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Original Study

Determining the Incidence of Drug-Associated Acute Kidney Injury in Nursing Home Residents

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A B S T R A C T

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Objective: Although acute kidney injury (AKI) is well studied in the acute care setting, investigation of AKI in the nursing home (NH) setting is virtually nonexistent. The goal of this study was to determine the incidence of drug-associated AKI using the RIFLE (Risk, Injury, Failure, Loss of kidney function, or End-Stage kidney disease) criteria in NH residents.

Design/Setting/Participants/Measurements: We conducted a retrospective study between February 9, 2012, and February 8, 2013, for all residents at 4 UPMC NHs located in southwest Pennsylvania. The TheraDoc™ Clinical Surveillance Software System, which monitors laboratory and medication data and fires alerts when patients have a sufficient increase in serum creatinine, was used for automated case detection. An increase in serum creatinine in the presence of an active medication order identified to potentially cause AKI triggered an alert, and drug-associated AKI was staged according to the RIFLE criteria. Data were analyzed by frequency and distribution of alert type by risk, injury, and failure.

Results: Of the 249 residents who had a drug-associated AKI alert fire, 170 (68.3%) were women, and the mean age was 74.2 years. Using the total number of alerts ($n = 668$), the rate of drug-associated AKI was 0.35 events per 100 resident-months. Based on the RIFLE criteria, there were 191, 70, and 44 residents who were classified as AKI risk, injury, and failure, respectively. The most common medication classes included in the AKI alerts were diuretics, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEIs/ARBs), and antibiotics.

Conclusion: Drug-associated AKI was a common cause of potential adverse drug events. The vast majority of cases were related to the use of diuretics, ACEIs/ARBs, and antibiotics. Future studies are needed to better understand patient, provider, and facility risk factors, as well as strategies to enhance the detection and management of drug-associated AKI in the NH.

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Acute kidney injury (AKI) is defined as the rapid loss of kidney function, occurring over hours or days and resulting in the accumulation of metabolic waste products and the dysregulation of

extracellular volume and electrolyte homeostasis.¹ AKI is diagnosed on the basis of clinical history and laboratory data, as measured by serum creatinine (SCr), or based on a rapid reduction in urine

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output.² The 3 main types of AKI are prerenal, intrinsic, and postrenal, and drugs can cause each type.¹ There had not been a standardized definition of AKI until the Risk, Injury, Failure, Loss of kidney function, or End-stage kidney disease (RIFLE) criteria were proposed for its diagnosis by the Acute Dialysis Quality Initiative group.³

The RIFLE criteria for diagnosis and staging of AKI have been widely validated.⁴ Indeed, multiple studies have demonstrated a significant association between the RIFLE criteria and important clinical outcomes, such as morbidity (eg, hospitalization) and mortality across patient care settings.^{5–9} Furthermore, existing evidence supports the predictive validity of the RIFLE criteria to identify groups of hospitalized patients with increased risk of the need for renal replacement therapy and/or death.^{5–9} There is now emerging evidence of the long-term risks associated with AKI (even after apparent resolution), including the development of cardiovascular disease, chronic kidney disease, and death.^{10–12} Thus, early recognition and management of AKI is critical to prevent morbidity and mortality.

Although AKI is well studied in the acute care setting, investigation of AKI in the nursing home (NH) setting is virtually nonexistent even though NH residents are at high risk of developing AKI. First, NH residents (given their older demographics) have a number of cellular, structural, functional, and hemodynamic changes in the kidney. These changes contribute to a gradual decrease in renal function, and estimates suggest that 50% of NH residents have chronic kidney disease, placing them at high risk for AKI.^{13,14} Second, older NH residents have a higher incidence of hypertension, diabetes mellitus, atherosclerosis, and heart failure, which increases the risk of developing AKI. Third, older NH residents have high rates of polypharmacy, as a direct result of treating multiple comorbidities. Polypharmacy may expose NH residents to potentially nephrotoxic medications and drug-drug interactions, which can increase the risk of developing AKI.¹⁵

To the best of our knowledge, no prior studies have examined drug-associated AKI in the NH setting. In this article, we present a retrospective analysis of drug-associated AKI alerts detected by the TheraDoc™ Clinical Surveillance Software System (Hospira, Inc, Lake Forest, IL), which monitors laboratory and medication data and fires alerts when patients have a sufficient increase in SCr as determined by the RIFLE criteria. The data presented here were collected in advance of a cluster randomized controlled trial funded by the Agency for Healthcare Research and Quality (AHRQ). The primary goal of the AHRQ-funded study is to determine the impact of a multicomponent intervention carried out by consultant pharmacists on the detection and management of adverse drug events (ADEs) in the NH setting.¹⁶ As an initial set of steps to improve early recognition and management of AKI, determine the consultant pharmacist resources needed, and enhance the understanding of its epidemiology, we sought to determine the incidence of drug-associated AKI by using the RIFLE criteria in NH residents.

Methods

Study Design

We conducted our study within UPMC Senior Communities, which is the largest long-term care organization in southwestern Pennsylvania, as well as the largest nationally that is part of an integrated health care delivery system. UPMC Senior Communities has approximately 2500 beds, of which 752 are located in the NH setting. There are 6 UPMC NHs, all of which are nonprofit, academically affiliated, and not part of a national chain. Four of the 6 NHs (2 urban and 2 suburban) have the same health information technology infrastructure and were included in the study. The number of beds in

these NHs ranged from 50 to 179. We assessed all residents in the 4 NHs between February 9, 2012, and February 8, 2013. This study was approved by the University of Pittsburgh Institutional Review Board. Ethics approval was provided by the University of Pittsburgh.

Detection of Drug-Associated AKI

We used the SCr part of the RIFLE criteria to operationally define AKI into risk, injury, or failure. *Risk* was defined as an increase in SCr of 1.5 times from baseline, *injury* as a doubling of SCr from baseline, and *failure* as a tripling of SCr from baseline, or a SCr > 4 mg/dL with an acute rise >0.5 mg/dL. Similar to other studies that have assessed AKI, we defined the baseline SCr as the lowest value (nadir SCr) that was recorded for the patient in the preceding year (including the current NH admission).^{17–19} No additional indices (eg, urine sodium or fractional excretion of sodium) were drawn to determine the underlying type of AKI.

In addition to the RIFLE criteria, the patient had to be concurrently prescribed at least one medication that has been reported in the literature to be associated with AKI. The development of the knowledge base of medications associated with AKI and used for this determination has been previously described.^{20,21} Briefly, by using a validated approach, a list of potentially causative medications was reviewed, edited, and agreed on by an expert panel consisting of 2 clinical pharmacist/pharmacoepidemiology researchers, 2 geriatric clinical pharmacists, and a geriatrician (see [Appendix 1](#) for medications associated with AKI).

We used the TheraDoc™ Clinical Surveillance Software System, which is licensed for use in the UPMC System, including the 4 participating NHs, to automate the detection of drug-associated AKI. The TheraDoc™ system integrates data from several disparate information source systems used by the select NHs, including admission/discharge/transfer, pharmacy, and laboratory. These data are integrated in real time, so that they appear in TheraDoc™ within seconds of being entered into the source system. After consensus was reached on rule parameters, the AKI detection rule was developed by TheraDoc™ programmers with oversight by our investigative team. A sample drug-associated AKI alert can be seen in [Figure 1](#).

Data Cleaning and Analysis

To analyze the included AKI alerts, a series of exclusionary steps were taken ([Figure 2](#)). The final dataset included 668 drug-associated AKI alerts involving 249 unique individuals. Descriptive statistics (means, SDs, frequencies) were used to summarize all variables for the sample, including the frequency and distribution of alert type by risk, injury, and failure. We characterized the number of unique residents, their gender, age, and baseline SCr. We also calculated the frequency of medication classes associated with the drug-associated AKI alerts, and further categorized the medication classes by AKI alert type. All analyses were conducted using SAS version 9.2 (SAS Institute, Inc, Cary, NC).

Results

Of the 249 residents who had a drug-associated AKI alert fire, 170 (68.3%) were women, and the mean $\pm$ SD age was 74.2 ± 14.0 years. The baseline SCr was 0.90 ± 0.64 mg/dL. During the study period, there were a total of 1475 admissions, providing 188,426 resident-days with an average length of stay of 75 days. The average length of stay for each of the 4 individual NHs was 69, 90, 92, and 120 days.

Using the total number of alerts ($n = 668$), the rate of drug-associated AKI among these residents was 0.35 cases per 100

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