Accuracy of Kidney Failure Risk Equation in Transplant Recipients

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An increasing number of kidney transplants are being performed worldwide. At present, patients with failing kidney allografts comprise a significant proportion (5%) of patients beginning dialysis.[1] Accurately predicting the risk of end-stage kidney disease (ESKD) in transplant patients may help clinical decision making to individualize patient care and improve access planning for dialysis and retransplantation. Kidney transplantation is the treatment of choice for ESKD, as it improves both mortality and morbidity compared with dialysis modalities.[2,3]

Several models have been developed to predict kidney allograft failure,[4] but many of them require a renal biopsy and are not simple to use in day-to-day clinical decision making. Tangri *et al.*[5] developed the Kidney Failure Risk Equation (KFRE) for patients with native chronic kidney disease. It accurately predicts the risk of needing renal replacement therapy at 2 and 5 years. The equation relies on age, sex, estimated glomerular filtration rate (eGFR) and spot urine albumin-creatinine ratio. The KFRE has been adopted as a tool for predicting the need for renal replacement therapy in several jurisdictions.[6] Although the KFRE has been validated in several populations,[7] to our knowledge, the KFRE has not been validated in populations that have received a kidney transplant. This study assesses the accuracy of the KFRE in renal transplant recipients.

RESULTS

A total of 956 kidney transplants were performed at The Ottawa Hospital between January 1, 2000, and December 31, 2014. Data were collected on 877 kidney transplants. Seventy-nine patients did not have adequate data to calculate KFRE or had died before reaching the 1-year point.

Patient characteristics are shown in Table 1. Data to calculate KFRE were available on 877 patients (living donors $n = 414$; eGFR < 60 $n = 488$) at 12 months, 801 patients (living donors $n = 386$; eGFR < 60 $n = 400$) at 24 months, and 547 patients (living donors $n = 264$; eGFR < 60 $n = 269$) at 60 months. Mean age was 51 and most patients were white. The most common cause of kidney disease was glomerulonephritis.

When comparing 2-year KFRE predictions with observed ESKD events, the receiver operating characteristic curve values ranged from 0.73 to 0.93 for different time periods of calculation (Table 2 and Figure 1). The 5-year KFRE risk prediction receiver operating characteristic values ranged from 0.72 to 0.78 for different time periods of calculation (Table 2 and Figure 1). Number of patient deaths with graft function was significantly higher than observed ESKD events.

Sensitivity analysis between living and deceased donors did not reveal any major difference. The receiver operating characteristic values ranged from 0.67 to 0.96 for different time periods. We could not calculate 5-year KFRE risk separately for deceased donors because there was only one outcome in this group. A second sensitivity analysis stratified by eGFR of <60 and $\geq$ 60 ml/min per 1.73 m^2 revealed better risk prediction of 2- and 5-year risk at the 12-month time point (Table 2). For eGFR $<$ 60 ml/min per 1.73 m^2, the receiver operating characteristic values for 2-year KFRE predictions to observed ESKD events, ranged from 0.64

Table 1. Kidney transplant recipient characteristics, $N = 887$

Age, yr, mean (SD)	51 (14.1)
Female, *n* (%)	340 (38.3)
White, *n* (%)	762 (86.0)
Asian, *n* (%)	41 (4.6)
Black, *n* (%)	48 (5.4)
Other, *n* (%)	38 (4.0)
Living donor, *n* (%)	426 (48)
Cause of kidney disease	
Glomerulonephritis, *n* (%)	207 (23)
Polycystic kidney disease, *n* (%)	100 (11.3)
Diabetes, *n* (%)	168 (18.9)
Hypertension, *n* (%)	39 (4.4)
Other, *n* (%)	122 (13.8)
Unknown, *n* (%)	251 (28.3)
eGFR,[a] ml/min per 1.73 m^2, mean (SD)	
At 12 mo	58.4 (22)
At 24 mo	61.1 (22)
At 60 mo	61.2 (23)
ACR, mg/mmol, median (IQR)	
At 12 mo	2 (1–6)
At 24 mo	2.2 (1–7)
At 60 mo	2.8 (1–10)

ACR, albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; IQR, interquartile range.
[a]Calculated by Chronic Kidney Disease–Epidemiology Collaboration equation.[11]

to 0.93 and for eGFR $\geq$ 60 ml/min per 1.73 m^2, it was 0.51 to 0.74. We could not calculate 2-year KFRE risk separately for eGFR $\geq$ 60 for 24- and 60-month time points because there was only one outcome in these 2 groups.

DISCUSSION

Our data reveal that KFRE can be used to predict ESKD with good accuracy in kidney transplant recipients at 2 and 5 years in patients surviving at least 1 year post-transplant. Nephrologists can use the KFRE to guide aggressiveness of treatment when issues such as late rejection, malignancy, or infection develop and there is a high predicted risk of ESKD in the near future. This information may also help guide transition away from a calcineurin inhibitor–based regimen. Nephrologists also can use this model to refer patients back to transplant centers when there is a high risk of graft failure. Patients also can benefit from the KFRE while considering retransplantation, and it may encourage living donation. If retransplantation is not an option, it could be used to make access planning for dialysis more efficient.

Fifteen studies have assessed predictors for allograft failure in kidney transplant recipients.[4] None are in widespread use, as they require variables that are not easily and readily available to most clinicians, whereas variables used by the KFRE are readily available and routinely measured.

Our data indicate that the KFRE can be used to predict ESKD in transplant populations. This is in spite of the etiology and pathophysiology of kidney allograft failure being different, compared with native kidney disease. There are several pathological processes that can lead to graft loss, such as calcineurin inhibitor toxicity, chronic antibody-mediated rejection, and acute rejection.[8] Transplanted kidneys also are thought to be more susceptible to acute kidney injury[9] and display an accelerated senescence compared with native kidneys (S1). In addition, the accuracy of GFR calculated by the Chronic Kidney Disease–Epidemiology Collaboration equation (S2) has been questioned in renal transplant recipients (S12–15). Despite the differences between transplant and nontransplant populations, the KFRE risk estimate seems to be reasonable to use in the clinical care of patients with a kidney transplant. We did not have data to calculate 8 variable KFRE, which may improve further risk prediction in this population.

Limitations to our study should be noted. This study was conducted at a single center where recipients are followed in a subspeciality transplant clinic for the duration of their kidney transplant. However, our outcomes are similar to other centers in Canada.[10] The dataset was not complete, as a small number of patients did not have the required tests done to calculate KFRE at different time points, but we were

Table 2. End-stage kidney disease outcomes from time of KFRE Calculation

Time point of KFRE calculation	No. (%) reaching end-stage kidney disease	No. (%) of deaths	Area under ROC curve (95% CI), all	Area under ROC curve (95% CI), eGFR < 60	Area under ROC curve (95% CI), eGFR ≥ 60
2 yr from KFRE calculation					
12 mo ($n = 877$)	18 (2.1)	27 (3.1)	0.76 (0.73–0.79)	0.79 (0.75–0.83), $n = 488$	0.66 (0.61–0.71), $n = 389$
24 mo ($n = 801$)	13 (1.6)	21 (2.6)	0.93 (0.91–0.95)	0.93 (0.90–0.96), $n = 400$	Unable to calculate, $n = 401$
60 mo ($n = 547$)	8 (1.5)	24 (4.4)	0.73 (0.69–0.77)	0.64 (0.58–0.70), $n = 269$	Unable to calculate, $n = 278$
5 yr from KFRE calculation					
12 mo ($n = 877$)	37 (4.2)	63 (7.2)	0.72 (0.69–0.70)	0.76 (0.72–0.80), $n = 488$	0.64 (0.60–0.69), $n = 389$
24 mo ($n = 801$)	29 (3.6)	56 (7.0)	0.78 (0.75–0.80)	0.87 (0.83–0.90), $n = 400$	0.51 (0.46–0.56), $n = 401$
60 mo ($n = 547$)	19 (3.5)	42 (7.7)	0.77 (0.73–0.80)	0.73 (0.68–0.79), $n = 269$	0.74 (0.68–0.79), $n = 278$

CI, confidence interval; KFRE, Kidney Failure Risk Equation; ROC, receiver operating characteristic.

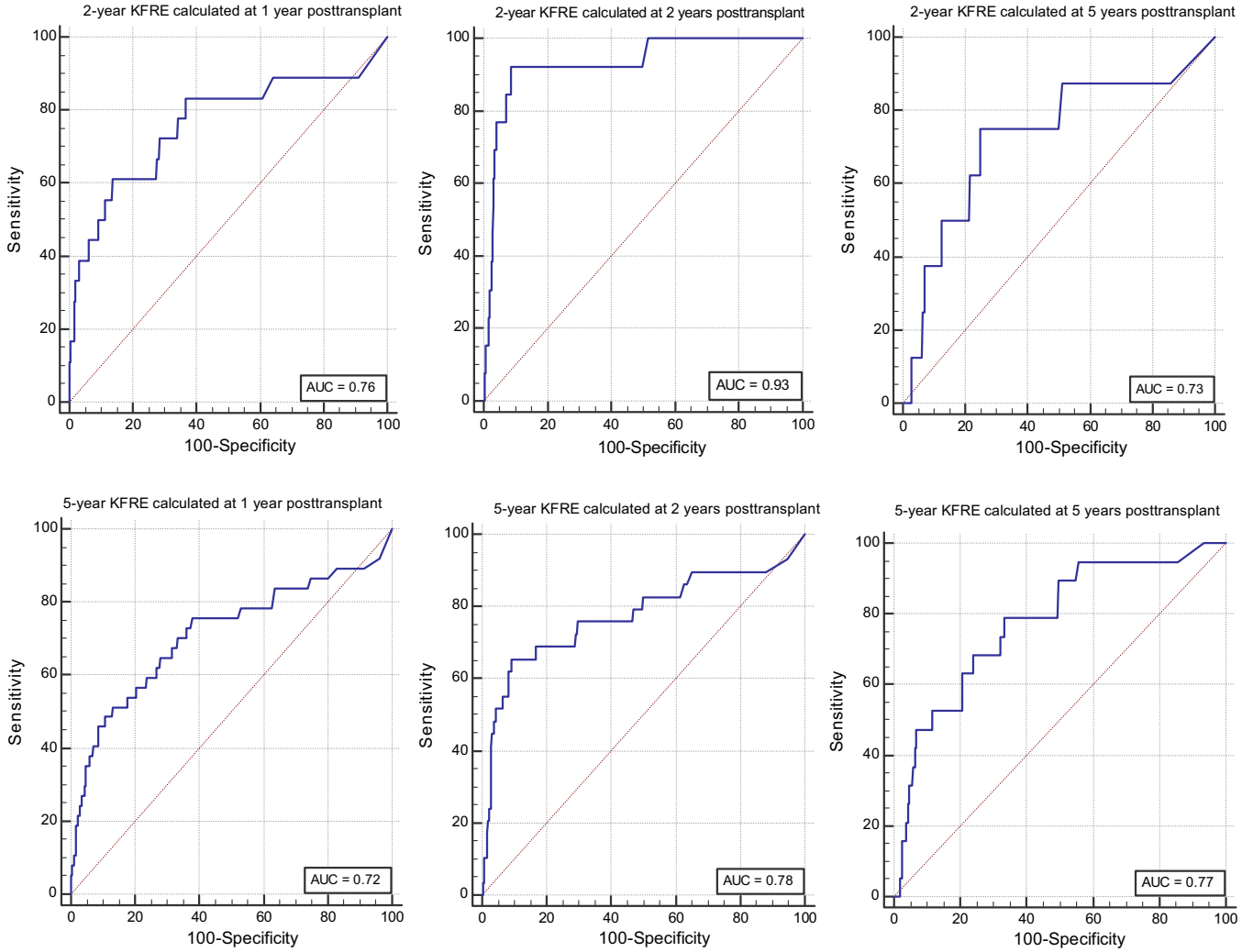

Figure 1. Receiver operating characteristic curve figures. AUC, area under the curve; KFRE, Kidney Failure Risk Equation.

able to obtain data on >90% of the patients. We did not have data on use of antirejection medications or on rejection episodes of patients. Although the number of patients included in the study was large, the number of outcomes recorded during the study period was moderate. We may not be able to extrapolate our results to patients surviving with kidney transplant to later time points, as we calculated the KFRE at only 1, 2, and 5 years posttransplant. Finally, 86% of the population was white, and the racial homogeneity of the study population means that the results might not be generalizable to other settings.

Strengths of our study include the large number of patients, a robust outcomes assessment, and that all laboratory data were extracted directly from the laboratory system at the center.

CONCLUSION

The KFRE is a useful tool to prognosticate kidney transplant recipients for ESKD at different time points if they have survived without ESKD for 1 year. Clinicians should use the KFRE for prognostication of their patients, and high-risk patients should be referred back to transplant centers (if followed elsewhere), aggressiveness of treatment should be assessed when there is a high risk of ESKD in the short term, and consideration should be given to prepare high-risk patients for dialysis or retransplantation.

DISCLOSURE

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Study Methods.

Supplementary References.

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Acute Kidney Injury Following Eastern Russell's Viper (*Daboia siamensis*) Snakebite in Myanmar

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Snakebite is a neglected tropical disease of global importance affecting at least 2.5 million people with more than 100,000 deaths annually.[1,2] Morbidity and mortality are high in countries such as Myanmar, where recent hospital data reported 15,000 to 20,000 cases per year with case-fatality ratio of 10.9%.[3] Experience elsewhere suggests that hospital-based data may underestimate the actual burden of snakebite by more than two-thirds.[4,5]

To assess outcomes of snakebite cases at Mandalay General Hospital, we established a clinical data collection system. This major hospital serves as a regional referral center for snakebite. In this region of Myanmar, Eastern Russell's Viper (ERV; *Daboia siamensis*) snakebite is of the utmost importance given the high incidence of acute kidney injury (AKI) following envenoming.[6,7]

The primary purpose of this clinical audit, which represents one arm of an Australian Department of Foreign Affairs and Trade–funded foreign aid project to improve the outcomes of snakebite patients in Myanmar,[8] is to provide accurate information to local health authorities to improve health care policies and resource allocation. In addition, we wanted to examine the clinical variables that affect the development of AKI following ERV envenoming. We report 12 months of observational data pertaining to ERV snakebites.