RENAL REPLACEMENT THERAPY IN CRITICALLY ILL CONGENITAL HEART DISEASE

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PCHC IJN
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Aims of the presentation

Important topic;

- AKI is common in PCICU and associated with poor clinical outcomes especially in patient with CHD
- AKI in PCICU: Definitions
- Indications and types of RRT in AKI in PCICU
- Controversies and issues in CRRT in PCICU
Renal Replacement Therapy

- Standard therapy in PICU

- Expertise is required as:
  - wide variation of size (2-100kg)
  - Variety of disease associated with AKI
  - Variety of technique

- The overall mortality in CHD children that receive RRT ranges from 3.3-12.7% with average length of stay increased from 4.5 to 12.7 days
CHD and Acute kidney injury (AKI)

- AKI is a frequent complication (40-60%) of pediatric cardiac surgery
- AKI is associated with significant morbidity (longer ventilation, inotropic support and ICU stay)
- Increase risk of mortality in pediatric cardiac surgical cases
- Fluid overload (FO) is associated with morbidity and mortality
- Survivors of AKI can progress into Chronic Kidney disease (CKD)
**Cardiorenal syndrome in Heart failure**

- Renal injury is common in heart failure
- Cause is LCOS, persistent vasoconstriction, nephrotoxic drugs, contrast agents, sepsis and high CVP
- Myocardial dysfunction leads to renal dysfunction
- Decrease urine output and fluid overload aggravates clinical deteriorations
- Associated with longer length of stay, high cost and increased risk of in-hospital mortality
- Poor outcome
Acute Kidney Injury – definition

Many definitions (>30) of AKI exist in the literature;

• Hallmarks of AKI definitions;
  - Rise in plasma creatinine from baseline  Fall in (e)GFR
  - Fall in urine output (not essential)

Standardised definitions needed;

• pRIFLE (renal dysfunction, injury, failure, loss of kidney function, ESRD) standardised definition proposed in 2007
• Other standardised definitions: AKIN/KDIGO
**Acute Kidney Injury – definition**

**Modified RIFLE criteria in critically ill children with acute kidney injury**

A Akcan-Arikan¹, M Zappitelli¹, LL Loftis², KK Washburn¹, LS Jefferson² and SL Goldstein¹

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**Table 6 | Pediatric-modified RIFLE (pRIFLE) criteria**

<table>
<thead>
<tr>
<th>Estimated CCI</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk eCCI decrease by 25%</td>
<td>&lt;0.5 ml/kg/h for 8 h</td>
</tr>
<tr>
<td>Injury eCCI decrease by 50%</td>
<td>&lt;0.5 ml/kg/h for 16 h</td>
</tr>
<tr>
<td>Failure eCCI decrease by 75% or eCCI &lt; 35 ml/min/1.73 m²</td>
<td>&lt;0.3 ml/kg/h for 24 h or anuric for 12 h</td>
</tr>
<tr>
<td>Loss Persistent failure &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td></td>
</tr>
<tr>
<td>(persistent failure &gt; 3 months)</td>
<td></td>
</tr>
</tbody>
</table>

eCCI, estimated creatinine clearance; pRIFLE, pediatric risk, injury, failure, loss and end-stage renal disease.
Acute Kidney Injury - definition

- 150 admissions to PICU
- 82% AKI occurred in the initial week
- pRIFLE max:
  - 48.8% = R  26% = I  25.2% = F
- AKI defined by pRIFLE associated with longer LOS (PICU and hospital)
- pRIFLE max commonly reached early in admission

Table 1 | Comparison of characteristics of patients with versus without AKI

<table>
<thead>
<tr>
<th></th>
<th>Control n=27 (18%)</th>
<th>AKI by RIFLE n=123 (82%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.0±0.0 (1.25)</td>
<td>0.3±0.3 (4.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>21.7±18.1 (12.0)</td>
<td>26.1±23.6 (16.0)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>103.9±38.2 (67.0)</td>
<td>104.7±38.4 (102.2)</td>
</tr>
<tr>
<td>PRISM II</td>
<td>12.4±7.2 (13.0)</td>
<td>15.4±8.6 (16.0)</td>
</tr>
<tr>
<td>Baseline eGFR (ml/min/1.73 m²)</td>
<td>132±46 (119)</td>
<td>159±100 (129)</td>
</tr>
<tr>
<td>Peak mean arterial pressure (mm Hg)</td>
<td>15.0±8.2 (17.0)</td>
<td>17.2±9.2 (14.0)</td>
</tr>
<tr>
<td>Days ventilated</td>
<td>10.7±13.1 (8.0)</td>
<td>15.8±18.7 (9.0)</td>
</tr>
<tr>
<td>PICU length of stay</td>
<td>10.1±6.2 (9.0)</td>
<td>18.0±24.3 (11.0)**</td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>20.5±16.6 (14.0)</td>
<td>36.6±40.1 (22.0)**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Categorical variables, N (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>11 (40.7)</td>
<td>41 (33.3)</td>
</tr>
<tr>
<td>African-American</td>
<td>5 (18.5)</td>
<td>25 (20.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8 (29.6)</td>
<td>55 (44.7)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (11.1)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (40.7)</td>
<td>56 (45.5)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>17 (63)</td>
<td>89 (72.4)</td>
</tr>
<tr>
<td>Hematology/oncology</td>
<td>1 (3.7)</td>
<td>15 (12.2)</td>
</tr>
<tr>
<td>Cardiology</td>
<td>2 (7.4)</td>
<td>20 (16.3)</td>
</tr>
<tr>
<td>Other</td>
<td>14 (52)</td>
<td>55 (44.7)</td>
</tr>
<tr>
<td>Admitting diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>11 (41)</td>
<td>40 (33)</td>
</tr>
<tr>
<td>SIRS/sepsis/septic shock</td>
<td>5 (18.5)</td>
<td>33 (26.8)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>6 (22)</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (18.5)</td>
<td>38 (30.9)</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for pressors</td>
<td>13 (48.2)</td>
<td>66 (53.7)</td>
</tr>
<tr>
<td>Need for RRT</td>
<td>0</td>
<td>11 (8.9)</td>
</tr>
<tr>
<td>28-Day mortality</td>
<td>3 (11.1)</td>
<td>18 (14.6)</td>
</tr>
</tbody>
</table>

AKI, acute kidney injury; eGFR, estimated creatinine clearance; PICU, pediatric intensive care unit; RIFLE, risk, injury, failure, loss and end-stage renal disease.

*P < 0.05; **P < 0.005

1PRISM, Pediatric Risk of Mortality II score.
2Other includes the following diagnostic categories: endocrine, failure to thrive, gastrointestinal, rheumatologic, neurological (cerebral palsy, and epilepsy), orthopedic, pulmonary, psychiatric.
3SIRS, systemic inflammatory response syndrome.
4RRT, renal replacement therapy.
How is AKI defined clinically?

- Different criteria have been used in clinical practice and in literature to define and stage AKI (RIFLE\textsuperscript{1,2} and AKIN\textsuperscript{1,3})
- The KDIGO Clinical Practice Guideline for Acute Kidney Injury unifies these criteria in a single definition:\textsuperscript{1}

AKI can be clinically defined as any one of the following:\textsuperscript{1}

- Increase in SCr by \(\geq 0.3 \text{ mg/dL} (\geq 26.5 \text{ µmol/L})\) within 48 hours
- Increase in SCr to \(\geq 1.5\) times baseline within the past 7 days
- Urine volume <0.5 mL/kg/hour for 6 hours

\textbf{References:}

KDIGO Clinical Practice Guidelines severity staging for AKI

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR ≥0.3 mg/dL (≥26.5 μmol/L) increase</td>
<td>&lt;0.5 mL/kg/hour for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>&lt;0.5 mL/kg/hour for ≥12 hours</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dL (≥353.6 μmol/L) OR Initiation of RRT OR in patients &lt;18 years, a decrease in eGFR to &lt;35 mL/minute per 1.73 m²</td>
<td>&lt;0.3 mL/kg/hour for ≥24 hours OR Anuria for ≥12 hours</td>
</tr>
</tbody>
</table>

eGFR, estimated glomerular filtration rate
KDIGO recommends that AKI should be managed according to the stage of disease.

<table>
<thead>
<tr>
<th>High risk</th>
<th>AKI Stage</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinue all nephrotoxic agents when possible</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Ensure volume status and perfusion pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider functional hemodynamic monitoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor serum creatinine and urine output</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid hyperglycemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider alternatives to radiocontrast procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Non-invasive diagnostic workup**
- Consider invasive diagnostic workup

**Check for changes in drug dosing**
- Consider Renal Replacement Therapy
- Consider ICU admission

Avoid subclavian catheters if possible

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Fluid overload (FO)

- In critically ill with or without AKI is associated with increase morbidity and mortality
- 20% conferred greater odds of death in the presence of Multiorgan dysfunction
- **Basu et al.** showed association of early postoperative fluid overload and poor outcome
- **Wilder et al.** postoperative fluid overload is surrogate marker of AKI and risk factor for poor outcome
- Recent studies demonstrated early use of PD in infants after CPB is associated with shorter ventilation and inotropic usage, Lower MORTALITY
Epidemiology & Outcome of Acute Kidney Injury In Paediatric Patients Treated With Renal Replacement Therapy In Malaysia

Lim HN¹, Pee S¹, Yap YC², Sidhu S², Eng C³, Lee ML³, Wanjazilah WI⁴, Liaw L⁵, Khairulfaizah MK⁶, Yap SL⁷, Anisuraya G⁸

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²Department of Paediatrics, Hospital Kuala Lumpur, Wilayah Persekutuan, Malaysia
³Department of Paediatrics, Hospital Tuanku Jaafar, Seremban, Negeri Sembilan, Malaysia
⁴Department of Paediatrics, Hospital Selayang, Selangor, Malaysia
⁵Department of Paediatrics, Hospital Pulau Pinang, Pulau Pinang, Malaysia
⁶Institut Jantung Negara, Wilayah Persekutuan, Malaysia
⁷Department of Paediatrics, Hospital Umum Sarawak, Kuching, Sarawak, Malaysia
⁸Department of Paediatrics, Hospital Serdang, Selangor, Malaysia
Total events of severe AKI, N = 360

Note: Cardiac centres are marked in red.
Incidence

Total Number of Admissions: 406,966

Number of admissions at ICU setting: 44,790

360 cases of Severe AKI in total

Severe AKI rate in ICU: 6.4 per 1000 ICU admissions

Severe AKI rate: 0.88 per 1000 hospital admissions

70 cases in non-ICU setup

290 cases in ICU setup

70 cases in non-ICU setup

290 cases in ICU setup
Aetiology of Severe AKI

- Sepsis: 26%
- Hypoperfusion: 42%
- Glomerular Disease: 16%
- HUS: 7%
- Tumour lysis syndrome: 3%
- Other: 6%
- Nephrotoxin: 3%
- IEM: 2%
- Obstructive uropathy: 1%

**Majority due to community-acquired forms of AKI**
Median eGFR at onset of AKI was 54.30 ml/1.73m²/min (24.1,88.1). Stage of pRIFLE was of Loss in two-thirds of the cohort at presentation (67.5%).
A one way Welch ANOVA was conducted which showed that the mean eGFR at initiation of dialysis is significantly different between the groups, p=0.0005.

Games-Howell post hoc analysis suggest statistically significant lower threshold of initiating dialysis at IJN (cardiac centre) compared to the rest of the participating centre, p=0.0005.
Mortality

Incidence rate of death due to severe AKI is 2.5 per 10,000 hospital admissions

~28.6% of children with AKI
## Predictors of Death

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>pVALUE</th>
<th>ODDS RATIO</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.25</td>
<td>0.94</td>
<td>0.83-1.05</td>
</tr>
<tr>
<td>Gender</td>
<td>0.80</td>
<td>0.93</td>
<td>0.52-1.66</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0.005</td>
<td>0.21</td>
<td>0.11-0.43</td>
</tr>
<tr>
<td>Concomitant clinical sepsis</td>
<td>0.024</td>
<td>2.00</td>
<td>1.10-3.63</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0.58</td>
<td>0.66</td>
<td>0.15-2.93</td>
</tr>
<tr>
<td>Needed 2 or more inotropes</td>
<td>0.025</td>
<td>0.205</td>
<td>0.05-0.82</td>
</tr>
</tbody>
</table>
• Median eGFR at onset was 54.3 (IQR24.1,88.1) and initiation of dialysis was 19.3 (IQR10.2,36.2).

• Upon discharge, median eGFR was 59.8(IQR27.2,97.110.2,).

• By a year post AKI, majority showed good recovery with median eGFR at 93.9  (IQR68.9,115.4)

- A third who survived had eGFR less than 60ml/1.73m²/min
- 2% progressed to end stage renal failure.
RESULTS

A total of 6493 eligible patients were included into the study cohort.

<table>
<thead>
<tr>
<th>Subject Test</th>
<th>Group</th>
<th>Non Parametric Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AKI [N=237]</td>
<td>Non-AKI [N=6256]</td>
</tr>
<tr>
<td>Bypass Time (min)</td>
<td>200.5 (158.0, 255.8)</td>
<td>94.0 (65.0, 139.0)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>110.00 (70.5, 165.5)</td>
<td>53.0 (34.0, 85.0)</td>
</tr>
<tr>
<td>X Clamp (min)</td>
<td>7.0 (4.0, 12.0)</td>
<td>1.0 (1.0, 2.0)</td>
</tr>
<tr>
<td>Ventilation (days)</td>
<td>9.5 (6.0, 16.0)</td>
<td>2.0 (1.0, 4.0)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>8.0 (5.0, 11.0)</td>
<td>2.0 (1.0, 3.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>AKI</th>
<th>Non AKI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>212</td>
<td>6211</td>
<td>6423</td>
</tr>
<tr>
<td>Death</td>
<td>25 (10.55%)</td>
<td>45 (0.72%)</td>
<td>70 (1.08%)</td>
</tr>
<tr>
<td>Total</td>
<td>237 (3.7%)</td>
<td>6256 (96.3%)</td>
<td>6493</td>
</tr>
</tbody>
</table>

Chi Square Test: p < 0.001
The incidence of AKI in children who underwent cardiac surgery with CPB was 3.7%

Risk factors;
- Longer CPB, aortic cross-clamp time, inotropes
- ECMO support

AKI associated with prolonged mechanical ventilation, increased hospital stay and mortality

Mortality rate AKI 10.55% versus non AKI 0.72%
Indication for RRT

- Indications similar to adults, with some unique features in children e.g. Inborn errors of metabolism.
- From ppCRRT registry:
  - Indications for CRRT 90% related to AKI
  - 29% FO
  - 13% electrolyte abnormalities
  - 46% both FO and electrolyte abn
  - 3% to eliminate fluid restriction

<table>
<thead>
<tr>
<th>Indications for RRT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td>Non-renal</td>
</tr>
<tr>
<td>Oliguria/anuria</td>
<td>Fluid-overload</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Inborn errors of metabolism</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Azotemia/uraemia symptoms</td>
<td>Drug overdose/toxins</td>
</tr>
<tr>
<td>Hyperphosphataemia</td>
<td></td>
</tr>
</tbody>
</table>
Risk factor for AKI—younger age, preexisting renal dysfunction, complex cardiac lesion, prolonged CPB, circulatory arrest, LCOS, central venous hypertension, hypotension and hypoalbuminemia

Conservative- diuretics and to increase perfusion pressure

Indication of RRT;
1- refractory electrolytes abnormalities
2-prevention or treatment of fluid overload
3-need to provide adequate nutritional support

Kwiatkowski etal-use of PD catheter (even without active dialysis) was associated with earlier negative balance, extubation, reduce inotropes and fewer electrolytes imbalance.
### Types of RRT

- PD
- HD
- CRRT

➢ Choice depends on clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>HD</th>
<th>CRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular access</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Complexity</td>
<td>Low</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>Systemic anticoagulation</td>
<td>No</td>
<td>Frequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Toxin removal</td>
<td>Moderate</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Fluid removal</td>
<td>Moderate</td>
<td>Moderate</td>
<td>High</td>
</tr>
<tr>
<td>Use in haemodynamic</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>instability?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use in abdominal surgery?</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Adapted from Roger’s Pediatric Intensive Care Table 37.2
Peritoneal dialysis

- PD is the oldest form of RRT
- Safe and effective form of RRT after repair of CHD and fluid overload after CPB, Common choice in small children
- Low cost, No anticoagulation
- Usually tenckhoff catheter
- Bidirectional exchange of fluid and solutes across the peritoneal membrane
- Clearance depends on:
  - Volume of PD (usually 10-20ml/kg)
  - Fluid Dwell time (usually 20-40 mins)
  - Osmolality of PD fluid (varied dextrose concentration (1.5% / 4.25%)
- Complications relatively rare:
  - Peritonitis
  - Drainage / filling problems
  - Fluid imbalance
Cardiopulmonary interaction

- PD common form of RRT after CPB
- Effective even in LCOS/Hypotension
- Potential increase in ventilator requirement and reducing CO
- Start with 10ml/kg and try to reach 30ml/kg (effective removal of solutes)
Peritoneal dialysis

➢ Advantages;
  • No exposure to blood products
  • Continuous ultrafiltration with less potential for hemodynamic instability secondary to sudden fluid shift

➢ Limitations of PD;
  • Does not provide urgent clearance of acute intoxication e.g. hyperkalemia/uremia
  • Not feasible for patients with congenital anomalies e.g. gastrochisis
  • Omphalocele or adhesion from abdominal surgery
  • Lost of IG leads to risk of peritonitis/sepsis
  • Dialysate can damage the peritoneal membrane
Peritoneal Dialysis
Continuous Renal Replacement Therapy

Definition:

“Any extracorporeal blood purification Therapy intended to substitute for impaired renal function over an extended period of time and applied for or aimed at being applied for 24 hours/day.”

Reference:
CRRT

- Gentler form of fluid / solute removal (e.g. hemodialysis)
- Suitable for haemodynamic instability
- Initially CAVH (1950s) Now pump-driven CVVH
- Provides solute clearance by diffusion and / or convection
- CVVH: Exclusively convection
Hemodialysis Flow Path

- Blood Circuit
- Dialysis Circuit
- Haemofilter
- Dialysis fluid
- Water from RO system
- Drain
- Concentrate

Patient
Continuous Renal Replacement Therapy

- Different types of CRRT:
  - SCUF - Slow Continuous Ultrafiltration
  - CVVH - Continuous Veno-Venous Hemofiltration
  - CVVHD - Continuous Veno-Venous Hemodialysis
  - CVVHDF - Continuous Veno-Venous
  - Hemodiafiltration

Reference:
**In a nutshell - Therapies of CRRT**

<table>
<thead>
<tr>
<th></th>
<th>SCUF</th>
<th>CVVH</th>
<th>CVVHD</th>
<th>CVVHDF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principal Transport Mechanism</strong></td>
<td>Ultrafiltration</td>
<td>Ultrafiltration Convection</td>
<td>Ultrafiltration Diffusion</td>
<td>Ultrafiltration Convection Diffusion</td>
</tr>
</tbody>
</table>
Ultrafiltration is the movement of fluid through a semi-permeable membrane driven by a pressure gradient.
Convection is the movement of solutes with fluid flow, also known as solute drag. This movement of fluid is consequence of transmembrane pressure (TMP) gradient.

Reference:
Continuous Veno-Venous Hemofiltration
Acute Kidney Injury – CRRT

- Issues / controversies with CRRT:
  - Access
  - Modality
  - Timing
  - Anticoagulation
  - Use of CRRT in small children
CRRT: access

- Longer circuit survival associated with larger bore catheters and internal jugular site

From: Hackbarth et al. a report from the PPCRRRT registry. Int J Artif Organs 30:1116–1121
CRRT: timing

- Determining optimal timing of initiation of CRRT in ICU is a high priority research goal

- Strong evidence that fluid overload in ICU is associated with worse outcomes

- Modem et al, CCM 2014
  - Single-centre, observational study 190 PICU pts on CRRT (AKI / FO)
  - Overall mortality 47%
  - Survivors commenced CRRT earlier in admission compared with non-survivors
  - 2d vs 3.4d (p=0.001)
CRRT: anticoagulation

- CRRT in children:
  Elevated risk of clotting of adults:
  - Lower blood flows
  - Smaller catheters

- Commonest options:
  - Heparin or Citrate

- Multi-centre evaluation of anticoagulation

- Heparin vs citrate ppCRRT registry: 138 patients

No diff in circuit life
Higher risk of bleeding in heparin group

Brophy et al. Nephrol Dial Transplant 2005
Acute Kidney Injury – CRRT: small children

- CRRT uniquely difficult in small children

- Vascular access may be limited – 5Fr catheters associated with poor filter lifespan

- Relatively high blood flow relative to blood volume

- Higher circuit volume relative to blood volume  Risk of hypothermia

- ppCRRT registry:
  - 84 children < 10kg
  - Higher mortality (67%) vs >10kg (36%)
  - But technology and expertise improving
Acute Kidney Injury – CRRT: complications

- Complications of CRRT in PICU: Prospective, observational study Single-centre in Spain

- 174 PICU patients on CRRT (43% <1 yr of age) High complication rate.

- Main complications:
  - Catheterization-related: 13 pts. (7.4%) – hematoma, bleeding, venous congestion
  - Hypotension: 53 pts. (30.4%)
  - Hemorrhage: 18 pts. (10.3%)
  - Electrolyte disturbance: common

Santiago et al, Critical Care 2009
Conclusion

- AKI in CHD is common after cardiac surgery and associated with worse clinical outcomes

- Early recognition and aggressive prevention and treatment of AKI result in decline in morbidity and mortality

- Fluid overload is an independent predictor of mortality in CHD patient with AKI

- PD is the preferred mode of RRT in PCICU with reasonable good outcome
THANK YOU
Acute Kidney Injury – CRRT: small children

Ronco
Lancet 2014

CarpeDiem
Miniaturise
d CRRT

2.9kg MODS / FO
5cm, 22g catheter
>400hrs CRRT
Acute Kidney Injury - aetiology

- **Pre-renal:**
  - volume depletion / redistribution of circulation / decreased CO
- **Renal:**
  - ATN / ischaemia / toxins / nephritis / glomerulonephritis / vascular / congenital
- **Post-renal:**
  - obstructive uropathy

- Commonest cause of **pre-renal** AKI worldwide = dehydration from gastroenteritis

- Commonest cause of **renal** AKI worldwide = HUS

- But most AKI now seen in PICU is secondary to other primary or systemic disease e.g. Post cardiac surgery / ATN / sepsis / nephrotoxic medication
CRRT: dose

- High dose vs. lower dose of ultrafiltration
- 35ml/kg/hr vs. 20ml/kg/hr
- Historical evidence from adult studies for better outcome with higher dose
- Large multi-centre trials show no survival benefit for higher dose:
  - Acute Renal Failure Network study
    - 1124 adults with AKI
    - 60 day survival equivalent in high dose and low dose
  - RENAL study
    - 1508 adults AKI
    - Just CVVHDF
    - No survival benefit at 90 days

Bellomo et al NEJM 2009
Renal Replacement Therapy

Intermittent
- Intermittent haemodialysis
- Prolonged Intermittent Renal Replacement Therapy

Continuous
- Peritoneal Dialysis
- Continuous Renal Replacement Therapy
CRRT: timing

- Effect of degree of fluid overload at time of initiation of CRRT
- Cohort of PICU pts on CRRT, ppCRRT registry
- 153 patients
- 3% increase in mortality for 1% increase in FO

Sutherland et al Am J Kidney Disease 2010
Recognize that AKI in acutely ill patients is associated with adverse short- and long-term outcomes:

- Morbidity (CKD, CVD, infection)
- Mortality

Identify AKI as a potential risk factor for CKD among survivors of acute illness

- New CKD or worsened CKD

Understand how the differences among RRT modalities may influence long-term renal recovery after AKI

AKI, acute kidney injury; CKD, chronic kidney disease; CVD, cardiovascular disease; RRT, renal replacement therapy
Adsorption is molecular adhering to surface or interior of a semi permeable membrane.
Acute Kidney Injury in PICU – the future

Need RCTs – currently lacking in this area in pediatrics cf adults
ppRRT registry is a good start
More collaborative data and research needed
AKI biomarker-based decision algorithms may help detect and predict need for RRT
Emerging technology and expertise (e.g. Carpediem)
Prismaflex® System

- User friendly system for individualized CRRT prescriptions
- Leading in development of extracorporeal blood purification and fluid management
- Versatility to facilitate use of a wide range of treatment strategies
- Patients’ safety in mind
Continuous Veno-Venous Hemodialysis
What is AKI?

- AKI is a clinical syndrome characterized by a rapid reduction in renal excretory function\(^1,2\)
- In severe AKI, RRT is often needed to support renal function
  - RRT may be required temporarily until renal function recovers\(^3\)
  - In a proportion of patients, the need for RRT may become permanent\(^3\)
- AKI is distinct from CKD
  - CKD = GFR <60 mL/min/1.73 m\(^2\) for ≥3 months, irrespective of the presence or absence of kidney damage\(^4\)

GFR, glomerular filtration rate
Intermittent Renal Replacement Therapy

- Intermittent Renal Replacement Therapy
  - Intermittent Haemodiagnosis
  - Prolonged Intermittent Renal Replacement Therapy
    - Extended Daily Dialysis
    - Sustained Low Efficiency Dialysis

Reference:
Acute Kidney Injury – CRRT: modality

- Does it make a difference to **outcome**?
- No strong evidence to favour one modality
- Observational (ppCRRT registry) evidence of improved survival when using convective methods (vs. CVVHD) in cohort of stem-cell transplant patients
- 59% vs. 27% p<0.05

**Choice** of modality:

- ppCRRT registry: 344 children on CRRT in US: CVVHD: 48% CVVHDF: 30% CVVHF: 21%  

Choice tends to be centre-dependent

**Theoretical improved clearance of:**
- small solutes with diffusion
- middle-sized solutes with convection
Continuous Renal Replacement Therapy

Peritoneal Dialysis

Continuous Renal Replacement Therapy
Pre vs. Post Filter Dilution

**Pre Dilution**
- Reduces risk of filter clotting
- May prolonged filter life
- Reduces effective clearance

Reference:
Kellum et al. 2010. Continuous Renal, ork, Oxford University Press.
CRRT Therapy Sets

The main functional unit of the CRRT circuit, where blood is processed for solute and/or fluid removal.
**CRRT Therapy Set – Prismaflex M Sets**

**AN69 Membrane**

Symmetrical hydrogel structure. ie. AN69

**PAES Membrane**

Microporous asymmetric membranes, ie Polysufone / PAES.

**CRRT (especially CVVH) with the AN 69 membrane, provide more adsorptive capability** as compared to other microporous asymmetric membranes; because the entire breadth of the membrane is in contact with the blood compartment and thus more accessible for adsorption.

**Adsorption enables the removal of inflammatory cytokines.**

Reference:
## CRRT Therapy Sets – Prismaflex M Sets and oXiris

<table>
<thead>
<tr>
<th></th>
<th>Prismaflex M60</th>
<th>Prismaflex M100</th>
<th>Prismaflex oXiris</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow range (ml / min)</td>
<td>50 – 180</td>
<td>75 – 400</td>
<td>0 – 450</td>
</tr>
<tr>
<td>Minimum patient weight (kg)</td>
<td>11</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Blood volume in set ± 10 % (ml)</td>
<td>93</td>
<td>152</td>
<td>189</td>
</tr>
</tbody>
</table>
## Indications for Renal Replacement Therapy

**Renal Replacement Therapy**¹  
_(excretory function only)_

### Life threatening changes
- Fluid balance
- Electrolyte control
- Acid–base regulation

**Initiate emergently**

### Patient medical condition
- Hemodynamically unstable
- Acute brain injury
- Generalized brain edema
- Increased intracranial pressure

### Preference to initiate with CRRT

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## Renal Support Therapy²

- Immune modulation in sepsis
- Volume balance in multi organ dysfunction / failure
- Nutritional support
- Volume removal in refractory Congestive Heart Failure
- Alleviate ARDS induces respiratory acidosis

---

**Reference:**
Slow Continuous Ultrafiltration
Pre vs. Post Filter Dilution

Post Dilution
- Increases risk of filter clotting.
- Increased need of anticoagulant
- No reduction of effective clearance

Reference:
Kellum et al. 2010. Continuous Renal Replacement Therapy. New
# Indications for CRRT Initiation

<table>
<thead>
<tr>
<th>Description</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uremic complications</td>
<td>Encephalopathy, Pericarditis, Bleeding</td>
</tr>
<tr>
<td>Serum urea</td>
<td>≥ 36mmol/l (100 mg/dl)</td>
</tr>
<tr>
<td>Potassium</td>
<td>≥ 6mmol/l, ECG abnormalities</td>
</tr>
<tr>
<td>Magnesium</td>
<td>≥ 4mmol/l, Anuria, Absent deep tendon reflexes</td>
</tr>
<tr>
<td>Serum pH</td>
<td>≤ 7.15</td>
</tr>
<tr>
<td>Urine output</td>
<td>&lt; 200 ml /12 hours, Anuria</td>
</tr>
<tr>
<td>Diuretic-resistant organ edema (i.e. pulmonary edema) in the presence of AKI</td>
<td></td>
</tr>
</tbody>
</table>

Criteria for CRRT initiation

RENAL Trial

<table>
<thead>
<tr>
<th>Criteria for CRRT</th>
<th>Serum Creatinine</th>
<th>Urine Output</th>
<th>BUN</th>
<th>Serum Potassium</th>
<th>Volume Overload (with AKI)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>RENAL Initiation Criteria for CRRT</td>
<td>&gt; 3.4 mg/dl (&gt;300 μmol/L)</td>
<td>&lt; 100 mL/6h*</td>
<td>&gt; 70 mg/dl (&gt;25 mmol/L)</td>
<td>&gt; 6.5 mEq/L (&gt;6.5 mmol/L)</td>
<td>Clinically significant organ edema</td>
<td>&lt; 7.2</td>
</tr>
<tr>
<td>Normal Patient Values</td>
<td>0.6–1.5 mg/dl (53–133 μmol/L)</td>
<td>&gt; 30 mL/h</td>
<td>8–25 mg/dl (2.9–8.9 mmol/L)</td>
<td>3.5–5 mEq/L (3.5–5.0 mmol/L)</td>
<td></td>
<td>7.35–7.45</td>
</tr>
</tbody>
</table>

*unresponsive to fluid resuscitation measures

Acute Kidney Injury – indication for RRT

- Diagnosis associated with AKI from ppCRRT registry

### Table 2: Primary diagnosis and survival for pediatric patients receiving continuous renal replacement therapy (CRRT) (Prospective Pediatric Continuous Renal Replacement Therapy Registry)

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number of patients</th>
<th>Number of survivors</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>81</td>
<td>48</td>
<td>59%</td>
</tr>
<tr>
<td>Stem cell transplant</td>
<td>55</td>
<td>25</td>
<td>45%</td>
</tr>
<tr>
<td>Cardiac disease/transplant</td>
<td>41</td>
<td>21</td>
<td>51%</td>
</tr>
<tr>
<td>Renal disease</td>
<td>32</td>
<td>27</td>
<td>84%</td>
</tr>
<tr>
<td>Liver disease/transplant</td>
<td>29</td>
<td>9</td>
<td>31%</td>
</tr>
<tr>
<td>Malignancy (w/o tumor lysis)</td>
<td>29</td>
<td>14</td>
<td>48%</td>
</tr>
<tr>
<td>Ischemia/shock</td>
<td>19</td>
<td>13</td>
<td>68%</td>
</tr>
<tr>
<td>Inborn error of metabolism</td>
<td>15</td>
<td>11</td>
<td>73%</td>
</tr>
<tr>
<td>Drug intoxication</td>
<td>13</td>
<td>13</td>
<td>100%</td>
</tr>
<tr>
<td>Tumor lysis syndrome</td>
<td>12</td>
<td>10</td>
<td>83%</td>
</tr>
<tr>
<td>Pulmonary disease/transplant</td>
<td>11</td>
<td>5</td>
<td>45%</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>5</td>
<td>71%</td>
</tr>
</tbody>
</table>
Acute Kidney Injury – PD

- BCH PD prescription
- Includes cross-flow PD
- In BCH, mostly used in post-cardiac surgery AKI in infants.
Acute kidney injury (AKI) is common among hospitalized pediatric patients.

Epidemiological data on pediatric AKI in Malaysia is lacking.

This study involved 9 major tertiary hospitals across East and West Malaysia. To date, this is a pioneer study in Malaysia on pediatric AKI.

We hope to generate data that would assist in future evidence-based decision making in terms of health policy.
RENAL REPLACEMENT THERAPY

First mode of RRT:
- CRRT: 10.5%
- PD: 49.2%

4 out of 145 patients on HD had to switch to PD (2.75%) while 2 out of 177 patients were converted to HD from PD (1.13%).

Median eGFR at onset of AKI was 54.30 ml/1.73m²/min (24.1, 88.1). Stage of pRIFLE was of Loss in two-thirds of the cohort at presentation (67.5%).
• Incidence of severe AKI is low BUT with increased risk of mortality.
• Majority caused by community-acquired forms of AKI.
• PD was the most frequently utilized modality of renal replacement therapy.
• Short term renal outcome amongst survivors appears promising.
• Establishment of a prospective and population-specific data collection will provide the true incidence and burden of paediatric AKI.
• These observation helps in developing both vertical (disease-specific) and horizontal (investment on infrastructure and human resources) programming of future paediatric healthcare services.
**Acute Kidney Injury – CRRT**

From ppCRRT registry:

CVVH: 21%
CVVHD: 48%
CVVHDF: 30%

*Symons et al 2007*

---

**Edwards life sciences**

**Table 7 Comparison of mortality in studies of critically ill children on CRRT**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study characteristics</th>
<th>Country</th>
<th>Number of patients</th>
<th>Age and weight</th>
<th>PRISM score</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldstein</td>
<td>2001</td>
<td>Retrospective single centre</td>
<td>USA</td>
<td>21</td>
<td>0.5–18 years (mean 8.8 years)</td>
<td>15.4</td>
<td>57</td>
</tr>
<tr>
<td>Ponikvar</td>
<td>2002</td>
<td>Retrospective single centre</td>
<td>Slovenia</td>
<td>21</td>
<td>Only newborns and infants</td>
<td>Not measured</td>
<td>57</td>
</tr>
<tr>
<td>Symons</td>
<td>2003</td>
<td>Retrospective single centre</td>
<td>USA</td>
<td>85</td>
<td>Less than 10 kg</td>
<td>Not measured</td>
<td>38</td>
</tr>
<tr>
<td>Folland</td>
<td>2004</td>
<td>Retrospective single centre</td>
<td>USA</td>
<td>113</td>
<td>2.5–14.3 years (mean 9.6 years)</td>
<td>13</td>
<td>39</td>
</tr>
<tr>
<td>Shiga</td>
<td>2004</td>
<td>Retrospective single centre</td>
<td>Japan</td>
<td>60</td>
<td>Neonates and children</td>
<td>Non measured</td>
<td>48</td>
</tr>
<tr>
<td>Pichler</td>
<td>2007</td>
<td>Retrospective single centre</td>
<td>Austria</td>
<td>115</td>
<td>50 patients less than 1 year</td>
<td>15.9</td>
<td>43</td>
</tr>
<tr>
<td>Symons</td>
<td>2007</td>
<td>Prospective multicentre</td>
<td>USA</td>
<td>344</td>
<td>0–25 years 80% more than one year</td>
<td>12</td>
<td>42</td>
</tr>
<tr>
<td>Hayes</td>
<td>2009</td>
<td>Retrospective single centre</td>
<td>USA</td>
<td>75</td>
<td>0–19 years (median 5.8 years)</td>
<td>13</td>
<td>45</td>
</tr>
<tr>
<td>Santiago</td>
<td>2009</td>
<td>Prospective single centre</td>
<td>Spain</td>
<td>174</td>
<td>0–22 years (mean 4.3 years)</td>
<td>14.7</td>
<td>35</td>
</tr>
</tbody>
</table>

*Symons et al ICM 2010*
Objectives

➢ To determine the incidence of severe AKI amongst hospitalized children in Malaysia.
➢ To describe the etiology, patient survival and renal outcome of severe AKI.
➢ To identify potential predictors of death in severe paediatric AKI.