RESEARCH LETTER

Kidney Failure Risk Equation Thresholds for Multidisciplinary Kidney Care Referrals: A Validation Study

To the Editor:

Chronic kidney disease (CKD) is a highly prevalent and morbid condition. Disease progression is variable, and predicting the risk of requiring kidney replacement therapy (KRT) becomes increasingly important in advanced CKD (estimated glomerular filtration rate <30 mL/min/1.73 m^2).[1] The Kidney Failure Risk Equation (KFRE) is a widely used tool for estimating risk of requiring KRT.[2] As it does not consider the competing risk of death, it tends to overestimate KRT initiation. It has been validated across heterogenous settings, including advanced CKD.[3-5] The Ontario Renal Network introduced the 2-year 4-variable KFRE (KFRE-2) >10% as a criterion for referral of patients followed by general nephrologists to multidisciplinary CKD clinics. These clinics consist of nephrologists, nurses, dieticians, pharmacists, and social workers who collaborate to delay and manage CKD progression and provide education regarding transitioning to end-stage kidney disease. Patients and providers have reported KFRE-guided multidisciplinary CKD clinic referral improves care delivery.[6] Although the KFRE has been extensively externally validated, a recent systematic review identified that its clinical applications and impact on care have been understudied.[7] We explored using KFRE risk thresholds to guide clinical decision making in advanced CKD.

We conducted a retrospective cohort study using 2 independent multidisciplinary CKD clinic cohorts in Kingston, Ontario. The derivation cohort included prevalent patients followed in multidisciplinary clinic in 2013. The validation cohort included incident patients between 2018 and 2020, and all prevalent patients seen at least once in the clinic in 2018, excluding those from the derivation cohort. Patients with prior kidney transplantation were excluded. Baseline KFRE-2 scores were calculated using the urinary albumin-creatinine ratio and estimated glomerular filtration rate associated with the index clinic visit. The primary outcome was KRT initiation, defined as preemptive transplant or starting dialysis within 2 years of the index visit. Sensitivity, specificity, and positive (PPV) and negative predictive values (NPVs) were reported across the range of predicted risk probabilities to determine clinically useful thresholds. Item S1 and Table S1 include further details about methodology.

There were 442 and 590 patients in the derivation and validation cohorts, respectively. The cohorts had similar baseline demographics (Table 1). Median KFRE-2 scores and urinary albumin-creatinine ratios were higher in the validation cohort, likely reflecting changes in provincial criteria for multidisciplinary CKD clinic eligibility (KFRE-2 >10%) implemented in 2018, resulting in fewer low-risk patients in the later validation cohort. At 2 years, there were 90 (20%) KRT initiation events in the development cohort and 179 (30%) events in the validation cohort.

Although the 10% risk threshold (current eligibility standard) displayed excellent sensitivity in the derivation cohort, with few patients who had predicted risk <10% going on to initiate KRT, and the specificities were low, with 52% of patients who did not initiate KRT having predicted risk >10% (Table 2). The 30% threshold, however, remained fairly sensitive (76%) and was more specific (80%), with few false positives exceeding this threshold. NPV was also high, with 93% of patients who had lower predicted risk not initiating KRT within 2 years, and PPV was modest (48%), indicating that only approximately half of patients with risk above this threshold initiated KRT. Thus, a 30% KFRE-2 threshold may be more reasonable to guide multidisciplinary clinic referral. Patients below this threshold would still need careful management under general nephrology care to slow CKD progression, whereas those who progress could then be transferred to a multidisciplinary clinic. This

Table 1. Baseline Patient Characteristics

	Derivation N = 442	Validation N = 590
Mean age (SD), y	73 (12)	69 (13)
Female, n (%)	196 (44)	220 (37)
Race, n (%)		
White	427 (97)	517 (88)
Black	2 (0.45)	2 (0.34)
Indigenous	6 (1.4)	38 (6.4)
Asian	4 (0.90)	17 (2.9)
Other	3 (0.68)	5 (0.85)
Unknown	0 (0)	11 (1.9)
Median urine albumin: creatinine (Q1, Q3), mg/mmol	30 (5, 120)	94 (19, 232)
<3, n (%)	81 (18)	10 (1.7)
3-30, n (%)	141 (32)	120 (20)
>30, n (%)	220 (50)	460 (78)
Median eGFR CKD-EPI[a] (Q1, Q3), mL/min/1.73 m^2	20 (15, 25)	19 (12, 24)
CKD etiology		
Diabetic nephropathy, n (%)	204 (46)	274 (46)
Hypertensive nephrosclerosis, n (%)	120 (27)	90 (15)
Glomerulonephritis, n (%)	18 (4)	43 (7)
Polycystic kidney disease, n (%)	12 (3)	16 (3)
Other, n (%)	88 (20)	167 (28)
Comorbid conditions		
Diabetes mellitus, n (%)	248 (56)	373 (63)
Hypertension, n (%)	N/A	405 (69)
Median KFRE-2 score (Q1, Q3)	15 (5, 35)	29 (19, 59)

Abbreviations: CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; KFRE, Kidney Failure Risk Equation; N/A, not available; Q, quartile; SD, standard deviation.
[a]2009 CKD-EPI eGFR equation.

Table 2. Performance Characteristics of KFRE-2 Thresholds

Derivation Cohort	10%	20%	30%	40%	50%	60%	70%	80%	90%
Sensitivity	90%	78%	**76%**	62%	52%	39%	26%	16%	5%
Specificity	48%	66%	**80%**	**88%**	**92%**	95%	97%	99%	100%
PPV	30%	36%	48%	56%	63%	68%	72%	74%	80%
NPV	95%	93%	93%	90%	89%	86%	84%	83%	81%
AUC (95% CI)	0.83 (0.78-0.88)								
Validation Cohort	10%	20%	30%	40%	50%	60%	70%	80%	90%
Sensitivity	97%	83%	**74%**	64%	55%	47%	37%	26%	12%
Specificity	10%	48%	**67%**	**81%**	**89%**	93%	97%	98%	100%
PPV	32%	41%	49%	59%	68%	75%	83%	87%	91%
NPV	87%	86%	85%	84%	82%	80%	78%	75%	72%
AUC (95% CI)	0.78 (0.73-0.82)								

Abbreviations: AUC, area under the curve; CI, confidence interval; KFRE, Kidney Failure Risk Equation; NPV, negative predictive value; PPV, positive predictive value.

could enable more appropriate allocation of costly, finite resources required for multidisciplinary care to those with the greatest need and spare low-risk patients undue anxiety.

The 40%-50% thresholds in the derivation cohort were highly specific (88%-92%), indicating most patients who did not initiate KRT had predicted risk below these thresholds, but sensitivities were modest (52%-62%), indicating many patients who initiated KRT had lower KFRE scores. Negative predictive values were high, with most patients below these thresholds not initiating KRT (89%-90%), and the PPVs (56%-63%) indicated more than half the patients with higher predicted risk initiated KRT. Thus, using KFRE-2 ≥40%-50% to guide KRT education and planning could prevent unnecessary, expensive, and potentially invasive interventions. This is in keeping with the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) recommendation of 10%-20% 1-year predicted risk for KRT planning, the KDOQI (Kidney Disease Outcomes Quality Initiative) recommendation of ≥50% 2-year risk for vascular access referrals, and the draft 2023 KDIGO CKD recommendation of >40% 2-year risk for education and KRT preparation.[8-10]

The 30% threshold in the validation cohort was similarly sensitive to the derivation cohort (74% vs 76%) albeit somewhat less specific (67% vs 80%). Likewise, the characteristics were comparable at the 50% threshold with high specificities (89% vs 92%). Based on the KFRE-2 performance characteristics in 2 independent advanced CKD cohorts, we propose using KFRE-2 ≥30% to guide referral to multidisciplinary clinic programs and KFRE-2 ≥50% to guide referrals for modality education, transplant, and access planning. These thresholds require further validation in diverse settings, including cohorts with less advanced CKD managed by general nephrology, as well as impact studies on patient outcomes and resource utilization.

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SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Item S1: Detailed Methods

Table S1: Observed KRT and Death at 2 Years

ARTICLE INFORMATION

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