AKI
Current Awareness Bulletin
April 2018

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Title: Pragmatic studies for acute kidney injury: Consensus report of the Acute Disease Quality Initiative (ADQI) 19 Workgroup

Citation: Journal of Critical Care; Apr 2018; vol. 44; p. 337

Author(s): Peng, Zhiyong; Yu, Kaijiang; Ostermann, Marlies; Xi, Xiuling; Hsu, Raymond; Jean-Louis, Vincent; Prowle, John R; Du, Bin; Gallagher, Martin; Wang, Changsong; Murugan, Raghavan; Qiu, Haibo; Rimmelé, Thomas; Li, Jianguo; Forni, Lui G; Kashani, Kianoush; Ronco, Claudio; Kellum, John A

Objective: Acute kidney injury (AKI) has become a major medical and financial burden in China along with the rest of the world. There have been considerable advances in the understanding of the epidemiology and pathogenesis of AKI. However, there is no consensus regarding the optimal care for patients. The Acute Disease Quality Initiative (ADQI) 19 meeting focused on identifying and designing relevant and achievable AKI-related studies in China.

Materials & methods: The working group developed a list of preliminary questions and objectives and performed analysis of the existing literature. Relevant studies were identified through a literature search using the MEDLINE database and bibliographies of relevant research and review articles. We then used a two-step Delphi process to prioritize a research agenda and proposed specific study designs to address unmet needs.

Results: Important gaps in existing knowledge were identified and pragmatic studies were proposed in three distinct areas: care bundles for AKI prevention, renal replacement therapy (RRT) for AKI, and fluid management. In addition, the use of biomarkers to guide clinical trials was discussed.

Conclusions: Consensus was reached on a research agenda for AKI with a specific focus on pragmatic trials in China.

Title: Genetic variants and acute kidney injury: A review of the literature

Citation: Journal of Critical Care; Apr 2018; vol. 44; p. 203

Author(s): Larach, Daniel B; Engoren, Milo C; Schmidt, Ellen M; Heung, Michael

Objective: Limited data exists on potential genetic contributors to acute kidney injury. This review examines current knowledge of AKI genomics.

Materials and methods: 32 studies were selected from PubMed and GWAS Catalog queries for original data studies of human AKI genetics. Hand search of references identified 3 additional manuscripts. Results 33 of 35 studies were hypothesis-driven investigations of candidate polymorphisms that either did not consistently replicate statistically significant findings, or obtained significant results only in few small-scale studies. Vote-counting meta-analysis of 9 variants examined in >1 candidate gene study showed >=50% non-significant studies, with larger studies generally finding non-significant results. The remaining 2 studies were large-scale unbiased investigations: One examining 2,100 genes linked with cardiovascular, metabolic, and inflammatory syndromes identified BCL2, SERPINA4, and SIK3 variants, while a genome-wide association study (GWAS) identified variants in BBS9 and the GRM7/LMCD1-AS1 intergenic region. All studies had relatively small sample sizes (<2300 subjects). Study heterogeneity precluded candidate gene and GWA meta-analysis.
Conclusions: Most studies of AKI genetics involve hypothesis-driven (rather than hypothesis-generating) candidate gene investigations that have failed to identify contributory variants consistently. A limited number of unbiased, larger-scale studies have been carried out, but there remains a pressing need for additional GWA studies.

Title: Utility of electronic AKI alerts in intensive care: A national multicentre cohort study

Citation: Journal of Critical Care; Apr 2018; vol. 44; p. 185

Author(s): Holmes, Jennifer; Roberts, Gethin; Geen, John; Dodd, Alan; Selby, Nicholas M; Lewington, Andrew; Scholey, Gareth; Williams, John D; Phillips, Aled O

Objective: Electronic AKI alerts highlight changes in serum creatinine compared to the patient's own baseline. Our aim was to identify all AKI alerts and describe the relationship between electronic AKI alerts and outcome for AKI treated in the Intensive Care Unit (ICU) in a national multicentre cohort.

Methods: A prospective cohort study was undertaken between November 2013 and April 2016, collecting data on electronic AKI alerts issued.

Results: 10% of 47,090 incident AKI alerts were associated with ICU admission. 90-day mortality was 38.2%. Within the ICU cohort 48.8% alerted in ICU. 51.2% were transferred to ICU within 7 days of the alert, of which 37.8% alerted in a hospital setting (HA-AKI) and 62.2% in a community setting (CA-AKI). Mortality was higher in patients transferred to ICU following the alert compared to those who had an incident alert on the ICU (p<0.001), and was higher in HA-AKI (45.3%) compared to CA-AKI (39.5%) (35.0%, p=0.01). In the surviving patients, the proportion of patient recovering renal function following, was significantly higher in HA-AKI alerting (84.2%, p=0.004) and CA-AKI alerting patients (87.6%, p<0.001) compared to patients alerting on the ICU (78.3%).

Conclusion: The study provides a nationwide characterisation of AKI in ICU highlighting the high incidence and its impact on patient outcome. The data also suggests that within the cohort of AKI patients treated in the ICU there are significant differences in the presentation and outcome between those patients that require transfer to the ICU after AKI is identified and those who develop AKI following ICU admission. Moreover, the study demonstrates that using AKI e-alerts provides a centralised resource which does not rely on clinical diagnosis of AKI or coding, resulting in a robust data set which can be used to define the incidence and outcome of AKI in the ICU setting.

Title: Acute kidney injury: emerging pharmacotherapies in current clinical trials.

Citation: Pediatric Nephrology; May 2018; vol. 33 (no. 5); p. 779-787

Author(s): Benoit, Stefanie Woolridge; Devarajan, Prasad

Abstract: Acute kidney injury (AKI) is a significant source of morbidity and mortality in pediatric patients, affecting more than one quarter of critically ill children. Despite significant need, there are no targeted therapies to reliably prevent or treat AKI. Recent advances in our understanding of renal injury and repair signaling pathways have enabled the development of several targeted pharmaceuticals. Here we review emerging pharmacotherapies for AKI that are currently in clinical trials. Categorized by their general mechanism of action, the therapies discussed include anti-inflammatory agents (recAP, AB103, ABT-719), antioxidants (iron chelators, heme arginate), vasodilators (levosimendan),
apoptosis inhibitors (QPI-1002), and repair agents (THR-184, BB-3, mesenchymal stem cells).

Title: Assessment of hydration status using bioelectrical impedance vector analysis in critical patients with acute kidney injury.

Citation: Clinical Nutrition; Apr 2018; vol. 37 (no. 2); p. 695-700
Author(s): Hise, Ana Cláudia da Rosa; Gonzalez, Maria Cristina

Objective: The state of hyperhydration in critically ill patients with acute kidney injury (AKI) is associated with increased mortality. Bioelectrical impedance vector analysis (BIVA) appears to be a viable method to access the fluid status of critical patients but has never been evaluated in critical patients with AKI. The objective of this study is to evaluate the hydration status measured using BIVA in critical patients under intensive care at the time of AKI diagnosis and to correlate this measurement with mortality.

Methods: We assessed the fluid status measured using BIVA in 224 critical patients at the time of AKI diagnosis and correlated it with mortality. To interpret the results, BIVA Software 2002 was used to plot the data from the patients studied on the 95% confidence ellipses of the RX c plane for comparisons between groups (non-survivors, survivors). Variables such as mechanical ventilation, vasoactive drug, and sepsis, among others, were collected.

Results: The impedance vector analysis conducted using BIVA Software 2002 indicated changes in the body compositions of patients according to the 95% confidence ellipse between the vectors R / H and X c / H of the group of survivors and the group of deceased patients. Hotelling’s test (T^2 = 21.2) and the F test (F = 10.6) revealed significant differences (p < 0.001) between the two groups. These results demonstrate that patients who died presented with a greater hydration volume at the time of AKI diagnosis compared with those who survived. In addition to the hydration status measured using BIVA, the following were also correlated with death: diagnosis at hospitalization, APACHE II score, length of hospital stay, RIFLE score, maximum organ failure, sepsis type, hemoglobin, and AF.

Conclusions: The fluid status assessment measured using BIVA significantly demonstrated the difference in hydration between survivors and non-survivors among critically ill patients with AKI.

Title: Acute Kidney Injury: It's not just the 'big' burns.

Citation: Injury; Feb 2018; vol. 49 (no. 2); p. 213-218
Author(s): Kimmel, L.A.; Wilson, S.; Walker, R.G.; Singer, Y.; Cleland, H.

Objective: Acute Kidney Injury (AKI) complicates the management of at least 25% of patients with severe burns and is associated with long term complications. Most research focuses on the patients with more severe burns, and whether the same factors are associated with the development of AKI in patients with burns between 10 and 19% total body surface area (TBSA) is unknown. The aims of this study were to examine the incidence of, and factors associated with, the development of AKI in patients with %TBSA≥10, as well as the relationship with hospital metrics such as length of stay (LOS).

Methods: Retrospective medical record review of consecutive burns patients admitted to The Alfred Hospital, the major adult burns centre in Victoria, Australia. Demographic and
injury details were recorded. Factors associated with AKI were determined using multiple logistic regression.

**Results:** Between 2010 and June 2014, 300 patients were admitted with burn injury and data on 267 patients was available for analysis. Median age was 54.5 years with 78% being male. Median %TBSA was 15 (IQR 12, 20). The AKI incidence, as measured by the RIFLE criteria, was 22.5%, including 15% (27/184) in patients with %TBSA 10-19. Factors associated with AKI included increasing age and %TBSA (OR 1.05 p<0.001) as well as increased surgeries (p<0.041) and a cardiac comorbidity (p<0.01). All patients with renal comorbidity developed AKI. In the %TBSA 10-19 cohort, only increasing age (OR 1.05 p<0.001) was associated with AKI. After accounting for confounding factors, the probability of discharge from hospital in Non-AKI group was greater than for the AKI patients at all time points (P<0.001).

**Conclusion:** This is the first study to show an association between patients with %TBSA 10-19 and AKI. Given the association between AKI and complications, prospective research is needed to further understand AKI in burns with the aim of risk reduction.

**Title:** Pediatric acute kidney injury induced by concomitant vancomycin and piperacillin–tazobactam.

**Citation:** Pediatrics International; Feb 2018; vol. 60 (no. 2); p. 136-141

**Author(s):** Abouelkheir, Manal; Alsubaie, Sarah

**Background:** Vancomycin is very commonly used in combination with piperacillin–tazobactam (PTZ) as the initial empiric treatment for moderate–severe infection, whenever coverage for both methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa is required. The combination of vancomycin and PTZ in adults has recently been reported to significantly increase the risk of acute kidney injury (AKI) relative to vancomycin monotherapy; such reports in pediatrics, however, are sparse.

**Methods:** A retrospective chart review was conducted of pediatric patients, aged 0–14 years, who were admitted to the general wards or intensive care unit and developed AKI after receiving vancomycin and PTZ concomitantly for >48 h. AKI is defined as a decrease in estimated glomerular filtration rate ≥50% from baseline. Cases were identified by reviewing the Adverse Drug Reaction program database at King Saud University Medical City in Saudi Arabia from January 2015 to June 2016.

**Results:** Eight children admitted to the present hospital and who received concomitant vancomycin and PTZ treatment for pneumonia (n = 7) or febrile neutropenia (n = 1) developed drug-induced nephrotoxicity. Drug Interaction Probability Scale (DIPS) score for causation assessment was 9 in all cases (highly probable).

**Conclusion:** Caution in utilizing the combination of vancomycin and PTZ is warranted in pediatric patients. Health-care professionals should be vigilant if this combination is to be initiated, and ensure close monitoring of renal function. Antibiotic therapy de-escalation should be considered as soon as culture results are available.

**Title:** Contrast-associated acute kidney injury is a myth: Yes.

**Citation:** Intensive Care Medicine; Jan 2018; vol. 44 (no. 1); p. 104-106

**Author(s):** Ehrmann, Stephan; Aronson, Doron; Hinson, Jeremiah
Abstract: An editorial is presented which discusses misconceptions associated with contrast-associated acute kidney injury. It mentions that contrast medium (CM) administration is widely cited as a leading cause of hospital-acquired acute kidney injury (AKI). It presents information on risk factors for AKI which contributes to contrast media (CM) and also presents information on contrast media and acute kidney injury in patients undergoing percutaneous intervention.

Title: Contrast-associated acute kidney injury is a myth: No.

Citation: Intensive Care Medicine; Jan 2018; vol. 44 (no. 1); p. 107-109
Author(s): Weisbord, Steven; Cheryon, Damien

Abstract: An editorial is presented which discusses impact of intravascular contrast over kidney. It mentions that iodinated contrast has adverse effects on mitochondrial enzyme activity and membrane function and contributes to apoptosis of renal tubular epithelial cells. It presents information on pathophysiology of acute kidney injury following intravascular contrast administration.

Title: Contrast-associated acute kidney injury is a myth: We are not sure.

Citation: Intensive Care Medicine; Jan 2018; vol. 44 (no. 1); p. 110-114
Author(s): Kashani, Kianoush; Levin, Adeera; Schetz, Miet

Abstract: An editorial is presented which discusses contrast-associated acute kidney injury (CA-AKI). Topics discussed include information on the impact of contrast media on the AKI incidence; determination of contrast dose as a significant risk factor of CA-AKI both in experimental settings and in humans undergoing cardiac angiography and impact of intravenous hydration combined with cytoprotective drugs over prevention of CA-AKI.

Title: Association Between Early Caffeine Citrate Administration and Risk of Acute Kidney Injury in Preterm Neonates: Results From the AWAKEN Study.

Citation: JAMA Pediatrics; Apr 2018; p. e180322
Author(s): Harer, Matthew W; Askenazi, David J; Boohaker, Louis J; Carmody, J Bryan; Griffin, Russell L; Guillett, Ronnie; Selewski, David T; Swanson, Jonathan R; Charlton, Jennifer R; Neonatal Kidney Collaborative (NKC)

Objectives: To examine the association between caffeine citrate administration and AKI in preterm neonates in the first 7 days after birth and to test the hypothesis that caffeine administration would be associated with reduced incidence and severity of AKI.

Design, Setting, and Participants: This study was a secondary analysis of the Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN) study, a retrospective observational cohort that enrolled neonates born from January 1 to March 31, 2014. The dates of analysis were October 2016 to December 2017. The setting was an international, multicenter cohort study of neonates admitted to 24 participating level III or IV neonatal intensive care units. Participants met the original inclusion and exclusion criteria of the AWAKEN study. Additional exclusion criteria for this study included participants greater than or equal to 33 weeks’ gestation at birth, admission after age 7 days, use of theophylline
in the neonatal intensive care unit, or lack of data to define AKI. There were 675 preterm neonates available for analysis.

**Exposure:** Administration of caffeine in the first 7 days after birth.

**Main Outcomes and Measures:** The primary outcome was the incidence of AKI (based on the modified neonatal Kidney Disease: Improving Global Outcomes [KDIGO] definition) in the first 7 days after birth. The hypothesis that caffeine administration would be associated with reduced AKI incidence was formulated before data analysis.

**Results:** The study cohort (n = 675) was 55.4% (n = 374) male, with a mean (SD) gestational age of 28.9 (2.8) weeks and a mean (SD) birth weight of 1285 (477) g. Acute kidney injury occurred in 122 neonates (18.1%) in the first 7 days after birth. Acute kidney injury occurred less frequently among neonates who received caffeine than among those who did not (50 of 447 [11.2%] vs 72 of 228 [31.6%], P < .01). After multivariable adjustment, administration of caffeine remained associated with reduced odds of developing AKI (adjusted odds ratio, 0.20; 95% CI, 0.11–0.34), indicating that for every 4.3 neonates exposed to caffeine one case of AKI was prevented. Among neonates with early AKI, those receiving caffeine were less likely to develop stage 2 or 3 AKI (adjusted odds ratio, 0.20; 95% CI, 0.12–0.34).

**Conclusions and Relevance:** Caffeine administration in preterm neonates is associated with reduced incidence and severity of AKI. Further studies should focus on the timing and dosage of caffeine to optimize the prevention of AKI.

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**Title:** Incidence, Predictors, and Impact on Six-Month Mortality of Three Different Definitions of Contrast-Induced Acute Kidney Injury after Coronary Angiography.

**Citation:** The American journal of cardiology; Apr 2018; vol. 121 (no. 7); p. 818-824

**Author(s):** Guillon, Benoit; Ecarnot, Fiona; Marcucci, Charles; Ducloix, Didier; Chatot, Marion; Badoz, Marc; Bonnet, Benjamin; Chopard, Romain; Frey, Pierre; Meneveau, Nicolas; Schiele, François

**Abstract:** We assessed incidence, predictors, and impact on 6-month mortality of contrast-induced acute kidney injury (CI-AKI) after coronary angiography with or without percutaneous coronary intervention in patients with acute coronary syndrome (ACS), according to 3 different CI-AKI definitions. Serum creatinine (sCr) was assessed at baseline and 48 to 72 hours after procedure to classify patients into 3 CI-AKI groups: Group 1: increase in sCr ≥25% over baseline but absolute increase <0.5 mg/dl; Group 2: absolute increase ≥0.5 mg/dl; Group 3: absolute increase ≥0.3 mg/dl or ≥50% over baseline. The association between CI-AKI and all-cause 6-month mortality was assessed using multivariate Cox regression. Among 1,002 patients included, median age was 68 [57 to 79] years. The sample had the following characteristics: 70% men, 25% diabetics, 22% had a history of myocardial infarction, 21% had baseline estimated glomerular filtration rate (as calculated by the Modification of Diet in Renal Disease) 25% in the remaining 844 (84.2%). CI-AKI was significantly associated with 6-month all-cause mortality using the definitions for Group 2 (hazard ratio 3.1, 95% confidence interval [CI] 1.5 to 6.6, p = 0.002) and Group 3 (hazard ratio 2.03, 95% CI 1.03 to 4.0, p = 0.04), but not Group 1. In conclusion, based on the definition used for CI-AKI, CI-AKI is observed in 6% to 15.7% of patients. An increase of 25% over baseline sCr does not identify high-risk patients. CI-AKI defined as an increase in sCr >0.3 mg/dl identifies 15.7% of the population at 2-fold higher risk of mortality.
Title: Furosemide Response Predicts Acute Kidney Injury After Cardiac Surgery in Infants and Neonates.

Citation: Pediatric Critical Care Medicine: a Journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies; Apr 2018; vol. 19 (no. 4); p. 310-317

Author(s): Borasino, Santiago; Wall, Kevin M; Crawford, Jack H; Hock, Kristal M; Cleveland, David C; Rahman, Fazlur; Martin, Kimberly D; Alten, Jeffrey A

Objective: Cardiac surgery-induced acute kidney injury occurs frequently in neonates and infants and is associated with postoperative morbidity/mortality; early identification of cardiac surgery-induced acute kidney injury may be crucial to mitigate postoperative morbidity. We sought to determine if hourly or 6-hour cumulative urine output after furosemide in the first 24 hours after cardiopulmonary bypass could predict development of cardiac surgery-induced acute kidney injury and other deleterious outcomes.

Design: Retrospective chart review.

Setting: Pediatric cardiac ICU.

Patients: All infants younger than 90 days old admitted to the cardiac ICU from October 2012 to December 2015 who received at least one dose of furosemide in the first 24 hours after cardiopulmonary bypass surgery.

Interventions: None.

Measurements and Main Results: Ninety-nine patients met inclusion and exclusion criteria. In total, 45.5% developed cardiac surgery-induced acute kidney injury. Median time between cardiopulmonary bypass and furosemide was 7.7 hours (interquartile range, 4.4-9.5). Six-hour cumulative urine output was 33% lower (p = 0.031) in patients with cardiac surgery-induced acute kidney injury. Area under the curve for prediction of cardiac surgery-induced acute kidney injury was 0.69 (p = 0.002). Other models demonstrated urine output response to furosemide had significant area under the curves for prediction of peak fluid overload greater than 15% (0.68; p = 0.047), prolonged peritoneal dialysis (area under the curve, 0.79; p = 0.007), prolonged mechanical ventilation (area under the curve, 0.79; p < 0.001), prolonged hospitalization (area under the curve, 0.62; p = 0.069) and mortality (area under the curve, 0.72; p = 0.05).

Conclusions: Urine output response to furosemide within 24 hours of cardiopulmonary bypass predicts cardiac surgery-induced acute kidney injury development and other important morbidity in children younger than 90 days old; prospective validation is warranted.

Title: High incidence of acute kidney injury during chemotherapy for childhood acute myeloid leukemia.

Citation: Pediatric blood & cancer; Apr 2018; vol. 65 (no. 4)

Author(s): Du Plessis, Liezl; Rassekh, Shahrad Rod; Mammen, Cherry

Objectives: Childhood acute myeloid leukemia (AML) is a rare and heterogeneous disease. Pediatric data on the epidemiology of acute kidney injury (AKI) in AML are limited. We report on the incidence of AKI in childhood AML and the risk factors associated with AKI episodes.

Methods: A retrospective cohort of 53 patients (≤18 years), with de novo AML, receiving chemotherapy over a 10-year period. All serum creatinine (SCr) levels during therapy-related hospitalizations were assessed to stage AKI episodes as per Kidney Disease: Improving
Global Outcomes criteria. Severe AKI was defined as AKI stages 2 or 3 and urine output criteria were not used. AKI risk factors were assessed independently in both cycle 1 alone and combining all chemotherapy cycles.

**Results:** AKI developed in 34 patients (64%) with multiple AKI episodes in 10 patients (46 total episodes). Twenty-four severe AKI episodes occurred in 23 patients (43.4%) with a mean duration of 26.1 days (SD 7.3). In cycle 1, hyperleukocytosis was not predictive of AKI, but severe sepsis was an independent risk factor of severe AKI (odds ratio [OR]: 13.4; 95% CI 1.9-94.9). With cycles combined, all subjects with AKI had severe sepsis and older age (≥10 years) was associated with severe AKI (OR: 20.8; 95% CI 3.8-112.2).

**Conclusions:** There was a high incidence of AKI in our AML cohort with a strong association with older age (≥10 years) and severe sepsis. Larger prospective studies are needed to confirm the high burden of AKI and risk factors in this susceptible population.

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**Title:** Paradigms of acute kidney injury in the intensive care setting.

**Citation:** Nature reviews. Nephrology; Apr 2018; vol. 14 (no. 4); p. 217-230

**Author(s):** Kellum, John A; Prowle, John R

**Abstract:** Acute kidney injury (AKI) is a heterogeneous clinical syndrome that has multiple aetiologies, variable pathogenesis and diverse outcomes. However, these heterogeneities are not reflected in current approaches to the diagnosis and, to some degree, treatment of AKI. For example, congestive heart failure and dehydration can produce identical changes in serum creatinine level and urine output (parameters that are used to define AKI); however, they differ vastly in their physiological contexts and demand completely opposite treatments. AKI is often still considered to be a homogeneous clinical entity, which implies a uniform pathogenesis and a well-defined prognosis. As a consequence, efforts to find effective AKI treatments have been hampered by a lack of clear clinical classifications for various types of AKI. In addition, subclassification of AKI into subclinical phenotypes - for example, on the basis of protein biomarkers and other in vitro diagnostics that take into account disease aetiology and underlying pathogenesis - might be necessary to develop therapeutic approaches that effectively target the widely differing pathomechanisms of AKI. In this Review, we discuss the major subtypes of AKI that are associated with sepsis, major surgery, renal hypoperfusion and nephrotoxin exposure - situations that are typically seen in the intensive care setting. We consider differences and similarities in their phenotype, pathogenesis and outcomes and how this information might be used to guide treatment.

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**Title:** Cystatin C predicts acute kidney injury and mortality in cirrhotics: A prospective cohort study.

**Citation:** Liver International: official journal of the International Association for the Study of the Liver; Apr 2018; vol. 38 (no. 4); p. 654-664

**Author(s):** Maiwall, Rakhi; Kumar, Awinash; Bhardwaj, Ankit; Kumar, Guresh; Bhadoria, Ajeet S; Sarin, Shiv K

**Objective:** Acute kidney injury is a frequent and ominous complication in cirrhosis. An episode of AKI damages the functional nephron mass, compromising the renal functional reserve. We aimed to study the incidence of AKI, probability of subsequent episodes, whether AKI itself predisposes to future AKI and the reliability of serum cystatin C(sCyC) as a biomarker in a prospective cohort of cirrhotics.
**Patients & Methods:** Five hundred and thirty-one cirrhotics without ongoing AKI were followed for development/resolution of AKI. Predictive models for AKI and mortality were developed and validated (Gr. A, Derivative cohort \( n = 273 \), Gr. B, Validation Cohort \( n = 258 \)).

**Results:** 365 episodes of AKI occurred in 233 patients; yielding a mean of 1.56 episodes of AKI per patient. In Gr. A and B, 97 (35.5%) and 78 (30%) patients had prior AKI episodes and were predisposed to further attacks (Gr. A, HR 3.9, 95% CI 2.7-5.6, Gr. B, HR 3.6, 95% CI 2.5-5.4). AKI was thus an independent predictor of the development of new AKI \( (P < .05) \) and this risk increased significantly with increase in the number of AKI episodes \( (P < .001) \). S.CysC but not s.Cr was an independent predictor of new AKI on multivariate analysis. “AKI-Score” incorporating CysC; and the addition of Cyst into components of MELD, that is the “MELD-Cystatin” score predicted the development of AKI and mortality, respectively, and performed significantly better than the MELD and CTP scores.

**Conclusions:** An episode of AKI itself predisposes to subsequent attacks of AKI in cirrhotics. Scores incorporating CysC can accurately predict the development of AKI and mortality in these patients.

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**Title:** Overexpressed SIRT6 attenuates cisplatin-induced acute kidney injury by inhibiting ERK1/2 signaling.

**Citation:** Kidney international; Apr 2018; vol. 93 (no. 4); p. 881-892

**Author(s):** Li, Zhongchi; Xu, Kang; Zhang, Nannan; Amador, Gabriel; Wang, Yanying; Zhao, Sen; Li, Liyuan; Qiu, Ying; Wang, Zhao

**Abstract:** Sirtuin 6 (SIRT6) is a NAD+-dependent deacetylase associated with numerous aspects of health and physiology. Overexpression of SIRT6 has emerged as a protector in cardiac tissues against pathologic cardiac hypertrophy. However, the mechanism of this protective effect is not fully understood. Here, both in vivo and in vitro results demonstrated that SIRT6 overexpression can attenuate cisplatin-induced kidney injury in terms of renal dysfunction, inflammation and apoptosis. In addition, SIRT6 knockout aggravated kidney injury caused by cisplatin. We also found that SIRT6 bound to the promoters of ERK1 and ERK2 and deacetylated histone 3 at Lys9 (H3K9) thereby inhibiting ERK1/2 expression. Furthermore, inhibition of ERK1/2 activity eliminated aggravation of kidney injury caused by SIRT6 knock out. Thus, our findings uncover the protective effect of SIRT6 on the kidney and define a new mechanism by which SIRT6 regulates inflammation and apoptosis. This may provide a new therapeutic target for kidney injury under stress.

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**Title:** Predicting acute kidney injury: current status and future challenges.

**Citation:** Journal of nephrology; Apr 2018; vol. 31 (no. 2); p. 209-223

**Author(s):** Pozzoli, Simona; Simonini, Marco; Manunta, Paolo

**Abstract:** Acute kidney injury (AKI) is characterized by an acute decline in renal function and is associated to increased mortality rate, hospitalization time, and total health-related costs. The severity of this ‘fearsome’ clinical complication might depend on, or even be worsened by, the late detection of AKI, when the diagnosis is based on the elevation of serum creatinine (SCr). For these reasons, in recent years a great number of new tools, biomarkers and predictive models have been proposed to clinicians in order to improve diagnosis and prevent the development of AKI. The purpose of this narrative paper is to
review the current state of the art in prediction and early detection of AKI and outline future challenges.

Title: Association between chloride content of intravenous fluids and acute kidney injury in critically ill medical patients with sepsis.

Citation: Journal of critical care; Apr 2018; vol. 44; p. 363-367
Author(s): Jaynes, Megan P; Murphy, Claire V; Ali, Naeem; Krautwater, Annalise; Lehman, Amy; Doepker, Bruce A

Title: Chronic kidney disease after acute kidney injury associated with intravenous colistin use in survivors of severe infections: A comparative cohort study.

Citation: Journal of critical care; Apr 2018; vol. 44; p. 244-248
Author(s): Meraz-Muñoz, Alejandro; Gomez-Ruiz, Ismael; Correa-Rotter, Ricardo; Ramirez-Sandoval, Juan C

Objective: The use of colistin for multi-drug resistant (MDR) infections has led to an increase of colistin-associated acute kidney injury (AKI). Nevertheless, information on long-term renal prognosis is scarce. We aimed to determine the predictors of chronic kidney disease (CKD) in survivors of MDR-infections with colistin-associated AKI.

Methods: A retrospective cohort of patients with colistin-associated AKI was compared with controls (survivors of severe infections who developed AKI matched by age, sex, diabetes, vancomycin exposure, and baseline kidney function). The primary outcome was the development of CKD after 6 months of follow-up.

Results: From 2011 to 2015, 122 patients with MDR infections received colistin. Among 72 survivors, 29 (40%) had colistin-associated AKI. After 6 months, 22 of them (75%) progressed to CKD (G3 in 21/22) compared with 16 (27%) in 58 controls (P5g was an independent predictor of progression to CKD (OR: 14.1, 95% CI: 2.6-75.7).

Conclusion: Colistin-associated AKI had a substantial risk for the latter development CKD, and consequently, these patients should be tightly monitored.

Title: Novel acute kidney injury biomarkers: their characteristics, utility and concerns.

Citation: International urology and nephrology; Apr 2018; vol. 50 (no. 4); p. 705-713
Author(s): Beker, Braian M; Corleto, Mateo G; Fieiras, Cecilia; Musso, Carlos G

Abstract: Acute kidney injury (AKI) consists of a rapid renal function decline which usually increases serum urea and creatinine levels. Since kidney injury begins by inducing biological and molecular changes which evolve to cellular damage, biomarkers could be used as tools for monitoring early AKI appearance, and predicting its recovery. Among the main AKI biomarkers the neutrophil gelatinase-associated lipocalin, cystatin C, kidney injury molecule-1, monocyte chemotactic peptide-1, N-acetyl-β-D-glucosaminidase, interleukin-18, liver-type fatty acid-binding protein, netrin-1, cycle arrest markers, endogenous ouabain, selenium-binding protein 1, and BPIFA2 marker, have been described. Even though novel biomarkers seem to be more helpful to early detect AKI and/or predict the need for renal replacement, and mortality compared to serum creatinine, more comprehensive studies are still required to determine their clinical utility.
**Title: Is the dose and mode of administration of dipyrone associated with acute kidney injury?**

**Citation:** European journal of anaesthesiology; Apr 2018; vol. 35 (no. 4); p. 316-318

**Author(s):** Stamer, Ulrike M; Stüber, Frank

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**Title: Risk factors and mortality rate in premature babies with acute kidney injury.**

**Citation:** Journal of clinical laboratory analysis; Mar 2018; p. e22441

**Author(s):** Elmas, Ahmet Taner; Tabel, Yılmaz; Özdemir, Ramazan

**Objective:** Acute kidney injury (AKI) is a common morbidity in neonatal intensive care units and associated with poor outcome. This study aimed to determine the prevalence of AKI and provide a demographic data and risk factors associated with the mortality and morbidity.

**Methods:** This is a retrospective study included 105 premature babies. Diagnosis of AKI was based on neonatal KDIGO classification criteria. The babies were stratified into two groups according to AKI status during the hospitalization. Clinical and laboratory characteristics of the AKI group were compared to non-AKI group.

**Results:** AKI occurred in 21 (20.0%) of 105 premature babies, and mortality rate in these babies was 61.9%. Lower gestational weeks, lower Apgar scores at 5 minutes, lower systolic blood pressures, and inotropic supports were independent risk factors for the development of AKI in preterm babies (P < .05, for each). Oliguria, preeclampsia/eclampsia, resuscitation at birth, lower diastolic blood pressure, patent ductus arteriosus (PDA), inotropic support, and furosemide treatment were associated with the mortality (P < .05, for each).

**Conclusions:** Prenatal risk factors and medical interventions are associated with AKI, and AKI is associated with increased morbidity and mortality. Therefore, identification of AKI is very important in this vulnerable population and it should be performed as quickly as possible in all babies who are at high risk for developing of AKI.

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**Title: Use of Proton Pump Inhibitors and the Risk of Acute Kidney Injury Among Patients with Rheumatoid Arthritis: Cohort Study.**

**Citation:** Drug safety; Mar 2018

**Author(s):** Svanström, Henrik; Lund, Marie; Melbye, Mads; Pasternak, Björn

**Objective:** Recent observational studies have indicated that use of proton pump inhibitors may be associated with adverse renal outcomes. The objective of this study was to investigate whether the use of proton pump inhibitors increases the risk of acute kidney injury among patients with rheumatoid arthritis.

**Methods:** We conducted the study as a historical prospective cohort study, including patients with rheumatoid arthritis, 30-84 years of age, during 2004-2015. Among these, we identified and matched episodes of use and non-use of proton pump inhibitors (control episodes) 1:4 on the propensity score, including 24,579 episodes of use of proton pump inhibitors and 98,230 control episodes. The primary outcome was a first diagnosis of acute kidney injury and the secondary outcome was any serious renal event (acute kidney injury or chronic kidney disease). The primary time point for analysis was 120 days after study entry.

**Results:** The incidence rate of acute kidney injury was 2.2 per 1000 person-years during episodes of use of proton pump inhibitors and 0.9 during control episodes. Use of proton
pump inhibitors was associated with a significantly increased risk of acute kidney injury (hazard ratio 2.30, 95% confidence interval 1.26-4.20). The absolute risk difference was 40 (95% confidence interval 8-99) events of acute kidney injury per 100,000 episodes of use of proton pump inhibitors. Use of proton pump inhibitors was also associated with a significantly increased risk of the secondary outcome of any serious renal event (hazard ratio 2.61, 95% confidence interval 1.80-3.80).

**Conclusions:** This cohort study among patients with rheumatoid arthritis found a significantly increased risk of acute kidney injury associated with the use of proton pump inhibitors. These findings may help inform clinical decision making when considering the risks and benefits of proton pump inhibitor treatment in rheumatoid arthritis.

**Title:** Ischemic acute kidney injury and klotho in renal transplantation.

**Citation:** Clinical biochemistry; Mar 2018

**Author(s):** Panah, Fatemeh; Ghorbanihaghjo, Amir; Argani, Hassan; Zarmehri, Maryam Asadi; Ahmad, Saeed Nazari Soltan

**Abstract:** Post-transplant ischemic acute kidney injury (AKI), secondary to ischemia reperfusion injury (IRI), is a major problem influencing on the short and long term graft and patient survival. Many molecular and cellular modifications are observed during IRI, for example, tissue damage result production of reactive oxygen species (ROS), cytokines, chemokines, and leukocytes recruitment which are activated by NF-κB (nuclear factor kappa B) signaling pathway. Therefore, inhibiting these processes can significantly protect renal parenchyma from tissue damage. Klotho protein, mainly produced in distal convoluted tubules (DCT), is an anti-senescence protein. There is increasing evidence to confirm a relationship between Klotho levels and renal allograft function. Many studies have also demonstrated that expression of the Klotho gene would be down regulated with IRI, so it will be used as an early biomarker for acute kidney injury after renal transplantation. Other studies suggest that Klotho may have a renoprotective effect for attenuating of kidney injury. In this review, we will discuss pathophysiology of IRI-induced acute kidney injury and its relation with klotho level in renal transplantation procedure.

**Title:** Identification of Patients Expected to Benefit from Electronic Alerts for Acute Kidney Injury.

**Citation:** Clinical journal of the American Society of Nephrology: CJASN; Mar 2018

**Author(s):** Biswas, Aditya; Parikh, Chirag R; Feldman, Harold I; Garg, Amit X; Latham, Stephen; Lin, Haiqun; Palevsky, Paul M; Ugwuowo, Ugochukwu; Wilson, F Perry

**Objectives:** Electronic alerts for heterogenous conditions such as AKI may not provide benefit for all eligible patients and can lead to alert fatigue, suggesting that personalized alert targeting may be useful. Uplift-based alert targeting may be superior to purely prognostic-targeting of interventions because uplift models assess marginal treatment effect rather than likelihood of outcome.

**Design, Setting, Participants & Measurements:** This is a secondary analysis of a clinical trial of 2278 adult patients with AKI randomized to an automated, electronic alert system versus usual care. We used three uplift algorithms and one purely prognostic algorithm, trained in 70% of the data, and evaluated the effect of targeting alerts to patients with higher scores in the held-out 30% of the data. The performance of the targeting strategy was assessed as the interaction between the model prediction of likelihood to benefit from alerts...
and randomization status. The outcome of interest was maximum relative change in creatinine from the time of randomization to 3 days after randomization.

**Results:** The three uplift score algorithms all gave rise to a significant interaction term, suggesting that a strategy of targeting individuals with higher uplift scores would lead to a beneficial effect of AKI alerting, in contrast to the null effect seen in the overall study. The prognostic model did not successfully stratify patients with regards to benefit of the intervention. Among individuals in the high uplift group, alerting was associated with a median reduction in change in creatinine of -5.3% (P=0.03). In the low uplift group, alerting was associated with a median increase in change in creatinine of +5.3% (P=0.005). Older individuals, women, and those with a lower randomization creatinine were more likely to receive high uplift scores, suggesting that alerts may benefit those with more slowly developing AKI.

**Conclusions:** Uplift modeling, which accounts for treatment effect, can successfully target electronic alerts for AKI to those most likely to benefit, whereas purely prognostic targeting cannot.

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**Title:** Biopsy-proven vancomycin-induced acute kidney injury: a case report and literature review.

**Citation:** BMC nephrology; Mar 2018; vol. 19 (no. 1); p. 72

**Author(s):** Sawada, Anri; Kawanishi, Kunio; Morikawa, Shohei; Nakano, Toshihiro; Kodama, Mio; Mitobe, Mitihito; Taneda, Sekiko; Koike, Junki; Ohara, Mamiko; Nagashima, Yoji; Nitta, Kosaku; Mochizuki, Takahiro

**Background:** Vancomycin is the first-line antibiotic for methicillin-resistant Staphylococcus aureus and coagulase-negative strains. The risk of vancomycin-induced acute kidney injury increases with plasma vancomycin levels. Vancomycin-induced acute kidney injury is histologically characterized by acute interstitial nephritis and/or acute tubular necrosis. However, only 12 biopsy-proven cases of vancomycin-induced acute kidney injury have been reported so far, as renal biopsy is rarely performed for such cases. Current recommendations for the prevention or treatment of vancomycin-induced acute kidney injury are drug monitoring of plasma vancomycin levels using trough level and drug withdrawal. Oral prednisone and high-flux haemodialysis have led to the successful recovery of renal function in some biopsy-proven cases.

**Case Presentation:** We present the case of a 41-year-old man with type 1 diabetes mellitus, who developed vancomycin-induced acute kidney injury during treatment for Fournier gangrene. His serum creatinine level increased to 1020.1 μmol/L from a baseline of 79.6 μmol/L, and his plasma trough level of vancomycin peaked at 80.48 μg/mL. Vancomycin discontinuation and frequent haemodialysis with high-flux membrane were immediately performed following diagnosis. Renal biopsy showed acute tubular necrosis and focal acute interstitial nephritis, mainly in the medullary rays (medullary ray injury). There was no sign of glomerulonephritis, but mild diabetic changes were detected. He was discharged without continuing haemodialysis (serum creatinine level, 145.0 μmol/L) 49 days after initial vancomycin administration.

**Conclusions:** This case suggests that frequent haemodialysis and renal biopsy could be useful for the treatment and assessment of vancomycin-induced acute kidney injury, particularly in high-risk cases or patients with other renal disorders.
Title: Association between preoperative renin-angiotensin system inhibitor use and postoperative acute kidney injury risk in patients with hypertension.

Citation: Clinical nephrology; Mar 2018
Author(s): Xu, Nana; Long, Qian; He, Ting; Liu, Xing; Dai, Haijiang; Lu, Yao; Wen, Jia; Wu, Qiaoyu; Yuan, Hong

Objective: To determine whether preoperative renin-angiotensin system (RAS) inhibitor use within 7 days of noncardiac surgery is associated with a lower incidence of postoperative acute kidney injury (AKI) in hypertensive patients.

Materials & Methods: We retrospectively analyzed 12,545 hypertensive patients undergoing noncardiac surgery at the Third Xiangya Hospital of Central South University from February 2007 to November 2015. According to the use of RAS inhibitors within 7 days of surgery, the patients were divided into a RASI group and a non-RASI group. We used a multivariable logistic regression model and propensity score matching (PSM) analysis to examine the association between preoperative RAS inhibitor use and postoperative AKI incidence.

Results: Among the 12,545 hypertensive patients undergoing noncardiac surgery who met the inclusion/exclusion criteria, 18.74% received preoperative RAS inhibitor treatment within 7 days of surgery. After PSM, 2,192 patients in each group were matched successfully. The incidence of postoperative AKI in the RASI group was significantly lower than that in the non-RASI group (7.39% vs. 12.32%, p < 0.001). The multivariable logistic regression analysis and the PSM analysis demonstrated similar associations between preoperative RAS inhibitor use and postoperative AKI incidence. This association was modified by the presence of preoperative congestive heart failure (CHF) (p-value for the interaction: 0.027), and the observed association was not evident in patients without CHF (CHF: adjusted odds ratios (ORs): 0.47; 95% CI: 0.31 - 0.70 vs. no CHF: adjusted OR: 0.80; 95% CI: 0.62 - 1.03).

Conclusion: The preoperative use of RAS inhibitors in hypertensive patients was associated with a lower incidence of AKI following noncardiac surgery, and this association was not significant in the subgroup population without CHF.

Title: Acute Kidney Injury in Critically Ill Patients: A Prospective Randomized Study of Tidal Peritoneal Dialysis Versus Continuous Renal Replacement Therapy.

Citation: Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy; Mar 2018
Author(s): Al-Hwiesh, Abdullah; Abdul-Rahman, Ibrahim; Finkelstein, Fredric; Divino-Filho, Jose; Qutub, Hatem; Al-Audah, Nadia; Abdelrahman, Abdalla; El-Fakhirany, Nazeek; Nasr El-Din, Mohammed; El-Salamony, Tamer; Noor, Abdulsalam; Al-Shahrani, Mohammed; Al-Otaibi, Khalid

Abstract: Few studies have discussed the role of peritoneal dialysis (PD) in managing acute kidney injury (AKI) in critically ill patients. The present study compares the outcome of AKI in intensive care unit (ICU) patients randomized to treatment with tidal PD (TPD) or continuous venovenous hemodiafiltration (CVVHDF). One hundred and twenty-five ICU patients with AKI were randomly allotted to CVVHDF, (Group A, N = 62) or TPD, (group B, N = 63). Cause and severity of renal injury were assessed at the time of initiating dialysis. The primary outcome was hospital mortality at 28 days, and secondary outcomes were time to recovery of renal function, duration of stay in the ICU, metabolic and fluid control, and
improvement of sensorial and hemodynamic parameters. No statistically significant differences were observed between groups in regard to patients' characteristics. The survival at 28 days was significantly better in the patients treated with TPD when compared to CVVHDF (69.8% vs. 46.8%, P < 0.01). Infectious complications were significantly less (P < 0.01) in the TPD group (9.5%) when compared to the CVVHDF group (17.7%). Recovery of kidney function (60.3% vs. 35.5%), median time to resolution of AKI and the median duration of ICU stay of 9 days (7-11) vs. 19 days (13-20) were all in favor of TPD (P < 0.01). This study suggests that there are better outcomes with TPD compared to CRRT in the treatment of critically ill patients with AKI.

Title: Renal regeneration after Acute Kidney Injury.

Citation: Nephrology (Carlton, Vic.); Mar 2018
Author(s): Coelho, Silvia; Cabral, Guadalupe; Lopes, José António; Jacinto, António

Abstract: Acute kidney injury is common and associated with negative renal and patient outcomes. The human kidney has a real but limited regeneration capacity. Understanding renal regeneration may allow us to manipulate this process and thus develop therapeutic weapons to improve patients' outcome. In the first part of this paper we discuss the clinical factors associated with renal recovery: baseline patient particularities, acute kidney injury characteristics and the medical approach taken in the short and long-term. In the second part, the cellular and molecular mechanisms underlying renal regeneration are explored. The immune system seems to have an important role first promoting inflammation and then tissue healing. Other players, such as cellular senescence, mitochondrial dysfunction, renal hemodynamics and metabolic reprogramming also have a role in renal regeneration. We aim to develop a short review of renal regeneration, offering a holistic view of this process.

Association of plasma neutrophil gelatinase-associated lipocalin with acute kidney injury and clinical outcome in cardiac arrest survivors depends on the time of measurement.

Citation: Biomarkers: biochemical indicators of exposure, response, and susceptibility to chemicals; Mar 2018 ; p. 1-8
Author(s): Cho, Yong Soo; Lee, Byung Kook; Lee, Dong Hun; Jung, Yong Hun; Lee, Sung Min; Park, Jung Soo; Jeung, Kyung Woon

Objective: The optimal timing for measurement of neutrophil gelatinase-associated lipocalin (NGAL) level to predict acute kidney injury (AKI) and prognosis in cardiac arrest (CA) survivors has not been elucidated. We aimed to compare the diagnostic and prognostic performance of NGAL levels after return of spontaneous circulation (ROSC) and at 48 h after CA.

Methods: We included 231 adult cardiac arrest survivors who underwent targeted temperature management between May 2013 and December 2016. The primary outcome was stage 2 and 3 AKI (high stage AKI), and the secondary outcomes were in-hospital mortality and neurologic outcome. Sixty-one (26.4%) developed high stage AKI, 50 (21.6%) died, and 152 (65.8%) had a poor neurologic outcome.

Results: NGAL level at 48 h (0.876; 95% confidence interval [CI], 0.826-0.916) had a higher area under receiver operating characteristic curve than NGAL level after ROSC (0.694; 95% CI, 0.631-0.753). Both NGAL levels were independently associated with high stage AKI. NGAL level at 48 h (1.001; 95% CI, 1.000-1.002) remained a significant predictor for in-
hospital mortality, while neither of the NGAL levels were independently associated with neurologic outcome.

**Conclusions:** NGAL at 48 h after CA seems to be a robust predictor for high stage AKI and in-hospital mortality.

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**Title:** Describing pediatric acute kidney injury in children admitted from the emergency department.

**Citation:** Pediatric nephrology (Berlin, Germany); Mar 2018

**Author(s):** Hanson, Holly R; Babcock, Lynn; Byczkowski, Terri; Goldstein, Stuart L

**Objective:** To define those children who develop acute kidney injury (AKI) within 48 h of admission from the emergency department (ED) and ascertain patient-related factors in the ED associated with AKI.

**Methods:** Retrospective, cohort study of children, birth to 19 years, admitted to a tertiary pediatric hospital from the ED between January 2010 and December 2013 who had serum creatinine (Scr) drawn as part of clinical care. AKI was defined as a 50% increase in Scr above baseline, as measured within 48 h of hospital presentation. Multivariable logistic regression was performed to determine factors associated with AKI by comparing those with and without kidney injury on hospital presentation.

**Results:** Of all ED admissions, 13,827 subjects (27%) were included; 10% developed AKI. Of kids with AKI, 75% had a measured Scr consistent with AKI while in the ED, 36% were admitted to the intensive care unit, and 2% died (all significantly more than children without AKI). Young age, history of AKI or solid organ transplant, receipt of intravenous fluids or central venous access in the ED, and admission to intensive care were factors independently associated with AKI (AUC = 0.793, 95% CI 0.78-0.81).

**Conclusions:** One in 10 children who had Scr measured and were admitted to a tertiary pediatric hospital had AKI on or within 48 h of presentation. Inherent characteristics, identifiable in the ED, are associated with an increased risk of AKI. Future research should focus on improving AKI recognition in the ED by the development of a risk stratification tool.

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**Title:** Trends in Hospitalizations for Acute Kidney Injury - United States, 2000-2014.

**Citation:** MMWR. Morbidity and mortality weekly report; Mar 2018; vol. 67 (no. 10); p. 289-293

**Author(s):** Pavkov, Meda E; Harding, Jessica L; Burrows, Nilka R

**Abstract:** Acute kidney injury is a sudden decrease in kidney function with or without kidney damage, occurring over a few hours or days. Diabetes, hypertension, and advanced age are primary risk factors for acute kidney injury. It is increasingly recognized as an in-hospital complication of sepsis, heart conditions, and surgery (1,2). Its most severe stage requires treatment with dialysis. Acute kidney injury is also associated with higher likelihood of long-term care, incidence of chronic kidney disease and hospital mortality, and health care costs (1,2). Although a number of U.S. studies have indicated an increasing incidence of dialysis-treated acute kidney injury since the late 1990s (3), no data are available on national trends in diabetes-related acute kidney injury. To estimate diabetes- and nondiabetes-related acute kidney injury trends, CDC analyzed 2000-2014 data from the National Inpatient Sample (NIS) (4) and the National Health Interview Survey (NHIS) (5). Age-standardized rates of acute kidney injury hospitalizations increased by 139% (from 23.1 to 55.3 per 1,000 persons)
among adults with diagnosed diabetes, and by 230% (from 3.5 to 11.7 per 1,000 persons) among those without diabetes. Improving both patient and provider awareness that diabetes, hypertension, and advancing age are frequently associated with acute kidney injury might reduce its occurrence and improve management of the underlying diseases in an aging population.

**Title:** Attributable Risk and Time Course of Colistin-Associated Acute Kidney Injury.

**Citation:** Clinical journal of the American Society of Nephrology : CJASN; Mar 2018

**Author(s):** Miano, Todd A; Lautenbach, Ebbing; Wilson, F Perry; Guo, Wensheng; Borovskiy, Yuliya; Hennessy, Sean

**Objectives:** Despite colistin's longstanding reported association with nephrotoxicity, the attributable risk and timing of toxicity onset are still unknown. Whether substantial toxicity occurs during the initial 72 hours of exposure has important implications for early treatment decisions. The objective of this study was to compare colistin-exposed patients with a matched control group given other broad spectrum antibiotics.

**Design, Setting, Participants & Measurements:** We conducted a retrospective cohort study in patients treated for multidrug-resistant Pseudomonas, Klebsiella, or Acinetobacter spp. Colistin-exposed patients were matched to unexposed controls using propensity scores. AKI was defined according to the Kidney Disease Improving Global Outcomes creatinine criteria. Incidence rate ratios and risk differences of AKI in the matched cohort were estimated with the generalized estimating equation Poisson regression model. Risk factors for AKI were tested for effect modification in the matched cohort.

**Results:** The study included 150 propensity-matched pairs with similar types of infection, similar delays to effective treatment, and similar baseline characteristics. Incidence of AKI was 77 of 150 (51%) in the colistin group versus 33 of 150 (22%) in matched controls (risk difference, 29%; 95% confidence interval, 19 to 39), corresponding to a number needed to harm of 3.5. Early toxicity was apparent, because AKI risk was higher in colistin-exposed patients at 72 hours of exposure (incidence rate ratio, 1.9; 95% confidence interval, 1.1 to 3.5). In both groups, hospital mortality in patients who experienced AKI was lower if kidney function returned to baseline during hospitalization. The effect of colistin exposure on AKI risk varied inversely according to baseline hemoglobin concentration.

**Conclusions:** Colistin is associated with substantial excess AKI that is apparent within the first 72 hours of treatment. Colistin's toxicity varied according to baseline hemoglobin concentration.

**Title:** Incidence and perioperative risk factors for early acute kidney injury after radical cystectomy and urinary diversion.

**Citation:** Urologic oncology; Mar 2018

**Author(s):** Furrer, Marc A; Schneider, Marc P; Burkhard, Fiona C; Wuethrich, Patrick Y

**Objective:** Early postoperative acute kidney injury (AKI) is associated with increased morbidity and mortality following major surgery. Only few reports exist on postoperative AKI and specifically its risk factors after radical cystectomy (RC) and urinary diversion (UD). We aimed to identify risk factors for AKI in patients undergoing RC and UD.

**Methods:** In an observational single-center cohort study, 912 consecutive bladder cancer patients undergoing RC and UD from 2000 to 2016 were evaluated for risk factors for AKI.
Multiple logistic regression analysis was performed to model the association between variables and AKI.

**Results:** Early postoperative AKI occurred in 100/912 patients (11%). An increased risk was seen in patients with surgery lasting >400 minutes, male and obese patients (>25 kg/m²). Independent predictors were duration of surgery (P = 0.020), intraoperative blood loss (P = 0.049), preoperative serum creatinine values (P = 0.004), intraoperative administration of crystalloids (P = 0.032), body mass index (P = 0.031), and fluid balance (P = 0.006). Patients with AKI had a longer hospitalization time (18d vs 17d, P = 0.040). Limitations include the potential bias due to the design as a case series with prospectively collected data with some missing values.

**Conclusions:** An increased risk for AKI was seen in patients with an operative time >400 minutes. Hence, in this group of patients the role of postoperative fluid management for preserving renal function should be considered. Further independent predictors of postoperative AKI were male sex, obesity, intraoperative blood loss, and a low preoperative plasma creatinine. So especially in male and obese patients, optimized perioperative nephroprotective strategies are of importance.

**Title:** Acute kidney injury after high dose etoposide phosphate: A retrospective study in children receiving an allogeneic hematopoietic stem cell transplantation.

**Citation:** Pediatric blood & cancer; Mar 2018

**Author(s):** Barnoud, Delphine; Pinçon, Claire; Bruno, Bénédicte; Béné, Johana; Gautier, Sophie; Lahoche, Annie; Petitpain, Nadine; Vasseur, Michèle; Barthélémy, Christine; Décaudin, Bertrand; Simon, Nicolas; Odou, Pascal

**Objective:** Etoposide phosphate (EP; single injection, 60 mg/kg) followed by total body irradiation (TBI) at 12 Gy has been used as an allogeneic stem cell transplantation (allo-SCT) conditioning regimen for children since 2010. In our institution, EP has been suspected of leading to acute nephrotoxicity. The aim of this study was to assess the potential renal toxicity of EP in this context.

**Materials & Methods:** A retrospective study was carried out on children hospitalized between 2007 and 2015 for allo-SCT with TBI-based myeloablative conditioning associated with cyclophosphamide (CY, 60 mg/kg/day × 2 days) or EP. The primary endpoint of the study was the occurrence of acute kidney injury (AKI). Additional endpoints were time to recovery for children with AKI, survival, and treatment-related mortality.

**Results:** Thirty-five patients were analyzed (CY: 22 vs. EP: 13). AKI occurred more frequently in the EP group than in the CY one (69% vs. 27%, adjusted odds ratio 6.0, 95% confidence interval [CI] [1.145; 31.445], P = 0.03). The median time to recovery was estimated at 3 days, 95% CI (2; 17), with CY and 11 days 95% CI (5; 18) with EP (adjusted hazard ratio of recovery for EP vs. CY 0.262, 95% CI [0.071; 0.969], P = 0.04). No significant difference was highlighted between the two treatments for survival or for treatment-related mortality.

**Discussion:** This study shows that EP at high dosage or one of its excipients is probably responsible for AKI, as compared to CY. Further studies are required to explore the origin of this adverse effect.
Title: Pre-operative anaemia, intra-operative hepcidin concentration and acute kidney injury after cardiac surgery: a retrospective observational study.

Citation: Anaesthesia; Mar 2018
Author(s): Karkouti, K; Yip, P; Chan, C; Chawla, L; Rao, V

Abstract: Acute kidney after cardiac surgery is more common in anaemic patients, whereas haemolysis during cardiopulmonary bypass may lead to iron-induced renal injury. Hepcidin promotes iron sequestration by macrophages: hepcidin concentration is reduced by anaemia and increased by inflammation. We analysed the associations in 525 patients between pre-operative anaemia (haemoglobin < 130 g.l⁻¹ in men and 26.4 μmol.l⁻¹ or > 50% creatinine increase during the first two days after cardiac surgery. Rates of pre-operative anaemia and postoperative kidney injury were 109/525 (21%) and 36/525 (7%), respectively. The median (IQR [range]) intra-operative hepcidin concentration was 20 (10-33 [0-125]) μg.l⁻¹ and was lower in anaemic patients than those who were not: 15 (4-28 [0-125]) μg.l⁻¹ vs. 21 (12-33 [0-125]) μg.l⁻¹, respectively, p = 0.002. Four variables were independently associated with postoperative kidney injury, for which the beta-coefficients (SE) were: minutes on cardiopulmonary bypass, 0.016 (0.004), p < 0.001; intra-operative hepcidin concentration, 0.032 (0.008), p < 0.001; pre-operative anaemia, 1.97 (0.56), p < 0.001; and Cleveland clinic risk score, 0.88 (0.35), p = 0.005. Contrary to generally increased rates of kidney injury in patients with higher hepcidin concentrations, rates of kidney injury in anaemic patients were lower in patients with higher hepcidin concentrations, beta-coefficient (SE) -0.037 (0.01), p = 0.007. In cardiac surgical patients the rate of postoperative acute kidney injury predicted by the Cleveland risk score might be adjusted for pre-operative anaemia and intra-operative cardiopulmonary bypass time and hepcidin concentration. Pre-operative correction of anaemia, reduction in intra-operative bypass time and modification of iron homeostasis and hepcidin concentration might reduce acute kidney injury.

Sources Used:
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