The Relationship Between Medication Discrepancies and Hospitalization Risk Among Patients With Advanced CKD

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Medication discrepancies are common in medicine, posing an ongoing threat to safe patient care. Discrepancies can be defined as any difference between the physician's records and the medications that the patient actually takes, including related dose and frequency. In clinical practice, medication discrepancies are common, occurring in 34% to 95% of patients newly admitted to hospitals.[1,2] The results of a systematic review indicated that 11% to 59% of discrepancies were clinically relevant,[3] and that 39% could potentially cause moderate to severe harm.[1]

We have previously reported that medication discrepancies are particularly common in patients with advanced chronic kidney disease (CKD; estimated glomerular filtration rate 0 to 30 ml/min per 1.73 m^2) not yet on dialysis, with 55% of patients having at least 1 discrepancy.[4] It is likely that mismatches between patients' medication use and the physician's record are more of a problem in chronic diseases. These patients are often treated with a large number of drugs[5] and are cared for by multiple physicians. This is certainly true in advanced CKD, in which care can become fragmented because of the large number of collaborating care providers and suboptimal communication.

The relationship between medication discrepancies and subsequent hospitalizations has been rarely studied in advanced CKD.[6] There are clear reasons to believe that such a relationship would exist. Patients with advanced CKD probably have a high rate of hospitalizations. Improper use of medications could lead to hospitalizations through adverse effects of misused drugs, medical complications, and diminution of anticipated efficacy. In the current study we have analyzed the relationship between the number medication discrepancies in advanced CKD and the risk for hospitalizations over up to a year of follow-up.

RESULTS

We enrolled 713 patients with stage 4 to 5 CKD into the baseline cohort, with characteristics displayed in Table 1. The population skewed toward older age, with 62.7% being >65 years. There was a minor underrepresentation of Hispanic patients; comprising only 9% of patients. The vast majority of patients were hypertensive and approximately 50% had diabetes mellitus. During the 1-year assessment period, 23 patients died and 33 patients reached end-stage renal disease. A further 5 patients were lost to follow-up.

A total of 392 patients (55.0% of the study population) had at least 1 medication discrepancy. The median number of discrepancies per patient (in patients with at least 1 discrepancy) was 2, (interquartile range, 1–4). A total of 646 patients (90.6%) had 0–5 discrepancies, 56 (7.8%) had 6–10 discrepancies, and 11 (1.5%) had more than 10 discrepancies. Types of discrepancies included patients taking a medication not on the nephrologist's list, patients not taking a medication on the nephrologist's list, different doses, and different dose frequencies. Medication classes with a greater number of discrepancies were cardiovascular, vitamins, bone and mineral disease agents, diuretics, analgesics, and diabetes medications.

The number of hospitalizations per patient ranged from 0–6, with a mean of 0.64 ± 0.96 (Table 2). The leading causes were cardiovascular (31%), infections (19%), other respiratory (16%), and gastrointestinal (9%). The number of hospitalizations within up to 1 year of follow-up was significantly and positively

Table 1. Patient characteristics at baseline

Variable	$N = 713$
Age, yr	
18–35	35 (4.9)
36–50	71 (10.0)
51–70	259 (36.3)
>70	348 (48.8)
Sex	
Female	310 (43.5)
Male	403 (56.5)
Race	
Asian	38 (5.3)
Black or African American	174 (24.4)
Other or multiracial	67 (9.4)
White	434 (60.9)
Ethnicity	
Hispanic	64 (9.0)
Non-Hispanic	649 (91.0)
Hypertension	
Yes	662 (92.8)
No	51 (7.2)
Diabetic	
Yes	364 (51.1)
No	349 (48.9)
Heart failure	
Yes	181 (25.4)
No	532 (74.6)
Smoker	
Yes	41 (5.8)
No	666 (93.4)
Not specified	6 (0.8)
Insurance group	
Medicaid	65 (9.1)
Medicare	443 (62.1)
Private	131 (18.4)
No insurance	74 (10.4)
Number of medication discrepancies	
0–5	646 (90.6)
6–10	56 (7.9)
>10	11 (1.5)
Estimated glomerular filtration rate (ml/min per 1.73 m^2)	
0–10	79 (11.1)
11–20	339 (47.5)
>20–30	295 (41.4)

Values are n (%).

Table 2. Distribution of the number of hospitalizations per patient

Number of hospitalizations per patient	Frequency	Percent
0	419	58.8
1	188	26.4
2	63	8.8
3	33	4.6
4	5	0.7
5	4	0.5
6	1	0.1

By multivariate analysis, after backward variable selection,[1] in the zero-inflation model, the only significant factor associated with being in the group of no hospitalization in 1 year was the number of medication discrepancies (odds ratio, 0.59; 95% confidence interval [CI], 0.43–0.82; $P = 0.0016$) (Table 4). Stated otherwise, if the number of medication discrepancies increased by 1, the patient would be less likely to have no 1-year hospitalizations (the odds of having no 1-year hospitalizations would decrease by 41%). In the count model, among patients who had at least one 1-year hospitalization, the number of medication discrepancies was significantly associated with hospitalization risk. For each additional discrepancy there was an increase in the rate of 1-year hospitalizations by 9% (rate ratio [RR], 1.09; 95% CI, 1.06–1.13; $P = 0.0003$). Other factors significantly associated with the number of hospitalizations in 1 year were age, reduced estimated glomerular filtration rate, and a diagnosis of diabetes. Specifically, with age being increased by 1 year, the expected rate of 1-year hospitalizations increases by 1% (RR, 1.01; 95% CI, 1.00–1.02; $P = 0.0028$). For estimated glomerular filtration rate being increased by 1 ml/min per 1.73 m^2, the expected rate of 1-year hospitalization decreases by 2% (RR, 0.98; 95% CI, 0.97–0.99; $P = 0.0107$). Patients with diabetes had increased rate of 1-year hospitalization of 40% (RR, 1.40; 95% CI, 1.15–1.72; $P = 0.001$). The number of medications patients took was a predictor of hospitalizations by simple analysis but not by multivariate analysis because it was highly correlated to the number of medication discrepancies ($r = 0.71$, $P = 0.0001$).

DISCUSSION

We found a strong and independent association between the number of medication discrepancies and subsequent 1-year risk for hospitalizations among patients with advanced CKD. Other significant risk factors for hospitalization included older age, lower estimated glomerular filtration rate, and a diagnosis of diabetes mellitus. These latter risk factors have been previously reported on. A previous study by Tuttle et al.[6] found a large number of medication problems after hospital discharge in CKD. In contrast to their findings of patients after a

associated with the number of medication discrepancies. With 0–5 discrepancies, the mean number of hospitalizations was 0.55 ± 0.88, from 6–10 discrepancies the mean increased to 1.34 ± 1.13, and for >10 discrepancies the mean was 2.18 ± 1.60, $P = 0.0001$. In comparing patients with no discrepancies with other patients, we found a significantly reduced rate of 1-year hospitalizations (0.4 ± 0.7 vs. 0.8 ± 1.1, $P < 0.0001$). Other patient characteristics that were significantly associated with the number of hospitalizations were increasing patient age, white race, diagnosis of diabetes mellitus, insurance by Medicare or no insurance, and increasing number of medications (Table 3).

Table 3. Mean number of hospitalizations based on patient characteristics

Variable	Hospitalizations within 1 year, mean (SD)	P value
Age (yr)		0.018
18–35	0.37 (0.55)	
36–50	0.44 (0.77)	
51–70	0.64 (1.05)	
>70	0.71 (0.94)	
Sex		0.95
Female	0.64 (0.97)	
Male	0.64 (0.95)	
Race		0.02
Asian	0.55 (1.08)	
Black or African American	0.50 (0.89)	
Other or multiracial	0.66 (1.07)	
White	0.70 (0.95)	
Ethnicity		0.95
Hispanic	0.58 (0.79)	
Non-Hispanic	0.65 (0.97)	
Hypertension		0.052
Yes	0.66 (0.96)	
No	0.43 (0.90)	
Diabetic		0.002
Yes	0.76 (1.03)	
No	0.52 (0.86)	
Heart failure		0.144
Yes	0.70 (0.94)	
No	0.62 (0.96)	
Smoker		0.443
Yes	0.41 (0.63)	
No	0.66 (0.97)	
Not specified	0.50 (0.84)	
Insurance group		0.004
Medicaid	0.37 (0.72)	
Medicare	0.65 (0.97)	
Private	0.57 (0.89)	
No insurance	0.93 (1.10)	
Number of medication discrepancies		0.0001
0–5	0.55 (0.88)	
6–10	1.34 (1.13)	
>10	2.18 (1.60)	
Estimated glomerular filtration rate (ml/min per 1.73 m^2)		0.288
0–10	0.66 (1.04)	
11–20	0.72 (1.06)	
>20	0.55 (0.80)	
Number of medications		0.0001
0–5	0.47 (0.80)	
6–10	0.56 (0.91)	
>10	1.18 (1.16)	

Table 4. Multivariable analysis for 1-year hospitalizations

Zero-inflation model

Variables	Odds ratio (95% confidence interval)	P value
Number of medication discrepancies	0.59 (0.43–0.82)	0.0016

Count model

Variables	Rate ratio (95% confidence interval)	P value
Age	1.01 (1.00–1.02)	0.0028
Glomerular filtration rate	0.98 (0.96–0.99)	0.0040
Diabetic (yes vs. no)	1.36 (1.11–1.68)	0.0036
Number of medication discrepancies	1.09 (1.05–1.13)	0.0003
Number of medications	1.01 (0.99–1.03)	0.6418

Other factors include medication changes made by multiple doctors involved in care that might now have been communicated to the nephrologist.

Medication discrepancies have the potential to lead to patient harm through failure to achieve efficacy, adverse events, and unanticipated drug interactions. In a recent study, 17.1% of medication discrepancies were considered to be serious or potentially life-threatening.[7] To the extent that medication discrepancies can diminish efficacy or increase risk, then it is reasonable to consider a hypothesis that they could be associated with, or a direct cause for, some hospitalizations. Our finding that the 2 were strongly and independently associated lends credence to the hypothesis. As for any association, there cannot be an assertion of causality. Despite multivariate testing, residual confounding is always a risk.

In the care of patients with advanced CKD, nephrologists play a central role in medication management. Decreased renal excretion affects pharmacokinetics and risk profile of prescribed drugs. This, combined with polypharmacy, inadequate communication between care providers, suboptimal electronic health records, and the effect of frequent hospitalizations all act to create a highly fraught process. Our finding that the greater the number of medication discrepancies associates strongly with hospitalization risk implies a need for more comprehensive management, rigorous medication review and reconciliation, and improved medical informatics linking care providers, pharmacies, hospitals, and insurance companies.[8]

Strengths of the current study include the number of patients studied, the extensive data available to the investigators, and the very comprehensive nursing medication review. Limitations include the retrospective nature of the analysis, which limits the ability to query for certain additional data points. For example, we do not have data on how the nephrologists maintained their electronic medication lists or how patients used information on over-the-counter medications. A potential limitation might be the process for

hospital discharge, our study was focused on apparently stable patients with CKD.

Medication discrepancies are a reflection of a number of different factors that complicate medication management in chronically ill patients. In a previous study,[4] we found a diagnosis of heart failure, white race, hypertension, and the number of medications to be associated with increased number of discrepancies.

ascertainment of hospitalizations. However, in contrast to large database epidemiology studies, this direct methodology probably had a greater sensitivity to find hospitalizations and extract meaningful data.

In conclusion, we found a strong and independent relationship between number of medication discrepancies and risk for subsequent 1-year hospitalizations in advanced CKD. This relationship could have important clinical implications. Further study of interventions to improve medication review and reconciliation in advanced CKD would be particularly helpful.

DISCLOSURE

All the authors declared no competing interests.

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The Psychosocial Impact of a Diagnosis of Hypertension in Pediatric Patients

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The most recent US Preventive Services Task Force statement on hypertension (HTN) screening in the pediatric population states that "current evidence is insufficient to assess the balance of benefits and harms," and suggests that blood pressure (BP) screening should not be routine practice in asymptomatic children.[1] The recommendation was based on inadequate evidence that routine screening in children is sufficiently accurate, that it identifies those who will have HTN or cardiovascular disease in adulthood, and the absence of studies documenting that treatment of HTN in childhood reduces cardiovascular morbidity and mortality later in life. The US Preventive Services Task Force found minimal evidence to assess potential harms of routine BP screening, citing a single investigation of adverse effects of diagnosing children with HTN by measuring school absence rates.[2]

In contrast, the American Academy of Pediatrics and the American Heart Association recommend, based on Grade C evidence, measuring BP annually beginning at age 3 years in healthy children and adolescents without risk factors for HTN (e.g., family history, obesity, kidney disease, vascular anomalies, or use of medications that increase BP).[3] There is no mention of the