Kidney Diseases

Research Article

Kidney Dis
DOI: 10.1159/000531329

Received: August 13, 2022
Accepted: May 23, 2023
Published online: June 6, 2023

Development and Validation of a Nomogram for Renal Survival Prediction in Patients with Autosomal Dominant Polycystic Kidney Disease

Xiaomei Wang[a, b] Rui Zheng[c] Zhende Liu[d] Ling Qi[a] Liang Gu[a]
Xiaoping Wang[a] Shan Zhu[a] Mingyue Zhang[e] Danya Jia[a] Zhen Su[a]

[a]Department of Nephrology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China; [b]Department of Nephrology, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou, China; [c]Department of Critical Care Medicine, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China; [d]Research Center for Intelligent Supercomputing, Zhejiang Laboratory, Hangzhou, China; [e]Department of Radiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China

Keywords
Nomogram · Autosomal dominant polycystic kidney disease · Renal survival · Prediction model · End-stage renal disease

Abstract
Introduction: Due to the wide variation in the prognosis of autosomal dominant polycystic kidney disease (ADPKD), prediction of risk of renal survival in ADPKD patients is a tough challenge. We aimed to establish a nomogram for the prediction of renal survival in ADPKD patients. ***Methods:*** We conducted a retrospective observational cohort study in 263 patients with ADPKD. The patients were randomly assigned to a training set (N = 198) and a validation set (N = 65), and demographic and statistical data at baseline were collected. The total kidney volume was measured using stereology. A clinical prediction nomogram was developed based on multivariate Cox regression results. The performance and clinical utility of the nomogram were assessed by calibration curves, the concordance index (C-index), and decision curve analysis (DCA). The nomogram was compared with the height-adjusted total kidney volume (htTKV) model by receiver operating characteristic curve analysis and DCA. ***Results:*** The five independent factors used to construct the nomogram for prognosis prediction were age, htTKV, estimated glomerular filtration rate, hypertension, and hemoglobin. The calibration curve of predicted probabilities against observed renal survival indicated excellent concordance. The model showed very good discrimination with a C-index of 0.91 (0.83–0.99) and an area under the curve of 0.94, which were significantly higher than those of the htTKV model. Similarly, DCA demonstrated that the nomogram had a better net benefit than the htTKV model. ***Conclusion:*** The risk prediction nomogram, incorporating easily assessable clinical parameters, was effective for the prediction of renal survival in ADPKD patients. It can be a useful clinical adjunct for clinicians to evaluate the prognosis of ADPKD patients and provide individualized decision-making.

Xiaomei Wang, Rui Zheng, and Zhende Liu have contributed equally to this work.

karger@karger.com
www.karger.com/kdd

Correspondence to:
Zhen Su, cnsuzhen@wmu.edu.cn

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the fourth most common cause of end-stage renal disease (ESRD) and accounts for 5–10% of all ESRD [1, 2]. It is caused by genetic mutations in which the two main pathogenic genes are polycystin 1 (PKD1) (about 80%) and polycystin 2 (PKD2) (about 15%) [3, 4], although more than 1,400 pathogenic mutations have been reported that can result in ADPKD [4]. These mutations lead to the development and irreversible expansion of bilateral renal cysts, resulting in the progressive deterioration of renal function [5]. The incidence of ADPKD is approximately 1:1,000–1:2,500 [6–8], with 50% of these patients reaching ESRD between the ages of 50 and 60 years [9]. Due to the causal heterogeneity, the prediction of renal prognosis in ADPKD patients is a challenging task for clinicians. There is thus a significant need for the development of convenient and reliable models for the prediction of renal survival to optimize the treatment of patients with ADPKD.

Previous studies have reported a variety of key predictors associated with ADKPD progression, including PKD1 mutation [9], total kidney volume (TKV) [9], early eGRF decline [10, 11], female with multiple pregnancies [12], hypertension [11, 13, 14], age [11, 15], male [9, 11], obesity [16], and proteinuria [14], among others [2, 17, 18]. Of these, height-adjusted total kidney volume (htTKV) and mutations in PKD1 are the most commonly used prognostic indicators [19]. Currently, there is no single predictor that can fully predict the prognosis of ADPKD patients. Combining a series of predictive indicators may thus provide a superior predictive capability.

To date, ADPKD remains an incurable disease. Previously, treatment for patients with ADPKD has been geared toward the management of the clinical manifestations and complications, such as blood pressure control, pain relief, urinary tract infection, and kidney stones [20]. With advancements in research into the molecular mechanism of ADPKD, targeted therapy has been considered an effective treatment [21]. Drugs that can inhibit the growth of cysts have been found to be effective in slowing the rapid progression of polycystic kidney disease, but they are less effective during the early and late stages of the disease. Therefore, an effective predictive model will not only enable prognosis prediction but also the identification of patients who are most likely to benefit from early intervention [18, 22, 23].

There are few reports on prognostic models of ADPKD-related renal survival in the Chinese population. In this study, we explored predictive factors associated with ADPKD prognosis to identify a combination of several variables that could predict the progression of ADPKD to ESRD. We then developed and internally validated a nomogram to support treatment decision-making in Chinese patients with ADPKD.

Methods

Research Design and Participants

This was a single-center retrospective observational cohort study. Patients who were diagnosed with ADPKD were consecutively documented between January 2006 and December 2019 at the First Affiliated Hospital of Wenzhou Medical University and followed up until July 2022.

The inclusion criteria were as follows: (1) diagnosis of ADPKD using unified ultrasound diagnostic criteria [24]; (2) age ≥18 years; (3) patients underwent abdominal computed tomography (CT) or magnetic resonance imaging (MRI) scans at baseline with complete visualization of the kidneys on the images; (4) baseline estimated glomerular filtration rate (eGFR) >15 mL/min/1.73 m^2; (5) at least two follow-up measurements of serum creatinine before the development of ESRD. The exclusion criteria were as follows: (1) patients who had received renal replacement therapy at baseline; (2) incomplete CT or MRI images that affected the analysis; (3) no baseline and follow-up data; (4) follow-up time of less than 4 months and did not reach ESRD; (5) acute kidney injury at baseline. Consequently, a total of 263 patients with ADPKD were enrolled in the present study.

The patients were randomly assigned to a training set ($N = 198$) and a validation set ($N = 65$) using R software. This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University.

Data Collection and Follow-Up

Data were extracted from the electronic medical record system of the hospital. Patient demographic and clinical data were collected, including sex, age, body mass index, htTKV, family history, fertility history, medical history (e.g., hypertension, polycystic liver disease, hepatitis B, fatty liver, diabetes mellitus, urinary tract infection, kidney bleeding, abdominal wall hernia, kidney stones, and malignant tumors), and baseline laboratory parameters (e.g., serum creatinine, urea, nitrogen, uric acid, hemoglobin, albumin, hematuria, and proteinuria). Creatinine levels were measured enzymatically. The eGFR was calculated using the CKD-EPI equation. The baseline TKV was measured by standard abdominal CT or MRI scans and three-dimensional reconstruction using analysis software (ITK-SNAP Documentation: version 3.x). Renal volume was measured by stereology, which is consistent with the guidelines of the Mayo Clinic. The measurements of kidney volume were performed independently by two blinded and experienced clinicians, and any disagreements were resolved through discussion. The CT and MRI readings were equivalent and did not systematically overestimate or underestimate the TKV [23].

The endpoint of this study was progression to ESRD (with ESRD defined as eGFR <15 mL/min per 1.73 m^2). Renal survival was defined as the time from the baseline assessment to ESRD (in months). In addition, the patients who did not develop ESRD were classified as having censored values at the time of the last follow-

up. After the first evaluation, patients were regularly followed up and monitored in the internal medicine clinic, and laboratory examinations were performed when indicated.

Statistical Analysis

The normality of the data distribution of all variables was assessed by the Kolmogorov-Smirnov test. Continuous variables with normal distribution were expressed as mean ± standard deviation, whereas continuous variables with non-normal distribution were described as the median and interquartile range. Categorical variables were expressed as numbers (percentages).

The χ^2 test (categorical variables), one-way ANOVA (normally distributed variables), or Kruskal-Wallis H test (non-normally distributed variables) were used to analyze the differences between different groups. Due to the potential prognostic value of the clinical variables, univariate Cox regression analysis was used for the preliminary identification of clinical risk factors related to renal survival in the training set. All factors with $p < 0.05$ in the univariate Cox analysis were included in the multivariate Cox regression. The backward stepwise selection of the Akaike Information Criteria (AIC) was used to identify the significantly relevant variables [25]. The hazard ratios and 95% confidence intervals were computed.

Significant variables identified by the multivariate Cox regression were used to construct a nomogram for the prediction of 3- and 5-year renal survival. The performance of the nomogram was evaluated by discrimination and calibration analyses in the training and validation sets. Discrimination was measured by Harrell's concordance index (C-index) [26], and calibration was evaluated using calibration plots. The calibration plot was a graphic representation of the relationship between the observed frequencies and the predicted probabilities, with a bootstrapped sample. Furthermore, receiver operating characteristic analysis was conducted to assess and compare the discrimination of the nomogram to the htTKV model for the prediction of 3- and 5-year survival using the area under the curve (AUC) values. To evaluate the clinical utility of the nomogram, decision curve analysis (DCA) was carried out to quantify the net income under different threshold probabilities [27]. All statistical analyses were performed in R software (version 3.4.4, http://www.R-project.org) and Empower Stats software (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA). p values <0.05 were considered statistically significant. R libraries and codes used in this study were presented in the online supplementary materials (for all online suppl. material, see https://doi.org/10.1159/000531329).

Results

Patient Characteristics

The clinical characteristics of the 198 ADPKD patients in the training cohort and 65 patients in the validation cohort are shown in Table 1. The median follow-up time was 53 months (31–81.5) and 45 months (28–71) for training and validation sets, respectively. Of the 263 ADPKD patients, 175 patients (66.5%) showed renal survival during follow-up, while 88 patients (33.5%) developed ESRD.

Identification of Factors Associated with Renal Survival

Univariate Cox regression analysis (Table 2) showed that baseline age, htTKV, eGFR, hypertension, hemoglobin, albumin, uric acid, serum urea, and urine protein were significantly associated with renal survival, and these variables were included in the multivariate regression analysis. The multivariate analysis confirmed that age ($p = 0.008$), htTKV ($p = 0.036$), eGFR ($p < 0.001$), hypertension ($p < 0.001$), and hemoglobin ($p < 0.001$) were independently associated with renal survival (Table 2), and all of these factors constituted the final model based on the backward stepwise selection of the Akaike Information Criteria (AIC) (Table 3). Overall, ADPKD patients with larger TKVs, early onset of hypertension, lower eGFR, and lower hemoglobin were at higher risk of progression to ESRD. On the other hand, albumin, uric acid, blood urea nitrogen, and urine protein were not independently associated with renal survival.

Development of the Nomogram

Based on the final stepwise (stepAIC) selected multivariate Cox regression model, a nomogram (Fig. 1) with five independent factors (age, htTKV, eGRF, hypertension, and hemoglobin) was established to predict the 3-year and 5-year probabilities of renal survival in the training set. Briefly, the nomogram located the position of each variable on the corresponding axis, and a straight line was drawn from the point on the axis to obtain the number of points. The points were summed, and a straight line was drawn from the total-point axis to the 3- and 5-year renal survival axes to predict the risk of progression in ADPKD patients.

Performance and the Clinical Utility of the Nomogram

To validate the performance of the nomogram, an internal verification using a 1,000-times bootstrapped calibration test was performed. The nomogram demonstrated an excellent difference in estimating the likelihood of renal survival, with an unadjusted C-index of 0.91 (95% confidence interval: 0.83–0.99) and a bootstrap-corrected C-index of 0.90. In addition, the calibration plot showed that the prediction of renal survival corresponded with the actual survival data in the training set (Fig. 2a, c) and the validation set (Fig. 2b, d).

The nomogram was compared with the htTKV model in the training and validation sets to further evaluate its predictive ability. Receiver operating characteristic analysis indicated that the nomogram was superior to htTKV alone (3-year AUC 0.910 vs. 0.681 for the training set, 0.941 vs. 0.732 for the validation set, and 5-year AUC

Table 1. Characteristics of patients in the training set and validation sets

Parameters, median [25–75p]/number (%)	Training set, *n* = 198	Validation set, *n* = 65	*p* value
Gender			0.173
Female, *n* (%)	86 (43.4)	22 (33.8)	
Male, *n* (%)	112 (56.6)	43 (66.2)	
Age, years	49.0 [40.2–58.8]	52.0 [38.0–60.0]	0.561
htTKV, mL/m	687.7 [455.0–1,125.0]	613.2 [456.5–950.1]	0.224
eGFR, mL/min/1.73 m^2	77.1 [48.7–101.6]	65.6 [38.1–98.3]	0.389
BMI, kg/m^2	22.5 [21.0–24.6]	23.7 [20.3–25.6]	0.059
Hemoglobin, g/L	125.0 [112.0–139.8]	130.0 [117.0–144.0]	0.124
Albumin, g/L	40.3 [36.8–44.1]	42.5 [37.4–45.5]	0.066
Uric acid, μmol/L	349.5 [274.5–415.8]	415.5 [296.8–492.0]	0.002
Serum urea, mmol/L	6.5 [5.3–8.4]	7.3 [5.6–10.1]	0.121
Renal survival, months	53.0 [31.0–81.5]	45.0 [28.0–71.0]	0.134
Family history, yes, *n* (%)	85 (42.9)	33 (51.6)	0.228
Fertility history, *n* (%)			0.338
Men and no birth	125 (63.1)	46 (70.8)	
1–2 (one or two pregnancies)	58 (29.3)	13 (20.0)	
>2 (three or more pregnancies)	15 (7.6)	6 (9.2)	
Viral hepatitis B, yes, *n* (%)	20 (10.1)	5 (7.7)	0.566
Fatty liver, yes, *n* (%)	15 (7.6)	6 (9.2)	0.669
Abdominal wall hernia yes, *n* (%)	8 (4.0)	2 (3.1)	0.725
Kidney stones, yes, *n* (%)	77 (38.9)	23 (35.4)	0.614
Polycystic liver, yes, *n* (%)	164 (82.8)	53 (81.5)	0.812
Urinary tract infection, yes, *n* (%)	43 (21.7)	10 (15.4)	0.269
Diabetes, yes, *n* (%)	8 (4.0)	5 (7.7)	0.239
Malignant tumor, yes, *n* (%)	17 (8.6)	7 (10.8)	0.596
Hypertension, yes, *n* (%)	152 (76.8)	49 (75.4)	0.820
Urine protein, yes, *n* (%)	67 (34.0)	25 (39.1)	0.462
Hematuria, yes, *n* (%)	61 (31.0)	15 (23.4)	0.250
Kidney bleeding, yes, *n* (%)	38 (19.2)	8 (12.3)	0.205

htTKV, height-adjusted total kidney volume; eGFR, estimated glomerular filtration rate; BMI, body mass index.

0.963 vs. 0.743 for the training set, 0.928 vs. 0.710 for the validation set) in predicting the 3-year probability of renal survival (Fig. 3a, b) and the 5-year probability of renal survival (Fig. 3c, d). Lastly, DCA was used to compare the clinical utility of the nomogram to that of the model based on htTKV. This showed that the screening strategy of the nomogram using the estimates for the likelihood of renal survival provided a better net benefit than htTKV alone (Fig. 4).

Discussion

Based on the demographic and clinical characteristics data from a cohort of Chinese ADPKD patients, we developed and validated a visual nomogram model for ADPKD patients to predict kidney prognosis. Earlier age, larger baseline TKV, lower eGFR, lower hemoglobin, and hypertension were significantly associated with renal survival. In this study, the baseline age is associated with prognosis. It is not that younger patients have a worse prognosis, but rather that patients who experience symptoms at an earlier age have a worse prognosis, which is consistent with clinical observations. The nomogram accurately predicted the probability of renal survival, with a bootstrapped corrected C-index of 0.90.

The number of patients with ESRD is increasing yearly, leading to significant medical expenses that place a heavy socioeconomic burden on the patients, families, and the country [28, 29]. Given that there are significant differences in the natural history of individuals with polycystic kidney disease, some patients will rapidly progress to ESRD before the age of 40, while others do not need renal replacement therapy during their lives. Current knowledge of the molecular mechanisms underlying polycystic kidney disease has confirmed that a variety of drugs can

Table 2. Cox regression models of variables associated with renal survival outcomes

	Renal survival					
	univariate analysis			multivariate analysis		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Gender (male vs. female)	1.34	0.86–2.09	0.196			
Age, years	1.02	1.01–1.04	0.008	0.97	0.94–0.99	0.008
BMI, kg/m^2	1.04	0.97–1.11	0.257			
htTKV, mL/m	1.00	1.00–1.00	<0.001	1.00	1.00–1.00	0.036
eGFR, mL/min/1.73 m^2	0.95	0.94–0.96	<0.001	0.94	0.92–0.95	<0.001
Family history (yes vs. no)	1.16	0.76–1.77	0.490			
Fertility history						
Men and no birth	Reference	Reference	Reference			
1–2 (one or two pregnancies)	0.80	0.48–1.33	0.383			
>2 (three or more pregnancies)	1.94	0.96–3.93	0.066			
Viral hepatitis B (yes vs. no)	1.12	0.56–2.23	0.756			
Fatty liver (yes vs. no)	0.37	0.12–1.17	0.092			
Abdominal wall hernia (yes vs. no)	0.34	0.05–2.42	0.280			
Kidney stones (yes vs. no)	0.87	0.56–1.37	0.561			
Polycystic liver (yes vs. no)	1.72	0.83–3.57	0.144			
Urinary tract infection (yes vs. no)	0.77	0.45–1.32	0.340			
Diabetes (yes vs. no)	1.62	0.70–3.73	0.256			
Malignant tumor (yes vs. no)	0.76	0.31–1.87	0.547			
Hypertension (yes vs. no)	2.45	1.30–4.62	0.006	3.62	1.76–7.44	<0.001
Hemoglobin, g/L	0.98	0.97–0.99	<0.001	0.98	0.96–0.99	<0.001
Albumin, g/L	0.97	0.94–1.00	0.028	1.02	0.98–1.07	0.358
Uric acid, μmol/L	1.01	1.00–1.01	<0.001	1.00	1.00–1.00	0.335
Serum urea, mmol/L	1.19	1.15–1.24	<0.001	1.05	0.99–1.11	0.120
Urine protein (yes vs. no)	3.26	2.10–5.04	<0.001	1.42	0.87–2.30	0.160
Hematuria (yes vs. no)	1.20	0.77–1.87	0.425			
Kidney bleeding (yes vs. no)	1.39	0.85–2.27	0.191			

htTKV, height-adjusted total kidney volume; eGFR, estimated glomerular filtration rate; BMI, body mass index; HR, hazard ratio; CI, confidence interval.

Table 3. Stepwise (stepAIC)-selected model from the multivariate Cox regression analysis

Parameters	Coefficient	HR	95% CI	*p* value
Age, years	−0.0454	0.956	0.931–0.981	<0.001
htTKV, mL/m	0.0003	1.000	1.000–1.001	0.139
eGFR, mL/min/1.73 m^2	−0.0636	0.938	0.924–0.954	<0.001
Hypertension, yes, *n* (%)	1.5055	4.507	1.639–12.394	0.004
Hemoglobin, g/L	−0.0251	0.975	0.962–0.989	<0.001

htTKV, height-adjusted total kidney volume; eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, confidence interval.

slow down the growth of kidney cysts, leading to opportunities for targeted therapy. Thus, an effective prognostic model is essential for the selection of high-risk patients for which intervention can be instituted early. Moreover, the use of a prognostic model can improve the patient's knowledge and understanding of the individual risk of progression to ESRD. Our low-risk, low-cost model identifies patients likely to show rapid disease progression, which will aid clinical decision-making in individualized management plans.

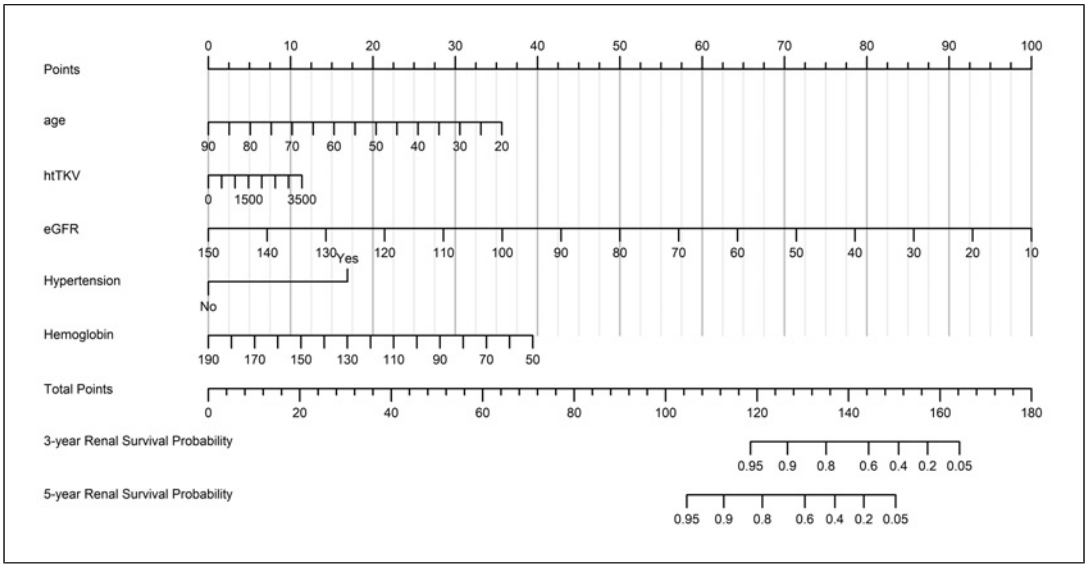

Fig. 1. Nomogram was constructed using the factors age, htTKV, eGRF, hypertension, and hemoglobin to estimate the probabilities of 3- and 5-year renal survival in patients with ADPKD.

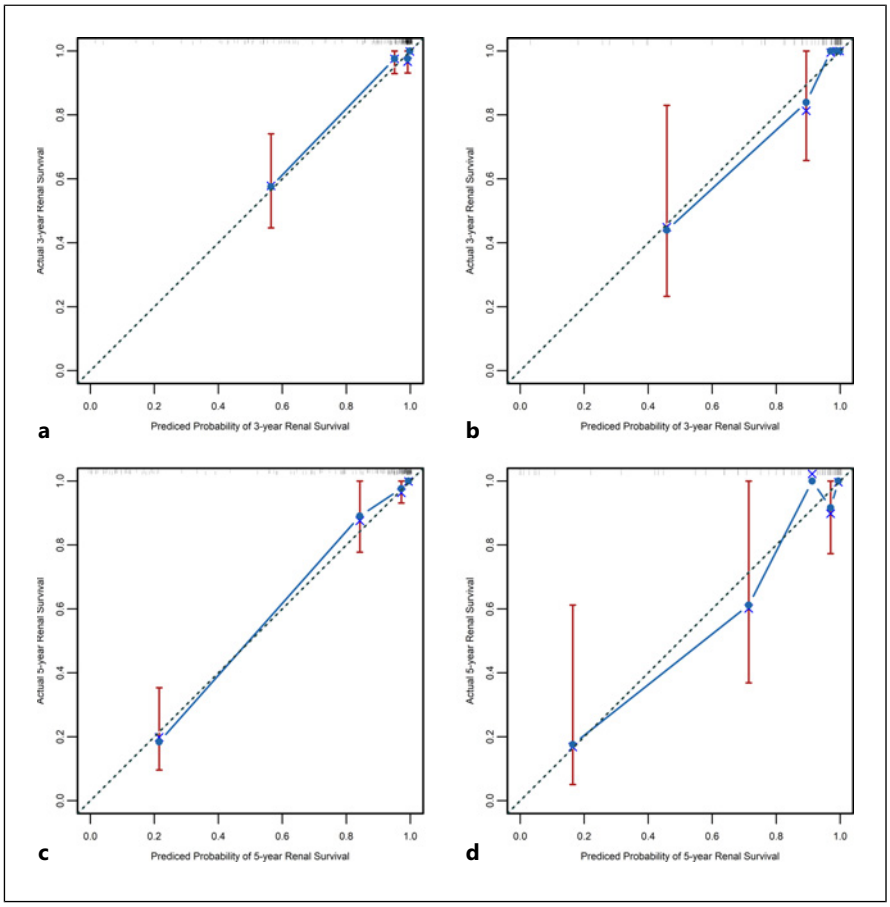

Fig. 2. Validation of the predictive performance of the nomogram in estimating renal survival probability. **a** Three-year probability of renal survival in the training cohort. **b** 3-year probability of renal survival in the validation cohort. **c** 5-year probability of renal survival in the training cohort. **d** 5-year probability of renal survival in the validation cohort.

Several studies have confirmed that the htTKV is an important predictor of eGFR decline, resulting in its use as a prognostic biomarker in clinical trials [30]. The study by Chapman et al. [30] (the CRISP cohort study) found that an htTKV >600 mL/m predicted the risk of stage 3 CKD over an 8-year follow-up. A further study using a

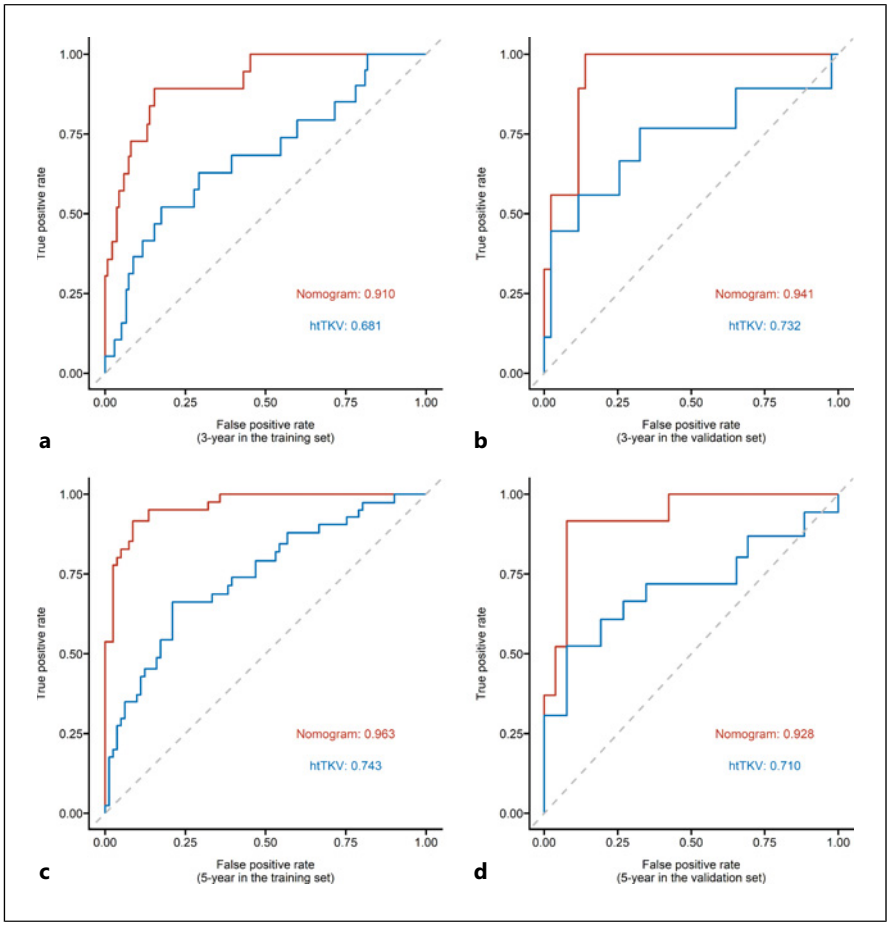

Fig. 3. Comparison of receiver operating characteristic (ROC) curves for prediction of renal survival probability. ROC curves for the nomogram and htTKV in the 3-year renal survival probability in the training (**a**) and validation sets (**b**). ROC curves for the nomogram and htTKV in the 5-year renal survival probability in the training (**c**) and validation sets (**d**).

median follow-up of 13 years found that the TKV was associated with a 57% decline in GFR and progression to ESRD [31]. Irazabal et al. [23] established an image-based model utilizing baseline age and htTKV to predict the GFR decline in ADPKD patients with typical imaging findings. However, this model was less accurate for patients with atypical imaging findings. The present study also confirmed that htTKV was a biomarker of renal prognosis. However, our nomogram displayed better predictive performance and clinical utility than htTKV for predicting the likelihood of ESRD development [32]. Additionally, the nomogram, compiled using five independent factors (age, htTKV, eGRF, hypertension, and hemoglobin), quantified the magnitude of the association of each of these five factors with the likelihood of progression to ESRD.

In addition, mutation in PKD1 is another factor that is often used for prognostication in many studies, whereby patients with PKD1 mutations have a more severe clinical phenotype and younger age at presentation with kidney failure (median age 54.3 [52.7–55.9] vs. 74.0 [67.2–80.8] years) than patients with PKD2 mutations [9, 33]. However, the prognosis of individuals with the same genetic mutations varies. Interestingly, Yu et al. [31] have reported that genotype is no longer an independent predictor after adjustment for baseline htTKV.

The PROPKD score developed by Cornec-Le Gall et al. [34] is a new algorithm for predicting kidney survival in ADPKD patients [35]. This was based on four variables, including the genotype, and the total scores of these predictors were categorized into three types of ESRD risk, namely, low-risk, medium-risk, and high-risk, which corresponded to the ages of ESRD development at 70.6, 56.9, and 49 years old, respectively. Given that PROPKD scoring requires genetic analysis, the associated high cost has limited its use in clinical practice. In addition, based on the patient data in the TEMPO 3:4 placebo group [36], McEwan et al. [20] proposed the ADPKD-OM model which predicts annual changes in TKV and eGFR. This model appears appropriate for patients with early disease and good renal function, but it is not effective in predicting the late stage of the disease.

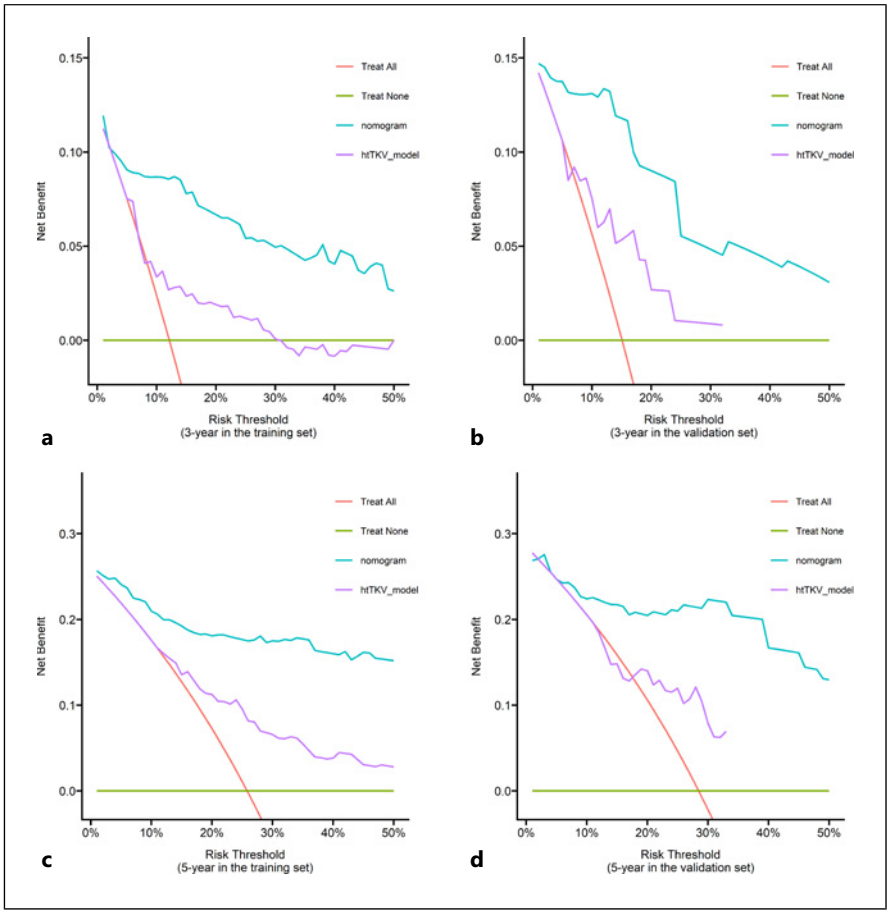

Fig. 4. DCA of the nomogram. Decision curves of the nomogram and htTKV to predict 3-year renal survival probability in the training (**a**) and validation sets (**b**), and 5-year renal survival probability in the training (**c**) and validation sets (**d**).

Li et al. [36] constructed a nomogram based on MRI T1 and T2 radiomic features for the evaluation of renal function in ADPKD. Using univariate logistic regression analysis, the radiomic nomogram model showed an AUC of 0.8435 in the assessment of the risk of GFR <60 mL/min per 1.73 m^2. However, this was a small-sample cross-sectional study, and more data support is needed.

Our study incorporated clinical variables that may be related to prognosis, albeit without including the variable of gene mutation. As is well known, genetic testing is not only costly but also not available in most hospitals. Besides, the genotype is the main determinant of the baseline TKV, as has been shown in several studies, and is thus an external manifestation of the genotype that fully represents the predictive value of genotype in the model [31]. Therefore, our predictive model has wider applicability and generalizability and thus provides valuable prognostication for the Chinese ADPKD population.

To our knowledge, our risk model represents the first that uses a nomogram for the prediction of renal survival in ADPKD patients. Nomograms are widely used in tumor prognosis as they enable individualized risk estimation based on the specific characteristics of patients and diseases. The role of the nomogram in the prognosis and management of chronic diseases is increasingly accepted by clinicians [37]. The most important consideration regarding the use of nomograms is the need to further evaluate their discrimination, calibration, and clinical applicability. Generally, despite their excellent performance in risk prediction, nomograms are less accurate in capturing clinical results with a certain level of deviation or calibration error. Therefore, we conducted a DCA to ascertain the judgment of the nomogram in its clinical utility. This method is based on the threshold probability of obtaining a net benefit and provides novel insights into clinical outcomes [27]. The DCA for the prediction nomogram in ADPKD patients revealed that the screening strategy based on this nomogram for estimating the likelihood of renal survival brought better net benefit than htTKV alone.

The strengths of this study included the construction of a predictive model based on a real patient cohort in China that was completely independent of other predictive models. Our nomogram simply and clearly predicted the 3- and 5-year probabilities of renal survival in ADPKD patients, which would assist patients and clinicians in estimating the possible course of the disease and thus in strategizing a treatment plan. However, there were limitations to our study. First, the TKV was assessed by CT or MRI, of which MRI has the advantage of reduced radiation exposure. Second, the predictive nomogram was based on retrospective data from a single center, and thus future multi-center prospective studies with larger sample sizes investigating different races or populations are required for further validation of the reliability of the nomogram and its applicability in different healthcare settings.

In conclusion, this study described the construction of a nomogram that incorporated age, htTKV, eGFR, hypertension, and hemoglobin. The nomogram showed excellent performance in both the training and validation sets for predicting the likelihood of renal survival. It can thus be a useful clinical adjunct for clinicians to evaluate the prognosis of ADPKD patients and provide individualized decision-making. It is especially valuable for clinicians when strategizing treatment recommendations for ADPKD patients with rapid disease progression.

Acknowledgments

The authors thank the colleagues in the Department of Nephrology, the First Affiliated Hospital of Wenzhou Medical University, for their great support and selfless help during this study. The authors would also like to thank the doctors in the Department of Radiology, the First Affiliated Hospital of Wenzhou Medical University, for their help in the measurement of polycystic kidney volume.

Statement of Ethics

This study protocol was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University, approval number [2020-228]. As the data are anonymous, the requirement for informed consent was waived by the same Ethics Committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This work was supported by grants from the National Natural Science Foundation of China (81671403, 30871179) for Zhen Su, Zhejiang Provincial Health Science and Technology Foundation of China (2021KY203) for Zhen Su, and Special Support Plan for High-level Talents in Wenzhou – Famous Doctors in Wenzhou for Zhen Su.

Author Contributions

Xiaomei Wang was involved in study design, data collection, analysis, interpretation of results, and drafting the manuscript. Rui Zheng and Zhende Liu were involved in analysis, interpretation of results, and writing of the manuscript. Zhen Su was involved in study design, interpretation of results, and critical review of the manuscript. Ling Qi, Liang Gu, Xiaoping Wang, Shan Zhu, Mingyue Zhang, and Danya Jia were involved in data collection and writing of the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

Data are not publicly available due to ethical reasons. Further inquiries can be directed to the corresponding author.

References

1 Willey C, Kamat S. Stellhorn R, Blais J. Analysis of nationwide data to determine the incidence and diagnosed prevalence of autosomal dominant polycystic kidney disease in the USA. Kidney Dis. 2019;5(2):107–17.
2 Chapman AB, Devuyst O, Eckardt KU, Gansevoort RT, Harris T, Horie S, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a kidney disease – improving global outcomes (KDIGO) controversies conference. Kidney Int. 2015;88(1):17–27.
3 Wilson PD. Polycystic kidney disease. N Engl J Med. 2004;350(2):151–64.
4 Cornec-Le Gall E, Audrézet MP, Le Meur Y, Chen JM, Férec C. Genetics and pathogenesis of autosomal dominant polycystic kidney disease: 20 years on. Hum Mutat. 2014;35(12):1393–406.
5 Shaw C, Simms RJ, Pitcher D, Sandford R. Epidemiology of patients in England and Wales with autosomal dominant polycystic kidney disease and end-stage renal failure. Nephrol Dial Transplant. 2014;29(10):1910–8.
6 Lanktree MB, Haghighi A, Guiard E, Iliuta IA, Song X, Harris PC, et al. Prevalence estimates of polycystic kidney and liver disease by population sequencing. J Am Soc Nephrol. 2018;29(10):2593–600.
7 Willey CJ, Blais JD, Hall AK, Krasa HB, Makin AJ, Czerwiec FS. Prevalence of autosomal dominant polycystic kidney disease in the European Union. Nephrol Dial Transplant. 2017;32(8):1356–63.
8 Cornec-Le Gall E, Alam A, Perrone RD. Autosomal dominant polycystic kidney disease. Lancet. 2019;393(10174):919–35.
9 Cornec-Le Gall E, Audrézet MP, Chen JM, Hourmant M, Morin MP, Perrichot R, et al. Type of PKD1 mutation influences renal outcome in ADPKD. J Am Soc Nephrol. 2013;24(6):1006–13.
10 Torres VE, King BF, Chapman AB, Brummer ME, Bae KT, Glockner JF, et al. Magnetic resonance measurements of renal blood flow and disease progression in autosomal dominant polycystic kidney disease. Clin J Am Soc Nephrol. 2007;2(1):112–20.

11 Chen D, Ma Y, Wang X, Yu S, Li L, Dai B, et al. Clinical characteristics and disease predictors of a large Chinese cohort of patients with autosomal dominant polycystic kidney disease. PLoS One. 2014;9(3):e92232.
12 Chapman AB, Johnson AM, Gabow PA. Pregnancy outcome and its relationship to progression of renal failure in autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 1994;5(5):1178–85.
13 Schrier RW, McFann KK, Johnson AM. Epidemiological study of kidney survival in autosomal dominant polycystic kidney disease. Kidney Int. 2003;63(2):678–85.
14 Ozkok A, Akpinar TS, Tufan F, Kanitez NA, Uysal M, Guzel M, et al. Clinical characteristics and predictors of progression of chronic kidney disease in autosomal dominant polycystic kidney disease: a single center experience. Clin Exp Nephrol. 2013;17(3):345–51.
15 Higashihara E, Nutahara K, Okegawa T, Shishido T, Tanbo M, Kobayasi K, et al. Kidney volume and function in autosomal dominant polycystic kidney disease. Clin Exp Nephrol. 2014;18(1):157–65.
16 Nowak KL, You Z, Gitomer B, Brosnahan G, Torres VE, Chapman AB, et al. Overweight and obesity are predictors of progression in early autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 2018;29(2):571–8.
17 Schrier RW, Brosnahan G, Cadnapaphornchai MA, Chonchol M, Friend K, Gitomer B, et al. Predictors of autosomal dominant polycystic kidney disease progression. J Am Soc Nephrol. 2014;25(11):2399–418.
18 Ong ACM, Devuyst O, Knebelmann B, Walz G; ERA-EDTA Working Group for Inherited Kidney Diseases. Autosomal dominant polycystic kidney disease: the changing face of clinical management. Lancet. 2015;385(9981):1993–2002.
19 Woon C, Bielinski-Bradbury A, O'Reilly K, Robinson P. A systematic review of the predictors of disease progression in patients with autosomal dominant polycystic kidney disease. BMC Nephrol. 2015;16:140.
20 McEwan P, Bennett Wilton H, Ong ACM, Ørskov B, Sandford R, Scolari F, et al. A model to predict disease progression in patients with autosomal dominant polycystic kidney disease (ADPKD): the ADPKD Outcomes Model. BMC Nephrol. 2018;19(1):37.
21 Weimbs T, Shillingford JM, Torres J, Kruger SL, Bourgeois BC. Emerging targeted strategies for the treatment of autosomal dominant polycystic kidney disease. Clin Kidney J. 2018;11(Suppl 1):i27–38.
22 Gansevoort RT, Arici M, Benzing T, Birn H, Capasso G, Covic A, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. Nephrol Dial Transplant. 2016;31(3):337–48.
23 Irazabal MV, Rangel LJ, Bergstralh EJ, Osborn SL, Harmon AJ, Sundsbak JL, et al. Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. J Am Soc Nephrol. 2015;26(1):160–72.
24 Pei Y, Obaji J, Dupuis A, Paterson AD, Magistroni R, Dicks E, et al. Unified criteria for ultrasonographic diagnosis of ADPKD. J Am Soc Nephrol. 2009;20(1):205–12.
25 Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15(4):361–87.
26 Harrell F, Califf R, Pryor D, Lee K, Rosati RA. Evaluating the yield of medical tests. JAMA. 1982;247(18):2543–6.
27 Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making. 2006;26(6):565–74.
28 Szczech LA, Lazar IL. Projecting the United States ESRD population: issues regarding treatment of patients with ESRD. Kidney Int. 2004;66(90):S3–7.
29 Saran R, Robinson B, Abbott KC, Bragg-Gresham J, Chen X, Gipson D, et al. US renal data system 2019 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis. 2020;75(1 Suppl 1):A6–7.
30 Chapman AB, Bost JE, Torres VE, Guay-Woodford L, Bae KT, Landsittel D, et al. Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. Clin J Am Soc Nephrol. 2012;7(3):479–86.
31 Yu ASL, Shen C, Landsittel DP, Harris PC, Torres VE, Mrug M, et al. Baseline total kidney volume and the rate of kidney growth are associated with chronic kidney disease progression in Autosomal Dominant Polycystic Kidney Disease. Kidney Int. 2018;93(3):691–9.
32 Kattan MW, Leung DHY, Brennan MF. Postoperative nomogram for 12-year sarcoma-specific death. J Clin Oncol. 2002;20(3):791–6.
33 Hateboer N, v Dijk MA, Bogdanova N, Coto E, Saggar-Malik AK, San Millan JL, et al. Comparison of phenotypes of polycystic kidney disease types 1 and 2. European PKD1-PKD2 Study Group. Lancet. 1999. 353;(9147):103–7.
34 Cornec-Le Gall E, Audrézet M, Rousseau A, Hourmant M, Renaudineau E, Charasse C, et al. The PROPKD score: a new algorithm to predict renal survival in autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 2016;27(3):942–51.
35 Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Grantham JJ, Higashihara E, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. N Engl J Med. 2012;367(25):2407–18.
36 Li X, Liu Q, Xu J, Huang C, Hua Q, Wang H, et al. A MRI-based radiomics nomogram for evaluation of renal function in ADPKD. Abdom Radiol. 2022;47(4):1385–95.
37 Balachandran V, Gonen M, Smith J, DeMatteo RP. Nomograms in oncology: more than meets the eye. Lancet Oncol. 2015;16(4):e173–80.