RESEARCH LETTER

Self-reported Urine Volume in Hemodialysis Patients: Predictors and Mortality Outcomes in the International Dialysis Outcomes and Practice Patterns Study (DOPPS)

To the Editor:

The prognostic importance of residual kidney function (RKF) for maintenance hemodialysis (HD) patients has previously been recognized.[1-6] In previous studies, monitoring of RKF typically required urine collection preceding the HD session and a predialysis blood sample from the end of collection to compute the renal clearance of urea/creatinine (ie, urinary urea/creatinine divided by serum concentration[2,4,5]) and more specifically, renal Kt/V_{urea}.[3] Urine volume, the prerequisite for RKF, can also be estimated by patient self-report.[7] In the present analysis of the DOPPS, we evaluated predictors and outcomes of self-reported urine volume; specifically, whether a positive response to the question: "Did the patient have urine output > 200 mL/d or 1 cup/day at the time of enrollment?" was associated with mortality during follow-up periods of 2 to 3 years.

We included 37,575 patients from 2002-2015 (Table S1). Urine volume at baseline was available from patient reports as a dichotomous variable (≤200 vs >200 mL/d) at DOPPS entry. Additional data collection in phase 5 allowed more detailed analyses for 8,388 patients with patient-reported urine volume by 4 categories (≤200, 200-499, 500-999, ≥1,000 mL/d), collected at 4-month reporting intervals. Analyses of cross-sectional associations between urine volume and patient characteristics and treatment factors were conducted using descriptive statistics (and multivariable logistic regression models for supplementary tables). Cox regression was used to estimate associations between urine volume and all-cause mortality.

Patient characteristics by reported urine volume status are shown in Table 1. Self-reported urine volume > 200 mL/d was inversely associated with HD vintage (Fig 1A; Fig S1 has data by region; Fig S2 has data by region, DOPPS phase, and vintage).

All factors listed in Table 1 were also analyzed by phase and region (Table S2), but only vintage was recognizable as a consistent predictor of urine volume > 200 mL/d. We therefore used logistic regression to determine adjusted associations between patient characteristics and urine volume > 200 mL/d (Table S3). Positive associations with urine volume > 200 mL/d included lower vintage, region (proportion with urine volume > 200 mL/d was lowest in North America); lower IDWG, younger age, PKD, absence of congestive heart failure, prescription of diuretics, RAAS inhibition, and IV iron. Inverse associations with urine volume > 200 mL/d included longer treatment time, higher Kt/V, higher dialysate sodium concentrations, and PPI prescription.

Adjusted associations of urine volume status and urine volume treated as a 4-category variable with all-cause mortality are shown in Fig 1B and C. Self-reported urine volume > 200 mL/d and higher urine volume categories were inversely associated with mortality (all HRs reported in the legend; for various levels of all-cause mortality risk adjustment, by region, see also Fig S3).

In this largest international study of urine volume to date,[1-9] the following modifiable factors were consistently associated with higher reported urine volume: lower IDWG; use of diuretics, RAAS inhibition, or IV iron; and nonuse of a PPI. Among nonmodifiable factors, consistent associations with urine volume were observed for lower vintage category, PKD, and absence of congestive heart failure.

Several previous studies demonstrated that survival was better when patients maintained RKF[1-7] (definitions for RKF: urinary clearance of urea and creatinine,[2] renal Kt/V_{urea},[3] renal urea clearance > 1 mL/min,[4] renal urea clearance,[5] glomerular filtration rate calculated from 24-hour urine and estimated glomerular filtration rate calculated from serum urea and creatinine concentration).[6] The present analysis confirms the previous survival results of Shafi et al,[7] which showed for incident HD patients that urine output of at least 1 cup daily was associated with better survival.

The associations between self-reported urine volume and dialysate sodium concentrations (higher, by indication, in patients with lower blood pressure),[10] prescription of RAAS inhibition and IV iron, and not prescribing PPIs require further analysis to determine whether associations are causal. Whether patients with vs without urine volume should be managed differently deserves further study.

Among the study limitations, cross-sectional analyses of urine volume prevalence as the outcome may be limited by selection bias, temporal ambiguity (exposure before loss of urine volume?), and reverse causation (loss of urine volume can influence the exposure). The mortality analysis may be biased by unmeasured confounders, overadjustment for mediators, or lead-time bias (patients starting dialysis earlier may have higher urine volume and lower mortality). Despite these limitations, the findings indicate value to routinely asking patients a simple question about urine output, especially now that timed urine samples are no longer collected routinely in most US dialysis units.

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Table 1. Distributions of Covariates by Reported Urine Volume: ≤200 Versus >200 mL/d

	≤200 mL/d	>200 mL/d	All
No. of patients	22,644	14,931	37,575
Patient Demographic Factors			
Region			
Europe	45%	63%	52%
Japan	25%	15%	21%
North America	30%	22%	26%
Vintage			
≤90 d	8%	21%	13%
90 d-0.9 y	15%	36%	24%
1-1.9 y	13%	17%	14%
2-2.9 y	10%	8%	9%
3-4.9 y	16%	9%	13%
>5 y	38%	9%	27%
Vintage, y	5.6 ± 6.4	1.8 ± 3.3	4.1 ± 5.7
Age, y	64 ± 14	64 ± 15	64 ± 15
Male sex	58%	63%	60%
Black race	8%	5%	7%
Diagnoses and Comorbid Conditions			
Primary ESKD cause: type 2 diabetes	24%	26%	25%
Primary ESKD cause: PKD	5%	6%	5%
Coronary artery disease	43%	41%	42%
Cerebrovascular	17%	16%	16%
Congestive heart failure	30%	28%	29%
Hypertension	82%	87%	84%
Peripheral vascular disease	27%	27%	27%
Other cardiovascular disease	35%	30%	33%
Cancer	14%	15%	14%
Diabetes	38%	43%	40%
Gastrointestinal bleed	5%	5%	5%
HIV positive	1%	1%	1%
Lung disease	12%	12%	12%
Neurologic disease	12%	10%	11%
Psychiatric disorder	16%	16%	16%
Recurring cellulitis	9%	8%	8%
Measured Patient Factors			
Body mass index, kg/m^2	24.8 ± 5.9	25.7 ± 5.7	25.2 ± 5.9
Postdialysis SBP, mm Hg	134 ± 24	138 ± 22	135 ± 23
Albumin, g/dL	3.7 ± 0.5	3.7 ± 0.5	3.7 ± 0.5
Normalized PCR, g/kg/d	1.00 ± 0.24	0.95 ± 0.24	0.98 ± 0.24
Potassium, mEq/L	5.0 ± 0.8	4.8 ± 0.8	4.9 ± 0.8
Creatinine, mg/dL	9.2 ± 3.0	7.8 ± 2.8	8.7 ± 3.0
Treatments			
RAAS inhibition[a]	37%	43%	39%
Diuretic	18%	52%	31%
IV iron therapy	62%	71%	65%
PPI	42%	42%	42%
Single-pool Kt/V	1.49 ± 0.31	1.37 ± 0.33	1.44 ± 0.32
IDWG, % body weight	4% ± 2%	3% ± 2%	3% ± 2%
Treatment time, min	235 ± 34	230 ± 36	233 ± 35
Dialysate sodium concentration, mEq/L	140 ± 2	139 ± 2	140 ± 2

Note: Continuous variables given as mean ± standard deviation. Data for urine volume, demographic factors, diagnoses, comorbid conditions, and measured patient factors taken from study entry for each patient; patients not limited to prevalent cross-section taken at the beginning of each phase.
Abbreviations: ESKD, end-stage kidney disease; IDWG, interdialytic weight gain; IV, intravenous; PCR, protein catabolic rate; PKD, polycystic kidney disease; PPI, proton pump inhibitor; SBP, systolic blood pressure.
[a]Angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or aldosterone antagonist.

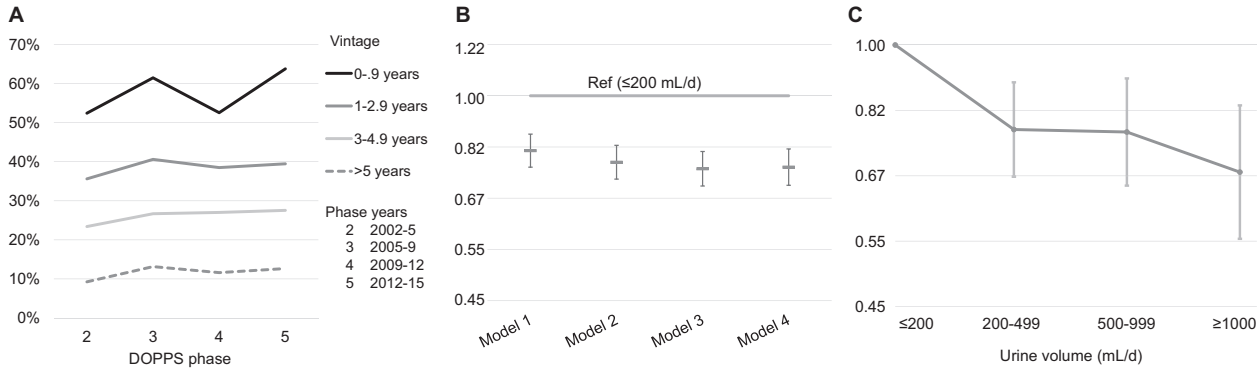

Figure 1. Self-reported urine volume and mortality. (A) Patients reporting urine volume > 200 mL/d, by DOPPS phase and vintage category. (B) Association of all-cause mortality of patients with reported urine volume > 200 vs ≤ 200 mL/d, using different covariate adjustments for each model. Model 1, adjusted for DOPPS phase, demographic factors, diagnoses, and comorbid conditions (hazard ratio [HR], 0.81; 95% confidence interval [CI], 0.77-0.85); model 2, + measured patient factors (HR, 0.77; 95% CI, 0.73-0.81); model 3, + dialysis treatment factors (HR, 0.75; 95% CI, 0.71-0.79); model 4, + medications (HR, 0.76; 95% CI, 0.72-0.80). Table 1 lists the variables adjusted for under each category (eg, demographic factors). Data for urine volume, demographic factors, diagnoses, comorbid conditions, measured patient factors, dialysis treatment factors, and medications taken from study entry for each patient; patients not limited to prevalent cross-section taken at the beginning of each phase. (C) Association between urine volume category (vs ≤200 mL/d) and all-cause mortality, based on model 4, among patients in DOPPS phase 5 (urine volume categories were not reported in earlier phases). Data for urine volume, demographic factors, diagnoses, comorbid conditions, and measured patient factors taken from study entry for each patient; patients not limited to prevalent cross-section taken at the beginning of phase 5. Compared with patients reporting urine volume < 200 mL/d, HRs were 0.77 (95% CI, 0.67-0.89), 0.77 (95% CI, 0.65-0.90), and 0.68 (95% CI, 0.55-0.83) for urine volumes of 200-499, 500-999, and ≥ 1,000 mL/d, respectively.

Supplementary Material

Supplementary File (PDF)

Figures S1-S3, Item S1, Tables S1-S3.

Article Information

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Support: Global support for ongoing DOPPS Programs is provided without restriction on publications by a variety of funders (details in https://www.dopps.org/AboutUs/Support.aspx). All grants were made to Arbor Research Collaborative for Health and not to coauthors directly. None of the funders had any role in study design; collection, analysis, and interpretation of data; writing the report; or the decision to submit this report for publication.

Financial Disclosure: Dr Jadoul received consulting fees/served on paid advisory boards of Astellas and MSD; lecture fees from AbbVie, Amgen, Astellas, Fresenius Vifor, Menarini, and MSD; and grant support from Amgen, Janssen-Cilag, Otsuka, Roche, and MSD. Dr Yamamoto received lecture fees from Chugai Pharmaceutical and Kyowa Hakko Kirin. The remaining authors declare that they have no other relevant financial interests.

Acknowledgements: Heather Van Doren, senior medical editor with Arbor Research Collaborative for Health, provided editorial assistance on this manuscript.

Peer Review: Received September 10, 2018. Evaluated by 2 external peer reviewers, with direct editorial input from a Statistics/Methods Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form February 27, 2019.

Publication Information: © 2019 by the National Kidney Foundation, Inc. Published online Month X, XXXX with doi 10.1053/j.ajkd.2019.02.012

References

1. Maiorca R, Brunori G, Zubani R, et al. Predictive value of dialysis adequacy and nutritional indices for mortality and morbidity in CAPD and HD patients. A longitudinal study. *Nephrol Dial Transplant*. 1995;10(12):2295-2305.
2. Shemin D, Bostom AG, Laliberty P, Dworkin LD. Residual renal function and mortality risk in hemodialysis patients. *Am J Kidney Dis*. 2001;38(1):85-90.

3. Termorshuizen F, Dekker FW, van Manen JG, et al. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. *J Am Soc Nephrol*. 2004;15(4):1061-1070.
4. Vilar E, Wellsted D, Chandna SM, Greenwood RN, Farrington K. Residual renal function improves outcome in incremental haemodialysis despite reduced dialysis dose. *Nephrol Dial Transplant*. 2009;24(8):2502-2510.
5. Obi Y, Rhee CM, Mathew AT, et al. Residual kidney function decline and mortality in incident hemodialysis patients. *J Am Soc Nephrol*. 2016;27(12):3758-3768.
6. Lee MJ, Park JT, Park KS, et al. Prognostic value of residual urine volume, GFR by 24-hour urine collection, and eGFR in patients receiving dialysis. *Clin J Am Soc Nephrol*. 2017;12(3):426-434.
7. Shafi T, Jaar BG, Plantinga LC, et al. Association of residual urine output with mortality, quality of life, and inflammation in incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. *Am J Kidney Dis*. 2010;56(2):348-358.
8. Drechsler C, de Mutsert R, Grootendorst DC, et al. Association of body mass index with decline in residual kidney function after initiation of dialysis. *Am J Kidney Dis*. 2009;53(6):1014-1023.
9. Jansen MA, Hart AA, Korevaar JC, et al. Predictors of the rate of decline of residual renal function in incident dialysis patients. *Kidney Int*. 2002;62(3):1046-1053.
10. Hecking M, Karaboyas A, Rayner H, et al. Dialysate sodium prescription and blood pressure in hemodialysis patients. *Am J Hypertens*. 2014;27(9):1160-1169.