RESEARCH LETTER

Inpatient Native Kidney Biopsies and Glomerular Disease: Utilization and Diagnostic Trends in the United States, 2006-2015

To the Editor:

Kidney biopsy is necessary for definitive diagnosis of many parenchymal kidney diseases, particularly glomerular diseases. It can be performed in inpatient or outpatient settings and by nephrologists or radiologists, and in recent years, real-time image guidance has become standard.[1] Many factors may affect inpatient native kidney biopsy use related to glomerular disease, including changing admission patterns and criteria, changing diagnostic trends, and perhaps changing illness patterns.[2] We investigated trends in inpatient native kidney biopsies related to glomerular disease in US adults, 2006 to 2015.

We used National Inpatient Sample (NIS) data from January 1, 2006, to September 30, 2015. The NIS is an all-payer database of inpatient health care in the United States, containing data from more than 7 million hospital stays each year.[3] It is a 20% stratified sample of discharges from community hospitals and allows weighted estimates on more than 35 million hospitalizations per year.[3] NIS is publicly available administrative data, use is not considered human subjects research, and consent was not required. We identified patients 18 years or older who underwent kidney biopsy (identified from *International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] procedure code 55.23) and categorized by age. We excluded persons with a transplanted kidney or kidney tumor.

Presence of glomerular disease and categorization into 4 glomerular disease categories was inferred from *ICD-9-CM* discharge codes (Figs 1 and S1; Tables S1-S3). Patients could be categorized into either or both nephritic/proliferative and nephrotic categories. Diabetic glomerular disease was inferred from the presence of nephrotic and diabetic kidney disease codes with absence of nephritic/proliferative codes. Paraprotein kidney disease was inferred from nephritic or nephrotic codes plus a paraproteinemia code. Incidence rates were adjusted using census year measures. We used appropriate survey methods and trendweights.[4,5] Linear trends were estimated using weighted least-squares regression.[6] For day of kidney biopsy and lengths of stay, median and interquartile range were plotted, and linear trends were tested using quantile regression. Plots used smoothing.

Estimated inpatient kidney biopsies identifying glomerular disease increased from 9,600 (95% CI, 8,648-10,550) in 2006 to 15,920 (95% CI, 15,067-16,773) in 2015 (yearly increase of 732 [95% CI, 633-831]), corresponding to an increase from 4.3 (95% CI, 3.9-4.7) per 100,000 adults in 2006 to 6.4 (95% CI, 6.1-6.8) in 2015. P for trends < 0.001.

The proportion of inpatient biopsies with glomerular disease increased from 53.8% (95% CI, 51.9%-55.8%) in 2006 to 64.7% (95% CI, 63.2%-66.3%) in 2015 (P for trend < 0.001). Growth in the number of biopsies with glomerular disease was noted in all age groups. Population-indexed growth was highest in those older than 70 years and lowest in those aged 18 to 39 years. Growth in absolute numbers was highest among those aged 40 to 69 years. By diagnostic category, growth was largest in paraprotein-related kidney diseases among all age groups (Fig 1).

Kidney biopsies identifying glomerular disease were performed on day of hospitalization median 4 (interquartile range, 2-7); there was no evidence of change over time (Fig 2A). Of those with glomerular disease, an estimated 2.9% (95% CI, 2.6%-3.1%) of patients died during the biopsy hospitalization. There was an absolute decline of 0.21% per year (95% CI, 0.06%-0.37%; $P = 0.01$) in inpatient mortality. The decline was most pronounced among those 70 years or older, in whom there was an absolute decline of 0.71% per year (95% CI, 0.39%-1.04%; $P = 0.001$; Fig 2B).

We found increasing inpatient native kidney biopsies with glomerular disease in US adults, not explained by demographic or hospitalization trends. Increasing total inpatient native kidney biopsies has previously been reported from an NIS analysis.[7] We found that population-indexed growth in biopsies with glomerular disease was highest among the oldest patients, perhaps related to low complication rates and improved therapies for many glomerular diseases. It is also notable that kidney biopsies in paraprotein-related kidney disease displayed the largest growth. Despite increased use of inpatient kidney biopsies, especially in older age groups, hospitalization mortality rates are decreasing overall, a finding most pronounced in the oldest group. Kidney biopsies are increasingly recognized as essential and safe procedures to understand heterogeneous kidney diseases and move toward personalized therapy in both the clinical and research domains.[8,9] This improved safety with the use of image guidance has been demonstrated in a recent large meta-analysis.[2] The observed increasing paraprotein-related kidney disease may be due to increasing recognition of this diverse entity.[10]

Important limitations of our study were dependence on *ICD-9-CM* discharge codes to try to glean kidney diagnoses (in particular, there are no codes for paraprotein-related kidney disease so we attempted to infer that diagnosis from combinations of codes; uncertain diagnoses may be coded; we are unable to differentiate changes in true diagnoses from changes in coding patterns) and use of weights that were not derived for the subpopulation of interest.

Inpatient kidney biopsy use in glomerular disease is increasing in US adults, most rapidly in older patients, perhaps related to increasing recognition of the

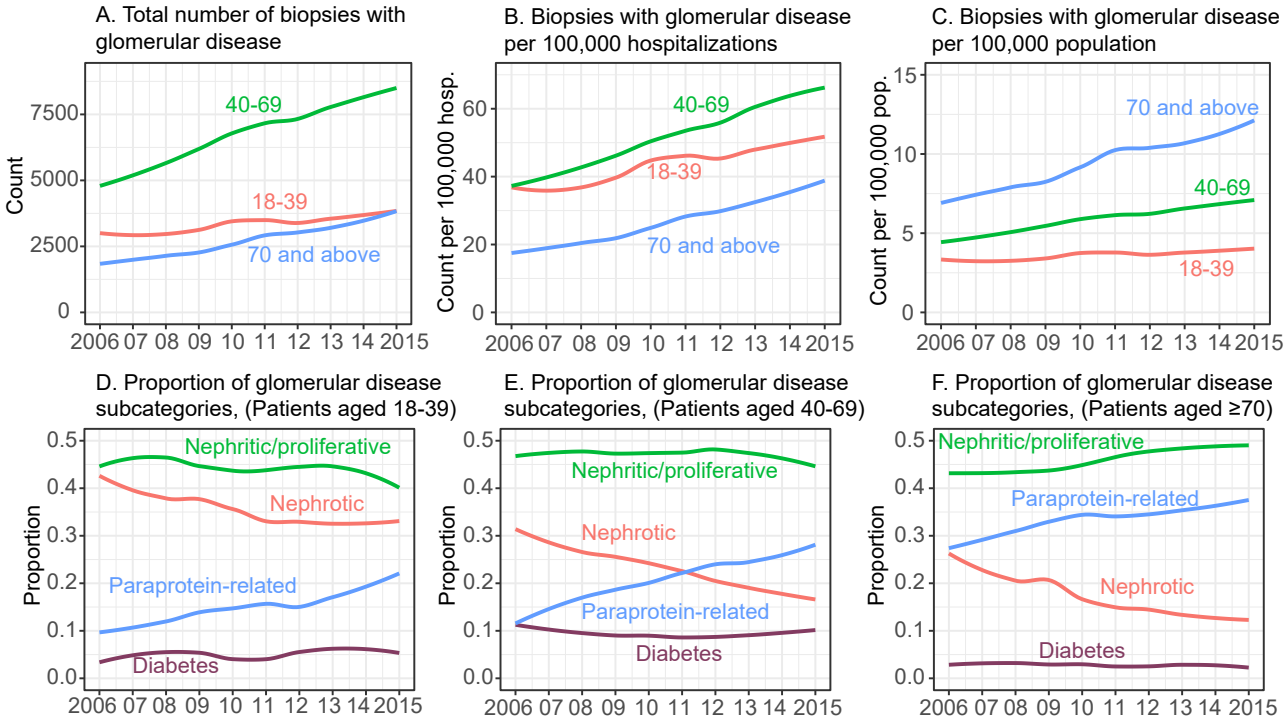

Figure 1. (A-C)* Estimated trends in inpatient kidney biopsies with glomerular disease in the United States, 2006 to 2015. (D-F)† Estimated trends in 4 glomerular disease diagnostic categories, 2006 to 2015, as proportions of kidney biopsies identifying glomerular disease. **P* values for trends: (A) $P < 0.001$ for 70 years and older and 40- to 69-year age group; $P = 0.001$ for 18- to 39-year age group. (B) $P < 0.001$ for each age group. (C) $P < 0.001$ for 70 years and older and 40- to 69-year age group; $P = 0.002$ for 18- to 39-year age group. †*P* values for trends. (D) Diabetes: $P = 0.12$; nephrotic: $P = 0.03$; nephritic/proliferative: $P = 0.37$; paraprotein-related: $P < 0.001$. (E) Diabetes: $P = 0.48$; nephrotic: $P < 0.001$; nephritic/proliferative: $P = 0.96$; paraprotein-related: $P < 0.001$. (F) Diabetes: $P = 0.41$; nephrotic: $P = 0.005$; nephritic/proliferative: $P = 0.22$; paraprotein-related: $P = 0.01$. Note: Numbers are weighted estimates using the National Inpatient Sample. Presence of glomerular disease and subcategories thereof (nephritic/proliferative, nephrotic, paraprotein-related, and diabetes) were inferred from *International Classification of Diseases, Ninth Revision, Clinical Modification* discharge code patterns (Fig S1; Tables S1-S3). Patients could be categorized into both nephritic/proliferative and nephrotic categories (resulting in the sum of proportions being slightly >1 for each year), but all other glomerular disease combinations were mutually exclusive (Fig S1). Abbreviations: hosp, hospitalization; pop, population.

relative safety of the procedure and the importance of accurate kidney disease diagnosis and targeted therapies.

Vinh V. Tran, MD, Carl P. Walther, MD, MS

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Algorithm for differentiating into 4 glomerular disease kidney categories by *ICD-9-CM* diagnostic codes (nephritic/proliferative, nephrotic, paraprotein-related, diabetic).

Table S1. Diagnostic codes for glomerular disease, diabetic kidney disease, and paraproteinemia.

Table S2. Diagnostic codes for nephritic/proliferative glomerular diseases.

Table S3. Diagnostic codes for nephrotic glomerular diseases.

ARTICLE INFORMATION

Authors' Affiliations: Department of Medicine, Baylor College of Medicine (VHT); and Selzman Institute for Kidney Health, Section of Nephrology, Department of Medicine, Baylor College of Medicine, Houston, TX (CPW).

Authors' Contributions: Research idea and study design: VVT, CPW; data acquisition: CPW; statistical analysis: CPW; data analysis/interpretation: VVT, CPW; supervision or mentorship: CPW. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Support: Dr Walther is supported by the National Institute of Diabetes and Digestive and Kidney Diseases (grant/award number: K23DK122131).

Financial Disclosure: The authors declare that they have no relevant financial interests.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Peer Review: Received April 21, 2021, as a submission to the expedited consideration track with 2 external peer reviews. Direct editorial input from the Statistical Editor and the Editor-in-Chief. Accepted in revised form June 27, 2021.

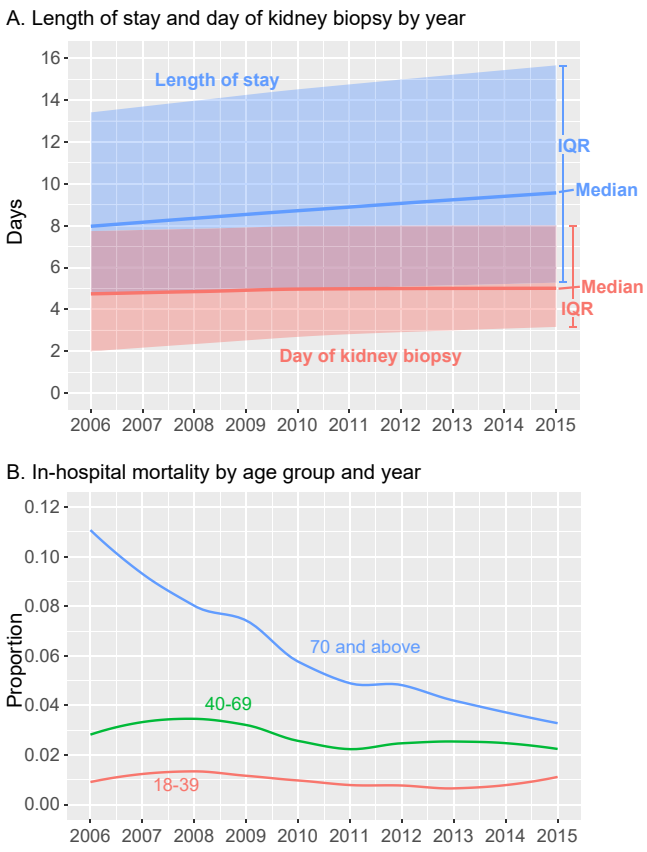

Figure 2. (A) Length of stay and hospitalization day of kidney biopsy, for inpatient stays with glomerular disease diagnosed by inpatient kidney biopsy.* (B) In-hospital mortality estimates for hospitalizations in the United States in which kidney biopsy diagnosed glomerular disease, 2006 to 2015, by age group (18-39, 40-69, and ≥70 years). *Trend for median day of kidney biopsy did not differ from 0 (change per year, 0.00 [95% CI, −0.02 to 0.02; P = 1.00]). Increasing trend for median length of stay was significant (change per year, 0.14 [95% CI, 0.11 to 0.18]; P < 0.001). Note: Day of admission was taken as day 1 of hospitalization. Abbreviation: IQR, interquartile range.

Publication Information: © 2021 The Authors. Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). Published online August 11, 2021 with doi 10.1016/j.xkme.2021.06.013

REFERENCES

1. Luciano RL, Moeckel GW. Update on the native kidney biopsy: core curriculum 2019. *Am J Kidney Dis*. 2019;73(3):404-415.
2. Poggio ED, McClelland RL, Blank KN, et al. Systematic review and meta-analysis of native kidney biopsy complications. *Clin J Am Soc Nephrol*. 2020;15(11):1595-1602.
3. Agency for Healthcare Research and Quality. Introduction to the HCUP National Inpatient Sample (NIS) 2015. Issued November 2017. www.hcup-us.ahrq.gov. Accessed April 1, 2021.
4. Heeringa SG, West BT, Berglund PA. *Applied Survey Data Analysis*. 2nd ed. CRC Press; 2017.
5. Houchens R, Ross D, Elixhauser A. Final Report on Calculating National Inpatient Sample (NIS) Variances for Data Years 2012 and Later. 2015. HCUP Methods Series Report # 2015-09. US Agency for Healthcare Research and Quality; December 14, 2015.
6. Bao Y, Sturm R. How do trends for behavioral health inpatient care differ from medical inpatient care in US community hospitals? *J Mental Health Policy Econ*. 2001;4(2):55-64.
7. Charu V, O'Shaughnessy MM, Chertow GM, Kambham N. Percutaneous kidney biopsy and the utilization of blood transfusion and renal angiography among hospitalized adults. *Kidney Int Rep*. 2019;4(10):1435-1445.
8. de Boer IH, Alpers CE, Azeloglu EU, et al. Rationale and design of the Kidney Precision Medicine Project. *Kidney Int*. 2021;99(3):498-510.
9. Srivastava A, Palsson R, Kaze AD, et al. The prognostic value of histopathologic lesions in native kidney biopsy specimens: results from the Boston Kidney Biopsy Cohort Study. *J Am Soc Nephrol*. 2018;29(8):2213-2224.
10. Hogan JJ, Alexander MP, Leung N. Dysproteinemia and the kidney: core curriculum 2019. *Am J Kidney Dis*. 2019;74(6):822-836.