NARRATIVE REVIEW

CKD as an Underrecognized Threat to Patient Safety

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Chronic kidney disease (CKD) is common, but underrecognized, in patients in the health care system, where improving patient safety is a high priority. Poor disease recognition and several other features of CKD make it a high-risk condition for adverse safety events. In this review, we discuss the unique attributes of CKD that make it a high-risk condition for patient safety mishaps. We point out that adverse safety events in this disease have the potential to contribute to disease progression; namely, accelerated loss of kidney function and increased incidence of end-stage renal disease. We also propose a framework in which to consider patient safety in CKD, highlighting the need for disease-specific safety indicators that reflect unsafe practices in the treatment of this disease. Finally, we discuss the hypothesis that increased recognition of CKD will reduce disease-specific safety events and in this way decrease the likelihood of adverse outcomes, including an accelerated rate of kidney function loss and increased incidence of end-stage renal disease.

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INDEX WORDS: Patient safety; chronic kidney disease; disease recognition; medical errors.

Patient safety has been identified as a high-priority area for improvement in health care. In 1999, the Institute of Medicine issued a report entitled "To Err Is Human: Building a Safer Health System" that included the widely cited statistic that 44,000 to 98,000 in-hospital deaths occurring each year were caused by medical errors.[1] The Agency for Healthcare Research and Quality (AHRQ) has taken the lead in guiding efforts in improvement of patient safety and reducing medical errors.[2-5] However, despite their efforts, these improvements have been slow in coming across the health system.[6] Definitions of safety incidents vary, and in an effort to apply standards in measurement of patient safety across hospitals and health systems, the AHRQ established a set of patient safety indicators (PSIs).[2] Using these PSIs, several investigators have identified variations in patient safety events across hospitals,[7,8] by payer status,[9] and with varying demographic factors, including race and ethnicity.[10]

Despite the acceptance of the AHRQ PSIs as a set of tools to evaluate patient safety, these measures have many shortcomings.[11] First, the AHRQ PSIs capture only a portion of the type of events that might be included in the domain of patient safety. Others use alternative definitions of patient safety and place a greater emphasis on medication errors,[12] which are absent from the AHRQ PSIs. Moreover, the AHRQ PSIs optimally are used to evaluate in-hospital incidents, which are only a subset of all patient safety events. Also, the AHRQ PSIs generally have low incidence rates in the hospital population and often require large sample surveys to assess trends and test hypotheses. This could occur partly because the AHRQ PSIs are heavily weighted to surgical and obstetric misadventures. However, it is plausible and likely that the majority of patient safety problems are in the growing population of Americans who have chronic medical ailments, including chronic kidney disease (CKD).

In this review, we discuss the various aspects of CKD that make it a uniquely high-risk condition for both general and disease-specific adverse safety events. We assert that new efforts are needed to formally define PSIs that are specific to CKD and derived from the unique disease attributes described. We propose the use of the

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Donabedian structure-process-outcome paradigm as a foundation for the consideration of disease-specific patient safety in CKD.[11,13] We also discuss the potential role of increased disease recognition as a key structural intervention necessary to reduce the incidence of CKD-specific safety events and in turn reduce the incidence of adverse disease outcomes, including hastened kidney function loss and incidence of end-stage renal disease (ESRD).

CKD IS A HIGH-RISK CONDITION FOR ADVERSE SAFETY EVENTS

CKD is becoming increasingly prevalent in the United States,[14,15] and with its complexity and preponderance of comorbidities, this disease often requires frequent hospitalizations and prolonged length of hospital stay and has an increased cost of care.[16-18] The diagnosis of CKD frequently is underrecognized,[19-21] and the failure to recognize CKD in patients who are frequent users of the health system is a lost opportunity to initiate recommended treatments for the disease and minimize threats to patient safety.

In a national cohort of veterans receiving care at the Veterans' Health Administration with at least 1 hospitalization during fiscal year 2004 to 2005 and an outpatient creatinine level for determination of estimated glomerular filtration rate, we examined whether CKD was a risk factor for the incidence of AHRQ-established PSIs. We showed that CKD was a significant risk factor for several AHRQ PSIs and showed a stepwise increase in risk of a composite of all PSIs with decreasing kidney function. We concluded that CKD was a risk factor for the general AHRQ-derived PSIs, but noted that these indicators tended to be uncommon in a general population and did not have a high degree of relevance in patients with a chronic medical condition, such as CKD. It was clear from the study that a set of disease-specific safety indicators were needed for CKD.[22]

Manifestations of CKD that relate to patient safety can range from sequelae of the disease that are improperly managed to consequences of misguided therapeutic interventions used in this highly comorbid disease population and are listed in Box 1. Many of these are not mutually exclusive and have the potential to relate to others on the list. These clinical events are not included in the AHRQ-derived set of PSIs, but comprise the basis for a disease-specific set of safety events in patients with CKD. Although there is a substantial body of literature describing these events, there has been minimal consideration of them within the context of patient safety or the extent to which they fit on the spectrum, ranging from inadequately managed disease sequelae to unanticipated iatrogenic complications of a treatment or intervention.

Box 1. Features of Chronic Kidney Disease and Its Management That Relate to Patient Safety

1. Medication errors[23-26]
   a. Improper dosing
   b. Inappropriate prescription
   c. Inadequate monitoring
2. Hyperkalemia[27,28]
3. Hypoglycemia[29,30]
4. Other electrolyte intoxication
   a. Hypermagnesemia[31,32]
   b. Hyperphosphatemia[33]
5. Diagnostic testing
   a. Iodinated contrast[34,35]
   b. Gadolinium[36]
6. Cardiovascular disease
   a. Missed diagnoses[37]
   b. Improper management (hemorrhage, restenosis)[38,39]
7. Fluid, RAAS blocker, diuretic mismanagement[40-42]
   a. Hypotension
   b. Azotemia
   c. CHF exacerbation
8. Acute kidney injury[43-45]
9. Miscellaneous
   a. Hip fracture[46]
   b. Deep vein thrombosis[47]
   c. Multiresistant bacterial infection[48]

Abbreviations: CHF, congestive heart failure; RAAS, renin-angiotensin-aldosterone system.

ADVERSE SAFETY OUTCOME IN CKD: ACCELERATION OF KIDNEY FUNCTION LOSS

A patient safety event typically is defined as an unintended incident that usually results in a hospitalization, prolonged length of hospital stay, unexpected injury, or death. With CKD, the unintended consequences of a patient safety event must be broadened to include progression of disease. The rate of kidney function decrease associated with CKD is variable. The most sig-

nificant risk factors include proteinuria, uncontrolled hypertension, and lack of diabetes control. Although beneficial therapies are available, such as renin-angiotensin-aldosterone system blockers, these are limited in their ability to successfully arrest kidney disease progression in most patients. With the absence of curative therapies, an important tactic to slow progression in patients with CKD is to minimize nephrotoxic exposures, which may accelerate the rate of kidney function loss. The National Kidney Foundation's Kidney Disease Outcome Quality Initiative (KDOQI) Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification, places emphasis on practices to be avoided because they confer unreasonable risks to patients with CKD.[49] Guidelines 2 and 13 of that report discuss minimizing exposure to medications that contribute to disease progression and identifying several potential factors that might lead to acute episodes of kidney injury and contribute to the net loss of kidney function over time. Figure 1 shows the clinical course of a theoretical, but typical, patient with CKD who has been subject to such exposures. These common exposures have the potential to accelerate disease beyond the baseline rate of kidney function decay. The importance of identifying these safety events is emphasized because they are often preventable. The identification and prevention of CKD-related safety events offer an opportunity to reduce the adverse outcomes associated with CKD, namely, the accelerated decrease in kidney function and the incidence of ESRD.

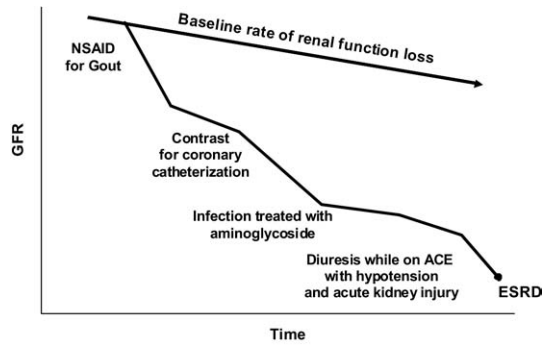

Figure 1. A theoretical patient with chronic kidney disease is subject to several events that might be classified as preventable and related to patient safety. These events contribute to an accelerated rate of kidney function decay. Abbreviations: ACE, angiotensin-converting enzyme (inhibitor); ESRD, end-stage renal disease; GFR, glomerular filtration rate; NSAID, nonsteroidal anti-inflammatory drug.

ESTABLISHING A ROBUST FRAMEWORK TO SURVEY PATIENT SAFETY IN CKD

Given the shortcomings of the current tools to evaluate patient safety, investigators at the AHRQ have proposed a framework for future efforts in this area and targeted at different populations.[13] This framework is basic in its elements, but intended to be acceptable across multiple disease domains and flexible in its ability to incorporate the disparate types of events that can fit into the rubric of patient safety. The conceptual scheme is based on the Donabedian[13] classic structure-process-outcome model of quality measures.[4] Figure 2 offers a schematic showing how the Donabedian model can be applied to the unique circumstances of CKD. As outlined next, important steps are necessary to tailor the Donabedian model to address patient safety in CKD.

Structural Measures

Structural measures include dimensions of infrastructure, process, or systems that contribute to the environment that affects patient safety. These are not directly attributable to individuals or care providers, although structural conditions may create circumstances that have the potential to lead to unintended consequences for a patient or an error by a provider. The pivotal structural aspect of the health care system that is likely to contribute to patient safety in CKD is lack of disease recognition. This includes the absence of cues that alert providers to the unique specifications for care in a patient with CKD. As described, it is well documented that the majority of patients with CKD and their associated impaired kidney function often are not recognized. Improving disease recognition might reduce medical errors; however, overcoming the problem of poor disease recognition may be more challenging than first realized given the broad environment in which CKD patients dwell. As shown in Fig 2, patients with CKD may encounter health agents and receive interventions in a wide variety of venues, including the hospital, clinic, pharmacy, nursing home, ambulance, or medicine cabinet. Therefore, strategies to increase disease recognition must attempt to go

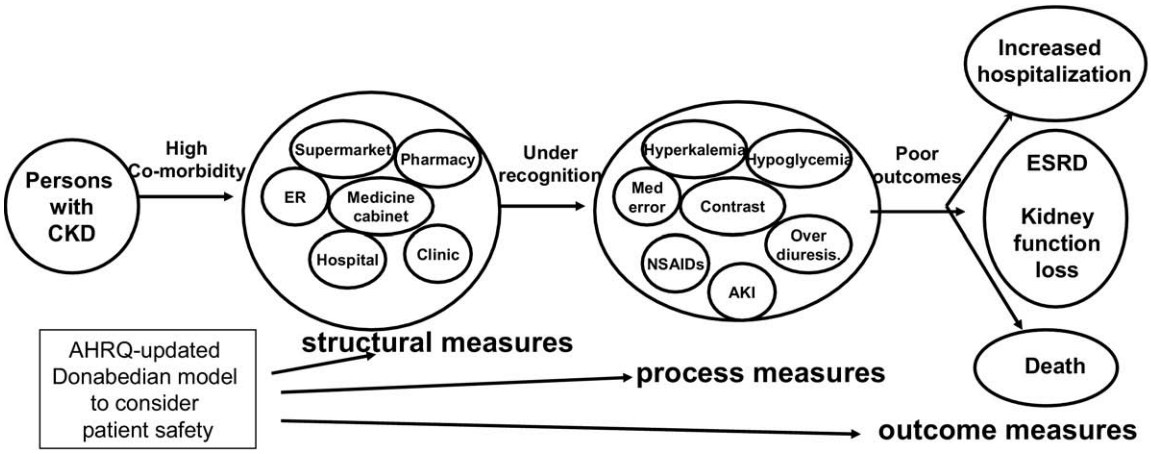

Figure 2. The Donabedian structure-process-outcome framework[13] applied to the chronic kidney disease (CKD) model. The model proposes a causal link between the disease-specific structural deficit of poor disease recognition and adverse disease outcomes, mediated through several candidate disease-specific safety measures. Abbreviations: AHRQ, Agency for Healthcare Research and Quality; AKI, acute kidney injury; ER, emergency room; ESRD, end-stage renal disease; NSAID, nonsteroidal anti-inflammatory drug.

beyond those center-based systems already established to improve disease recognition.

Process Measures

Process measures include practices, lifestyles, interventions, or treatments that are ill advised, improper, misused, overused, or omitted. These actions may be implemented by providers or patients and include medication errors or unsafe medical practices. However, classification of a medical action as related to safety is based on the clinical context. For example, a treatment may be indicated for one disease state, but not be appropriate for another. Moreover, what makes a practice or treatment unsafe or use of a medication an error is not necessarily based on the occurrence of an unintended (iatrogenic) event, but rather the potential for such an occurrence. The unique aspects of CKD described previously lead to a condition with the rich potential for unsafe practices, injudicious treatments, and medical errors. The byproducts of such actions can include serious adverse outcomes. Although candidate safety measures are listed in Box 1 and shown in Fig 2, a validated list of such CKD-specific patient safety process measures has not been established. A prerequisite to any intervention related to safety will be the consensus acceptance of a set of such safety indicators specific to CKD. However, any patient safety indicator specific to CKD must meet certain criteria to be useful. The safety indicators must be relatively common, substantiating their significance as a health problem. They must be relevant to the disease process, with a link to adverse outcomes that are significant in the disease. Finally, and perhaps most importantly, the safety measure must be preventable.

Outcome Measures

Outcome measures include adverse safety events and the realization of the potential consequences of high-risk structural and process measures. These would include a medical injury, manifest toxicity from a medication error, iatrogenic illness, nosocomial infections, disease progression related to an inappropriate medical action, and death related to medical treatment or accident. It is well known that patients with CKD are at increased risk of adverse disease outcomes, including loss of kidney function, ESRD, hospitalization, and death. However, it is not known to what extent these adverse outcomes are related to patient safety events. Confirmation of a relationship between safety process measures and disease-specific outcomes, as shown in Fig 2, is critical because prevention of the former may have a significant role in reducing the incidence of the latter.

IMPROVING CKD-SPECIFIC PATIENT SAFETY: A NEW APPROACH TO SLOWING DISEASE PROGRESSION

Establishing an association between CKD recognition and patient safety is an important first step to developing new approaches to treating this disease, for which added emphasis is placed on health services in addition to the use of medical therapies. With a clear definition of CKD-specific safety indicators developed within the structure-process-outcome paradigm outline shown in Fig 2, investigators can move forward with studies and demonstration projects designed to improve patient safety and assess the extent to which this reduces adverse disease outcomes. Such efforts should include interventions intended to alter the key structural deficiency affecting patients with CKD: poor disease recognition. Previous work has shown the benefit in reducing medication errors of computer-based systems that alert providers to impaired kidney function when prescribing in-hospital medications.[23,50] However, efforts to increase the recognition of CKD does not necessarily ensure that appropriate therapy is given.[51-53] The most recent surveys of practice patterns in large practice or health network settings have shown either persistent shortfalls in recognition of moderate CKD or marginal improvement in adherence to consensus-based practice guidelines for CKD.[54,55] Moreover, innovative strategies that transmit alerts about the condition of a patient with CKD across all dimensions of the health care landscape are required because many of the exposures that relate to patient safety are present not only in the hospital, but also in the community and home.

Although efforts to increase recognition of CKD across a patient's domain may be a challenge, there are still opportunities to improve patient safety in this disease population, which is frequently hospitalized. The preponderance of cardiovascular disease (CVD) in patients with CKD who present to the hospital represents a target for efforts to reduce safety-related adverse events. Several aspects of prudent CVD management, when implemented in patients with CKD, may lead to preventable adverse safety events. Exposure to iodinated contrast agents with coronary catheterization can lead to acute kidney injury.[34,35] However, kidney-sparing tactics can be used as means to reduce acute episodes of kidney function loss in patients with CKD and a clear indication for coronary catheterization.[56,57] Additionally, patients with CKD often present with atypical cardiac symptoms, which may mislead providers away from indicated CVD treatments, but with increased awareness of the atypical manifestations of CVD in patients with CKD, adverse outcomes may be prevented.[37] Moreover, patients with recognized coronary artery disease are often treated with thrombolysis, percutaneous angioplasty, or stents, which may lead to iatrogenic safety events in patients with CKD, such as early restenosis or hemorrhage, which can be minimized with attention to the high rate of complications in patients with CKD.[38,39]

The hospital setting is also a place for frequent misuse of medications, including those that contribute to accelerated loss of kidney function or other complications. Increased recognition of CKD would be an effective means to ensure avoidance of nonsteroidal anti-inflammatory drugs, aminoglycosides, or other agents that are ill advised in patients with this disease.[24,25] Additionally, patients might receive electrolyte-based preparations that are poorly handled in patients with CKD, such as magnesium-containing antacids or laxatives[32] or phosphate-containing purgatives.[33] Many hospitals have computer-based alerts to guide proper use of drugs in the setting of CKD, and these have been shown to be an effective means to reduce medical errors.[23,50] Alternatively, the pharmacist may have a key role in team rounds to ensure proper use of drugs in hospitalized patients who might have CKD.[58] This is especially helpful for physicians who have a significant challenge in accessing critical information on a broad set of disease processes, such as CKD, that are active in the complex hospitalized patient.[59] However, the effectiveness of these interventions is predicated on screening for CKD, which may not necessarily be universal in hospitalized patients.

Another potential source of CKD-specific safety events in hospitalized patients is the undermanaged patient with congestive heart failure who receives diuretics or treatment with a renin-angiotensin-aldosterone system blocker. Patients who have unrecognized CKD and who receive such treatment are at high risk of symptomatic

hypotension, azotemia, or acute kidney injury.[41,42] Recognition of impaired kidney function and appropriate longitudinal management by either the primary provider or an appropriate nephrology consultant may avert many of these safety events, which often contribute to accelerated loss of kidney function.

Because patients with CKD are at risk of safety events in many settings, not the least of which is the hospital, it is unclear how to increase recognition of CKD beyond the boundaries of the hospital. Certainly hospitalized patients are a captive audience and can be provided with increased education to enhance their understanding of the relationship between recognition of CKD and patient safety events. Educated patients are the most committed stakeholders in their own medical care and can carry this message to other encounters out of the hospital and in this way have a role in improving their safety.

Interventions that increase CKD recognition may have an important role in reducing patient safety events and, in turn, alter disease progression and reduce the incidence of ESRD. Although there is good reason to consider CKD as an important disease modifier in the realm of patient safety, there also is likely to be a unique and perhaps pivotal role of patient safety and medical errors in the epidemic of kidney disease. The best expectation of current therapies for this disease is slowing the rate of kidney function loss in most patients. Additional interventions, such as those directed at patient safety, that provide incremental benefit in treatment should be considered and sought out. Improving patient safety in CKD may offer an important opportunity to alter the progression of disease in a significant portion of the affected population and in this way reduce the incidence of ESRD.

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