Database Research in Acute Kidney Injury: Time to Take Stock?

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In God we trust, all others must bring data.” This is a memorable quote from W.E. Deming, a highly influential engineer and statistician whose theories on systems, variation, and industrial process have had global influence, notably in the field of health care quality improvement. The availability of clinical data, its quality, and its systematic use underpin our efforts in health service improvement, epidemiology, and clinical trials, and in the developing field of data science.

Database research into acute kidney injury (AKI) has improved our understanding of this syndrome, providing insights into its acute and comorbid risk factors, its incidence in a range of scenarios, and its association with the development of complications and long-term sequelae. Such research is advantaged in that researchers may directly access primary biological data—specifically serum creatinine measurements, and, to a lesser extent, urine volumes—that are widely available and define the clinical syndrome, its evolution, its severity, and recovery. This has advantages over database research that relies on the accuracy of bedside diagnosis, its documentation, and clinical coding. There are, however, potential drawbacks to such database-driven diagnosis where clinical validation has not occurred. Specifically, it is necessary to ensure that appropriate thresholds for data-driven case ascertainment have been reached.

There are key considerations for the researcher undertaking database research in AKI. First, the baseline serum creatinine must be defined and determined. Second, the signifiers of AKI (ie, rate and extent of serum creatinine rise from this baseline, or oliguria) must be ascertained. Finally, one must establish the extent of renal recovery evidenced by a fall in serum creatinine or reconstitution of urine volume and whether significant complications or adverse outcomes (such as the need for kidney replacement therapy) have occurred. Ideally such methodology should be standardized such that AKI database research may be compared.

In 2012 KDIGO published its consensus guidance on the definition of AKI. This included diagnostic and staging criteria based on relative changes in serum creatinine, urine volumes, and need for kidney replacement therapy. This invaluable contribution consolidated prior ground-breaking work on AKI definitions by the RIFLE and AKIN researchers. Since then, the KDIGO criteria have been operationalized in multiple clinical and research contexts. They have been successfully utilized not only in epidemiological studies on AKI incidence and outcomes, but also as end points in clinical prevention and therapeutic trials, in mobilization of AKI-alerting functions in electronic health record (EHR) systems, and, more recently, as a target for predictive artificial intelligence tools.

In this issue of AJKD, Guthrie et al present their important findings on the use of AKI KDIGO classification criteria in AKI database research. They have appraised this issue through 2 approaches. First, they have systematically reviewed all published research studies using KDIGO AKI definitions for the first 5 years after their publication in 2012. The authors have demonstrated significant heterogeneity in how the KDIGO definitions have been applied. This variation included whether and how baseline serum creatinine has been determined, which part of the AKI definition set has been used to determine whether AKI has occurred, and the methodology to define renal recovery. In the second part of their study Guthrie et al convened a panel of clinical and epidemiological experts and, using a 2-step modified Delphi process, they explored the level of consensus on key methodological issues. Consensus was achieved in some areas, but was lacking in others that mapped broadly to the variation in methodology seen in the prior literature review.

So we are agreed on where we disagree. How do we now move forward?

First, Guthrie et al have helpfully summarized clear areas of consensus that can inform researchers undertaking AKI epidemiological studies, while highlighting areas where controversy remains. For the latter areas researchers should consider methodologies carefully, qualifying their approach.

Second, further collaborative efforts to refine AKI detection and staging criteria, such as the KDIGO initiative, might reasonably attempt to provide clarity on such (now well-defined) areas of difficulty, bearing in mind the practical application of using an enhanced definition for database analysis. The forging of absolute consensus in the AKI community may not be achievable, and the greater good of standardization should be a pragmatic goal. Guidance on data quality, minimal datasets, transparent reporting of methodology, and best practice methods of retrospective AKI database analysis would be helpful supplemental resources to revised guidance. Such guidance could reasonably be tested in the field—with real-life databases in different contexts—prior to finalization and dissemination. We must, however, balance this evolving methodological rigor with an acknowledgement of global inequality of access to health care data. In our most

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challenged health care environments we may need data that are “just good enough” to inform much-needed local improvement efforts.13

AKI-defining changes in serum creatinine or urine volume are, ultimately, a surrogate end point for more significant clinical events such as the development of life-threatening metabolic complications, fluid overload, physiological deterioration, need for kidney replacement therapy, and long-term kidney damage. A consistent framework for evaluation of AKI outcomes will further support such database research. A sensible framework of this type has now been proposed and is in widespread use.14

Retrospective epidemiological database research in AKI will always have a key role in exploring novel questions in specific patient populations. Refining our existing approach, as outlined, will provide further progress, but we should remain optimistic regarding other potential advances in data science and AKI care. Effective data visualization with real-time clinical validation may allow us to assess baselines and trajectory of change and to log validated AKI episodes in the EHR systems that populate our research databases.15

Machine learning tools may allow us to survey creatinine datasets with novel biomarkers that may provide more reliable models for predicting, for example, chronic kidney disease post-AKI.17 We may also expand our datasets with novel biomarkers that may provide more reliable and rapid evaluation of kidney damage, its etiology, and attendant changes in renal excretory capacity.16,17 Such novel biological variables may enhance classical classification of AKI and populate our AKI databases of the future. Meanwhile, real-time monitoring of kidney function in high-risk contexts remains a tantalizing prospect and, if operational, could track and archive AKI evolution and its causation prospectively.20

Guthrie and colleagues have provided a valuable next step evaluating AKI database research, against a backdrop of significant progress in the last decade. Their work provides a timely reminder for the AKI community to celebrate success while taking stock of problems with our current methodologies and plan next steps. This will ensure our data-driven understanding of AKI evolves further. One can easily imagine that Deming himself would have viewed such an iterative, critical approach to improving the quality of AKI research with approval.

References