Temporal Trends in AKI: Insights from Big Data

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"Hiding within these mounds of data is knowledge that could change the life of a patient or change the world." This quote by Atul Butte, a preeminent data scientist, perfectly encapsulates the alluring promise of big data for biomedical research. Using large, national administrative datasets is attractive to epidemiologic researchers for a variety of reasons. They allow for many more observations than would be feasible with primary data collection, they allow researchers to conduct sophisticated multilevel analyses because of a large sample size, and they require little to no institutional review board approval. In addition, because of their representative nature, trends and observations obtained from these datasets are likely to generalize nationally.

The Nationwide Inpatient Sample (NIS), maintained by the Agency for Healthcare Research and Quality, is such a database. It contains data on hospitalizations at about 1000 hospitals across the United States, comprising a 20% sample of hospitals (1,2). The sampling varies from year to year. Sampling is stratified across five criteria (geographic region, public versus private, urban versus rural, teaching versus nonteaching, and bed size). Data available through the NIS include patient demographics, The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses and procedures, hospital charges and length of stay, discharge disposition, anonymous physician and hospital identifiers, and hospital characteristics (*e.g.*, geographic region, teaching status, and bed size).

AKI is common in hospitalized patients and can affect >5% of hospitalizations, and it is associated with high morbidity and mortality (3). Moreover, there is growing evidence that sequelae of AKI include poor long–term survival, increased risk of readmissions, incident and worsening CKD, and progression to ESRD (4–6). These consequences also lead to increased disability, decreased quality of life, and disproportionate burden on health care resources. The incidence of nondialysis-requiring AKI has increased when assessed in either communities or hospitalized patients (7). Most studies on the temporal trends of AKI requiring dialysis (AKI-D) were restricted to certain geographic regions and/or critical care settings (8–10).

The use of national databases for AKI epidemiology research has been restricted by the poor validity of administrative codes (11). By using an innovative approach in the NIS, combining diagnosis and procedure codes capturing AKI-D incidence with high fidelity and using the US Census data, Hsu *et al.* (12) showed in 2013 that the population–level incidence rates of AKI-D increased by >10% per year, with a near tripling in the absolute number of annual patients. However, adjustment for AKI risk factors, including acute heart failure, sepsis, and critical illness, and cardiac catheterizations only explained a fraction of this rise.

In this issue of the *Clinical Journal of the American Society of Nephrology*, Hsu *et al.* (13) build on their prior work by attempting to explain the reasons responsible for the temporal rise in AKI-D. Hsu *et al.* (13) again show that, from 2007 to 2009, the population incidence of AKI-D increased by 11% per year. Hsu *et al.* (13) also used the clinical classifications software to group a large variety of ICD-9-CM codes into clinically relevant categories, showing that temporal trends in acute and chronic disease categories (sepsis, hypertension, respiratory failure, coagulation/hemorrhagic disease, shock, and liver disease) accounted fully for this rise in AKI-D. Changes in procedures did not contribute to the rise in AKI-D. In addition, even if they excluded admissions with a concurrent diagnosis of ESRD, thus minimizing misclassification of hospitalizations, this temporal increase persisted.

Hsu *et al.* (13) need to be commended for conducting a rigorous and statistically complex study to identify predictors of increasing trends in AKI-D. This is especially important in a time when the public health burden of AKI and attendant CKD has attained critical importance. With the failure of several therapies aimed at preventing worsening of AKI (14), acute intermittent and continuous RRTs remain the cornerstone of severe AKI management. However, we may have approached a therapeutic threshold for both intermittent and continuous RRTs, beyond which there is no benefit to intensifying dialysis (15,16). Thus, early identification of those patients with AKI who are likely to worsen and need RRT as well as those who are likely to recover is of paramount importance from a public health perspective. This paper represents a strong effort to outline in broad strokes the comorbidities responsible for the increase in AKI-D (13).

The analysis, however, has limitations, most of which are representative of any analysis using large datasets (13). Although the NIS is a large dataset, it is not granular, lacking laboratory measurements, readmission information, and long-term outcomes. Thus, determination of whether this increasing trend is indicative of true rise in disease versus earlier initiation of dialysis by physicians is yet to be determined, although ascertainment of dialysis need by creatinine-based criteria is inadequate at best. In addition, the comorbidities explaining the rise were determined by administrative codes, which have varying

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validity, especially with chronic comorbidities (17). Also, the NIS data lack longitudinal information, and being deidentified, they lack linkage to other registries (including the US Renal Data System); thus, long–term ESRD outcomes cannot be defined with AKI-D.

In addition, this study presents an enigma (13). Although the prevalence rate of ESRD has been increasing (likely because of improved life expectancy), the incidence rate has been stable since 2010 (18). Thus, if AKI-D raises ESRD risk (as evidenced by several other epidemiologic studies) (19,20) and if incident AKI-D is on the rise, which this study indicates, why is the annual incidence rate of ESRD not rising in parallel? This might be possible if AKI-D conferred such an excess risk of mortality that patients died before getting to ESRD. However, the excess mortality attributed with AKI and AKI-D has been stable or declining (9). The second possibility is that, because AKI begets AKI (21,22), AKI-D increases the risk of additional admissions with AKI-D (even with recovery of renal function), and thus, the number of AKI-D hospitalizations could be inflated without an actual increase in the number of individual patients with AKI-D per year. This process may be at play; the NIS fails to capture this distinction, because all hospitalizations are deidentified and readmissions cannot be tracked.

Another point that this study engenders is far more pessimistic. If the rise in AKI-D is truly explained by rising comorbidities, the sheer variety of comorbidities that are responsible for the rising trend is daunting. Because of this heterogeneity in risk factors and etiologies, searching for a long-awaited therapy to prevent or ameliorate AKI is going to be extremely unlikely. Because of the complex and overlapping nature of AKI, it is conceivable that each patient with AKI will need a different therapeutic strategy, or subphenotyping of AKI using molecular, imaging, and other tools may be necessary to use the correct intervention. Although some generic pleuripotent prevention strategies to reduce the risk of AKI seemed to be promising (low chloride fluids, steroids, statins, and remote ischemic preconditioning), recent studies have not been able to confirm their efficacy, putting the scientific community back at square one for finding preventive or treatment strategies for AKI (23–29).

In summary, this big data study (13) provides a valuable foundation for future larger studies using longitudinal granular data from health care systems as well as currently ongoing cohort studies to delineate the epidemiology and precipitants of AKI-D (30). This, in turn, would provide early risk stratification for those hospitalized patients who are at highest risk of developing AKI-D. Understanding this epidemiology will play a vital role in diminishing the public health burden of this devastating condition.

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Disclosures

None.

References

1. Agency for Healthcare Research and Quality: Healthcare Cost and Utilization Project. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed July 1, 2014
2. Steiner C, Elixhauser A, Schnaier J: The healthcare cost and utilization project: An overview. *Eff Clin Pract* 5: 143–151, 2002
3. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW: Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 16: 3365–3370, 2005
4. Chawla LS, Eggers PW, Star RA, Kimmel PL: Acute kidney injury and chronic kidney disease as interconnected syndromes. *N Engl J Med* 371: 58–66, 2014
5. Chawla LS, Amdur RL, Amodeo S, Kimmel PL, Palant CE: The severity of acute kidney injury predicts progression to chronic kidney disease. *Kidney Int* 79: 1361–1369, 2011
6. Bagshaw SM: Short- and long-term survival after acute kidney injury. *Nephrol Dial Transplant* 23: 2126–2128, 2008
7. Rewa O, Bagshaw SM: Acute kidney injury-epidemiology, outcomes and economics. *Nat Rev Nephrol* 10: 193–207, 2014
8. Hsu C-Y, McCulloch CE, Fan D, Ordoñez JD, Chertow GM, Go AS: Community-based incidence of acute renal failure. *Kidney Int* 72: 208–212, 2007
9. Wald R, McArthur E, Adhikari NKJ, Bagshaw SM, Burns KEA, Garg AX, Harel Z, Kitchlu A, Mazer CD, Nash DM, Scales DC, Silver SA, Ray JG, Friedrich JO: Changing incidence and outcomes following dialysis-requiring acute kidney injury among critically ill adults: A population-based cohort study. *Am J Kidney Dis* 65: 870–877, 2015
10. Metcalfe W, Simpson M, Khan IH, Prescott GJ, Simpson K, Smith WC, MacLeod AM; Scottish Renal Registry: Acute renal failure requiring renal replacement therapy: Incidence and outcome. *QJM* 95: 579–583, 2002
11. Grams ME, Waikar SS, MacMahon B, Whelton S, Ballew SH, Coresh J: Performance and limitations of administrative data in the identification of AKI. *Clin J Am Soc Nephrol* 9: 682–689, 2014
12. Hsu RK, McCulloch CE, Dudley RA, Lo LJ, Hsu CY: Temporal changes in incidence of dialysis-requiring AKI. *J Am Soc Nephrol* 24: 37–42, 2013
13. Hsu RK, McCulloch CE, Heung M, Saran R, Shahinian VB, Pavkov ME, Burrows NR, Powe NR, Hsu C-Y; Centers for Disease Control and Prevention Chronic Kidney Disease Surveillance Team: Exploring potential reasons for the temporal trend in dialysis-requiring AKI in the United States. *Clin J Am Soc Nephrol* 11: 14–20, 2016
14. Jo SK, Rosner MH, Okusa MD: Pharmacologic treatment of acute kidney injury: Why drugs haven't worked and what is on the horizon. *Clin J Am Soc Nephrol* 2: 356–365, 2007
15. Pannu N, Klarenbach S, Wiebe N, Manns B, Tonelli M; Alberta Kidney Disease Network: Renal replacement therapy in patients with acute renal failure: A systematic review. *JAMA* 299: 793–805, 2008
16. Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E, Schein RM, Smith MW, Swanson KM, Thompson BT, Vijayan A, Watnick S, Star RA, Peduzzi P; VA/NIH Acute Renal Failure Trial Network: Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med* 359: 7–20, 2008
17. Quach S, Blais C, Quan H: Administrative data have high variation in validity for recording heart failure. *Can J Cardiol* 26: 306–312, 2010
18. USRDS: 2013 USRDS Anual Data Report. Available at: http://www.usrds.org/2014/view/v2_01.aspx. Accessed November 23, 2015
19. Wald R, Quinn RR, Luo J, Li P, Scales DC, Mamdani MM, Ray JG; University of Toronto Acute Kidney Injury Research Group: Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. *JAMA* 302: 1179–1185, 2009
20. Hsu CY, Chertow GM, McCulloch CE, Fan D, Ordoñez JD, Go AS: Nonrecovery of kidney function and death after acute on chronic renal failure. *Clin J Am Soc Nephrol* 4: 891–898, 2009
21. Siew ED, Parr SK, Abdel-Kader K, Eden SK, Peterson JF, Bansal N, Hung AM, Fly J, Speroff T, Ikizler TA, Matheny ME: Predictors of recurrent AKI [published online ahead of print August 11, 2015]. *J Am Soc Nephrol* doi:ASN.2014121218
22. Thakar CV, Parikh PJ, Liu Y: Acute kidney injury (AKI) and risk of readmissions in patients with heart failure. *Am J Cardiol* 109: 1482–1486, 2012
23. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M: Association between a chloride-liberal vs chloride-restrictive

intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA* 308: 1566–1572, 2012
24. Young P, Bailey M, Beasley R, Henderson S, Mackle D, McArthur C, McGuinness S, Mehrtens J, Myburgh J, Psirides A, Reddy S, Bellomo R; SPLIT Investigators; ANZICS CTG: Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit: The SPLIT Randomized Clinical Trial. *JAMA* 314: 1701–1710, 2015
25. Molnar AO, Coca SG, Devereaux PJ, Jain AK, Kitchlu A, Luo J, Parikh CR, Paterson JM, Siddiqui N, Wald R, Walsh M, Garg AX: Statin use associates with a lower incidence of acute kidney injury after major elective surgery. *J Am Soc Nephrol* 22: 939–946, 2011
26. Billings F, Wagner C, Hendricks P, Shi Y, Petracek M, Brown N: High Dose Perioperative Atorvastatin and Acute Kidney Injury Following Cardiac Surgery. Available at: https://www.asn-online.org/education/kidneyweek/2015/KW15_Late-Breakers.pdf. Accessed November 23, 2015
27. Garg AX, Whitlock R: Effect of Methylprednisolone on Acute Kidney Injury in Patients Undergoing Cardiac Surgery with Cardiopulmonary Bypass. Available at: https://www.asn-online.org/education/kidneyweek/2015/KW15_Late-Breakers.pdf. Accessed November 23, 2015
28. Zarbock A, Schmidt C, Van Aken H, Wempe C, Martens S, Zahn PK, Wolf B, Goebel U, Schwer CI, Rosenberger P, Haeberle H, Görlich D, Kellum JA, Meersch M; RenalRIPC Investigators: Effect of remote ischemic preconditioning on kidney injury among high-risk patients undergoing cardiac surgery: A randomized clinical trial. *JAMA* 313: 2133–2141, 2015
29. Hausenloy DJ, Candilio L, Evans R, Ariti C, Jenkins DP, Kolvekar S, Knight R, Kunst G, Laing C, Nicholas J, Pepper J, Robertson S, Xenou M, Clayton T, Yellon DM; ERICCA Trial Investigators: Remote ischemic preconditioning and outcomes of cardiac surgery. *N Engl J Med* 373: 1408–1417, 2015
30. Go AS, Parikh CR, Ikizler TA, Coca S, Siew ED, Chinchilli VM, Hsu C-Y, Garg AX, Zappitelli M, Liu KD, Reeves WB, Ghahramani N, Devarajan P, Faulkner GB, Tan TC, Kimmel PL, Eggers P, Stokes JB; Assessment Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury Study Investigators: The assessment, serial evaluation, and subsequent sequelae of acute kidney injury (ASSESS-AKI) study: Design and methods. *BMC Nephrol* 11: 22, 2010

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See related article, "Exploring Potential Reasons for the Temporal Trend in Dialysis-Requiring AKI in the United States," on pages 14–20.