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A "generalized wayfinding" paradigm for improving AKI understanding and classification: insights from the Dutch registries

Vaar *et al.* has recently highlighted the need to define acute kidney injury (AKI) subphenotypes in order to develop specific approaches for prevention, early diagnosis, and appropriate treatment of AKI.[1] Although Kidney Disease Improving Global Outcome (KDIGO) 2012 Criteria increased awareness on AKI, serum creatinine (sCr) and urinary output (UO) levels are driven by different functional and organic kidney modifications. Factors such as comorbidities, the acute organ failures, and nephrotoxic drugs may further contribute to the heterogeneity of the underlying AKI pathophysiology.[2] Furthermore, AKI is associated with very different short- and long-term outcomes. We investigated AKI onset in 52,863 patients using the Dutch National Intensive Care Evaluation (NICE) Registry. Approximately 50% of patients had renal impairment at day one of ICU admission intended as renal replacement therapy (RRT) or sCr>1.1 mg/dL (97.5 µmol/L) or a UO<0.5 mL/kg/h. The remaining patients were followed during ICU stay and AKI incidence was classified according to the highest and lowest levels of sCr and UO criteria as per KDIGO Guidelines (*i.e.*, sCr alone [sCr] or both sCr and UO criteria [sCr+UO]). AKI incidence during ICU admission increased from 4.1% (sCr) to 18.8% (sCr+UO). However, the impact of AKI on mortality markedly differed among the two classifications suggesting that UO may have a lower prognostic impact than sCr. We observed similar findings using the AmsterdamUMCdb during the 4th Digital Critical Care Datathon organized by the European Society of Intensive Care Medicine (ESICM). Although the two databases may present a partial overlap of included patients, the AmsterdamUMCdb provides more information regarding the ICU stay.[3] Similarly to the NICE Registry, among 18,050 patients with available data, 45.4% had renal impairment at the ICU admission and the overall AKI incidence raised from 3.7% (sCr) to 17.2% (sCr+UO). ICU-mortality differed especially for stage 2, dropping from 39.6% (sCr) to 8.8% (sCr+UO). Notably, a consistent proportion of patients recovers from the renal impairment at admission and develops a second AKI during the ICU stay (Figure 1). The AKI incidence, recurrence, and prognosis (*i.e.*, need of RRT at the ICU discharge and mortality) were different and partially predictable according to patient's characteristics. Our results support the need to change the paradigm of AKI Classification aiming at identifying AKI subphenotypes.[1] Therefore, in this perspective, a generalization of the "wayfinding" approach proposed by Adler-Milstein may be a winning strategy.[4] Rather than predicting diagnostic labels of AKI, new technologies should help clinicians to interpret the context of the disease and provide cues to guide them. One possible approach is to explore the underlying AKI pathophysiology such as monitoring real-time microcirculation to estimate renal perfusion and oxygen delivery. Such informative and accurate quantitative data will lead to develop targeted therapies tackling renal pathophysiological processes. Simultaneously, machine learning (ML) algorithms may improve their ability to cluster patients with unique prognostic and predictive enrichment. While the current approach prioritizes the AKI diagnosis, a "generalized wayfinding" strategy has the potential of supporting clinicians to prioritize what should be feasible for the patient care, either be a diagnostic test or a therapeutic intervention. Eventually, research efforts should aim at the increase of our patient's prognosis. Although the there is still an open debate on technical and ethical aspects for the bedside applicabil-

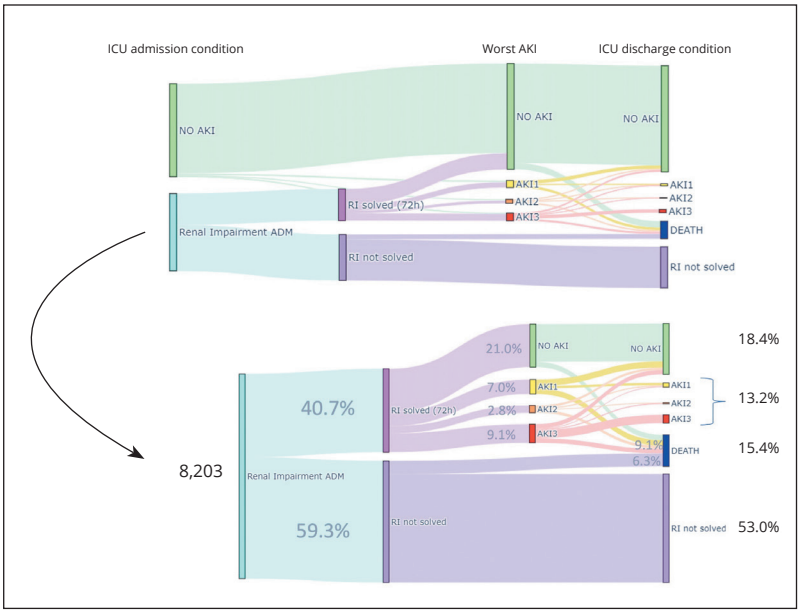

Figure 1.—A, B) Evolution of AKI during admission to the ICU using only serum creatinine values to define AKI according to KDIGO 2012 consensus criteria. The Sankey plot (A) describes the evolution during ICU stay of patients with renal impairment and patients with normal renal function at the admission. Moving along the graph (B) from left to right describes the percentage of patients with renal impairment that normalize and do not normalize the renal function within 72 hours. Furthermore, it is reported the worst AKI stage reached during the ICU admission and at the discharge or death in patients with no AKI at the ICU admission and in patients that normalize renal function within 72 hours.
AKI: acute kidney injury; ADM: admission; ICU: Intensive Care Unit; RI: renal impairment.

ity of ML-based tools in the prediction of organ failure – such as accountability and interpretability – the novel advancement in the ML literature opens new scenarios for clinical applications. These include the possibility to adopt fair learning techniques and domain adaptation strategies to mitigate unwanted bias and to minimize the domain shift problem in specific subgroups. Overall, we believe that the crosstalk between the complexity of the ML techniques with new technologies that provide data on pathophysiological mechanisms behind the organ impairments is an ambitious but promising frontier to improve the clinical practice. This will be only possible thanks to the robust collaboration among all key professionals including engineers, data scientists, clinicians, managers, and companies – as all of them will take part to the process of a better patient care. In conclusion, bedside usability of ML-based algorithms, the availability of a big amount of high-quality data fitting in an adequate technological infrastructure, and a strategy aimed at promoting a new digital culture may be a key strategy to improve patients' outcome.[5]

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