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Estimated Glomerular Filtration Rate Decline at 1 Year After Minimally Invasive Partial Nephrectomy: A Multimodel Comparison of Predictors

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Article info

Abstract

Background: Long-term renal function after partial nephrectomy (PN) is difficult to predict as it is influenced by several modifiable and nonmodifiable variables, often intertwined in complex relations.

Objective: To identify variables influencing long-term renal function after PN and to assess their relative weight.

Design, setting, and participants: A total of 457 patients who underwent either robotic (n = 412) or laparoscopic PN (n = 45) were identified from a multicenter international database.

Outcome measurements and statistical analysis: The 1-yr estimated glomerular filtration rate (eGFR) percentage loss (1YPL), defined as the eGFR percentage change from baseline at 1 yr after surgery, was the outcome endpoint. Predictors evaluated included demographic data, tumor features, and operative and postoperative variables. Bayesian multimodel analysis of covariance was used to build all possible models and compare the fit of each model to the data via model Bayes factors. Bayesian model averaging was used to quantify the support for each predictor via the inclusion Bayes factor (BF_{incl}). High-dimensional undirected graph estimation was used for network analysis of conditional independence between predictors.

Results and limitations: Several models were found to be plausible for estimation of 1YPL. The best model, comprising postoperative eGFR percentage loss (PPL), sex, ischemia technique, and preoperative eGFR, was 207 times more likely than all the

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other models regarding relative predictive performance. Its components were part of the top 44 models and were the predictors with the highest BF_{incl}. The role of cold ischemia, solitary kidney status, surgeon experience, and type of renorraphy was not assessed.

Conclusions: Preoperative eGFR, sex, ischemia technique, and PPL are the best predictors of eGFR percentage loss at 1 yr after minimally invasive PN. Other predictors seem to be irrelevant, as their influence is insignificant or already nested in the effect of these four parameters.

Patient summary: Kidney function at 1 year after partial removal of a kidney depends on sex, the technique used to halt blood flow to the kidney during surgery, and kidney function at baseline and in the early postoperative period.

1. Introduction

Partial nephrectomy (PN) is the standard treatment for T1 renal masses [1]. In comparison to radical nephrectomy, PN is associated with a lower incidence of chronic kidney disease (CKD) while maintaining similar oncologic and safety outcomes [2]. Preservation of kidney function is critical in patients with pre-existing comorbidities, solitary renal malignancies, or bilateral cancers, as it can influence the risk of mortality from other causes [3].

Immediate and long-term renal function after PN is affected by several modifiable and nonmodifiable variables, including demographic, disease-related, intraoperative, and postoperative factors, often intertwined in complex relations [4].

In this study we sought to identify which variables influence long-term renal function and to assess their relative weight in determining the percentage change in estimated glomerular filtration rate (eGFR) at 1 yr after minimally invasive PN.

A Bayesian multimodel comparison was applied to objectively compare the predictive performance of all possible combinations of predictors while balancing estimation errors and overfitting risks. Using Bayesian model averaging, it was possible to weight each predictor across all models and give information on its overall predictive performance and plausibility.

2. Patients and methods

2.1. Patient population

An international, multicenter, institutional review board–approved, retrospective study including patients undergoing laparoscopic or robot-assisted PN at five academic institutions (three from Europe and two from USA) between 2013 and 2019 was conducted. Inclusion criteria were (1) adult patients diagnosed with a localized renal tumor (T1 or T2); (2) undergoing robotic or laparoscopic PN; and (3) with a complete description of preoperative and postoperative characteristics, including up to 1-yr follow-up data. The following exclusion criteria were applied: (1) patients undergoing radical nephrectomy or nonsurgical treatments; (2) pediatric patients; and (3) patients with a transplanted kidney or a history of multiple PNs on the same kidney.

2.2. Data collection

Demographic data and baseline characteristics included age, sex, ethnicity, hypertension, diabetes mellitus status, body mass index, American Society of Anesthesiologists score, solitary kidney status, preoperative hemoglobin. eGFR was calculated using the CKD-Epidemiology Collaboration equation. Hypertension was defined as systolic blood pressure of $\geq$140 mm Hg or diastolic blood pressure of $\geq$90 mm Hg or taking antihypertensive medication. Information on tumor and operative details included pathological tumor size, Radius, Endophytic, Nearness to collecting system, Anterior/posterior, and Location (RENAL) score, surgical approach, clamping technique, warm ischemia time (WIT), operative time, estimated blood loss (EBL), and intraoperative complications. Postoperative data included eGFR at discharge, length of stay, and postoperative complications. eGFR postoperative percentage loss (PPL) was calculated as the percentage difference between baseline eGFR and eGFR at discharge: (preoperative eGFR − postoperative eGFR) × 100 / preoperative eGFR.

The functional outcome endpoint was the 1-yr eGFR percentage loss (1YPL), defined as the eGFR percentage change from baseline at 1 year after surgery: (eGFR at 1 yr − preoperative eGFR) × 100 / preoperative eGFR.

2.3. Statistical analysis

To predict 1YPL, analysis of covariance (ANCOVA) with multiple continuous and categorical variables was performed. To objectively identify models that balance estimation errors and overfitting risk, a Bayesian multimodel comparison was used. In Bayesian statistics, the prior beliefs (prior distribution of the model and the parameter probability) are updated with inclusion of the likelihood of data in the posterior beliefs (posterior distributions). The likelihood of data is the relative support from data for alternative hypotheses and is quantified using Bayes factors (BFs). With Bayesian multimodel ANCOVA it is possible to overcome the uncertainty derived from the use of only one model by comparing the predictive performance of all possible combinations of predictors and calculating the relative plausibility of each model relative to the others. Furthermore, Bayesian model averaging can be used to weight each predictor across all models and give information on its overall predictive performance and plausibility [5]. In the first step, we performed a Bayesian model comparison and calculated the posterior model probability P(M|data) to evaluate the relative plausibility of each model across the entire model space; we used the model BF (BF_M) as an indicator of model predictive performance, or model likelihood, which measures how many times the data were more likely to occur under a specific model than all the others averaged across the space. BF_{01} was used to

represent the relative predictive performance (likelihood) of the best model with respect to the model considered [6]. For the model prior probability P(M), we chose a uniform model prior and imposed that all models were equally likely before seeing the data [7]. In the second step, we used a Bayesian model averaging approach to choose which variable is useful in predicting 1YPL and quantified the support for each predictor as its posterior inclusion probability P(incl|data), which is the probability of including it in a model after observing the data. P(incl|data) is the sum of P(M|data) for the models including a given variable. We compared the predictive performance of predictors in terms of BF_{excl}, which is the ratio between the likelihood of models excluding a predictor and models including it. In this way, the data are BF_{excl} times more likely to occur under the models that do not include a predictor than the models that include it. BF_{incl} represents the reciprocal of BF_{excl}. The percentage error was used to quantify the proportional error associated with BF estimation and reflects the percentage accuracy in predicting the value of each BF. We also reported the model-averaged effect size for each parameter (regression coefficient β) to assess the weight of each predictor in estimating 1YPL. The mean β was calculated by averaging the β values assumed for the predictor across all models and weighted by the P(M|data). Standard deviation (SD) and the 95% credible interval for estimates are also reported. We chose the Jeffrey-Zellner-Siow distribution for the β prior probability. To explain the mutual dependence between variables, we performed a network analysis of conditional independence between relevant predictors using the high-dimensional undirected graph estimation method; in the resulting acyclic graph, variables are shown as nodes and conditional dependences as edges [8]. All statistical analyses were carried out using JASP (version 0.14; JASP Software Ltd., Warrington, UK).

3. Results

Data were collected for 1359 patients. Six patients were excluded because of pediatric age, and 896 were excluded because of incomplete preoperative, postoperative, or follow-up data. A total of 457 patients undergoing robotic (n = 412) or laparoscopic PN (n = 45) were thus included in the study cohort. Demographic data and baseline characteristics are shown in Table 1. There were no differences in available characteristics between the included and excluded patients. No violation of model assumptions for ANCOVA was observed (Supplementary Fig. 1).

The analysis showed that several models of varying complexity are plausible for estimation of 1YPL (Table 2). The best model, comprising sex, preoperative eGFR, ischemia technique, and PPL, was 207 times more likely than all the others averaged across the model space. For all the predictors in this model, the likelihood increased after seeing the data. The second-best model includes the same predictors with the addition of age (BF_M 122.6). The relative predictive performance of the third-best model (comprising ischemia technique, PPL, and preoperative eGFR) is 81 times higher than the average performance of the other models. The components of this model (ischemia technique, PPL, and preoperative eGFR) are part of the top 44 models with the highest P(M|data) values.

Comparison between the group of models not including PPL and the group of models including PPL showed that the data were extremely less likely (BF_{excl} 4.441E-16) to occur under the former (Table 3). The data were less likely to occur under the group of models not including preoper-

Table 1 – Demographics and baseline characteristics for the 457 patients.

Variable	Result [a]
Age (yr)	61 (17)
Body mass index (kg/m^2)	26.1 (5.11)
Preoperative hemoglobin (g/dl)	14.3 (1.9)
Preoperative eGFR (ml/min/1.73 m^2)	87.36 (25.34)
eGFR at discharge (ml/min/1.73 m^2)	76.52 (33.22)
PPL (%)	9.11 (25.41)
eGFR at 1 yr (ml/min/1.73 m^2)	71.78 (23.59)
PPL at 1 yr (%)	10.31 (13.04)
RENAL score	6 (3)
Tumor size (cm)	2.8 (1.9)
Operative time (min)	144 (63)
Warm ischemia time (min)	16 (10)
Length of stay (d)	5 (3)
Sex	
Male	286 (62.6)
Female	171 (37.4)
Race (Black)	
Yes	29 (6.3)
No	428 (93.7)
Hypertension [b]	
Yes	166 (36.3)
No	291 (63.7)
Diabetes mellitus	
Yes	46 (10.1)
No	411 (89.9)
Solitary kidney	
Yes	19 (4.1)
No	438 (95.8)
Partial nephrectomy approach	
Robot-assisted	404 (88.4)
Laparoscopic	53 (11.6)
Ischemia technique	
Clampless	47 (10.3)
Selective	107 (23.4)
Full	303 (66.3)

PPL = postoperative percentage eGFR loss; eGFR = estimated glomerular filtration rate.
[a] Results are presented as mean (SD) for continuous variables and n (%) for categorical variables.
[b] Defined as systolic blood pressure of ≥140 mm Hg or diastolic blood pressure of ≥90 mm Hg or taking antihypertensive medication.

ative eGFR (BF_{excl} 0.02), ischemia technique (BF_{excl} 0.034), and sex (BF_{excl} 0.458). The other variables (preoperative hemoglobin, hypertension, diabetes, tumor size, RENAL score, WIT, and EBL) were all worse predictors than those mentioned above.

Mean β coefficients supported the importance of PPL, preoperative eGFR, sex, and ischemia technique in predicting 1YPL; specifically, the 95% credible interval for the regression coefficient did not include 0 for any of these variables (Supplementary Table 1). For sex, the 95% credible interval ranged from −4 to −0.4, demonstrating that male sex is a protective factor for renal function because it reduces the extent of 1YPL. The 95% credible interval for all the other variables included the null effect.

Network analysis of conditional independence showed that 1YPL was highly dependent on PPL and moderately dependent on preoperative eGFR and EBL; inverse dependence was observed between 1YPL and male sex (Fig. 1).

4. Discussion

This study demonstrates that several models are plausible for predicting renal loss at 1 yr after minimally invasive

Table 2 – Model comparison for the top 20 models in predicting eGFR percentage loss at 1 yr after minimally invasive partial nephrectomy.

Models	P(M)	P(M|data)	BF_M	BF_{01}	Error (%)
Sex (male) + ischemia technique + PPL + PeGFR	8E-06	0.00158	207.1	1	
Sex (male) + ischemia technique + PPL + PeGFR + age	8E-06	0.00093	122.6	1.57	1.573
Ischemia technique + PPL + PeGFR	8E-06	0.00062	81.45	2.28	1.689
Ischemia technique + PPL + PeGFR + age	8E-06	0.00033	43.75	4.1	1.467
DM + sex (male) + ischemia technique + PPL + PeGFR	8E-06	0.0003	38.74	4.61	1.842
Sex (male) + ischemia technique + HTN + PPL + PeGFR + age	8E-06	0.00026	34.67	5.14	1.702
Sex (male) + ischemia technique + HTN + PPL + PeGFR	8E-06	0.00026	34.64	5.14	1.86
Sex (male) + ischemia technique + PPL + PeGFR + WIT	8E-06	0.00022	29.23	6.06	1.57
Sex (male) + ischemia technique + PPL + PeGFR + age + WIT	8E-06	0.0002	26.33	6.71	1.602
Sex (male) + ischemia technique + PPL + PeGFR + tumor size	8E-06	0.0002	26.01	6.79	1.57
DM + sex (male) + ischemia technique + PPL + PeGFR + age	8E-06	0.00018	24.09	7.32	1.699
Sex (male) + ischemia technique + PPL + PeGFR + EBL	8E-06	0.00017	22.91	7.68	1.569
DM + ischemia technique + PPL + PeGFR	8E-06	0.00016	20.59	8.53	1.858
Ischemia technique +iHTN + PPL + PeGFR	8E-06	0.00015	19.82	8.86	1.729
Sex (male) + ischemia technique + PPL + PeGFR + tumor size + age	8E-06	0.00015	19.15	9.16	1.604
Ischemia technique + HTN + PPL + PeGFR + age	8E-06	0.00014	18.76	9.35	1.574
Sex (male) + ischemia technique + PPL + PeGFR + age + EBL	8E-06	0.00013	16.62	10.5	1.616
Ischemia technique + PPL + PeGFR + WIT	8E-06	9.3E-05	12.22	14.3	1.464
DM + ischemia technique + PPL + PeGFR + age	8E-06	8.6E-05	11.28	15.4	1.584
Ischemia technique + PPL + PeGFR + tumor size	8E-06	8.1E-05	10.62	16.4	1.465

eGFR = estimated glomerular filtration rate; PeGFR = preoperative eGFR; PPL = postoperative percentage eGFR loss; HTN = hypertension; DM = diabetes mellitus; WIT = warm ischemia time; EBL = estimated blood loss; P(M) = prior model probability; P(M|data) = posterior model probability; BF_M = model Bayes factor; BF_{01} = relative Bayes factor of the best model against the model considered.

Table 3 – Analysis of effects.

Effects	P(incl|data)	P(excl|data)	BF_{excl}	BF_{incl}
PPL	1	4.44E-16	4.44E-16	2.25E+15
Preoperative eGFR	0.98	0.02	0.02	50.000
Ischemia technique	0.967	0.033	0.034	29.412
Sex (male)	0.686	0.314	0.458	2.183
Age	0.378	0.622	1.646	0.608
Body mass index	0.331	0.669	2.021	0.495
Preoperative hemoglobin	0.234	0.766	3.278	0.305
Diabetes mellitus	0.185	0.815	4.411	0.227
Hypertension	0.183	0.817	4.478	0.223
Warm ischemia time	0.181	0.819	4.524	0.221
Operative time	0.174	0.826	4.734	0.211
Surgical technique	0.155	0.845	5.453	0.183
Tumor size	0.132	0.868	6.564	0.152
Estimated blood loss	0.123	0.877	7.104	0.141
ASA score	0.094	0.906	9.614	0.104
Length of stay	0.048	0.952	19.747	0.051
RENAL score	0.025	0.975	39.493	0.025

ASA = American Society of Anesthesiologists; eGFR = estimated glomerular filtration rate; PPL = eGFR postoperative percentage loss; P(incl|data), posterior inclusion probability (the probability of including the predictor in a model after seeing the data); P(excl|data) = posterior exclusion probability, reciprocal of P(incl|data); BF_{excl} = relative likelihood of the models excluding the predictor against the models including it; BF_{incl} = reciprocal of BF_{excl}.

PN. We found that the best model includes sex, preoperative eGFR, ischemia technique, and PPL. All the models containing these four variables exhibited an increase in probability after seeing the data and showed greater predictive performances than the models including all or some of the remaining variables. Model averaging and network analysis of conditional independence confirmed these results. Several points regarding these findings deserve more detailed consideration.

Unlike most studies in the literature, we chose percentage eGFR loss to evaluate functional loss after minimally invasive PN. Several previous models used the ultimate eGFR or progression to stage III CKD as the endpoint [9–12]. Choice of a similar criterion might lead to deceptive results because the dependent variable is directly calculated from the same variables (ie, age, sex, or serum creatinine) that it is tested against. This always results in identification of those variables as important predictors of the outcome.

Other studies evaluated predictors of significant eGFR loss, defined as a reduction of >25% from baseline eGFR [13–15]. This endpoint resolved the above-mentioned limitation, as it is not necessarily influenced by variables used in eGFR formulas. Nonetheless, those studies chose only a subset of predictors to build a model containing the covariates considered relevant. Consequently, inference in all previous studies was carried out without taking into account the uncertainty derived from the use of only one model among all possible models; furthermore, the weight of each predictor was specific to a particular model and cannot give information on its overall predictive performance (likelihood) provided by the data [5]. This process can ultimately lead to overestimation of model precision and may provide biased estimates.

We took account of model space uncertainty by using Bayesian model averaging, in which the full range of models contribute to estimates and predictions. In this way, a
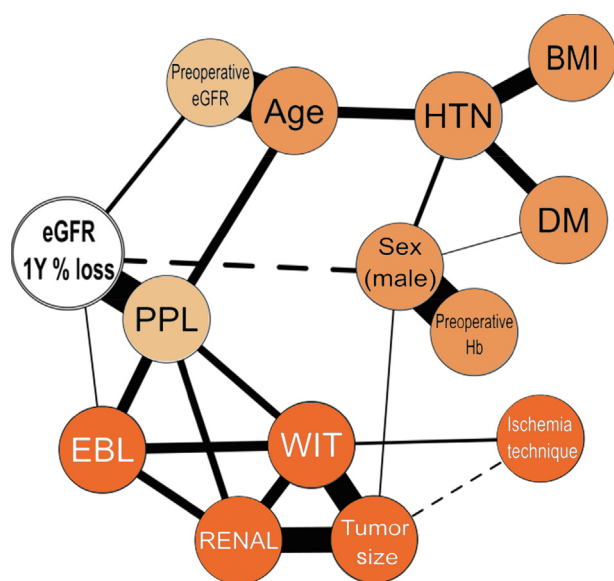
Fig. 1 – Network analysis of conditional independence between the variables evaluated using high-dimensional undirected graph estimation. Variables are shown as nodes and conditional dependences as edges, with direct dependences as solid lines and inverse dependences as dashed lines. PPL = postoperative percentage estimated glomerular filtration rate (eGFR) loss; HTN = hypertension; DM = diabetes mellitus; WIT = warm ischemia time; EBL = estimated blood loss; BMI = body mass index; Hb = hemoglobin; RENAL = RENAL nephrometry score; 1Y = 1 yr.

summary of the importance and consistency of each predictor can be provided. Regression coefficients that have a mean value close to zero will have very limited importance in predicting the independent variable; furthermore, predictors with a 95% credible interval that includes the null effect will influence the outcome in an opposite way, depending on the model considered, thus proving to be inconsistent. Specifically, calculation of the posterior mean and the 95% credible interval for the regression coefficients showed that PPL, preoperative eGFR, and sex retained their predictive performance throughout the entire model space: possible values for their regression coefficients were all above or below the null effect ($\beta = 0$). Interestingly, β values for sex ranged from -4 to -0.4, demonstrating that male sex is a protective factor for renal function because it reduces the extent of 1YPL. All the other variables proved unreliable, with a 95% credible interval whose extreme values were of opposite signs.

Previous studies tested the use of the acute kidney injury (AKI) categories of the Acute Dialysis Quality Initiative as predictors of long-term renal failure after PN. The Risk, Injury, Failure, Loss, and End-stage (RIFLE) criteria define AKI as an abrupt loss of kidney function resulting in a >25% reduction in eGFR from baseline [16]. It has been shown that AKI increases the risk of mortality and CKD development in patients with underlying medical conditions [17,18] but it was not thought to affect these outcomes when occurring in patients undergoing PN [19,20]. However, recent studies showed that both the presence and duration of AKI increase the risk of long-term renal failure in this type of patient as well [14,21]. Nonetheless, the RIFLE criteria may be inappropriate for patients undergoing

renal surgery; in these patients the increase in eGFR may be due to both surgical excision and ischemic damage, with relative contributions that are difficult to differentiate diagnostically and prognostically [18].

We did not use a cutoff value to define AKI in our study; instead, we evaluated acute renal failure in terms of PPL. This choice might offer some benefits, including avoiding the negative consequences of dichotomization such as loss of effect size and the risk of misclassification, allowing comparison with other continuous covariates of long-term eGFR and yielding a more detailed prediction of functional recovery [22].

We not only confirmed that PPL has noticeable repercussions for long-term function but also demonstrated that PPL is the most important factor affecting 1YPL. Unlike AKI, PPL seems to be useful for predicting long-term functional deterioration even when the percentage eGFR loss is <25%; moreover, it is essential to precisely quantify the extent of PPL as a continuous variable, as it is linearly related to the outcome (Supplementary Fig. 2). An interesting difference between our study and the current literature is that PPL is a better predictor than all the other surgical variables tested, including WIT, tumor size, RENAL score, and EBL. In addition, all these variables showed little support from the data, because models that do not include them are more likely than models that use them as predictors. Finally, it should be considered that renal function decline related to postoperative acute injury could be influenced by consequent hypertrophy of the remnant healthy kidney parenchyma. Studies with longer follow-up have shown that the impact of these modifiable parameters has a progressively lower influence on functional outcomes, while other comorbidities or de novo vascular diseases may have a significant impact on long-term outcomes [13,23].

Several studies found that WIT was a crucial factor in predicting eGFR change [24–27]. Other studies downgraded its role and concluded that as long as WIT is below a safe threshold (25–30 min) its duration does not significantly affect long-term eGFR [10,28–30].

A large body of literature has focused on the percentage of parenchymal mass preserved (PPMP) as the key determinant of remaining renal function, with WIT playing only a minor role [28,31]. For instance, both Simmons et al [10] and Ginzburg et al [15] found that PPMP and baseline eGFR, but not WIT, were independently associated with long-term renal function after PN. Other authors found that inclusion of PPMP in multivariable linear regression led to loss of significance for WIT in predicting eGFR at 3 mo [31] or later [32]. It must be noted that PPMP assessment is not immediate and requires dedicated three-dimensional rendering software to compare preoperative and postoperative renal computed tomography scans performed with intravenous contrast.

WIT and PPMP are closely related and difficult to decouple [33]. Large and complex tumors are usually associated with great parenchymal excision, extensive devascularization, and secondary damage due to reconstruction [9,34,35]. All of these factors are associated with longer WIT and smaller PPMP, which in turn are strongly related to PPL [35–37], thus causing multicollinearity between all

these variables. This is clearly shown by analysis of the network structure for variable dependence. Specifically, each node in the network graph represents a single variable and each edge represents the conditional dependence of two variables given all the others. Two variables initially found to be correlated (ie, marginally dependent) can become conditionally independent (no direct edge between the two nodes) when their correlation is explained by a third variable that is strongly related to both. For instance, after introducing PPL into the model, WIT and 1YPL become conditionally independent, because WIT influences the outcome via PPL. In addition, when conditionally independent predictors are added to a model already containing conditional dependent variables, they are unlikely to increase model predictivity. In our analysis, models containing both WIT and PPL performed worse than models containing only PPL because the influence of WIT on 1YPL is already nested in the PPL effect.

Our database does not have complete data for PPMP, so we did not evaluate this variable. However, PPMP should not add any benefit to our models; when several variables related to PPMP, including pathological size, RENAL score, and tumor stage [35], were added to a model containing PPL, the derived models did not have higher likelihood. In other words, these variables related to PPMP are unable to explain the residual variance, achieving a worse overall predictive performance. This does not mean that WIT and PPMP are not important in determining long-term renal function, but most of their effect is mediated by PPL, which represents the best predictor of eGFR at 1 yr after surgery.

Age, hypertension, body mass index, and diabetes mellitus have all been identified as risk factors for CKD onset and could also be involved in greater long-term functional loss [9,11,31]. Contrasting results have been found for the role of sex [11,31,38]. We believe that these findings may be strongly influenced by the study design and choice of endpoint, as they are all associated with lower baseline renal function. We evaluated the role of clinical variables including age, diabetes, obesity, hypertension, and preoperative hemoglobin in determining 1YPL. Model averaging analysis showed that only age was clearly related to 1YPL; its effect is largely mediated by PPL and it retains a marginal effect if it is added as an independent predictor.

Some studies suggest that selective clamping of artery branches [39] or the zero-ischemia approach [40] gives a significantly higher chance of parenchymal sparing compared to hilar clamping. Our results indicate that ischemia technique is a useful predictor of 1YPL as shown by its BF_{incl} of 29.4, which means that its inclusion increased the predictive performance of models nearly 30-fold.

Several reports found no significant difference in the reduction in eGFR between surgical approaches [31,38,41]. Our study confirms these findings by demonstrating that the data were less likely to occur under the group of models including surgical technique as a predictor.

Our study is characterized by several limitations. It is a retrospective study and thus selection and detection biases cannot be excluded. Our population came from high-volume centers and all PNs were performed by highly experienced surgeons; therefore, our findings may not apply to other health care settings. In this study, data for 1359 patients were collected, with 896 excluded owing to incomplete data. This is largely because of the strict inclusion criteria applied; a large proportion of these patients lacked 1-yr follow-up data and no statistical inference for these patients is possible; This might introduce a selection bias and impact the generalizability of the findings. We were not able to draw any conclusions regarding the role of cold ischemia, solitary kidney status, surgeon experience, or renorraphy techniques; the likelihood and magnitude of long-term functional loss may be affected by each of these.

5. Conclusions

Several models are plausible for predicting renal loss at 1 yr after minimally invasive PN. Our analysis suggests that the best model should include sex, ischemia technique, preoperative eGFR, and PPL. All the predictive models containing these four variables had higher probability and showed greater predictive performance than models including all or some of the remaining variables. Compared to other tools, these predictors are immediate and readily available. PPL is useful for predicting long-term functional decline even when the percentage loss is less than 25%, since it is linearly related to 1YPL. Other predictors seem to be irrelevant, as their influence is insignificant or already nested in the effect of these four parameters.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.02.005.

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