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RESEARCH LETTER

Prediction of kidney function in deceased donor kidney transplant recipients

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As patients with chronic kidney disease progress to kidney failure, kidney replacement therapy, dialysis or kidney transplantation (KTx), is needed. However, a critical shortage of kidney donors is associated with long wait times globally [1]. To address this issue, various strategies have been implemented, including the utilization of kidneys from expanded criteria donors, especially deceased donors. However, deceased donor KTx shows poorer outcomes than living donor KTx. These postoperative differences have led many transplant candidates to refuse deceased donor kidneys, resulting in inadequate utilization of donated organs due to misallocation.

To improve kidney allocation efficiency, non-invasive methods for evaluating donated kidneys, such as the Kidney Donor Risk Index (KDRI) [2], have been developed to optimize kidney allocation and predict graft outcomes before transplantation. However, some studies indicate that their predictive value may vary across populations [3]. Directly applying these methods to South Korea, with its distinct environmental conditions, poses significant challenges [4]. The rising number of patients awaiting repeat kidney transplantation [5] highlights the need to consider not only post-transplant survival rates but also long-term kidney function. However, current methods of predicting kidney function in recipients of deceased-donor kidneys remain inadequate.

This study aimed to predict three-year kidney function in recipients of deceased donor transplants using machine learning regression models based solely on pre-transplant variables. By identifying key donor-and-recipient factors influencing three-year post-transplant kidney function in the Korean population, the models predicted recipient three-year post-transplant estimated Glomerular Filtration Rate (eGFR) as a measure of kidney function. This approach offers a non-invasive, pre-surgical tool to support clinical decision-making and reduce the risk of transplant failure.

We collected 3022 observational records between May, 2014 and December, 2021 from the Korean Organ Transplantation Registry (KOTRY) [6]. We then analyzed the records to predict three-year kidney function (i.e., eGFR) of recipients after deceased-donor KTx, and to identify risk factors influencing the three-year post-transplant eGFR. The dataset includes the pre-transplant characteristics of the deceased donors and recipients, along with comprehensive 7-year follow-up records after KTx. Recipients regularly visited the hospital for graft function monitoring, with eGFR assessments at specific intervals, i.e., at sixth months, first year, second year, and every subsequent year until the seventh year. eGFR was measured by the CKD-EPI equation [7].

Data preprocessing was conducted to handle missing and abnormal data. After data preprocessing, 38 pre-transplantation variables from 871 data points were selected for the prediction task. The feature variables are presented in Table 1. In the table, continuous data are expressed as mean ± standard deviation (SD). Categorical data are expressed as quantity and percentage. The average age of donors was 48.1 years with a 14.5 SD, of whom 70.6% were male and 98.6% were Korean. The average age of recipients was 51.3 years with a 10.6 SD, of whom 57.9% were male

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Table 1 Dataset characteristics

Feature variable	Overall ($n=871$)	Training set ($n=696$)	Test set ($n=175$)	p-value
Donor feature Age, years	48.1 ± 14.5	48.5 ± 14.0	46.6 ± 16.5	0.42
Gender (Male), *n*	615 (70.6%)	490 (70.4%)	112 (64.0%)	0.45
Race (1 Korean), *n*	859 (98.6%)	687 (98.7%)	174 (99.4%)	0.54
Blood (A), *n*	297(34.1%)	249 (35.8%)	58 (33.1%)	0.02 (< 0.05)
Blood (B), *n*	234 (26.9%)	175 (25.1%)	48 (27.4%)	
Blood (O), *n*	224 (25.7%)	183 (26.3%)	41 (23.5%)	
Blood (AB), *n*	116 (13.3%)	89 (12.8%)	28 (16%)	
Blood RH (+), *n*	870 (99.9%)	695 (99.9%)	175 (100%)	0.82
Cold Ischemic time, min	281.9 ± 129.2	281.9 ± 126.3	284.5 ± 140.2	2.37
BMI (Body Mass Index), kg/m^2	23.4 ± 3.7	23.3 ± 3.7	23.7 ± 3.6	0.0001 (< 0.05)
Height, cm	167.2 ± 10.5	167.6 ± 9.3	165.7 ± 14.4	0.19
Weight, kg	65.7 ± 13.1	65.6 ± 12.7	66.0 ± 14.6	9.92
eGFR	74.6 ± 40.4	73.5 ± 40.0	78.7 ± 41.7	1.21
Cause of brain death (0), *n*	73 (9.3%)	57 (8.2%)	16 (9.1%)	0.003 (< 0.05)
Trauma (1), n	285 (32.7%)	226 (32.5%)	16 (9.1%)	
Underlying disease (2), n	384 (44.1%)	311 (44.7%)	73 (41.7%)	
Suicide (3), n	109 (12.5%)	84 (12.1%)	25 (14.3%)	
ICH (Intra-Cerebral Hemorrhage), Cerebral infarction (4), n	20 (2.3%)	18 (2.6%)	2 (1.1%)	
Absence of treatment, *n*	78 (9.0%)	63 (9.1%)	15 (8.6%)	0.36
Dopamine, *n*	387 (44.4%)	305 (43.8%)	82 (46.9%)	0.003 (< 0.05)
Noradrenaline, *n*	661 (75.9%)	523 (75.1%)	138 (78.9%)	0.11
Vasopressin, *n*	220 (25.3%)	178 (25.6%)	42 (24.0%)	0.78
CRRT (Continuous Renal Replacement Therapy), *n*	61 (7.0%)	50 (7.2%)	11 (6.3%)	0.53
ECMO (Extra-Corporeal Membrane Oxygenation), *n*	23 (2.6%)	20 (2.9%)	3 (1.7%)	0.13
Smoking status (never), *n*	433 (49.7%)	347 (49.9%)	86 (49.1%)	0.70
Smoking amount, pack/year	6.8 ± 11.6	6.5 ± 11.3	7.9 ± 13.0	0.02 (< 0.05)
Diabetes, *n*	112 (12.8%)	88 (12.6%)	24 (13.7%)	0.003 (< 0.05)
Type of diabetes (Type 1), *n*	3 (0.3%)	3 (0.4%)	0 (0%)	0.99
Hypertension, *n*	214 (24.6%)	180 (25.9%)	34 (19.4%)	0.43
Cardiovascular conditions (0), *n*	836 (95.98%)	667 (95.83%)	169 (96.6%)	0.99
AMI (Acute Myocardial Infarction) (1), *n*	10 (1.15%)	7 (1%)	3 (1.7%)	
Angina (2), *n*	13 (1.5%)	11(1.58%)	2 (1.1%)	
CHF (Congestive Heart Failure) (3), *n*	2 (0.23%)	2 (0.29%)	0(0%)	
Other (4), *n*	10 (1.15%)	9 (1.3%)	1 (0.6%)	
History of cancer (0), *n*	853 (97.9%)	681 (97.8%)	172 (98.3%)	0.64
Respiratory (lung) (1), *n*	1 (0.1%)	1 (0.1%)	0 (0%)	
Gastrointestinal (2), *n*	4 (0.5%)	3 (0.5%)	1 (0.6%)	
Hepatobiliary pancreas (3), *n*	1 (0.1%)	1 (0.1%)	0 (0%)	
Breast thyroid (5), *n*	5 (0.6%)	3 (0.5%)	2 (1.1%)	
Other (7), *n*	7 (0.8%)	7 (1%)	0	
Other conditions (0), *n*	174 (22.3%)	135 (19.4%)	29 (22.3%)	0.003 (< 0.05)
Recipient feature Gender (Male)	504 (57.9%)	392 (56.3%)	112 (64%)	0.15
Age, years	51.3 ± 10.6	48.5 ± 14.0	51.3 ± 10.7	0.25
Race (1 Korean)	868 (99.7%)	694 (99.7%)	174 (99.4%)	0.13

Table 1 (continued)

Feature variable	Overall ($n=871$)	Training set ($n=696$)	Test set ($n=175$)	p-value
Height, cm	164.4 ± 8.6	164.1 ± 8.4	165.5 ± 9.1	0.0004 (< 0.05)
Weight, kg	62.3 ± 11.7	61.8 ± 11.4	64.5 ± 12.6	3.19
BMI, kg/m^2	23.0 ± 3.3	22.8 ± 3.2	23.4 ± 3.5	0.05
Blood (A), *n*	307 (35.2%)	249 (35.8%)	58 (33.2%)	0.016 (< 0.05)
Blood (B), *n*	226 (26.0%)	178 (25.6%)	48 (27.4%)	
Blood (O), *n*	204 (23.4%)	163 (23.4%)	41 (23.4%)	
Blood (AB), *n*	134 (15.4%)	106 (15.2%)	28 (16%)	
Blood RH (+), *n*	867 (99.5%)	692 (99.4%)	175 (100%)	0.81
Recipient/Donor Mismatch (0), *n*	122 (14%)	94 (13.5%)	28 (16%)	0.70

BMI Body mass index, *ICH* Intracerebral hemorrhage, *CRRT* Continuous renal replacement therapy, *ECMO* Extracorporeal membrane oxygenation, *AMI* Acute myocardial infarction, *CHF* Congestive heart failure, *R/D Mismatch* recipients-donor human leukocyte antigen mismatch

and 99.7% were Korean. The data were split into 80% in the training set and 20% in the test set. The training set and test set were a well-balanced split.

We employed a repeated tenfold cross-validation strategy in the training process to enhance performance and minimize model bias, and we performed feature selection to identify the important features that affected post-transplant kidney function. In the feature selection process, a backward elimination technique and feature permutation importance were used to achieve best model performance. Ultimately, the optimal prediction model and the corresponding set of important features were identified.

In this prediction task, we employed several machine learning regression algorithms. The algorithms included K-nearest neighbor, random forest regression, support vector regression, linear ridge regression, linear lasso regression, kernel ridge regression, Bayesian ridge regression, and gradient boosting regression. We sought the optimal hyperparameters of models using the random search strategy. We compared the models' performance and checked the feature importance in the prediction process. Then we performed prediction optimization by choosing different feature subsets and the models for the best performance. We optimized the feature subset predictors and regression models iteratively. Finally, we selected the model which had the best performance that was evaluated by mean absolute error.

The linear lasso regression model achieved the best performance with the lowest mean absolute error of 17.017, followed by Bayesian ridge regression with a mean absolute error of 17.131, while all the other models yielded mean absolute error values greater than 17.5. The optimized model incorporated the following feature subset: donor factors (i.e., age, height, weight, cause of brain death, history of cancer, other diseases prior to donation, vasopressor use, history of hypertension, smoking status, annual smoking amount for smokers, and pre-donation eGFR); recipient factors (i.e., age, gender, weight, and blood type); and donor–recipient human leukocyte antigen mismatch (i.e., Recipient/Donor Mismatch) status.

The results are overall consistent with those found in other studies [2, 8, 9]. Our study yields lower performance compared to Jeon et al. [9], because Jeon's model predicts post-donation kidney function in living donors, while our study predicts post-transplant kidney function in recipients of deceased donor kidneys. Donor recovery depends on surgical healing and compensatory kidney adaptation, whereas recipient outcomes are affected by unpredictable factors such as rejection, infection, delayed graft function, and immunosuppressive therapy, making prediction more challenging.

This study underscores the importance of identifying which donor-and-recipient risk factors influence graft function following KTx from deceased donors. Additionally, measuring each factor's impact on graft function could help develop a future non-invasive evaluation scoring system. This tool could improve assessment of deceased-donor kidneys, boost transplantation rates and enable more efficient allocation in order to benefit a greater number of kidney failure patients.

However, the dataset was limited in size and lacked long-term (> 10 years) follow-up, the study could not reliably predict kidney function beyond three years, and the results may be subject to bias. To overcome this limitation, the KOTRY will consistently collect and manage data on kidney transplantation.

We will try to collect more data and prepare for external validation. Regarding methodology, we plan to explore the application of deep learning-based methods to enhance our model's predictive accuracy. Moreover, we aim to set up and validate novel approaches for identifying the key risk factors that affect the long-term function of kidney transplants.

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Author contributions Xiaohong Yu worked on the data analysis, data preprocessing, modeling selection, training, and writing of the manuscript. Jaehoon (Paul) Jeong and Joonseok Oh participated in the research design, writing of the manuscript, and the critical revision of article. All authors have read and agreed to the published version of the manuscript.

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Data availability The data was obtained from the KOTRY. To protect the privacy of the patients, the dataset in this study has been anonymized and replaced by serial numbers.

Declarations

Conflict of interest All authors have no conflicts of interest to declare.

Ethical approval This study was approved by the Institutional Review Boards of all participating centers in the Korean Organ Transplantation Registry (KOTRY). The study protocol was conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and the 2008 Declaration of Istanbul. The approval number from the coordinating center (Seoul National University Hospital) was H-1312-087-543.

Informed consent Written informed consent was obtained from all living donors and recipients prior to inclusion in the KOTRY database. For deceased donor transplants, consent was obtained from the recipients before data entry into the registry. The requirement for informed consent was waived by the Institutional Review Board.

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