ABSTRACTS

THE 22nd INTERNATIONAL CONFERENCE ON ADVANCES IN CRITICAL CARE NEPHROLOGY

AKI & CRRT 2017

MARCH 7-10, 2017
SAN DIEGO, CALIFORNIA

MANCHESTER GRAND HYATT

Updates in ICU Medicine: Controversies, Challenges and Solutions

Jointly Provided by
UC San Diego
School of Medicine
and
CRRT, INC.

crrtonline.com
ABSTRACT INDEX

EPIDEMIOLOGY AND OUTCOMES FROM AKI

1. Impact of Hospital Volume on Acute Kidney Injury and its Association with Mortality in Severe Sepsis Hospitalizations…………7
   Ankit Sakhuja
2. Impact Of Preoperative Renal Dysfunction On Postoperative Renal Function And Outcomes In Heart Transplant Patients - A Single Center Experience……………………………………………………8
   Saresh Rao K G
3. Our Experience With Continuous Renal Replacement Therapy In Patients On Veno Arterial ECMO……………………………………9
   Suresh Rao K G
4. Epidemiology Of Acute Kidney Injury In Children, a Tertiary Centre Experience ……………………………………………………9
   Werner Keenswijk
5. Acute Kidney Injury in Intensive Care Unit Patients: A Prospective PopulationBased Study in Brazilian Amazon ………………11
   Fernando Melo
   Fernando Melo
7. Delay on Acute Kidney Injury Diagnosis in Critically Ill Patient: A Snapshot on Brazilian Amazon ……………………………12
   Fernando Melo
8. Validation of 4 Prediction Scores For Cardiac Surgery Associated Acute Kidney Injury In Chinese Patients …………………13
   Wenhaa Jiang
9. Epidemiology, Risk factors and Survival of AKI patients treated by CRRT- A Study from Rural Indian Landscape ……………………14
   Krishnaswamy Sampathkumar
10. Obstructive Uropathy as a Cause of Acute Kidney Injury in Patients with Severe Sepsis…………………..………………15
    Ghassan Bandak
11. Dialysis-Requiring Acute Kidney Injury in Patients with Disseminated Candidiasis………………………………………..16
    Mehrshid Resni
12. Early initiation of continuous renal replacement therapy may improve outcome in patients with acute kidney injury ………17
    Young Ki Son
13. Efficacy of various Estimated Creatinine Clearance methods in comparison with measured GFR (Tc99m DTPA clearance) in Indians ………………………………………………………………………………………………18
    Rishi Nigam
14. Clinical Outcomes of Acute Kidney Injury Patients with Prolonged Continuous Renal Replacement Therapy Dependence ………18
    Harin Rhee
15. RENAL REPLACEMENT THERAPY PRACTICES FOR CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY IN CHINA: RESULTS OF A PHYSICIAN SURVEY ……………………………………………………19
    Li Yang
16. The Outcome of Metformin-Associated Lactic Acidosis Accompanied by Acute Kidney Injury ………………………………………21
    Sang Mok Yeo
17. Improvement of Postoperative Cardiac Function of Patients with Preoperative Renal Dysfunction can Reduce the Risk of Postoperative Acute Kidney Injury ……………………………………22
    Yimei Wang
18. Observational Study of CRRT for AKI in Severe Sepsis/Septic Shock Patients - A Single Centre Pilot Study …………………23
    Abdul Ansari
    Yimei Wang
20. The Clinical Outcomes of Colistin induced Acute Kidney Injury………………………………………………………………25
    Sang Mok Yeo
21. The Impact of Fluid Overload on Outcomes in Pediatric Patients treated with Extracorporeal Membrane Oxygenation: Results from a Multi-Centre Retrospective Cohort Study ……………………………………26
    David Selewski
22. Patient Centered Outcomes in Continuous Renal Replacement Therapy: Functional Outcome of ………………………………………27
    Pediatric Continuous Renal Replacement Therapy Survivors
    Mallory Kent
23. The Impact of Disease Severity on Paradoxical Association between Body Mass Index and Mortality in Patients with Acute Kidney Injury Undergoing Continuous Renal Replacement Therapy …………………………28
    Hae-Ryoung Yun
24. Severity, Outcome and Renal Replacement Therapy (RRT) for Acute Kidney Injury (AKI) in a Mixed Pediatric Intensive Care Unit (PICU) - A Retrospective Analysis, 2005 and 2015 ………………………………………………………29
    Sophie Fincher
25. Association between different stages of AKI and risk of long-term mortality ……………………………………………………………30
    Jonah Powell-Tuck
RESEARCH IN AKI

35. The Clinical Significance of Alkaline Phosphatase Activity in Patients with Septic Acute Kidney Injury ………………………………………39
Seung Don Baek
36. Outcomes of recurrent acute kidney injury in tropics ……………………………………………………………………………………40
Anupma Kaul
37. Pro-Enkephalin, Prediction of Renal Dysfunction and Short and Longer Term Prognosis in Acute Heart Failure - a GREAT Network Study ……………………………………………………………………………………41
Leong Ng
Jifu Jin
39. Association Between Renal Recovery after Acute Kidney Injury and Long-Term Mortality after Transcatheter Aortic Valve Replacement …………………………………………………………………………………………43
Wisit Cheungpasitporn
40. Role of Elevated Red Cell Distribution Width On Acute Kidney Injury Patients after Cardiac Surgery …………………………………44
Zhaoqing Zou
41. Blood Urea Nitrogen to serum Creatinine ratio is an accurate predictor of outcome in Diarrhea-associated Hemolytic Uremic Syndrome ………………………………………………………………………………………45
Werner Keenswijk
42. A 2-year old Boy Presenting with Circulatory Failure, a Case Report of Streptococcal Toxic Shock Syndrome ………………………46
Werner Keenswijk
43. Another Atypical Case of Acute Kidney Injury or not? ………………………………………………………………………………………47
Werner Keenswijk
44. An Atypical Case of a 2 year-old boy with Acute Kidney Injury, A Race Against Time …………………………………………………48
Werner Keenswijk
45. Daytime continuous veno-venous hemofiltration as a treatment for tumorlysis syndrome in children …………………………………49
Yamei Wang
46. Tim-3/Gal-9 pathway activation ameliorates renal ischemia reperfusion injury by shifting the balance of activated CD4+ T cell immune response in mice ……………………………………………………………………………………………45
Yamei Wang
47. Autophagy protects against contrast induced tubular epithelial injury ………………………………………………………………………51
Moo Yong Park
48. Plasma Concentration of Pro-enkephalin upon Admission to the Emergency Department Predicts Development of Acute Kidney Injury in Patients with Sepsis ……………………………………………………………………………………………………51
Mari Rosenqvist
49. Long term effects of remote ischemic preconditioning on kidney function in high risk cardiac surgery patients: Follow-up results from the RenalRIP trial …………………………………………………………………………………………………………52
Alexander Zarbock
50. Urinary Exosomal Activating Transcriptional Factor 3 as the Early Diagnostic Biomarker for Sepsis-Induced Acute Kidney Injury …………………………………………………………………………………………………………………………53
Wiwat Chancharoenthana
51. Hyperuricemia increases the risk of acute kidney injury: a systematic review and meta-analysis ……………………………………………………………...54
Xialian Xu
52. A Novel Adsorbent System Rapidly Clears Amlodipine from Human Blood ...............................................................55
   Vincent Capponi
53. A Novel Adsorbent System Rapidly Clears Verapamil from Human Blood ...............................................................55
   Vincent Capponi
54. A Risk Scoring Model To Predict Progression Of Renal Dysfunction In Patients With Chronic Kidney Disease Complicated With Contrast-induced Nephropathy ...............................................................56
   Seonghoon Kim
55. Urinary TIMP-2 and IGFBP7 for the Prediction of Acute Kidney Injury Following Cardiac Surgery ........................57
   yimei wang
   Nigar Sekercioglu
57. Vitamin D and C deficiency is common in critically ill patients with severe acute kidney injury ........................................59
   Danielle Bear
58. Risk Of Mortality And Acute Kidney Injury During Hospitalization After Major Surgery ........................................61
   Shengnan Li
59. Associations Between Fluid Balance and Outcomes in Critically Ill Children: A Systematic Review and Meta-Analysis ........61
   Alobaidi Rashid
60. IGFBP-7/TIMP-2 and pro-enkephalin levels in Acute kidney injury: results from the FROG ICU study .................................63
   Matthieu Legrand
61. High Intensity Intermittent Resistance Training Causes Muscle Damage and Increase of Biomarkers indicative of Acute Kidney Injury in Healthy Individuals ..................................................65
   Tania Spada
62. Effects of Remote Ischemic Preconditioning on the Innate Immune Response in Humans In Vivo ...........................................66
   J. Zwaag
63. The Regulative Roles of TIMP-2 on Cell Cycle in AKI in HK-2 Cells Stimulated by LPS ....................................................67
   Yi-Ming Li
64. Plasma Proenkephalin to Monitor Kidney Function Following Cardiac Surgery .................................................................68
   E. Peters
65. FGF23 levels and patient/renal outcome at 3 months in dialysis dependent AKI ............................................................69
   Krishan Gupta
66. Plasma Proenkephalin to Monitor Kidney Function in Critically Ill Sepsis Patients ............................................................69
   G. Leijte
67. Modulation of IGFBP7 and TIMP2 Expression and Secretion by Clinically Relevant Insults In Vitro .......................................70
   David Emlet
68. Cell-cycle Arrest Biomarkers [TIMP2][IGFBP7] for Risk Stratification of Acute Kidney Injury in Patients with Sepsis ........71
   Marco Fiorentino
69. Unveiling Incidence and Outcomes of Subclinical AKI in the ICU .................................................................................72
   Javier Neyra
70. Serum Bilirubin is Associated with Lower Incidence of Acute kidney Injury;
   A Basic Science Mechanism behind a Clinical Outcome .........................................................................................73
   Arnaldo Lopez-Ruiz
71. Performance of Sequential Biomarkers for Predicting a More Precise AKI Phenotype .....................................................74
   Rajit Basu

RRT TECHNIQUE CHARACTERISTICS

72. CRRT in the United States: A Practice Survey ................................................................................................................75
   Paul McCarthy
73. Extracorporeal Blood Therapies in a Neurointensive Care Unit: A Retrospective Review ....................................................76
   Paul McCarthy
74. Compared of Measured vs Online Urea Kinetics in Patients with Acute Kidney Injury .......................................................77
   Yifei Zhang
75. Does the Site of Calcium Infusion Affects the Mean Circuit Life in Pediatric CRRT? ......................................................78
   Francisco Flores
76. Changing Blood Primed CRRT Circuits Using a Reservoir Bag and a SINGLE Machine ..............................................79
   Daryl Ingram

RRT APPLICATIONS AND TARGETED INTERVENTION

77. Pediatric Acute Renal Replacement Simulation Workshop .........................................................................................80
   Mostafa Elbaba
78. IPE Simulation Enhances the Quality of Care in Neonatal Hyperammonemia .................................................................81
   Mostafa Elbaba
79. Incidence of Complications During Continuous Renal Replacement Therapy ...............................................................82
   Rafae Avila
80. Anticoagulation on Continuous Renal Replacement Therapy in Acute Liver Failure patients ...........................................82
     Vaishali Solao
81. Comparison Of Early Onset Versus Late Onset High Volume CRRT in Acute Kidney Injury (AKI) Patients With Septic Shock .................................................................84
     RANA JIT CHATTERJEE (CHATTOPADHYAY)
82. Renal Replacement Therapy in ECMO, Modalities, Access And Safety Profile: Experience Of An ECMO Centre in a Developing Country ..............................................................................84
     SANDEEP DEWAN
83. Plasma Exchange for Paediatric Non-renal Disease Indications and Outcomes: A Single Centre Experience ......................................................85
     Saravanan Margabandhu
84. Back From The Cold .........................................................................................87
     Azeem Mohammed
85. Use of Continuous Renal Replacement Therapy (CRRT) in Osmotherapy for Cerebral Edema in Acute Liver Failure ...........................87
     EWALOLA IJADUOLA
86. Kinetic Estimated Glomerular Filtration Rate as a Predictor of Successful Continuous Renal Replacement Therapy Weaning ..........................89
     Teruhiko Yoshida
87. Combined Usage of Extracorporeal Membrane Oxygenation And Continuous Renal Replacement Therapy Circuit in a Neonate - First Case Report From India ............................................................89
     Kanav Anand
88. Use Of Continuous Renal Replacement Therapy In Successful Management Of A Neonate With Maple Syrup Urine Disease .................90
     Kanav Anand
89. CRRT : Profile of Practic Patterns from a tertiary care Hospital in South India .........................................................................................91
     SreeBhusan Raju
90. Regional Citrate Anticoagulation for Continuous Renal Replacement Therapy in Severe Burn Injury Patients: Patient and Circuit Outcomes at the Singapore General Hospital ..................................................92
     Riece Koniman
91. Arterial Continuous Renal Replacement Therapy: A complication of the past? ..................................................................................93
     Ruba Sarsour
92. Early Experience with Phoxillum as Post-Replacement Fluid in AKI Patients Treated with Continuous Veno-Venous Hemodiafiltration (CVVHDF) ...........................................................................94
     Ewalola Ijaduola
93. Regional Citrate Anticoagulation CRRT in a Small Child After BiDirectional Cavopulmonary Anastomosis (Glenn operation) ............95
     Dorela Haxhiademi

NEW TECHNOLOGY

94. A Novel Electronic Device for Measuring Urine Flow Rate ..................................................................................96
     Aliza Goldman
95. Experience Of Extracorporeal Therapy-OXIRIS For Sepsis In Indian Tertiary Care Hospital .................................................................98
     SUHAS MONDHE
96. Broad adsorption of sepsis-related pathogen and damage-associated inflammatory mediators from whole blood using porous sorbent beads ......................................................................99
     Maryann Gruda
97. Cytokine Removal in Sepsis: Does Their Levels Co-relate With Outcome ..................................................................................100
     Deepak Govil
98. Cytokine Adsorption In Sepsis: Correct Timing Can Predict The Favourable Outcome .................................................................102
     Deepak Govil
99. Polymyxin B-immobilized Hemoperfusion and Mortality in Critically Ill Patients with Sepsis/Septic Shock: A Systematic Review and Meta-Analysis .........................................................................................103
     Tomoko Fujii
100. Performance Evaluation of the VITROS® NEPHROCHECK® Test* .....................................................................................104
     Godwin Ogbonna
101. Automating Urine Output Measurements To Improve Acute Kidney Injury Diagnosis And Management ...........................................104
     Jay Joshi

RRT RESEARCH

102. The Effect of Blood Transfusion on Continuous Renal Replacement Therapy (CRRT) Circuit Survival and Percent Change in Fluid Overload (PCFO) in Critically Ill Children .........................................................................................106
     Dawn Eding
103. Prediction of Citrate Accumulation from Initial Lactate Concentrations and Lactate Kinetics During Regional Citrate Anticoagulation in CRRT ...........................................................................107
     Torsten Slowinski

continued
104. Incidence of metabolic and electrolyte disturbances caused by decrease of filter clearance during regional citrate anticoagulated continuous veno-venous dialysis (rca-cvvhd) .................................................................107
   Torsten Slowinski

105. The influence of hypophosphatemia on outcomes during continuous renal replacement therapy in critically ill patients with acute kidney injury .................................................................108
   Ho Sik Shin

106. Incidence of Hypocalcemia in Pediatric Patients Receiving Continuous Renal Replacement Therapy and Tandem Therapeutic Plasma Exchange.........................................................................................109
   Tara Haworth

107. First Report from the Multi-Center Adult CRRT Registry (CRRTnet) .................................................................110
   Stuart Goldstein

108. Comparison of the Interleukin-6 Clearance between AN69ST and Polysulfone Membrane Filters .................................................................111
   Mariko Sawada

109. Adequate fluid balance affects outcome of adult patients undergoing extracorporeal membrane oxygenation treatment ....112
   Min-Uk Cha

110. Association of Vascular Access Flow and Volume Status on Fistula Arm by Bio-impedance Analysis in Hemodialysis ....113
    HYUNG JONG KIM

111. Intradialytic Hypotension in Acute Kidney Injury: A Systematic Review ........................................................................113
    Adrianna Douvris

112. Improvement of Respiratory Condition Treated with Polymyxin B-immobilized Fiber Column Direct Hemoperfusion for Acute Respiratory Distress Syndrome Accompanied by Neonatal Meningitis .................................................................114
    Hayashi Masako

    Soo Min Jang

114. Masked hypercalcemia and bone fractures with prolonged continuous renal replacement therapy (CRRT) ......................116
    Peace Imani

115. Influence of Hemodialysis Frequency on Cefepime Probability of Target Attainment in Critically Ill Patients .....................117
    Soo Min Jang

    Marcella Frediani

**NURSING ISSUES**

117. Continuous Renal Replacement Therapy (CRRT) ..................................................................................................119
    Isagani Marquez

118. Improved Assessment of Continuous Renal Replacement Therapy (CRRT) Nursing Competency ..................................................120
    Kathryn Plomaritas
Impact of Hospital Volume on Acute Kidney Injury and its Association with Mortality in Severe Sepsis Hospitalizations

Ankit Sahuja1, Kianoush Kashani1, Robert C Albright1

1 Mayo Clinic, Rochester, MN, USA

INTRODUCTION: Severe sepsis is an important cause of mortality in the hospitals. Acute kidney injury requiring dialysis (AKI-D) is an important complication in severe sepsis with its incidence on the rise. AKI-D is also an important cause of mortality in this population. Hospital volume has been shown to be associated with mortality in severe sepsis; however, it is unclear if it also affects development of AKI-D. As nephrology care and timely availability of dialysis facilities can be dependent on hospital volume, it is also plausible that the effect of hospital volume on mortality is modified by presence of AKI-D. We therefore designed this study to look into the impact of hospital volume on development of AKI-D and to see if AKI-D modifies its effect on mortality.

METHODS: Using data from Nationwide/National Inpatient Sample Database from years 2000-2013 we identified adult patients (≥18 years age) with severe sepsis using ICD-9-CM codes. We then identified patients with AKI-D while excluding patients with end stage renal disease and those with renal transplant. Multivariable regression models were used to assess the impact of annual hospital volume of severe sepsis admissions on AKI-D and mortality. We modeled hospital volume using restricted cubic splines to account for its non-linear relationship with AKI-D and mortality. A priori interaction term between AKI-D and hospital volume was assessed in model for mortality.

RESULTS: There were total 9,420,920 (95% CI 9,140,196-9,701,644) severe sepsis admissions of which 4.5% (424,403) had AKI-D. Patients with AKI-D tended to be <80 years age (84.5% vs 70.5%; p<0.001), males (57.9% vs 50.1%; p<0.001) and blacks (14.8% vs 11.9%; p<0.001). On adjusted analysis hospital volume was associated with odds of developing AKI-D but in a non-linear fashion (Fig 1a). Similarly, hospital volume showed a non-linear association with mortality with differential effect based on presence of AKI-D (interaction p<0.001) (Fig 1 b).

CONCLUSIONS: Annual hospital volume of severe sepsis admissions is associated with both risk of developing AKI-D and mortality though both these relationships are non-linear. Effect of hospital volume on mortality varies in a non-linear fashion based on presence or absence of AKI-D.
Impact Of Preoperative Renal Dysfunction On Postoperative Renal Function And Outcomes In Heart Transplant Patients - A Single Center Experience

Suresh Rao K G\(^1\), Muralikrishna T\(^1\), Ravikumar R\(^1\), Balakrishnan K R\(^1\)

\(^{1}\text{Fortis Malar Hospital}\)

Purpose of study: Preoperative GFR < 35 ml/min is considered as a relative contraindication to heart transplant. However majority of the times renal dysfunction is secondary to heart failure. Once the cardiac function improves post heart transplant, the renal parameters tend to improve. They may develop AKI requiring renal replacement therapy.

Methods used: this is a single centre retrospective analytic study. Relevant data of the heart transplant patients during the period 2012 to 2016 is collected from medical records and analysed. Summary of the results: A total of 114 patients underwent heart transplantation during this period. Preoperative workup includes calculation of creatinine clearance. if the creatinine clearance is < 80 ml/min further renal workup was done. If the renal workup did not showed significant renal disease, then heart transplant alone is considered. All of our patients received induction Immunosuppression therapy with basiliximab and steroids.

Out of the 114 patients, 39 had preoperative creatinine clearance less than 35 ml/min. In the preoperative period 6 had renal shut down that did not improve with all the medical measures and required renal replacement therapy. Post heart transplant 15 patients had renal shut down requiring renal replacement therapy. 3 patients had to receive second dose of basiliximab as calcineurin inhibitors could not be started early postoperative period.

Amongst the 39 patients who had preoperative GFR < 35 ml/min there were 11 deaths. None of the patients, who had preoperative renal shutdown that did not improve with medical measures and were on dialysis, survived. None of those who survived had episodes of renal shut down or worsening of renal function at 1 year follow up.

Conclusion: preoperative GFR of less than 35 need not be considered as a contraindication for heart transplant. Many of these patients will have good outcome if the Immunosuppression therapy is tailored to the clinical situation. Preoperative renal shutdown requiring dialysis is associated with poor post transplant outcomes. Further research is needed in identifying the ideal renal parameter based on which the decision of transplant can be done.
**Our Experience With Continuous Renal Replacement Therapy In Patients On Veno Arterial ECMO**

Suresh Rao K G¹, Ajay Aravind¹, Balakrishnan K R¹

¹Fortis Malar Hospital

Purpose of Study: The observed mortality in heart failure patients waiting for heart transplantation varies from 3 to 11%/1. ECMO is used to resuscitate these patients when there is cardiovascular collapse. Acute renal failure and fluid retention is often seen in these patients. Continuous renal replacement therapy provides an effective way of managing the renal dysfunction. We share our experience with CRRT on ECMO as a bridge to heart transplant.

Methods: 130 heart failure patients were registered for heart transplant between 2010 to 2016 were taken up for the study. 40 patients required ECMO for cardiovascular deterioration. 15 patients required CRRT. 5 patients required both ECMO and CRRT. Fluid retention, metabolic acidosis, hyperkalemia and uremic status were the common indications for CRRT.

Summary of the results: 9 out of 15 heart failure patients who required CRRT had successful heart transplantation. 5 patients had normal renal function post heart transplant. 5 patients on ECMO required CRRT. Renal function was recovered in 2 patients and CRRT was stopped. 3 patients expired on CRRT and ECMO.

Conclusions: ECMO with CRRT presents the high risk group for heart transplant. However CRRT is an effective way of managing the renal dysfunction in this subset of patients.

**Epidemiology Of Acute Kidney Injury In Children, a Tertiary Centre Experience**

Werner Keenswijk¹, Johan Vande Walle¹

¹Ghent University Hospital

Background: To assess the burden of mortality and morbidity of acute kidney injury (AKI) in children we performed an epidemiological study aimed at:
1. Analyzing the incidence, male/female ratio, etiology and age at presentation
2. Assessing outcome of children with AKI measured by mortality, duration of PICU stay and development of Chronic Kidney Disease (CKD)

Methods: Electronic patient files were searched between the 1st of January 2008 and the 1st of January 2015 for patients presenting with or developing AKI at the Ghent University Hospital, a tertiary referral
center in Belgium. Patients between the ages of 1 month and 18 years were included. AKI was classified according to the pediatric Rifle criteria while the cause of AKI was defined as the major underlying disease.

Results: Of the 28295 children admitted to the Ghent University Hospital between 1st January 2008 and 1st January 2015, 167 episodes of AKI were identified, equaling 5.9 cases per 1000 children. Diarrhea-associated Hemolytic uremic syndrome (D+HUS) was the most frequent cause (20.3%) peaking during the summer months, followed by cardiac surgery (13.7%), medication-related nephrotoxicity (13.2%) and acute Glomerulonephritis (12%). The median age of children admitted with AKI was 6.1 years (range 0.1-17) and 50.8% of cases were male. Twenty five (15%) children died while 27 (16%) developed CKD.

Conclusions: D+ HUS was the most common cause of AKI and is associated with significant long term and short term morbidity, posing a significant burden on a patient level but also on the society as a whole. Active surveillance and additional measures to decrease infections with Shiga Toxin producing Enterohemorrhagic E.coli infections are highly recommended.
Acute Kidney Injury in Intensive Care Unit Patients: A Prospective Population Based Study in Brazilian Amazon

FERNANDO F MELO¹, ANA CAROLINE F BEZERRA¹, ETIENNE MACEDO³, RAVINDRA L MEHTA³, EMMANUEL A BURDMANN², DIRCE M ZANETTA²

¹ACRE FEDERAL UNIVERSITY, ²UNIVERSITY OF SAO PAULO, ³UNIVERSITY OF CALIFORNIA - UCSD

Background: The Brazilian Amazon region is a resource constrained, impoverished area with limited health care facilities. The epidemiology of Acute Kidney Injury (AKI) in this region has not been described.

Methods: We performed a prospective study of the risk factors and incidence of AKI in patients admitted to all Intensive Care Units (ICU’s) in Rio Branco (Acre), an Amazon region, from Feb 2014 to Feb 2016. Patients were screened at ICU admission and diagnosed with AKI based on modified KDIGO criteria and their course recorded through hospital discharge. AKI was characterized as community acquired (CAAKI) if AKI developed prior to hospital admission and hospital acquired (HAAKI) if developed during the hospital stay.

Results: Of 1494 patients admitted, 1046 fulfilled selection criteria. A third of the patients developed AKI before ICU admission, only 6% were CAAKI. AKI incidence was 43.8%, with 61.9%, 19.5% and 18.6% Stage 1, 2 and 3 respectively and 5.4% received dialysis. Associated etiological factors for AKI included surgery (30.3%), hemodynamic instability (24%), and respiratory failure (19.2%). Only 1.7% had tropical diseases. Risk factors for AKI included use of nephrotoxic antibiotics (OR 8.6, p<0.001), antiinflammatory drugs (OR 1.7, p=0.002), anemia (OR 3.8, p=0.001) and fluid balance over 1500 ml/24h (OR 1.6, p=0.003). AKI was associated with a higher ICU mortality (AKI 55.9% vs non AKI 13.9%, p<0.001). In a logistic regression model AKI mortality was associated with mechanical ventilation (OR 3.6, p<0.001), use of vasoactive drugs (OR 2.4, p=0.03) shock (OR 2.2, p<0.001), and use of antibiotics (OR 2.5, p<0.001).

Conclusions: AKI is common in ICU patients in the western Brazilian Amazon with few hospitalizations for tropical diseases and similar etiologies, risk factors and outcomes as developed countries; however with higher mortality rates that may represent the economic conditions and poor access to health care.
Epidemiology of Acute Kidney Injury in the Intensive Care Unit: A Systematic Review

FERNANDO F MELO¹, ANA CAROLINE F BEZERRA¹, ETIENNE MACEDO³, RAVINDRA L MEHTA¹, EMMANUEL A BURDMANN², DIRCE M ZANETTA¹

¹ACRE FEDERAL UNIVERSITY, ²UNIVERSITY OF SAO PAULO, ³UNIVERSITY OF CALIFORNIA – UCSD

Background: AKI is commonly encountered in Intensive Care Unit (ICU) patients across the world; however, the epidemiology of Acute Kidney Injury (AKI) in the developed and developing world has not been systematically examined.

Methods: We conducted a systematic review of published studies (2005–2015) identified in PUBMED, CENTRAL, LILACS, and IBECs databases using the search terms “acute kidney injury” and “intensive care unit”. We examined the differences in AKI incidence, severity (based on KDIGO criteria) and associated mortality and describe geographic variations based on the gross national income.

Results: We identified 94 studies: 60 from developed countries and 34 from developing countries. Of these, 75.5% used KDIGO equivalent criteria; however, we found 10 different definitions for oliguria and 19 different definitions for baseline creatinine. The frequency of AKI was higher in studies using KDIGO equivalent criteria (34.3% vs 24.3%), with lower mortality rates (median 29% vs median 42.5%). There were no differences in incidence of AKI between developed and developing countries. However, the need for RRT, ICU length of stay and mortality rates were higher in developing countries.

Conclusions: Despite the attempt to standardize the criteria for defining AKI, there is still no uniformity in the settings for “baseline creatinine” or “oliguria”. Differences in ICU length of stay, need for RRT and mortality rates may reflect differences in the entry criteria and the social conditions, access to health care and hospital infrastructure.

Delay on Acute Kidney Injury Diagnosis in Critically Ill Patient: A Snapshot on Brazilian Amazon

FERNANDO F MELO¹, ANA CAROLINE F BEZERRA¹, ETIENNE MACEDO³, RAVINDRA MEHTA³, EMMANUEL BURDMANN², DIRCE M ZANETTA²

¹ACRE FEDERAL UNIVERSITY, ²UNIVERSITY OF SAO PAULO, ³UNIVERSITY OF CALIFORNIA - UCSD

Background: There are deficiencies in the recognition and management of patients who developed Acute Kidney Injury (AKI) in Intensive Care Unit (ICU) that can result delay in treatment and inappropriate referral to nephrologist, leading to worse outcomes as need for dialysis, recovery and mortality rates.

Methods: We performed a prospective study of AKI incidence in patients admitted to all ICU’s in Rio Branco, state capital of Acre, from Feb 2014 to Feb 2016. We used medical records to compare the
Results: We studied 1046 patients. Among 43.8% of patients who developed AKI in ICU, there were agreement of the diagnosis day in only 14.5%, in 65% the clinician did not make the diagnosis and in 8.2% it was delayed. Thirty seven percent of the delayed diagnosis patients presented AKI grade III. Dialysis was offered to only 0.3% of nondiagnosed patients in contrast with 31.3% in those who had timely diagnosis (p <0.001). The APACHE II score was lower in those nondiagnosed compared with those who had timely diagnosis (17.5 vs. 27, p <0.001). ICU and hospital stay were higher when diagnosis was delayed compared with timely diagnosis patients (10 vs. 8, p <0.001 and 21 vs 16, p <0.001, respectively). Mortality was also higher in those nondiagnosed and delayed diagnosed patients, compared with those who had timely diagnosis (61.8% vs 68.3% vs 40%, p <0.001).

Conclusions: In the vast majority of our patients, the clinic diagnosis of AKI was not done or occurred later. This fact may have contributed to delay on completion of dialysis, increased length of ICU and hospital stay and higher mortality rates. It is necessary to increase awareness of AKI in ICU and disseminate knowledge.
patients, according to KDIGO AKI definition, none of the 4 models above is good at predicting CSA-AKI or RRT-AKI.

9

Epidemiology, Risk factors and Survival of AKI patients treated by CRRT- A Study from Rural Indian Landscape.

Krishnaswamy Sampathkumar¹, Rajiv Andrew¹, Ratchagan Saravanan¹, Shakthi Kumar¹, Adithya Nayak¹, Sivaraj Anandan ¹

¹Meenakshi Mission Hospital

AIM OF THE STUDY - AKI encountered in ICU is commonly accompanied by shock which precludes the use of Intermittent Hemodialysis. But less than 10% of ICUs in India provide CRRT services. This retrospective cohort study of patients treated with CRRT for AKI was undertaken in our renal centre catering to rural population of South India.

Methods- Consecutive patients who were treated with CRRT during the period formed the Study Group. The mode of CRRT was uniformly CVVHDF [Prismaflex - Baxter]. Replacement was prefiltre. APACHE II score was calculated at the start of CRRT initiation. Survivors and Non survivors were compared using various clinical and biochemical risk factors. Student's t-test for quantitative variables and Chi-square (χ²) test for qualitative variables were used for comparison. p<0.05 was significant. Period of Study- June 2015 to October 2016. Primary Outcome was In hospital survival.
Results-There were 127 patients who developed AKI requiring CRRT out of the total admission of 1544 in ICU during the period [8.2 %]. 12 [9%] of these patients could not afford CRRT. The rest of 115 patients were treated with CRRT and formed the study group. Mean age was 50 +/− 8 years. 66% were males. Community acquired AKI [89%] was more common than hospital acquired AKI [11%]. Medical [63%] etiology was more common than Surgical [28%] and Obstetric [7.8%] Medical causes included Septic shock [58%], cardiogenic shock [20%], Hepatorenal syndrome [9.5%] and Pancreatitis [7.8%]. Emphysematous Pyelonephritis [8], scrub typhus [2], and Dengue shock syndrome [2] were encountered. Vascular access was mostly via Femoral vein [94%]. CVVHDF was heparin free in 53% of sessions. 78% required ventilatory support. The Primary Outcome of in hospital survival was 42%. It was predicted by higher Mean BP [72 mm Hg vs 62 mm Hg (p <0.01)], Lower APACHEII score [24 vs 29 (p = <0.001)], higher S.Bicarbonate [20 vs 17 mEq/L (p = < 0.11)] and higher serum albumin [3 versus 2.3 G/d L (p =0.006)] and less ionotropic support. Diabetic status, S.Creatinine, ventilator requirement and Effluent volume had no influence.

Conclusion- The etiological factors of AKI treated with CRRT has different profile from those encountered in developed countries in the rural landscape of India. Survival was predicted by higher mean Blood Pressure with lower APACHE II score. Higher cost of the CRRT is a significant barrier to its widespread utilisation.

Obstructive Uropathy as a Cause of Acute Kidney Injury in Patients with Severe Sepsis

Ghassan Bandak1, Ankit Sakhuja1, Mahrukh Rizvi1, Kianoush Kashani1

1Mayo Clinic

INTRODUCTION: Acute kidney injury (AKI) is an important complication of severe sepsis and the incidence of AKI requiring dialysis (AKI-D) is on the rise. Though renal imaging is often performed as a part of AKI workup, its utility is unclear especially as the majority of AKI in severe sepsis is attributed to acute tubular necrosis. We designed this study to study the utilization of renal imaging and proportion of obstructive uropathy among the patients with severe sepsis who develop AKI-D.

METHODS: Using data from Nationwide/National Inpatient Sample database from years 2000-2013 we identified adult patients (aged ≥20 years) with severe sepsis using ICD-9-CM codes. Those with kidney transplant or with end-stage kidney disease were excluded. We then identified those who developed AKI-D during the same admission using ICD-9-CM codes. The use of renal ultrasound and CT was identified using ICD-9-CM procedure codes. We performed a linear regression to assess trends of utilization of renal ultrasound imaging over the study period. Due to the low incidence of obstructive uropathy, we have combined years as shown in Figure 1 for reporting trends over time.

RESULTS: Of 9,389,639 (95% CI: 9,110,088-9,669,191) admissions with severe sepsis, AKI-D was identified in 423,212 (4.5%) of admissions. Those with AKI-D were younger (84.5% were <80 years old vs. 70.4%; p<0.001), males (57.9% vs. 50.1%; p<0.001) and blacks (14.8% vs. 11.9%; p<0.001). Overall, renal imaging was used in 1.6% of patients with AKI-D. Of the patients who underwent renal imaging, 6.3% had evidence of obstructive uropathy. The trend has been decreasing (p=0.008). However, the proportion of patients with obstructive uropathy among those imaged has increased though the trend did not achieve statistical significance (n=0.06) – Fig 1.
CONCLUSIONS: Obstructive uropathy appears to be an uncommon cause of AKI-D among patients with severe sepsis. Though the utilization of renal imaging is on the decline, the yield of renal imaging has increased over the years.

Dialysis-Requiring Acute Kidney Injury in Patients with Disseminated Candidiasis

Mahrukh S Rizvi¹, Ankit Sakhuja¹, Ghassan Bandak¹, Kianoush Kashani¹

¹Mayo Clinic

INTRODUCTION: Severe sepsis is a significant cause of morbidity & mortality and acute kidney injury (AKI) is an important complication in patients with severe sepsis. Patients with severe sepsis who have disseminated candidiasis are prone to worse outcomes; however, the literature on dialysis-requiring acute kidney injury (AKI-D) in this population is sparse. We designed this study to understand the epidemiology and outcomes of AKI-D in septic patients with disseminated candidiasis.

METHODS: Using data from National/Nationwide Inpatient Sample database from 2000-2013, we identified patients >20 years of age with severe sepsis using ICD-9-CM codes. Those with kidney transplant or with end-stage kidney disease were excluded. We then used ICD-9-CM codes to identify those with disseminated candidiasis and AKI-D. We studied the proportion of patients with and without disseminated candidiasis who develop AKI-D. We also assessed if disseminated candidiasis is an independent risk factor for the development of AKI-D using a multivariable regression model adjusting for patient characteristics, hospital characteristics, individual acute organ dysfunctions, need for mechanical ventilation, and primary payer.
RESULTS: Of total 9,389,639 (95% CI: 9,110,088-9,669,191) admissions with severe sepsis, 1% (102,525) had disseminated candidiasis. Those with disseminated candidiasis were younger (48.7% vs. 37.5% were <65 years old; p<0.001) and blacks (14.5% vs. 12.0%; p<0.001). Mortality was higher in patients with disseminated candidiasis (30.2% vs. 25.8%; p<0.001). 9.7% of patients with disseminated candidiasis developed AKI-D in comparison to 4.4% of those with an alternative cause of severe sepsis (p<0.001). In an adjusted model, disseminated candidiasis was an independent risk factor for AKI-D with an odds ratio of 1.63 (95% CI: 1.55-1.73).

CONCLUSIONS: Disseminated candidiasis is associated with increased risk of mortality and is an independent risk factor for development of AKI-D in patients with severe sepsis. Further studies are needed to explore this relationship.

12

Early initiation of continuous renal replacement therapy may improve outcome in patients with acute kidney injury

Young Ki Son

Dong-A University, Busan, South Korea

Background
Renal replacement therapy improved considerable outcome in the treatment of acute kidney injury, the optimal timing of initiation of CRRT in critically ill patients with AKI is still controversy. However, early initiation may improve benefits in controlling volume, toxin, acid-base balance, and other complication. In this study, we tried to determine whether the early initiation may reduce mortality in AKI patients.

Methods
We retrospective reviews the medical records of all ICU patients who received CRRT at Dong-A University hospital from March 2014 to September 2016. At the starting time, patients were classified into two group by RIFLE classification:
Group 1 (early initiation); risk, injury by RIFLE classification
Group 2 (delayed initiation); failure by RIFLE classification

Results
The total number of patients who required CRRT in ICU was 145. The average age of the 145 patients was 59.0 ± 18.2 years and 95 patients were male. The treatment duration was 78 ± 38.2 hours. Early initiation group (n=78) and delayed group (n=67) completed follow-up at 90 days. Early initiation of RRT significantly reduced 90-day mortality (28 of 77 patients [36.3%]) compared with delayed initiation of RRT (43 of 67 patients [64.1%]; hazard ratio [HR], 0.48 [95%CI, 0.35 to 0.87]; difference, −14.4% [95%CI, −28.1% to −2.6%]; P = .03). Duration of RRT and length of hospital stay were significantly shorter in the early group than in the delayed group (RRT: 7.4 days in the early group vs 19.3 days in the delayed group (P = .03).

Conclusions
Early initiation of CRRT may be improve outcome in patients with acute kidney injury.
Efficacy of various Estimated Creatinine Clearance methods in comparison with measured GFR (Tc99m DTPA clearance) in Indians

Rishi K Nigam¹, Mukul Mathur²

¹Rajiv Gandhi College, Barkatullah University, Bhopal, India, ²Jawaharlal Nehru Cancer Hospital & Research Center, Bhopal

Background: The aim of this study was to compare measured glomerular filtration rate (GFR) with estimates of GFR derived from various estimated creatinine clearance methods of Jelliffe, Cockcroft and Gault, and 4MDRD equations in Indian population.

Methods: We enrolled 80 patients in the study. GFR was determined by technetium-99m diethyl triamine penta-acetic acid (Tc99mDTPA) clearance. Height, body weight and serum creatinine were measured, and GFR and creatinine clearance (CrCl) estimates calculated by various equations. Spearman's correlation was used to assess relationships between measured GFR (Tc99mDTPA clearance) and estimated clearances using the three formulae. Difference between the measured GFR and estimated clearances compared with measured GFR were examined to determine whether prediction error was independent from measurement magnitude. Analyses of differences were used to determine bias and precision. Bias was assessed by mean percentage error (MPE), calculated as the percentage difference between the estimated clearances for each formula and measured GFR. A positive bias indicates overestimation of GFR, and a negative bias indicates underestimation. Relationships were also assessed by gender and varying levels of renal function: GFR <60 ml/ min, and GFR >60 ml/ min.

Results: The mean measured GFR was 77.2 ml/ min (range 17 to 152 ml/ min). The mean bias (mean percentage error) was -4.9, -10.3 and -1.57% respectively for the, Jelliffe, Cockcroft and Gault, and 4MDRD formulas, respectively. The 4 MDRD formula overestimates the GFR in patients having GFR less than 60ml/ min, whereas it underestimates for GFR more than 60ml/ min.

Conclusions: 4 MDRD equation seems to be most efficient in estimating GFR in Indian population.

Clinical Outcomes of Acute Kidney Injury Patients with Prolonged Continuous Renal Replacement Therapy Dependence

Harin Rhee¹, Geum-Suk Jang¹, In- Seong Park², Il- Young Kim², Sang-Heon Song¹, Eun-Young Seong¹, Dong-Won Lee², Soo-Bong Lee², Ihm-Soo Kwak¹

¹Pusan National University Hospital, ²Yangsan-Busan National University Hospital

Introduction
Continuous renal replacement therapy (CRRT) is useful for hemodynamically unstable patients needed renal replacement therapy. Usually, CRRT can be terminated or changed to intermittent hemodialysis in 10 days when patient's renal function is recovered or patients become hemodynamically stable. However, there are some cases that needed prolonged CRRT treatment. This study aims to describe clinical features and outcomes of acute kidney injury (AKI) patients with CRRT dependence for more
than 14 days.

Methods
This is a single center, retrospective study of AKI patients who underwent CRRT for more than 14 days from January 2013 to December 2015. Baseline patient characteristics and the causes of CRRT initiation were checked by medical chart review. The 30-days, 90-days and 180-days of patient survival were verified by individual phone call.

Results
A total of 7.4(64/863) % of patients underwent CRRT for more than 14 days because of the not recovery from the unstable hemodynamic conditions. 53.1% of the patients were male, and there mean ages were 63.84±12.56 years old. The most common cause of CRRT initiation was septic AKI (56.9%) and the second most common cause was acute pulmonary edema (25.1%). 56.9% of the patients had hypertension, 16.7% of the patients had congestive heart failure and 9.7% of the patients had chronic kidney disease. Their mean SOFA score and APACHEII score was 11.15±3.14 and 24.69±6.07, respectively. After mean duration of 20.47±9.93 days of CRRT, 45.9% of the patients were dead. Among the survived 54.1% of the patients, 32.8% of the patients switched to intermittent hemodialysis and the 21.3% of the patients could wean the CRRT. A total of 6.4% of the patients progressed to the end stage renal disease needed maintenance dialysis at the time of discharge. In the dialysis non-dependent survivors, the mean eGFR at the time of discharge was 65.08±73.91 mg/dL. The 30-days, 90-days and 180-days of patients survival was 23.8%, 22.2% and 19.0%.

Conclusion
Even though long term patient survival rate is very low, there were patients who survived from long duration of CRRT with relatively fair renal function. Thus, CRRT should not be abandoned in the case of prolonged CRRT requirement.

15

RENEAL REPLACEMENT THERAPY PRACTICES FOR CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY IN CHINA: RESULTS OF A PHYSICIAN SURVEY

Li Yang1, William, R Clark2, Xiaohong Ding3, Haibo Qiu4, Zhaohui Ni5, Ping Chang6, Ping Fu7, Jiarui Xu3, Minmin Wang1, Claudio Ronco8

1 Baxter Healthcare, Shanghai, China, 2School of Biomedical Engineering, Purdue University, West Lafayette (IN), USA, 3Department of Nephrology, Zhongshan Hospital, Fudan University, 4Department of Critical Care Medicine, Nanjing Zhongda Hospital, Southeast University, Nanjing, China, 5Department of Nephrology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, 6Department of ICU, Zhujiang Hospital, Southern Medical University, Guangzhou, China, 7Division of Nephrology, West China Hospital of Sichuan University, Chengdu, China, 8International Renal Research Institute of Vicenza (IRRIV), San Bortolo Hospital, Vicenza, Italy

Objectives: To characterize contemporary dialytic management of AKI patients in China, especially with respect to the utilization of CRRT.

Method: The online survey queried both nephrologists and critical care physicians across a wide spectrum of hospitals about factors influencing initial RRT modality selection. For patients initially treated with CRRT, data related to indication, timing of treatment initiation, dose, anticoagulation technique, and duration of therapy were also collected.
Results: 200 volunteers (100 nephrologists and 100 intensivists) were included in the analysis (Table 1). Among AKI patients considered RRT candidates, the survey indicated 15.1% (95% CI, 12.3%-17.9%) did not actually receive dialysis at Chinese hospitals. For all patients who received RRT, 63.9% (95% CI, 56.4%-71.3%) were treated initially with CRRT and 24.8% (95% CI, 19.2%-30.3%) with IHD (P<0.001). An overwhelming majority of intensive care patients were treated initially with CRRT (86.6%; 95% CI, 79.8-93.4%) while it was the initial modality in only 44.6% (95% CI, 33.5-55.7%) of patients treated in a nephrology department (P<0.001) (Figure 2). Overall CVVH was the most commonly prescribed modality (42%), followed by CVVHDF (35%) and CVVHD (23%). Anticoagulation for CRRT with either unfractionated heparin or low-molecular weight heparin was reported as being prescribed in two-thirds of patients. Approximately 70% of respondents overall reported prescribing a CRRT dose in the range of 20-30 mL/kg/hr. The most common average prescribed time (50% of respondents) fell in the 10-20 hr range, with only 18% in the 20-24 hr range. Moreover, 32% of respondents reported an average prescribed value of less than 10 hrs per day. And this practice pattern was much more common in nephrology programs (48%) versus intensive care unit programs (16%) (P<0.001) (Figure 4). Timing of RRT initiation was the most important factor felt to influence both survival and renal recovery, being listed by 80% of participants in each case (Figure 3).

Conclusion: CRRT was the first-choice modality used to treat AKI in China and CVVH was the most common CRRT technique used. Our analysis demonstrates both similarities and differences between RRT practices for AKI in China and those in the developed world. While some of these differences are driven by non-medical factors, future studies should explore these issues further to harmonize RRT practices in China with those in the rest of the world.

<table>
<thead>
<tr>
<th></th>
<th>Tier 1</th>
<th>Tier 2</th>
<th>Tier 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34%</td>
<td>34%</td>
<td>33%</td>
</tr>
<tr>
<td>Hospital Class</td>
<td>Class 3</td>
<td>Class 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>70%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Department</td>
<td>ICU</td>
<td>Nephrology</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Job title</td>
<td>Vice/Chief</td>
<td>Attending</td>
<td>Resident</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>50%</td>
<td>20%</td>
</tr>
<tr>
<td>CRRT experience</td>
<td>&lt;1 year</td>
<td>1-3 years</td>
<td>&gt;3 years</td>
</tr>
<tr>
<td>ICU</td>
<td>13%</td>
<td>19%</td>
<td>68%</td>
</tr>
<tr>
<td>Nephrology</td>
<td>9%</td>
<td>30%</td>
<td>61%</td>
</tr>
<tr>
<td>Class 3</td>
<td>9%</td>
<td>24%</td>
<td>67%</td>
</tr>
<tr>
<td>Class 2</td>
<td>15%</td>
<td>27%</td>
<td>58%</td>
</tr>
<tr>
<td>Vice/Chief</td>
<td>2%</td>
<td>10%</td>
<td>88%</td>
</tr>
<tr>
<td>Attending</td>
<td>13%</td>
<td>21%</td>
<td>66%</td>
</tr>
<tr>
<td>Resident</td>
<td>21%</td>
<td>56%</td>
<td>23%</td>
</tr>
</tbody>
</table>
The Outcome of Metformin-Associated Lactic Acidosis Accompanied by Acute Kidney Injury

Sang Mok Yeo\(^1\), Woo Yeong Park\(^1\), Yaerim Kim\(^1\), Seong Sik Kang\(^1\), Kyubok Jin\(^1\), Sung Bae Park\(^1\), Seungyeup Han\(^1\)

\(^1\)Department of internal medicine, Keimyung University School of Medicine

Background: Metformin has become the treatment of choice for diabetic patients. However, metformin can cause to a fatal metabolic acidosis, called metformin-associated lactic acidosis (MALA). The purpose of our study is to investigate the outbreak of MALA and the outcome of cases treated by renal replacement therapy.

Methods: We retrospectively analyzed 12 patients who admitted to the intensive care unit (ICU) with severe lactic acidosis and acute kidney injury between 2006 and 2016. We defined acute kidney injury (AKI) by KDIGO guidelines. Among the 12 patients, 2 patients were excluded because they were ESRD patients undergoing dialysis.
Results: The median age at diagnosis with MALA was 74 (interquartile range [IQR] 64, 78) years. The mean length of hospital stay was 12 (IQR 7, 15) days and the mean duration of ICU was 5.0 (IQR 1.5, 6.8) days. Severity score by Acute Physiology and Chronic Health Evaluation II (APACHE II) was 29 (IQR 22, 34). The mean pH and concentration of lactate at admission were 6.99 ± 0.21 and 15.2 ± 6.7 mmol/L. The mean serum creatinine level was 7.5 ± 4.7 mg/dL and the median initial urine volume and 24 hour urine volume were 16.5 (range 0, 43.8) mL/h and 145 (range 22.5, 776.3) mL. The causes of AKI were dehydration (58.3%) and infection (41.7%). The mean maintenance dose of metformin was 1445 ± 1018 mg and each patient was taken according to the estimated glomerular filtration rate. Eleven patients were treated for continuous renal replacement therapy (CRRT). Lactic acidosis was corrected after CRRT for a short period of an average of 1.7 days. Two patients died from sudden cardiac arrest during treatment.

Conclusion: MALA is a rare, but life-threatening condition. In order to prevent this complication, we should pay attention to the appropriate dose of metformin according to glomerular filtration rate and the risk factors of AKI. Immediate CRRT treatment should be applied when MALA occurs.

Improvement of Postoperative Cardiac Function of Patients with Preoperative Renal Dysfunction can Reduce the Risk of Postoperative Acute Kidney Injury

Yimei Wang¹, Bo Shen¹, Jiarui Xu¹, Wuhua Jiang¹, Jiawei Yu¹, Wenlv lv¹, Jianzhou Zou¹, Chunsheng Wang², Xiaojian Ding¹, Jie Teng¹

¹Department of Nephrology, Zhongshan Hospital, Shanghai, China, ²Department of Cardiovascular Surgery, Zhongshan Hospital.

Objective: To evaluate the impact of improvement of cardiac function after cardiac surgery on the renal outcome in patients with preoperative renal dysfunction (RD).

Method: Data from patients underwent cardiac surgery from April 2011 to Feb 2015 were collected. RD was defined as preoperative SCr>1.2 (female)/1.5(male) mg/dL. Reversible renal dysfunction (RRD) was defined when patients with preoperative RD but not met the CKD diagnosis. Cardiac function improve (CFI) group = ΔEF>0%, Cardiac function not improve (CFNI) group = ΔEF≤0%. ΔEF = postoperative LVEF - preoperative LVEF.

Results: Of 8661 patients, there were 7903(91.2%) cases in preoperative normal renal function (Normal) group and 758(8.8%) in RD group. RD group was further divided into RRD group (n=622, 82%) and CKD group (n=136, 18%). The AKI incidence in RRD group was significantly lower than in CKD group (39.5% vs 61.8%, P<0.01). The AKI incidence in RRD and CKD group were both significantly higher than in Normal group (39.5% vs. 30%, P=0.002; 61.8% vs. 30%, P<0.01). Sub-group analysis showed that there was no statistical significance of AKI incidence between Normal group and RRD+CFI group (30.0% vs. 30.9%, P=0.729), but much higher in other sub-groups. Of the 758 preoperative RD patients, there were 431(57%) in CFI group and 327(43%) in CFNI group. The AKI incidence in CFI group was significantly lower than in CFNI group(32.2% vs 58.4%, P<0.01). Multivariate logistic regression analysis showed that RRD and CKD were all independent risk factors for postoperative AKI, and sub-group analysis showed that only RRD+CFI did not add the risk of AKI. The independent risk factors of postoperative AKI in RD patients included age, male, RRD+CFNI,
CKD+CFNI, aorta surgery, CPB time, intraoperative hypotension, while improved cardiac function can reduce the risk.

Conclusion: Preoperative RD was always the independent risk factor of postoperative AKI in patients undergo cardiac surgery, no matter CKD or RRD. Improved postoperative cardiac function can significantly reduce the risk of AKI. Most RD patients were RRD, and cardiac function of most RD patients can be improved after surgery. RRD+CFI did not add the risk of postoperative AKI which may be useful to broaden the indication of surgery.

---

**Observational Study of CRRT for AKI in Severe Sepsis/Septic Shock Patients – A Single Centre Pilot Study**

Abdul S Ansari¹, Rajiv J Shah¹

¹Nanavati hospital

Aims & Objectives: To study the effects of CRRT (Continuos Renal Replacement Therapy) on hemodynamic parameters, on markers of inflammation and to determine survival at 28 days

Methodology: 22 patients with severe sepsis/septic shock (sepsis definition 2012) were started on CRRT for AKI (Acute Kidney Injury) (KDIGO criteria). Patient’s biochemical parameters and APACHE II score were noted before initiating CRRT and were serially followed up. Daily assessment of need of CRRT was done in all patients. CRRT was terminated once the indication seized. If there was any intervention, filter clotted, CRRT was restarted immediately.

Summary of the results: Out of 22 patients of severe sepsis/septic shock with AKI initiated on CRRT, 11 survived (50% survival). Although mean lactate level of survivors was higher on day 0 than non survivors (61.7 versus 47.96 mg/dl), but they had a steady decline in their lactate levels over the next 4 days of therapy. Delta lactate between day 1 and day 2 of survivors was +9.55 v/s -12.4 of non survivors. In survivors lactate clearance of 15.47% in 24 hrs and 40.34% in 48 hrs. Lactate rise of 25.85% and 46.14% at 24 and 48 hours respectively was seen in non survivors.

Mean APACHE II score of both the groups was significantly different (29 vs 34 in survivors and non survivors respectively. This shows the overall sickness severity of the patient population. At baseline both the groups had non-significant difference in bicarbonate levels and arterial pH. A steady rise in bicarbonate was highly suggestive of survivors and improvement in pH with complete compensation on day3 was a characteristic finding in all survivors.

Although starting CRP (C reactive protein) of non survivors was significantly higher than survivors, a steady decline in CRP after day 2 differentiated amongst survivors and non survivors. Gradual reduction in vasopressor requirement by day 3 was another consistent finding in all survivors.

Conclusion: Severe sepsis/septic shock is often complicated by AKI resulting in severe acidosis and worsening hemodynamics. This combination has a fatal outcome if not treated in time. Our study patients had 50% survival rate on CRRT -an improving lactate, bicarbonate, pH, CRP and reduced vasopressor need all suggest reduced mortality.
Impact of Preoperative Hidden Renal Dysfunction on Postoperative Acute Kidney Injury and Long-term Outcome after Cardiac Surgery

Yimei Wang¹, Bo Shen¹, Jiarui Xu¹, Wuhua Jiang¹, Jiawei Yu¹, Wenlv Lv¹, Jianzhou Zou¹, Chunsheng Wang², Xiaqiang Ding¹, Jie Teng¹

¹Department of Nephrology, Zhongshan Hospital, Shanghai, China, ²Department of Cardiovascular Surgery, Zhongshan Hospital, Shanghai, China

Objective: Studies have confirmed that preoperative renal dysfunction was the high risk factor for acute kidney injury (AKI) and long-term outcome. But the risk of patients with hidden renal dysfunction is not clear.

Methods: Patients underwent cardiac surgery and without preoperative renal dysfunction (SCr ≤ 106µmol/L & eGFR ≥ 60ml/min/1.73m2) from 2012.4 to 2012.12 were enrolled. Normal renal function (Normal group)= eGFR ≥ 90ml/min/1.73m2. Hidden renal dysfunction (Hidden dysfunction group)= 60 ≤ eGFR < 90ml/min/1.73 m2 . Hidden group was further divided into 2 sub-groups: Mild (75 ≤ GFR < 90ml/min/1.73 m2) and Moderate hidden dysfunction (60 ≤ GFR < 75ml/min/1.73 m2) group. The main endpoints were postoperative AKI (KDIGO 2012) and long term mortality and progressive CKD (GFR ≤ 30ml/min per 1.73 m2 or ESRD) in a follow up of 2 years.

Results: There were 1632 (93.6%) patients without renal dysfunction among the total of 1744 patients underwent cardiac surgery. There were 59.1% (n=965) in Normal group and 40.9% (n=667) in Hidden dysfunction group. The total AKI incidence was 35.4% (n=578) and was much higher in Hidden dysfunction group than in Normal group (39.3% vs. 32.7%, P<0.01). In the Hidden dysfunction group, there were 62.5% (n=417) in Mild group and 37.5% (n=250) in Moderate hidden dysfunction group. AKI incidence was much higher in Moderate group than in Mild hidden dysfunction group (35.5% vs. 45.6%, P=0.01), but there was no statistical significance of AKI incidence between Mild hidden dysfunction group and Normal group (32.7% vs. 35.5%, P=0.321). After 2 year period followed up, the accumulated survival rates in Hidden dysfunction group was much lower than in Normal group (86.8% vs. 93.3%, P<0.01), the incidence of progressive CKD were much in Hidden dysfunction group was much higher than in Normal group (6.0% vs. 2.4%, P<0.01). Cox proportional hazards regression model showed that age, diabetes, moderate hidden dysfunction (60≤GFR<75 ml/min/1.73m2), cardiopulmonary bypass time, length of ICU stay were the independent risk factors for progressive CKD.

Conclusion: Preoperative hidden renal dysfunction was common in patients undercardiac surgery, with a high prevalence of 40.9%. The AKI incidence of these patients was much higher and 2 year outcome was much worse than patients with normal renal function. Moderate hidden dysfunction (60≤GFR<75 ml/min/1.73m2) was the independent risk factor for long-term progressive CKD after adjusted for other risk factors.
The Clinical Outcomes of Colistin induced Acute Kidney Injury

Sang Mok Yeo¹, Woo Yeong Park¹, Yaerim Kim¹, Seong Sik Kang¹, Kyubok Jin¹, Sung Bae Park¹, Seungyeup Han¹

¹Department of Internal Medicine, Keimyung University School of Medicine

Background: Colistin has become a major antibiotic against multidrug-resistant bacteria such as Acinetobacter baumannii and Pseudomonas aeruginosa. However, use of colistin can cause acute kidney injury (AKI). The purpose of our study is to investigate the risk factors and clinical outcomes of patients had AKI after colistin treatment.

Methods: We retrospectively analyzed patients who admitted to our hospital and use of colistin during admission from Jan. 2014 to Dec. 2015. We compared clinical findings between AKI group and non-AKI group matched age, baseline eGFR and diabetes mellitus as comorbidity.

Results: The mean age at admission was 68 ± 13 years. The median length of hospital stay was 41 (interquartile range [IQR] 24, 72) days and the median duration of ICU was 9 (IQR 0, 32) days. AKI was occurred in 26 (61.9%) patients and 12 (28.6%) patients died. Acute Physiology and Chronic Health Evaluation II score was 22.2 ± 6.3. The mean daily dose of colistin and cumulative dose during hospitalization were 279 ± 87 and 2,707 ± 1,784 mg, respectively. Most common cause of using colistin was pneumonia (57.1%) and main microorganism was Acinetobacter baumannii (81.0%). Duration of ICU and total hospital stay was longer in AKI group than non-AKI group. The cumulative dose of colistin was higher in AKI group than non-AKI group.

Conclusion: Nephrotoxicity is a critical adverse event of colistin. AKI is occurred more frequently when cumulative dose of colistin is higher. AKI is extending hospitalization period. In order to prevent this complication, we should pay attention to the appropriate dose of colistin according to GFR and the risk factors of AKI.
The Impact of Fluid Overload on Outcomes in Pediatric Patients treated with Extracorporeal Membrane Oxygenation: Results from a Multi-Centre Retrospective Cohort Study

David T Selewski¹, David J Askenazi², Brian C Bridges³, David S Cooper⁴, Geoffrey M Fleming³, Matthew L Paden⁵, Mark Verway⁶, Rashmi Sahay⁷, Eileen King⁷, Michael Zappitelli⁶

¹Department of Pediatrics & Communicable Diseases, University of Michigan Medical School, Ann Arbor, Michigan USA, ²Department of Pediatrics, University of Alabama Birmingham, Birmingham, Alabama USA, ³Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee USA, ⁴Department of Pediatrics, The Heart Institute, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio USA, ⁵Department of Pediatrics, Emory University, Atlanta, Georgia USA, ⁶Department of Pediatrics, McGill University Health Centre, Montreal, Canada, ⁷Division of Biostatistics and Epidemiology, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio USA

Objective: Extracorporeal membrane oxygenation (ECMO) is a life-saving therapy for children with severe cardiac and/or respiratory failure. ECMO patients are at increased risk of acute kidney injury (AKI), fluid overload (FO) and often receive renal support therapy. We aim to evaluate the incidence and impact of FO at ECMO initiation, and peak FO during ECMO on ECMO duration, survival to ECMO decannulation and hospital discharge.

Design/ methods: Retrospective cohort study performed in six tertiary children’s hospital intensive care units of patients < 18 years of age treated with ECMO for ≥ 24 hours from January 1, 2007 to December 31, 2011. FO was calculated at the initiation of ECMO and during ECMO by cumulative ins/outs.

Results: 756 patients were included in the study. Survival to ECMO decannulation was 74.9% (n=566) and survival to hospital discharge was 57.7% (n=436). Median FO at ECMO initiation was 8.8% (IQR 0.3, 19.2) and it differed between hospital survivors and non-survival, though not between ECMO survivors and non-survivors. Median peak FO on ECMO was 30.9% (IQR 15.4, 54.8); lower in patients who survived ECMO (27.2% vs. 44.4%, p<0.0001) and survived to hospital discharge (24.8% vs. 43.3%, p<0.0001). During ECMO, 84.8% had a peak FO ≥ 10%; 67.2% of patients had a peak FO of ≥ 20% and 29% of patients had a peak FO of ≥ 50%.

FO at ECMO initiation and peak FO during ECMO were associated with duration of ECMO. After adjusting for AKI, pH at ECMO initiation, non-renal complications, ECMO mode, centre and patient age, the degree of fluid overload at ECMO initiation (p =0.03) and the peak fluid overload on ECMO (p<0.0001) predicted duration of ECMO in survivors.

Multivariable analysis showed that peak fluid overload (for each 10% rise) on ECMO predicted mortality on ECMO (adjusted OR 1.09, 95% CI 1.04-1.14). Fluid overload at ECMO initiation (aOR 1.13, 95% CI 1.05-1.22) and peak fluid overload (aOR 1.17, 95% CI 1.11-1.23) both predicted hospital mortality.

Conclusions: Fluid overload occurs commonly and is independently associated with adverse outcomes including increased mortality and increased duration of ECMO support in a broad pediatric ECMO population. These results suggest that FO is a potential target for intervention to improve outcomes in children on ECMO.
Patient Centered Outcomes in Continuous Renal Replacement Therapy: Functional Outcome of Pediatric Continuous Renal Replacement Therapy Survivors

Mallory B Kent¹, Molly Vega¹, Laura Loftis¹, Mona McPherson¹, Jeanine Graf¹, Ayse A Arikan¹

¹Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA

With improving support options and the accompanying improvement in patient survival, patient centered outcomes such as quality of life and functional status are under the spotlight in clinical studies. Pediatric continuous renal replacement therapy (CRRT) patients now have an improved survival rate of >60% compared to <40% only a decade ago.

We aimed to review the functional outcomes of pediatric CRRT patients at intensive care unit (PICU) and hospital discharge. METHODS: Retrospective cohort study of CRRT patients at Texas Children’s Hospital during 2014-2015. Primary outcome was functional outcome assessed using the Functional Status Score (FSS) (ranging from 6 (fully functional) to – 30 (comatose). Modified CRTT on ECMO was excluded from analysis. RESULTS: Seventy-four patients received 723 days of CRRT (mean 21.5), 43% females, median age 6 years (IQR 1 – 13). Twenty percent of patients had no co-morbidity, 14% had only one, and 66% had two or more comorbidities on PICU admission. Mean PELOD on admission was 19.5, and highest oxygenation index (OI) score was 17.4. Duration of sedation and neuromuscular blockade was 12.5 days( IQR 2 - 32) and 2 days (IQR 0 - 8), respectively. CRRT duration was 12 days (IQR 4 - 24), and 32 patients (43%) went on to receive hemodialysis. Survival was 64% (47/75), Median FSS score was 16 (IQR 10 - 27) on admission, 13.5 (IQR 9 - 30) on ICU discharge, and 11.5 (IQR 8 - 30) on hospital discharge. Of the surviving patients, 48% had an improved FSS score on discharge. Ten patients (21%) were discharged with new G-tubes, four (8.5%) received a tracheostomy during admission, and three were ventilator dependent (6%) on hospital discharge. FSS score at PICU or ICU discharge was not correlated with number of days on CRRT, CRRT indication, or percent fluid overload, but it was, strongly correlated with degree of malnutrition at time of CRRT start, (p = 0.001) duration of sedation (p = 0.032), and highest OI (p = 0.001). In multivariable analyses, number of days on sedation (p = 0.004) was the only independent predictor of FSS at discharge in CRRT survivors.

CONCLUSION: Though pediatric CRRT patients overall have favorable functional outcomes at PICU and hospital discharge, they remain at risk for new disability and require close follow up for adequate rehabilitation and development. Duration of sedation might be a modifiable risk factor to improve functional outcome in survivors.
The Impact of Disease Severity on Paradoxical Association between Body Mass Index and Mortality in Patients with Acute Kidney Injury Undergoing Continuous Renal Replacement Therapy

Hae-Ryong Yun¹, Hyounghae Kim¹, Youn Kyung Kee¹, Changhyun Lee¹, Shinchan Kang¹, Jung Tak Park¹, Tae Ik Chang², Tae-Hyun Yoo¹, Shin-Wook Kang¹, Seung Hyeok Han¹

¹Kidney Disease Research Yonsei University, ²Division of Nephrology, Department of Internal Medicine, National Health Insurance Service Medical Center, Ilsan Hospital, Goyang, Gyeonggi-do, Republic of Korea

Background: Association between high body mass index (BMI) and survival benefit in chronically ill patients is confounded by comorbid conditions such as nutritional status and inflammation. Patients with acute kidney injury (AKI), particularly those receiving continuous renal replacement therapy (CRRT), are highly catabolic and more susceptible to loss of energy. Herein, we evaluated whether disease severity can modify the relationship between BMI and mortality.

Methods: We conducted an observational study in 573 patients who had undergone CRRT owing to various causes of AKI between 2010 and 2014. Patients were categorized into four groups according to BMI quartiles (Q1< 20.9, Q2 21.0 – 23.5, Q3 23.6 – 26.5, and Q4 ≥ 26.6). More severe disease was defined as serum albumin < 3.0 mg/dL and sepsis-related organ failure assessment (SOFA) score ≥ 13. The study endpoint was defined as death that occurred within 30 days after the initiation of CRRT.

Results: There were no significant differences in sex, kidney function, comorbidity index, and SOFA score among the four BMI quartile groups. In a multivariable analysis adjusted for sex, blood pressure, estimated glomerular filtration rate, septic AKI, Charlson comorbidity score, SOFA score, CRRT prescription, white blood cell count, and albumin, higher BMI was significantly associated with a lower risk of death. Compared to Q1, hazard ratios (HR) for Q2, Q3, and Q4 were 0.75 (95% confidence interval [CI] 0.56-1.00), 0.69 (0.51-0.92) and 0.59 (0.44-0.80), respectively. This association remained unaltered in high severity group (HR [95% CI] for Q2: 0.79 [0.56-1.13]; Q3: 0.58 [0.40-0.84]; Q4: 0.59 [0.40-0.85]), whereas no such relationship was seen in low severity group.

Conclusion: This study showed that a protective effect of high BMI was observed in AKI patients undergoing CRRT only in more severe patients, and was lost in less severe patients.
Severity, Outcome and Renal Replacement Therapy (RRT) for Acute Kidney Injury (AKI) in a Mixed Pediatric Intensive Care Unit (PICU) - A Retrospective Analysis, 2005 and 2015

Sophie Fincher\textsuperscript{1}, Barry Wilkins\textsuperscript{1}

\textsuperscript{1}Children's Hospital at Westmead

Objectives: To investigate severity and outcome of AKI in PICU, using creatinine criteria.

Methods: 955 consecutive admissions over one year in 2005 and 1244 in 2015 were screened for high plasma creatinine (enzymatic, peak >1.5x baseline or >1.5x upper normal limit), subgroups Mild (1.5x creatinine), Intermediate (2x) and Severe (3x), and for oliguria >6 hours. Use of RRT and outcome were recorded.

Results: In 2005 249 patients (26%) had AKI (9.5% Mild, 9.2% Intermediate, 7.3% Severe). In 2015 247 patients (19.9%) had AKI (9.3% Mild, 6.3% Intermediate, 4.3% Severe). In 2005 36 patients died (4%), all but 8 in AKI. In 2015 23 patients died (1.8%), all but 9 in AKI. Although death was always explainable by the underlying illness, oliguria (at least one period >12 hours), uraemia >17 mmol/L and creatinine >3x were strongly associated with death (p < 0.01) in both years. AKI mortality was 10.8% in 2005 (19% in the severe group, 8% in the lower groups). AKI mortality was lower in 2015, 5.7% overall (11% in the severe group, 4% in the lower groups), 1% in both years in patients without AKI. An additional 13% of patients had 1.5-2.9x creatinine fluctuations but staying within normal limits for age, and mortality for these was zero in both years. All but four surviving patients recovered renal function. Paediatric Index of Mortality (PIM2) predicted overall PICU mortality well (standardised mortality ratio SMR\textsubscript{PIM2} 0.80), but AKI increased the risk of mortality relative to PIM2, SMR 2.0 for the severe group, 1.0 for milder groups, and 0.2 for non-AKI patients. 15% of AKI patients in 2005 and 18% in 2015 received RRT (7% haemofiltration and 8% peritoneal dialysis in 2005; 4% and 14% in 2015). Cardiopulmonary bypass patients had a higher incidence of AKI but lower severity and mortality.

Conclusions: AKI incidence, by the above creatinine criteria, is high, 26% and 20% in the two years. AKI increases risk of mortality, correlating with severity and occurs in most PICU deaths. Most AKI is benign (89-94% recovery with <1% chronic renal failure). Creatinine criteria must be applied with clinical judgement in diagnosing AKI and predicting mortality.
Association between different stages of AKI and risk of long-term mortality

Jonah Powell-Tuck¹, Hugh Leonard¹, Ryan Haines¹, Marlies Ostermann¹, Salma Ayis²

¹Guy’s & St Thomas Hospital, ²NIHR Biomedical Research Centre, King’s College London, Division of Health and Social Care Research, London SE1, UK

Background: There is increasing evidence that patients with severe acute kidney injury (AKI) have an increased risk of short- and long-term complications, including mortality. Little is known about the long-term prognosis of patients with less severe AKI.

Aim: To investigate whether there is an association between any stage of AKI and long-term mortality in critically ill patients admitted to the Intensive Care Unit (ICU).

Methods: We analysed the electronic database of all patients admitted to the ICU of a tertiary care centre between 2004 – 2008. Using the KDIGO classification, we determined the worst stage of AKI during stay in ICU. Patients with pre-existing end-stage renal failure were excluded. Patients were followed up to June 2016. Mortality data were collected from the medical notes and a national register. We examined the associations between AKI severity and mortality risk at 1 and 5 years after hospital discharge, using Cox regression models.

Results: Of 3,097 eligible patients, 1457 (47.1%) had no AKI, 776 (25.1%) had AKI stage I, 166 (5.4%) had AKI stage 2, and 698 (22.5%) had AKI stage 3. Adjusting for age and pre-existing chronic conditions, AKI stage 2 was independently associated with an increased risk of death at 1 and 5 years. (Table 1)

Conclusions: Patients with AKI stage 2 had a significantly higher risk of mortality at 1 and 5 years after hospital discharge compared to patients without AKI. 1 and 5 year mortality of patients with AKI stage 1 was not significantly different from that of patients without AKI. Older age and pre-existing chronic condition were strong predictors of death, and important confounders of the associations between AKI severity and mortality. Further analyses are necessary to investigate the impact of acute severity of illness.

<table>
<thead>
<tr>
<th>Maximum AKI stage</th>
<th>1 year mortality</th>
<th>5 year mortality</th>
<th>1 year mortality</th>
<th>5 year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (adjusted)</td>
<td>95% CI</td>
<td>p-value</td>
<td>HR (adjusted)</td>
</tr>
<tr>
<td>no AKI</td>
<td>1.0</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>AKI stage I</td>
<td>1.07</td>
<td>0.84 - 1.35</td>
<td>0.59</td>
<td>1.02</td>
</tr>
<tr>
<td>AKI stage II</td>
<td>1.66</td>
<td>1.16 - 2.38</td>
<td>0.01</td>
<td>1.33</td>
</tr>
<tr>
<td>AKI stage III</td>
<td>1.16</td>
<td>0.91 - 1.47</td>
<td>0.23</td>
<td>1.10</td>
</tr>
<tr>
<td>Confounding factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age 16 - 19</td>
<td>1.0</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>age 20 - 59</td>
<td>1.48</td>
<td>0.47 - 4.65</td>
<td>0.50</td>
<td>1.17</td>
</tr>
<tr>
<td>age 60 - 79</td>
<td>3.40</td>
<td>1.09 - 10.63</td>
<td>0.04</td>
<td>3.00</td>
</tr>
<tr>
<td>age 80 or older</td>
<td>5.66</td>
<td>1.78 - 18.02</td>
<td>0.00</td>
<td>5.71</td>
</tr>
<tr>
<td>chronic conditions</td>
<td>2.72</td>
<td>2.15 - 3.43</td>
<td>0.00</td>
<td>2.33</td>
</tr>
</tbody>
</table>
Assessment of Community and in-Hospital Acquired Acute Kidney Injury in the Clinical Emergency Department in a Tertiary University Latin-American Hospital – a Prospective Study

Flavia B Azevedo1, Lia Marçal1, Herlon Martins2, Irineu Velasco2, Veronica Costa e Silva3, Leila Antonangelo4, Luis Yu1, Dirce Maria T Zanetta5, Emmanuel A Burdmann1

1LIM - 12, Division of Nephrology, University of Sao Paulo Medical School, São Paulo, SP, Brazil, 2Division of Emergency, University of Sao Paulo Medical School, São Paulo, SP, Brazil, 3Cancer Institute, Sao Paulo, SP, Brasil, 4Clinical Pathology Division, University of Sao Paulo Medical School, São Paulo, SP, Brazil, 5University of Sao Paulo Public Health School, São Paulo, SP, Brazil

Prospective studies comparing the frequency and outcomes of community and in-hospital acquired acute kidney injury (AKI) in patients admitted to the Emergency Department (ED) are scarce, especially in developing countries.

The aims of this study were to compare the frequency, characteristics and outcomes of community-acquired AKI (CAKI), and early in-hospital developing AKI diagnosed by RIFLE or/and KDIGO serum creatinine (SCr) criteria in patients admitted to the ED through a referred emergency room (ER) of a tertiary university hospital in a developing country.

Inclusion criteria were patient ≥ 18 years old hospitalized in the ED through the ER. Exclusion criteria were refuse to sign the informed consent, length of stay in the ED < 48h, chronic kidney disease stage 5, terminal patients on palliative care, renal transplant, and patients not suitable for long-term outcome. Patients were assessed up to the hospitalization day 7 or discharge, whatever happened first. SCr (mg/dl) was assessed at admission and daily or every 48 h. Patients were classified as: no-AKI, CAKI, AKI by RIFLE (ARIFLE), AKI by KDIGO (AKDIGO) and AKDIGO positive ARIFLE negative (K+R-). The analyzed outcomes were length of in-hospital stay (LoS, d), ICU admission (%), and in-hospital (IH) mortality. Data are presented as median (minimum-maximum values) or percent (%). Statistical significance is p<0.05.

Five hundred two patients were included, age 62y (19-98y), gender 53.6% male, LoS 7 (2-132d). Causes of hospitalization were pulmonary (25.5%), gastric (14.5%), cardiovascular (10.2%), and other (49.8%). Overall IH mortality was 15.1%.

Comparison of groups is shown in the table below (* p<0.05 vs no AKI; IH mortality was significantly different among groups (p<0.0001); frequency of ICU admission was significantly different among groups (p=0.0052))

In conclusion, the frequency of AKI at admission or developing in the first 7 days of hospitalization was high in the clinical emergency department. KDIGO criteria diagnosed more patients than RIFLE. CAKI, ARIFLE and AKDIGO patients were admitted more frequently to the ICU, suggesting higher clinical severity. In-hospital mortality of AKI patients was significantly higher than non-AKI. CAKI showed high prevalence and mortality, similar to AKI diagnosed by RIFLE or KDIGO criteria.

<table>
<thead>
<tr>
<th></th>
<th>no AKI</th>
<th>CAKI</th>
<th>ARIFLE</th>
<th>AKDIGO</th>
<th>K+ R -</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (n)</td>
<td>52.2 (262)</td>
<td>19.5 (98)</td>
<td>17.9 (90)</td>
<td>28.3 (142)</td>
<td>10.4 (52)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>58 (20-90)</td>
<td>64 (19-98)*</td>
<td>64 (22-98)</td>
<td>64 (21-98)</td>
<td>65 (21-91)</td>
</tr>
<tr>
<td>LoS (d)</td>
<td>5.0 (2-132)</td>
<td>8.0 (2-49)</td>
<td>9.0 (2-95)*</td>
<td>8.5 (2-95)</td>
<td>4.0 (2-78)</td>
</tr>
<tr>
<td>ICU (%)</td>
<td>19.1</td>
<td>25.5</td>
<td>33.7</td>
<td>29.6</td>
<td>17.3</td>
</tr>
<tr>
<td>IH mortality (%)</td>
<td>8.4</td>
<td>18.4</td>
<td>27.3</td>
<td>25.3</td>
<td>13.5</td>
</tr>
</tbody>
</table>
Urinary Output Measurement Is Essential for Early Diagnosis of AKI after Major Elective Non-Vascular Abdominal Surgeries

Graziela R de Souza¹, Lia Marçal¹, Leila Antonangelo², Regis Tironi¹, Dirce Maria T Zanetta³, Luis Yu¹, Emmanuel Burdmann¹

¹LIM - 12, Division of Nephrology, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, ²Clinical Pathology Division, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, ³Public Health School, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil

The incidence of acute kidney injury (AKI) after major surgeries is high. Prospective data on AKI post major elective abdominal surgeries are scarce. The aim of this on-going study is to assess incidence and outcomes of early AKI comparing RIFLE and KDIGO serum creatinine (SCr) and urinary output (UO) criteria in patients submitted to major elective non-vascular abdominal surgeries admitted to ICU. 171 patients were prospectively evaluated from 09 2015 to 11 2016, peri-operatively and from the ICU admission up to 7 days. SCr (mg/dl) was assessed pre surgery and once a day up to 7 d or ICU discharge. Hourly UO (ml/kg/h) was measured daily. Outcomes were AKI diagnosis, ICU and hospital length of stay (LoS), and mortality (in-hospital, 30 d and 90 d). Data are mean ± SD or %.

Patients’ age was 54±16 y, 59% female, hospital LoS was 17.0±16.6 d, ICU LoS was 3.0±1.7 d and mortality was 7.0%.

Using RIFLE, 101 patients (59.1%) developed AKI: 5 by SCr, 76 by UO and 20 by SCr+UO criteria, respectively. Using KDIGO definition, 102 patients (59.6%) developed AKI: 6 by SCr, 67 by UO and 29 by SCr+UO criteria, respectively. The majority of patients were RIFLE stage R (81.2%) and KDIGO stage I (81.4%).

AKI patients were older (5.7±13 vs. 50±17 y non-AKI, p=0.0056), had longer hospital LoS (20.1±19.7 vs. 12.4±8.5 d non-AKI, p=0.0012), longer ICU LoS (3.3±2.0 vs. 2.5±0.8 d non-AKI, p=0.0168) and increased mortality (9.8 vs. 2.3% non-AKI, NS).

Patients with AKI (KDIGO definition) diagnosed by changes in UO, SCr+UO and SCr criteria presented, respectively, hospital LoS of 19±19, 24±22, and 14±10 days (NS), ICU LoS of 3±1, 5±3 and 4±3 days (p<0.001 UO vs. SCr+UO) and mortality of 4.5, 6.9 and 83.3% (p<0.0001), respectively. If the SCr criteria alone were utilized for AKI diagnosis, a total of 25 patients in RIFLE group and 35 in the KDIGO group would be overlooked.

In conclusion, the use of both SCr and UO criteria in RIFLE and KDIGO definitions showed high prevalence of early AKI, which was associated to unfavorable outcomes in this population. UO seems to be pivotal for early AKI recognition in this context, since the use of SCr criteria alone would miss a high number of AKI diagnosis, both in RIFLE and KDIGO definitions.
Trends in Acute Kidney Injury after Cardiac Surgery in Zhongshan Hospital, 2009 to 2014

Yimei Wang, Zhouping Zou, Jie Teng, Jiarui Xu, Wuhua Jiang, Bo Shen, Yi Fang, Zhe Luo, Chunsheng Wang, Xiaoqiang Ding

1Zhongshan Hospital, Fudan University, Shanghai, China

Aim: Acute kidney injury (AKI) is a common and severe complication of cardiac surgery. We examined the trends in incidence of AKI after cardiac surgery in a 2000-bed hospital of China prospectively to evaluate the impact of AKI on in-hospital mortality.

Methods: Cardiac surgery patients of Zhongshan Hospital, Fudan University, Shanghai from 2009 to 2014 were screened by the hospital medical database. The presence and severity of AKI were assessed by the KDIGO criteria. The primary endpoint was in-hospital mortality and the secondary endpoint was renal outcomes.

Results: 13786 cardiac surgeries were performed from 2009 to 2014. The median age of patients was 56 (45-64) years, 56.8% were male. The AKI incidence was 33.8% (25.0% in stage 1, 5.7% in stage 2, 4.1% in stage 3), increased during the six years from 29.9% to 39.6% (P<0.05). 279 patients received renal replacement therapy. Complete, partial and no renal recovery was observed in 32.7%, 55.1% and 12.2% of AKI patients, respectively. There was no significantly statistical difference in AKI-RRT incidence during the six years. Among AKI patients, 345 (7.4%) died with no change in survival over time. Multivariate logistic regression analysis showed that male, Age (per 10-year increase), chronic heart failure (NYHA stage III-IV), pre-operative estimated glomerular filtration rate (eGFR)<60 mL/min/1.73m², cardiopulmonary bypass time, proteinuria and blood platelet count were risk factors for AKI after cardiac surgery.

Conclusion: AKI is prevalent in the cardiac surgery patients. Slight elevations of serum creatinine are associated with significantly increased mortality. The incidence of AKI after cardiac surgery is rising from 2009 to 2014, but in-hospital mortality remained high without significant decline. The prevention and treatment of AKI demand urgent improvement.

Nutritional therapy to prevent progression of Acute Kidney Injury to Chronic Kidney Disease: Design and Methods

Krishan L Gupta, Vivek Kumar, Etienne Macedo, Ravinndra Mehta

1Postgraduate Institute of Medical Education and Research, Chandigrah, 2UCSD Department of Nephrology San Diego, 4I

Background Acute Kidney Injury (AKI) has been recognized as an important risk factor for Chronic Kidney Disease (CKD). In CKD, dietary protein restriction is used to mitigate its progression by reducing intra-glomerular pressure. We believe that post AKI, the kidney is vulnerable to the metabolic demands and dietary protein control may facilitate renal recovery and retard progression to CKD.
Methods This will be a pilot, single center, open label, randomized, controlled trial of adult subjects who would be recovering from an episode of Stage 2/3 AKI at the Postgraduate Institute of Medical education and Research, Chandigarh, India. The subjects will be randomized to a low protein and Ketosteril® (LPD-K) or ad-lib diet for 3 months. The randomization procedure will be non-stratified, using random permuted blocks of 4 subjects to guarantee groups of equal size throughout the study. After the 3-month period, subjects will continue ad lib diet and followed for additional three months. Clinical and laboratory investigations details would be recorded every 2 weeks for first 3 months and finally, at the end of 6 months. The primary objective is change in nutritional status (as measured by anthropometry, subjective global assessment, nutrition biomarkers and bioelectrical impedance) at 6 months. The secondary objectives are rate and degree of recovery of renal function at 3 months and proportion of patients who progress to one CKD stage higher than their baseline at 3 months and 6 months.

Relevance Recent data suggest that when dietary compliance is achieved in CKD patients, LPD-K diet is feasible for the majority and rate of decline in glomerular filtration rate is significantly lower on LPD-K than on low protein diet alone. Protein restriction has not been studied at all in AKI. It is possible that, by the same mechanisms, LPD-K will reduce the tubular workload in the recovering kidney, ameliorate further tubular damage, and enhance recovery of renal function, or at least retard the progression to CKD. If successful, it will set the stage for a larger trial and might become one of the first interventions to decrease development of CKD following AKI.

30

AKI – Changing Spectrum of Epidemiology and Aetiology: Experience form Tertiary Care Hospital in South India

SreeBhushan Raju1, vamsi nagalla1, ramesh boora1, anvesh golla1, krishna prasad1

1Nizams Institute of Medical Sciences

Introduction: Epidemiology of AKI in developing countries differs from that of the developed world. The etiology also varies based on the geographical variations with in the country. We evaluated the epidemiology and etiology of AKI patients admitted in to our highest referral medical institute of the state.

Materials and Methods: 
We retrospectively analysed the data of 500 consecutive patients with AKI who admitted in to our institute since January 2015. We collected the data from the portal of health insurance scheme provided free to all the patients below the poverty line (BPL) by the local government. All the clinical data including the aetiology , choice of Renal replacement therapy and the outcome were analysed. Results: Most of the patients (45%) were young below 40 years of age and elderly (>65 years) constituted significantly in 25%. Sepsis was the most frequent cause constituting 78 % with (45%) and obstructive uropathy due to stone disease. Community acquired pneumonia and Cellulitis were seen. Malaria was seen in <2 % and acute gastroenteritis was in 4 % of the patients and other infections like salmonella, scrub typhus, dengue, leptospira were in less than 2% of total cases. The source of sepsis could not be identified in 8 % ; Septic shock was seen in 32 % and mechanical ventilation was required in 12%. Acute pancreatitis, drug induced including contrast agent related AKI, AKI due to poisoning, crystal induced nephronathy. Multiple mveloma and rhabdomvolvsis were the other significant etiologies. was
the most frequent comorbid condition seen in 37% and renal stone disease in 8%. Interimemt Hemodialysis (IHD) was given to 92% and peritoneal dialysis in 3%. Mortality was significant in those who required mechanical ventilation and septic shock. Renal recovery was seen in 38% and progression to dialysis dependent state was seen in 15%.

Conclusions: There is change in the spectrum of AKI cases admitted in tertiary care hospital among the BPL patients. Tropical infections have become less frequent and complications with AKI became predominant. IHD was the most preferred choice and mortality was attributed to comorbidities. Renal recovery was seen in those with short duration of symptoms.

31

Comparison of Acute Kidney Injury Diagnosed by KDIGO and Modified KDIGO Criteria and Acute Kidney Disease among 11,909 Patients Hospitalized in a Tertiary University Hospital

Felipe Ledesma¹, Leila Antonangelo², Dirce Maria Zanetta³, Luis Yu¹, Emmanuel Burdmann¹

¹LIM - 12, Division of Nephrology, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, ²Division of Clinical Pathology, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, ³Division of Epidemiology, University of Sao Paulo Public Health School, Sao Paulo, SP, Brazil

The term acute kidney disease (AKD) has been used for patients with a serum creatinine (SCr) increase that did not satisfy acute kidney injury (AKI) definition by KDIGO criteria, but occurred in a period < 3 months. Information on the prevalence and outcomes of those patients are scarce.
The aim of this study was to assess the prevalence and outcomes of AKD patients as compared to AKI patients diagnosed by KDIGO or modified KDIGO criteria in a large (1,000 beds) general tertiary university hospital.
During the year of 2015, there were 35,067 hospitalizations in the assessed university hospital. Among those 18,686 had SCr measured during hospitalization. We analyzed 11,909 hospitalizations in patients ≥18 years old, who had at least two SCr measurements during hospitalization. We divided the patients in four groups: no-AKI, AKI by KDIGO definition, AKI by modified KDIGO definition (SCr did not increase, but actually decreased ≥0.3 mg/dl in 48 hours or ≥50% within 7 days), and AKD (SCr increase ≥0.3 mg/dl or ≥50% in a period larger than 7 days but smaller than 3 months). Age, gender, time of hospitalization, and intra-hospital mortality were assessed. Results are presented as median (25%-75% interquartile) or frequency (%). Statistical significance was defined as p<0.05.
The age of the analyzed group (11,909 patients) was 56.0 y (40.2-67.6 y), hospitalization length of stay (LoS) was 9.43 d (5.13-18.06 d) and overall mortality was 12%. Comparisons among groups are in the table below (*p<0.05 vs non-AKI; &p<0.05 vs. KDIGO and modified KDIGO; # p<0.0001 vs. others).
In conclusion, there was a large prevalence of patients with AKI diagnosed by KDIGO criteria among the patients who had at least 2 SCr measured during hospitalization. These patients were significantly older and had significantly higher mortality as compared to non-AKI. The group of patients with AKI by modified KDIGO criteria was significantly older and had similar mortality as non-AKI patients. There was a low prevalence of AKD among the studied patients. AKD patients were significantly younger, had a significantly higher frequency of female gender, had significantly longer hospital LoS and significantly lower in-hospital mortality, as compared to the KDIGO AKI group.

*table on following page*
32

Risk of AKI in Patients Receiving Antibiotic Therapy at the Time of Cardiac Catheterization

Cheri Lehmann¹, Parker Lehmann², Udayan Bhatt¹

¹The Ohio State University, ²New Albany High School

Introduction: Acute kidney injury (AKI) is a significant complication seen in patients undergoing cardiac catheterization. Also, antibiotic use is commonly seen in hospitalized subjects. The epidemiology and contribution of antibiotics to post-cardiac catheterization AKI have not been fully explored. On this basis, the purpose of this study is to examine the concomitant use of antibiotics at the time of cardiac catheterization, in terms of frequency of occurrence and impact on the development of AKI.

Methods: After institutional approval, hospitalized patients undergoing cardiac catheterization over a six-month period were identified. Patients with end-stage renal disease were excluded. Demographic data were obtained. All medications administered, laboratory studies and vital signs on the day of cardiac catheterization were extracted. Serum creatinine (SCr) values were also obtained from the day prior to and 2 days after the imaging procedure. The change in SCr from the day prior to imaging to 2 days after the procedure was then calculated (Δ_Cr). Univariate linear regression was performed to explore the association between change in SCr and antibiotic use. Finally, univariate and multivariate logistic regression was performed to examine the risk of AKI (defined as a change in SCr of > 0.3mg/dL) in patients undergoing heart catheterization and antibiotic use.

Results: Complete records for 437 heart catheterizations were obtained. Antibiotic classes administered with a frequency of > 2% along with Δ_Cr are shown below. A statistically significant increase in creatinine was experienced in subjects receiving vancomycin at the time of catheterization. The adjusted odds ratio for developing AKI in subjects receiving vancomycin at the time of cardiac catheterization was 2.97 (95% CI: 1.12, 7.90; p=0.029).

Conclusions: Vancomycin use was associated with a statistically significant increase in serum creatinine 48 hours after heart catheterization. Based on our data, the odds of AKI after heart catheterization in subjects who had also received vancomycin on the day of the procedure was 2.97 times higher than in subjects who did not receive vancomycin. This was after adjustment for demographic and clinical variables. This study demonstrates the possible additive nephrotoxicity of vancomycin and cardiac catheterizations.

*table on following page*
<table>
<thead>
<tr>
<th>Antibiotic Class</th>
<th>Use with Cardiac Cath (%)</th>
<th>Delta_Cr</th>
<th>p-value</th>
<th>Adj. OR for AKI</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>7.32</td>
<td>0.159</td>
<td>0.015</td>
<td>2.97</td>
<td>1.18, 11.47</td>
</tr>
<tr>
<td>Macrolides</td>
<td>3.98</td>
<td>0.102</td>
<td>0.246</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP/SMX</td>
<td>2.29</td>
<td>0.102</td>
<td>0.370</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>8.70</td>
<td>-0.069</td>
<td>0.737</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillins</td>
<td>10.53</td>
<td>-0.037</td>
<td>0.729</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinalones</td>
<td>2.52</td>
<td>-0.052</td>
<td>0.997</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

33

Mortality Risk Factors In Community-Acquired Acute Kidney Injury

Jonathan Chavez-Iñiguez¹, Ricardo Rubio-Reynoso¹, Miguel Ibarra-Estrada², Melinia Amador-Jimenez¹, Jose Montalban-Castellanos¹, De la Torre-Campos Librado¹, Garcia-Gracia Guillermo¹

¹Hospital Civil de Guadalajara, ³Instituto Jaliscience de Oncologia

Background: Community-acquired Acute kidney Injury (CA-AKI) remains a high risk factor for mortality. The 0by25 initiative promotes the increase of CA-AKI awareness. However, there is little evidence on the risk factors associated to mortality in CA-AKI.

Methods: Prospective cohort from a tertiary-care hospital. We compared 78 CA-AKI patients with 150 non-AKI patients seen at the emergency department. The main outcome was mortality. Mann–Whitney and chi-square or Fisher’s exact tests where used when appropriate. We constructed receiver operating characteristic curves (ROC) for variables predicting death. Multivariate logistic regression was performed to identify factors associated with death.

Results:

Conclusion
In CA-AKI patients serum creatinine >1.55mg/dL on admission is significantly associated with death and it is a good predictor of mortality.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>adjunsted OR</th>
<th>95% IC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute abdomen</td>
<td>3.67</td>
<td>0.84-16.0</td>
<td>0.08</td>
</tr>
<tr>
<td>Analgesia</td>
<td>0.18</td>
<td>0.02-1.30</td>
<td>0.09</td>
</tr>
<tr>
<td>Vasopressor requirement</td>
<td>2.86</td>
<td>0.60-13.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>1.67</td>
<td>0.30-9.12</td>
<td>0.55</td>
</tr>
<tr>
<td>Diastolic arterial pressure</td>
<td>2.05</td>
<td>0.30-14.0</td>
<td>0.46</td>
</tr>
<tr>
<td>Serum creatinine &gt;1.55 mg/dL</td>
<td>3.66</td>
<td>1.02-13.73</td>
<td>0.049</td>
</tr>
</tbody>
</table>

figure on following page
Risk Factors for Mortality in Patients with Acute Kidney Injury Treated with Continuous Renal Replacement Therapy

Yoojin Lee¹, Bongsoo Park¹, Yangwook Kim¹, Sihyung Park¹

¹Department of internal medicine, nephrology service, Inje university Haeundae Paik Hospital, Busan, Korea

Introduction
Continuous renal replacement therapy (CRRT) is a widely used treatment modality in hemodynamically unstable acute kidney injury (AKI) patients, but mortality rate of AKI is still high. We aim to identify the risk factors for mortality in CRRT-treated AKI patients.

Method
As retrospective study, the data related with CRRT was collected since March 2010 till December 2015. The duration of CRRT, AKIN criteria by creatinine or urine volume, presence of complete anuria, BUN and creatinine ratio, bilirubin, mean blood pressure (BP), systolic BP and other comorbidities were analyzed to know which factors associated with death.

Result
CRRT was applied to 184 patients due to AKI among the total number of 838 CRRT users. Among the various variables, creatinine (2.87 ± 1.34 vs. 3.92 ± 2.6 mg/dL), creatinine ratio changes (2.89 ± 1.4 vs. 4 ± 2.9), lowest mean BP (67.07 ±14.01 vs 75.45 ± 16.07 mmHg) and systolic BP (90.02 ± 19.24 vs. 105.27 ± 20.7 mmHg) were lower and bilirubin (6.13 ± 7.86 vs. 1.93 ±1.98) was higher in non-survival group (N= 164) than survival group (N=20). The bilirubin (r= 0.24, p = 0.001) and systolic BP (r=-0.25, p = 0.01) were only correlated with death in multivariable analysis. The relative risk was 4.54 with septic shock (r = 0.22, p = 0.001) and 6.06 with malignancy (r = 0.16, p = 0.008). In subgroup analysis with non-survival group, total CO2 contents (16.1 ± 6.2 vs 18.4 ± 4) and systolic BP (84.3 ±
17.9 vs 92.7 ± 19) were lower in death within 48 hours group. The relative risk was 3 with malignancy (r= 0.26, p = 0.001) and 1.48 with septic shock (r = 0.08, p= 0.275)

Conclusion
Patients with CRRT are very fragile regardless of their causes and have high mortality risk. According to our study, the time to CRRT (early or late) did not affect survival. However, comorbidity especially malignancy, other organ damage and systolic blood pressure were closely related with mortality than the level of AKI damage.

RESEARCH IN AKI

35

The Clinical Significance of Alkaline Phosphatase Activity in Patients with Septic Acute Kidney Injury

seung don baek1, seulgi shin1, hyang-sook park1, mi-soon kim1, eun kyoung lee2, so mi kim2, jai won chang1

1 asan medical center, 2 dankook university college of medicine

Purpose: Evidences suggested that alkaline phosphatase attenuate inflammatory response in sepsis by lipopolysaccharide detoxification and adenosine triphosphate dephosphorylation. We sought to determine alkaline phosphatase (AP) activity change during septic acute kidney injury (AKI) and clinical parameters influenced by AP activity.

Methods: In a retrospective study of the patients who underwent continuous renal replacement therapy (CRRT) due to septic AKI, we investigated the baseline, follow-up AP activity on day 3 and the associated outcomes.

Results: We analyzed baseline AP activity of 155 patients and day 3 AP activity of 123 patients. Baseline AP activity of 90 (59–133) U/L increased to 105 (79–156) U/L on day 3, of which liver and bone isoforms increased significantly, but intestine isoforms did not reach statistical significance. Baseline AP activity did not show an association with renal and inflammatory biomarkers, or outcomes. Also, it did not differ significantly between 75 survivors and 80 non-survivors (p=0.155). Day 3 AP activity increased in 70.6% of patients with mean difference of 19 (-3 to 53) U/L. Day 3 AP activity showed weak correlation with length of ICU stay (r=0.205, p=0.023) and length of hospital stay (r=0.190, p=0.036). However, day 3 AP activity did not correlate with survival (r=-0.035, p=0.698).

Conclusion: Endogenous AP activity modestly, but significantly increased in 70.6% of patients with septic AKI. Follow-up AP activity was associated with morbidity. However, neither baseline nor follow-up AP activity was associated with survival.

figure on following page
Outcomes of recurrent acute kidney injury in tropics

Anupma kaul\textsuperscript{1}, Dharmendra bhaduaria\textsuperscript{1}, R.K. Sharma\textsuperscript{1}, Narayan Prasad\textsuperscript{1}, Amit Gupta\textsuperscript{1}

Background- Acute kidney injury (AKI) is now an established and preventable cause for chronic Kidney disease. Poor outcome of Acute Kidney Injury is influenced by severity and duration of AKI. We hypothesize that recurrent episodes of acute kidney injury are associated with adverse renal and patient related outcome.

Methods- Study was undertaken to look into etiological risk factors for recurrent AKI and its effect on renal and patient related outcome. This retrospective analytical study was conducted at tertiary care health care centre from northern part of India from January 2003 to December 2013. All patients with the diagnosis of "acute renal failure" or "acute kidney injury" as their hospital admission diagnosis was identified and individuals with recurrent Acute Injury were included in the study.

Results- Recurrent acute kidney injury was found in 21 (0.56\%) of 3698 patients who presented with acute kidney injury during the 10 years period. Topical infections were the most common etiology of recurrent AKI followed by rhabdomyolysis and intravascular hemolysis leading to pigment nephropathy. Acute tubular necrosis was the most common histopathological diagnosis among patients biopsied. As the episodes of AKI increased from 2 to \textgreater 2 episodes, there was poor immediate as well as late renal outcome. 50\% were protienuric and 87.5\% were hypertensive at 1 year among patients who had \textgreater 2 episodes of AKI while it was 15.3\% and 7.69\% among patients having < 2 episodes respectively.

Conclusion- Recurrent episodes of AKI are associated with poor patient and renal outcome suggesting that each episode of acute kidney injury needs close evaluation and follow up following hospital discharge with particular attention to renal outcomes.
Pro-Enkephalin, Prediction of Renal Dysfunction and Short and Longer Term Prognosis in Acute Heart Failure - a GREAT Network Study

Leong L Ng1, Iain B Squire1, Donald J Jones2, Joachim Struck3, Zaid Sabti4, Tobias Breidthardt4, Christian Mueller4, Mattia Arrigo5, Etienne Gayat5, Alexandre Mebazaa5

1 University of Leicester, Department of Cardiovascular Sciences and NIHR Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester LE3 9QP, United Kingdom, 2 University of Leicester, Department of Cancer Studies, Leicester Royal Infirmary, Leicester LE1 5WW, United Kingdom, 3 Sphingotec GmbH, Hennigsdorf, Germany, 4 Cardiovascular Research Institute Basel (CRIB) and Department of Cardiology, University Hospital Basel, Switzerland, 5 U942 Inserm; APHP, Hôpitaux Universitaires Saint Louis Lariboisière; Université Paris Diderot, Paris, France

Purpose of the study

Pro-Enkephalin (penKid) and its receptors are widely distributed. Enkephalins are cardiodepressors and difficult to measure directly. PenKid is a stable surrogate plasma analyte of labile enkephalins and has been shown in various acute disease conditions including sepsis and acute myocardial infarction to predict renal dysfunction and adverse outcome. Cardiorenal syndrome is common in acute heart failure (AHF) and portends poor prognosis. In this study we assessed the prognostic value of penKid levels in AHF, identified levels that may be useful in clinical decisions and assessed its use for predicting cardiorenal syndrome.

Methods

In a multicentre study we measured penKid in 1908 (1186 male, mean age 75.66±11.74 years) AHF patients. The primary end-point was all cause mortality at 1-year; secondary endpoints were in-hospital mortality, all-cause mortality or heart failure rehospitalisation within 1 year and in-hospital worsening renal function, defined as a rise in plasma creatinine ≥ 26.5 µmol/L or 50% above the admission value within 5 days of presentation.

Results

During 1 year follow-up 518 patients died. Measures of renal function were the major determinants of penKid levels. PenKid independently predicted worsening renal function (Odds ratio 1.58[1.24-2.00, P<0.0005]) with a model ROC area of 0.69. PenKid was associated with the degree of worsening renal function. Multivariable Cox regression models showed penKid level was an independent predictor of 1 year mortality (hazard ratio HR 1.43[95%CI 1.23-1.67, P<0.0005]) and 1 year death and/or heart failure (HR 1.27[1.10-1.45, P=0.001]). PenKid independently predicted outcomes at 3 or 6 months. PenKid levels were independent predictors of in-hospital mortality, predominantly down-classifying risk in survivors when added to clinical scores and levels <133.3 pmol/L and >211.3 pmol/L detected low and high-risk patients, respectively.

Conclusions

Plasma penKid reflects the cardio-renal status in AHF, and elevated penKid levels are independently prognostic for worsening of renal function, death in-hospital and during short or long-term follow-up.
Impact of Dilution effect of Fluid Balance on the Early Detection of Cardiac Surgery Associated Acute Kidney Injury

Jifu Jin\textsuperscript{1}, Jiarui Xu\textsuperscript{1}, Wuhua Jiang\textsuperscript{1}, Yamin Zhuang\textsuperscript{2}, Bo Shen\textsuperscript{1}, Jiawei Yu\textsuperscript{1}, Wenlv Lv\textsuperscript{1}, Chunsheng Wang\textsuperscript{2}, Xiaoqiang Ding\textsuperscript{1}, Jie Teng\textsuperscript{1}

\textsuperscript{1}Department of Nephrology, Zhongshan Hospital, Shanghai Medical College, Fudan University, Shanghai, China, \textsuperscript{2}Department of Cardiovascular Surgery, Zhongshan Hospital, Shanghai Medical College, Fudan University, Shanghai, China

Objective: The volume overload of patients with cardiac surgery is common, which is closely related to the occurrence, development and prognosis of cardiac surgery associated acute kidney injury (CSA-AKI). Dilution effect of volume overload of cardiac surgery patients could delay early diagnosis of CSA-AKI. The purpose of the study is to investigate the effect of volume overload on the timing of diagnosis and prognosis of AKI with off pump coronary artery bypass grafting (OPCABG).

Design: Retrospective analysis study.

Setting: Fudan University-affiliated Zhongshan hospital: single center.

Patients: 122 consecutive patients undergoing elective OPCABG from January to June 2015.

Measurements and Methods: AKIN criteria was used to classify CSA-AKI. Fluid input and output were recorded for 48 hours post-operatively. Urine output was recorded every 6 hours for 24 hours post-operatively. Serum creatinine was daily recorded and adjusted for weight-corrected fluid balance and patients were categorized into three groups: group A (No AKI before or after adjustment); group B (AKI only after adjustment); group C (AKI both before and after adjustment).

Results: Among 122 patients with weight and baseline creatinine available, only 1 patient in group C received CRRT treatment and all patients were discharged successfully from hospital. After adjusting for weight and volume balance, the incidence of CSA-AKI increased from 18.8\% (23/122) to 30.3\% (37/122) (p<0.05). In patients with AKI only after adjustment (group B), ICU stay and total hospitalization time were significantly higher than those in group A (3.3±0.9 vs 1.8±1.5d, p<0.05; 13.3±3.7 vs 11.3±3.3d, p<0.05), however no significant difference was observed when compared with group C (3.3±0.9 vs 2.5±1.1d, p>0.05; 13.3±3.7 vs 14.0±2.5d, p>0.05). Also, the mechanical ventilation time in group B was significantly longer than group A (2.1±0.6 vs 1.3±0.9d, p<0.05), but approximated that of group C (p>0.05).

Conclusion: The dilution effect of volume overload in the patients with OPCABG could influence the level of serum creatinine concentration, which may delay early classification of AKI. In order to improve the sensitivity of detection of cardiac surgery associated AKI, serum creatinine should be adjusted according to the volume balance and basic weight level.
Association Between Renal Recovery after Acute Kidney Injury and Long-Term Mortality after Transcatheter Aortic Valve Replacement

Wisit Cheungpasitporn¹, Charat Thongprayoon¹, Wonngarm Kittanamongkolchai¹, Narat Srivali¹, Kianoush B Kashani¹

¹Mayo Clinic, Rochester, MN, USA

Background: This study aimed to examine the association between acute kidney injury (AKI) following transcatheter aortic valve replacement (TAVR) and renal outcomes at hospital discharge and long-term mortality.

Methods: We included all adult patients undergoing TAVR for aortic stenosis from January 1, 2008, through June 30, 2014, and survived until hospital discharge at a quaternary referral hospital. AKI was defined as an increase in serum creatinine of 0.3 mg/dL or a relative increase of 50% from baseline. Renal outcome at the time of discharge was evaluated by comparing the discharge serum creatinine to the baseline serum creatinine. Complete renal recovery (CR) occurred if there was no AKI at discharge, whereas partial renal recovery (PR) took place if there was AKI but no need for renal replacement therapy at discharge. No renal recovery (NR) happened when there was a need for renal replacement therapy at discharge.

Results: 374 patients were included in the analysis. Ninety-eight (26%) patients developed AKI during hospitalization, of which 55 (15%) had CR, 39 (10%) had PR, and 4 (1%) had NR. AKI development was significantly associated with increased risk of 2-year mortality (STS risk-adjusted OR 2.26; 95% CI 1.45-3.48). The 2-year mortality rate was 34% in AKI patients with CR, 43% with PR and 75% with NR compared with 20% in non-AKI patients (Figure 1, p<0.001). After adjusting for STS risk score, CR (HR 1.82; 95% CI 1.02-3.09), PR (HR 2.59; 95% CI 1.38-4.57) and NR (HR 10.31; 95% CI 2.49-28.40) after AKI remained significantly associated with increased risk of 2-year mortality.

Conclusion: In a cohort of patients undergoing TAVR for aortic stenosis, increased mortality was observed in all AKI patients and there was a progressively higher risk of death reversely correlating with the extent of AKI recovery.
Role of Elevated Red Cell Distribution Width On Acute Kidney Injury Patients after Cardiac Surgery

Zhouping Zou¹, Jiarui Xu¹, Yi Fang¹, Bo Shen¹, Yimei Wang¹, Zhonghua Liu¹, Jianzhou Zou¹, Jie Teng¹, Xiaqiang Ding¹, Chunsheng Wang²

¹Department of Nephrology, Zhongshan hospital, Fudan University, Shanghai, Shanghai, China
²Department of cardiology surgery, Zhongshan hospital, Fudan University, Shanghai, Shanghai, China

Objective
This research was to explore the association between the elevated red cell distribution width (RDW) and the risk of morbidity and mortality rate for developing acute kidney injury after cardiac surgery (CS-AKI).

Methods
Clinical data of 10274 patients undergoing cardiac surgery, which included demographic data of pre-operation, intra-operation, post-operation were prospectively collected from January 2009 to December 2014. AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) and was staged according to the serum creatinine (Scr) and urine output. The elevated RDW was defined as the difference between RDW of 24 hours after cardiac surgery and the latest RDW before cardiac surgery.

Results
The mean age of the patients was 53.3±13.6 years. The overall CS-AKI incidence was 32.8% (n=3365) with a hospital mortality of 5.5% (n=185). The elevated RDW in AKI patients was higher than those without AKI [0.5% (0.1%,1.0%) vs 0.3% (0.0,0.6%), P<0.001]. The elevated RDW were 0.4% (0.1%,0.9%), 0.5% (0.2%,1.0%), 0.8% (0.3%,1.7%) in AKI 1,2,3 stage, respectively (P=0.02). The elevated RDW in AKI patients who died during the hospitalization was higher than those who survived[1.1% (0.4%,2.0%) vs 0.4% (0.1%,0.9%), P<0.001, respectively] ; In contrast, no significant difference in elevated RDW was found in the non-AKI patients between the death and survival groups [0.4% (-0.1%,0.9%) vs 0.3%(0.0,0.6%), P=0.875, respectively]. The independent risk factors that were computed from the multivariate logistic regression model were age, gender, body mass index(BMI), blood urea nitrogen(BUN), elevated RDW, uric acid, CPB(additional 30min). Estimated the ROC AUC showed that elevated RDW had moderate discriminative power for AKI development and hospital mortality (AUC = 0.600, 0.714, respectively).

Conclusion
The elevated RDW may be an independent prognostic factor for development, severity, and poor prognosis of AKI after cardiac surgery. Also, it may be efficient to early diagnose and predict prognosis of AKI after cardiac surgery by enhancing the supervision of elevated RDW.
Blood Urea Nitrogen to serum Creatinine ratio is an accurate predictor of outcome in Diarrhea – associated Hemolytic Uremic Syndrome

Werner Keenswijk\textsuperscript{1}, Jill Vanmassenhove\textsuperscript{1}, Ann Raes\textsuperscript{1}, Evelyn Dhont\textsuperscript{1}, Johan Vande Walle \textsuperscript{1}

\textsuperscript{1}Ghent University Hospital, Ghent, Belgium

Diarrhea-associated Hemolytic Uremic Syndrome (D+HUS) is a common thrombotic microangiopathy during childhood and early identification of parameters predicting poor outcome could enable timely intervention.

This study aims to establish the accuracy of BUN-to-serum Creatinine ratio at admission, in addition to other parameters in predicting the clinical course and outcome.

Records were searched for children between 1st January 2008 and 1st January 2015 admitted with D+HUS. A complicated course was defined as developing one or more of the following: neurological dysfunction, pancreatitis, cardiac or pulmonary involvement, hemodynamic instability and hematologic complications whilst poor outcome was defined by death or development of Chronic Kidney Disease. 34 children were included from which 11 with a complicated disease course/ poor outcome. Risk of a complicated course/ poor outcome was strongly associated with oliguria (p=0.000006) and hypertension (p=0.00003) at presentation. In addition, higher serum Creatinine (p=0.000006) and sLDH (p=0.02) with lower BUN-to-serum Creatinine ratio (p=0.000007) were significantly associated with development of complications. A BUN-to-sCreatinine ratio $\leq 40$ at admission was a sensitive and highly specific predictor of a complicated disease course/ poor outcome.

Conclusion: A BUN-to-serum Creatinine ratio can accurately identify children with D+HUS at risk for a complicated course and poor outcome.
A 2-year old Boy Presenting with Circulatory Failure, a Case Report of Streptococcal Toxic Shock Syndrome

Werner Keenswijk1, Johan Vande Walle1

1Ghent University Hospital, Ghent, Belgium

This is a report of a 2-year old boy referred to the PICU with circulatory failure and Acute Kidney Injury (AKI). In the preceding days diarrhea and fever were present. At presentation a very ill but still responsive child with cyanosis of hands and feet, tachycardia and respiratory distress was seen. Oxygen saturation and blood pressure could not be obtained probably because of poor circulation. Several purpuric lesions on his face, hands and scrotum were seen. His blood count showed leukocytosis with normocytic anemia and thrombocytopenia. Elevated serum Creatinine, BUN and liver enzymes were seen in addition to high Creatine Kinase (CK) and LDH levels. There was considerable coagulopathy and low Complement component 3 (C3) levels. He received immediate fluid resuscitation and antibiotics but deteriorated and was placed on mechanical ventilation with addition of vasopressors. His condition improved over the next two days but fluid overload and worsening of AKI dominated the clinical picture with increasing CK levels. Sepsis, atypical Hemolytic Uremic Syndrome and Lupus nephritis were important differential diagnostic considerations. The timing and modality of renal replacement therapy in light of fluid overload and hemodynamic instability provided an additional clinical challenge. We decided to start Continuous Venovenous Hemofiltration (CVVH) even though eGFR was >20 ml/min/1.73m² in light of significant fluid overload. Ultrafiltration was gradually increased and CVVH was continued for 11 days without significant problems.

Blood cultures remained negative but serology showed very high Anti Streptolysin O titers leading to the diagnosis of Toxic shock syndrome caused by Group A β-haemolytic streptococcal infection. Streptococcal toxic shock syndrome (STSS) is a toxin mediated life threatening illness characterized by acute hypotension, coagulopathy, renal dysfunction, increased liver enzymes, respiratory distress and soft tissue necrosis or myositis and an erythemato-macular rash. STSS is rare in early childhood and associated with a high case fatality rate (30-60%). Several recent pediatric critical care studies emphasize that timely initiation of renal replacement therapy in light of fluid overload is an important treatment strategy in preventing AKI-related mortality. He recovered completely and was discharged in good condition.
Another Atypical Case of Acute Kidney Injury or not?

Werner Keenswijk1, Johan Vande Walle1

1Ghent University Hospital, Ghent, Belgium

A 12-year old boy presented at the pediatric department with persistent non bilious vomiting and anuria. There was no fever or diarrhea and no signs of a respiratory infection. His medical history was negative besides episodes of vomiting during periods of stress from the age of 7 years. At physical examination moderate dehydration was seen. His laboratory results showed metabolic alkalosis and elevated serum Creatinine and BUN with hyperphosphataemia and hyperparathyroidism. His urinalysis didn’t show abnormalities. A renal ultrasound showed large kidneys with increased cortical echogenicity and corticomedullary differentiation. After IV rehydration he recovered well clinically with normalization of diuresis and cessation of vomiting. Hyperphosphataemia and hyperparathyroidism together typically are more associated with CKD than AKI and the ultrasound image was atypical for acute tubular necrosis. We decided to perform a renal biopsy which showed normal glomeruli but tubules filled with amorphous material consistent with the microscopic presentation of hyperoxaluria. He was suspected of Primary Hyperoxaluria and treatment was commenced consisting of pyridoxine (Vitamine B 6), hyperhydration and magnesium supplementation. Genetic testing for Primary Hyperoxaluria was negative. We noticed that his growth chart showed stunted growth from the age of 9 years and he confirmed to having episodes of vomiting almost every night for the past 2 years. A hypotonic duodenography showed subobstruction at the duodeno-jejunal junction and this was confirmed at gastroscopy where a complete torsion of the distal duodenum and stomach traction was seen. On laparascopy a malrotation with chronic volvulus without vascular compromise were seen and corrected. The hyperoxaluria was thought to be secondary to the chronic intermittent intestinal obstruction with malabsorption. Enteric hyperoxaluria is responsible for 5% of cases of hyperoxaluria and is often seen secondary to (fat) malabsorption with increased enteric oxalate absorption. It is usually secondary to conditions such as intestinal surgery, bacterial overgrowth syndrome and Inflammatory Bowel Disease. After surgery his growth improved with cessation of vomiting and serum Creatinine settling around 0.9 mg/dl (CKD stage 2).
An Atypical Case of a 2 year- old boy with Acute Kidney Injury, A Race Against Time

Werner Keenswijk¹, Johan Vande Walle¹

¹Ghent University Hospital, Ghent, Belgium

An interesting report of a 2-year old boy with persistent spiking fever and signs of acute kidney injury (AKI) is presented.

Initially he had presented with high fever, respiratory symptoms, vomiting, abdominal pain and cervical lymphadenopathy. He was treated with oral amoxicillin and Ibuprofen for a suspected upper respiratory tract infection but had to be admitted to a local hospital 3 days later because of persistent fever. Bacterial sepsis was suspected and antibiotics were switched to intravenous amoxicillin-clavulanate but without improvement.

His condition worsened and high spiking fever persisted even though repeated cultures remained negative. An elevated serum creatinine and BUN were also noted and suspicion of a tubulointerstitial nephritis secondary to sepsis arose. Upon presentation an ill looking tachycardic child was noted with a normal blood pressure, normal oxygen saturation. Additionally bilateral conjunctivitis, periorbital edema, a hyperemic pharynx, dry cracked lips with blood crusts and cervical lymphadenopathy were also noted. Several petechiae were noticeable on his shoulders and axillary pits. His laboratory results showed slight anemia and thrombopenia with leukocytosis with significantly elevated C-reactive protein (282 mg/L). Elevated serum Creatinine (2.0 mg/dl) and Blood Urea Nitrogen (103 mg/dl) was seen but electrolytes were within normal range. In addition increased coagulation times and slightly increased liver enzymes were seen. Renal ultrasound showed enlarged swollen kidneys with increased corticomedullary differentiation suggestive of renal vasculitis.

Although in the differential diagnosis, septic AKI was initially suspected, Kawasaki disease (KD) was eventually considered as the working diagnosis, leading to IV Immunoglobulin administration even though the patient at the time did not completely fulfil the criteria. Fever subsided and renal function recovered soon thereafter. He developed peeling of fingertips of hands with severe thrombocytosis in the second week and with this fulfilled the criteria of complete KD. We present this case aiming to increase awareness amongst clinicians concerning AKI as a potential manifestation of Kawasaki disease hereby enabling timely treatment to prevent the potentially fatal complications of this disease. In addition this case also illustrates the potential added value of early ultrasound imaging in differentiating causes of AKI.
Daytime continuous veno-venous hemofiltration as a treatment for tumorlysis syndrome in children

Yamei Wang¹, Yuhong Tao¹

¹Department of Pediatrics, West China Second University Hospital, Sichuan University; Chengdu, Sichuan, China

Background: This study aimed to evaluate the therapeutic efficacy and safety of continuous veno-venous hemofiltration (CVVHF) for the treatment of tumor lysis syndrome (TLS) in children.

Methods: Eight TLS patients who were hospitalized in West China Second University Hospital of Sichuan University for hemopurification between January 2011 and July 2015 were enrolled and treated with CVVHF for 8–12 h during the daytime every day. Their urine output, renal function, serum electrolytes, uric acid levels, and adverse reactions to hemopurification were monitored.

Results: The eight patients enrolled were aged 5–14 years; seven were male and one was female. There were five cases of acute lymphoblastic leukemia and three cases of lymphoma. All patients exhibited acute kidney injury (AKI), including four cases of stage 2 AKI and four cases of stage 3 AKI. All patients also had hyperphosphatemia, and there were four cases of hyperkalemia, four cases of hyperuricemia, and two cases of hypocalcemia. All patients received 1–10 CCVHF treatments with a total treatment duration of 8–80 h. All patients’ urine output, renal function, serum uric acid levels, potassium, phosphate, and calcium levels all returned to normal, but recovery of renal function is relatively slow. No significant adverse reactions were found after treatment following discharge from hospital. In the 6-month follow-up period, seven patients survived and one died from pneumonia caused by Stenotrophomonas maltophilia.

Conclusions: Daytime CVVHF is a safe and effective treatment for TLS in children.
Tim-3/Gal-9 pathway activation ameliorates renal ischemia reperfusion injury by shifting the balance of activated CD4+ T cell immune response in mice

Yamei Wang¹, Yuhong Tao¹

¹Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China

Background: Renal ischemia reperfusion injury (IRI) is characterized by kidney inflammation, and activation of CD4+ T cells play a pivotal role in the development of renal IRI. Lectin family member galectin-9 (Gal-9) is identified as a T-cell immunoglobulin domain and T mucin domain protein-3 (Tim-3) ligand, and Tim-3/Gal-9 interaction acts as a specific inhibitor of immune response.

Objective The purpose of this study was to study whether activation of Tim-3/Gal-9 pathway can ameliorate renal IRI by shifting the balance of activated activated CD4+ T cell immune response in mice.

Methods: Expression of renal Gal-9 and Tim-3 were detected in mice with left renal IRI at baseline, day 3, 10 after renal IRI. The percentage of Th1, Th17 and Foxp3+ Tregs in KMNCs and their mRNA expression in kidney also were measured. Then, recombinant adeno-associated virus 9 (rAAV9) carrying Gal-9 was injected to mice two weeks before kidney IRI surgery to overexpress Gal-9 and activate Tim-3/Gal-9 pathway. Then, the CD4+ T cell subsets and cytokines in kidney were evaluated at day 3 and 10.

Results: The expression of Gal-9 and Tim-3 in the IR kidney at day 3 and 10 increased significantly compared with injured kidney at baseline (P<0.05). The percentage of Foxp3+ Treg in CD4+ T cells and Foxp3 mRNA was up-regulated with time. Compared with normal control kidney, the mRNA levels of Foxp3, Gal-9 and Tim-3 of kidney at day 3, 10 after renal IRI were increased in IRI kidney. Compared with empty virus group at 3 days and 10 days after IRI, over-expression of Gal-9 can reduce tubular damage in the healing phase of renal IRI. Protein plex results showed that the expression levels of inflammatory cytokines including TNF-α, IFN-γ, IL-17 and IL-6 was decreased, while the expression level of IL-10 was increased. The mRNA level of Foxp3 in kidney, the percentage of Foxp3+ Treg cells in IRI kidneys was increased. However, the proportions of Th1, Th17 cells and the gene levels of T-bet and RORyt were decreased. In the bilateral renal IRI model, the mice mortality was decreased after rAAV-Gal-9 intervention.

Conclusions: Activation of Tim-3/Gal-9 pathway can ameliorate damage in kidney and increase the survival rate of mice after renal IRI, inhibit the Th1 and Th17 cell-mediated immune responses, and promote the proliferation of Foxp3+ Treg in kidney after renal IRI, which may be an important mechanism for renal protection of Gal-9/Tim-3 pathway activation.
Autophagy protects against contrast induced tubular epithelial injury

Moo Yong Park\textsuperscript{1}, Byung Chul Yu\textsuperscript{1}, Soo Jeong Choi\textsuperscript{1}, Jin Kuk Kim\textsuperscript{1}, Seung Duk Hwang\textsuperscript{1}, Geum Ha Jang\textsuperscript{1}

\textsuperscript{1}Soonchunhyang University, Bucheon

Background
Radiocontrast-induced nephropathy (RCN) is common cause of acute kidney injury in hospital. However, preventing and treating strategies against developing RCN were very limited. The role of autophagy in the pathogenesis of RCN remains undetermined, therefore we investigated its role in RCN.

Methods
We examined the expression of autophagic and apoptotic proteins during progression of contrast (idoxanol) induced injury to renal tubular epithelial cells (RTEC). To determine protective role of autophagy against contrast induced injury, we inhibit autophagy with small interference RNA (siRNA) for ULK1, and measured the changes of cell viability and induction of apoptotic and autophagy protein for 48hr.

Results
After RTEC exposure to contrast media, cell viability was decreased at 3 hours, but increased after 24 hours and 48 hours. Apoptosis was observed as early as 1hr after contrast exposure as indicated by induction of caspase 3 and 8 and they were increased at 48hr. However, autophagy, indicated by LC3 and autophagy-related gene protein 7 (ATG7), was detected at 3hr after contrast exposure, and induction of LC3 and ATG7 were further increased up to 48hr. The increase in cell viability of RTEC, which was observed at 24 and 48 hours after RTEC exposure to contrast media, was suppressed by inhibiting autophagy with ULK1 siRNA.

Conclusions
Autophagy plays cytoprotective role in contrast induced RTEC injury and it may occur independently of apoptosis.

Plasma Concentration of Pro-enkephalin upon Admission to the Emergency Department Predicts Development of Acute Kidney Injury in Patients with Sepsis

Mari Rosenqvist\textsuperscript{1}, Joachim Struck\textsuperscript{2}, Andreas Bergmann\textsuperscript{2}, Olle Melander\textsuperscript{1}

\textsuperscript{1}Faculty of Medicine, Lund University, Sweden, \textsuperscript{2}Sphingotec GmbH, Hennigsdorf, Germany

BACKGROUND and OBJECTIVE: Plasma concentration of pro-enkephalin (pro-ENK) independently predicts incidence of chronic kidney disease in the population and in sepsis, pro-ENK has been shown to correlate strongly inversely with renal function and associate with acute kidney injury (AKI). Here, we tested if pro-ENK predicts development AKI and mortality in patients with sepsis admitted to the
Emergency Department (ED).

METHODS: We measured pro-ENK in 327 patients with sepsis (≥2SIRS criteria + suspected infection) upon admission to the ED at Skåne University Hospital, Malmö, Sweden and followed the patients for development of AKI within 7 days. Quartiles of pro-ENK (lowest quartile as referent) were related to risk of AKI development within 7 days using logistic regressions adjusted for age and sex. AKI was defined as a creatinine increase >44 µmol/L (>0.5 mg/dL) between any two measurements, requirement for acute dialysis or an increase in creatinine of >50% with an initial value >160 µmol/L (>2.0 mg/dL).

RESULTS: Fifty patients (15%) developed AKI within 7 days and the risk of AKI increased significantly with quartile of pro-ENK (P_trend<0.001). The odds ratio (OR) for AKI in the top (median pro-ENK=161 pmol/L, range 118-824 pmol/L) versus bottom (median pro-ENK 44.9, range 10.9-58.1 pmol/L) quartile of pro-ENK was 18.8 (95% CI=5.05-69.8; P<0.001). When excluding patients who had known renal disease prior to the ED visit (n=22), the result remained highly significant (P_trend over quartiles <0.001) and patients in the top versus bottom quartile of pro-ENK had an OR of 23.2 (95% CI=5.8-92.6; P<0.001). Patients who died within 7 days (n=15, 4.6%) had significantly higher pro-ENK than 7-day survivors (P=0.003) and 47% of patients who died had developed AKI.

CONCLUSION: Pro-ENK measured upon admission to the ED in sepsis patients strongly predicts development of AKI within 7-days, especially in patients without prior renal disease. AKI occurs in almost half of sepsis patients who die during the first 7 days of hospitalization.

---

49

Long term effects of remote ischemic preconditioning on kidney function in high risk cardiac surgery patients: Follow-up results from the RenalRIP trial

Alexander Zarbock¹, John A Kellum², Mira Küllmar¹, Dennis Görlich³, Melanie Meersch¹

¹Department of Anesthesiology, Intensive Care and Pain Medicine, University of Muenster, Muenster, Germany, ²Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, PA, USA, ³Institute of Biostatistics and Clinical Research, University of Münster, Münster, Germany

Purpose of the study: In a multicenter randomized trial, we enrolled patients at high risk for acute kidney injury (AKI) as identified by a Cleveland-Clinic-Foundation-Score ≥6. We enrolled 240 patients at four hospitals and randomized them to remote ischemic preconditioning (RIPC; three cycles of 5 min ischemia and 5 min reperfusion in one upper arm after induction of anesthesia) or sham-RIPC (control). We found that RIPC reduced AKI in high risk patients undergoing cardiac surgery. We now report on the effects of RIPC on 90-day-outcomes.

Methods: In this follow-up study to the RenalRIP-trial, we examined the effect of RIPC on the composite endpoint major adverse kidney events consisting of mortality, need for renal replacement therapy, and persistent renal dysfunction (≥ 0.5 mg/dl increase in serum creatinine) at 90 days (MAKE90). Secondary outcomes were persistent renal dysfunction and dialysis dependence in patients with AKI.

Results: RIPC significantly reduced the occurrence of MAKE at day 90 (17/120 (14.2%)) compared to control (30/120 (25.0%); absolute risk reduction, 10.8%; 95% CI: 0.9%-20.8%; n=0.034). In those
patients who developed AKI after cardiac surgery 2/38 subjects in the RIPC group (5.3%) and 13/56 subjects in the control group (23.2%) failed to recover renal function by day 90 (absolute risk reduction, 17.9%; 95% CI, 4.8%-31.1%; p=0.020). AKI biomarkers were also increased in patients reaching the MAKE at day 90 endpoint compared to patients who did not.

Conclusion: Remote ischemic preconditioning significantly reduced the 3-month incidence of a composite endpoint MAKE at day 90 consisting of mortality, need for renal replacement therapy, and persistent renal dysfunction in high risk patients undergoing cardiac surgery. Furthermore, remote ischemic preconditioning enhanced renal recovery in patients with AKI.

50

Urinary Exosomal Activating Transcriptional Factor 3 as the Early Diagnostic Biomarker for Sepsis-Induced Acute Kidney Injury

Wiwat Chancharoenthana¹, Tanaporn Panich², Poorichaya Somparn³, Jiraphorn Issara-Amphorn ², Nattiya Hirankarn³, Asada Leelahavanichkul³

¹Division of Nephrology and Hypertension, Department of Medicine, Princess Chulabhorn College of Medical Sciences, Chulabhorn Royal Academy of Science (CRAS), Bangkok, Tha, ²Immunology Unit, Department of Microbiology, Chulalongkorn University, Bangkok, Thailand 10330, ³Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand 10330

Background: An early sepsis-induced acute kidney injury (sepsis-AKI) biomarker is currently in needed. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is a candidate of sepsis-AKI biomarker but with different cut-point values. Urinary exosomal activating transcriptional factor 3 (uATF3) has been mentioned as an interesting biomarker.

Methods: We conducted experiments in mice and a prospective, multicenter study in patients as a proof of concept that urine exosome is an interesting biomarker. An early expression of ATF3 in kidney of CD-1 mice at 6h after cecal ligation and puncture implied the possibility of uATF3 as an early sepsis-AKI biomarker. Increase serum creatinine (Scr) >0.3 mg/dL from the baseline was used as an AKI diagnosis and urine was analyzed for uATF3 and uNGAL. Patients with baseline Scr at admission >1.5 mg/dL were excluded.

Results: The analysis showed higher Scr, uNGAL and uATF3 in patients with sepsis-AKI in comparison with patients with sepsis-non-AKI and healthy volunteers. A fair correlation, r² =0.47, between uATF3 and uNGAL was showed in sepsis-AKI group with Scr >2 mg/dL. To see if uATF3 could be an early sepsis-AKI biomarker, urine sample was collected daily during the first week of the admission. In sepsis-AKI and sepsis-non-AKI groups, uNGAL were 367±43 ng/mL and 183±23 ng/mL, respectively; and uATF3 were 19±4 ng/mL and 1.4±0.8 ng/mL, respectively. With the mean value of uNGAL and uATF3 in sepsis AKI as a cut-off level, AUROC of uNGAL and uATF3 were 64% (95%CI 0.54 to 0.74) and 84% (95%CI 0.77 to 0.91), respectively.

Conclusions: Urine exosome is an interesting source of urine biomarker and uATF3 is an interesting sepsis-AKI biomarker.

figure on following page
Hyperuricemia increases the risk of acute kidney injury: a systematic review and meta-analysis

Xialian Xu¹, Jiachang Hu¹, Nana Song¹, Rongyi Cheng¹, Ting Zhang¹, Xiaoqiang Ding¹

¹Zhongshan Hospital of Fudan University

Background: Mounting evidence indicated that the elevated serum concentration of uric acid was associated with an increased risk of acute kidney injury (AKI). Our goal was to systematically evaluate the correlation of serum uric acid (SUA) level and incidence of AKI by longitudinal cohort studies.

Methods: We searched electronic databases and the reference lists of relevant articles. 18 cohort studies with 75,200 patients were analyzed in this random-effect meta-analysis. Hyperuricemia was defined as SUA levels greater than 360-420µmol/L (6-7 mg/dl), which was various according to different studies. Data including serum uric acid, serum creatinine, and incidence of AKI and hospital mortality were summarized using random-effects meta-analysis.

Results: The hyperuricemia group significantly exerted a higher risk of AKI compared to the controls (odds ratio OR 2.24, 95%CI 1.76-2.86, p<0.01). Furthermore, there is less difference of the pooled rate of AKI after cardiac surgery between hyperuricemia and control group (34.3% vs 29.7%, OR 1.24, 95%CI 0.96-1.60, p=0.10), while the rates after PCI were much higher in hyperuricemia group than that in control group (16.0% vs 5.3%, OR 3.24, 95%CI 1.93-5.45, p<0.01). In addition, there were significant differences in baseline renal function at admission between hyperuricemia and control groups in most of the included studies. The relationship between hyperuricemia and hospital mortality was not significant. The pooled pre-operative SUA levels were higher in AKI group than that in the non-AKI group.

Conclusions: Elevated SUA level showed an increased risk for AKI in patients and measurements of SUA may help stratify risks for AKI in these patients.
A Novel Adsorbent System Rapidly Clears Amlodipine from Human Blood

Vincent J Capponi1, Wendell T Young1, Eric J Lavonas2, Phillip P Chan1

1CytoSorbents Medical, Inc., 2Denver Health Medical Center, Denver, CO

Abstract:
Background: Calcium channel blockers are not effectively removed by current extracorporeal removal techniques, such as hemodialysis or charcoal hemoperfusion. CytoSorb is a perfusion cartridge containing a novel sorbent polymer, approved and marketed in Europe for the removal of excess cytokines in sepsis.

Objectives: To determine whether a cartridge containing polymeric beads can efficiently clear amlodipine from human blood.

Methods: 20 mg amlodipine was added to 4 liters of citrate-anticoagulated whole human blood and stirred to equilibrate. This blood was then recirculated through a Cole-Parmer Masterflex L/S Digital Drive blood circuit at a rate of 300 mL/minute. In the experimental arm, a saline-primed 300-mL CytoSorb cartridge was installed in-line with the circuit. Whole blood samples were obtained prior to amlodipine instillation, following equilibration, and after 0, 15, 30, 60, 120, and 180 minutes of blood recirculation. Whole blood amlodipine concentrations were determined using previously-validated ultra performance liquid chromatography methods. The lower level of quantification (LLQ) was 0.25 mg/L whole blood. Two experimental and two control runs were performed.

Results: All quality control checks were within 15% of their respective nominal values. At the start of recirculation, whole blood amlodipine concentrations were 5.44 (+/-0.63) mg/L in the experimental and 4.70 (+/-0.16) mg/L in the control arms. In the experimental arm, amlodipine concentrations were 3.20 (+/-0.42) mg/L after 15 minutes of recirculation, 1.93 (+/-0.15) mg/L at 30 minutes, 1.02 (+/-0.36) mg/L at 60 minutes, 0.62 (+/-0.15) mg/L at 120 minutes, and 0.35 (+/-0.12) mg/L after 180 minutes. Amlodipine removal was therefore 41.3% after 15 minutes of perfusion, 64.6% after 30 minutes, 81.3% after 60 minutes, 88.7% after 120 minutes, and 93.5% after 180 minutes of recirculation. Amlodipine concentrations in the control arms were 107.2% of baseline after 180 minutes.

Conclusion: Perfusion over polymer beads efficiently removes amlodipine from whole human blood.

A Novel Adsorbent System Rapidly Clears Verapamil from Human Blood

Vincent J Capponi1, Wendell T Young1, Eric J Lavonas2, Phillip P Chan1

1CytoSorbents Medical, Inc., 2Denver Health Medical Center, Denver, CO

Abstract:
Background: Calcium channel blockers are not effectively removed by current extracorporeal removal techniques, such as hemodialysis or charcoal hemoperfusion. CytoSorb is a perfusion cartridge containing a novel sorbent polymer, approved and marketed in Europe for the removal of excess cytokines in sepsis.
Objectives: To determine whether a cartridge containing polymeric beads can efficiently clear verapamil from human blood.

Methods: 10 mg verapamil was added to 4 liters of citrate-anticoagulated whole human blood and stirred to equilibrate. This blood was then recirculated through a Cole-Parmer Masterflex L/S Digital Drive blood circuit at a rate of 300 mL/minute. In the experimental arm, a saline-primed 300-mL CytoSorb cartridge was installed in-line with the circuit. Whole blood samples were obtained prior to verapamil instillation, following equilibration, and after 0, 15, 30, 60, 120, and 180 minutes of blood recirculation. Whole blood verapamil concentrations were determined using previously-validated ultra performance liquid chromatography methods. The lower level of quantification (LLQ) was 0.25 mg/L whole blood. Two experimental and two control runs were performed.

Results: All quality control checks were within 15% of their respective nominal values. At the start of recirculation, whole blood verapamil concentrations were 2.50 (+/- 0.09) mg/L in the experimental and 2.23 (+/- 0.31) mg/L in the control arms. In the experimental arm, verapamil concentrations were 0.87 (+/- 0.001) mg/L at 15 minutes, 0.31 (+/- 0.04) mg/L at 30 minutes, and below LLQ thereafter. Verapamil removal was therefore 65.1% after 15 minutes of perfusion, 87.4% after 30 minutes, and 90% or greater at 60, 120, and 180 minutes. Verapamil concentrations in the control arm decreased 10.5% from baseline at 180 minutes.

Conclusion: Perfusion over polymer beads efficiently removes verapamil from whole human blood.

54

A Risk Scoring Model To Predict Progression Of Renal Dysfunction In Patients With Chronic Kidney Disease Complicated With Contrast-induced Nephropathy

Seonghoon Kim¹, Seung Don Baek¹, Eun Kyoung Lee², So Mi Kim², Jai Won Chang¹

¹Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, ²Dankook University Hospital, Dankook University College of Medicine, Cheonan, Republic of Korea

Introduction
The contrast-induced nephropathy (CIN) occurs more frequently in patients with lower estimated glomerular filtration rate (eGFR). Since CIN may be associated with the progression of chronic kidney disease (CKD), it would be important to predict the risk of irreversible renal damage prior to contrast-enhanced Computed Tomography (CT).

Methods
We retrospectively analyzed 18,278 enhanced CTs performed in 9,097 CKD patients with estimated GFR less than 60 mL/min/1.73 m² for at least 3 months, from January 2013 to December 2014. We investigated 1-year renal outcomes in CKD patients complicated by CIN (increase ≥25% and/or ≥0.5 mg/dL in serum creatinine within 3 days after CT) between the progression (defined as reduction of estimated GFR ≥25% at 1 year) and the non-progression groups. A risk score of 4, 5, 6, 7, or 7 was assigned to diabetes, baseline estimated GFR <45 mL/min/1.73 m², hypertension, repeated contrast exposure, and congestive heart failure, respectively. Using the sum of risk scores, we developed a risk scoring model to predict progression of renal dysfunction in CKD patients who were complicated by CIN.

Results
The overall occurrence of CIN was 5.8% (1,051/18,278) of all enhanced CTs performed, in 7.6% (689/9,097) of the total CKD patients. Among 689 patients, 465 were excluded due to incomplete data.
follow-up loss, or death. Among the remaining 224 patients, 70 (31.3%) patients had progression of renal dysfunction at 1 year. The aggravation of azotemia at 1-month later after CIN compared with baseline serum creatinine level, was more severe in the progression group (1.84 ± 0.75 mg/dL at baseline vs. 2.46 ± 1.13 mg/dL at 1-month, p < 0.001) than in the non-progression group (1.67 ± 0.60 vs. 1.69± 0.83, p = 0.827). The risk scoring model demonstrated that the risk of progression of renal dysfunction increased with the sum of risk score in CKD patients complicated by CIN (c statistic = 0.735).

Conclusions
Although our risk scoring model needs to be validated in another population, our study suggested the possibility of predicting the risk of progression of renal dysfunction in CKD patients complicated by CT contrast administration.

55

Urinary TIMP-2 and IGFBP7 for the Prediction of Acute Kidney Injury Following Cardiac Surgery

yimei wang1, zhoupeng zou1, jifu jin1, jie teng1, jiarui xu 1, bo shen1, wuhua jiang1, zhe luo1, chunsheng wang1, xiaoqiang ding1

1Zhongshan Hospital, Fudan University, Shanghai, China

Background
Acute kidney injury (AKI) following cardiac surgery is common and associated with poor patient outcomes. Yet, early risk assessment for development of AKI remains a challenge. The combination of urinary tissue inhibitor of metalloproteinase 2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7) has been shown to be an excellent predictor of AKI following cardiac surgery, but reported studies are for predominately non-Asian populations. In this study, we investigated for the first time the ability of TIMP-2 and IGFBP7 to predict AKI in patients undergoing cardiac surgery at a tertiary care hospital in China.

Methods
Adult patients were prospectively enrolled at Zhongshan hospital in Shanghai, China. The primary analysis was prediction of AKI and stage 2-3 AKI (defined by Kidney Disease: Improving Global Outcomes criteria) by [TIMP-2]*[IGFBP7] measured 4 hours after postoperative ICU admission assessed using receiver operating characteristic curve (ROC) analysis. Kinetics of [TIMP-2]*[IGFBP7] following ICU admission were also examined in a subset of patients.

Results
We prospectively enrolled 57 cardiac surgery patients, of which 20 (35%) developed AKI and 6 (11%) developed stage 2-3 AKI. The area under the ROC curve (AUC) of [TIMP-2]*[IGFBP7] at 4 hours after ICU admission was 0.80 (95% confidence interval (CI): 0.68-0.91) for development of AKI and 0.83 (95% CI: 0.69-0.96) for development of stage 2-3 AKI. Urinary [TIMP-2]*[IGFBP7] values at 4 hours after ICU admission were significantly (p < 0.001) higher in patients who developed AKI than in patients who did not develop AKI (mean (standard error) of 1.08 (0.34) (ng/mL)2/1000 and 0.29 (0.05) (ng/mL)2/1000, respectively). The time-profile of [TIMP-2]*[IGFBP7] suggests the markers started to elevate by the time of ICU admission in patients who developed AKI and either decreased or remained flat in patients without AKI.
Conclusion
The combination of urinary TIMP-2 and IGFBP7 identifies patients at risk for developing AKI following cardiac surgery. The test performance reported previously from studies in the United States and Europe was confirmed in the Chinese patient population.

A Critical Appraisal of Acute Kidney Injury Clinical Practice Guidelines Using the AGREE II Instrument

Nigar Sekercioglu1, Reem Al-Khalifah2, Jason Busse1, Gordon Guyatt1

1McMaster University, Hamilton, Ontario, Canada, 2Pediatric Endocrinology, King Saud University, Riyadh, Saudi Arabia

Background & Purpose of the Study: Acute kidney injury (AKI) represents a rapid decline in kidney function as a result of kidney damage or failure, and is strongly associated with increased morbidity and mortality. Management of AKI, globally is highly variable due to knowledge-to-action gaps and inconsistent access to resources. Clinical practice guidelines can provide important guidance and, when evidence warrants strong recommendations, can help to minimize variability in care; however, evaluating the trustworthiness of recommendations requires appraisal of guideline quality. The objective of this systematic survey is to critically appraise clinical practice guidelines (henceforth referred to as guidelines) addressing management of AKI.

Methods: We systematically searched MEDLINE, the National Guideline Clearinghouse, Guideline International Network, and Turning Research into Practice, without language restrictions, up to December 2016. We imported all citations into the Covidence online software program. Guidelines that address diagnosis, monitoring or management of AKI in adult or pediatric populations were eligible for our review. We restricted our review to guidelines that generate their own recommendations, versus those that adapt or adopt existing guideline recommendations. We evaluated the most recent version of each guideline, if multiple versions existed. We excluded guidelines addressing prevention of AKI and those specific to kidney transplant recipients.

Teams of two reviewers, independently and in duplicate, screened titles and abstracts and potentially eligible full text reports to determine eligibility, and will appraise the reporting quality of AKI guidelines using the Advancing Guideline Development, Reporting and Evaluation in Health Care instrument II (AGREE). The AGREE II instrument (www.agreetrust.org) contains 23 items divided into six domains: scope and purpose (questions 1-3); stakeholder involvement (questions 4-6); rigour of development (questions 7-14); clarity of presentation (questions 15-17); applicability (questions 18-21); and editorial independence (questions 22-23) (Table 1). A seven-point scale is used to answer each question with a range of options from 1 (strongly disagree) to 7 (strongly agree). We will calculate standardized scores ranging from 0% to 100% for each domain. We will report mean values (SD) when data is normally distributed, and median values (inter-quartile range; IQR) when it is not.
Search Strategies:

A MEDLINE:
The search strategy for OvidSP MEDLINE (1946 to December Week 1 2016) retrieved a total of 1454 of which 1254 were unique references not duplicated in our other searches. The strategy includes a combination of MeSH descriptors and free text terms for AKI

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy for MEDLINE:

1 azotemia/ or azotemi*.mp. (3226)
2 uremia/ or uremi*.mp. (34373)
3 1 or 2 (372405)
4 acute kidney injury.mp. or exp Acute Kidney Injury/ (46170)
5 acute kidney injury/di, dt, ep, mo [Diagnosis, Drug Therapy, Epidemiology, Mortality] (10292)
6 (acute adj3 (kidney or renal)).ti,ab. (46219)
7 4 or 5 or 6 (62530)
8 3 or 7 (1138)
9 renal insufficiency, acute/ or acute failure, acute/ (38892)
10 8 or 9 (62530)
11 (systematic: review: or systematic: overview).tw. (105889)
12 guideline*.ti,ab. or practice guideline.pt. (277758)
13 11 or 12 (372405)
14 10 and 13 (1454)

Vitamin D and C deficiency is common in critically ill patients with severe acute kidney injury

Danielle Bear¹, Jennifer Summers², Katie Lei¹, Kathryn Chan¹, John Smith¹, Lynda Cameron¹, Janet Peacock², Marlies Ostermann¹

¹Guy's & St Thomas Hospital, ²NIHR Biomedical Research Centre, King's College London, Division of Health and Social Care Research, London SE1, UK

Background: Vitamin deficiency has been reported in patients with acute kidney injury (AKI) receiving continuous renal replacement therapy (CRRT). However, little is known about the vitamin status of patients with AKI not receiving CRRT. We aimed to investigate the degree and severity of vitamin deficiency in patients with AKI treated with and without CRRT.
Methods: We prospectively recruited adult patients with KDIGO AKI stage 2 or 3 admitted to the critical care units of two London teaching hospitals. Patients receiving total parenteral nutrition or vitamin supplements were excluded. Serial blood samples were taken to measure plasma concentrations of vitamin B1, B6, B12, C and D and folate during a 6-day follow up period. In an intention-to-treat analysis, we compared patients who were on CRRT at time of enrolment with those not on CRRT.

Results: Fifty-five patients were included in the analysis (31 patients with CRRT and 24 patients without CRRT). There were no significant differences in baseline characteristics between both groups. More than 50% of patients had plasma vitamin D and vitamin C concentrations below the reference range throughout the 6-day follow up period, including at baseline. (Figure 1) There were no significant differences between the CRRT and non-CRRT group.

Conclusions: Deficiency of Vitamin D and C is very common in patients with AKI and independent of treatment with CRRT. Further research is necessary to investigate the role of vitamin supplementation.
Risk Of Mortality And Acute Kidney Injury During Hospitalization After Major Surgery

Shengnan Li, Shu Wang, Xiaoyan Wen, John Kellum

1 Center for Critical Care Nephrology, CRISMA, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA, 2 Department of Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA

Background: Acute kidney injury (AKI) is a common postoperative complication. Recent studies have shown that, among ICU patients following major surgery, AKI occurred in 11.8-33%. Severity of AKI has shown to be independent risk factor for death. The aim of this study was to identify patients with increased risk for AKI and to determine potential modifiable risk factors that could be targeted.

Methods: In this observational cohort study, we analyzed data on 4120 patients admitted to any of 8 ICUs at the University of Pittsburgh Medical Center after major surgery (thoracic, vascular, general, neurosurgical and trauma) from 2000-2008. We extracted data on demographics, health characteristics and type of surgery. Outcomes were maximum AKI stage defined by full KDIGO criteria, ICU and hospital stay, 90 day and 1 year mortality and major adverse kidney events (MAKE: defined as composite of death, use of renal replacement therapy, or persistence of renal dysfunction truncated at 1 year). Multivariate logistic regression was used to determine preoperative risk factors.

Results: 2744(66.7%) patients developed AKI. Patients developing AKI were older (61±17 vs 54±18 years), but with similar baseline serum creatinine (1.12±0.68 vs 0.83±0.23 mg/dl). Preoperative risk factors include age, gender, history of diabetes, hypertension and liver transplantation, anemia, aminoglycosides, and diuretics. Compared to patients who did not develop AKI, those patients with postoperative AKI experienced prolonged ICU (10 vs 4 days) and hospital (24 vs 12 days) stay, higher 1 year mortality (29.0% vs 15.6%), and more were MAKE positive (29.3% vs 15.6%).

Conclusions: Advanced age, male sex, and history of diabetes, hypertension, liver transplantation, and anemia, as well as use of aminoglycosides and diuretics all identified high risk for postoperative AKI. Anemia and blood pressure are potential modifiable risk factors.

Associations Between Fluid Balance and Outcomes in Critically Ill Children: A Systematic Review and Meta-Analysis

Alobaidi Rashid, Catherine Morgan, Rajit K Basu, Erin Stenson, Robin Featherstone, Sumit R Majumdar, Sean M Bagshaw

1 University of Alberta, Edmonton, AB, Canada, 2 Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA

Background: After initial resuscitation of critically ill children, excessive fluid accumulation may lead to adverse events and increased mortality. However, the available evidence has not yet been rigorously synthesized. Therefore, we undertook a formal systematic review and meta-analysis.
Methods:
We searched MEDLINE, EMBASE, Cochrane Library, trial registries, and selected grey literature from inception through July 2016. We included observational studies and trials of children admitted to pediatric intensive care units (PICU) that described fluid balance or fluid overload (FO) and that reported outcomes of interest. Primary outcome was mortality, secondary outcomes included measures of treatment intensity and organ failure. Two reviewers independently screened studies and extracted data.

Results:
Of 6814 studies identified, 37 studies (31 cohort studies, 4 case-control studies, and 2 trials; n=6368 children) included. Six fluid metrics were used to describe fluid balance: cumulative or peak %FO (30 studies), cumulative or peak % weight change (4 studies), net fluid balance in relation to weight (5 studies), and net fluid balance in relation to body surface area (1 study). Twenty-one studies (57%) explicitly defined FO thresholds: >5% (n=3), >10% (n=14), >15% (n=1), and >20% (n=9). Fluid overload, however defined by investigators, was associated with increased in-hospital mortality (Odds Ratio [OR], 3.71; 95% CI, 2.67-5.17; p <0.0001, I2=41%, 14 studies, n=2307). Survivors had lower FO% than non-survivors (Mean Difference [MD], -7.5; 95% CI, -10.4 to -4.6; P<0.0001, I2=80%, 18 studies, n=2228). After adjusting for illness severity, there was 7% increase in mortality for every 1% increase in FO (OR, 1.07; 95% CI, 1.03-1.11; P=0.001, I2=64%, 7 studies, n=2580). Fluid overload was associated with longer duration of mechanical ventilation (MD, 1.13 days; 95% CI, 0.68-1.59; P<0.0001, I2=93%, 4 studies, n=623), prolonged mechanical ventilation (>72hrs) (OR,1.89; 95% CI, 1.05-3.40; P=0.03, I2=0%, 2 studies, n=468), and acute kidney injury (OR, 2.98; 95% CI, 1.88, 4.73; P<0.0001, I2=23%, 4 studies, n=1297).

Conclusion:
There were considerable variations in the methods used to define FO in critically ill children. Nevertheless, FO is significantly associated with morbidity and mortality in critically ill children. Future research to define FO and assess interventional strategies to prevent or mitigate avoidable fluid accumulation is needed.
**IGFBP-7/TIMP-2 and pro-enkephalin levels in Acute kidney injury: results from the FROG ICU study**

Matthieu Legrand¹, Etienne Gayat², Malha Sadoune³, Antoine Vieillard-Barron⁵, Jean-Marie Launay³, Marie-Celine Fournier³, Nicolas Deye⁶, Alexandre Mebazaa²

¹Anesthesiology, Critical Care and Burn Unit, St-Louis Hospital, Paris, France, ²Anesthesiology and Critical Care, Lariboisière hospital, Paris, ³Inserm 942, ⁵ICU, Hôpital Ambroise-Paré, Boulogne-Billancourt, ⁶Medical ICU, Lariboisière hospital

Introduction: Acute kidney injury (AKI) has been associated with an increased risk of death and poor outcome in critically ill patients. Plasma penKid has been suggested to be a biomarker of interest of AKI. The objective of this study was to explore the predictive value of PenKid for AKI in a cohort of critically ill patients and to compare with an AKI biomarker assay (Nephrocheck®, combo of insulin-like growth factor binding protein-7 and Tissues inhibitor metalloprotease-2) considered as a sensitive and specific biomarker of AKI.

Methods: This was an ancillary study of The French and euRopean Outcome reGistry in Intensive Care Units (FROG-ICU) study was a multicenter observational study. The protocol has previously been described [2]. After excluding patients who died during the first 24 hours, with chronic kidney disease, and patients with missing Scr at admission, 1836 patients remained. The present cohort includes a random sampling of 200 patients based on the renal-item of the Simplified organ failure assessment (renalSOFA=0, n=80; renalSOFA =1, n=40; renalSOFA =2, n=40; renalSOFA =3, n=40). Primary endpoint was AKI, defined by KDIGO definition using the creatinine criteria. The association between Nephrocheck® level and AKI as assessed by univariate analysis and with area under the ROC curve.

Results: Patients characteristics are summarized in Table 1. PenKid level showed a stepwise increase with renalSOFA stage at admission. Median (and IQR) of PenKid in patients with renalSOFA = 0 was 47 (33-67)- within the normal range, renalSOFA = 1 was 86 (62-112), renalSOFA = 2 was 116 (87-159), renalSOFA = 3 was 248 (135-305), p<0.0001. Nephrocheck in patients with renalSOFA = 0 was 0.44 (0.21-0.97), renalSOFA = 1 was 0.75 (0.28-2.04), renalSOFA = 2 was 0.64 (0.28-2.47), renalSOFA = 3 was 1.79 (0.36-4.27), p<0.0001 while Scr was 80 (60-90), 140 (140-170), 230 (210-250) and 400 (380-430) µmol/L respectively, p<0.0001. 057 pg/mL [30-114] and 110 pg/mL [63-220], respectively (p<0.001). For Nephrocheck, Odd ratio for AKI was 1.41 [0.74-2.81] 0.3-2, p=0.30 and 7.2 [2.7-18.3] with >2.0; p<0.001. Area under the ROC curve for AKI was 0.832 [0.771 - 0.885] for PenKid and 0.697 [0.62 - 0.77] for Nephrocheck.

Conclusion: PenKid level appears to be closely associated to AKI stage in ICU patients and be a biomarker of renal function in opposition to Nephrocheck, biomarkers of renal injury.

*table and figure on following page*
<table>
<thead>
<tr>
<th>All patients (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Septic shock</td>
</tr>
<tr>
<td>SAPS-2</td>
</tr>
<tr>
<td>In-ICU mortality</td>
</tr>
<tr>
<td>Kidney biomarkers</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
</tr>
<tr>
<td>Creatinin (µmol/L)</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
</tr>
<tr>
<td>pen-KID</td>
</tr>
<tr>
<td>NephroCheck</td>
</tr>
</tbody>
</table>

![Box plots showing pen-KID and NephroCheck scores across KDIGO stages.](image)
High Intensity Intermittent Resistance Training Causes Muscle Damage and Increase of Biomarkers indicative of Acute Kidney Injury in Healthy Individuals

Tania Spada\textsuperscript{1}, José M Rodrigues da Silva\textsuperscript{2}, Lucila Francisco\textsuperscript{2}, Lia Marçal\textsuperscript{3}, Leila Antonangelo\textsuperscript{3}, Dirce Maria T Zanetta\textsuperscript{4}, Luis Yu\textsuperscript{1}, Emmanuel A Burdmann\textsuperscript{1}

\textsuperscript{1}LIM - 12, Division of Nephrology, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, \textsuperscript{2}University of Guarulhos, Guarulhos, SP, Brazil, \textsuperscript{3}Division of Pathology, University of Sao Paulo Medical School, Sao Paulo, SP, Brazil, \textsuperscript{4}Division of Epidemiology, University of Sao Paulo Public Health School, Sao Paulo, SP, Brazil

High intensity resistance training (HIRT) is currently very popular because of the possibility of achieving positive results with short exercise sessions. On the other hand, its striking intensity might cause adverse effects. The aim of this study was to evaluate whether a HIRT session causes muscle damage and changes in biomarkers of acute kidney injury (AKI).

Fifty-eight healthy volunteers (age median 24 y; 50% male; body mass index 24±3) were evaluated. They were submitted to a 4 minutes HIRT session, preceded by 5 min warm-up. A Borg CR10 Scale for pain (CR10P), blood and urinary samples were collected before (baseline), 2 and 24h after the HIRT session. Immediately after the HIRT session, all individuals completed a Borg Rating of Perceived Exertion Scale (RPE). Blood samples were analyzed for serum creatinine (SCr, mg/dl), CPK (IU/l) and myoglobin (Myo, g/l)) and urinary samples for Cr, NGAL (UNGAL, ng/mgCr), IL-18 (ng/mgCr), calbindin (Cal, ng/mgCr) and µalbuminuria (µalb, µg/ mgCr). Data (medians) were compared by Friedman test followed by Dunn´s post-test or Repeated Measures ANOVA followed by Tukey-Kramer post-test (p<0.05).

RPE was 15 denoting hard effort. CR10P increased on 2h (from 0 to 1.5, p<0.001) and on 24h (4, p<0.001 vs. baseline). CK increased on 2h (from 123 to 153, p<0.001) and 24h (340, p<0.001 vs. baseline). Myo increased on 2h (from 21 to 89, p<0.001) and remained high on 24h (39, p<0.001 vs. baseline). SCr was similar on baseline and on 2h (0.91 and 0.90) and increased on 24h (0.94, p<0.05 vs. 2h). UNGAL increased on 2h (from 18 to 33, p<0.01) and was similar to baseline on 24h (16, p<0.01 vs. 2h). IL-18 increased on 2h (from 0.015 to 0.026, p<0.001) and returned to baseline on 24h (0.015, p<0.01 vs. 2h). Cal increased on 2h (from 27 to 55, p<0.001) and was similar to baseline on 24h (36, p<0.05 vs. 2h). Values of µalb increased on 2h (from 4.3 to 20.0, p<0.001) and returned to baseline on 24h (3.3, p<0.001 vs. 2h).

In conclusion, a single session of HIRT in young, healthy individuals caused significant elevations in CK, myoglobin, SCr, microalbuminuria and urinary biomarkers indicative of early renal tubular injury. These results demonstrated that a single HIRT session was associated to rhabdomyolysis and AKI.
Effects of Remote Ischemic Preconditioning on the Innate Immune Response in Humans In Vivo

J. Zwaag¹, E. Peters¹, R. Beunders¹, J.A. Kellum², P. Pickkers¹, M. Kox¹

¹Department of Intensive Care Medicine, Radboud university medical center, Radboud Center for Infectious Diseases (RCI), Nijmegen, The Netherlands. ²Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

Introduction: Remote Ischemic Preconditioning (RIPC) using a tourniquet to temporary cut off blood supply to the arm has been shown to reduce the rate of acute kidney injury following cardiac surgery. Animal studies have shown an ‘early window of protection’ in the 1-2 hours after RIPC as well as a ‘late window of protection’ 12-24 hours after RIPC. Several mechanisms have been suggested to mediate the protective effects of RIPC, of which modulation of the immune response is an important candidate. Here, we aimed to determine the effect of single and repeated RIPC on the innate immune response in humans in vivo.

Methods: We performed a randomized controlled study in 30 healthy male volunteers assigned to the single-dose (SD) RIPC group, multiple-dose (MD) RIPC group, or control group (n=10 per group). The SD RIPC group received 1 dose of RIPC, consisting of 4 cycles of 5-minute ischemia of the arm followed by 5 minutes of reperfusion just before administration of 2 ng/kg lipopolysaccharide (LPS). The MD RIPC group received one dose of RIPC per day during the 6 days before the endotoxemia experiment day, and 1 dose just before LPS administration. The control group received LPS without RIPC. Urinary TIMP2*IGFBP7 levels, which were previously found to sharply increase directly following RIPC [1] were determined before and immediately after RIPC. Cytokines were determined in plasma.

Results: In both groups receiving RIPC, increased levels of urinary TIMP2*IGFBP7 were found after RIPC (Figure 1). LPS administration resulted in a typical increase in body temperature, flu-like symptoms, and hemodynamic changes, with no differences between groups. Administration of LPS resulted in a profound increase in plasma levels of the pro-inflammatory cytokines TNF-α, IL-6, and IL-8 as well as the anti-inflammatory cytokine IL-10. No differences in plasma levels of these cytokines were observed between the different groups (Figure 2).

Conclusion: RIPC was effectively induced, as confirmed by the increase in urinary TIMP2*IGFBP7 levels, but did not affect the innate immune response in vivo in humans. Previously reported beneficial effects of RIPC do not appear to be mediated through modulation of innate immunity.
The Regulative Roles of TIMP-2 on Cell Cycle in AKI in HK-2 Cells Stimulated by LPS

Yi-Ming Li¹, Zhiyong Peng¹

¹Wuhan University Zhongnan Hospital

Purpose of the study: The mechanisms of septic acute kidney injury (AKI) are not well understood. The renal tubule epithelial cell cycle arrest is one of the possible mechanisms. The urine tissue inhibitor of metalloproteinase 2 (TIMP-2) was reported to be increased in patients with moderate to severe AKI, but it was unknown why it was increased. We aimed to evaluate the role of TIMP-2 in AKI in human kidney 2 cell (HK-2).

Methods: AKI was induced in HK-2 cell with lipopolysaccharide (LPS) stimulus. At 0, 1, 1.5, 2, 2.5 and 3h after LPS the mRNA expression level of TIMP-2 was evaluated by quantificational real-time polymerase chain reaction (qRT-PCR). Furthermore, the expression of Rb, CDK4 and cyclin D1 was also measured by qRT-PCR. DNA content of renal tubule epithelial cells was analyzed using flow cytometer at 24h after LPS.

Results: After LPS stimulation, the mRNA expression level of TIMP-2 was increased at 2h (Fig 1A). Meanwhile, the mRNA expression level of Rb, CDK4 and cyclin D1 was reduced (Fig1B). Furthermore, the cell cycle of HK-2 was arrested in G1, and the percentage of G1 was decreased after the silence of TIMP-2 (Fig1C).

Conclusion: The data suggest that TIMP-2 is early increased after AKI, by which induces renal tubule epithelial cell cycle arrest through regulating Rb, CDK4 and cyclin D1. The antagonist of the TIMP-2 expression will ameliorate the cell cycle arrest.
Plasma Proenkephalin to Monitor Kidney Function Following Cardiac Surgery

E. Peters¹, R. van Groenendael¹, E. Kooistra¹, W. Claassen¹, J. Gerretsen¹, W.J. Morshuis², M. Kox¹, L. van Eijk¹, P. Pickkers¹

¹Department of Intensive Care Medicine, Radboud university medical center, Nijmegen, The Netherlands, ²Department of Cardiac Surgery, Radboud university medical center, Nijmegen, The Netherlands

Introduction: Acute kidney injury (AKI) is a major complication in patients who undergo cardiac surgery and is independently associated with prolonged hospitalization and death. The diagnosis of AKI is hampered by the lack of accurate markers to assess kidney function. A promising novel candidate is plasma proenkephalin (penKid), a stable surrogate marker for enkephalins; endogenous opioid ligands that turn out to be a biomarker for kidney function. Currently, there is limited information to what extent proenkephalin predicts the rise in plasma creatinine. Therefore, we investigated the kinetics of proenkephalin following cardiac surgery and related this to creatinine levels on the post-operative day.

Methods: In this prospective pilot study, 35 patients (>18 yrs) undergoing elective on-pump coronary artery bypass grafting, with or without valve replacement, were enrolled. Blood was collected pre-operatively (baseline), on the day of surgery before incision, at the end of extracorporeal circulation (EC), at 2, 4 and 6 hours following end of EC, and on the post-operative day to determine plasma proenkephalin and creatinine levels. Patients were divided in those who showed an increase in creatinine of ≥5% on the post-operative day (‘AKI-group’) compared to baseline (set to 100%), to those who did not (‘No-AKI-group’).

Results: Patients (31 males) had a median [IQR] age of 67 [63-74] yrs and a baseline creatinine of 78 [58-94] µmol/L. Ten patients showed a ≥5% increase in creatinine on the post-operative day (AKI-group) and increased from 93 [82-103] to 100 [91-172] µmol/L, while those who did not increase (No-AKI-group) went from 84 [78-97] to 77 [68-91] µmol/L. Two, 4 and 6 hours following end of EC, creatinine levels were not significantly increased in the AKI-group compared to the No-AKI-group. Baseline proenkephalin levels were 57 [57-77] pmol/L in the AKI-group and 58 [57-81] pmol/L in the No-AKI-group (p=0.7). A significant difference in the increase in proenkephalin between the AKI- and No-AKI-group occurred already 6 hours (t=6) following end of EC (increase to 117 [100-152]% vs. 100 [93-112]% of baseline; p<0.05). Proenkephalin levels at t=6 correlated with creatinine levels on the post-operative day (r=0.63, p<0.0001; Figure 1).

Conclusion: These pilot results indicate that proenkephalin predicts the rise in creatinine following cardiac surgery. Plasma proenkephalin may serve as an early marker to monitor kidney function in this population.
FGF23 levels and patient/renal outcome at 3 months in dialysis dependent AKI

Krishan L Gupta¹, TIRTHANKAR MOHANTY¹, Raja Ramachandran¹, Ashok Yadav¹

¹Postgraduate Institute of Medical Education and Research, Chandigrah

Introduction: AKI may be associated with adverse outcome including CKD and increased mortality and elevated levels of FGF23 have been observed in such patients. We tried to ascertain the association between FGF23 levels and renal outcome at 3 months in dialysis requiring AKI patients. Material and methods: We enrolled dialysis requiring adults with AKI who did not have any underlying CKD or other clinical conditions associated with perturbations of calcium and phosphate metabolism. At enrolment samples for calcium, phosphate, intact parathyroid hormone (iPTH), 25-OH-Vit-D and FG23 were drawn just prior to the first dialysis. The samples were centrifuged, and stored in aliquots at -80°C. Subjects were closely monitored during the hospital stay for the development of clinical endpoints (Death or recovery of renal function). Following discharge, they were evaluated monthly for the next 3 months. The statistical analysis was performed with the IBM SPSS statistics version 21 while the graphs were created with Graphpad Prism version 6. Results: During the one-year study period, 48 (M-27 & F-21) patients with mean age was 39.65±15.69 (range 18-74) years were enrolled. Thirty-six (75%) had developed AKI secondary to medical causes and 6 (12.5%) each due to surgical and obstetric causes. The mean serum creat. was 5.77±3.14 (range, 1.6-14.7) mg/dl. The median corrected serum calcium and phosphorus level were 8.90(IQR, 8.28-9.66) mg/dl and 4.50(IQR, 3.25-5.50) mg/dl, respectively. The median vitamin D value was 3.61(IQR,3.60-10.04) ng/ml and iPTH was 91.55 (IQR,36.52-269.67) pg/ml. The median albumin was 2.20(IQR,1.75-2.57) mg/dl. and FGF23 level among the cases was 35.15(IQR, 8.28-85.23) pg/ml. By the end of 3 months, 27 (73%) cases expired. Twenty-five (68%) died during the same admission, while two (5%) died within 3 months of discharge. Out of the 10 alive patients 9 (90%) had completely recovered their renal functions and 1 (10%) had partial renal recovery in 3 months. Patients who died had significantly higher FGF 23 compared to patients who survived (14.37(IQR, 4.82-60.00) vs 4.65(IQR,4.31-8.18), p-0.039). Predictive value of FGF23 for death was assessed by ROC curve analysis. Accuracy of FGF23 in predicting death was fair(AUC-0.733). At a cutoff point of 22.77 pg/ml, FGF23 predicted mortality with a sensitivity and specificity of 70% and 78% respectively. Conclusion: In dialysis, dependent AKI patients FGF23 predicts death with

Plasma Proenkephalin to Monitor Kidney Function in Critically Ill Sepsis Patients

G. Leijte¹, R. van Groenendael¹, L. van Eijk¹, M. Kox¹, E. Peters¹, P. Pickkers¹

¹Department of Intensive Care Medicine, Radboud university medical center, Radboud Center for Infectious Diseases, Nijmegen, The Netherlands

Introduction: Deterioration of kidney function in critically ill patients is an important concern, as it is independently associated with morbidity and mortality. Diagnosis of AKI is currently hampered by the lack of accurate markers to assess kidney function, as conventional creatinine-based methods to assess GFR are known to be insensitive, late, and inaccurate. Plasma clearance of iohexol, an iodine contrast agent that is exclusively filtered in the glomerulus, has been shown to be equally accurate in determining GFR as inulin clearance, the current gold standard. Nevertheless, iohexol is currently not
used in clinical practice as it is as time-consuming and its determination is laboursome. A promising novel candidate to assess kidney function is plasma proenkephalin (penKid), a stable surrogate marker for enkephalins; endogenous opioid ligands that turn out to be a biomarker for kidney function. Here, we determined to what extent proenkephalin reflects the GFR in sepsis patients.

Methods: In this prospective pilot study, we included 24 septic patients admitted to the ICU. All patients received an intravenous bolus of 1 mL iohexol. During the subsequent 6-hour window, blood was sampled 4 times to construct the iohexol plasma disappearance curve. Plasma proenkephalin and creatinine were determined once. Urine was collected cumulatively over the same 6-hour period to determine the endogenous creatinine clearance (ECC).

Results: Patients had a median [IQR] iohexol-GFR of 45 [15-75] ml/min. Both ECC (60 [19-155] ml/min) as well as plasma proenkephalin (63 [31-124] pmol/L) correlated strongly with the iohexol-GFR (r=0.93, p<0.001 and r= -0.95, p<0.001, respectively) (Figure 1).

Conclusion: These pilot results indicate that a single measurement of plasma proenkephalin strongly correlates with the true GFR in sepsis patients. Therefore, plasma proenkephalin may serve as a more feasible marker to assess kidney function in this population. Results need to be confirmed in larger cohorts and other patient groups.

---

**Modulation of IGFBP7 and TIMP2 Expression and Secretion by Clinically Relevant Insults In Vitro.**

David R Emlet¹, Seth Morrisroe¹, Alicia Frank¹, John A Kellum¹

¹University of Pittsburgh

Purpose: Our group has recently identified variable constitutive expression and secretion of the AKI biomarkers Insulin-Like Growth Factor Binding Protein 7 (IGFBP7) and Tissue Inhibitor of Metalloproteinases-2 (TIMP2) in model systems of primary human kidney proximal and distal tubule epithelial cells in vitro. In this study, we assessed modulation of these biomarkers in models of the clinically relevant insults ischemia, trauma/surgery, and nephrotoxicity. Methods: Primary human kidney tubule epithelial cells of proximal and distal tubule origin were immunoaffinity isolated from cortical cell cultures with antibodies directed against Aminopeptidase N (APN) and Mucin-1 (MUC-1)
respectively, using the Dyanbead pan-mouse IgG system. Isolated proximal and distal tubule cells were cultured on transwell permeable supports in serum-free media to form monolayers. For insult testing, monolayer cells were subjected to oxygen-nutrient deprivation, or treatment with hemoglobin, myoglobin, gentamicin, or amphotericin B. Cell lysates and conditioned media were assessed for IGFBP7 and TIMP2 levels, initiation of an inflammatory response, and cell death. Results: Oxygen-nutrient deprivation (as an in vitro model of ischemia) demonstrated that deprivation suppressed the secretion of both biomarkers, and reperfusion caused an early transient increase of secretion of both markers, including a burst of IGFBP7 in distal cells where a very low level of constitutive secretion is observed. Initial studies on the nephrotoxins gentamicin and amphotericin B suggest that both may suppress the secretion of both markers at 6 and 24 hours, in both tubule cell types, and both nephrotoxic insults may elicit an inflammatory response preferentially in proximal tubule cells. Lastly, in the model of trauma/surgery, hemoglobin and myoglobin demonstrated variable effects on secretion of both markers in proximal and distal tubule cells, hemoglobin enhanced cell death in both cell types, and myoglobin elicited an inflammatory response preferentially in proximal tubule cells. Conclusion: Together, these data show that IGFBP7 and TIMP2 are indeed modulated by various clinically relevant kidney insults, and that different insults affect these molecules in different ways. This in vitro system will be a useful tool to further investigate the potential role of these markers in the etiology of AKI.

68

Cell-cycle Arrest Biomarkers [TIMP2]*[IGFBP7] for Risk Stratification of Acute Kidney Injury in Patients with Sepsis

Marco Fiorentino1, Christopher Keener1, Ali Smith1, John A Kellum1

1Center for Critical Care Nephrology, CRISMA, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA

Purpose of the study: Acute kidney injury (AKI) is associated with both short- and long-term adverse outcomes in patients with sepsis. Standard criteria for AKI, like serum creatinine (sCr) and urine output (UO), are poor, late and non-specific diagnostic tools, measuring renal function, but not renal injury. The aim of this study is to analyze the performance of cell-cycle arrest biomarkers tissue inhibitor metallopeptase-2 (TIMP2) and IGF-binding protein 7 (IGFBP-7) in addition to standard criteria for early prediction of severe sepsis-associated AKI.

Methods: We analyzed data from 1243 patients with septic shock enrolled in the ProCESS trial of early goal-directed therapy, for which biomarkers at admission and at 6 hour were available. TIMP2 and IGFBP-7 were measured and their product (Nephrocheck test) was combined with clinical parameters for AKI (sCr and UO). The primary endpoint is the development of severe AKI (KDIGO stage 3), renal replacement therapy (RRT) and death in the first 7 days of enrollment. We analyzed the frequency of the outcomes and the odds ratios (ORs) for each combination, compared to the reference combination (normal sCr, UO and [TIMP2]*[IGFBP-7] ≤ 0.3 ng/ml2/1000).

Results: Excluding patients with stage 3 AKI at admission, and those with missing data we analyzed 732 patients with hour 0 data and 785 patients with available parameters at hour 6 (Figure 1). The percentage of patients with all the three parameters negative at hour 0 who achieved the endpoint was low (5.7%). Interestingly, this percentage was significantly higher in patients with no AKI by sCr and UO but [TIMP2]*[IGFBP-7] positive (16.2% vs 5.7%, p=0.02) and the odds of developing the endpoint was three times higher compared to the reference group (OR 3.03. 95%CI 1.27-7.22). Similarly, the
percentage of patients with sCr negative, UO negative, and [TIMP2]*[IGFBP-7] negative at hour 6 who reached the endpoint was low (7%). However when only [TIMP2]*[IGFBP-7] was positive (sCr and UO negative), this percentage was significantly higher (17.8% vs 7%, p<0.001) and the odds for the endpoint was similar to that for hour 0 data (OR 2.85, 95%CI 1.33-6.1).

Conclusions: Early assessment of [TIMP2]*[IGFBP-7] in the first 6 hours of admission in ICUs may significantly improve the ability to predict hard outcomes (severe AKI, RRT and death within 7 days) in apparently “asymptomatic” septic patients (normal sCr and UO).

Unveiling Incidence and Outcomes of Subclinical AKI in the ICU

Javier A Neyra¹, Victor E Prado², Xilong Li², Katherine Bosler², Robert D Toto², Orson W Moe²

¹University of Kentucky Medical Center, ²University of Texas Southwestern Medical Center

Background: AKI carries adverse outcome. The incidence or prognosis of subclinical AKI is unknown. High serum cystatin C with normal creatinine may signify subclinical AKI in the ICU. We compared renal outcomes of patients with subclinical AKI in reference to patients with established AKI and no AKI.

Methods: Data from a prospective case-control study of 106 ICU patients were analyzed. Patients with baseline eGFR <60 or kidney transplant were excluded. Subclinical AKI was defined as serum cystatin C ≥0.7 mg/L and absence of KDIGO-AKI criteria. Established AKI was defined as KDIGO stage ≥2 criteria and serum cystatin C ≥0.7 mg/L. Incident CKD consisted of eGFR <60 and at least 25% lower than baseline. Creatinine ratio was defined as the ratio of follow-up serum creatinine / baseline value. Results: 54 (51%) patients had established AKI. Among patients without established AKI, 32 of 52 (62%) had subclinical AKI, and 20 (38%) had no AKI. Sepsis was more frequent in established AKI.
patients and cardiovascular surgery, in subclinical AKI patients. We found important differences in outcomes between the groups (Table).

Conclusions: Subclinical AKI occurred in almost two-thirds of patients without established AKI in the ICU. Subclinical AKI is a distinct AKI phenotype that carries adverse long-term renal outcome.

<table>
<thead>
<tr>
<th>Table</th>
<th>No AKI</th>
<th>Subclinical AKI</th>
<th>Established AKI</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital death, %</td>
<td>0%</td>
<td>3%</td>
<td>48%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>90-day creatinine ratio, mean, SD</td>
<td>0.96 ± 0.14</td>
<td>1.08 ± 0.28</td>
<td>2.39 ± 2.24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6-month creatinine ratio, mean, SD</td>
<td>1.03 ± 0.15</td>
<td>1.13 ± 0.29</td>
<td>1.51 ± 0.76</td>
<td>0.01</td>
</tr>
<tr>
<td>CKD at 1 year, %</td>
<td>0%</td>
<td>16%</td>
<td>27%</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**70**

**Serum Bilirubin is Associated with Lower Incidence of Acute kidney Injury; A Basic Science Mechanism behind a Clinical Outcome**

Arnaldo Lopez-Ruiz1, Luis A Juncos2, Mahrukh Rivzi1, Karl A Nath1, Kianoush Kashani1

1Mayo Clinic, Rochester-MN, USA, 2University of Mississippi Medical Center, Jackson-MS, USA

Acute kidney injury (AKI) is mainly due to increased renal inflammation, oxidative stress and endothelial dysfunction. Bilirubin is an endogenous product of the metabolism of heme proteins with potent anti-oxidative/anti-inflammatory effects synthetized by heme-oxygenase-1 (HO-1) and biliverdin reductase. Previous studies have shown that inducing HO-1 activity protects against renal injury in part via increasing bilirubin levels.

We tested whether increased HO-1 activity and bilirubin levels confer protection against AKI. The study was divided into 2 aims. Aim 1: Evaluate if systemic induction or blockade of HO-1 has a beneficial or deleterious impact on the renal function of animals with ischemia-reperfusion induced AKI (IR-AKI). Aim 2: Evaluate if increased serum bilirubin in patients admitted to ICU correlates with decreased incidence of AKI and/or AKI requiring dialysis.

Aim 1: we infused an HO-1 inducer (CoPP 50 µmol/kg) or inhibitor (SnPP 30 µmol/kg) before inducing AKI by bilateral renal pedicle clamping in rats. We randomized 4 groups of rats (n=6): 1) Sham, 2) IR/AKI/Control, 3) IR-AKI/CoPP, 4) IR-AKI/SnPP. We measured serum creatinine, urine NGAL and harvested the kidney to measure intra-renal bilirubin (HO-1 activity). Aim 2: We studied 10,283 patients from Olmsted County MN-USA admitted to ICU from 2006 through 2014, and compared by ordinal logistic regression whether increased serum bilirubin in patients admitted to ICU correlates with decreased incidence of AKI and/or AKI requiring dialysis.

Aim 1; animals treated with CoPP had less severe AKI than IR/AKI-control as demonstrated by reduced plasma creatinine (1.24 vs. 1.81 mg/dl) and urine NGAL (415 vs. 863 UI/ml). These animals had higher levels of intra-renal bilirubin (463 vs. 268 pMoles/mg). Animals treated with SnPP developed more severe AKI (creatinine 2.4 vs. 1.81 mg/dl and NGAL 1215 vs. 415 UI/ml) and had decreased intra-renal bilirubin production (191 vs. 268 pMoles/mg) compared to IR/AKI control. Aim 2, analysis of the cohort (adjusted to APACHE III, nephrotoxic exposures and length of ICU stay) showed a significant
association between increased level of bilirubin on admission to ICU and decreased incidence of AKI (p<0.001, R2 0.26) and less AKI requiring RRT (p<0.001, R2 0.13).

Our data in animals and humans suggest that an increased level of bilirubin is associated with lower incidence of AKI and AKI requiring dialysis. Therapies targeting the activity HO-1 may confer protection against AKI.

Performance of Sequential Biomarkers for Predicting a More Precise AKI Phenotype

Rajit K Basu1, Erin Stenson1, Margaret R Ninemire1, Shina Menon2, Stuart L Goldstein1

1Cincinnati Children's Hospital Medical Center, 2Seattle Children's Hospital

Critical illness is managed dynamically. Integrated into context, markers of injury are followed over time and trends in these laboratory parameters (e.g., co-oximetry, lactate, troponin) help guide management. Although novel AKI biomarkers may have a time advantage over serum creatinine (SCr), responding earlier to injury, all are derived and validated in static fashion, as single measurements. Very little published data explores the utility of assessing biomarkers as they change over time. Additionally, even though fluid accumulation is a significant, modifiable aspect of the AKI syndrome, the prediction of fluid overload (FO) by either changes in creatinine or biomarkers is underexplored. Leveraging data from a single center, prospective observational study of AKI in children requiring the intensive care unit (ICU) (NCT:01735162), we tested the hypotheses that sequential biomarker measurements were superior to static or sequential changes in SCr or static biomarker measurements for prediction of both AKI and significant FO. The primary outcome variables were 1) Severe AKI: defined as SCr-KDIGO Stage 2-3 between ICU Days 2 and 7 and 2) FO% maximum in the first 7 ICU days determined by the ratio of the net fluid balance to admission ICU weight. Creatinine elevation over baseline was assessed on the day of admission and ICU Day 1 and urinary neutrophil gelatinase associated lipocalin (uNGAL) level was measured consecutively on Day 1. In 164 patients studied through Day 7, severe AKI occurred in 30 (18.3%) patients and FO>20% occurred in 47 (28.7%) patients. In patients with available biomarker data, the positive likelihood ratios (LR) increased for sequential measurements compared to static measurements for both severe AKI and significant FO (Table 1). In non-septic patients, sequential uNGAL demonstrated a significant predictive superiority over sequential SCr (LR: 5.6 (1.8-17.4) vs. 1.6 (0.5-5.2)). Taken together, we suggest that sustained elevation in biomarker levels offers a heightened and more refined prediction of a severe AKI phenotype than either changes in serum creatinine or single measurements of a biomarker. The timing of these measurements is early (Day 1 of critical illness), potentially offering a considerable time-based management advantage in the care of critically ill patients suffering AKI (all patients receiving renal replacement therapy had consecutive uNGAL > 500 ng/ml on Day 1). Confirmation in larger populations is warranted.
CRRT in the United States: A Practice Survey

Paul McCarthy\textsuperscript{1}, Veena Nandwani\textsuperscript{2}, Alison Grazioli\textsuperscript{3}, Farhan Ali\textsuperscript{3}, Ami Patel\textsuperscript{1}

\textsuperscript{1}Dept of Nephrology, University of Maryland, \textsuperscript{2}Trauma/Critical Care, University of Maryland, \textsuperscript{3}Departments of Nephrology and Critical Care, University of Maryland

Purpose: To find areas for research & to improve practice, the continuing renal replacement therapies (CRRT) committee at our center made a survey on CRRT delivery.

Methods: The survey was sent to US physicians. Requested respondents were program directors in nephrology & critical care as well physicians on an email list kept by the department of nephrology at the University of Maryland.

Results: The response rate was 11%. Respondents included 80\% from teaching hospitals, 70\% nephrologists & 55\% from centers of 500 or less beds. Most responding work in the Northeast. 80\% of CRRT programs are run by nephrology with 20\% managed by Intensivists or co-managed with nephrology. Nephrology training is required for CRRT privileges at most centers. 10\% of centers have further requirements for CRRT privileges. Half of nephrology training programs require fellows to have a minimum case volume and/or didactic sessions related to CRRT. Common modalities for renal replacement in intensive care units (ICUs) are intermittent hemodialysis (iHD), continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD) & indications are volume overload, electrolytes abnormalities & acidosis. Most dose therapy at 20 – 30ml/kg/hr. Many anticoagulation practices exist: 34\% of centers always use anticoagulation and 19\% never do. Half of centers use no anticoagulation at least in part and 5\% use citrate in all cases. Common reasons to stop CRRT are urine output, filter clotting & calculated creatinine clearance. Hemodynamic stability was often sited for stopping CRRT, however, this was not a survey question. A divergence of practice on volume assessment and time spend with patients on CRRT existed. Physical exam and central venous pressure (CVP) are used to assess volume for nephrologists, ultrasound & pulmonary artery catheter (PAC) are also used. Most nephrologists spend 30 minutes or less a day with patients on CRRT. Intensivists use ultrasound, physical exam & arterial waveform analysis for volume assessment & rarely use CVP or PAC. The majority of Intensivists spend over 30 minutes a day with patients on CRRT.

Conclusion: Most CRRT is managed by nephrologists. There are no universal training requirements specific for CRRT. Agreement exists on dosing of CRRT & indications, with volume overload sited most often. Nephrologists and Intensivists assess volume differently. Variations exist in anticoagulation strategies and when to stop therapy.
Extracorporeal Blood Therapies in a Neurointensive Care Unit: A Retrospective Review

Paul J McCarthy¹, Derek Hatfield², Michael Armahizer³, Melissa Motta⁴

¹University of Maryland/Nephrology, ²University of Maryland School of Medicine, ³University of Maryland Department of Pharmacy, ⁴University of Maryland/Neurocritical Care

Purpose: Continuous renal replacement therapy (CRRT) & therapeutic plasma exchange (TPE) are extracorporeal therapies provided in our neurointensive care unit (NICU). For quality improvement & to identify areas for research, our group keeps a case registry

Methods: A retrospective review of 100 cases using the Gambro® Prismaflex system (70 CRRT & 30 TPE) from mid 2103 to late 2016 are reported. Demographics, indications, anticoagulation, dosing, therapy duration, vascular access, & complications are reviewed.

Results: For the 70 CRRT cases 44 patients were male & 26 were female with an average age of 55 (19 – 80). Indications for CRRT include volume overload, acidosis, hyperkalemia, uremia & end stage renal disease with cerebral edema. Most are managed with continuous venovenus hemofiltration (CVVH). Slow continuous ultrafiltration and continuous venovenous hemodiafiltration are used rarely. No anticoagulation is used in most cases with heparin or citrate used rarely. Most prescriptions are written at 30 ml/kg/hr. & the average delivered dose is 21 ml/kg/hr. Average time of therapy is 5 days (1 – 23). The main access location is the right internal jugular vein (31 patients). Complications have included 2 catheter related infections, 1 hematoma, 1 severe vascular injury and 2 deep venous thrombi.

For the 30 TPE cases 13 patients were female and 7 were male. The average age is 48 (18 – 73). indications include Guillain-Barre syndrome, myasthenia gravis, transverse myelitis, encephalitis, chronic inflammatory demyelinating polyradiculoneuropathy, & catastrophic antiphospholipid syndrome. Heparin anticoagulation is used in all cases. All exchanges are dosed between 1.2 & 1.5 plasma volumes & total exchanges have ranged from 4 to 7. The main access location is the right internal jugular vein (18). Therapy is delivered in a timelier manor compared to historical controls from our hematology apheresis service. Complications include 1 catheter related infection, minor bleeding, non-clinically significant coagulopathy & on 2 occasions a partial exchange (1 plasma volume) due to a catheter malfunction.

Conclusions: Reported are results from a review of 100 extracorporeal blood purification cases in a NICU. CVVH is the most common CRRT modality and most cases are done without anticoagulation. The average delivered dose is 21 mg/kg/min which meet KDIGO guidelines. TPE is used for a variety of neurologic indications is delivered more efficiently.
Compared of Measured vs Online Urea Kinetics in Patients with Acute Kidney Injury

Yifei F Zhang¹, Anitha Vijayan¹

¹Washington University in St Louis

Background
For patients with acute kidney injury (AKI) who require intermittent hemodialysis (IHD), KDOQI guidelines recommend a target single pool Kt/V (spKt/V) of 1.4, or at least 1.2, 3 times per week. Currently, the standard method of monitoring dialysis adequacy for patients with AKI is by calculating spKt/V using pre and post dialysis serum BUN. This requires additional blood draws associated with nursing and laboratory costs. The laboratory charge for BUN is $77 per test at our institution. Online urea kinetic monitor systems, such as continuous dialysate UV-adsorbance monitoring, can potentially measure the spKt/V more quickly while avoiding the expense of additional blood tests. These systems had been used for ESRD patients during outpatient dialysis, but have not been critically examined for use in AKI patients receiving inpatient dialysis.

Objective
The objective of this retrospective pilot study was to compare spKt/V calculated using pre and post dialysis BUN with spKt/V measured by an online urea monitoring system using UV-adsorbance. We hypothesized that online urea monitoring will be as accurate as measured spKt/Vurea.

Method
After approval from the Washington University IRB, we conducted a retrospective analyses of the collected data. We reviewed medical records of 20 patients who received at least one hemodialysis session for AKI over a 14 month period. A number of physiologic variables related to hemodialysis were extracted. For a single dialysis session per patient, spKt/V was calculated via Daugirdas equation using pre and post dialysis BUN, and compared to Kt/V measured by dialysate urea monitoring using UV-adsorbance. Preliminary data were analyzed via paired T test for means.

Results
Preliminary data analyzed with Paired T-Test for Means showed a T Statistic of 1.56, with a T Critical Two-Tail Statistic of 2.09, and therefore no statistical significant difference between spKt/V calculated using pre/post dialysis BUN.

Conclusion
In our small, limited study, preliminary data suggests that there’s no statistically significant difference between the spKt/V calculated via pre and post serum BUN compared to the spKt/V measured by continuous dialysate urea monitoring using UV-adsorbance. A larger prospective study will be needed to determine whether dialysate UV-adsorbance monitoring can be used as a less costly alternative for monitoring dialysis adequacy for patients with AKI.

*figure on following page*
Does the Site of Calcium Infusion Affects the Mean Circuit Life in Pediatric CRRT?

Francisco X Flores¹, Jolyn Morgan², Teresa Mottes², Joseph Ratcliff², Stuart Goldstein¹

¹Cincinnati Children's Hospital Medical Center, ²Center Acute Care Nephrology, Cincinnati Children's Hospital Medical Center

Purpose: Adequate vascular access (VA) and anticoagulation are important determinants of continuous renal replacement therapy (CRRT) delivery to pediatric patients (pts) with acute kidney injury (AKI). Regional citrate is the preferred anticoagulation (RCA) method in pediatric CRRT and small patients often do not have available separate access (SA) for a separate calcium infusion; therefore centers have to rely on the venous port (VP) of the CRRT access to provide the calcium infusion needed to maintain pt’s serum calcium levels at target range. We assessed if use of VP resulted in decrease CRRT filter life or worse VA function.

Method: This study is an institutional review board approved retrospective review of pediatrics pts with AKI treated with CRRT and received RCA at Cincinnati Children’s Hospital from January 1, 2015 until December 1, 2016.

Results: Data from 74 pts and 320 circuits were reviewed. 76 venous catheters were placed, 55 internal jugular (72%), 19 femoral (25%), 1 subclavian (1.3 %), 1 trans-lumbar (1.3 %). Due to VA malfunction, tissue plasminogen activator (tPA) was used in 79 episodes, 27 in 8 Fr (36%), 16 in 11.5 Fr (20%), 16 in 10 Fr (20 %), 11 in 9 Fr (14%), 5 in 7 Fr (6.5 %) and 2 in 14 Fr (2.5%). RCA was provided to all CRRT circuits and calcium was infused to pts via the VP of VA in 283 of the circuits (88%) and a SA in 37 circuits (12%). Median [IQR] circuit life (MCL) was 53.3 [25.5, 69.6] hours with VP calcium infusion vs. 42.8[21.1, 59.5] hours with SA calcium infusion (p=0.03). 74 (26%) VP vs. 5 (14%) SA circuits required tPA (p= 0.17). MCL for VP vs. SA circuits which required tPA was 45.6[15.8, 66.9] vs 24.5[6.7, 46.8] hours (p=0.30). Unplanned circuit changes for VP vs. SA were 129/284 [45%] vs 29/49 [59.1%] (p=0.08).

Conclusions: We suggest that while calcium infusion via VP maybe associated with increased need of tPA, the higher MCL we observed demonstrates VP calcium infusion is effective for RCA in pediatric CRRT and may be preferable to save cannulation of a separate vessel.
Changing Blood Primed CRRT Circuits Using a Reservoir Bag and a SINGLE Machine

Daryl Ingram¹, Suzanne Gurosky¹, David Askenazi¹

¹Pediatric and Infant Center for Acute Nephrology (PICAN) Children's of Alabama, University of Alabama at Birmingham

Background: Over the last several years, microtechnology innovations have brought great progress in development of machines that use smaller filters, smaller bloodlines, simpler interfaces, and allow for smaller vascular access. We have adapted the Aquadex Pureflow™ to provide renal support in CVVH mode to small children as it has a) the extracorporeal volume (amount of blood outside the body when the machine is running) is approximately 33 ml (about 1/3 the volume of standard CRRT machines) and b) allows for smaller intravenous catheters to run these small machines.

In infants who have an extra-corporeal volume of 10% or greater, we perform a blood prime (pRBC’s, sodium bicarbonate, and calcium gluconate infusion). When a circuit needs to be changed out routinely, we use the existing blood from the current circuit to prime the new circuit. By avoiding another blood prime, we minimize blood exposure, avoid thromocytopenia and coagulation factor dilution that comes if new pRBC’s are used to initiate the procedure. As the blood has been dialyzing for days, it is as physiologic as the baby’s plasma. However, there are times when a second machine is not available.

Methods: We performed a retrospective analysis of our clinical database to evaluate a procedure using a single Aquadex™ and a reservoir bag for the filter change. The procedure involves four steps. 1) Disconnect patient from current circuit; 2) Rinse blood back from current circuit into sterile bag; 3) Use sterile bag of blood to prime new circuit on SAME machine; 4) Reconnect patient and resume CRRT with new circuit on new machine.

Results: Between 7/29/2016 and 11/7/2016, we have performed this circuit change out with a single Aquadex™ machine 9 times on 2 patients. We were able to initiate 9/9 (100%) of these circuits without initiation problems. All patients remained hemodynamically stable without need for interventions. All circuits lasted over 30 hours with 6/9 (67%) lasting until time for routine change out and 3/9 (33%) clotted circuits. The mean circuit life was 63.0 +/- 14.5 hours.

Conclusions: CRRT circuits for children who require a blood prime, can be changed using a SINGLE machine. This procedure is safe, simple, easy-to-learn and minimizes exposure to new blood products with excellent hemodynamic stability.
Pediatric Acute Renal Replacement Simulation Workshop

Mostafa A Elbaba

Hamad Medical Corporation

The goal of this workshop is to highlight the different interventions required for acute kidney injury in the pediatric critical care conditions. Learners of different levels will be immersed in simulation scenarios of AKI in children from supportive management only up to CRRT. The inter-professional hands-on activities will enhance learners to take the decision and adjust the therapy in renal replacement treatment of different modalities. Peritoneal dialysis and intermittent hemodialysis pros and cons with indications and prescription will be discussed during the debriefing stage of simulation session. The CRRT is the modality of choice for critically ill child with AKI; it has a special concern during the workshop. The author will focus on CRRT indications, precautions, prescription and connection. The structure of the workshop starts by opening and introduction followed by small simulation sessions of 10 minutes each. Each session is followed by 20 minutes debriefing that will enhance the learning objectives of each scenario. The instructor is expert and qualified pediatric nephrologist, healthcare educator and simulation educator. The workshop targeted audiences are mainly those who work in the field of pediatric but it is also very useful for adult nephrologists for 2 reasons; the first is the pediatric view of dialysis modality that can be applied to small adults and the second is the simulation-based education and inter-professional education that is extremely needed in most of health professions. A similar curriculum can be planned, designed and implemented in adult renal replacement in AKI as well.
IPE Simulation Enhances the Quality of Care in Neonatal Hyperammonemia

Mostafa Elbaba

1Hamad Medical Corporation

BACKGROUND: Rapid blood clearance through continuous renal replacement therapy (CRRT) should be considered for neonatal hyperammonemia when medical therapy will not rapidly clear the ammonia and irreversible brain damage might occur. The complexity of extracorporeal blood clearance might affect the quality of care in that critical time. Inter-professional education (IPE) simulation-based training can fill the gaps of the multidisciplinary collaborative team management and improve the outcome in neonatal hyperammonemia. The purpose of this study is to evaluate the effectiveness of IPE collaborative practice in the management of neonatal hyperammonemia through the simulation training.

METHODS One full day IPE simulation workshop was conducted in our institute for pediatric CRRT multidisciplinary team quality training. The Prismaflex® System from Gambro for CRRT and neonatal manikin were used. After theoretical background, the inter-professional team practiced hands-on the CRRT for 90 minutes. Simulation specialist facilitated the scenario over three phases with advocacy-inquiry and plus-delta debriefing formats in between the phases for 180 minutes. Two tools were used to assess the workshop learning outcome. The first was a self-assessment pre & post surveys. The second was the expert facilitator’s assessment through a standardized checklist.

RESULTS The results showed a significant improvement in CRRT cognitive learning and psychomotor skills among the team as documented by the pre and post surveys. Inter-professional education and collaborative practice was also improved by the third phase compared to the prior two phases and their debriefing. This was observed by the means score improvement of the standardized checklist that documented by the experts in the field.

CONCLUSIONS This neonatal CRRT simulation training demonstrated a very effective learning achievement that can improve the patient outcome in real situation of neonatal hyperammonemia. We recommend simulation workshop or in-site (point of care) simulation training to enhance the quality of care of complex neonatal management.
Incidence of Complications During Continuous Renal Replacement Therapy

Rafael Avila 1, Nestor Carrizo1, Marta Filippi1, Agustin Fernandez 1

1Hospital Cullen

INTRODUCTION. Acute kidney injury (AKI) is a common and life threatening complication of critical illness in the intensive care unit. Continuous renal replacement therapy is specially performed to treat severe AKI in patients hemodynamically unstable or for all other critical medical conditions such as heat stroke, rhabdomyolysis, electrolyte and metabolic disturbances. The real incidence of complications related to CRRT in adult patients remain not very well studied.

OBJECTIVES. Report the incidence of mechanical, metabolic, and hemodynamic complications during CRRT.

METHODS. We reviewed 45 patients’ records who had undergone to CRRT during a 2-year period.(2014-2015). We collected demographic, severity of illness and outcomes in patients on CRRT and also we looked for complications attributable to the procedure itself (mechanical, metabolic, hemodynamic).

RESULTS. During the 2-year-period of the study, a total of 5912 CRRT treatment hours were performed on a total of 45 patients. Of these 78% were male, mean age was 39 years. APACHE II 20 (7), ICU LOS days 20(7), ICU mortality 67%. Duration of CRRT used, hours 133 (106). CVVHDF was performed in a vast majority 96%. The more frequent complications found were calcium and potassium disturbances, metabolic alkalosis and hypothermia.

CONCLUSIONS. The incidence of complication in our study was relatively high. Although most of the reported complications were not life threatening, a significant number of patients suffered complications, including new onset hypotension, major electrolyte abnormalities and hypothermia.

Anticoagulation on Continuous Renal Replacement Therapy in Acute Liver Failure patients

Dr. Vaishali Solao1, Dr. Priya Kenkre1, Dr. Hepal Vora1, Dr. Ruhi Kohli1, Dr. Sanjay Walke1, Dr. Sandeep Seth1, Dr. Nikhil Ramdasi1, Dr. Zaheer Virani1, Dr. Vibhor Borkar1, Dr. Samir Shah1

1Global Hospitals

PURPOSE
Cerebral edema followed by herniation remains an important life threatening complication of acute liver failure [ALF]. Hyperammonemia contributes majorly to cerebral edema along with inflammation. Significant ammonia clearance can be achieved by continuous venovenous hemodiafiltration [CVVHDF] without having an impact on hemodynamic parameters. A major challenge in ALF patients on continuous renal replacement therapy [CRRT] is the choice of anticoagulation. Available choices are heparin, citrate, prostacyclin or no anticoagulation. Use of citrate in liver failure is majorly restricted due
to perceived higher risk of toxicity. We present our experience with anticoagulation of CRRT circuit in ALF.

METHODS
We performed a single centre retrospective analysis of prospectively collected data of 49 ALF patients. Data collected included demographic data, detailed data of CRRT, etiology of ALF, anticoagulation on CRRT, citrate protocol- total calcium, ionized calcium serum, ionized calcium circuit, calcium gap, lactate, ammonia, pH, bicarbonate, disease severity scores, venous access and complications.

RESULTS SUMMARY
Median peak arterial ammonia level was 186 mmol/L[71-902]. Median ammonia reduction in first 48 hours was 36.4% [0.7-76%].median circuit life span was 27 hours [7-50] and median CVVHDF dose was 33.33 mL/kg/hour[25-48]. 8 patients received heparin [16.3%], 14 received citrate [28.5%] and 27 received intermittent NS flushes [55%]. The median circuit life span was 35.8 hours on heparin, 29.5 hours on citrate and 26 hours on saline. The median number of circuits on heparin was 3 [1-7], 2 [1-10] on citrate and 2 [1-5] on saline. On comparison of heparin versus citrate, there was no significant difference except for major bleeds [p-0.049]. 4 had major bleeds of which 2 were on heparin and 2 were on saline flushes. None had heparin induced thrombocytopenia. 4 patients had citrate accumulation with calcium gap > 2.5, but no metabolic acidosis or raised anion gap. In 3 out of these 4, citrate was continued after dose modification and discontinued in 1 due to severe hypocalcemia.

CONCLUSIONS
CRRT is an effective and safe modality to reduce raised ammonia levels in ALF. Anticoagulation is needed on CRRT for better efficacy and to prevent premature circuit clotting. Citrate could be used as an anticoagulant on CRRT in ALF though more robust data is needed. Saline flushes can also be used on CRRT effectively but larger numbered study is needed.

<table>
<thead>
<tr>
<th>Comparison Data</th>
<th>Heparin [n=8]</th>
<th>Citrate [n=14]</th>
<th>Saline flushes [n=27]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of circuits</td>
<td>28</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>Major bleeding, n[%]</td>
<td>2 [25%]</td>
<td>0</td>
<td>2 [7%]</td>
</tr>
<tr>
<td>Circuit life span [hours]-median [range]</td>
<td>35.8 [7-44]</td>
<td>29.5 [8.5-40]</td>
<td>26 [15.7-50]</td>
</tr>
<tr>
<td>Median CRRT dose [mL/kg/hour], [range]</td>
<td>29 [25-44.4]</td>
<td>34.77 [28.5-48]</td>
<td>33.3 [21-49]</td>
</tr>
<tr>
<td>Mortality, n[%]</td>
<td>3 [37.5%]</td>
<td>3 [21.4%]</td>
<td>7 [25.9%]</td>
</tr>
</tbody>
</table>
Comparison Of Early Onset Versus Late Onset High Volume CRRT In Acute Kidney Injury (AKI) Patients With Septic Shock.

RANAJIT CHATTERJEE(CHATTOPADHYAY)¹, RAKESH SINGHAL¹

¹SWAMI DAYANAND HOSPITAL, DELHI

Purpose: To compare early high volume hemodiafiltration (CVVHDF) with late high volume hemodiafiltration in patients of AKI with septic shock and its effect on mortality after 30 days posttreatment.

Methods used: It is a single centre, cross-sectional study enrolling 84 patients between age group 18-60 suffering from septic shock and AKI. 42 patients were enrolled in early onset high volume hemodiafiltration group (group-1) and equal number of patients was enrolled in late onset high volume hemodiafiltration group-2). Early is defined as those patients in whom CVVHDF was started at RIFLE-I and late is defined as those patients where CVVHDF was started at RIFLE-F. The mode of therapy in both was continuous venovenous hemodiafiltration (CVVHDF) with post filter replacement. The prescribed dose was 45ml/kg/hr which achieved a delivered dose of 40ml±2 ml/kg/hr. Patients on diuretics, previous kidney disease and patient below 18 years and above 60 years and negative balanced CRRT were excluded from the study. The mortality was compared in these patients at 30 days post treatment.

Summary of the results: There was significant decrease in and values of urea, creatinine, lactate, potassium, bicarbonate in the early high volume CVVHDF group (gr 1) when measured 24 hours after initiation of therapy. The early high volume hemodiafiltration group had significant lower mortality both at day 30 than the late high volume hemodiafiltration group.

Conclusion: Early high volume hemodiafiltration in patients of AKI with septic shock significantly decreases mortality in comparison to late high volume hemodiafiltration.

Renal Replacement Therapy in ECMO, Modalities, Access And Safety Profile: Experience Of An ECMO Centre in a Developing Country

SANDEEP DEWAN¹, MUNISH CHAUHAN¹, NITIN JAIN¹, POOJA WADWA¹, MONU DEWAN², MILIND TALEGAONKAR¹, KUMAR VISHAL¹, PRITEEMA CHANANA¹, SAMIR MALIK¹, SAURABH POKHARIYAL¹

¹FORTIS MEMORIAL RESEARCH INSTITUTE, GURGAON, HARYANA, INDIA, ²S.G.T MEDICAL COLLEGE, HOSPITAL AND RESEARCH INSTITUTE, GURGAON, HARYANA, INDIA

INTRODUCTION
ECMO (Extra Corporeal Membrane Oxygenation) is a lifesaving modality used in patients with severe organ dysfunctions. The incidence of Acute Kidney Injury (AKI) in these patients is very high. Continuous Renal Replacement Therapy (CRRT) is an accepted modality to manage fluid overload, AKI...
and metabolic disturbances in ECMO patients. In India, ECMO with CRRT is a rarely used modality and very few centres practice it. This review assesses the experience of a tertiary care centre in India of combining ECMO with CRRT during the first 3 years of inception.

METHOD
We collected data retrospectively of all the patients placed on ECMO from Dec 2013 to Dec 2016 at our centre. All data related to prevalence of AKI (by AKIN criteria), indications, modality and access for RRT and associated complications was collected. Outcome parameters like survival and net fluid balance were determined.

RESULTS
We recorded the data from 25 patients who underwent ECMO at our centre. Of these, 16 (64%) underwent some form of RRT while on ECMO. Eight patients each (50%) were Veno Arterial (VA) and Veno Venous (VV). Seven (43.7%) of these were on RRT pre ECMO which was continued on ECMO. The most common indication was AKI associated with metabolic acidosis. Fluid overload was the second commonest indication. The access most commonly used was one independent of the ECMO circuit (11 cases; 68.7%). ECMO circuit for RRT was used in 8 (50%) cases. A CRRT device was used in 5 of these cases and an inline hemofilter was used in 3 cases. In three cases, ECMO circuit access was switched over to independent access due to complications. Amongst the three complications two were damage to the CRRT filter due to high pressure gradients; and other was ECMO centrifugal pump failure due to microbubbles entering the circuit. Mortality rates were high on patients with CRRT and ECMO (14 of 16 cases, 87.5%) as compared to those without RRT (2 of 9; 22.2%). Irrespective of the requirement of RRT, the survivors on ECMO had a much lesser fluid balance than non survivors.

CONCLUSIONS
The incidence of AKI was high in our study and a majority required RRT. The associated mortality also was higher in these patients. Our study shows that CRRT is a safe technique for renal support and maintenance of fluid, electrolyte and acid base balance. Independent access was found to be safer and complication free in our patients. Patients with lesser fluid balance had better survival.

83

Plasma Exchange for Paediatric Non-renal Disease Indications and Outcomes: A Single Centre Experience

Saravanan Margabandhu¹, Rajeev A Annigeri¹, Suchitra Ranjith², Indira Jayakumar², Jayakumar Reddy², Meepa Thiyagarajan³, Shyamala J², Chitra Sundaramoorthy², Mahesh Janarthanan², Latha Viswanathan²

¹Apollo hospitals, Chennai, Tamilnadu, India , ²Apollo Children's hospital, Chennai, Tamilnadu, India

Objectives: We aimed to evaluate the role of plasma exchange and its outcome in children having non-renal disease.Methods:A retrospective chart review of children admitted between November 2015 and October 2016(1 year)to Apollo Children Hospitals,Chennai,India and requiring plasma exchange for non-renal indications was undertaken Plasma exchange was given as additive therapy along with primary treatment.Results:Ten children underwent plasma exchange with a male: female ratio of 3:2 and a mean age of 10 years(range 3-16 years).The indications were hemophagocytic lymphohistiocytosis(HLH)secondary to systemic lupus erythematosus SLE(n=2)and severe dengue sepsis(n=1),acute disseminated encephalomyelitis(ADEM)(n=2),acute neuromyelitis optica(n=1),thrombotic microangiopathy(TMA)secondary to snake bite envenomation(n=2),multi-organ
dysfunction syndrome (MODS) secondary to severe dengue sepsis (n=1) and catastrophic antiphospholipid antibody syndrome (APLA) secondary to SLE (n=1). All children received either 1.5 or 2 times plasma volume exchange (mean session - 4, range 1-6). Primary treatment were given along with plasma exchange (the details are given in table). Necessary investigations were carried out to make diagnosis of HLH, ADEM, TMA, etc. The mean duration of stay in hospital was 17.2 days (range 3-40 days) and follow-up was 2.6 months (range 3 days - 6 months), with majority of children (8/10, 80%) survived from the catastrophic illness at the time of discharge. Two children with snake envenomation had AKI and TMA picture. They showed good improvement after dialysis and plasma exchange. The child with catastrophic APLA (life threatening bilateral renal infaracts and mesenteric ischemia) showed good improvement. Two children (2/10, 20%) (HLH secondary to severe dengue sepsis/encephalitis (n=1) and acute neuromyelitis optica (n=1)) succumbed because of the disease per se in earlier (had high PRISM score = 35 at admission) and enterobacteriaeae sepsis (hospital acquired pneumonia) in later. One patient (n=1, 10%) had allergic reaction and one (n=1, 10%) had hypokalemia during or after the procedure whom were managed appropriately. None of our children had hypocalcemia, coagulopathy and hypotension secondary to the procedure. Conclusion: As all our paediatric patients were very sick at presentation, it mandated aggressive management like plasma exchange along with primary treatment. Introduction of such approach as additive therapy for non-renal indications showed early recovery from their illness.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years/ gender)</th>
<th>Diagnosis</th>
<th>Other co-morbidities</th>
<th>Indication for TPE</th>
<th>Volume of plasma exchanged</th>
<th>No. of TPE done</th>
<th>Replacement fluid</th>
<th>Treatment given</th>
<th>Duration of stay in hospital (in days)</th>
<th>Outcome</th>
<th>Follow-up at end (in months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 M</td>
<td>Dengue shock syndrome/MODS/ AKI/ ALI/ HLH</td>
<td>Secondary bacterial sepsis (Staphylococcus/Fungal peritonitis (Ascetisitis) (as per was on PD Acute Peritonal Dialysis initially)</td>
<td>ILH</td>
<td>Hemophagocytic Lymphohistiocytosis</td>
<td>1.5 TIMES</td>
<td>4 = 4 A D (ALTERNATIVE DAYS)</td>
<td>50/50 - FFP/ 95% ALBUMIN</td>
<td>PD initially for 4 days then CVVHD 30 ml/kg/hr given for 72 hours then SLED on AD - 4 sessions Antibiotics/Antifungals 1.5 gm/day</td>
<td>35</td>
<td>Improved</td>
</tr>
<tr>
<td>2</td>
<td>16 F</td>
<td>Systemic lupus crythromatosus</td>
<td>Cerebral lupus - optic neuritis/PRES &amp; HLH</td>
<td>ILH &amp; Severe Lupus</td>
<td>2 TIMES</td>
<td>3 = 3 D (DAILY)</td>
<td>50/50 - FFP/ 95% ALBUMIN</td>
<td>Methyl Prednisolone Pulse MP 30 mg/kg/day – 3 days followed by 2 A D 600 mg – 2 doses &amp; MDM 1.5 gm/xday</td>
<td>21</td>
<td>Improved</td>
<td>At 2 months - partially recovered PR, HLD - disappeared, vision difficulty plus</td>
</tr>
<tr>
<td>3</td>
<td>13 M</td>
<td>Systemic lupus crythromatosus</td>
<td>Class IV LN &amp; HLH</td>
<td>ILH</td>
<td>2 TIMES</td>
<td>5 = 3 D (Followed by) 2 A D</td>
<td>50/50 - FFP/ 95% ALBUMIN</td>
<td>MP 30 mg/kg/day – 5 days followed on steroid &amp; IV Cyclosporine 8 mg/kg/day – 3 days &amp; Pulse cyclophosphamide once in 15 days</td>
<td>14</td>
<td>Improved</td>
<td>At 2 months - HLH - CR, Renal - PR</td>
</tr>
<tr>
<td>4</td>
<td>8 M</td>
<td>Acute disseminated onchocholophylmyelitis</td>
<td>Respiratory failure</td>
<td>ADEM</td>
<td>1 TIMES</td>
<td>5 = 3 D/ 2 A D</td>
<td>50/50 - FFP/ 95% ALBUMIN</td>
<td>MP 30 mg/kg/day – 3 days, IVlg – 0.4 mg/kg/day – 5 days</td>
<td>16</td>
<td>Improved</td>
<td>At 6 months - CR</td>
</tr>
<tr>
<td>5</td>
<td>7 F</td>
<td>Acute disseminated onchocholophylmyelitis</td>
<td>NIL</td>
<td>ADEM</td>
<td>1 TIMES</td>
<td>5 = 3 D/ 2 A D</td>
<td>50/50 - FFP/ 95% ALBUMIN</td>
<td>MP 30 mg/kg/day – 3 days, IVlg – 0.4 mg/kg/day – 5 days</td>
<td>15</td>
<td>Improved</td>
<td>At 2 months - CR</td>
</tr>
<tr>
<td>6</td>
<td>7 M</td>
<td>Neuromyelitis optica (Devic’s disease)</td>
<td>Brainstem involvement/Autonomic instability</td>
<td>Acute severe demyelinating illness</td>
<td>1.5 TIMES</td>
<td>6 = 3 D/ 3 A D</td>
<td>75/25 - 5% ALBUMIN/FFP</td>
<td>MP 30 mg/kg/day – 5 days, IVlg – 0.4 mg/kg/day – 2 cycles</td>
<td>40</td>
<td>Improved</td>
<td>Explored, Cause: Enterobacter sepsis (Hospital associated pneumonia) NIL</td>
</tr>
<tr>
<td>7</td>
<td>3 M</td>
<td>Snake envenomation</td>
<td>TMA &amp; AKI</td>
<td>TMA</td>
<td>1 TIMES</td>
<td>5 = 3 D/ 2 A D</td>
<td>75/25 - 5% ALBUMIN/FFP</td>
<td>Anti-venom &amp; 3 session of Intravenous Hesodialysis IHD done</td>
<td>12</td>
<td>Improved</td>
<td>At 2 months - normal renal function, no peripheral MAHA (Microangiopathic hemolytic anemia)</td>
</tr>
<tr>
<td>8</td>
<td>15 F</td>
<td>Snake envenomation</td>
<td>TMA &amp; AKI</td>
<td>TMA</td>
<td>1 TIMES</td>
<td>2 = 2 D</td>
<td>75/25 - 5% ALBUMIN/FFP</td>
<td>Anti-venom &amp; 2 session of IHD done</td>
<td>8</td>
<td>Improved</td>
<td>At 1 month - normal renal function, no peripheral MAHA</td>
</tr>
<tr>
<td>9</td>
<td>13 M</td>
<td>Dengue encephalitis/MODS/ AKI/ ALI/ Faintness liver failure</td>
<td>NIL</td>
<td>MODS</td>
<td>2 TIMES</td>
<td>1</td>
<td>75/25 - 5% ALBUMIN/FFP</td>
<td>CVVHD 30 ml/kg/hr given for 48 hours &amp; other supportive</td>
<td>3</td>
<td>Improved</td>
<td>Explored, Cause: Disease per se NIL</td>
</tr>
<tr>
<td>10</td>
<td>15 F</td>
<td>Systemic lupus crythromatosus</td>
<td>Secondary APLA - Renal infect &amp; Mesenteric ischemia &amp; Class IV LN</td>
<td>Catastrophic APLA</td>
<td>2 TIMES</td>
<td>4 = 2 D/ 2 A D</td>
<td>75/25 - 5% ALBUMIN/FFP</td>
<td>MP 30 ml/kg/day – 3 days followed on steroid &amp; Pulse cyclophosphamide once in 15 days &amp; anti-coagulant</td>
<td>8</td>
<td>Improved</td>
<td>At 3 months - CR</td>
</tr>
</tbody>
</table>
Back From The Cold

Azeem A Mohammed¹, Ahmad A Kabbani¹, William T Poisson¹, Matthew Diamond¹

¹Augusta University Medical Centre

Continuous Renal replacement therapy (CRRT) can modulate core body temperature through modulation of the replacement fluid temperature. Although this has been theorized to be helpful in hypotension, there are no guidelines for a temperature setting during CRRT. We present a case where maintaining an optimal temperature during CRRT was of paramount importance to the overall patient management.

A 32 year old African American male presented to the emergency room with recurrent syncope and was notably pale and lethargic on arrival. Lab tests revealed a hemolytic anemia, with a hemoglobin at 3.3 g/dL, LDH at 991 U/L, haptoglobin at 1 mg/dL, positive C3 and total bilirubin at 4.3 mg/dL. A peripheral smear showing severe anemia, prominent agglutination and several granulocytes containing intracytoplasmic cryoglobulins was conclusive for cold agglutinin disease. Although steroids and plasmapheresis were started, patient’s condition worsened with the development of multiorgan failure, shock and oliguric renal failure from acute tubular necrosis.

We instituted emergent initiation of CRRT for correction of malignant hyperkalemia and acidosis in the setting of hemodynamic instability. Patient underwent 5 days of CRRT with concomitant plasmapheresis. To assist with the overall therapeutic warming strategy, the Replacement fluid was heated on an external heating device and via the CRRT machine to the maximum temperature of 38 C. He improved significantly with resolution of acidosis, and electrolyte derangements; he ultimately required rituximab to truncate the autoimmune hemolytic anemia. A repeat cold agglutinin assay confirmed IgG+ cold agglutinin disease with a positive Mycoplasma IgM thought to be the likely trigger of the autoimmune hemolytic anemia.

This case provides a unique perspective on temperature control during CRRT. Typically, cooling of dialysate or replacement fluid is used to bolster blood pressure in times of hemodynamic shock. In this setting, the reverse was utilized as a therapeutic benefit. While often overlooked as a part of the routine CRRT order set, this case highlights the important impact that temperature modulation can have on overall patient management, and should be carefully considered when approaching the CRRT prescription.

---

Use of Continuous Renal Replacement Therapy(CRRT) in Osmotherapy for Cerebral Edema in Acute Liver Failure

EWALOLA A IJADUOLA¹, ASHITA J TOLWANI ¹

¹University of Alabama at Birmingham

Background: We describe the use of CRRT in a patient with fulminant hepatic failure, hyperammonemia, and cerebral edema.

Methods: A 36-year-old woman with history of migraines was admitted to the ICU for emergent liver transplant after an acetaminophen overdose. She consumed >6 grams of acetaminophen daily for 4 days with an acetaminophen level of 63mg/dl. She had a Glasgow Coma Scale of 7 and 1+ Deep Tendon
reflexes with posturing movements. She was intubated, Fosphenytoin and N-Acetyl cysteine administered and a CAT scan of the head showed diffuse white matter hypo attenuation suggestive of diffuse cerebral edema. She was given intravenous mannitol 1gm/kg followed by 3% saline at 50 ml/hr with goal serum sodium of 150-155meq/L. Nephrology was consulted for assistance with ammonia removal in view of cerebral edema. Continuous Veno-Venous Hemodiafiltration (CVVHDF) was initiated using bicarbonate-based solutions (Na 140meq/L, HCO3 35meq/L, K 4meq/L, Ca 3meq/L) given as both Pre-filter replacement fluid (RF) at 2L/hr and Dialysate at 2L/hr; 3% saline was given as Post-filter RF at 200 ml/hr rather than as a systemic infusion. The prescribed dose of CVVHDF was 52 ml/kg/hr to facilitate ammonia removal. We monitored electrolytes every 4 hours with only one adjustment made to reduce the 3% saline to 100 ml/hr when the serum sodium increased to 157meq/L. She had an emergent liver transplant in 72 hours and CVVHDF discontinued with significant neurologic improvement.

Results: This showed INR:12, Total Bilirubin:4.3mg/dl, Aspartate Transaminase: 4874U/L, Alanine Transaminase: 5319U/L, creatinine:0.7mg/dl, Ammonia: 444micromol/L decreased to 225micromol/L after 12hrs of CVVHDF and Serum Sodium maintained at 150-155meq/L with CVVHDF

Conclusions: This case demonstrates a potential to utilize the CRRT circuit as a useful adjunct in ammonia clearance while providing osmotherapy in severe encephalopathy prior to liver transplantation.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>DAY 1</th>
<th>DAY 2 (CRRT Started)</th>
<th>DAY 3</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>133</td>
<td>142</td>
<td>154</td>
<td>133-145meq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.7</td>
<td>3.1</td>
<td>3.6</td>
<td>3.1-5.1meq/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>101</td>
<td>105</td>
<td>120</td>
<td>97-108meq/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>16</td>
<td>25</td>
<td>24</td>
<td>22-32meq/L</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>9</td>
<td>8</td>
<td>6</td>
<td>5-22mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.0</td>
<td>0.8</td>
<td>0.6</td>
<td>0.4-1.2mg/dL</td>
</tr>
<tr>
<td>Glucose</td>
<td>383</td>
<td>106</td>
<td>97</td>
<td>70-99mg/dL</td>
</tr>
<tr>
<td>Calcium</td>
<td>7.8</td>
<td>8.2</td>
<td>8.1</td>
<td>8.4-10.2mg/dL</td>
</tr>
<tr>
<td>Ionized Calcium</td>
<td>1.12</td>
<td>1.02</td>
<td>1.08</td>
<td>1.12-1.32mmol/l</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.7</td>
<td>2.0</td>
<td>1.8</td>
<td>1.7-2.5mg/dl</td>
</tr>
<tr>
<td>Phosphate</td>
<td>2.3</td>
<td>1.4</td>
<td>2.1</td>
<td>2.4-5.0mg/dl</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>16</td>
<td>13</td>
<td>10</td>
<td>4-16meq/L</td>
</tr>
<tr>
<td>Aspartate Transaminase</td>
<td>5566</td>
<td>5148</td>
<td>3773</td>
<td>12-39U/L</td>
</tr>
<tr>
<td>Alanine Transaminase</td>
<td>5074</td>
<td>3066</td>
<td>1461</td>
<td>7-52U/L</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>104</td>
<td>138</td>
<td>135</td>
<td>37-117U/L</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>4.3</td>
<td>4.9</td>
<td>5.2</td>
<td>0.3-1.4mg/dL</td>
</tr>
<tr>
<td>Direct Bilirubin</td>
<td>2.7</td>
<td>2.7</td>
<td>2.8</td>
<td>0.0-0.3mg/dL</td>
</tr>
<tr>
<td>Ammonia</td>
<td>444</td>
<td></td>
<td>222</td>
<td>12-60micromol/L</td>
</tr>
<tr>
<td>Serum osmolarity</td>
<td></td>
<td>311</td>
<td>324</td>
<td>280-305mOsm/KgH2O</td>
</tr>
<tr>
<td>PH</td>
<td>7.351</td>
<td>7.516</td>
<td>7.505</td>
<td>7.35-7.45</td>
</tr>
<tr>
<td>Lactate</td>
<td>4.2</td>
<td>4.6</td>
<td>4.3</td>
<td>0.5-2.2 mmol/L</td>
</tr>
</tbody>
</table>
Kinetic Estimated Glomerular Filtration Rate as a Predictor of Successful Continuous Renal Replacement Therapy Weaning

Teruhiko Yoshida¹, Ryo Matsuura¹, Yohei Komaru¹, Yoshihisa Miyamoto¹, Kohei Yoshimoto¹, Yoshifumi Hamasaki¹, Eisei Noiri¹, Masaomi Nangaku¹, Kent Doi¹

¹The University of Tokyo, Bunkyo-ku, Tokyo, JAPAN

Purpose of the study: No standardized criteria for successful continuous renal replacement therapy (CRRT) weaning currently exist. When to stop CRRT is one of the most important clinical issues to be resolved on CRRT practice. Kinetic estimated glomerular filtration rate (kinetic eGFR) is a recently revisited indicator to estimate GFR in acute setting by the simple formula with baseline and two recent serum creatinine (sCr) values. We evaluated the predictive value of kinetic eGFR for CRRT weaning.

Methods used: We performed a retrospective single-center cohort study. Patients received CRRT for acute kidney injury (AKI) between May 2015 and April 2016 in the intensive care unit of The University of Tokyo Hospital (Tokyo, JAPAN) were analyzed. Successful CRRT weaning was defined as neither resuming CRRT during 48 hours nor receiving intermittent hemodialysis during 7 days from the CRRT termination. We reviewed medical records and identified factors associated with successful CRRT weaning by receiver operating characteristic (ROC) curve analysis.

Summary of Results: 52 patients who received CRRT for AKI were analyzed. Their baseline sCr and eGFR were 0.99 [0.74-1.38] mg/dl and 51.9 [38.4-78.1] ml/min/1.73m². 38 weaned patients and 14 un-weaned patients were identified. sCr, kinetic eGFR and urine volume of day0 (the day of CRRT stop) and day1 (the next day of CRRT stop) were all good predictive parameters for CRRT weaning with area under the curve (AUC)-ROC > 0.7. Kinetic eGFR of day1 had the best AUC 0.87 [0.73-0.94] with the cut-off value of 20.58 ml/min/1.73m². Kinetic eGFR of day1 combined with urine volume of day0 had AUC 0.92 [0.82-0.97].

Conclusion: This study proposed the utility of kinetic eGFR as a predictive parameters for CRRT weaning. Combination of kinetic eGFR and urine volume could be a clinically available indicator for CRRT weaning.

Combined Usage of Extracorporeal Membrane Oxygenation And Continuous Renal Replacement Therapy Circuit in a Neonate - First Case Report From India

Kanav Anand¹, P K Pruthi¹, Shivani Bansal¹, Shraddha Lohia¹, Raja Joshi¹, Reena K Joshi¹, Neeraj Agarwal¹

¹Sir Ganga Ram Hospital, New Delhi, Delhi, India

Purpose of the study :
Extracorporeal membrane oxygenation (ECMO) is a modality of treatment used in the intensive care unit (ICU) to provide cardiac support in cardiac failure and/or to improve gas exchange in patients with
life-threatening respiratory failure when conventional therapeutic methods fail to sustain sufficient oxygenation and/or the removal of carbon dioxide. Continuous Renal replacement therapy (CRRT) is added to ECMO for the treatment of acid-base imbalance, electrolyte imbalance, renal insufficiency and fluid overload. We report a neonate on respiratory ECMO for whom renal replacement was initiated in the form of combined CRRT and ECMO circuit. As per literature search, this is the first such case report from India.

Methods and Results:
A male neonate with unremarkable antenatal history, weighing 2.5 kg, born at 36 weeks of gestation who immediately cried after birth, had respiratory distress syndrome for which he received surfactant therapy. Child developed persistent pulmonary hypertension for which he was started on inhaled nitric oxide (iNO) therapy. Initially the child responded well and pulmonary pressures dropped. iNO was tapered after 72 hours. Subsequently he had rebound pulmonary hypertension, which did not respond to high frequency ventilation, sildenafil and iNO therapy. Worsening of oxygenation index and pulmonary hemorrhage indicated the use of ECMO. On ECMO, oxygenation index and metabolic parameters improved. Inline hemofiltration was done for fluid overload. Child’s renal and hepatic functions deteriorated for which CRRT was initiated in parallel circuit to ECMO. After initiating CRRT renal and liver functions improved, fluid management eased out along with a decrease in ventilatory settings.

Conclusion:
CRRT is potentially the most efficacious renal replacement therapy for fluid management and rapid clearance of toxins and metabolites, in a child with hemodynamic instability. Connecting the CRRT device to the ECMO circuit improves the handling of the CRRT device thus increasing the efficacy of CRRT. As per currently available literature this is the first neonate from India who was effectively and safely managed on ECMO and CRRT combination circuit.

88

Use Of Continuous Renal Replacement Therapy In Successful Management Of A Neonate With Maple Syrup Urine Disease

Kanav Anand1, P K Pruthi1

1Sir Ganga Ram Hospital, New Delhi, Delhi, India

Purpose of the study:
Maple syrup urine disease is rare disorder of inborn error of metabolism which can lead to severe neurological manifestations and may be fatal. Herein, we report a neonate presenting within first week of life with seizures secondary to maple syrup urine disease (MSUD), who showed good neurological improvement following Continuous Renal Replacement Therapy (CRRT).

Methods and Result:
A term male neonate appropriate for gestational age with birth weight 2960g, born to a 28 years old primigravida. He developed poor sucking, decreased activity and decreased urine frequency on seventh day of life. On eight day of life he developed subtle seizures following which he was admitted in NICU. Antenatal history was unremarkable and there was no history of consanguinity. He was investigated and his tandem mass spectroscopy showed raised levels of leucine, isoleucine and valine and genetic analysis revealed compound heterozygous mutations, c.1065 delT (p.Ala355AlafsX34) and c.293T>G (p.Val98Gly) in exons 10 and 3, respectively in BCKDHB gene, thus confirming the diagnosis of classical MSUD. This neonate was successfully treated with continuous renal replacement therapy
(CRRT) via umbilical line, which led to decrease in the blood levels of ammonia, branched chain amino acids and also neurological improvement during acute crisis. This is the first case report of a neonate with MSUD being successfully treated with CRRT from India.

Conclusion:
In a child with MSUD, in case of neurological depression immediate elimination of toxic metabolites is of utmost importance to prevent irreversible damage. CRRT is potentially the most efficacious renal replacement therapy for rapid clearance of branched chain amino acids.

CRRT: Profile of Practic Patterns from a tertiary care Hospital in South India

SreeBhushan Raju¹, Vamshi Nagalla¹, Ramesh Boora¹, Rajesh Goli¹

¹Nizams Institute of Medical Sciences

CRRT: Clinical Profile form a Tertiary care hospital in south India

Introduction: CRRT is not performed in patients with AKI despite an indication in several hospitals in India due to non-availability of resources and cost of therapy. We aim to study the profile of patients who underwent CRRT for various indications.

Materials and Methods:
We retrospectively analysed the data of our patients who underwent CRRT between January 2015 to November 2016. We collected all the clinical parameters related to the patients as well as the data related to the technique of CRRT. We analysed the complications during CRRT and the outcome.

Results:
A total of 92 patients (Age: 53.3 + 16.2 years/ Males – 61) underwent CRRT during the study period. AKI was the indication for CRRT in 62 and a complication of CKD in rest of patients. The indications for initiation of CRRT include septic shock ( 67), hyperkalaemia ( 48), Fluid overload ( 35) , severe metabolic acidosis ( 88) , encephalopathy ( 45) and Oligo-anuria (65). Mechanical ventilation (MV) was required in 78. Post operative patients were 42, predominantly following cardiac surgery. Major complications were Hypokalaemia (90), hypomagnesaemia( 88) and hypophosphatemia ( 82). Duration of CRRT was 68.4 + 48.9 hours. Mortality during the procedure was seen in 32 and renal recovery noted in 24. In-hospital mortality after completion of CRRT was seen in 12. Mortality was more in those who required MV for more than 72 hours.

Conclusions: CRRT is a viable option in septic shock patients both in AKI as well as the CKD patients. Significant renal recovery was seen in those with AKI and mortality was high in those required MV despite renal recovery.
Regional Citrate Anticoagulation for Continuous Renal Replacement Therapy in Severe Burn Injury Patients: Patient and Circuit Outcomes at the Singapore General Hospital

Riece Koniman¹, Su Hooi Teo¹, Hui Hua Li¹, Si Jack Chong¹, Bien Keem Tan¹, Han Khim Tan¹, Manish Kaushik¹

¹Singapore General Hospital

Introduction: Early continuous renal replacement therapy (CRRT) is associated with improved outcomes in severe burn injury (SBI) complicated by acute kidney injury (AKI). Recurrent surgical procedures and bleeding risk limit the use of heparin anticoagulation. Literature on experience of CRRT with regional citrate anticoagulation (RCA) in burn patients is scarce. At Singapore General Hospital (SGH), since 2015, all SBI patients requiring CRRT receive continuous veno-venous hemodiafiltration (CVVHDF) with RCA, using commercially prepared solutions. The SGH protocol incorporates a continuous delivery of Magnesium (Mg) in post-filter fluid to counter hypomagnesaemia associated with RCA. Our study reports on patient and technique outcomes of CRRT with RCA in SBI patients admitted to SGH.

Methods: This retrospective study included all SBI patients who received CRRT at SGH from 1 March 2015-29 February 2016. Data regarding demographics, metabolic control, clinical outcomes of patients and CRRT technique and circuit outcomes were reviewed from electronic and written case records of patients.

Results: A total of 11 patients (90.9% males) received CRRT. The median age was 40 years [Inter Quartile Range (IQR) 32, 51] and median total body surface area burn was 71% [IQR 60, 74]. AKI was multi-factorial in 45.5%; with pre-renal (54.5%), hypotension and sepsis (36.4% each) as most common etiologies. At CRRT initiation: median serum creatinine was 130 micromol/L [IQR 103, 151], median fluid balance was positive 10216 mL [IQR 5479, 13333]. Median urine output was 310 mL [IQR 255, 375] and 675 mL [IQR 587.5, 1085] in 6 and 12 hours preceding CRRT, respectively. The median duration of CRRT with RCA was 5 days [IQR 4, 13]. There were 79 filters changed among all the patients, with total filter duration of 2149.8 hours. 45.6% of filters were stopped prematurely for procedures and had median filter life of 20 hours [IQR 11.9, 38.1]. 27.8% of the filters clotted with median filter life 18.5 hours [IQR 14.0, 35.88]. 17.7% were changed due to high pressure and had median filter life 27.7 hours [IQR 2.8, 45.7]. 78.5% of the 200-recorded Mg readings were >0.74mmol/L. 30-day and in-hospital patient mortality was 27.2% and 54.5% respectively. All survivors recovered from AKI and were dialysis-free at discharge.

Conclusion: In patients with SBI and AKI, CRRT with RCA was safe and effective. Continuous post-filter Mg replacement may be considered to reduce risk of hypomagnesaemia.
Arterial Continuous Renal Replacement Therapy: A complication of the past?

Ruba Sarsour¹, Saed Awadallah¹, Mary J Barchman¹

¹East Carolina University

Purpose: After experiencing a serious safety event at our tertiary care institution in which continuous renal replacement therapy (CRRT) was run through a vascath placed in an artery, we established a protocol to prevent such sentinel events. Since critically ill patients frequently have hypotension requiring pressor support, inadvertent arterial placement of dialysis access can occur frequently despite the use of ultrasound guidance.

Methods: We educated the Intensive Care Unit (ICU) nursing staff of our purpose and methods and identified 10 patients requiring CRRT. Using the placed vascath, we attached a pressure transducer to the venous port and obtained a central venous pressure (CVP) reading as well as a tracing of the waveform. With the same technique we used the pigtail (the ‘third’ lumen) of the vascath and obtained a CVP to confirm that the CVP measured from both the venous and pigtail ports were similar. We then connected the vascath to the CRRT machine (NxStage) and documented “venous” pressures which is reflected by flow sensors prior to initiating CRRT. We then started CRRT and documented venous pressures at target blood flow rate (BFR). We also measured CVP using the pigtail while CRRT was running at target BFR.

Results: All 10 patients had a venous waveform to confirm venous access. The CVP pressures ranged from 5-21 for vascaths placed in the internal jugular vein. CVP was -2 for a patient that had vascath placed in a femoral vein. Higher CVP values of 17-21 were seen in patients that had elevated right heart pressures. CVP pressures remained the same at target BFR. The ranges of venous pressures obtained on the CRRT machine did not correlate with the CVPs.

Conclusion: Although obtaining a CVP using the vascath prior to initiating CRRT is an extra step, it was not time consuming or expensive per the nursing staff. It will ensure that CRRT is performed through proper venous access and avoid inadvertent arterial catheter placement which can have potentially serious consequences. The venous waveform will confirm placement in a venous vessel even when appropriate catheter placement is questionable. In general, the nursing staff relies on venous pressures ‘measured’ by the CRRT machine, however as seen in our results, these values do not correspond with the actual vessel pressure and can vary depending on the patient’s hemodynamics, anatomy and medical history, and hence are not reliable for identifying proper placement of the vascath.

*Table on following page*
Early Experience with Phoxillum as Post-Replacement Fluid in AKI Patients Treated with Continuous Veno-Venous Hemodiafiltration (CVVHDF)

Ewalola A Ijaduola 1, Jared Cook1, Rajesh G Speer1, Keith M Wille1, Ashita J Tolwani1

1University of Alabama at Birmingham

Purpose: Hypophosphatemia is a common complication in patients on Continuous Renal Replacement Therapy (CRRT). Phosphate supplementation remains essential in the care of these critically ill patients with acute kidney injury (AKI). There are few studies examining the use of phosphate-containing CRRT solutions as a method of phosphate supplementation. We hypothesized that administration of a commercially available phosphate-containing replacement fluid (Phoxillum) delivered post-filter with continuous veno-venous hemodiafiltration (CVVHDF) would decrease the need for supplemental phosphate replacement in patients with hypophosphatemia.

Methods: We retrospectively reviewed AKI patients on CVVHDF who developed hypophosphatemia, and assessed their clinical response, first to standard phosphate supplementation therapy, and subsequently to a phosphate-containing replacement fluid. All patients received CVVHDF using a Prismaflex device and a post-filter replacement fluid at 200 cc/hr between April - November 2016. We collected daily laboratory values, including serum phosphorus levels, and recorded daily oral and IV phosphate supplementation. After patients received 72 hours of CVVHDF, we examined the daily phosphate supplementation requirement (IV and oral) while on CRRT. After a minimum of 3 additional days, we changed the post-filter replacement fluid to Phoxillum B22K 4/0 (which contains 1 mmol/L of HPO42-) but maintained the same rate of 200 cc/hr. We compared the daily amount of phosphate supplementation required prior to and after addition of Phoxillum.

Summary: To date, five patients are included in this analysis. Median (range) age was 67 years (41 – 79), and were 3 (60%) were male. All patients had acute tubular necrosis due to sepsis. Median (range) CRRT dose was 35 ml/kg/hr (30.2 – 42.6). Median (range) phosphate supplementation required before Phoxillum was 24.8 mmol per day (16 – 41); median (range) phosphate supplementation required after Phoxillum was administered was 37.6 mmol per day (0 – 39.7), p=0.74 for group comparisons. There

<table>
<thead>
<tr>
<th>Venous Pressures on Nxstage machine before CRRT started</th>
<th>CVPs before Nxstage machine at target BFR</th>
<th>Venous Pressures on Nxstage machine before CRRT started</th>
<th>CVPs at target BFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>181</td>
<td>15</td>
<td>198</td>
<td>15</td>
</tr>
<tr>
<td>15</td>
<td>21</td>
<td>137</td>
<td>21</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>138</td>
<td>17</td>
</tr>
<tr>
<td>-5</td>
<td>-2</td>
<td>126</td>
<td>-2</td>
</tr>
<tr>
<td>30</td>
<td>5</td>
<td>202</td>
<td>5</td>
</tr>
<tr>
<td>69</td>
<td>12</td>
<td>220</td>
<td>12</td>
</tr>
<tr>
<td>26</td>
<td>5</td>
<td>161</td>
<td>5</td>
</tr>
<tr>
<td>0</td>
<td>7</td>
<td>-75</td>
<td>7</td>
</tr>
<tr>
<td>50</td>
<td>5</td>
<td>152</td>
<td>5</td>
</tr>
<tr>
<td>45</td>
<td>17</td>
<td>205</td>
<td>17</td>
</tr>
</tbody>
</table>
were no other observed acid-base abnormalities.

Conclusion: Providing Phoxillum only as post-filter replacement fluid at 200 cc/hr with CVVHDF did not reduce the need for phosphate supplementation in the majority of patients studied. Additional studies may help to identify how best to deliver Phoxillum in a cost-effective manner to correct hypophosphatemia associated with CRRT.

---

**Regional Citrate Anticoagulation CRRT in a Small Child After BiDirectional Cavopulmonary Anastomosis (Glenn operation)**

Dorela Haxhiademi\(^1\), Elisa Barberi\(^1\), Alexandru Morosan\(^1\), Riccardo Moschetti\(^1\), Susan Gwuine\(^1\), Bruno Murzi\(^1\), Paolo Del Sarto\(^1\)

\(^1\)Ospedale del Cuore, Fondazione Toscana Gabriele Monasterio, Massa, Italy

Case report
Andrei is 15 month old, 9.4 kg male with heterotaxy syndrome of the right atrial isomerism type, with Complete Atroioventricular Canal Defect, Total Anomalous Intracardiac Pulmonary Venous Return, Double Outlet Right Ventricular and Pulmonary Stenosis. In the first days of November 2016 he underwent a Bidirectional Superior Cavo-Pulmonary Anastomosis (Bidirectional Glenn - BDG) with additional pulmonary flow. The patient’s postoperative course was complicated by persistent tachyarrhythmia and low cardiac output syndrome causing AKI. The initial treatment with diuretics failed and on POD 9 the child presented oligoanuria, high creatininemia, hyperpotasemia and metabolic acidosis. Preload is the most important determinant for cardiac output in BDG (patients with 1 1/2 ventricle circulation) making CVVH management more tricky than usually.

At the time of the onset of AKI, the child was in spontaneous breathing with HFNC and was already in aspirin (antiaggregation needed to prevent thrombosis of the superio cavo-pulmonary anastomosis). In order to avoid systemic anticoagulation, we decided to use regional citrate anticoagulation of the CRRT circuit. Regional citrate anticoagulation in adult patients that undergo CRRT for AKI after cardiac surgery is the treatment of choice in our hospital.

With an uneventful eco-guided procedure a 8 French, double lumen catheter was placed in the Femoral Vein. We used an AV400S filter (PSu) with a surface area of 0,75 m\(^2\) and a standard adult blood line. The total priming volume of the filter and the blood line was 199 mL. The initial blood flow rate was 10 mL/minute and was gradually increased to 50 mL/minute within 2 hours; dialysate flow was 600 mL/min and extraction flow 20 mL/hour. Dyalisate K2 Ci-Ca solution (Sodium 133 mmol/L, Potassium 2 mmol/L, Calcium 0 mmol/L, Magnesium 0,75 mmol/L, Chloride 116,5 mmol/L, Sodium Bicarbonate 20 mmol/L, glucose 1g/L ) in combination with sodium citrate 4% solution and continuous calcium replacement were used.

The hemodynamic profile was stable and there was no need for vasopressor support. The child presented steady improvement, spontaneous diuresis and normalization of creatininemia, allowing weaning from the CRRT on POD 16. Andrei was discharged from ICU on POD 23 and from hospital on POD 30. He is in sinus rhythm, with a good functioning superior cavo-pulmonary anastomosis and has a creatinine level of 0,32 and clearance of creatinine 55mL/min.

*figure on following page*
A Novel Electronic Device for Measuring Urine Flow Rate

Aliza Goldman¹, Hagar Azran¹, Tal Stern¹, Dafna Wilner², Mor Grinstein¹

¹RenalSense, ²Hadassah Medical Center, Jerusalem, Israel

Introduction: Currently, most vital signs in the ICU are electronically monitored. However, clinical practice for urine output (UO) measurements still requires manual recording of data subject to human errors. UO is an underutilized biomarker for the indication of kidney function, fluid balance and hemodynamic status. The use of a medical device that provides accurate data of UO in real-time can help better define kidney function, patient fluid status, and response to diuretic treatments.

Methods: The RenalSense Clarity RMS™ sterile sensor kit incorporates the sensor within a standard sterile urinary catheter drainage tube and monitors urine flow in real-time as it exits the Foley catheter. For this study, the RenalSense drainage bag included a urinometer for the nursing staff to record UO as...
per standard practice. The drainage bag was placed on a scientific scale (gold standard) for validation of the sensor measurements. Sensor measurements and nursing staff manual records of UO were compared to the scale data. The sensor was connected by a cable to a laptop computer using software designed by RenalSense (Clarity RMS monitor). 1000 hours of UO data from 20 patients were collected.

Results: 1000 study hours analyzed showed a statistically significant correlation between the urine flow as measured by the Clarity RMS device and the scale of \( r=0.9562 \) (95% CI: [0.9503, 0.9613], \( p<0.0001 \)). Between the urine flow as measured by the nurse and the scale, the correlation was \( r=0.8691 \) (95% CI: [0.8522, 0.8840], \( p<0.0001 \) (Fig 1). The differences between the device and the scale were found to be significantly smaller than the differences between the nurse and the scale (paired t-test p-value: <0.0001). Common human errors with regard to the UO information included missing hours of data, imprecise records of hourly output, and an incomplete picture of patient fluid balance. Graphical presentation of electronic data showed real-time response to repeated diuretic administration.

Conclusions: Our observations have shown that electronically recorded data of UO is more consistent, reliable, and accurate than nursing records. Automated urine monitoring provided observation of diuretic response in real-time with continuous graphic monitoring of UO; highlighting possible applications of this tool for future decisions as to timely diuretic and fluid administration, furosemide stress tests, and dose response.
Experience Of Extracorporeal Therapy-OXIRIS For Sepsis In Indian Tertiary Care Hospital

SUHAS D MONDHE\textsuperscript{1}, VIKRANTH REDDY\textsuperscript{1}, SRIKANTH GUNDLAPALLI\textsuperscript{1}, SANTOSH HEDAU\textsuperscript{1}, MONIKA YACHHA\textsuperscript{1}, GIRISH KUMTHEKAR\textsuperscript{1}, MOHAMMED IMRAN\textsuperscript{1}, YUVRAJ SAWANT\textsuperscript{1}

\textsuperscript{1}CARE HOSPITALS, ROAD NUMBER 1, BANJARA HILLS, HYDERABAD, TELANGANA, INDIA 500034

Purpose of study: Despite usage of antibiotics, the mortality in septic shock is high. An extracorporeal therapy for sepsis can be used as an adjunct therapy in such patients along with appropriate antibiotics. This study was done to analyze our experience of extracorporeal therapy- OXIRIS for patients in septic shock

Method of study- Observational study

Summary of Results

Case 1): 59 yr. male, case of chronic liver disease, Nonalcoholic Steatohepatitis in 2009. Gradually developed portal hypertension and hepatopulmonary syndrome. Model of End stage Liver Disease score was 8. Child Pugh score was 8/15. Underwent split liver transplant on 25/5/16. Being stable post-surgery, was started on triple immunosuppression. He received multiple blood product transfusions. Total leucocyte count increased and persistently high. Platelet count dropped to 5700/microliter. He was started on broad spectrum antibiotics and antifungals after sending blood, urine culture. Initiated on renal replacement therapy in form of SLED for decreasing urine output & increased cumulative balance. Hypotension worsened requiring dual inotropic support. Decision was taken to switch over to CRRT from SLED. As the patient had worsening sepsis with septic shock an adjunct therapy along with appropriate antibiotics i.e. extracorporeal sepsis therapy- OXIRIS was started. Total 3 OXIRIS sessions were done. Hemodynamics improved after 1 st session. Inotropes decreased. Heparin was not used due to thrombocytopenia. Blood culture grew Enterococcus and Aspergillus. Patient succumbed due to severe sepsis.

Case 2): 70 yr. female, hypertensive on Losartan, had fever for 5 days. She had hypotension & dyspnea. Started on non-invasive ventilation. AKI was due to septic shock and drugs. Psoas abscess was diagnosed and drained. Pus grew multidrug resistant Klebsiella, started on Meropenem and Colistin. Oxiris was done for refractory shock with source control along with antibiotics. With single session of the OXIRIS patient became normotensive, afebrile and inotropes could be weaned off. CRRT de-escalated to SLED.

Conclusion: The use of such therapies early in the course of the treatment is crucial for early improvement, decreasing the ICU stay, decreasing organ supports. This decrease in vasopressor requirement & decrease in days of ICU stay may also be important aspect of these therapies. As India is a low income country, extra corporeal therapy like OXIRIS is expensive and availability is less.

table on following page
<table>
<thead>
<tr>
<th>PATIENT</th>
<th>CAUSE OF AKI</th>
<th>MODE OF RRT</th>
<th>OXIRIS SESSIONS</th>
<th>BLOOD CULTURE</th>
<th>TIME TO INITIATE RRT</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT 1</td>
<td>SEPTIC SHOCK, IMMUNOSUPPRESSION, FLUID OVERLOAD</td>
<td>SLED TO CRRT</td>
<td>3</td>
<td>ENTEROCoccus FAECIUM, ASPERGILLOSIS</td>
<td>66 HRS.</td>
<td>INOTROPES DECREASED, PATIENT SUCCUMBED</td>
</tr>
<tr>
<td>PATIENT 2</td>
<td>NON-STEROIDAL ANTI-INFLAMMATORY DRUGS, SEPTIC SHOCK</td>
<td>CRRT TO SLED</td>
<td>1</td>
<td>MULTI-DRUG RESISTANT KLEBSIELLA</td>
<td>5 HRS 30 MIN</td>
<td>INOTROPES STOPPED, PATIENT AFEBRILE AND IMPROVED</td>
</tr>
</tbody>
</table>

---

**96**

**Broad adsorption of sepsis-related pathogen and damage-associated inflammatory mediators from whole blood using porous sorbent beads**

Maryann C Gruda¹, Karl-Gustav Ruggeberg¹, Pamela O'Sullivan¹, Tamaz Guilashvili¹, Andrew Scheirer¹, Tom D Golobish¹, Vincent J Capponi¹, Phillip P Chan¹

¹CytoSorbents Medical, Inc.

Introduction: This study set out to quantify the ability of CytoSorb hemoadsorbent polymer beads (CytoSorbents Corporation, USA) to adsorb a broad selection of inflammatory pathogen-associated molecular pattern molecules (PAMPs), damage-associated molecular pattern molecules (DAMPs) and cytokines from whole blood in a single compartment, in vitro recirculation system. PAMPS, such as bacterial exotoxins, cause either direct damage or trigger an immune response in the host to fight infection leading to the production of high levels of cytokines and the release of DAMPS into the bloodstream, which can trigger a maladaptive systemic inflammatory response syndrome (SIRS) that can further contribute to organ injury. The benefits of cytokine reduction using extracorporeal blood filtration with hemoadsorbant porous polymer beads has been demonstrated in septic animals, yet the adsorption of other toxins and inflammatory factors may also contribute to the observed benefits.

Materials and Methods
Purified proteins S100A8, complement C5a, procalcitonin, HMGB-1, MIP1-alpha, IL-6, IFN-gamma, TNF-alpha, Staph aureus alpha-toxin (alpha-hemolysin), enterotoxin TSST-1, aflatoxin B1 and T-2 toxin were added to citrated whole bovine blood at expected clinical concentrations and recirculated through a 20 mL CytoSorb polymer-filled device or control (no bead) device at a flow rate of 140 ml/min for five hours. Plasma was analyzed by ELISA.

Results
Hemoperfusion of whole blood through porous polymer bead devices for five hours reduced the levels
of a broad spectrum of DAMPS, PAMPS and cytokines (Table 1). Levels of the inflammatory proteins were reduced by <20% during the five hour hemoperfusion through a control device.

<table>
<thead>
<tr>
<th>DAMPs</th>
<th>Initial Concentration (ng/mL)</th>
<th>% Removal at 5 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>C5a (8.2 kDa)</td>
<td>25</td>
<td>98 ± 1.3</td>
</tr>
<tr>
<td>Procalcitonin (13 kDa)</td>
<td>15</td>
<td>96 ± 0.7</td>
</tr>
<tr>
<td>S100-A8 (20 kDa)</td>
<td>50</td>
<td>93 ± 0.5</td>
</tr>
<tr>
<td>HMGB-1 (25 kDa)</td>
<td>100</td>
<td>83 ± 7.4</td>
</tr>
<tr>
<td>PAMPs</td>
<td>(microgram/mL)</td>
<td></td>
</tr>
<tr>
<td>Aflatoxin (0.3 kDa)</td>
<td>10</td>
<td>98 ± 0.1</td>
</tr>
<tr>
<td>T-2 toxin (0.4 kDa)</td>
<td>2</td>
<td>97 ± 4.5</td>
</tr>
<tr>
<td>TSST-1 (24 kDa)</td>
<td>1.5</td>
<td>83 ± 3.2</td>
</tr>
<tr>
<td>S. aureus alpha-toxin (33 kDa)</td>
<td>10</td>
<td>100 ± 0</td>
</tr>
<tr>
<td>Cytokines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIP1-α (8kDa)</td>
<td>400</td>
<td>98 ± 3.1</td>
</tr>
<tr>
<td>IFN-Ɣ (25 kDa)</td>
<td>400</td>
<td>79 ± 13</td>
</tr>
<tr>
<td>IL-6 (26 kDa)</td>
<td>3000</td>
<td>82 ± 14</td>
</tr>
</tbody>
</table>

97

**Cytokine Removal in Sepsis: Does Their Levels Co-relate With Outcome**

Deepak Govil¹, Sachin Gupta¹, Shrikanth Srinivasan¹, Sweta J Patel¹, Jagadeesh K N¹, Mozammil Shafi¹, Deeksha S Tomar¹, Vipal Chawla¹, Ashish Srivastava¹, Jahnabee Sarna¹

¹Institute of Critical Care & Anesthesia, Medanta The Medicity

Introduction:
Septic patients have a higher incidence of multiorgan failure, higher ICU stay and higher mortality. The cytokines, both pro and ant-inflammatory ones are released during an inflammatory insult and they play an important role in the pathogenesis of multiorgan failure and septic shock. The blood purification techniques have been used for few years but the co-relation of cytokine levels with mortality reduction has not been studied.

Purpose of study:
Retrospective data collection of 10 critically ill septic patients who underwent oXiris membrane based Continuous Renal Replacement Therapy (CRRT) and the co-relation of changes in cytokine levels measured during the therapy with the outcome of the patient.
Method:
We collected the retrospective data on critically ill septic patients who underwent oXiris membrane based CRRT. As a practice, cytokine levels are measured for all patients who undergo blood purification therapies. These levels are also measured every 12 hourly for next 72 hours. We also noted the trend in need for vasopressors, oxygenation index and urine output. We also noted the outcome of the patient.

Result:
The IL-6 and IL-10 levels were very high in all patients who underwent oXiris CRRT. The cytokines levels showed a downward trend by an average of 36% in six patients at the first measurement during the therapy. The rest four patients did not show any appreciable change. The reduction in cytokine levels also co-related with reduction in vasopressor (22%) in the first 12 hours and an increase in urine output (17%). At the end of 72 hours, six patients had almost 70% reduction in cytokine levels and the need for vasopressor reduced by 58% whereas the four patients had an unmeasurable change in cytokine levels. All these four patients died within next 2 days whereas only one patient died from the remaining six patients. The PaO2/FiO2 ratio improved in the patients which showed decrease in cytokine levels post oXiris therapy.

Conclusion:
Cytokine reduction co-related strongly with response of the blood purification therapies and also can predict a favourable outcome of the patient.
Cytokine Adsorption In Sepsis: Correct Timing Can Predict The Favourable Outcome

Deepak Govil1, Sachin Gupta1, Shrikanth Srinivasan1, Sweta J Patel1, Jagadeesh K N1, Mozammil Shafi1, Deeksha S Tomar1, Vipal Chawla1, Rahul Harne1, Nalin Talwar1

1Institute of Critical Care & Anesthesia, Medanta The Medicity

Introduction:
Gram negative infections release a host of cytokines which cause detrimental effects on various organs. This cytokine storm is one of the most important determinant in pathogenesis of multiorgan failure. Blood as a target for adjuvant therapies, the purification methods have been practiced in last few years but with mixed responses. There have been many reports about cytokine filtration but none have emphasized on the timing of application of such therapies.

Purpose of study:
Retrospective data collection of 15 critically ill septic patients who underwent oXiris membrane based Continuous Renal Replacement Therapy (CRRT) and the response of this therapy based on the timing of initiation.

Method:
We collected the retrospective data on critically ill septic patients who underwent oXiris membrane based CRRT. We noted the time of initiation of this therapy in the patients after they were diagnosed to be having a septic etiology for multiorgan dysfunction. The Sequential Organ Failure Assessment (SOFA) score, need for vasopressor at T=0, T=24, T=48 and T=72 hrs and stabilisation of hemodynamics was also noted. We also noted the effect on mortality in these patients.

Result:
Ten patients underwent oXiris within 3 hours of achieving adequate fluid resuscitation as per the surviving sepsis campaign. Rest of the five patients were applied oXiris only when patients were on high vasopressor support and established multiorgan dysfunction as a last resort option. The early group had an average vasopressor reduction by 36% within first 12 hours of initiation of therapy as compared to only 10% reduction in late group. The SOFA scores also showed a reduction over 72 hours of therapy in the early group whereas it remained higher in the later group. The average mean arterial pressure (MAP) increased by 38% in the early group as compared to only 10% in the later group. The early group also showed a trend towards increase in urine output as compared to the late group. Seven patients survived in the early group whereas only one survived in the later group.

Conclusion:
Early application of oXiris membrane blood purification filter can have a beneficial outcome in septic critically ill patients. These techniques should not be used as a last resort option and the cytokine removal should be targeted before end organ damage has been established.

<table>
<thead>
<tr>
<th>Delta % change over 72 hours</th>
<th>Early Group</th>
<th>Late Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasopressor reduction</td>
<td>68</td>
<td>20</td>
</tr>
<tr>
<td>SOFA scores reduction</td>
<td>72</td>
<td>18</td>
</tr>
<tr>
<td>MAP increase</td>
<td>58</td>
<td>14</td>
</tr>
<tr>
<td>Urine output increase</td>
<td>48</td>
<td>12</td>
</tr>
</tbody>
</table>
Polymyxin B-immobilized Hemoperfusion and Mortality in Critically Ill Patients with Sepsis/Septic Shock: A Systematic Review and Meta-Analysis

Tomoko Fujii1, Riki Ganeko2, Yuki Kataoka3, Toshi A Furukawa4, Robin Featherstone5, Sean M Bagshaw6

1Department of Epidemiology and Preventive Medicine, Kyoto University Graduate School of Medicine, Kyoto, Kyoto, Japan, 2Department of Surgery, Kyoto University Hospital, Kyoto, Kyoto, Japan, 3Department of Respiratory Medicine, Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Hyogo, Japan, 4Department of Health Promotion and Human Behavior, Kyoto University Graduate School of Medicine, Kyoto, Kyoto, Japan, 5Alberta Research Center for Health Evidence (ARCHE), Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada, 6Department of Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

Importance: Polymyxin-B immobilized hemoperfusion (PMX-HP) is an adjuvant therapy for sepsis or septic shock that clears circulating endotoxin through binding to polymyxin-immobilized fibers during hemoperfusion.

Objective: To evaluate the efficacy, safety and effectiveness of PMX-HP for adult patients with sepsis or septic shock.

Data Sources: MEDLINE, EMBASE, Cochrane Library, Health Technology Assessment Database, Cumulative Index to Nursing and Allied Health Literature, Pubmed, and “Igaku Chuo Zasshi”, National Institute of Health Clinical Trials Register, World Health Organization International Clinical Trials Registry Platform, University Hospital Medical Information Network Clinical Trials Registry, reference lists, and experts in the critical care nephrology and manufacturer of a PMX-HP column.

Study Selection: Randomized controlled trials comparing PMX-HP with standard therapy in critically ill patients with sepsis or septic shock.

Data Extraction and Synthesis: Two reviewers independently extracted trial-level aggregated data including population characteristics, interventions, outcomes, and funding sources. The risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias, and the strength of evidence was adjudicated using the GRADE methodology.

Main Outcomes and Measures: 28-day all-cause mortality, changes in organ dysfunction scores, and serious adverse events.

Results: Six trials (856 participants [range, 16-450]; mean age, 56.0-69.7 years) comparing PMX-HP vs sham or standard therapy fulfilled eligibility. Five out of the six trials were adjudicated to be of low risk of bias in the primary outcome of 28-day mortality. We observed the pooled risk ratio for 28-day mortality associated with PMX-HP to be 1.03 (95% confidence interval, 0.78 to 1.37; I2, 25%; 5 studies, 796 participants). We graded the quality of body of evidence as moderate. Changes in the Sequential Organ Failure Assessment score over 24 to 72 hours after treatment did not decrease with PMX-HP (Standardized mean difference, -0.38: 95%CI, -1.04 to 0.29; I2 83%; 4 studies, 347 participants). Serious adverse events attributed to therapy were poorly described.

Conclusions and Relevance: PMX-HP was not proven to reduce 28-day mortality. Available evidence does not support routine use PMX-HP for patients with sepsis or septic shock; however, future work should explore whether selected subgroups may derive benefit.
Performance Evaluation of the VITROS® NEPHROCHECK® Test*

Godwin Ogbonna¹, Sierra Clark¹, Shari Jackson¹, Jody Parsells¹, Souk Phonethepswath¹

¹Ortho Clinical Diagnostics, Rochester, NY, USA

Acute kidney injury (AKI) is a complex disorder with high mortality due to comorbidities and management challenges, especially in the critically ill patient. The VITROS® NEPHROCHECK® Test quantitatively measures Tissue Inhibitor of Metalloproteinase 2 (TIMP-2) and Insulin-like Growth Factor Binding Protein 7 (IGFBP-7) to generate an AKI risk index (AKIRISK™ Score). Patients with AKIRISK™ Score less than 0.3 are at low risk of developing AKI while those with values ≥ 0.3 are at high risk. We have evaluated the performance of the VITROS NEPHROCHECK Test on the VITROS 3600 Immunodiagnostic System and VITROS 5600 Integrated System. The test is linear across the range of 0.6 to 34.1 ng/mL for TIMP-2 and 2.2 to 482.2 ng/mL for IGFBP-7 resulting in an AKIRISK™ Score range of 0.001 to 16.4. Limits of Blank were determined to be 0.008 ng/mL and 0.006 ng/mL for TIMP-2 and IGFBP-7, respectively. Limits of Quantitation were determined to be 0.086 ng/mL for TIMP-2 and 0.106 ng/mL for IGFBP-7 respectively, resulting in an AKIRISK Score of 1.7x10⁻⁴. A 20-day precision study with pooled patient samples at mean AKIRISK Scores of 0.13, 0.51, 4.44, 10.16 resulted in within-laboratory percent coefficients of variation (%CV) of 7.5%, 5.9%, 5.5%, and 5.8% respectively on the VITROS 3600 and %CV of 5.7%, 6.3%, 8.5%, and 7.5%, respectively on the VITROS 5600 Integrated System. Potential interfering substances including acetoacetate, acetone, ammonia, albumin, creatinine, hemoglobin, myoglobin, pH (4.0 – 8.0), urea and uric acid were tested and shown not to interfere in the assay. The accuracy of the test was evaluated with 99 patient specimens spanning the assay measuring range against the Astute Medical NEPHROCHECK Test System (Astute) and the following linear regression statistics were obtained: VITROS = 1.14*Astute + 0.0126; (r) = 0.96. Fifty samples adjudicated for AKI risk were assayed using the VITROS NEPHROCHECK Test, and the data was analyzed for clinical performance. The sensitivity of the test was determined to be 90.0%, specificity of 60.0% with positive predictive value of 60% and negative predictive value of 90% for the Test. In conclusion, the assay demonstrated good precision, and acceptable clinical performance. (* under development)

Automating Urine Output Measurements To Improve Acute Kidney Injury Diagnosis And Management

Jay K Joshi¹, Alex Holterman¹, Jordan Altman¹

¹Output Medical, Chicago, IL, USA

Purpose:
To improve the measurement process of urine output to better understand how trends in urine output can impact real time clinical decision making. Our product addresses the limitations that exist in current medical technology using urine output specifically to diagnose Acute Kidney Injury (AKI). Urine output is an important vital sign used in treating patients with AKI. There is a direct correlation between patient mortality and the number of and duration of low urine output episodes. Currently, urine output data is
collected and recorded manually. ICU nurses can spend as much as 7% of their time in this effort and current methods fail to detect 23% of low urine output episodes.

Methods:
The device is an add-on adapter that fits between the Foley catheter and the distal tubing to measure urine output in customized, set intervals as the urine passes through. The technology in the device was developed through human factors analysis of ICU providers. In a benchtop test, we simulated the function of a kidney by varying the flow rate over time using a peristaltic pump while our device measured and displayed the data readings. The above graph shows the volumetric readings at intervals of 10 min and 1 hr.

Results:
The accuracy rates of our device were 97.5%.

Conclusion:
This device allows urine output to be measured in an automated manner with high accuracy. The future of Acute Kidney Injury (AKI) management will depend, in part, on predictive and diagnostic models and integration of data sets from multiple locations. These data sets include established lab markers, novel lab markers such as urinary biomarkers; and urine output. The problem with urine output is many measurements are not reliable, and are not used for clinical decision making or research. This alludes to potential research opportunities in evaluating urine output trends as an independent risk factor for AKI prognosis, mortality, and incidence of dialysis.

Through our device, we can study rates, and inflection points in those rates over time, and determine the subsequent incidence of key AKI events. This information would help physicians incorporate urine output trends into real time clinical decision making.
The Effect of Blood Transfusion on Continuous Renal Replacement Therapy (CRRT) Circuit Survival and Percent Change in Fluid Overload (PCFO) in Critically Ill Children

Dawn Eding¹, Yelena Davis², Nabil E Hassan¹, Diann Reischman³, Richard M Hackbarth¹

¹Helen Devos Children's Hospital, ²Michigan State University, ³Grand Valley State University

Purpose: Critically ill pediatric patients requiring CRRT are arguably some of the most severely ill patients in the ICU. Blood transfusion is common in these children and the associated inflammatory response along with activation of inflammatory mediators by the extracorporeal circuit could affect the coagulation milieu. However, little has been reported on the effect of transfusion on filter lifespan or its effect on fluid removal. The number of transfusions (nTx), the type of product transfused, and the total volume of transfusion (vTx) all might impact circuit life and efficacy of fluid removal during CRRT.

Methods: A single center, retrospective study of 91 consecutive pediatric CRRT patients admitted from 2008 through 2014 was undertaken to assess the effect of transfusion on circuit life and reduction in fluid overload during CRRT. Patients requiring ECMO where excluded. All patients were treated with CVVHDF using the Prismaflex CRRT device (Baxter, Deerfield, Il). Ninety-one percent of patients received citrate for circuit anticoagulation.

Results: In all, 209 filters were used in 91 patients. Filters exposed to transfusion were 3.58 times as likely to clot (p< .0001). However, those that did clot showed no correlation between lifespan and either nTx or vTx. Furthermore, there was no relationship between type of product transfused and circuit life, with the exception of a trend toward shorter life with cryoprecipitate (25 vs 51 hrs, p= .061). PCFO was significant for survivors, but not for non-survivors (median -27.5, p< .001 vs. -4.0, p= .845). Total filter hours were shorter for non-survivors 43.8 vs 65.3, but the difference was not statistically significant (p= .281). In the non-survivors only, there was a modest correlation between nTx or vTx and a greater PCFO (p= .013 and p=.042 respectively). Time on CRRT directly correlated with nTx or vTx, as well as with PCFO (p < .001).

Conclusions: Transfusion of any kind is associated with a 3.5 times greater risk of filter loss. However, the nTx, vTx, or type of transfusion, with the exception of cryoprecipitate, was not associated with circuit life. Survivors had a much greater reduction of their PCFO during CRRT than non-survivors, which was unexplained by time on CRRT, nTx or vTx. Non-survivors unexpectedly showed a modest positive correlation between nTx or vTx with reduction in PCFO which may be explained by the greater likelihood of transfusion with longer time on CRRT.
**Prediction of Citrate Accumulation from Initial Lactate Concentrations and Lactate Kinetics During Regional Citrate Anticoagulation in CRRT**

Torsten Slowinskiⁱ, Klemens Buddeⁱ, Annette Dahrlingerⁱ, Christin Schelterⁱ, Dmytro Khadzhynovⁱ

¹Charité Universitätsmedizin Berlin

Background: Citrate accumulation (CA) is a major complication of regional citrate anticoagulation (RCA) during continuous renal replacement therapy (CRRT). We studied the prediction of CA by lactate concentrations and lactate kinetics during the first 48 hours of treatment.

Methods: Patients (n=1061) treated with RCA-CRRT during a 3-year period were included in this retrospective cohort study and screened for CA. The mode of CRRT was continuous veno-venous hemodialysis (CVVHD) with use of a calcium-free and low-bicarbonate dialysate with RCA. CA was accessed by following signs: (1) a decrease of systemic iCa (<1.1 mmol/L); 2) a concomitant increase of total calcium concentration and, thus, an increase of total to ionized calcium ratio of greater than 2.25; 3) metabolic acidosis (pH <7.2 and/or base excess <-5 mmol/L) without, or with 4) an increased anion gap (>12 mmol/L).

Results: Incidence of CA during the first 48h of therapy was 2.26%. In patients with initially normal lactate (<2.2 mmol/L), elevated lactate (≥2.2 mmol/L), or severe hyperlactatemia (≥4 mmol/L) the incidence of CA was 0.77%, 4.67% and 6.33%, respectively. ROC-AUC of initial lactate concentration was 0.789 for CA prediction. Optimal cut-off from ROC (2.39 mmol/L) showed strong negative prediction (99.28%), but weak positive prediction (5.21%). In patients with CA, slope-intercept of lactate kinetic over 48h was positive and higher (+0.2 vs. -0.006 mmol/L/h, p<0.001). In patients with initial severe lactatemia (≥4 mmol/L) median lactate decrease at 6h, 12h, and 18h was -24.0%, -48.1%, and -59.4% in the non-accumulation group and higher in patients with CA (+9.8%, +20.5% and -2.3%, respectively; p<0.001).

Conclusions: Risk of CA during the first 48 hours of RCA-CVVHD is low even in patients with initial severe hyperlactatemia. Lactate kinetics rather than initially elevated lactate concentration should be considered for estimation risk of CA.

---

**Incidence of metabolic and electrolyte disturbances caused by decrease of filter clearance during regional citrate anticoagulated continuous veno-venous dialysis (rca-cvvhd)**

Torsten Slowinski¹, Detlef Kindgen-Milles², Dmytro Khadzhynov¹

¹University Hospital Charité, Berlin, Germany, ²Heinrich Heine Universität, Düsseldorf, Germany

Introduction: In all RCA protocols used for CRRT citrate is partially infused into patient and metabolized, thus leading to alkalization of blood and risk of metabolic alkalosis. When using trisodium citrate solution for RCA, protocol has to compensate for extra sodium, as well as for alkalization from metabolized citrate. In RCA-CVVHD using calcium-free, sodium-reduced, and bicarbonate-reduced dialysate (Ci-Ca Dialysate, Fresenius Medical Care) and calcium (Ca) substitution, filter clearance is
essential to maintain bicarbonate (BIC) and electrolyte control. In consequence, loss of filter clearance may cause metabolic alkalosis, hypercalcemia, and hypernatremia resistant to per protocol adaptations.

Methods: During a 6 months period 191 consecutive patients were treated with RCA-CVVHD on 6 ICUs of a university hospital and prospectively observed for disturbances consistent with loss of filter clearance.

Results: From 191 patients, 13 (6.8%) showed at least one episode of metabolic alkalosis with hypernatremia and hypercalcemia, resistant to per protocol adaptations. None of the circuits gave pressure alarm. Median filter run-time until change was 63 h (range: 8 to 72). Median BIC showed significant increase at time of filter replacement (33.9 mmol/L; 95%CI 31.5–36.4; max 42.0), compared to values 48 hours (25.6 mmol/L; 95%CI 24.5–29.3) before replacement (p=0.009). After filter change BIC decreased, reaching significant decrease at 24 h (27.9 mmol/L; 95%CI 27.0–30.7; p=0.037). Ionized Ca also showed significant increase (1.22 mmol/L; 95%CI 1.18–1.31; max. 1.39) compared to 48 h (1.16 mmol/L; 95% CI 1.11–1.20) before replacement (p=0.009). After filter change Ca decreased, reaching significant decrease after 16 h (1.11 mmol/L; 95%CI 1.05–1.15; p=0.038). Blood sodium increased until filter replacement (148 mmol/L; 95%CI 145–149; max 154) compared to 48 h before change (144 mmol/L; 95% CI 142–146) without reaching significance (p=0.140). After filter change sodium decreased to 141 mmol/L (95%CI 140-146) at 48 h (p=0.305).

Conclusions: During RCA-CVVHD using calcium-free, sodium- and bicarbonate-reduced dialysate the incidence of metabolic and electrolyte disturbances consistent with reduced filter clearance is high and can occur after short filter run-time. Metabolic alkalosis can be severe and immediate filter replacement is mandatory to correct disturbances. Further analysis is necessary to understand causes of early reduced filter clearance.

105

The influence of hypophosphatemia on outcomes during continuous renal replacement therapy in critically ill patients with acute kidney injury

Ho Sik Shin¹

¹Kosin University College of Medicine

Background: To assess the role of hypophosphatemia in major clinical outcomes in patients treated with low- or high-intensity continuous renal replacement therapy (CRRT)

Methods: We performed a retrospective analysis of data collected from 620 patients. We divided the patients into two different groups of CRRT intensity (more than or less than 40 mL/kg/hour of effluent generation) and measured serum phosphate level daily.

Results: We obtained a total of 1800 phosphate measurements on days 0, 1, and 2 and identified 49 patients (8%), 93 patients (15%), and 142 patients (23%) with hypophosphatemia on each of these respective days. In patients treated with lower-intensity CRRT, 23 episodes of hypophosphatemia/1000 patient days were identified, compared with 83 episodes/1000 patient days in patients receiving higher-intensity CRRT (P < 0.01). Multiple Cox proportional hazards analyses showed that APACHE score, utilization of vasoactive drugs, and arterial pH on the third CRRT day were significant predictors of mortality; however, serum phosphate level was not a significant contributor.

Conclusions: The APACHE score, use of vasoactive drugs, and arterial pH on the 2nd CRRT day were significant predictors of mortality. Hypophosphatemia might not be a major risk factor of increased mortality in patients treated with CRRT.
Incidence of Hypocalcemia in Pediatric Patients Receiving Continuous Renal Replacement Therapy and Tandem Therapeutic Plasma Exchange

Tara Haworth¹, Ji Lee³, Jennifer Morris¹, Katie Sigler¹, Ayse A Arikan², Poyyapakkam Srivaths²

¹Texas Children's Hospital, Houston, TX, USA, ²Baylor College of Medicine, Houston, TX, USA, ³Massachusetts General Hospital, Boston, MA, USA

Background: Therapeutic plasma exchange (TPE) is often performed in tandem with dialytic therapy in pediatric patients as vascular access and need for continuous dialysis would limit separate procedures. There is dearth of data regarding the incidence of hypocalcemia with tandem procedures.

Methods: Retrospective review to evaluate the incidence of hypocalcemia during continuous renal replacement (CRRT) and tandem TPE performed at our institution from January 2012 through December 2014.

Results: Twenty-three patients underwent 115 procedures; median of 4 tandem sessions (IQR 2.5-5.5) were instituted per patient. Demographics: Median age 2.5 yrs [IQR 0.96-9.50], 35% male, weight 14.7 kg [IQR 10.0-36.2], and BSA 0.56 m² [IQR 0.45-1.14]. Liver failure with coagulopathy was the most common indication (64.5%). Continuous venovenous hemodialfiltration and centrifugal based TPE was performed in all patients. The median CRRT clearance was 2,163 ml/1.73 m²/hr [IQR 1,985-3,364] and apheresis duration was 50 minutes [IQR 30.5-102.5]. Fresh frozen plasma (FFP) was the most common replacement fluid (96.5%); median FFP replacement volume was 2,333 mL/1.73 m² [2,044-2,994]. Regional anticoagulation with 3% citrate solution (ACD-A) was used to provide anticoagulation for both CRRT and TPE. Median ACD-A rate was 90 ml/hr [IQR 70-165]; intravenous (IV) calcium chloride infusion rate (2.16 mg/mL of elemental calcium) was 60 ml/hr [IQR 40-100]; inlet flow rate was 38.5 ml/min [IQR 26.3-50.0]; ratio 1.8 [IQR 1.2-2.3]. During tandem therapy, the median ionized calcium (iCa) was 1.12 mmol/L [IQR 0.96-1.19]; hypocalcemia (iCa <1.0 mmol/L) occurred in 52 procedures (45%). Calcium boluses were given during 40 procedures (35%). Diagnosis, age, or inlet
flow did not impact hypocalcemia occurrence. Earlier institution data had shown only 3% hypocalcemia with non-tandem TPE.

Conclusion: Hypocalcemia occurred in nearly half of TPE procedures in tandem with CRRT even with IV calcium replacement at 1.8 x inlet flow. Exogenous calcium supplementation should be preemptively increased in patients undergoing tandem therapy to prevent hypocalcemia.

First Report from the Multi-Center Adult CRRT Registry (CRRTnet)

Stuart L Goldstein1, Sean Bagshaw1, Michael Heung1, Andrew House1, Katrina Harper2, Robin Piazza1

1AKI Critical Care Research Foundation, Indianapolis, IN, USA, 2Technomics Research, Minneapolis, MN, USA

Background: CRRT is a commonly prescribed renal supportive therapy for critically ill patients with acute kidney injury (AKI). CRRT may be underutilized in adults because 1) no randomized studies show improved survival in patients receiving CRRT vs. intermittent hemodialysis (IHD) 2) perceived increased cost compared to IHD and 3) lack of available acute IHD or CRRT quality assurance data for benchmarking. We developed a multinational multicenter adult prospective CRRT Registry (CRRTnet) to 1) create a large prospective dataset of critically ill adults receiving CRRT as standard of care and integrate electronically stored CRRT machine data into the CRRTnet case report form matched to each patient encounter to 2) provide a robust patient and machine dataset to serve as an accessible adult CRRT benchmark platform for quality assurance and improvement. We now report data from the first 600 patients in CRRTnet.

Methods: Prospective, observational data registry from 2 US/3 Canadian adult CRRT programs initiated in 2012 with first patient enrollment in 2014. Electronic data entry occurs through secure website. CRRT machine electronic data uploaded from machine data cards. All sites received a waiver of informed consent from their IRB/REB. Non-parametric or linear regression analyses were used to assess for associations between pt age, SOFA score, percent fluid overload (%FO), CRRT dose and 28-day mortality and renal recovery.

Results: 605 patients (60% male, mean age 57.1+/-4.4 yrs have been enrolled. Mean APACHE II at ICU admission was 28.3+/-6.8. At CRRT initiation, mean SOFA score was 14.9+/-3.6 and median %FO was 5.7%. Mean CRRT effluent dose was 33.6+/-12.4 ml/kg/hour. Median filter lifespan was 36 hours. 28-day mortality was 37.6% (189/502 with 28-day data). 149/276 (54%) patients with available data had complete or partial renal recovery. Older age and higher SOFA scores were associated with mortality. %FO and higher SOFA scores were associated with increased ICU length of stay. Higher %FO at CRRT initiation was associated with increased risk of renal non-recovery.

Conclusion: The 28 day mortality in CRRTnet are similar to those reported in recent large acute RRT studies. The association between %FO and lack of renal recovery mirrors similar smaller single center study. With a target enrollment of 2000 patients, we believe CRRTnet will provide a unique benchmarking opportunity for CRRT patient and treatment related outcomes.
Comparison of the Interleukin-6 Clearance between AN69ST and Polysulfone Membrane Filters

Mariko Sawada¹, Tomohiro Hayashi¹, Masumi Saito², Sinichi Watabe¹, Kenji Waki¹, Yoshio Arakaki¹

¹Pediatrics, Kurashiki Central Hospital, ²Clinical Engineering, Kurashiki Central Hospital

Objectives:
The cytokine clearance during continuous hemodiafiltration (CHDF) depends on the characteristics of the membrane filter used. The acrylonitrile-co-methallyl sulfonate surface treated (AN69ST) membrane filter, which has been distributed since 2014 in Japan, has strong adsorption capacities. We evaluate the interleukin (IL)-6 clearance of the AN69ST and polysulfone (PS) membrane filters in a child with sepsis.

Methods:
The patient was a 4-year-old boy weighing 12 kg diagnosed septic shock and acute kidney injury due to gastric perforation and generalized peritonitis. He underwent CHDF to replace his renal function and remove the inflammatory cytokines. The TR55X dialysis machine (Toray Medical, Japan) was used with the following hemofilters: sepXiris 60 (AN69ST 0.6 m²; Baxter, USA) and Excelflo AEF-07 (PS 0.7 m²; Asahi KASEI Medical, Japan). Nafamostat mesylate was used as an anticoagulant, and the vascular access was an 8-Fr double lumen catheter inserted in his right internal jugular vein. The settings of CHDF were as follow: blood flow rate 30 mL/min, dialysate flow rate 750 mL/h, filtration flow rate 50 mL/h. The IL-6 samples were obtained at 1, 3, 6, 12, 18, and 24 h after the start of each CHDF session. The inlet plasma, outlet plasma, and filtrate IL-6 concentrations were measured. And the total, filtration, and adsorption clearances were calculated.

Results:
The range of inlet plasma IL-6 concentration was 67,000-192,000 pg/mL. Both membranes eliminated IL-6. AN69ST showed a higher clearance of IL-6 than did the PS membrane filter (9.4% vs. 5.1%; filtration clearance: 4.2% vs. 3.0%; absorption clearance: 5.2% vs. 2.1%). The filtration clearance did not change for 24 h in both membranes. The absorption clearance was dramatically decreased at 6 h in PS (from 8.0% to 0.9%) and AN69ST (from 10.9% to 2.8%) membrane filters.

Conclusion:
The results indicated the differences in the IL-6 clearance between AN69ST and PS membrane filters. The clearance of AN69ST is superior to that of PS membrane filter. The absorption clearance of IL-6 was reduced significantly at 6 h. These filters should be changed every 12 h to maintain their high adsorption performance.
Adequate fluid balance affects outcome of adult patients undergoing extracorporeal membrane oxygenation treatment

Min-Uk Cha¹, Hyoungnae Kim¹, Hae-Ryong Yun¹, Changhyun Lee¹, Shinchun Kang¹, Seung Hyeok Han¹, Tae-Hyun Yoo¹, Jung Tak Park¹, Shin-Wook Kang¹, Sejoong Kim²

¹Department of Internal Medicine, Institute of Kidney Disease Research, Yonsei University Colledge of medicine, Seoul, Republic of Korea, ²Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Background: Extracorporeal membrane oxygenation (ECMO) is an extracorporeal technique providing cardiorespiratory support in patients with circulatory or pulmonary failure. Frequently, large volumes of fluid resuscitation are needed to ensure sufficient preload in patients initiating ECMO. However, excessive over-hydration has been found to increase mortality in patients receiving ECMO. Therefore, in order to investigate the sufficient amount of fluid therapy for these patients, the association between cumulative fluid balance (CFB) and outcome was evaluated in patients undergoing ECMO.

Methods: Patients who underwent ECMO in Seoul National University Hospital or Yonsei University Severance Hospital between 2005 and 2016 were recruited. Cumulative fluid balance was calculated as the total fluid input minus total fluid output within the first 72 hours of ECMO initiation. Primary endpoint was mortality within 30 days after ECMO initiation.

Results: A total of 723 patients were enrolled. The mean age was 57.2 years and 66.9 % were male. The most common cause of ECMO was cardiovascular disease (42.2%) and veno-arterial ECMO was applied for 70% of patients. AKI was accompanied in 53.7% and continuous renal replacement therapy (CRRT) was applied in 366 (50.6%) patients. The mean CFB of the patients was 87.5 mL/kg. When the patients were divided into quartiles according to CFB, AKI occurred more frequently in highest CFB group (P < 0.001). The 30 day mortality rates after ECMO initiation were higher in the groups with higher CFB than those with lower CFB (P < 0.001). Multivariable analysis using Cox proportional hazard models revealed that, the risk of 30 day mortality significantly increased in patient groups with CFB values higher than 57.4 mL/kg compared to patients with patients with lower CFB (P < 0.001). This increased risk remained significant even after adjustment were made for propensity score (P = 0.005). Cubic spline model showed that mortality risk did not increase in patients with mild CFB increase. However, a significant increase in mortality risk was found in patients with CFB higher than 51.5 mL/kg.

Conclusion: Mortality risk increased in patients undergoing ECMO with excessive CFB. Adequate fluid resuscitation would be important in improving outcome in these patients.
Association of Vascular Access Flow and Volume Status on Fistula Arm by Bio-impedance Analysis in Hemodialysis

HYUNG JONG KIM¹, YounHee Lee¹, Jeong Hoon²

¹CHA Bundang Medical Center, CHA University, ²Seoul Bukbu Hospital

Background: Multi-frequency bioimpedance is a tool of body composition measure and can monitor changes in extracellular volume during dialysis. Arterio-venous fistula(aVF) could potentially affect fluid retention in the arm. We investigated whether multi-frequency bio-impedance could detect AVF stenosis or association of AVF with fluid retention in the AVF arm.

Methods: We measured the extracellular water(ECW) and total body water(TBW) in AVF arm following hemodialysis by multi-frequency bio-impedance (Inbody S10®) using an eight-electrode contact technique. We measured AVF or AVG flow by transonic ultrasonography using an ultrasound dilution technology (HD 03®) in hemodialysis.

Results: Total 73 patients (male 39 patients) were enrolled and the mean age of 58.20 ± 13.74 years. ECF/TBW ratio of fistula arm was a significantly higher than ECW/TBW ratio of non-fistula arm (0.387 ± 0.01 vs 0.379 ± 0.01; p<0.05).

ECW/TBW ratio of fistula arm was a significantly negative correlation with access flow level (mL/min) on fistula (p<0.05).
The 5kHz reactance of fistula arm was a significantly positive correlation with access flow level (mL/min) in fistula (p<0.05).

Conclusion: Absolute and also relative extracellular fluid volumes are increased in the fistula arm of hemodialysis. We thought that extracellular fluid volumes in the fistula arm were associated with access flow level (mL/min) and/or relative fistula stenosis. We suggest that multi-frequency bio-impedance can be a useful assistant tool of vascular access flow measure.

Intradialytic Hypotension in Acute Kidney Injury: A Systematic Review

Adrianna Douvris¹, Gurpreet Malhi ¹, Swapnil Hiremath ¹, Lauralyn McIntyre¹, Lindsey Sikora ¹, Catherine Weber ², Edward G Clark¹

¹University of Ottawa, Ottawa, ON, Canada , ²McGill University Health Centre, Montreal, QC, Canada

INTRODUCTION
Intradialytic hypotension (IDH) is a frequent complication of renal replacement therapy (RRT) in critically ill ICU patients with acute kidney injury (AKI). IDH exacerbates organ hypoperfusion, which may negatively impact outcomes such as renal recovery. We sought to systematically review RRT-related interventions that have been assessed with respect to their impact on IDH.

METHODS
We searched for observational studies and randomized controlled trials (RCTs) in Medline, Medline in
We also searched for unpublished studies in clinical trial registries and relevant conferences’ abstracts. Two reviewers independently screened studies for inclusion and performed data extraction. Study quality assessment was determined by two independent reviewers using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias assessment tool for RCTs.

RESULTS
We identified 13 studies meeting inclusion criteria: 8 RCTs and 5 observational studies that involved different RRT modalities including intermittent hemodialysis (7 studies), SLED (3 studies), and CRRT (3 studies). The definition of IDH varied widely across studies but was a common phenomenon with an overall incidence between 10 to 70%. We identified a maximum of 2 studies per RRT-related intervention assessed. Interventions included sodium modeling, ultrafiltration profiling, blood volume and dialysate temperature control, extended duration of SLED, variable CRRT pump speeds, changes in dialysate solutions, and use of different dialyzer membranes. Some strategies were employed in combination. A formal meta-analysis was not possible due to the heterogeneity of interventions, RRT modalities, IDH definitions, and outcomes assessed. Interventions identified as possibly reducing the incidence of IDH included use of higher dialysate sodium concentration, dialysate temperature control, and variable ultrafiltration rate, or a combination of those. In general, study quality was poor.

CONCLUSIONS
Currently, little high-quality data is available with respect to interventions for reducing the incidence of IDH in RRT-requiring AKI. Our review confirms that IDH is common across RRT modalities. Some RRT-related interventions may limit IDH and its consequences. As such, this remains a promising area for further study.

112

Improvement of Respiratory Condition Treated with Polymyxin B-immobilized Fiber Column Direct Hemoperfusion for Acute Respiratory Distress Syndrome Accompanied by Neonatal Meningitis

Hayashi Masako1, Sawada Mariko1, Shinichi Watabe1, Kazutoshi Ueda1, Tomohiro Hayashi1, Kenji Waki1, Yasunori Ueda2

1 pediatrics, Kurashiki central hospital, 2Hematology

Introduction
Polymyxin B-immobilized fiber column direct hemoperfusion (PMX) is an effective treatment method for severe sepsis and septic shock caused by gram-negative bacteria. We used PMX for neonatal meningitis caused by gram-positive bacteria that was complicated with acute respiratory distress syndrome (ARDS); PMX improved the respiratory symptoms.

Case
The case was a female infant born at a gestational age of 38 weeks and 5 days with a birth weight of 2698 g. congenital heart disease was identified as an underlying disease. At the age of 6 days, the case was diagnosed with bacterial meningitis, septic shock, and ARDS. Blood culture detected Streptococcus gallolyticus. Physical findings included retracted breathing, reticulated cyanosis. Heart rate was 173 bpm, Blood pressure could not be measured. Venous blood gas analysis indicated pH 6.772, pCO2 52.9 mFal/L, HCO3 7.7 mmol/L, BF -25.8 mmol/L, Lac 26 mmol/L. Blood tests indicated that white blood
count 24600 and that CRP 6.0 mg/dl, and cerebrospinal fluid examination revealed that the number of polymorphonuclear cells was elevated. PaO2/FiO2 ratio was 101, and x-ray findings indicated infiltration shadows in both lungs. Treatment consisting of antibiotics, IVIG, DOA 6 µg/k/g/min was performed, but since the case’s condition worsened, PMX was started. Vascular access was performed using a 6Fr double-lumen catheter. Dialysis was performed using a TR55X machine, the adsorption film used was Toraymyxin® PMX-01R, blood flow rate was 12 ml/min, and the anticoagulant used was nafamostat mesilate. PMX was performed a total of 2 times. As a result of the PMX, the blood IL-6 and cerebrospinal fluid IL-6 decreased from 57.1 to 5.9 and from 43296 to 321, respectively.

Conclusion
Due to the development of a variety of devices in recent years, extracorporeal blood purification can now be performed even on neonates. In the present case, the combined use of PMX allowed the treatment of gram-positive severe septicemia and the control of inflammatory mediators without sequelae. It has been reported that PMX is effective in cases of ARDS as well. Since there are only a limited number of cases in which PMX was used to treat neonates with anemia as a complication, there is no clear evidence of improvement in vital prognosis. Therefore, we look forward to further detailed study of complications and effectiveness when used on neonates.

113


Soo Min Jang, Bruce A Mueller

1University of Michigan College of Pharmacy, Ann Arbor, MI, USA

Background: Critically ill patients often require daily hemodialysis (HD) to maintain metabolic control, but drug dosing recommendations have been developed solely for thrice weekly HD. The purpose of this study was to use Monte Carlo Simulations (MCS) to predict if commonly used cefepime dose (1g every 24h) would reach pharmacodynamic (PD) target when the dose was given before or after dialysis treatment (preHD vs. postHD) in critically ill population.

Methods: A population pharmacokinetic (PK) model was developed for 4h daily HD as used in the VA/NIH ATN trial (blood flow rate of 360 mL/min and dialysate flow rate of 730 mL/min) and previously-published cefepime PK and demographic data on critically ill patients. A series of 5,000-subject MCS were completed for 1g every 24h before-HD and after-HD administration (preHD vs. postHD), and HD initiation relative to cefepime administration (HD early after cefepime dose vs. HD much later after HD). The goal of cefepime PD target is considered free cefepime concentration ≥ minimum inhibitory concentration (MIC) for ≥60% of the dosing interval (60% fT≥MIC). A probability of target attainment (PTA) of ≥90% for MIC of 8mg/L (against Pseudomonas aeruginosa) was considered to be an optimal dosing strategy.

Results: When cefepime was timed to be given after HD (postHD), ≥97% patients reached the PD target 60% fT≥MIC over 96 hours no matter when HD occurred (early or late after cefepime infusion). When cefepime was administered preHD and HD occurred late, only 33% met PTA. Worst case scenario was when cefepime was administered preHD and HD was then given early in the dosing regimen. In this scenario, only 9% reached the PD target over 96 hours of therapy and 0% reached the target in the first 24 h.
Conclusions: This analysis underscores the importance of when antibiotics should be given relative to HD. In this MCS analysis, most patients (≥97%) achieved the PD target of 60% fT ≥ MIC of 8 when 1g of cefepime was administered as postHD. However, most patients (<32%) failed to reach the PD goal when the dose was administered before HD was initiated. It is crucial to administer cefepime dose as post-HD regardless of when the HD is initiated in the drug dosing regimen.

![Mean 0-96 Hour PTA in IHD with 1g Cefepime](image)

**Figure 1:** Probability target attainments (PTA) for cefepime comparing cefepime administration before hemodialysis (preHD) vs. after hemodialysis (postHD), and when the HD was administered in drug dosing regimen (early vs. late) in 96 hours of therapy.

114

**Masked hypercalcemia and bone fractures with prolonged continuous renal replacement therapy (CRRT)**

Peace D Imani¹, Eileen D Brewer¹, Ayse Arikan¹, Poyyapakkam Srivaths¹

¹Baylor College of Medicine/ Texas Children's Hospital

BACKGROUND: CRRT is the preferred RRT modality for management of acute kidney injury (AKI) in critically ill patients. Although the majority of patients only require CRRT for several days, some patients need this treatment for a prolonged period. At our institution, CRRT treatment is performed with regional citrate anticoagulation (RCA). The effect of prolonged CRRT with RCA on bone health in children has not been described. We present the case of a patient treated with CRRT for 100 days, who developed bone fractures.

CASE: An 11-year-old girl with recent diagnosis of acute myeloblastic lymphoma and completion of an initial course of chemotherapy had septic shock secondary to Strep mirabilis and Strep oralis leading to multi organ failure. She developed oligoanuric AKI with poor response to intravenous furosemide, so CRRT with RCA was initiated to manage fluid overload and electrolyte and metabolic abnormalities as well as to maximize nutrition. CRRT prescription was dialysis/replacement fluid 2000 mL/hr/1.73m²
with blood flow rate (Qb) 150 mL/min (~4mL/kg), citrate (ACDA) rate 1.1 times Qb and calcium chloride (CaCl2) rate 0.6 times Qb. Qb remained constant throughout the weeks of treatment. Patient remained hemodynamically unstable preventing transition to intermittent RRT.

After 3-4 weeks on CRRT, the CaCl2 rate started to be lowered to maintain patient’s ionized calcium in the desired range and continued to be lowered from an initial CaCl2/ACDA ratio 0.5 to a very low 0.05 (10 fold decrease). Throughout the duration of CRRT, serum calcium, phosphorus and bicarbonate were mostly within normal range. Patient remained critically ill and confined to bed during CRRT. In week 13 on CRRT, routine chest x-ray was remarkable for diffuse demineralization and a non-displaced fracture of the right humeral neck. Additional imaging revealed generalized bone osteopenia and another fracture of the distal femoral metaphysis.

CONCLUSION: Children treated with prolonged CRRT with RCA may be at increased risk of fractures. Immobilization hypercalcemia, an indicator of bone demineralization, is masked in patients on CRRT with RCA, due to adjustments of CaCl2 rate to maintain desired blood calcium levels. With no adjustment of ACDA rate needed, CaCl2/ACDA ratio decreases remarkably and may be the only indicator of significant bone disease and masked hypercalcemia. A prospective study to further explore the pathophysiology of this phenomenon is needed.

115

Influence of Hemodialysis Frequency on Cefepime Probability of Target Attainment in Critically Ill Patients

Soo Min Jang1, Bruce A Mueller1

1University of Michigan College of Pharmacy, Ann Arbor, MI, USA

Background: The VA/NIH ATN trial compared daily vs. every other daily hemodialysis (HD) to determine whether dialysis dose intensity affected patient outcomes, but antibiotic dosing in both treatment arms was the same regardless of dialysis regimen. Some (Kielstein et al. NDT 2013) have suggested that suboptimal antibiotic dosing may have occurred in the intensive daily HD arm because of increased dialytic antibiotic clearance. The purpose of this study was to use Monte Carlo Simulations (MCS) to predict if commonly used cefepime dosing (1g every 24h) would reach pharmacodynamic (PD) targets for both daily HD treatment (QD) and every other day HD treatment (QOD) in critically ill patients.

Methods: Using previously-published pharmacokinetic (PK) and demographic data from critically ill patients with AKI, a population PK model was developed for QD and QOD of 4h HD as used in the VA/NIH ATN trial (blood flow rate of 360 mL/min and dialysate flow rate of 730 mL/min). A series of 5,000-subject MCS were performed for 1 g every 24h post-HD administration with varying frequencies (QD vs. QOD), different day of IHD initiation in QOD group relative to the first cefepime administration (HD on days 1&3 or 2&4 of cefepime therapy), and whether HD was administered soon after the cefepime dose (early HD) or at the end of the cefepime dosing interval (late HD). The PD target for cefepime was free cefepime concentration ≥ minimum inhibitory concentration (MIC) for ≥ 60% of the dosing interval (60% fT≥MIC) during the first 96h of therapy. The probability of target attainment (PTA) ≥90% for MIC of 8mg/L, which is a clinical susceptibility breakpoint for P. aeruginosa, was considered as an optimal therapy.
Results: Most patients (≥95%) reached the PD target 60% fT≥MIC over 96 hours of therapy regardless of HD frequency (QD vs. QOD), which day the dialysis was started from the first cefepime dose (day 1&3 vs. 2&4), and when the HD was initiated in the drug dosing regimen (early vs. late). In the first 24 h of cefepime therapy, all arms reached ≥89% PD attainment.

Conclusions: The MCS showed both HD frequency arms (QD vs. QOD) reached the optimal antibiotic dosing of 60% fT≥MIC when cefepime was administered as post-hemodialysis. Cefepime doses of 1g every 24h should achieve PD targets in 90% of critically ill patients receiving QD or QOD HD treatments.

![Mean 0-96Hour PTA in PostHD with 1g Cefepime](image)

**Figure:** Probability of target attainment (PTA) over 96h for cefepime in daily (QD) vs. every other day (QOD) hemodialysis (HD) and when the HD was administered soon after the dose (early) or at the end of the dosing interval (late).

**Efficacy and Safety of a Citrate Anticoagulation Protocol for Slow Extended Dialysis in Acute Kidney Injury Cancer Patients Using Path Batch Hemodialysis**

Marcella M Frediani1, Renato A Caires1, Antonio A Portela1, Fernanda C Coelho1, Elerson C Costalonga1, Emmanuel A Burdmann1, Ludhmila A Hajjar1, Veronica T Costa e Silva1

1University of Sao Paulo School of Medicine, Sao Paulo, SP, Brazil

Background: Data on citrate anticoagulation (CA) for hybrid dialysis therapies (HDT) are scarce and heterogeneous. Path Batch Hemodialysis (PBH) is well suited for HDT but clotting might be frequently observed, particularly in high risk patients. In this study we assessed a simple CA protocol in acute kidney injury (AKI) cancer patients treated by slow extended dialysis (SLED) using a PBH system.

Methods: We analyzed prospectively procedures (6 to 10 hours) performed with a PBH system in critically ill adult cancer patients in the Sao Paulo State Cancer Institute, from January 7 to April 7, 2015. Regional CA was performed according to an adapted protocol (Fiaccadori et al), using 4% sodium citrate and dialysate containing calcium at 5 mg/dL.
Results: Twenty four SLED sessions were performed in 11 AKI patients. Patients' characteristics were age 58 ± 13 y, 60% male, 13% on vasopressors and 9.1% on mechanical ventilation. Most (91%) patients had solid cancer (genitourinary 64%, gastrointestinal 9% and gynecologic 9%). More frequent AKI etiologic factors were sepsis (81.8%), surgery (45.5%) and obstructive uropathy (36.4%). Hospital mortality was 54.5%. The median number of SLED sessions per patient was 2 (1–3), median blood/dialysate flow (equal in PBH) was 180 (180–195) mL/min and median citrate flow at the end of session was 310 (280–320) mL/hr, corresponding to citrate level of 3.90 mmol/L in the circuit blood. Planned SLED duration was 6, 8, and 10 hours, respectively, in 25%, 71% and 4% of the procedures. The prescribed ultrafiltration (UF) was 2000ml (1500–2500). Halting of PBH due to clotting was recorded in only 3 sessions (12.5%). Overall, 95% of the prescribed dialysis time and 94% of prescribed UF were attained. Systemic ionized calcium (SCaI) at the end of SLED was 4.2 (3.9–4.5) mg/dL. Hypocalcemia (SCaI < 3.6 mg/dL) and metabolic alkalosis (serum bicarbonate > 30 mEq/L) rates were 8% and 4%, (N=96). No major bleeding, arrhythmia or relevant clinical event related to CA was observed. Hypotension (mean blood pressure <70 mmHg) was reported in 12.5% of sessions. PBH provided a satisfactory metabolic control (post session serum exams): Cr 2.4 (2.2–3.6) mg/dL; Ur 92 (50–117); Bic 26.6 (24.2–28.9) mEq/L; K 4.1 (3.7–4.7) mEq/L.

Conclusions: This is the first anticoagulation citrate-based protocol reported in SLED using PBH, which was safe and efficacious in this group of critically ill cancer patients with AKI.

NURSING ISSUES

117

Continuous Renal Replacement Therapy (CRRT)

Isagani I Marquez¹, Noel D Oabel¹

¹UC San Diego Health System

Background / Aim
Studies by other investigators have concluded that Continuous Renal Replacement Therapy (CRRT) decreases the mortality rate when limiting disruptions and time off the machine. It produces the best outcomes for CRRT patients. Continuation of the CRRT minimizes hemodynamic instability and provides fluid stability.

Plan / Do
2 patients with Acute Kidney Injury (AKI) were randomly chosen every month. Data was collected on these patients on the length of days they were on CRRT before changing the circuit. The reasons why the circuit was changed was also documented.

ACT
The data was gathered as part of a performance quality project. The skills and techniques used provide optimal patient outcomes while receiving CRRT without changing the circuit exceeding 24 to 72 hours. Systems are checked twice daily by the dialysis team. Daily monitoring include patient assessment.
reviewing laboratory results, hemodynamic status, flushing of the system to assess patency of filter as needed, and reviewing the sieving coefficient.

Conclusion
This study demonstrates that continuous CRRT without changing the circuit can lead to good patient outcomes such as transitioning to IHD and a decrease in mortality rate. The CRRT Sieving Coefficients were monitored twice daily and kept at a minimum of 80 percent before requiring to be changed. Circuit recirculation was also utilized. After blood is returned to the patient, a CRRT setup can be recirculated for 2 hours only per our policy. Mortality rate on patient on CRRT at UCSD was 35.5% in 2015 which is below the national average.

<table>
<thead>
<tr>
<th>Month</th>
<th>Longest days per patient per filter</th>
<th>Reason for change/stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>January</td>
<td>Patient 1 - 6 days Patient 2 - 3 days</td>
<td>Transition to IHD Expired</td>
</tr>
<tr>
<td>February</td>
<td>Patient 1 - 4 days Patient 2 - 6 days</td>
<td>Transfer to special bed Expired</td>
</tr>
<tr>
<td>March</td>
<td>Patient 1 - 3 days Patient 2 - 2 days</td>
<td>Expired</td>
</tr>
<tr>
<td>April</td>
<td>Patient 1 - 4 days Patient 2 - 6 days</td>
<td>Comfort care</td>
</tr>
<tr>
<td>May</td>
<td>Patient 1 - 5 days Patient 2 - 2 days</td>
<td>RN assessed to change</td>
</tr>
<tr>
<td>June</td>
<td>Patient 1 - 7 days Patient 2 - 3 days</td>
<td>Procedural</td>
</tr>
<tr>
<td>July</td>
<td>Patient 1 - 7 days Patient 2 - 1 day</td>
<td>Procedural</td>
</tr>
<tr>
<td>August</td>
<td>Patient 1 - 3 days Patient 2 - 5 days</td>
<td>Procedural Transition to IHD</td>
</tr>
<tr>
<td>September</td>
<td>Patient 1 - 4 days Patient 2 - 5 days</td>
<td>Transition to IHD</td>
</tr>
<tr>
<td>October</td>
<td>Patient 1 - 5 days Patient 2 - 7 days</td>
<td>RN assessed to change</td>
</tr>
<tr>
<td>November</td>
<td>Patient 1 - 2 days Patient 2 - 3 days</td>
<td>Transition to IHD</td>
</tr>
<tr>
<td>December</td>
<td>Patient 1 - 3 days Patient 2 - 3 days</td>
<td>Kidney func. improved</td>
</tr>
</tbody>
</table>

118

Improved Assessment of Continuous Renal Replacement Therapy (CRRT) Nursing Competency

Kathryn S Plomaritas¹, Erin Fraser¹

¹C.S. Mott Children's Hospital, University of Michigan Health System

PURPOSE OF STUDY: Assessing and maintaining nursing competency for performing continuous renal replacement therapy (CRRT) is a vital function of a CRRT program. There is currently no standard method to assess and maintain competency for CRRT. Although simulation has been used with positive results, it requires a very structured CRRT program to implement effectively and therefore is not accessible to all CRRT programs. We built a competency assessment tool that promotes understanding of the mechanics of the CRRT circuit and trouble shooting pressure and flow alarms on CRRT. Standardizing troubleshooting steps serves two purposes: it organizes interventions for the nurses and allows competency to be objectively measured. Considerations for this tool included ease of
implementation, and relevancy for units with high or low frequency of CRRT. METHODS: We identified understanding of the following topics to be vital for safe use of the CRRT machine: flow dynamics; pressure readings on and off ECMO; dialysis catheter management, and anticoagulation. We created a pre-intervention survey for all nurses caring for CRRT at bedside to identify learning needs. Nurses reported troubleshooting alarms as a learning need. Based on this feedback we developed a tool with methodical steps for troubleshooting each alarm. This tool divides nurses into 4 groups based on their ability to demonstrate actions and provide rationale: needs reorientation, needs follow-up, competent, and proficient/expert. Using this tool, nurses were tested 1:1 with an instructor on each alarm identified. The goal was for all users to demonstrate a minimum of competent skill level by the end of evaluation. Those identified as “needs follow up” were provided education on scene and given opportunity for return demonstration. Inability to demonstrate competency resulted in an action plan to achieve competency. Additionally, computer modules were created to supplement required knowledge of dialysis principles, anticoagulation, and calculating fluid balance. Nurses were given a post survey to assess the efficacy of this intervention on their CRRT skills. RESULTS: Currently 2 of 3 cohorts have completed the intervention and have overwhelmingly reported improved understanding of CRRT dynamics and ability to troubleshoot alarms (table 1). CONCLUSION: Creating a standardized evaluation tool to measure CRRT competency is a practical and effective solution for assessing and maintaining CRRT nursing competency.

<table>
<thead>
<tr>
<th>Post Intervention, Percentage of Nurses Reporting Improvement In:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to troubleshoot alarms</td>
<td>88.9%</td>
</tr>
<tr>
<td>Understanding of CRRT flow dynamics and pressure measurements</td>
<td>77.7%</td>
</tr>
<tr>
<td>Troubleshooting access and return alarms on the CRRT machine</td>
<td>86.7%</td>
</tr>
<tr>
<td>Troubleshooting scale/flow/alarms on the CRRT machine</td>
<td>73.3%</td>
</tr>
<tr>
<td>Understanding Citrate Anticoagulation</td>
<td>66.7%</td>
</tr>
<tr>
<td>Understanding how CRRT works? (Principles of CRRT)</td>
<td>60%</td>
</tr>
<tr>
<td>Understanding of flow dynamics between CRRT and ECMO</td>
<td>88.9%</td>
</tr>
<tr>
<td>Explaining how the CRRT machine measures pressures and generates alarms</td>
<td>71%</td>
</tr>
</tbody>
</table>