RESEARCH LETTER

Diuretic Use Among Patients Receiving Hemodialysis in the United States

To the Editor:

Aspects of volume management, including larger interdialytic weight gains, higher ultrafiltration rates, and chronic hypervolemia, are associated with adverse outcomes among individuals with kidney failure who are dependent on hemodialysis.[1] Prescribing diuretics for volume control is a mainstay of advanced chronic kidney disease treatment and peritoneal dialysis care; however, diuretic use in hemodialysis practice is inconsistent.[2,3] Observational studies have shown that diuretic use (vs. nonuse) is associated with lower risks of intradialytic hypotension and hospitalization among people receiving hemodialysis; however, firm conclusions are limited by potential confounding from the benefits of residual kidney function among diuretic users.[4,5] A small prospective study suggests that diuretics can increase urine volume in patients producing as little as 100 mL of urine per day.[6]

Diuretic use in hemodialysis practice is common in many regions, and 45% of European and 48% of Japanese patients continue diuretics after hemodialysis initiation.[5] In contrast, diuretic use among US patients declines after dialysis initiation.[3] Uncertainty regarding the efficacy and optimal dosing of diuretics likely contributes to this variation in practice. We undertook this study to describe the use of oral diuretics among US patients receiving hemodialysis.

Using 2017 data from the US Renal Data System and a cross-sectional design, we identified adults receiving center-based maintenance hemodialysis on July 1, 2017, with continuous Medicare coverage during the preceding 180 days and excluded those with prior kidney transplants (Fig S1). We used Medicare Part D prescription drug claims to determine the diuretic use status and calculated the proportion of patients taking a diuretic, overall and by diuretic type, on July 1, 2017. Among patients taking a loop diuretic, we determined their daily furosemide-equivalent dose. In a secondary analysis, we linked the US Renal Data System cohort to the database of a large US

Table 1. USRDS cohort characteristics overall and by diuretic use status

Characteristic	Overall N = 176,448	Diuretic User n = 22,296	Diuretic Nonuser n = 154,152	Std Diff[a]
Age, y	64 ± 14	66 ± 13	63 ± 14	0.17
Female	80,412 (46%)	10,527 (47%)	69,885 (45%)	0.04
Race				
White	94,129 (53%)	14,464 (65%)	79,665 (52%)	0.27
Black	70,535 (40%)	6,316 (28%)	64,219 (42%)	0.28
Other	11,784 (7%)	1,516 (7%)	10,268 (7%)	0.01
Hispanic	29,132 (17%)	3,611 (16%)	25,521 (17%)	0.01
Cause of ESKD				
Diabetes	85,305 (48%)	12,879 (58%)	72,426 (47%)	0.22
Hypertension	54,492 (31%)	6,011 (27%)	48,481 (31%)	0.10
Glomerular disease	14,819 (8%)	1,318 (6%)	13,501 (9%)	0.11
Cystic disease	3,884 (2%)	378 (2%)	3,506 (2%)	0.04
Other	17,948 (10%)	1,710 (8%)	16,238 (11%)	0.10
Dialysis vintage				
<1.0 y	6,683 (4%)	1,530 (7%)	5,153 (3%)	0.16
1.0-2.9 y	52,797 (30%)	9,880 (44%)	42,917 (28%)	0.35
≥3.0 y	116,968 (66%)	10,886 (49%)	106,082 (69%)	0.42
Arrhythmia	47,894 (27%)	6,438 (29%)	41,456 (27%)	0.04
Conduction disorder	19,477 (11%)	2,629 (12%)	16,848 (11%)	0.03
Dyslipidemia	110,427 (63%)	15,739 (71%)	94,688 (61%)	0.19
Heart failure	70,904 (40%)	10,917 (49%)	59,987 (39%)	0.20
Hypertension	154,865 (88%)	20,392 (91%)	134,473 (87%)	0.14
Ischemic heart disease	75,581 (43%)	10,864 (49%)	64,717 (42%)	0.14
Peripheral arterial disease	57,666 (33%)	7,634 (34%)	50,032 (32%)	0.04
Stroke	34,309 (19%)	4,467 (20%)	29,842 (19%)	0.02
Valvular disease	34,703 (20%)	4,675 (21%)	30,028 (19%)	0.04
Asthma or COPD	46,932 (27%)	6,982 (31%)	39,950 (26%)	0.12
Liver disease	21,637 (12%)	2,638 (12%)	18,999 (12%)	0.02

Note: Values are displayed as count (%) for categorical variables and as mean ± standard deviation for continuous variables. Figure S2 displays percentages of patients receiving hemodialysis who were diuretic users across US regions. Table S2 displays characteristics of the USRDS cross-sectional cohort and the subset of patients treated at the large dialysis organization.

Abbreviations: COPD, chronic obstructive pulmonary disease; ESKD, end-stage kidney disease; Std Diff, standardized difference; USRDS, US Renal Data System.

[a]Absolute standardized differences comparing diuretic users to diuretic nonusers. A standardized difference of >0.10 represents an imbalance between groups.

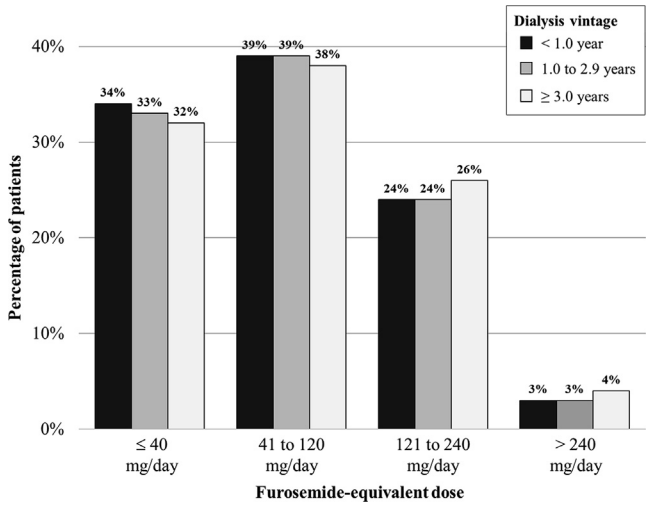

Figure 1. Furosemide-equivalent dosing among loop diuretic users stratified by dialysis vintage. Because percentages were rounded to the nearest whole number, the sum of the percentages within dialysis vintage categories may not add up to 100%.

dialysis organization and evaluated the frequency of 24-hour urine volume monitoring among diuretic users and nonusers. Item S1 reports the detailed methods.

Of 176,448 patients receiving hemodialysis who met the study criteria, 22,296 (13%) were taking a diuretic (Table 1). Overall, the study cohort was representative of the prevalent adult US population receiving hemodialysis.[2] Diuretic users (vs nonusers) were older, were newer to hemodialysis, were more likely to be White, and had a higher prevalence of cardiovascular conditions, including heart failure and hypertension. Among diuretic users, 90% were taking a loop diuretic, 8% were taking a thiazide or thiazide-like diuretic, 6% were taking a potassium-sparing diuretic, and <1% were taking a carbonic anhydrase inhibitor. Of the 20,097 loop diuretic users, 83% used furosemide, 9% used bumetanide, 7% used torsemide, and <1% used ethacrynic acid. Furosemide-equivalent dosing among loop diuretic users ranged from ≤20 mg/d (8%) to >320 mg/d (1%), and dosing did not differ by dialysis vintage (Fig 1). Only 28% of the loop diuretic users were taking doses of >80 mg of furosemide-equivalents per day. Moreover, the use of thiazide or thiazide-like diuretics and aldosterone antagonists without concomitant loop diuretic therapy was common (Table S1).

A total of 58,079 patients were in both the US Renal Data System and dialysis organization databases, including 6,659 (11%) diuretic users and 51,420 (89%) diuretic nonusers (Table S2). Overall, 3% of diuretic users and 2% of diuretic nonusers had a 24-hour urine volume measurement in the prior 180 days. The median urine volumes were 700 mL (interquartile range, 0-1,300 mL) and 200 mL (interquartile range, 0-1,000 mL) per 24 hours among diuretic users and nonusers, respectively. Among the 176 loop diuretic users with 24-hour urine volume measurements, urine volumes were similar regardless of dose; the median urine volumes were 700 mL (interquartile range, 100-1,200 mL) per 24 hours for patients taking ≤80 mg of furosemide-equivalents per day and 700 mL (interquartile range, 0-1,300 mL) per 24 hours for patients taking >80 mg of furosemide-equivalents per day.

Our analysis reveals substantial variation in diuretic use, dosing, and monitoring in the US hemodialysis practice. We found that diuretic dosing was particularly variable, with the majority of patients prescribed loop diuretics at furosemide-equivalent doses lower than what is recommended for patients with chronic kidney disease who are not dependent on dialysis.[7,8] In addition, 24-hour urine collections were strikingly infrequent, and measured urine volumes did not appear to correspond to dosing. Higher loop diuretic dosing is required to overcome physiologic changes related to kidney function decline, such as tubular resistance, impaired gastrointestinal absorption, and secondary hyperaldosteronism.[7] However, decreased kidney function impairs both renal and hepatic furosemide elimination pathways, prolonging the elimination half-life of furosemide.[9] Using too high of a loop diuretic dose can lead to tinnitus, ototoxicity, and other side effects. In addition, loop diuretics may compete for protein binding sites, increasing the risk of drug-drug interactions.[10] Such uncertainty regarding the risk-benefit balance of diuretic therapy in patients receiving hemodialysis likely, in part, underlies the observed variations in diuretic prescribing patterns.

This cross-sectional snapshot of diuretic use among US patients receiving hemodialysis reveals inconsistent and, in some cases, nonsensical prescribing patterns. Although clinicians may monitor urine output by means other than 24-hour urine collections, our findings also suggest the absence of a systematic approach to laboratory-based urine volume monitoring in hemodialysis care. Investigation of the efficacy, safety, and optimal dosing of diuretics in individuals with kidney failure who are dependent on hemodialysis is needed.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Flow diagram of study cohort creation.

Figure S2: Percentage of patients in the USRDS cross-sectional cohort using a diuretic by region of the U.S.

Item S1: Detailed methods.

Table S1: Combinations of diuretics used by patients in the USRDS cross-sectional cohort.

Table S2: Characteristics of the USRDS cross-sectional cohort and the subset of patients treated at the large dialysis organization.

ARTICLE INFORMATION

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