AKI
Current Awareness Bulletin
May 2020

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Title: Acute kidney injury biomarkers in the critically ill.

Citation: Clinica chimica acta; international journal of clinical chemistry; May 2020

Author(s): Pedroso, Luana Amaral; Nobre, Vandack; de Almeida, Claudmeire Dias Carneiro; da Silva Praxedes, Marcus Fernando; Guimarães, Nathália Sernizon; E Silva, Ana Cristina Simões; Martins, Maria Auxiliadora Parreiras

Abstract: Acute kidney injury (AKI) is a highly common complication in intensive care units (ICUs). Novel biomarkers might accelerate the detection and management of AKI. We performed a systematic review aiming to evaluate the performance of biomarkers for early AKI diagnosis in ICUs. MEDLINE, BVS, CINAHL, COCHRANE and EMBASE were searched for studies (2006-2019) on the use of biomarkers for AKI diagnosis. Preselected biomarkers were cystatin C, chitinase-3-like protein-1 (UCHI3L1), neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), kidney injury molecule-1 (KIM-1) and interferon-gamma-inducible protein 10 (IP-10/CXCL-10), measured in plasma or urine. Eleven articles with total of 2,289 patients were included. The most cited biomarker was NGAL (n=7 studies; 63.6%). Biomarkers with the highest sensitivity (se) and specificity (sp) were urinary heat shock protein (HSP-72) (se=100%; sp=90%) and urinary IL-18 (se=92%; sp=100%). All biomarkers’ performance was influenced by the presence of comorbidities or AKI etiology. Although some biomarkers showed good performance, there was no externally validated biomarker for early AKI diagnosis. Thus, from this review, we did not indicate a novel biomarker to be promptly used in clinical practice. Prospective studies with a large number of patients are needed to expand knowledge in this field.

Title: Timing of Initiation of Renal Replacement Therapy in Sepsis-Associated Acute Kidney Injury.

Citation: Journal of clinical medicine; May 2020; vol. 9 (no. 5)

Author(s): Agapito Fonseca, José; Gameiro, Joana; Marques, Filipe; Lopes, José António

Abstract: Sepsis-associated acute kidney injury (SA-AKI) is a major issue in medical, surgical and intensive care settings and is an independent risk factor for increased mortality, as well as hospital length of stay and cost. SA-AKI encompasses a proper pathophysiology where renal and systemic inflammation play an essential role, surpassing the classic concept of acute tubular necrosis. No specific treatment has been defined yet, and renal replacement therapy (RRT) remains the cornerstone supportive therapy for the most severe cases. The timing to start RRT, however, remains controversial, with early and late strategies providing conflicting results. This article provides a comprehensive review on the available evidence on the timing to start RRT in patients with SA-AKI.

Title: Acute Renal Failure/Acute Kidney Injury (AKI) Associated with Endovascular Procedures.

Citation: Diagnostics (Basel, Switzerland); May 2020; vol. 10 (no. 5)

Author(s): Krasinski, Zbigniew; Krasińska, Beata; Olszewska, Marta; Pawlaczyk, Krzysztof

Abstract: AKI is one of the most common underdiagnosed postoperative complications that can occur after any type of surgery. Contrast-induced nephropathy (CIN) is still poorly
defined and due a wide range of confounding individual variables, its risk is difficult to determine. CIN mainly affects patients with underlying chronic kidney disease, diabetes, sepsis, heart failure, acute coronary syndrome and cardiogenic shock. Further research is necessary to better understand pathophysiology of contrast-induced AKI and consequent implementation of effective prevention and therapeutic strategies. Although many therapies have been tested to avoid CIN, the only potent preventative strategy involves aggressive fluid administration and reduction of contrast volume. Regardless of surgical technique-open or endovascular-perioperative AKI is associated with significant morbidity, mortality and cost. Endovascular procedures always require administration of a contrast media, which may cause acute tubular necrosis or renal vascular embolization leading to renal ischemia and as a consequence, contribute to increased number of post-operative AKIs.

Title: Fyn Kinase: A Potential Therapeutic Target in Acute Kidney Injury.

Citation: Biomolecules & therapeutics; May 2020; vol. 28 (no. 3); p. 213-221

Author(s): Uddin, Md Jamal; Dorotea, Debra; Pak, Eun Seon; Ha, Hunjoo

Abstract: Acute kidney injury (AKI) is a common disease with a complex pathophysiology which significantly contributes to the development of chronic kidney disease and end stage kidney failure. Preventing AKI can consequently reduce mortality, morbidity, and healthcare burden. However, there are no effective drugs in use for either prevention or treatment of AKI. Developing therapeutic agents with pleiotropic effects covering multiple pathophysiological pathways are likely to be more effective in attenuating AKI. Fyn, a nonreceptor tyrosine kinase, has been acknowledged to integrate multiple injurious stimuli in the kidney. Limited studies have shown increased Fyn transcription level and activation under experimental AKI. Activated Fyn kinase propagates various downstream signaling pathways associated to the progression of AKI, such as oxidative stress, inflammation, endoplasmic reticulum stress, as well as autophagy dysfunction. The versatility of Fyn kinase in mediating various pathophysiological pathways suggests that its inhibition can be a potential strategy in attenuating AKI.

Title: Current Concepts on the Reno-Protective Effects of Phosphodiesterase 5 Inhibitors in Acute Kidney Injury: Systematic Search and Review.

Citation: Journal of clinical medicine; Apr 2020; vol. 9 (no. 5)

Author(s): Georgiadis, Georgios; Zisis, Ioannis-Erineos; Docea, Anca Oana; Tsarouhas, Konstantinos; Fragkiadoulaki, Irene; Mavridis, Charalampous; Karavitakis, Markos; Stratakis, Stavros; Stylianou, Kostas; Tsitsimpikou, Christina; Calina, Daniela; Sofikitis, Nikolaos; Tsatsakis, Aristidis; Mamoulakis, Charalampos

Abstract: Acute kidney injury (AKI) is associated with increased morbidity, prolonged hospitalization, and mortality, especially in high risk patients. Phosphodiesterase 5 inhibitors (PDE5Is), currently available as first-line therapy of erectile dysfunction in humans, have shown a beneficial potential of reno-protection through various reno-protective mechanisms. The aim of this work is to provide a comprehensive overview of the available literature on the reno-protective properties of PDE5Is in the various forms of AKI. Medline was systematically searched from 1946 to November 2019 to detect all relevant animal and human studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. In total, 83 studies were included for qualitative synthesis. Sildenafil is
the most widely investigated compound (42 studies), followed by tadalafil (20 studies), icariin (10 studies), vardenafil (7 studies), zaprinast (4 studies), and udenafil (2 studies). Even though data are limited, especially in humans with inconclusive or negative results of only two clinically relevant studies available at present, the results of animal studies are promising. The reno-protective action of PDE5Is was evident in the vast majority of studies, independently of the AKI type and the agent applied. PDE5Is appear to improve the renal functional/histopathological alternations of AKI through various mechanisms, mainly by affecting regional hemodynamics, cell expression, and mitochondrial response to oxidative stress and inflammation.

Title: AKI!Now Initiative: Recommendations for Awareness, Recognition, and Management of AKI.

Citation: Clinical journal of the American Society of Nephrology: CJASN; Apr 2020
Author(s): Liu, Kathleen D; Goldstein, Stuart L; Vijayan, Anitha; Parikh, Chirag R; Kashani, Kianoush; Okusa, Mark D; Agarwal, Anupam; Cerdá, Jorge; AKI!Now Initiative of the American Society of Nephrology

Abstract: The American Society of Nephrology has established a new initiative, AKI!Now, with the goal of promoting excellence in the prevention and treatment of AKI by building a foundational program that transforms education and delivery of AKI care, aiming to reduce morbidity and associated mortality, and to improve long-term outcomes. In this article, we describe our current efforts to improve early recognition and management involving inclusive interdisciplinary collaboration between providers, patients, and their families; discuss the ongoing need to change some of our current AKI paradigms and diagnostic methods; and provide specific recommendations to improve AKI recognition and care. In the hospital and the community, AKI is a common and increasingly frequent condition that generates risks of adverse events and high costs. Unfortunately, patients with AKI may frequently have received less than optimal quality of care. New classifications have facilitated understanding of AKI incidence and its impact on outcomes, but they are not always well aligned with AKI pathophysiology. Despite ongoing research efforts, treatments to promote or to hasten kidney recovery remain ineffective. To avoid progression, the current approach to AKI emphasizes the promotion of early recognition and timely response. However, a lack of awareness of the importance of early recognition and treatment among healthcare team members and heterogeneity of approaches within the healthcare teams assessing the patient remains a major challenge. Early identification is further complicated by differences in settings where AKI occurs (the community or the hospital), and by differences in patient populations and cultures between the intensive care unit and ward environments. To address these obstacles, we discuss the need to improve education at all levels of care and to generate specific guidance on AKI evaluation and management, including the development of a widely applicable education and an AKI management toolkit, engaging hospital administrators to incorporate AKI as a quality initiative, and raising awareness of AKI as a complication of other disease processes.

Title: Acute Kidney Injury: The Hidden Killer in the Ward.

Citation: Journal of Renal Care; Jun 2020; vol. 46 (no. 2); p. 72-73
Author(s): Nagalingam, Karen
Abstract: In this article the author talks about Acute kidney injury (AKI) which complicates hospital admission with mortality, and the cause of these deaths are multifactorial, however it has been repeatedly demonstrated that there is a link between fluid overload and mortality. It mentions that study by Faisal et al. (2018) highlights that National Early Warning Scores does not reflect illness severity in patients with AKI.

Title: Implementation of clinical decision support to manage acute kidney injury in secondary care: an ethnographic study.

Citation: BMJ Quality & Safety; May 2020; vol. 29 (no. 5); p. 382-389

Author(s): Bailey, Simon; Hunt, Carianne; Brisley, Adam; Howard, Susan; Sykes, Lynne; Blakeman, Thomas

Background: Over the past decade, acute kidney injury (AKI) has become a global priority for improving patient safety and health outcomes. In the UK, a confidential inquiry into AKI led to the publication of clinical guidance and a range of policy initiatives. National patient safety directives have focused on the mandatory establishment of clinical decision support systems (CDSSs) within all acute National Health Service (NHS) trusts to improve the detection, alerting and response to AKI. We studied the organisational work of implementing AKI CDSSs within routine hospital care.

Methods: An ethnographic study comprising nonparticipant observation and interviews was conducted in two NHS hospitals, delivering AKI quality improvement programmes, located in one region of England. Three researchers conducted a total of 49 interviews and 150 hours of observation over an 18-month period. Analysis was conducted collaboratively and iteratively around emergent themes, relating to the organisational work of technology adoption.

Results: The two hospitals developed and implemented AKI CDSSs using very different approaches. Nevertheless, both resulted in adaptive work and trade-offs relating to the technology, the users, the organisation and the wider system of care. A common tension was associated with attempts to maximise benefit while minimise additional burden. In both hospitals, resource pressures exacerbated the tensions of translating AKI recommendations into routine practice.

Conclusions: Our analysis highlights a conflicted relationship between external context (policy and resources), and organisational structure and culture (eg, digital capability, attitudes to quality improvement). Greater consideration is required to the long-term effectiveness of the approaches taken, particularly in light of the ongoing need for adaptation to incorporate new practices into routine work.

Title: Identification and validation of biomarkers of persistent acute kidney injury: the RUBY study.

Citation: Intensive Care Medicine; May 2020; vol. 46 (no. 5); p. 943-953

Author(s): Hoste, Eric; Bihorac, Azra; Al-Khafaji, Ali; Ortega, Luis M.; Ostermann, Marlies; Haase, Michael; Zacharowski, Kai; Wunderink, Richard; Heung, Michael; Lissauer, Matthew; Self, Wesley H.; Koyner, Jay L.; Honore, Patrick M.; Prowle, John R.; Joannidis, Michael; Forni, Lui G.; Kampf, J. Patrick; McPherson, Paul; Kellum, John A.; Chawla, Lakhmir S.
**Objective:** The aim of the RUBY study was to evaluate novel candidate biomarkers to enable prediction of persistence of renal dysfunction as well as further understand potential mechanisms of kidney tissue damage and repair in acute kidney injury (AKI).

**Methods:** The RUBY study was a multi-center international prospective observational study to identify biomarkers of the persistence of stage 3 AKI as defined by the KDIGO criteria. Patients in the intensive care unit (ICU) with moderate or severe AKI (KDIGO stage 2 or 3) were enrolled. Patients were to be enrolled within 36 h of meeting KDIGO stage 2 criteria. The primary study endpoint was the development of persistent severe AKI (KDIGO stage 3) lasting for 72 h or more (NCT01868724).

**Results:** 364 patients were enrolled of whom 331 (91%) were available for the primary analysis. One hundred ten (33%) of the analysis cohort met the primary endpoint of persistent stage 3 AKI. Of the biomarkers tested in this study, urinary C-C motif chemokine ligand 14 (CCL14) was the most predictive of persistent stage 3 AKI with an area under the receiver operating characteristic curve (AUC) (95% CI) of 0.83 (0.78-0.87). This AUC was significantly greater than values for other biomarkers associated with AKI including urinary KIM-1, plasma cystatin C, and urinary NGAL, none of which achieved an AUC > 0.75.

**Conclusion:** Elevated urinary CCL14 predicts persistent AKI in a large heterogeneous cohort of critically ill patients with severe AKI. The discovery of CCL14 as a predictor of persistent AKI and thus, renal non-recovery, is novel and could help identify new therapeutic approaches to AKI.

**Title:** Different applications of the KDIGO criteria for AKI lead to different incidences in critically ill patients: a post hoc analysis from the prospective observational SICS-II study.

**Citation:** Critical Care; Apr 2020; vol. 24 (no. 1); p. 1-8

**Author(s):** Wiersema, Renske; Jukarainen, Sakari; Eck, Ruben J.; Kaufmann, Thomas; Koeze, Jacqueline; Keus, Frederik; Pettilä, Ville; van der Horst, Iwan C. C.; Vaara, Suvi T.

**Objective:** Acute kidney injury (AKI) is a frequent and clinically relevant problem in critically ill patients. Various randomized controlled trials (RCT) have attempted to assess potentially beneficial treatments for AKI. Different approaches to applying the Kidney Disease Improving Global Outcomes (KDIGO) criteria for AKI make a comparison of studies difficult. The objective of this study was to assess how different approaches may impact estimates of AKI incidence and whether the association between AKI and 90-day mortality varied by the approach used.

**Methods:** Consecutive acutely admitted adult intensive care patients were included in a prospective observational study. AKI was determined following the KDIGO criteria during the first 7 days of ICU admission. In this post hoc analysis, we assessed whether AKI incidence differed when applying the KDIGO criteria in 30 different possible methods, varying in (A) serum creatinine (sCr), (B) urine output (UO), and (C) the method of combining these two into an outcome, e.g., severe AKI. We assessed point estimates and 95% confidence intervals for each incidence. Univariable regression was used to assess the associations between AKI and 90-day mortality.

**Results:** A total of 1010 patients were included. Baseline creatinine was available in 449 (44%) patients. The incidence of any AKI ranged from 28% (95%CI 25-31%) to 75% (95%CI 72-77%) depending on the approach used. Methods to estimate missing baseline sCr caused a variation in AKI incidence up to 15%. Different methods of handling UO caused a variation of up to 35%. At 90 days, 263 patients (26%) had died, and all 30 variations were associated with 90-day mortality.
Conclusions: In this cohort of critically ill patients, AKI incidence varied from 28 to 75%, depending on the method used of applying the KDIGO criteria. A tighter adherence to KDIGO definitions is warranted to decrease the heterogeneity of AKI and increase the comparability of future studies.

Title: Acute kidney injury in SARS-CoV-2 infected patients.

Citation: Critical Care; Apr 2020; vol. 24 (no. 1); p. 1-3
Author(s): Fanelli, Vito; Fiorentino, Marco; Cantaluppi, Vincenzo; Gesualdo, Loreto; Stallone, Giovanni; Ronco, Claudio; Castellano, Giuseppe


Citation: JAMA Network Open; Apr 2020
Author(s): Bhatraju, Pavan K.; Zelnick, Leila R.; Chinchilli, Vernon M.; Moledina, Dennis G.; Coca, Steve G.; Parikh, Chirag R.; Garg, Amit X.; Hsu, Chi-yuan; Go, Alan S.; Liu, Kathleen D.; Ikizler, T. Alp; Siew, Edward D.; Kaufman, James S.; Kimmel, Paul L.; Himmelfarb, Jonathan; Wurfel, Mark M.

Question: Is the trajectory of kidney function within 72 hours after acute kidney injury associated with 5-year clinical outcomes, such as chronic kidney disease, dialysis, and death?

Findings: Among 1538 participants in this prospective multicenter cohort study, the early recovery pattern after acute kidney injury was associated with long-term outcomes. In adjusted analyses, patients with a nonresolving recovery pattern after acute kidney injury had a 51% greater risk for the composite kidney-specific clinical outcome compared with patients with a resolving acute kidney injury recovery pattern, independent of traditional criteria to risk stratify patients with acute kidney injury.

Meaning: This study's finding suggest that the acute recovery pattern after development of acute kidney injury should be considered in evaluating the risk of long-term clinical outcomes.

Importance: The severity of acute kidney injury (AKI) is usually determined based on the maximum serum creatinine concentration. However, the trajectory of kidney function recovery could be an additional important dimension of AKI severity. Objective: To assess whether the trajectory of kidney function recovery within 72 hours after AKI is associated with long-term risk of clinical outcomes.

Design, Setting, and Participants: This prospective, multicenter cohort study enrolled 1538 adults with or without AKI 3 months after hospital discharge between December 1, 2009, and February 28, 2015. Statistical analyses were completed November 1, 2018. Participants with or without AKI were matched based on demographic characteristics, site, comorbidities, and prehospitalization estimated glomerular filtration rate. Participants with AKI were classified as having resolving or nonresolving AKI based on previously published definitions. Resolving AKI was defined as a decrease in serum creatinine concentration of 0.3 mg/dL or more or 25% or more from maximum in the first 72 hours after AKI diagnosis. Nonresolving AKI was defined as AKI not meeting the definition for resolving AKI.

Main Outcomes and Measures: The primary outcome was a composite of major adverse kidney events (MAKE), defined as incident or progressive chronic kidney disease, long-term dialysis, or all-cause death during study follow-up.
**Results:** Among 1538 participants (964 men; mean [SD] age, 64.6 [12.7] years), 769 (50%) had no AKI, 475 (31%) had a resolving AKI pattern, and 294 (19%) had a nonresolving AKI pattern. After a median follow-up of 4.7 years, the outcome of MAKE occurred in 550 (36%) of all participants. The adjusted hazard ratio for MAKE was higher for patients with resolving AKI (adjusted hazard ratio, 1.52; 95% CI, 1.01-2.29; P =.04) and those with nonresolving AKI (adjusted hazard ratio 2.30; 95% CI, 1.52-3.48; P <.001) compared with participants without AKI. Within the population of patients with AKI, nonresolving AKI was associated with a 51% greater risk of MAKE (95% CI, 22%-88%; P <.001) compared with resolving AKI. The higher risk of MAKE among patients with nonresolving AKI was explained by a higher risk of incident and progressive chronic kidney disease.

**Conclusions and Relevance:** This study suggests that the 72-hour period immediately after AKI distinguishes the risk of clinically important kidney-specific long-term outcomes. The identification of different AKI recovery patterns may improve patient risk stratification, facilitate prognostic enrichment in clinical trials, and enable recognition of patients who may benefit from nephrology consultation. This cohort study assesses whether the trajectory of kidney function recovery within 72 hours after acute kidney injury is associated with long-term risk of clinical outcomes.

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**Title:** Association of Contrast and Acute Kidney Injury in the Critically Ill: A Propensity-Matched Study.

**Citation:** CHEST; Apr 2020; vol. 157 (no. 4); p. 866-876

**Author(s):** Williams, Lisa-Mae S.; Walker, Gail R.; Loewenherz, James W.; Gidel, Louis T.

**Background:** Despite evidence that low osmolar radiocontrast media is not associated with acute kidney injury, it is important to evaluate this association in critically ill patients with normal kidney function.

**Methods:** This retrospective observational study included 7,333 adults with an ICU stay at a six-hospital health system in south Florida. Patients who received contrast were compared with unexposed control subjects prior to and following propensity score (PS) matching derived from baseline characteristics, admission diagnoses, comorbidities, and severity of illness. Acute kidney injury (AKI), defined as initial onset (stage I) or increased severity, was determined from serum creatinine levels according to Kidney Disease: Improving Global Outcomes guidelines.

**Results:** Based on 2,306 PS-matched pairs obtained from 2,557 patients who received IV contrast and 4,776 unexposed control subjects, the increase in AKI attributable to contrast was 1.3% (19.3% vs 18.0%; P =.273), and no association was found between contrast and the pattern of onset and recovery. Hospital mortality increased by 14.3% subsequent to AKI (18.0 vs 3.6; P < .001), but the risk ratio in relation to patients with stable AKI did not vary when stratified according to contrast. Multivariable regression identified sepsis, metabolic disorders, diabetes, history of renal disease, and severity of illness as factors that were more strongly associated with AKI.

**Conclusions:** In critically ill adults with normal kidney function, low osmolar radiocontrast media did not substantively increase AKI. Rather than limiting the use of contrast in ICU patients, efforts to prevent AKI should focus on the susceptibility of patients with sepsis, diabetes complications, high Acute Physiology and Chronic Health Evaluation scores, and history of renal disease.
Title: The conundrum of contrast-induced acute kidney injury.

Citation: Journal of Thoracic Disease; Apr 2020; vol. 12 (no. 4); p. 1721-1727
Author(s): Faraz Ul Haq, Mohammad; Yip, Cindy S.; Arora, Pradeep

Abstract: More than sixty years have elapsed since contrast induced nephropathy (CIN) was first described in the medical literature. This term has since been extensively explored, with a variety of studies conducted to investigate its incidence and various mechanisms examined to explain its pathophysiology. However, the topic of CIN remains one of controversy with a widely variable and often questionable incidence derived from various studies. The past two decades have seen a surge in reports questioning the existing of CIN altogether and if more harm is actually being caused to patients out of fear of this potential complication. We have attempted to review relevant studies regarding CIN and highlight the key points of its surmised understanding. The review has a higher focus on more recent literature and updates, in order to determine if an accurate estimate can be made on the incidence of CIN. While there was certainly no lack of material available, practically all the studies reviewed were limited by one or more significant drawbacks that limited the reliability of their conclusions regarding CIN. Based on the information reviewed, the strengths and the flaws encountered in other studies can be used to design a randomized control trial that may help in concluding the longstanding debate on this topic. However due to time, financial, and perhaps even ethical constraints such a trial will be difficult to arrange, and so a definitive answer on CI-AKI, and whether it really exist, may continue to elude clinicians.

Title: Contrast induced acute kidney injury in interventional cardiology: an update and key guidance for clinicians.

Citation: Reviews in Cardiovascular Medicine; Mar 2020; vol. 21 (no. 1); p. 9-23
Author(s): Ronco, Federico; Tarantini, Giuseppe; McCullough, Peter A.

Abstract: Contrast-induced acute kidney injury (CI-AKI) is a serious complication that can affect outcome and prognosis of patients undergoing percutaneous diagnostic and interventional procedures in catheterization laboratories. There have been advancements in case definition and epidemiology. Additionally strategies have emerged that are positioned to have impact in the catheterization laboratory for patients undergoing cardiovascular procedures. The aim of this review is to provide the state-of-the-art of diagnosis, prevention and management of CI-AKI in interventional cardiology.

Title: Impact of renal dysfunction and acute kidney injury on outcome in elderly patients with acute coronary syndrome undergoing percutaneous coronary intervention.

Citation: European heart journal. Acute cardiovascular care; May 2020 ; p. 2048872620920475
Author(s): De Rosa, Roberta; Morici, Nuccia; De Servi, Stefano; De Luca, Giuseppe; Galasso, Gennaro; Piscione, Federico; Ferri, Luca A; Piatti, Luigi; Grosseto, Daniele; Tortorella, Giovanni; Franco, Nicoletta; Lenatti, Laura; Misuraca, Leonardo; Leuzzi, Chiara; Verdeoia, Monica; Sganzerla, Paolo; Cacucci, Michele; Ferrario, Maurizio; Murena, Ernesto; Sibilio, Gerolamo; Toso, Anna; Savonitto, Stefano
Objective: Chronic kidney disease is common in patients admitted with acute coronary syndrome and its prevalence dramatically increases with age. Understanding the determinants of adverse outcomes in this extremely high-risk population may be useful for the development of specific treatment strategies and planning of secondary prevention modalities. The aim of this study was to assess the impact of baseline renal function and acute kidney injury on one-year outcome of elderly patients with acute coronary syndrome treated with percutaneous coronary intervention.

Methods: Patients aged 75 years and older with acute coronary syndrome undergoing successful percutaneous coronary intervention were selected among those enrolled in three Italian multicentre studies. Based on the baseline estimated glomerular filtration rate (eGFR) calculated using the Cockcroft-Gault formula \([\frac{(140 - \text{age}) \times \text{body weight} \times 0.85 \text{ if female}}{(72 \times \text{serum creatinine})^* 1.73 \text{ m2 of body surface area}}\]), patients were classified as having none or mild (eGFR \(\geq 60 \text{ ml/min/1.73 m2}\)), moderate (eGFR 30-59 ml/min/1.73 m2) or severe (eGFR <30 ml/min/1.73 m2) renal dysfunction. Acute kidney injury was defined according to the Acute Kidney Injury Network classification. All-cause and cardiovascular mortality, non-fatal myocardial infarction, rehospitalisation for cardiovascular causes, stroke and type 2, 3 and 5 Bleeding Academic Research Consortium bleedings were analysed up to 12 months.

Results: A total of 1904 patients were included. Of these, 57% had moderate and 11% severe renal dysfunction. At 12 months, patients with renal dysfunction had higher rates (\(P<0.001\)) of all-cause (4.5%, 7.5% and 17.8% in patients with none or mild, moderate and severe renal dysfunction, respectively) and cardiovascular mortality (2.8%, 5.2% and 10.2%, respectively). After multivariable adjustment, severe renal dysfunction was associated with a higher risk of all-cause (hazard ratio (HR) 2.86, 95% confidence interval (CI) 1.52-5.37, \(P=0.001\)) and cardiovascular death (HR 3.11, 95% CI 1.41-6.83, \(P=0.005\)), whereas non-fatal events were unaffected. Acute kidney injury incidence was significantly higher in ST-elevation myocardial infarction versus non-ST-elevation acute coronary syndrome patients (11.7% vs. 7.8%, \(P=0.036\) and in those with reduced baseline renal function (\(P<0.001\)), and it was associated with increased mortality independently from baseline renal function and clinical presentation.

Conclusion: Baseline renal dysfunction is highly prevalent and is associated with higher mortality in elderly acute coronary syndrome patients undergoing percutaneous coronary intervention. Acute kidney injury occurs more frequently among ST-elevation myocardial infarction patients and those with pre-existing renal dysfunction and is independently associated with one-year mortality.


Citation: Journal of the American Society of Nephrology : JASN; May 2020

Author(s): Batlle, Daniel; Soler, Maria Jose; Sparks, Matthew A; Hiremath, Swapnil; South, Andrew M; Welling, Paul A; Swaminathan, Sundararaman; COVID-19 and ACE2 in Cardiovascular, Lung, and Kidney Working Group

Title: Metformin-related lactic acidosis with acute kidney injury: results of a French observational multicenter study.

Citation: Clinical toxicology (Philadelphia, Pa.); May 2020; vol. 58 (no. 5); p. 375-382
**Author(s):** Corchia, Anthony; Wynckel, Alain; Journet, Julien; Moussi Frances, Julie; Skandrani, Nihel; Lautrette, Alexandre; Zafrani, Lara; Lewandowski, Elisabeth; Rebol, Pascal; Vrigneaud, Laurence; Djerada, Zoubir; Rieu, Philippe

**Objective:** Metformin-associated lactic acidosis (MALA) and metformin-induced lactic acidosis (MILA) remain controversial entities. Metformin toxic effect depends on accumulation to lead to lactic acidosis (LA), particularly during an episode of acute kidney injury (AKI). In MILA, no other condition contributing to LA is found. The aims of this study were to describe the characteristics and prognosis of AKI associated with LA in metformin users and to clarify the role of this drug in the different types of LA.

**Methods:** We performed a French multicenter retrospective study in diabetic patients treated by metformin presenting with LA in a context of AKI in 2015. 126 nephrology units (NU) and 23 intensive care units (ICU) were contacted. We individualized MILA and MALA patients in order to illustrate the role of metformin.

**Results:** We included 173 patients (109 MILA, 64 MALA). 103 patients presented without hemodynamic instability (82 MILA and 21 MALA) whereas 70 patients were shocked including 27 MILA. The shock was associated with death with an odds ratio (OR) of 12.92 (p < .001). Digestive disorders (DD) were strongly associated with MILA (p = .0001). MALA was significantly associated with shock (p < .0001). The mortality rate was higher in MILA (26%) when compared with MILA (7%). Dialysis performed in 133 patients was significantly associated with shock, kalemia, lactate and serum creatinine levels. In multivariate analysis, metformin level was independently associated with pH or lactate level only in MILA patients.

**Conclusions:** MILA is associated with DD and death is due to severe refractory acidosis leading to cardiovascular collapse attributed to metformin accumulation mainly via AKI. MALA patients are more frequently shocked and death is related to their underlying condition, metformin accumulation increasing LA.

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**Title:** Mild Acute Kidney Injury after Noncardiac Surgery Is Associated with Long-term Renal Dysfunction: A Retrospective Cohort Study.

**Citation:** Anesthesiology; May 2020; vol. 132 (no. 5); p. 1053-1061

**Author(s):** Turan, Alparslan; Cohen, Barak; Adegboye, Janet; Makarova, Natalya; Liu, Liu; Mascha, Edward J; Qiu, Yuwei; Irefin, Samuel; Wakefield, Brett J; Ruetzler, Kurt; Sessler, Daniel I

**Objective:** Perioperative acute kidney injury is common. However, it is unclear whether this merely represents a transient increase in creatinine or has prognostic value. Therefore, the long-term clinical importance of mild postoperative acute kidney injury remains unclear. This study assessed whether adults who do and do not experience mild kidney injury after noncardiac surgery are at similar risk for long-term renal injury.

**Methods:** This study is a retrospective cohort analysis of adults having noncardiac surgery at the Cleveland Clinic who had preoperative, postoperative, and long-term (1 to 2 yr after surgery) plasma creatinine measurements. The exposure (postoperative kidney injury) and outcome (long-term renal injury) were defined and staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) initiative criteria. The primary analysis was for lack of association between postoperative kidney injury (stage I vs. no injury) and long-term renal injury.

**Results:** Among 15,621 patients analyzed, 3% had postoperative stage I kidney injury. Long-term renal outcomes were not similar in patients with and without postoperative stage I injury. Specifically, about 26% of patients with stage I postoperative kidney injury still had
mild injury 1 to 2 yr later, and 11% had even more severe injury. A full third (37%) of patients with stage I kidney injury therefore had renal injury 1 to 2 yr after surgery. Patients with postoperative stage I injury had an estimated 2.4 times higher odds of having long-term renal dysfunction (KDIGO stage I, II, or III) compared with patients without postoperative kidney injury (odds ratio [95% CI] of 2.4 [2.0 to 3.0]) after adjustment for potential confounding factors.

Conclusions: In adults recovering from noncardiac surgery, even small postoperative increases in plasma creatinine, corresponding to stage I kidney injury, are associated with renal dysfunction 1 to 2 yr after surgery. Even mild postoperative renal injury should therefore be considered a clinically important perioperative outcome.


Citation: AJR. American journal of roentgenology; Apr 2020; p. 1-10

Author(s): Lee, Hung-Chi; Chua, Kai-I; Lu, Chia-Feng; Chiang, Yu; Wang, Hung-Jung; Hsieh, Kevin Li-Chun

Objective: The purpose of this study was to determine whether contrast medium volume and method of administration and baseline estimated glomerular filtration rate influence the efficacy of prophylactic hydration for prevention of acute kidney injury after contrast administration.

Materials and methods: An online search of PubMed conducted on August 25, 2017, produced a total of 697 studies. After the reports were reviewed, nine were included in this study. The extracted data on all patients in these studies were separated into a group that received prophylactic hydration and a group that did not. The following three parameters were used for subgroup analysis: contrast medium volume, contrast administration method, and baseline estimated glomerular filtration rate. The t test was performed, and study-level odds ratios with 95% CIs and p values were calculated. Tests of heterogeneity were conducted.

Results: When the volume of contrast agent administered exceeded 100 mL, hydration was beneficial in the prevention of contrast-induced acute kidney injury (odds ratio, 0.546). If the volume was less than 100 mL, hydration had no efficacy in preventing contrast-induced acute kidney injury (odds ratio, 0.917). Administration route and baseline estimated glomerular filtration rate exerted no effect on the efficacy of prophylactic hydration.

Conclusion: For patients who receive less than 100 mL of contrast medium, the prevalent practice for contrast-enhanced CT studies, prophylactic hydration may not be necessary, regardless of the estimated glomerular filtration rate or route of contrast administration. For patients undergoing procedures requiring administration of large volumes of contrast medium, however, hydration is recommended to prevent contrast-induced acute kidney injury.

Title: Impact of concomitant peripheral artery disease on contrast-induced acute kidney injury and mortality in patients with acute coronary syndrome after percutaneous coronary intervention.

Citation: Heart and vessels; Apr 2020
Author(s): Nakahashi, Takuya; Tada, Hayato; Sakata, Kenji; Yakuta, Yohei; Yoshida, Taiji; Tanaka, Yoshihiro; Nomura, Akihiro; Terai, Hidenobu; Horita, Yuki; Ikeda, Masatoshi; Namura, Masanobu; Takamura, Masayuki; Kawashiri, Masa-Aki

Abstract: Subclinical peripheral artery disease (PAD) might be associated with pathophysiology of contrast-induced acute kidney injury (CI-AKI). We hypothesized that concomitant PAD in patients with the acute coronary syndrome (ACS) would represent a high-risk subgroup with a greater incidence of CI-AKI, both of which lead to higher mortality after percutaneous coronary intervention (PCI). Six hundred and seventy-five consecutive patients with ACS who underwent PCI and examination of ankle-brachial index (ABI) were analyzed retrospectively. The presence of PAD was defined as an ABI < 0.9. We investigated whether (1) PAD was an independent predictor of CI-AKI (≥ 0.3 mg/dL or ≥ 50% relative increase in serum creatinine within 48 h after PCI) and (2) PAD and CI-AKI were independently associated with long-term mortality. Of the 675 patients with ACS, 114 (17%) exhibited PAD. The incidence of CI-AKI was significantly higher in PAD patients, compared with the remaining patients (12% vs. 4%, p < 0.001). Multivariate logistic regression analysis revealed that the presence of PAD was an independent predictor for the development of CI-AKI [odds ratio 2.50, 95% confidence interval (CI) 1.07-5.73, p < 0.05]. During the median 4-year follow-up, there were 65 incidents of all-cause death. In the multivariate Cox proportional hazard regression analysis, the presence of PAD [hazard ratio (HR) 2.08, 95% CI 1.17-3.65, p < 0.05] and CI-AKI (HR 2.23, 95% CI 1.08-4.26, p < 0.05) were associated with an increased risk of all-cause mortality. Assessment of ABI provides useful information for predicting CI-AKI and long-term mortality in patients with ACS after PCI.

Title: Pre-existing chronic kidney disease and acute kidney injury among critically ill patients.

Citation: Heart & lung: the journal of critical care; Apr 2020

Author(s): Abdalrahim, Maysoon S; Khalil, Amani A; Alramly, Manal; Alshlool, Khalid Nabeel; Abed, Mona A; Moser, Debra K

Objective: The impact of pre-existing chronic kidney disease (CKD) and acute kidney injury (AKI) on health outcomes in critically ill patients is unclear. Yet, CKD complicated by AKI in critically ill patients is common. This study aimed to compare risk of death within one-month of admission in critically ill patients with and without pre-existing CKD who developed AKI.

Methods: A multicenter retrospective comparative study using medical records review was conducted. Study participants consisted of 826 adult patients who received mechanical ventilation for at least 6 h in the critical care units from January 2012 to December 2017. Assessment of kidney function was established by serum creatinine. Severity and staging of AKI were defined using RIFLE criteria: Risk, Injury, Failure, Loss and End stage of renal disease. Chronic kidney disease was defined as eGFR > 60 ml/mg/1.73 m² on admission. Results: Pre-existing CKD was present in 55% of patients and 7% had AKI within 7 days of admission. The overall mortality rate among these patients was 87.3%. The mortality rate was highest in patients with CKD (70.1%) followed by that of patients without pre-existing CKD but with AKI (20.7%) and that of patients with pre-existing CKD (7.1%) and AKI. Risks associated with mortality were APACHE II score (1.03; 95% CI 1.02-1.05;P<0.001) and AKI (1.68; 95% CI 1.12-2.5;P<0.01) in patients with pre-existing CKD. Only APACHE-II (1.03; 95% CI 1.0-1.1; p < 0.001) was predictive of death in patients without pre-existing CKD.

Conclusion: Pre-existing comorbid CKD increases risks of death among critically ill patients compared to patients without CKD and regardless of whether they develop AKI or not. Early
identification of CKD and recognition of the risk for mortality among these patients may result in earlier intervention that could reduce mortality.

Title: Continuous Versus Intermittent Infusion of Vancomycin and the Risk of Acute Kidney Injury in Critically Ill Adults: A Systematic Review and Meta-Analysis.

Citation: Critical care medicine; Apr 2020
Author(s): Flannery, Alexander H; Bissell, Brittany D; Bastin, Melissa Thompson; Morris, Peter E; Neyra, Javier A

Objectives: Critically ill patients routinely receive vancomycin as empiric antibiotic therapy. A continuous infusion administration strategy may be superior to intermittent infusion by minimizing peak concentrations and variability thereby optimizing safety. We performed a systematic review and meta-analysis to investigate the impact of vancomycin infusion strategy on acute kidney injury in critically ill adults.

Data sources: A systematic search of MEDLINE, CINAHL, Web of Science, International Pharmaceutical Abstracts, and Google Scholar was undertaken.

Study selection: We included randomized controlled trials and observational studies evaluating acute kidney injury in critically ill adults comparing vancomycin administered by intermittent and continuous infusion. Secondary outcomes included mortality and pharmacokinetic target attainment.

Data extraction: Eleven studies were identified for analysis with baseline demographics, endpoints, protocol definitions, and outcomes extracted.

Data synthesis: When compared with intermittent infusion, continuous infusion was associated with a reduction in acute kidney injury in critically ill adults (odds ratio, 0.47; 95% CI, 0.34-0.65) and a 2.6 greater odds of pharmacokinetic target attainment (odds ratio, 2.63; 95% CI, 1.52-4.57). No difference in mortality was observed (odds ratio, 1.04; 95% CI, 0.80-1.35).

Conclusions: When administered via a continuous infusion, vancomycin is associated with a 53% reduction in the odds of acute kidney injury and a 2.6-fold higher odds of pharmacokinetic target attainment when compared with intermittent infusion without influencing overall mortality.

Title: 24-hour Serum Creatinine Variation Associates with Short- and Long-Term All-Cause Mortality: A Real-World Insight into Early Detection of Acute Kidney Injury.

Citation: Scientific reports; Apr 2020; vol. 10 (no. 1); p. 6552
Author(s): Yeh, Hung-Chieh; Lo, Yen-Chun; Ting, I-Wen; Chu, Pei-Lun; Chang, Shih-Ni; Chiang, Hsiu-Yin; Kuo, Chin-Chi

Abstract: Real-world evidence describing the variation in serum creatinine (S-Cre) within 24 hours and its prognostic value is unknown. We enrolled 14 912 adults who received two S-Cre measurements within 24 hours at a tertiary hospital between 2003 and 2016. The study population was divided into four groups according to the hospital service settings where the baseline and second S-Cre were measured: Group 1, Outpatient-to-Outpatient; Group 2, Outpatient-to-ED (emergency department) or Inpatient; Group 3, ED-to-ED or Inpatient; and Group 4, Inpatient-to-Inpatient. The main predictors were the difference between the two S-Cre measurements (ΔS-Cre) and the percent change (ΔS-Cre%). The
main outcomes were 30-day, 1-year, or 3-year all-cause mortality. A total of 6753 and 8159 patients with an increase and a decrease within-day ΔS-Cre, respectively. Among 6753 patients who had deteriorating ΔS-Cre or ΔS-Cre%, the adjusted hazard ratio (aHR) for 1-year all-cause mortality for each 0.1 mg/dL or 5% change in S-Cre was 1.09 (95% confidence interval [CI]: 1.07, 1.11) and 1.03 (95% CI: 1.03, 1.04). In 8159 patients with improving ΔS-Cre%, the aHR was 0.97 (95% CI: 0.94, 1.00). Groups 3 and 4 had statistically significant positive linear relationships between deteriorating ΔS-Cre% and 30-day and 3-year mortality. The optimal cut-offs for deteriorating ΔS-Cre% for predicting 30-day mortality were approximately 22% for Group 3 and 20% for Group 4. Inpatient within-day deteriorating ΔS-Cre% above 0.2 mg/dL or 20%, respectively, is associated with all-cause mortality. Monitoring 24-hour S-Cre variation identifies acute kidney injury earlier than the conventional criteria.

Title: Associated risk factors and outcomes of acute kidney injury in severe trauma: Results from the Spanish trauma ICU registry (RETRAUCI).

Citation: Anaesthesia, critical care & pain medicine; Apr 2020
Author(s): Chico-Fernández, Mario; Barea-Mendoza, Jesús Abelardo; Ormazabal-Zabala, Txoan; Moreno-Muñoz, Gerard; Pastor-Marcos, Diego; Bueno-González, Ana; Iglesias-Santiago, Alberto; Ballesteros-Sanz, María Ángeles; Pérez-Bárcena, Jon; Llompart-Pou, Juan Antonio

Objective: Acute kidney injury (AKI) constitutes a common complication after severe trauma. Our objective was to analyse the associated risk factors and outcomes of AKI in a large, multicenter sample of trauma ICU patients.

Materials and methods: Observational, prospective and multicenter nationwide registry (RETRAUCI). We included all patients admitted to the participating ICUs from November 2013 to May 2017. We analysed the impact of AKI evaluated by the Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease (RIFLE) definition. Comparison of groups was performed using Wilcoxon test, Chi-Square Test or Fisher’s exact test as appropriate. A multiple logistic regression analysis was performed to analyse associated factors to the development of AKI. Logistic regression was used to calculate AKI-related mortality. A p value < 0.05 was considered significant.

Results: During the study period, 5882 trauma patients were admitted. Complete data were available for 5740 patients. Among them, 871 had AKI (15.17%), distributed by RIFLE R 458 (7.98%), RIFLE I 234 (4.08%) and RIFLE F 179 (3.12%). Associated risk factors were: age (OR 3.05), haemodynamic instability (OR 2.90 to OR 8.34 depending on the severity of hypotension), coagulopathy (OR 1.82), rhabdomyolysis (OR 4.67) and AIS abdomen (OR 1.54). AKI was associated with mortality (crude OR 1.93 (1.59-2.36)), even after adjusting by potential confounders (adjusted OR 1.40 (1.13-1.73)).

Conclusion: In our large sample of trauma ICU patients we found an incidence of AKI of 15%, which was associated with an increased mortality.

Title: Pathophysiology of AKI to CKD progression

Citation: Seminars in Nephrology; Mar 2020; vol. 40 (no. 2); p. 206-215
Author(s): Sato Y.; Takahashi M.; Yanagita M.
Abstract: Acute kidney injury (AKI), defined as a rapid decrease in glomerular filtration rate, is a common and devastating pathologic condition. AKI is associated with significant morbidity and subsequent chronic kidney disease (CKD) development. Regardless of the initial insult, CKD progression after AKI involves multiple types of cells, including proximal tubular cells, fibroblasts, and immune cells. Although the mechanisms underlying this AKI to CKD progression have been investigated extensively over the past decade, therapeutic strategies still are lacking. One of the reasons for this stems from the fact that AKI and its progression toward CKD is multifactorial and variable because it is dependent on patient background. In this review, we describe the current understanding of AKI and its maladaptive repair with a focus on proximal tubules and resident fibroblasts. Subsequently, we discuss the unique pathophysiology of AKI in the elderly, highlighting our recent finding of age-dependent tertiary lymphoid tissues. Copyright © 2020 Elsevier Inc.

Title: Glucose and blood pressure-dependent pathways-the progression of diabetic kidney disease

Citation: International Journal of Molecular Sciences; Mar 2020; vol. 21 (no. 6)

Author(s): Patel D.M.; Bose M.; Cooper M.E.

Abstract: The major clinical associations with the progression of diabetic kidney disease (DKD) are glycemic control and systemic hypertension. Recent studies have continued to emphasize vasoactive hormone pathways including aldosterone and endothelin which suggest a key role for vasoconstrictor pathways in promoting renal damage in diabetes. The role of glucose per se remains difficult to define in DKD but appears to involve key intermediates including reactive oxygen species (ROS) and dicarbonyls such as methylglyoxal which activate intracellular pathways to promote fibrosis and inflammation in the kidney. Recent studies have identified a novel molecular interaction between hemodynamic and metabolic pathways which could lead to new treatments for DKD. This should lead to a further improvement in the outlook of DKD building on positive results from RAAS blockade and more recently newer classes of glucose-lowering agents such as SGLT2 inhibitors and GLP1 receptor agonists.

Sources Used:
The following databases are used in the creation of this bulletin: CINAHL, EMBASE & Medline.

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