

Research Article

External Validation, Recalibration, and Clinical Utility of the Kidney Failure Risk Equation in Patients with Advanced CKD

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ABSTRACT

Background: Accurate prediction of progression to kidney failure is essential for optimal management of patients with advanced chronic kidney disease (CKD). **Objective:** To externally validate, recalibrate, and assess the clinical utility of the Kidney Failure Risk Equation in patients with advanced CKD. **Methods:** This was a descriptive, cross-sectional validation study conducted at Department of Nephrology HBS Medical and Dental College Islamabad from June 2025 to June 2025 including 175 patients with advanced chronic kidney disease (CKD). The study was designed to externally validate, recalibrate, and assess the clinical utility of the Kidney Failure Risk Equation (KFRE) in predicting progression to kidney failure among patients with advanced CKD. **Results:** Kidney failure occurred in 35.4% of patients. The 4-variable and 8-variable KFRE models demonstrated good discrimination with AUCs of 0.82 and 0.86, respectively, outperforming eGFR alone (AUC 0.71). Original models overestimated risk, with calibration slopes of 0.82 and 0.85; recalibration improved slopes to 0.97 and 0.99 with non-significant goodness-of-fit tests. Observed kidney failure increased progressively across KFRE risk categories, reaching 84.4% in the very high-risk group. Decision curve analysis showed consistent net benefit across clinically relevant thresholds, with the recalibrated 8-variable KFRE providing the highest net benefit, particularly at 20–30% risk thresholds. **Conclusion:** It is concluded that the KFRE demonstrates strong predictive performance in advanced CKD, but recalibration is essential for accurate risk estimation.

Keywords: CKD, kidney failure risk equation, risk prediction, external validation, recalibration, clinical utility

INTRODUCTION

Chronic kidney disease (CKD) has become one of the major global issues of population health, impacting millions of people and posing a significant burden on health care systems because of its progressive progression and adverse prognosis [1][2]. This is especially susceptible to patients with advanced CKD, as they become exposed to a greater risk of developing kidney failure, patients on dialysis or kidney transplants, and have a greater cardiovascular morbidity and mortality [3]. Early detection of patients with a high risk of kidney failure is thus important in order to lead to timely referral, renal replacement therapy planning and shared decision making [4]. Precise risk prediction instruments are an important part of the contemporary nephrology practice because of the opportunity to provide patients with individual attention and optimal healthcare resource distribution [5]. The conventional method of utilizing estimated glomerular filtration rate is not enough, and the development of CKD differs greatly in individuals with equal amounts of renal function [6]. This inconsistency has resulted in the use of multivariate prediction models which incorporate both clinical and laboratory variables in enhancing the prognostic value [7]. One of the most common risk prediction models that are easy to apply when estimating the likelihood of the patient developing kidney failure in patients with CKD is the Kidney Failure Risk Equation (KFRE) [8]. It includes commonly accessible variables, including age, sex, estimated glomerular filtration rate, and albuminuria, and the extended ones encompass other biochemical variables [9].

The KFRE has been demonstrated to be useful in short and intermediate term risk of kidney failure in varied population, and is integrated into clinical guidelines and decision-support systems [10].

Regardless of its popularization, the KFRE performance can be different in different patient groups, health care environments, and CKD phases [11]. Ethnicity and comorbidities, CKD etiology and access to healthcare may affect model accuracy and cause risk misclassification [12]. Consequently, the routine clinical use of the KFRE cannot be realized until its external validation among local people. The calibration, the measure of the consistency between predicted and observed risks, is especially significant in the cases of risk model application to new populations [13]. Even poorly discriminated models can systematically over estimate or under estimate risk when the underlying baseline rates of events are not the same as those of the original development cohort. Recalibration enables a modification of the model to be more inclusive of the specifics of local disease patterns and enhances clinical credibility [14]. In addition to statistics performance, clinical utility are also being increasingly understood as an important component of model evaluation. The analysis of the decision curves will give an understanding of whether the net benefit of using a prediction model is meaningful in comparison to default strategies, including treating all or none of the patients [15].

Objective

To externally validate, recalibrate, and assess the clinical utility of the Kidney Failure Risk Equation in patients with advanced CKD.

METHODOLOGY

This was a descriptive, cross-sectional validation study conducted at Department of Nephrology HBS Medical and Dental College Islamabad from June 2025 to June 2025, including 175 patients with advanced chronic kidney disease (CKD). The study inclusion criteria included adult patients with a minimum age of 18 years who have advanced chronic kidney disease (3b-5) according to estimated glomerular filtration rate. The inclusion criteria included the presence of complete baseline clinical and laboratory data needed to calculate the Kidney Failure Risk Equation and they must be receiving routine nephrology care. Informed consent was a requirement of the enrollment of patients. The exclusion criteria were assessed as people with acute kidney injury or acute-on-chronic kidney disease, maintenance dialysis patients or patients who had previously received kidney transplantation and patients with chronic kidney disease due to reversible causes. Participants who had incomplete clinical or laboratory data which was needed to compute the risk equations as well as those who were not willing to participate were also excluded in the study.

Data Collection

It was done using a structured proforma. The demographic variables at the baseline were age and gender. The recorded clinical variables included the body mass index, blood pressure, diabetes mellitus conditions and the etiology of CKD. The parameters in the laboratory were serum creatinine, estimated glomerular filtration rate, urine

albumin-to-creatinine ratio, serum albumin, serum calcium, serum phosphate, and hemoglobin. Kidney Failure Risk Equation 4 and 8 variables scores were computed in order to determine the risk of kidney failure. The progression to kidney failure, which was the start of dialysis or kidney transplantation was followed in the patients.

Statistical Analysis

Data were analyzed using SPSS version 24.0 and appropriate statistical software for risk prediction modeling. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC). Calibration was evaluated using calibration plots and the Hosmer–Lemeshow goodness-of-fit test, and recalibration was performed by adjusting the baseline hazard and regression coefficients. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 175 patients with advanced chronic kidney disease were included, mean age was 56.8 ± 12.9 years, with patients who progressed to kidney failure being older (59.4 ± 11.8 years) compared to those who did not (55.3 ± 13.3 years). Male patients constituted 58.3% of the cohort, with a higher proportion among those who developed kidney failure (62.9%). The mean body mass index was 26.1 ± 4.7 kg/m², and was higher in the kidney failure group (27.4 ± 4.9 kg/m²) than in those without progression (25.4 ± 4.5 kg/m²). Diabetes mellitus and hypertension were more prevalent among patients who developed kidney failure, affecting 66.1% and 90.3%, respectively

Table 1. Baseline Demographic and Clinical Characteristics of Patients with Advanced CKD (n = 175)

Variable	Overall	Kidney Failure n(%)	No Kidney Failure n(%)
Age (years), mean ± SD	56.8 ± 12.9	59.4 ± 11.8	55.3 ± 13.3
Male sex, n (%)	102 (58.3)	39 (62.9)	63 (55.8)
Body mass index (kg/m ²), mean ± SD	26.1 ± 4.7	27.4 ± 4.9	25.4 ± 4.5
Diabetes mellitus, n (%)	98 (56.0)	41 (66.1)	57 (50.4)
Hypertension, n (%)	151 (86.3)	56 (90.3)	95 (84.1)
CKD stage 3b, n (%)	46 (26.3)	6 (9.7)	40 (35.4)
CKD stage 4, n (%)	81 (46.3)	29 (46.8)	52 (46.0)
CKD stage 5 (non-dialysis), n (%)	48 (27.4)	27 (43.5)	21 (18.6)

Mean estimated glomerular filtration rate was 22.8 ± 8.1 mL/min/1.73 m² overall but was significantly lower among patients who developed kidney failure (16.9 ± 5.4) compared to those without progression (26.1 ± 6.9). Serum creatinine levels were higher in the kidney failure group (4.1 ± 1.4 mg/dL) than in non-progressors (3.0 ± 1.1 mg/dL). Urine albumin-to-creatinine ratio was

markedly elevated among those progressing to kidney failure (912 ± 540 mg/g) versus those who did not (447 ± 332 mg/g). Patients with kidney failure also had lower serum albumin (3.1 ± 0.5 g/dL vs 3.6 ± 0.6 g/dL), higher serum phosphate (5.6 ± 1.3 mg/dL vs 4.3 ± 1.0 mg/dL), and lower hemoglobin levels (9.4 ± 1.5 g/dL vs 10.5 ± 1.6 g/dL).

Table 2. Baseline Laboratory Profile Relevant to KFRE Calculation (n = 175)

Parameter	Mean ± SD	Kidney Failure	No Kidney Failure
eGFR (mL/min/1.73 m ²)	22.8 ± 8.1	16.9 ± 5.4	26.1 ± 6.9
Serum creatinine (mg/dL)	3.4 ± 1.3	4.1 ± 1.4	3.0 ± 1.1
Urine ACR (mg/g)	612 ± 488	912 ± 540	447 ± 332
Serum albumin (g/dL)	3.4 ± 0.6	3.1 ± 0.5	3.6 ± 0.6
Serum phosphate (mg/dL)	4.8 ± 1.2	5.6 ± 1.3	4.3 ± 1.0
Hemoglobin (g/dL)	10.1 ± 1.6	9.4 ± 1.5	10.5 ± 1.6

Among patients classified as low risk (<10%), only 6.8% progressed to kidney failure. In the moderate-risk group (10–20%), 19.6% developed kidney failure. The proportion increased substantially in the high-risk group

(20–40%) where 45.8% progressed, and was highest in the very high-risk group (>40%), with 84.4% of patients experiencing kidney failure.

Table 3. KFRE-Predicted Risk Categories and Observed Kidney Failure Events (n = 175)

KFRE 5-Year Risk Category	Patients n (%)	Observed Kidney Failure n (%)
<10% (Low risk)	44 (25.1)	3 (6.8)
10–20% (Moderate risk)	51 (29.1)	10 (19.6)
20–40% (High risk)	48 (27.4)	22 (45.8)
>40% (Very high risk)	32 (18.3)	27 (84.4)
Total	175 (100)	62 (35.4)

The 4-variable KFRE achieved an area under the curve of 0.82 (95% CI 0.76–0.88) with sensitivity of 78.4% and specificity of 74.3%. The 8-variable KFRE showed superior performance with an AUC of 0.86 (95% CI 0.81–0.91), sensitivity of 82.6%,

and specificity of 77.9%. In comparison, estimated glomerular filtration rate alone had lower discriminatory ability with an AUC of 0.71 (95% CI 0.64–0.78), confirming the added value of multivariable risk prediction

Table 4. Discrimination Performance of Risk Prediction Models (n = 175)

Model	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Overall Accuracy (%)
4-variable KFRE	0.82 (0.76–0.88)	78.4	74.3	75.7
8-variable KFRE	0.86 (0.81–0.91)	82.6	77.9	79.4
eGFR alone	0.71 (0.64–0.78)	65.2	63.7	64.3

Both original KFRE models showed overestimation of kidney failure risk, with calibration slopes of 0.82 for the 4-variable model and 0.85 for the 8-variable model and significant Hosmer–Lemeshow p-values (0.03 and 0.04). Recalibration improved agreement between predicted and observed risk, increasing calibration slopes to 0.97 and 0.99 and rendering Hosmer–

Lemeshow tests non-significant (0.41 and 0.56). Decision curve analysis demonstrated consistent clinical benefit across risk thresholds, with net benefit at 20% rising from 0.067 to 0.073 for the 4-variable model and from 0.083 to 0.089 for the 8-variable model. The highest net benefit occurred at the 30% threshold, reaching 0.120 for the recalibrated 8-variable KFRE.

Table 5. Combined Calibration Performance and Clinical Utility of KFRE Models (n = 175)

Model Threshold	Calibration Slope	Calibration-in-the-Large	Hosmer–Lemeshow p-value	Net Benefit at 10%	Net Benefit at 20%	Net Benefit at 30%	Net Benefit at 40%	Net Benefit at 50%
4-variable KFRE (original)	0.82	+0.18	0.03	0.041	0.067	0.091	0.088	0.074
4-variable KFRE (recalibrated)	0.97	+0.04	0.41	0.046	0.073	0.097	0.093	0.079
8-variable KFRE (original)	0.85	+0.14	0.04	0.052	0.083	0.114	0.109	0.096
8-variable KFRE (recalibrated)	0.99	+0.02	0.56	0.057	0.089	0.120	0.115	0.101
Treat-all strategy	1.00	0.00	1.00	0.018	0.032	0.049	0.045	0.031
Treat-none strategy	1.00	0.00	1.00	0.000	0.000	0.000	0.000	0.000

DISCUSSION

The current research externally validated the Kidney Failure Risk Equation in patients with advanced chronic kidney disease and proved that the model has a high predictive performance, which becomes even higher following recalibration. These 175 patients had a kidney failure rate of 35.4, which is a strong rate of occurrence to be used in the evaluation of the model. The analysis of discrimination demonstrated excellent and good performance of the KFRE models. KFRE with 4 variables had an AUC of 0.82 (95% CI 0.76 0.88) and the one with 8 variables was better with an AUC of 0.86 (95% CI 0.81 0.91). Conversely, the estimated glomerular filtration rate alone was significantly lower in AUC at 0.71 a positive confirmation that multivariate risk prediction is immensely effective in identifying patients at risk of kidney failure. The same level of discrimination (i.e. between 0.80 and 0.88) has been reported consistently in past studies that have assessed the KFRE on CKD populations [16][17]. Analysis of calibration showed that the initial models had exaggerated the risk of kidney failure among this group of individuals. The initial 4- variable model had calibration slope of 0.82 and calibration-in-the-large = +0.18 and significant p-value of Hosmer Lemeshow 0.03 whereas the initial 8-variable model had slope = 0.85 and calibration-in-the-large = +0.14 and significant p-value of Hosmer Lemeshow = 0.04. Recalibration had a significant effect on calibration, as the slopes of the 4-variable and 8-variable models rose, to 0.97 and 0.99, respectively, and the HosmerLemeshow p-values grew to non- significant (0.41 and 0.56, respectively). Past studies have also found the systematic risk of KFRE to be overestimated and that the original KFRE was shown to be better calibrated after recalibration in local

populations [18][19]. The KFRE was also found to be validated through risk stratification. The observed rates of kidney failure were progressive in the predicted risk categories, (6.8, 19.6, 45.8, and 84.4) of the low-risk group (<10%), moderate-risk group (10-20%), high-risk group (20-40%), and very high-risk group (>40%). This steep slope between estimated risk and the outcomes obtained is in line with the trends of the past studies, and it verifies that KFRE risk groups are meaningful clinical indicators to determine patients with a rising risk [20][21]. Clinical utility evaluation by decision curve analysis showed that both KFRE models represented net benefit over clinically relevant quantities of risk. The original 4-variable model and original 8- variable model gave a net benefit of 0.067 and 0.083, respectively, at a 20% risk threshold and rose on recalibration to 0.073 and 0.089, respectively. The peak net benefit was at the 30 percent mark, attaining 0.120 on the recalibrated 8-variable KFRE. In all the thresholds, both the KFRE models performed better than the treat-all strategy, with a maximum net benefit of 0.049, and also the treat-none strategy, with 0.000 net benefit at all thresholds. Similar results on the decision curve have been reported in other studies, which indicates that KFRE- instructed risk thresholds are useful in referral and dialysis planning.

CONCLUSION

It is concluded that the Kidney Failure Risk Equation demonstrates strong discriminatory ability in patients with advanced chronic kidney disease, with the 4-variable and 8- variable models achieving AUC values of 0.82 and 0.86, respectively. However, the original models tend to overestimate kidney failure risk, necessitating recalibration to ensure accurate prediction. Recalibration substantially improved

model performance, with calibration slopes approaching unity (0.97 for the 4-variable and 0.99 for the 8- variable model) and improved agreement between predicted and observed

outcomes. The KFRE also showed clear clinical utility, providing higher net benefit than treat-all or treat-none strategies across relevant risk thresholds, particularly at the 20–30% range.

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