Too Many for Too Few: Finding Appropriate Nephrology Referrals for Patients With CKD That Optimize Outcomes

Chi D. Chu, Julio A. Lamprea-Montealegre, and Michelle M. Estrella

Kidney failure is a dire consequence of chronic kidney disease (CKD) progression and leads to substantial morbidity, mortality, and health care costs. Prompt referral to nephrology care is associated with improved clinical outcomes among patients with CKD. However, the severe shortage in the nephrology workforce precludes evaluation of all patients with CKD by a nephrologist. Thus, clinical guidelines recommend nephrology referral based on clinical criteria that primarily focus on advanced CKD stages. However, these criteria may still identify too many patients relative to the nephrology workforce. An alternative is to use risk prediction tools to guide referral based on patients’ risks for CKD progression. The Kidney Failure Risk Equation (KFRE) is based on 4 variables—age, sex, urinary albumin-creatinine ratio, and estimated glomerular filtration rate (eGFR)—and has been widely validated to predict 2- and 5-year risks of kidney failure among patients with CKD. However, its potential value in guiding nephrology referrals and impact on patient volumes and referral patterns have not been well established.

In this issue of AJKD, Duggal et al contrast the number of patients identified for referral using the VA/Department of Defense CKD clinical guidelines versus KFRE risk thresholds in a sample of nearly 400,000 patients with CKD in the VA Health Care System. A total of 66,276 patients met at least one laboratory criterion for nephrology referral, which included an eGFR <30 mL/min/1.73 m², severe albuminuria or proteinuria, or an eGFR decrease >5 mL/min/1.73 m² per year. The use of a 2-year KFRE risk ≥1% to guide referrals identified a similar number of patients, but these patients had a higher median KFRE risk (2.3%) than the patients who met the laboratory criteria (1.5%). This implies that the KFRE is more effective at selecting the highest-risk subset of patients.

These findings are consistent with prior studies and have important implications for CKD care delivery. In a UK primary-care cohort, a hybrid of National Institute of Health and Care Excellence (NICE) referral guidelines plus 5-year KFRE risk of ≥5% appeared to better capture patients in whom kidney failure would later develop compared with the guidelines alone, in addition to decreasing nephrology referrals. Another UK population-based study projected that the use of a 5-year KFRE risk threshold of 3% instead of the NICE criteria would significantly reallocate potentially referred and unreferred patients and identify patients at higher risk without substantially increasing the total number eligible for referral. In Manitoba, Canada, Hingwala et al found markedly reduced wait times for nephrology care after implementing a risk-based protocol to triage nephrology referrals, effectively returning low-risk patients (5-year KFRE risk <3%) to primary care with anticipatory guidance. Of note, the aforementioned health care systems are, like the VA Health Care System, integrated delivery systems. Whether similar results could be achieved in less integrated systems remains to be determined.

In the study of Duggal et al, the KFRE could not be calculated in nearly 41,000 patients as a result of missing albuminuria measurements, raising concerns for selection bias considering that kidney failure risk likely differs among patients with and without a measured urinary albumin-creatinine ratio. Despite the established value of albuminuria in risk stratification for kidney and cardiovascular outcomes, the incidence of albuminuria testing remains woefully low, even in this population of veterans who were actively engaged in care, as indicated by their having at least 2 primary care visits and 2 eGFR values. Selection for medications and therapeutic targets for hypertension and diabetes management hinges on albuminuria results. Furthermore, mainstay therapies for slowing CKD such as renin-angiotensin blockade and sodium/glucose cotransporter 2 (SGLT2) inhibitors are most beneficial among patients with albuminuria. Unfortunately, efforts to study, implement, and assess risk-based CKD care have been hindered by the absence of albuminuria testing, which is frequently missing in more than half of patients with CKD. As noted by Duggal et al, population health approaches focused on CKD care will not be possible without routine albuminuria testing to enable effective risk stratification.

Among patients who met laboratory thresholds for nephrology referral, most did so based on an eGFR <30 mL/min/1.73 m², and only 18% of these patients were referred. These observations underscore the challenges in optimizing CKD care coordination. Health systems seeking to optimize CKD care delivery will need to assess their nephrology workforce and choose referral criteria that identify the highest-risk subset of patients. In the study of Duggal et al, a combination of laboratory-based criteria plus a KFRE-based threshold reduced the potential number of patients eligible for referral by nearly half, but even that reduced figure could outstrip the apparent nephrology capacity. Of note, the study did not apply age restrictions and included elderly patients, for whom the benefits of nephrology referral and potential resulting interventions are...
controversial. In a prior study of more than 200,000 US veterans with CKD, the risk of death consistently exceeded the risk of progression to kidney failure among those aged at least 85 years; at an eGFR threshold of 30 mL/min/1.73 m², mortality risk generally exceeded risk of kidney failure in veterans at least 55 years of age.\(^\text{15}\) Therefore, future studies focused on nephrology referral interventions should balance risk and benefits in the elderly CKD population.

Furthermore, the present approaches to nephrology referral myopically focus on patients with very advanced CKD stages, with efforts aimed at slowing CKD progression and preparing for kidney replacement therapy rather than mitigating the greater threat of cardiovascular morbidity and mortality. The earlier stages of CKD represent a larger opportunity to substantially mitigate CKD progression and related cardiovascular complications. However, huge swaths of these patients are not receiving optimal, guideline-directed medical therapy,\(^\text{16}\) and primary care providers are unable to fully accommodate the CKD care of these patients in their practice.

So how do we address these complex challenges to provide optimal care to all patients with CKD within the constraints of our health care systems? Duggal et al note that risk prediction could guide alternative approaches, enabling nephrology expertise to extend to larger populations of patients with lower-risk CKD. However, aside from the well-recognized CKD knowledge gap, primary care providers grapple with competing clinical priorities during already taxed clinical appointments and often lack sufficient clinical support to execute recommendations from specialists.\(^\text{17}\) To drastically move the needle in improving CKD care delivery, future interventions will need to address these real-life challenges in creative ways. For example, machine-learning algorithms that predict the likelihood of a patient having CKD could increase CKD recognition and early disease management by automatically prompting CKD testing and, if needed, deploying guidance via a clinical decision support tool or e-consultation. Systems could use clinical dashboards to monitor CKD care quality metrics at the system level and provide automated timely performance feedback to clinicians.\(^\text{18}\) CKD clinical champions who interface between these tools and clinical providers could augment these approaches. Furthermore, incorporation of risk prediction could guide allocation of more limited resources, such as in-person nephrology referral and multidisciplinary care teams focused on managing advanced CKD and the transition to kidney failure therapies. Such interventions have already been implemented in some health systems, including risk-based nephrology referral at Kaiser Permanente\(^\text{19}\) and a CKD registry and e-consult platform in the San Francisco Health Network.\(^\text{20}\,\text{21}\)

Improving nephrology referral patterns so they identify patients who are most in need of specialized care is an important step toward reducing the kidney failure burden. However, we must reimagine how we deliver CKD care beyond the nephrology clinic to meaningfully improve care of the majority of patients with CKD.

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**Table 1. Studies of Risk-Based and Laboratory-Based Nephrology Referral Criteria**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Setting</th>
<th>Year</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Singh et al, 2017(^\text{16})</td>
<td>56,461 patients with CKD</td>
<td>Brigham and Women’s primary care network in Boston, MA</td>
<td>2013</td>
<td>Use of KDIGO referral criteria would have:</td>
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<td>- Resulted in 2,340 new referrals (67% increase over observed referral volume)</td>
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<td>- Accounted for 38% of existing nephrology patient volume</td>
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<td>Major et al, 2019(^\text{19})</td>
<td>17,077 patients with CKD</td>
<td>Primary-care cohort in UK</td>
<td>2004-2006</td>
<td>Use of hybrid criteria of 5-y KFRE ≥5% and UACR ≥70 mg/mmol (≥19 mg/g) vs 2014 NICE criteria would have:</td>
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<td>- Decreased eligible referral volume by 4.9% (from 879 to 836)</td>
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<td>- Reduced “false negatives” (patients not meeting referral eligibility but who would later experience kidney failure) from 41 to 34</td>
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<td>- Reduced eligible referral volumes to approximately two thirds of patient volume previously seen by nephrology</td>
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<td>Bhachu et al, 2021(^\text{18})</td>
<td>39,476 patients with CKD</td>
<td>Population-based cohort in UK</td>
<td>2016-2017</td>
<td>32% of patients identified by NICE criteria have KFRE risk &lt;3%</td>
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<td>- Use of a 5-y KFRE threshold ≥3% would yield similar eligible referral volume as 2014 NICE referral criteria (n = 8,663 vs 7,566, respectively); NICE criteria would miss 40% of patients with KFRE risk ≥3%.</td>
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<tr>
<td>Duggal et al, 2021(^\text{17})</td>
<td>399,644 veterans with CKD</td>
<td>VA Health Care System in US</td>
<td>2015-2016</td>
<td>Use of 2-y KFRE threshold of ≥1% would yield similar eligible referral volume as VA/DoD laboratory indications (72,948 vs 86,276, respectively); combination of laboratory-based criteria plus 2-y KFRE risk ≥1% would reduce eligible referral volume to 38,229 (42% reduction), which:</td>
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<td>- Still exceeds observed referral volume (n = 11,752)</td>
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<td>- Approximates the 37,560 patients with CKD already being seen by nephrology</td>
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</table>

Abbreviations: CKD, chronic kidney disease; DoD, Department of Defense; KDIGO, Kidney Disease: Improving Global Outcomes; KFRE, Kidney Failure Risk Equation; NICE, National Institute of Health and Care Excellence; UACR, urinary albumin-creatinine ratio.
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Support: Dr Estrella is supported by VA Health Services Research and Development grant SDR 20-387. Dr Lamprea-Montealegre is supported by University of California, San Francisco, Center for Aging in Diverse Communities/National Institute on Aging award P30AG015272. None of the funding sources had a role in the design or conduct of this research.

Financial Disclosure: None of the funding sources had a role in the design or conduct of this research.

Publication Information: Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. This is a US Government Work. There are no restrictions on its use. Published online month xx, xxxx with doi 10.1053/j.ajkd.2021.09.020

References