Contemporary Acute Kidney Injury Management

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ACUTE kidney injury (AKI) was discussed in a session chaired by Jolanta Malyszko, Medical University of Warsaw, Poland, and Danilo Fliser, Saarland University Medical Centre, Homburg, Germany, at the 60th European Renal Association (ERA) Congress, which took place in Milan, Italy, between 15th–18th June 2023. The moderators started by announcing that ERA has created a new working group on AKI.

ACUTE KIDNEY INJURY PREDICTION THROUGH BIOMARKERS AND CLINICAL MODELS

The first speaker, Greet De Vlieger, Katholieke Universiteit (KU) Leuven, Belgium, explained that AKI is a frequent complication that is often diagnosed late, and is associated with worse outcomes in the short- and long-term; therefore, its prediction is important, even though there is no curative treatment for it.

Subclinical AKI is more difficult to diagnose as there is no gold standard for its diagnosis; however, Kidney Disease Improving Global Outcomes (KDIGO) criteria can be used to diagnose AKI. This is indicated by an increase in serum creatinine or reduction of urinary output. However, the incidence of AKI can vary a lot within a single cohort based on how you apply these criteria.

Different types of biomarkers for AKI prediction include dysfunctional biomarkers, such as serum creatinine, and stress and damage biomarkers, which can be used in the subclinical phase of AKI. Stress biomarkers include tissue inhibitor of metalloproteinases, Dickkopf-3, whereas damage biomarkers that indicate injury to kidney cells include kidney injury molecule-1, IL-18, and neutrophil gelatinase-associated lipocalin.

In a large meta-analysis including over 38,000 patients, the most precise biomarker in predicting AKI was found to be neutrophil gelatinase-associated lipocalin in urine divided by creatinine in urine, whereas for severe AKI the most precise biomarker was tissue inhibitor metalloproteinases-2 x insulin-like growth factor-binding protein 7. A secondary analysis to the SAPHIRE trial showed that combining stress and functional biomarkers gave better accuracy in predicting Stage 2 or 3 AKI within the next 12 hours, and adverse kidney events in 30 days.

De Vlieger also presented the AKI predictor (KU Leuven, Belgium), a machine learning tool developed to predict AKI during the first week of intensive care unit (ICU) stay. This tool demonstrated good accuracy in predicting AKI, which increased as more data were gathered during the patient's stay.

Regarding AKI prediction models, De Vlieger explained that a meta-analysis showed even though 150 prediction models with good accuracy have been used over the years, with a quarter of them externally validated, and 40 of them using machine learning, none of them have actually been implemented in clinical practice. In a study predicting complications after surgery, data collected before and during hospital admission is used to make an estimation before surgery of post-operative complications in addition to a new estimation after surgery.

By using 135 features, this model can quite accurately predict complications after surgery, and it demonstrated a good predictive performance for AKI. Sub-phenotyping of patients in the ICU can be done by using different molecular analysis and biomarkers and machine learning, as well as by combining these two approaches.

In their concluding remarks, De Vlieger emphasised there is still a continuous quest for perfect biomarkers and despite the increased use of machine learning predictions in clinical models, few, if any, are used in clinical practice. De Vlieger predicts that in the future combining biomarkers and clinical models will be the most effective approach and that research will focus on subphenotyping use of machine learning tools and specific biomarkers in AKI phenotypes.

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ARTIFICIAL INTELLIGENCE GUIDING ACUTE KIDNEY INJURY PATIENT MANAGEMENT

Jay Koyner, University of Chicago, Illinois, USA, discussed artificial intelligence (AI) in medication dosing assistance, clinical decision support, and risk prediction. Koyner emphasised the need for AI in helping improve trends in AKI-associated mortality by citing a recent study that showed a significant but poor decrease in AKI-associated mortality over 11 years in veterans from the USA, emphasising that care of patients with Stage 2 AKI can be improved.

ARTIFICIAL INTELLIGENCE IN CLINICAL DECISION SUPPORT

Koyner went on to present a study that used e-alerts and educational activities to facilitate AKI care across hospitals, which showed improvements in care, even though 30-day mortality and AKI progression remained unchanged. Following implementation of the alert system, the likelihood of AKI recognition and fluid assessment increased, and more medication reviews and urinalyses were performed. In another alert study, no change in the development of AKI was detected but morbidity and mortality were improved in the patient population that was flagged as 'at risk'. In another study, the clinical team was alerted to the presence of AKI, enabling them to enhance care. However, even when orders with one click access to intravenous fluids or diuretics were given, no difference was observed in AKI progression, need of dialysis, death at 14 days, length of stay, or discharge rate. Interestingly, in non-teaching hospitals alerting the staff to the presence of AKI led to more diuretics and fluids being given, demonstrating the need of having AKI-trained staff caring for patients with AKI.

Clinical decision support has been successful in implementing care bundles and has demonstrated decreased mortality in certain studies, not necessarily associated with decreased rate in AKI, but in those specific alerts around nephrotoxin there is a clear decrease in AKI and AKI events.

MACHINE LEARNING

Currently, AKI phenotyping works by defining every type of AKI around changes in creatine whether this is due to a drug, sepsis, or cardiac arrest. Koyner emphasised the need to move away from this, possibly by using machine learning and incorporating all the information found in electronic records. One study used an ICU database to create three separate phenotypes of sepsis-associated AKI, each with different AKI event rates but also event rates regarding other organ system dysfunction. This enabled them to identify those who were most high risk, for example those who had a need for dialysis.

Koyner emphasised that AI tools need external validations and need to demonstrate that they can improve care and outcomes with earlier diagnosis. In their concluding remarks, Koyner explained that combining AI phenotypes and biomarkers has the potential to unlock new pathways to identify and treat AKI and its long-term complications and outcomes.

CLIMATE CHANGE: SUBTROPICAL CAUSES OF ACUTE KIDNEY INJURY IN EUROPE

Vivekanand Jha, The George Institute for Global Health India, New Delhi, India, and Imperial College, London, UK, introduced their talk by emphasising the great increases observed in temperature across Western European countries and the predictions that global temperatures will see new records in the next 5 years. They explained that climate change is going to be the greatest public health challenge of the 21st century, and underlined the high global burden of AKI of 13.3 million cases every year, which is particularly high in tropical developing countries with the majority of global deaths happening in low/middle income countries. Jha explained that AKI in tropical countries is linked to local ecosystem and culture, and that its presentation and outcomes are influenced by health-system level factors, not by individual hospital factors. According to Jha, climate change will have a major impact on AKI incidence; in fact, AKI related to climate change can be called a neglected disease, which needs a higher research focus.

Jha continued by emphasising that "the change that we are seeing is slowly shifting the host, environment, and pathogen equilibrium," explaining that climate change will lead to increased air temperature, change in quality and quantity of drinking water, migration and displacement, air pollution, and pandemics. The increase in urbanisation and the forced and voluntary migration observed both in Europe and the rest of the world will lead to increased frequency and vulnerability to established infectious disease and emergence of new infectious diseases. Jha explained that as a result of climate change and biodiversity loss, a number of infections are likely to increase, many of which have a direct impact on kidney health, such as malaria, dengue, leishmaniases, and severe acute respiratory syndrome.

Europe is increasingly vulnerable to infectious disease breakouts, Jha continued, due to an increasing occupational and residential exposure to vector-borne diseases, lack of natural immunity and vaccine development, and increased local mobility. Lack of flood barriers and ageing water infrastructure increase vulnerability to waterborne diseases, whereas foodborne diseases could develop due to breakdown of cold chain, and suboptimal preparation and processing of food. Change in environmental conditions can lead to changes in vector-host transmission. This, combined with a number of social factors, will lead to many types of kidney disorders for which Europe needs to remain prepared.

Finishing their presentation with a positive tone, Jha explained that there is a lot that can be done if we start now, including vaccine development, systems of monitoring importation risk, and elimination of vector breeding grounds. ●

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