External validation of yonsei nomogram predicting chronic kidney disease development after partial nephrectomy: An international, multicenter study

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Abbreviations
AKI = acute kidney injury
BMI = body mass index
CKD = chronic kidney disease
DM = diabetes mellitus
PN = partial nephrectomy
PPV = positive predictive value
RN = radical nephrectomy
RPN = robotic partial nephrectomy
WIT = warm ischemia time

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Abstract:

Objective: To externally validate Yonsei nomogram.

Methods: From 2000 through 2018, 3526 consecutive patients underwent on-clamp PN for cT1 renal masses at 23 centers were included. All patients had two kidneys, preoperative eGFR ≥60 ml/min/1.73 m2, and a minimum follow-up of 12 months. New-onset CKD was defined as upgrading from CKD stage I or II into CKD stage ≥III. We obtained the CKD-free progression probabilities at 1, 3, 5, and 10 years for all patients by applying the nomogram found at https://eservices.ksmc.med.sa/ckd/. Thereafter, external validation of Yonsei nomogram for estimating new-onset CKD stage ≥III was assessed by calibration and discrimination analysis.

Results and limitation: Median values of patients' age, tumor size, eGFR and follow-up period were 47 years (IQR: 47–62), 3.3 cm (IQR: 2.5–4.2), 90.5 ml/min/1.73 m2 (IQR: 82.8–98), and 47 months (IQR: 27–65), respectively. A total of 683 patients (19.4%) developed new-onset CKD. The 5-year CKD-free progression rate was 77.9%. Yonsei nomogram demonstrated an AUC of 0.69, 0.72, 0.77, and 0.78 for the prediction of CKD

stage ≥III at 1, 3, 5, and 10 years, respectively. The calibration plots at 1, 3, 5, and 10 years showed that the model was well calibrated with calibration slope values of 0.77, 0.83, 0.76, and 0.75, respectively. Retrospective database collection is a limitation of our study.

Conclusions: The largest external validation of Yonsei nomogram showed good calibration properties. The nomogram can provide an accurate estimate of the individual risk of CKD-free progression on long-term follow-up.

Key words: chronic kidney disease, external validation, functional outcomes, partial nephrectomy, Yonsei nomogram.

INTRODUCTION

Partial nephrectomy (PN) is the standard treatment of cT1 renal tumors when technically feasible.[1] Several studies showed that PN reduces the possibility of chronic kidney disease (CKD) development compared to radical nephrectomy (RN),[2–4] with similar oncological outcomes.[5] It is worth noting that CKD is a major health problem associated with increased risk of cardiovascular and overall mortality.[6]

Patients should be informed about the likelihood of surgical procedure success and understand the risks to help them making decisions. The nomogram is a practical and easy distinguishable tool that allows the clinician to calculate the probability of procedure success and facilitate patients' counseling. Of note, there are several nomograms that can predict renal function decline after renal surgery.[7–12] The first nomogram to predict renal insufficiency after RN and PN was introduced in 2006.[7] In 2009, Kim and colleagues assessed the risk of postoperative CKD after RN and PN, and the nomogram is consisted of age, weight, and tumor size.[8] Small number of patients, heterogeneity of the procedures (i.e., PN and RN), short-term follow-up, no external validation, and the use of serum creatinine in renal function assessment were drawbacks of both nomograms.[7,8]

Recently, two models for prediction of early postoperative renal failure and early postoperative CKD upstaging were developed.[9,10] Age, African race, ECOG performance status ≥1, diabetes mellitus (DM), hypertension (HTN), preoperative proteinuria, and larger tumor were associated with increased risk of early postoperative renal failure following RN and PN,[9] whereas, age, female gender, body mass index (BMI), baseline eGFR, and warm ischemia time (WIT) were predictors of early postoperative CKD upstaging after PN.[10] Following robotic partial nephrectomy (RPN), a nomogram was developed to predicts ≥25% reduction from baseline eGFR with an internally validated c-index of 73% and composed of the following variables age, sex, Charlson comorbidity index, baseline eGFR, RENAL nephrometry score, and acute kidney injury (AKI).[11]

We developed Yonsei nomogram to predict new-onset CKD stage ≥III occurrence following on-clamp PN in Korean patients with an internally validated c-index of 73%. However, absence of external validation and racial differences were main drawbacks of our nomogram which raised concerns about its generalizability.[12] Thus, in the present study we aimed to confirm our primary results through the external validation of Yonsei nomogram using a large multi-institutional cohort of patients.

METHODS

Study design and ethics

The present study is a retrospective international multicenter study. It was approved by the institutional review board of participating centers (IRB approval number: H1RI-11-Feb19-02).

Study population

We reviewed patients who received PN for cT1 renal tumors between 2000 and 2018 at 23 centers from Europe (Italy, UK, Germany, Spain, Belgium), North American (USA), Asia (South Korea, Saudi Arabia, Philippines) and Africa (Egypt). We excluded patients with solitary kidney (n = 151), preoperative eGFR <60 ml/min/1.73 m^2 (n = 226), multiple tumors (n = 124), follow-up <12 months (n = 437), incomplete or missed Yonsei nomogram variables (n = 513), history of kidney cancer or upper tract urothelial carcinoma (n = 40), metastatic disease (n = 21), conversion to RN (n = 61), and different clamp "selective and/or off clamp" or ischemia technique (n = 228). Of note, Korean patients of the original nomogram were not included in the present study.

Clinical variables

The demographic data of the external validation cohort includes age, BMI, gender, the American society of anesthesiologist (ASA) classification, tumor size (cm), tumor complexity assessed by R.E.N.A.L. nephrometry score, preoperative eGFR (ml/min/1.73 m^2), preoperative CKD classification, presence or absence of proteinuria, PN surgical technique (i.e., open PN, laparoscopic PN, or robotic-assisted PN), WIT, and chronic medial comorbidities such as DM and HTN.

Renal function follow-up

The preoperative renal function was evaluated based on the eGFR value, which was calculated using the Modification of Diet in Renal Disease (MDRD) formula.[13] During follow-up until the last outpatient visit, eGFR measurements were retrieved for patients at 1, 3, 5, and 10 years. The CKD staging before and after surgery was classified according to the National Kidney Foundation practice guidelines.[14] CKD stage I and stage II were defined as eGFR values of ≥90 and 89–60 ml/min/1.73 m^2, respectively. New-onset CKD "progression" was defined as decrease of eGFR from CKD stage I or

II into CKD stage ≥III (i.e., eGFR value <60 ml/min/1.73 m^2), on at least two subsequent measurements any time postoperatively.

Study outcomes

The primary endpoint of our study was to externally validate the Yonsei nomogram (Figure 1a) by estimating the probability of new-onset CKD free-progression in a large multi-institutional study.

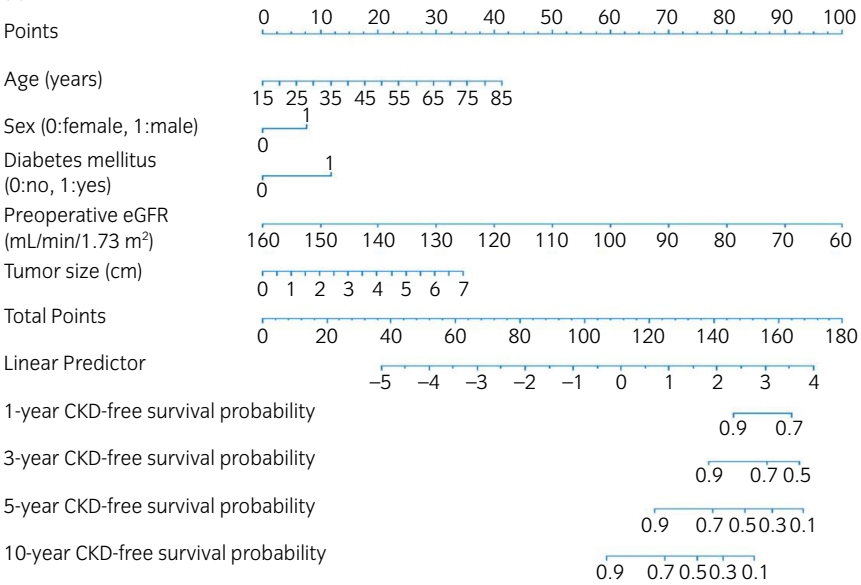
Online nomogram

An online version of Yonsei nomogram is available at https://eservices.ksmc.med.sa/ckd/ (Figure 1b). The nomogram is composed of five variables including, the patient's age (years), patient's gender (male or female), tumor size (cm), DM status (yes or no), and preoperative eGFR value (ml/min/1.73 m^2).[12] We used the online nomogram to evaluate each patient separately in the external validation cohort. After data entry, the software automatically calculated the probability of new-onset CKD free-progression at 1, 3, 5 and 10 years following PN (Figure 1b).

Statistical analysis

We report mean ± (SD) or median (IQR) for continuous variables, whereas categorical variables are described by their frequency (percentages). Kaplan–Meier plots was used to depict CKD-free progression rates. We used new-onset CKD

(a)



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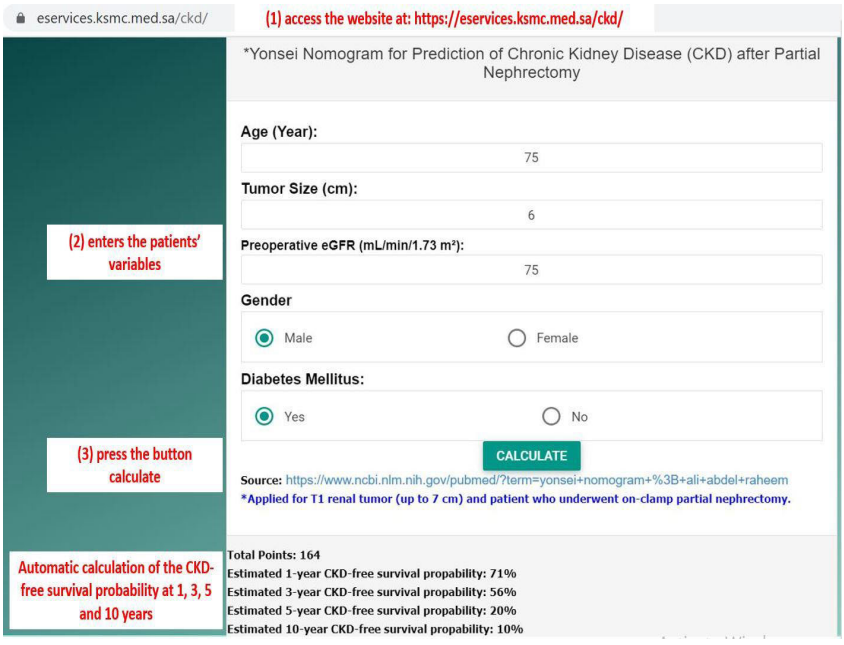


FIGURE 1 (a) The original Yonsei nomogram.[10] Each variable value is assigned a score on each axis, and the sum of scores "total points" is converted to a probability of observed events in the lowest scale. (b) The online calculator used for automatic calculation of the CKD-free survival probability at 1, 3, 5 and 10 years after on-clamp PN as follow: (1) access the website at: https://eservices.ksmc.med.sa/ckd/, (2) enters the patients' variables, and (3) press the button calculate. An example of a 75-years-old diabetic male, with a preoperative eGFR of 75 ml/min/1.73 m2 and a 6 cm renal mass is shown in the figure.

from observed CKD-free progression and the probability of new-onset CKD from CKD-free progression probability at 1, 3, 5, and 10 years to quantify model's discrimination and calibration performance.

Model's discrimination was measured by the C statistic or Harrell's concordance index,[15] i.e., the area under the receiver operating curve (ROC) curve (AUC). We used the bootstrap percentile method with 2000 replicates to obtain the 95% confidence interval (CI). The C-statistic can range from 0.5 to 1, a concordance index of 0.5 indicates that there is no predictive discrimination, whereas higher values indicate better predictive models and a higher ability to discriminate patients.

Calibration was quantified by the calibration slope and visualized[16] by plotting the observed versus predicted new-onset CKD across quantiles of predicted probabilities at 1, 3, 5, and 10 years. The calibration slope is the measure of agreement between the observed and the predicted risk and its value should be ideally equal 1. Calibration plots show the fitted logistic calibration curves along with a smooth non-parametric fit, obtained using locally weighted scatterplot smoothing. Moreover, grouped proportions vs. mean predicted probability in the group are displayed.

Statistical analysis was done using SPSS version 23 software (IBM SPSS Statistics, IBM Corp.) and R, version 4.0.0.[17] To compute AUC (CI), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), we used R library pROC.[18] While for calibration plots we used package rmda and package rms, respectively.[19] All tests were two-sided and statistical significance was set at 0.05.

RESULTS

Study population

Table 1 show the demographic data for external validation cohort and Yonsei nomogram development cohort. Between 2000 and 2018, 3526 patients met our inclusion criteria and were enrolled in the current study including 2384 males (67.6%). Median patients' age was 47 years (IQR: 27–65), median BMI was 26 kg/m^2 (IQR: 24–29) and median tumor size was 3.3 cm (IQR: 2.5–4.2). Preoperatively, median eGFR was 90.5 (IQR: 82.8–98) and the number of patients with CKD stage I and stage II were 1673 (47.4%) and 1853 (52.6%), respectively. At a median follow-up of 47 months, a total of 683 patients (19.4%) upgraded into CKD stage ≥III. The actuarial CKD-free progression rate at 1, 3, 5 and 10 years were 98.4%, 89.9%, 77.9%, and 35.8%, respectively (Figure 2).

TABLE 1 Descriptive statistics of external validation cohort and development cohort

Variables	External validation cohort	Development cohort
No. of patients	3526	698
Age (year), median (IQR)	54 (47–62)	52 (44–62)
BMI (kg/m^2), median (IQR)	26 (24–29)	24.1 (22.4–26.1)
Male, *n* (%)	2384 (67.6)	459 (65.8)
ASA score, *n* (%)		
1	1576 (44.7)	384 (55)
≥2	1946 (55.2)	314 (45)
DM, *n* (%)	578 (16.4)	69 (9.9)
HTN, *n* (%)	1501 (42.6)	221 (31.7)
Tumor size (cm), median (IQR)	3.3 (2.5–4.2)	2.5 (1.7–3.6)
R.E.N.A.L. score, median (IQR)	6 (6–9)	6 (5–8)
Baseline eGFR (ml/min/1.73m^2), median (IQR)	90.5 (82.8–98)	90.5 (80–102)
Proteinuria, *n* (%)	406 (11.5)	18 (2.6)
Preoperative CKD		
CKD I	1673 (47.4)	360 (51.6)
CKD II	1853 (52.6)	338 (48.4)
Last CKD		
CKD I	1017 (28.8)	309 (44.3)
CKD II	1826 (51.8)	298 (42.7)
CKD III	640 (18.2)	89 (12.8)
CKD IV	31 (0.9)	2 (0.3)
CKD V	12 (0.3)	0 (0)
New-onset CKD, *n* (%)	683 (19.4)	91 (13.1)
CKD free-progression probability (%)		
1-year	98.4	97.1
3-year	89.9	94.4
5-year	77.9	85.3
10-year	35.8	70.6
Surgical technique, *n* (%)		
Open PN	1465 (41.5)	245 (35.1)
Laparoscopic PN	536 (15.2)	95 (13.6)
Robotic PN	1525 (43.3)	358 (51.3)
WIT (min.), median (IQR)	22 (17–25)	28 (20–36.3)
Follow-up (months), median (IQR)	47 (27–65)	60 (44–74)

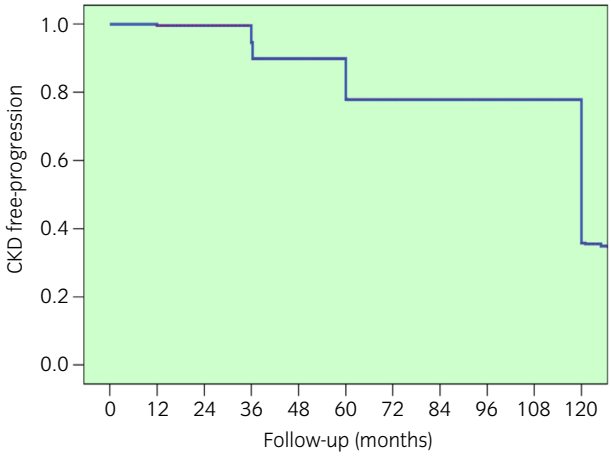
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension; IQR, interquartile range; PN, partial nephrectomy; SD, standard deviation; WIT, warm ischemia time.

Calibration and discrimination

For patients undergoing PN, Yonsei nomogram demonstrated an AUC of 0.69 (95% CI = [0.66; 0.73]), 0.72 (95% CI = [0.69; 0.74]), 0.77 (95% CI = [0.75; 0.79]), and 0.78 (95% CI = [0.76; 0.80]) for the prediction of new-onset CKD at 1, 3, 5, and 10 years, respectively (Figure 3). At best cut-off values according to Youden index method, i.e., 5%, 11%, 21%, 44%, the nomogram showed high specificity, good sensitivity, and high NPVs ranging from 72% to 86%, 50% to 73%, and 87% to 92%, respectively (Figure 3). The calibration plots showed that the risk model is well calibrated, indicating strong predictor effects. The calibration slope value was 0.77 at 1 year, 0.83 at 3 years, 0.76 at 5 years, and 0.75 at 10 years (Figure 4).

DISCUSSION

Postoperative renal function preservation is one of the main goals of PN. There is growing interest in evaluating preoperative predictors of renal function decline after PN, for proper patients' counseling regarding the optimal surgical procedure and treatment outcomes. Several risk factors were identified including, age, BMI, medical comorbidities, gender, tumor size, preoperative eGFR, type and duration of renal ischemia,



Duration (months)	0	12	36	60	120
No. of CKD events	0	16	141	468	619
No. of patients at risk	3526	3506	2369	1232	147

FIGURE 2 Kaplan–Meier curve showing CKD-free survival after PN

surgical approach (i.e., open, laparoscopic, and robotic), and quality and quantity of preserved renal parenchyma.[7–12,20–23] The surgical approach is one of the modifiable factors that might affect renal functional outcomes. At a median 5-yrs follow-up, LPN and OPN were associated with a significantly higher incidence of CKD upstaging compared with RPN (32%, 33.6%, and 20.5%, respectively).[24] In our cohort, the rate of new-onset CKD was lower in RPN (18.2%), compared to OPN (20.3%) and LPN (20.1%), however, the difference was not statistically significant between the three surgical approaches ($p = 0.330$).

Recently, several nomograms to predict postoperative renal function decline after PN were introduced.[7–12] Externally validation facilitates the dissemination and application of nomograms. Therefore, we aimed to first externally validate Yonsei nomogram as a prognostic tool to predict new-onset CKD stage ≥III development after on-clamp PN for cT1 tumors. In our previous study,[12] we analyzed 698 Korean patients, the rate of new-onset CKD ≥III was 13.1% at 5-yrs follow-up. Age (HR:1.041), DM (HR:1.921), male gender (HR:1.653), large tumors (HR:1.331) and lower preoperative eGFR (HR:0.937) were independent risk factors for CKD ≥III occurrence. The CKD-free survival rates at 1, 3, 5 and 10 years were 97.1%, 94.4%, 85.3% and 70.6%, respectively. This nomogram showed optimal accuracy and good calibration at internal validation (C-index was 0.85).[12] In the current multi-institutional study, we externally validated our primary nomogram using data of 3526 patients at a median follow-up of 47 months. A total of 683 patients (19.4%) of the external validation cohort developed new-onset CKD stage ≥III, compared to 13.1% in the development cohort (Table 1). This could be explained that patients in the external validation cohort were elder, had higher BMI, larger tumors, with increased rate of medical comorbidities compared to the development cohort. Of note, Asian patients have lower BMI than Western patients, and when the standard MDRD equation is applied, eGFR may be overestimated. Thus, the Japanese Society of Nephrology has recommended to use the modified equation for Japanese patients, so called "Modification of Diet in Renal Disease 2".[25] In the present study, we used the standard MDRD equation because the original Yonsei nomogram used the same equation in Korean patients, and we validated it among different races including Asian patients to test its geographical and racial validation. Interestingly, our results showed good calibration properties.

We tested the performance of the Yonsei nomogram by plotting the observed versus predicted new-onset CKD across quantiles of predicted probabilities at 1, 3, 5, and 10 years. Our results demonstrated a good accuracy of the nomogram an AUC of 0.72, 0.77, and 0.78 for the prediction of new-onset CKD at 3, 5, and 10 years, respectively. Moreover, the validated nomogram showed good calibration properties indicating strong predictor effects. The calibration slope value was 0.77, 0.83, 0.76, and 0.75 at 1, 3, 5, and 10 years respectively. In short, we found that the nomogram model could be used to compute new-onset CKD probability at different follow ups to decide whether to perform PN or opt for an alternative therapy such as RN or active surveillance. Consequently, the Yonsei nomogram fulfilled all the criteria to be a successful prediction tool to obtain accurate predictions of the individual risk of new-onset CKD occurrence after PN.

The decision to perform RN vs. PN remains a clinical challenge. Researchers are working hardly to introduce different models and equations that can help in estimation of post-operative renal function after renal tumors surgery to help making a decision. McIntosh and colleagues developed a model to identify patients at risk of post-operative eGFR of ≤45 ml/min/1.73m^2 and recommended them to receive PN instead of RN. Their multivariable analysis showed that increasing age ($p = 0.001$), female gender ($p < 0.001$), and increasing pre-operative creatinine ($p < 0.001$) were associated with renal function decline. An area under the curve

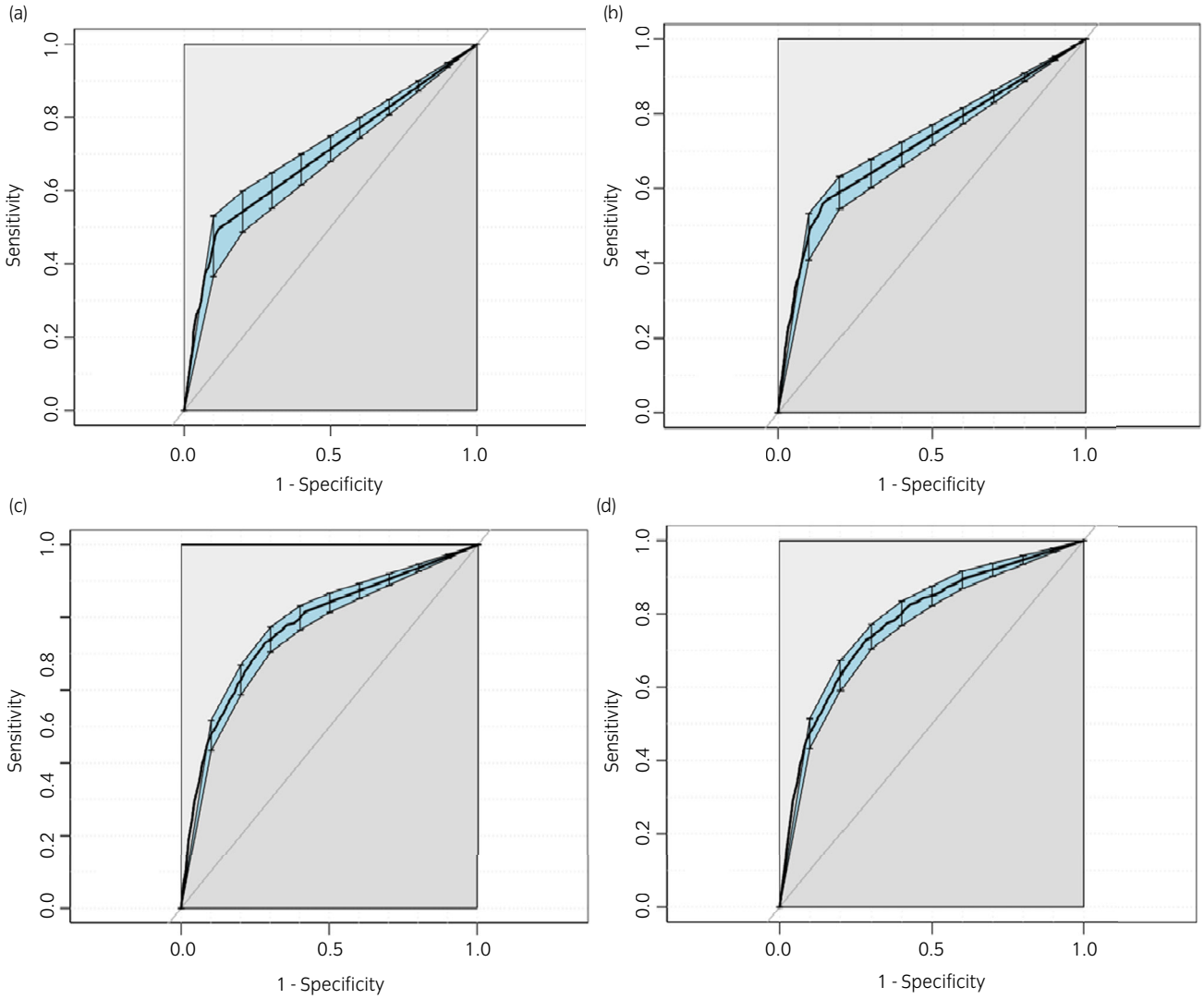


FIGURE 3 AUC of Yonsei nomogram in predicting CKD-free survival probability after PN: (a) at 1-year follow-up, with an AUC = 0.69 (95% CI 0.66; 0.73), sensitivity was 50%, specificity was 80%, PPV was 52% and NPV was 87%. (b) at 3-year follow-up, AUC = 0.72 (95% CI 0.69; 0.74), sensitivity was 56%, specificity was 86%, PPV was 49% and NPV was 89%. (c) at 5-year follow-up, AUC = 0.77 (95% CI 0.75; 0.79), sensitivity was 73%, specificity was 72%, PPV was 38% and NPV was 92%. (d) at 10-year follow-up, AUC = 0.78 (95% CI 0.76; 0.80), sensitivity was 73%, specificity was 72%, PPV was 38% and NPV was 92%.

(AUC) was 0.79. However, as with any predictive model built on a single dataset, their nomogram awaits external validation.[26] More recently, Aguilar Palacios et al introduced an equation = [35 + preoperative eGFR (× 0.65) − 18 (if RN) − age (× 0.25) + 3 (if tumor size >7 cm) − 2 (if diabetes)], to estimate postoperative new baseline eGFR at 3 to 12 months in patients being considered for RN or PN that can be easily implemented in daily clinical practice.[27]

No doubt that the variables constituted Yonsei nomogram[12] and other models[7–11] represent the strongest predictors of long-term renal function decline after PN including aging, male gender, DM and HTN, large tumors and lower baseline eGFR and creatinine. The unavoidable effect of aging, DM and HTN on renal function has been proved thoroughly in literature owing to decrease in renal blood flow, development of glomerular sclerosis and tubular interstitial fibrosis, thus the kidneys become at increased risk of CKD progression during long-term follow-up even after PN.[28,29] Furthermore, low preoperative eGFR reflects the quality of renal parenchyma[20] and is likely attributed to the frailty of the patient's general status, medical comorbidities, and aging. Moreover, resection of a large renal mass is expected to be associated with small quantity of residual renal parenchymal together with deep renography sutures. Of note, the quality and quantity of preserved renal parenchyma has emerged recently as an important factor affecting postoperative renal function.[30]

Of note, CKD increases the risk of cardiovascular and overall mortality.[6] And the cut-off eGFR value of CKD primarily related to PN or RN surgery (CKD-S) is not established yet. Wu et al. reported that patients with reduced new baseline eGFR (<45 ml/min/1.73m^2) have compromised survival. The postoperative CKD-S rate was 48% which is considered high, and this may be due to the inclusion of RN cases and 26% of patients had preoperative CKD.[31]

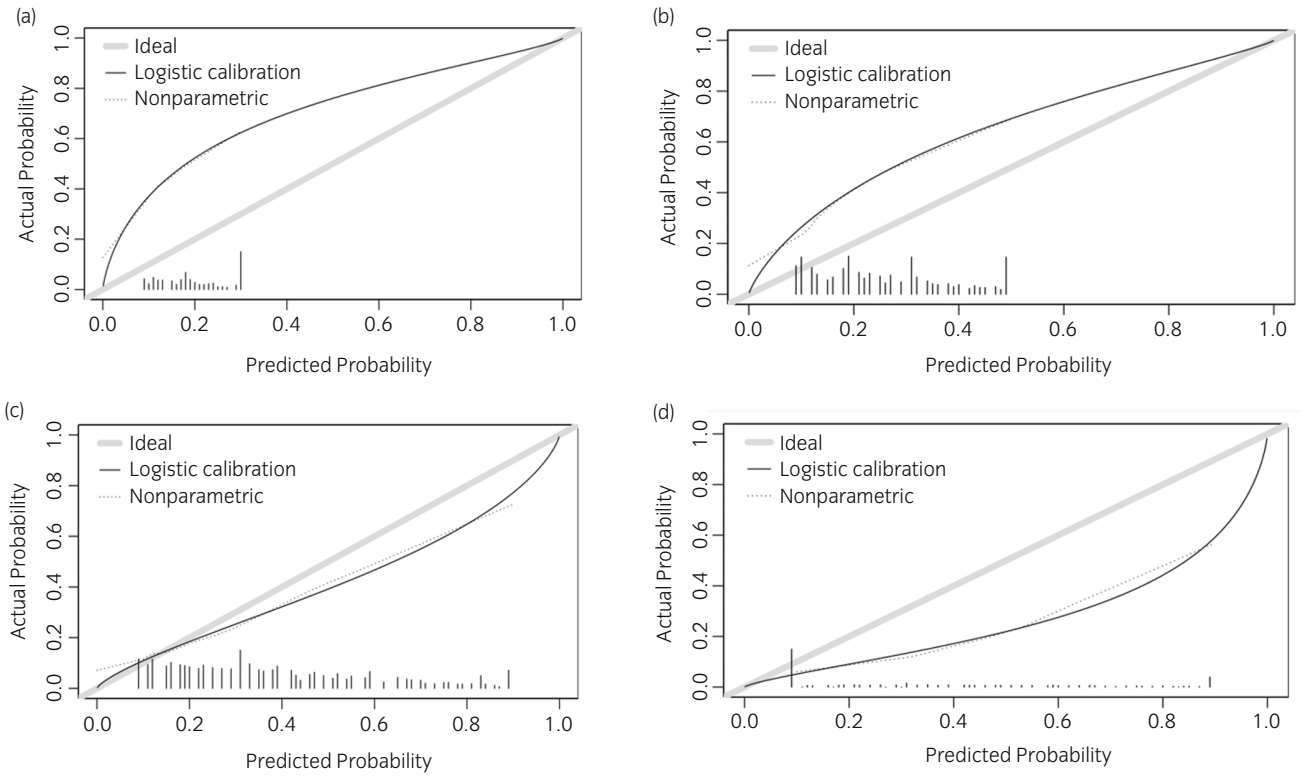


FIGURE 4 Calibration plots of observed and predicted new-onset CKD with locally weighted regression lines. (a) Nomogram-predicted probability of 1-year CKD-free survival, concordance index = 0.59, and calibration slope = 0.77. (b) Nomogram-predicted probability of 3-year CKD-free survival, concordance index = 0.65, and calibration slope = 0.83. (c) Nomogram-predicted probability of 5-year CKD-free survival, concordance index = 0.72, and calibration slope = 0.76. (d) Nomogram-predicted probability of 10-year CKD-free survival, concordance index = 0.78, and calibration slope = 0.75.

Moreover, they defined the new baseline eGFR as the highest eGFR between nadir and 6 weeks after surgery.[31] This definition also might increase the percentage of postoperative CKD (48%) as time was insufficient to full recovery. Recently, Dawidek and colleagues reported that the optimal renal function recovery following PN occurred by 6–12 weeks, and they concluded that this period should therefore be considered an appropriate endpoint for postoperative follow-up.[32] Unlike to their analysis,[31] we included patients who underwent PN only and those with preoperative eGFR >60 ml/min/1.73m^2, and this might explain the lower postoperative percentage (1.2%) of patients who have eGFR <45 ml/min/1.73m^2.

From the surgeon and patient's perspective identification of patients unlikely to benefit from PN is the main goal. This is an important step during counseling of patients before surgery. Yonsei nomogram provides a tool to identify patients with a high probability of a poor renal function outcome despite PN. The risks and benefits of each surgical approach must be measured properly before deciding the best treatment option for each patient. Generally, PN preserves renal parenchyma but may expose patients to higher perioperative complications than RN especially elderly comorbid patients with complex tumors.[22–26] For example, 75-years-old diabetic male, with a preoperative eGFR of 75 ml/min/1.73m^2 and a 6-cm renal mass. Based on Yonsei nomogram, the 3- and 5-years CKD-free progression probabilities following PN are 56% and 20%, respectively (Figure 1b). This information might be helpful during preoperative discussion with this patient, upon increased exposure to perioperative risks together with increased risk of CKD development at 5-years even after PN. Or to proceed with less morbid RN, putting in consideration equivalent oncological outcomes between both surgical approaches. In addition, based on our nomogram for patients who have high probability of developing CKD stage ≥III, they need close renal function monitoring and should be advised to follow certain reno-protective regimens to delay risk of CKD progression.[33]

Our research has some drawbacks merit discussion. First, the retrospective design of this study might carry a selection bias. Second, our results also apply to our study cohort only i.e. patients with two renal units, cT1 renal masses, preoperative eGFR ≥60 ml/min/1.73m^2 undergoing on-clamp PN. Third, renal function evaluation and follow-ups are based on eGFR values, with inability to use renal isotope scans to estimate function of the operated kidney. Indeed, the use of serial renal scans to follow-up renal function for each patient after PN seems to be not clinically applicable tool. Another drawback is the use of a standard MDRD equation which might over-estimate eGFR value, especially in patients with low BMI. Nevertheless, we have several strength points in our research. First, our study was the first that externally validated Yonsei nomogram. Second, the large sample size of patients included strengthens the significance of our results.

Third, various ethnicities were analyzed from four continents, 10 countries and 23 centers, and this characteristic will increase the generalizability and applicability of our findings. Fourth, our study did not focus on high-tertiary centers or expert surgeons only, thus our findings may apply to a community-based setting. Finally, the results of our study confirm that Yonsei nomogram is a potential tool to counsel patients undergoing PN about renal function outcomes prior to surgery. Finally, surgeons had wide range of surgical experiences and volume of centers were different, thus, the study represents real-world experience, and the results can be easily generalized.

In conclusion, the online Yonsei nomogram showed good calibration properties, and it provided an accurate prediction of new-onset CKD development following PN on long-term follow-up. These findings encourage the use of this model as a prognostic tool that can be used in PN treatment decision when counseling patients with renal tumors before surgery. In addition, patients with an increased risk of CKD≥III stage development should follow a renal protection program and be closely monitored after surgery.

AUTHOR CONTRIBUTIONS

Ali Abdel Raheem: Conceptualization; data curation; methodology; resources; software; writing – original draft; writing – review and editing. **Isotta Landi:** Data curation; formal analysis; investigation; methodology; software; validation. **Ibrahim Alowidah:** Conceptualization; data curation; methodology; supervision; writing – review and editing. **Umberto Capitanio:** Conceptualization; data curation; supervision; writing – review and editing. **Francesco Montorsi:** Conceptualization; data curation; methodology; supervision; writing – review and editing. **Alessandro Larcher:** Conceptualization; data curation; supervision; writing – review and editing. **Ithaar H. 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CONFLICT OF INTEREST

No conflict of interest is present at the time of submission.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

The study was approved by the institutional review board of participating centers (IBR approval number: H1RI-11-Feb19-02).

INFORMED CONSENT

N/A.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL

N/A.

ANIMAL STUDIES

N/A.

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Editorial Comment to External validation of Yonsei nomogram predicting chronic kidney disease development after partial nephrectomy: An international, multicenter study

One of the main goals of partial nephrectomy (PN) in patients with localized renal tumors is preventing the progression to chronic kidney disease (CKD) by sparing organ function. A nomogram predicting the risk of CKD development would help physicians counsel patients before surgery. The Yonsei nomogram was developed to predict the possibility of new-onset CKD after on-clamp PN in patients with clinical T1 disease.[1] It consists of five clinical parameters, including age, sex, diabetes, preoperative estimated glomerular filtration rate (eGFR), and tumor size and predicts the 1, 3, 5, and 10-year CKD-free survival probability. Although there have been other models for predicting the risk of CKD development, the lack of external validation has limited the use of these models in clinical practice.

Abdel Raheem et al. conducted an external validation study of the Yonsei nomogram with 3526 patients in mostly Western countries.[2] The area under the curve value was 0.69, 0.72, 0.77, and 0.78 for the prediction of new-onset CKD at 1, 3, 5, and 10 years, respectively. The authors concluded that this predictive model could provide an accurate estimate of the individual risk of CKD-free progression on a long-term follow-up not only in Asian patients, but also in those in other countries.

However, a major concern with the global use of this model is the evaluation of eGFR. The Modification of Diet in Renal Disease (MDRD) equation is commonly used to calculate eGFR.[3] It is well known that this equation was developed for the Caucasian population. The original MDRD equation may overestimate renal function in Asian patients due to a lower muscle mass than that of Caucasian patients.[4] The original MDRD equation improved the accuracy of GFR estimation in the Japanese population by a coefficient of 0.881.[4] Patients who developed new-onset CKD were 13.1% of the original Korean cohort, whereas they were 19.4% of the external validation cohort.[2] In addition, the overestimation of eGFR in Asian patients may have caused the miss determination of patients without CKD. Patients with mild CKD may have been included in the development cohort, which may have compromised the accuracy of the nomogram. This ethnical difference is a major barrier to the introduction of the MDRD equation globally. Thus, a new equation that accurately estimates eGFR is needed.

Nonetheless, the present study demonstrated the global versatility of the Yonsei nomogram developed for Asian patients. I am hopeful that the barrier against measuring eGFR in different ethnicities will be eliminated. As a result, nomograms that estimate renal function after treatment may show higher predictive accuracy.

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CONFLICT OF INTEREST

Tsunenori Kondo received honoraria from Pfizer, MSD, Takeda Pharmaceutical Company, and Ono Pharmaceutical.

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