls (n = 258) $18,463</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Total Postoperative LOS</th>
<th>cases with RRT 21.0 d</th>
<th>cases w/o RRT 10.0 d</th>
<th>Controls 5.0 d</th>
</tr>
</thead>
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<table>
<thead>
<tr>
<th>Mortality (%)</th>
<th>cases with RRT 37.0%</th>
<th>cases w/o RRT 8.2%</th>
<th>Controls 2.3%</th>
</tr>
</thead>
</table>

Dasta, 2008
Biomarkers for AKI

- **NGAL** - Neutrophil gelatinase – associated lipocalin
- Highly sensitive and specific predictor of AKI
- Collected from urine
- Increases 25-fold within 2 hours and declining 6 hours after surgery

Mao, 2013

- **KIM-1** - undetectable in normal kidney tissue, increases in ischemia and nephrotoxins
- **IL-18** - cytokine  Correlation between peak level and injury
- **Cystatin C** - correlates with severity of AKI

Calvert, 2012
Preventative treatment

- N-Acetylcysteine - Mucomyst
- Meta-analysis study concluded that combination of NAC and sodium bicarbonate substantially reduced the occurrence of AKI by 35%
- “Should be incorporated for all HIGH risk pts”.

Brown, 2009
Hemodilution in the setting of CPB

- current CPB management guidelines accepting extreme hemodilution may contribute to postoperative acute renal and other organ injury after cardiac surgery.

- Society of Thoracic Surgeons and Society of Cardiovascular Anesthesiologists recommending maintenance of hematocrit >21%

Calvert, 2013
Pharmacological Attempts at prevention of AKI

- Allopurinol
- Vitamin E - Antioxidants
- Pentoxifylline
- Erythropoietin (EPO)
- N-acetylcysteine
- Dopamine
- Fenoldopam
- Mannitol to CPB prime

• Effects of hydration prior to cardiac surgery:
  - in patients with renal dysfunction
  - IV 0.45% saline @ 1ml/kg/h 12 hours before surgery.
  - ”Prevents AKI”

Santana-Santos, 2014
• Buffalo NY VAMC
• 1358 pts post cardiac surgery
• 40% of their patients overall developed AKI

• Multiple regression – “Independent and significant association of AKI with PREOP use of ACEI/ARB”
• 28% higher risk for AKI post op in these pts.

• “settings where maintenance of GFR requires efferent arteriolar constriction, which is blocked by ACEI”

Arora, 2008
NSAID’s

• Approximately 70% of people 65 years or older use NSAIDs at least once per week, with half of them taking at least 7 doses per week. In 2000, more than 111 million prescriptions were written for NSAIDs in the United States, at an approximate cost of $4.8 billion

Fine, 2013
NSAID’s and AKI - MOA

- Adverse renal effects from these drugs are caused by two distinct pathological entities.
- **#1** - NSAIDs reduce renal plasma flow caused by a decrease in prostaglandins, which regulate vasodilation at the glomerular level. NSAIDs disrupt the compensatory vasodilation response of renal prostaglandins to vasoconstrictor hormones released by the body. Inhibition of renal prostaglandins results in acute deterioration of renal function after ingestion of NSAIDs.

- **#2** - Acute interstitial nephritis (AIN), which is characterized by the presence of an inflammatory cell infiltrate in the interstitium of the kidney. AIN is caused by an immunological reaction after NSAID exposure of about a week. AIN is now recognized as a major cause of drug induced AKI and accounts for about 15% of all patients with unexplained AKI.

Calvert, 2012
Recommendations

• Medicines and Healthcare Products Regulatory Agency regarding NSAID’s

• Should be avoided in all patients with hypovolemia and sepsis regardless of renal function.

Calvert, 2012
What ETCVSG has done since January 2015

• Changed order sets to discontinue ACE-I/ARB AND NSAID’s within 48 hours of surgery

• Discharged and electively admitted when anatomy and symptoms allow

• Presentations at all three facilities that perform OHS regarding AKI and goals

• Added AKI (KDIGO definition) field to STS database to allow capture of data points
“A lecture is nothing more than a series of empty words unless you apply strategies that help you change your behavior.”

Dr. Robert Cerfolia
President of Society of Thoracic Surgeons
Questions ?
References


*Stamou, et al. Stroke 2001; 32: 1508 -1513 Stroke after Coronary Artery Bypass


Fine, M.  Am J. Manag Care 2013; 19 (16 supp)” S267 – S 272  Quantifying the impact of NSAID’s – Associated Adverse Events