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Risk-Based Triage for Nephrology Referrals: The Time is Now

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Chronic kidney disease (CKD) is common, but progression to kidney failure requiring dialysis or kidney transplantation remains an uncommon event in patients with CKD.[1] Accurately predicting the risk of CKD progression can enable better patient-provider communication, a more appropriate transition from primary care to secondary care nephrology, and avoidance of referrals in those who are unlikely to progress to kidney failure. Subspecialty resources including nephrology may be more limited in universal health care systems such as the United Kingdom or Canada, and most patients with CKD are managed by primary care physicians.[1,2] In these settings, referral criteria are often used to guide the transition, and these criteria are typically based on single values or changes in estimated glomerular filtration rate (eGFR) as well as urine albumin to creatinine ratio.[1,2]

In several Canadian provinces, and in US health systems such as Kaiser Permanente, the kidney failure risk equation (KFRE), along with other criteria, is used to determine the need for nephrology referral.[3,4] In Manitoba, Canada, a risk of >3% over 5 years as determined by the KFRE has been a key component of the nephrology referral process. Its introduction has led to a reduction in wait times, and thereby improved access to care for patients at the highest risk of CKD progression.[4] More recently, a validation study of the KFRE in UK primary care suggested a threshold of >5 % over 5 years instead of the current criteria of an eGFR of <30 ml/min per 1.73 m^2 may reduce nephrology referral.[5] This change has been included in the draft CKD guidance by the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[6] Additional studies to examine the impact of these thresholds, either 3% or 5% over 5 years, on the number of generated nephrology referrals, and comparisons with current NICE criteria for referral are needed.

To address this question, Bhachu et al.[7] conducted a cross-sectional study of The Health Improvement Network, a well-described and generalizable primary care research database in the United Kingdom.[7] They examined the impact of a >3 % risk of kidney failure threshold for referral in comparison with current NICE criteria: (1) eGFR <30 ml/min per 1.73 m^2; (2) urine albumin to creatinine ratio ≥30 mg/mmol with hematuria; (3) urine albumin to creatinine ratio ≥70 mg/mmol and no diabetes; (4) a sustained decrease in eGFR of ≥25% or a sustained decrease in eGFR. The authors should be commended for using a prespecified published protocol for their analysis, a rarity in this type of research database study.

The authors started with a cohort of more than 3 million individuals in primary care from the The Health Improvement Network database and found 107,962 with a confirmed diagnosis of CKD. As expected, more than 30% of these individuals had diabetes, and more than 70% had a diagnosis of hypertension. Coronary heart disease and congestive heart failure were also very common in the CKD population. Only 36.6% of the patients had a measurement for albuminuria in the preceding 12 months despite guidelines endorsing it is for all individuals with CKD for staging and prognostication. This lack of albuminuria measurement, particularly in individuals without diabetes mellitus, is perhaps the biggest barrier to widespread implementation of the KFRE in primary care.

The authors then compared the NICE referral criteria based on the 2014 NICE CKD guidance to the KFRE-based threshold. Their principal finding was that for 85% of patients, both the NICE criteria and the KFRE-based criteria were concordant in recommending referral or

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nonreferral. However, when focusing on those recommended for referral using the current NICE criteria, there was significant divergence. For patients referred using the NICE criteria, 31.5% had a KFRE risk of <3 % over 5 years, and using the KFRE-based criteria, 40.2% of individuals with a risk >3% would not have met NICE criteria for referral. Taken together, these findings translated into 5869 (53.1%) of patients who fulfilled NICE and/or KFRE criteria (n = 11,049) being reclassified between primary and specialty care in either direction if the KFRE-based criteria replaced the NICE criteria.

Discordant results for referral between the KFRE and NICE criteria were primarily based on the sustained decrease in eGFR component of the NICE guidance. For this particular component, only 44.6% of patients meeting the NICE threshold met the KFRE threshold. In contrast, concordance ranged from 75% to 93% for the other NICE criteria and the KFRE threshold. These findings are important as they draw attention to an unexplained decline in eGFR in low-risk individuals, which often forms the trigger for nephrology referral from primary care. Whether this transient/sustained decline in eGFR represents true disease progression or it regresses to its baseline value over time remains unknown and is important to study. Equally important is the discordance of transient/sustained decline of 25% in eGFR with the KFRE threshold, and the relationship between both measures and downstream 5-year risk of kidney failure should be evaluated.

A recent study from Alberta, Canada, has shown that regression of CKD is as common as progression, and more common in older adults and in those with normal or mild albuminuria.[8] Given that age and albuminuria are components of the four-variable KFRE, these findings would suggest that the 44.6% of patients with a sustained decrease in eGFR and KFRE risk >3% are likely true progressors, and the 55.4% are individuals who are more likely to have regression to their baseline eGFR or stable disease. This would suggest that a KFRE-based threshold may be more appropriate to detect patients at longer-term risk of CKD progression and should replace referral criteria that rely on shorter-term changes in eGFR in otherwise low-risk individuals.

There are some important limitations that require consideration. First, the KFRE was developed in individuals with CKD stages G3A-G5 and should not be used to determine risk of CKD progression in patients with preserved kidney function.[9] Albuminuria is key risk factor for CKD progression and can be helpful in determining high-risk individuals who still have normal kidney function but are at risk for decline in the next 2 to 5 years. Second, the KFRE should not be the only criteria for nephrology referral, and nephrologists may be required to manage patients who are at low risk for CKD progression to dialysis, but have complex acid base or electrolyte disorders, suspected glomerulonephritis, polycystic kidney disease, and other diagnoses.

These findings suggest that a KFRE-based threshold may be an important addition to nephrology referral criteria in the United Kingdom and could replace criteria that use shorter-term changes in eGFR. Studies prospectively evaluating the longer-term impact of adding KFRE-based criteria to the NICE CKD referral guidance on patient and health system outcomes will be needed in the upcoming years.

DISCLOSURE

RM has received an education grant from AstraZeneca in relation to developing patient resources for the Kidney Failure Risk Equation. The John Walls Renal unit has received consultation fees from Roche Diagnostics in relationship to the clinical implementation of the Kidney Failure Risk Equation; RM has not been directly remunerated for this work. The remaining authors declared no competing interests.

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