Official Title: Prediction of Recipient Renal Function in Living Donor Kidney Transplantation Using Baseline Characteristics and Donor Renal Volume

ClinicalTrials.gov NCT Number:

Document Date: December 2, 2024

1. Purpose and Background

Kidney transplantation is the definitive treatment for end-stage renal disease (ESRD). Accurately predicting early post-transplant kidney function is critical for patient management and improving long-term outcomes. This study aims to develop a machine learning-based predictive model using baseline characteristics of recipients and donors, with a focus on donor kidney volume, to predict the lowest serum creatinine level within one year post-transplant.

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2. Study Design

- **Study Type**: Retrospective Cohort Study
- **Duration**: January 2006- March 2023
- **Setting**: Multicenter study conducted at Seoul National University Hospital, Severance Hospital, and Bundang Seoul National University Hospital.
- **Participants**: Living-donor kidney transplant recipients and their corresponding donors.

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3. Eligibility Criteria

Inclusion Criteria:

- Living-donor kidney transplant recipients and donors from the above centers.

Exclusion Criteria:

- Recipients or donors with follow-up duration less than 1 year.
- Recipients younger than 18 years old.
- Re-transplantation cases or recipients with simultaneous multi-organ transplantation.

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4. Data Collection and Management Plan

- Data was retrieved from hospital records and centralized in a unified dataset.
- Variables included demographic data, donor kidney volume (total and cortex), recipient-donor compatibility, and baseline laboratory data.

5. Primary and Secondary Outcomes

- **Primary Outcome**: Lowest serum creatinine level within one year post-transplant.
- **Secondary Outcomes**: Predictive performance metrics (MAE, RMSE, R^2), donor kidney volume correlations with recipient eGFR, and subgroup analyses by donor type.

6. Statistical Analysis

6.1 Statistical Software

All statistical analyses and data preprocessing will be conducted using the following software tools:

1. **R Software (Version 4.4.1)**:
   - Primary software for statistical analyses, including descriptive statistics, hypothesis testing, and data visualization.
2. **Python (Version 3.9)**:
   - Used for developing and validating machine learning models.

6.2 Predictive Model Development

Algorithms Used:

- Multiple Linear Regression (with and without variable selection)
- Elastic Net
- Generalized Additive Model (GAM)
- Random Forest
- Gradient Boosting (XGBoost)

Variable Selection Methods:

- Multiple Linear Regression: AIC-based stepwise selection.
- Elastic Net: LASSO regularization.
- GAM: Cross-validation for smoothing parameter selection.

- Tree-based models (Random Forest, Gradient Boosting, XGBoost): Feature importance evaluation based on cross-validation.

Hyperparameter Tuning:

- Grid search with 5-fold cross-validation will be used to optimize hyperparameters for machine learning models.

6.3 Model Evaluation

Performance Metrics:

1. **Mean Absolute Error (MAE)**:

   $\text{MAE}=\frac{1}{n}\sum_{i=1}^{n}|y_i - \hat{y}_i|$

   y_i: Actual value $\hat{y}_i$: Predicted value n=Number of observations

2. **Root Mean Square Error (RMSE)**:

   $\text{RMSE}=\sqrt{\frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}$

   y_i: Actual value $\hat{y}_i$: Predicted value n=Number of observations

3. **R-squared (R^2)** :

   $R^2 = 1 - \frac{SS_{res}}{SS_{tot}}$

   $SS_{res}=\sum_{i=1}^{n}(y_i - \hat{y}_i)^2$: Residual Sum of Square

   $SS_{tot}=\sum_{i=1}^{n}|y_i - \bar{y}_i|$: Total Sum of Squares

Internal Validation:

- Models will be evaluated using the internal validation set for all performance metrics.

External Validation:

- The final model will be tested on the external validation set to assess generalizability.

6.4 Subgroup Analysis

- Subgroups based on recipient characteristics (e.g., sex, age, baseline BMI) and donor variables (e.g., kidney volume) will be analyzed to evaluate heterogeneity in model performance.

6.5 Feature Importance Analysis

- Feature importance scores will be derived from tree-based models (Random Forest, XGBoost) to identify the most influential predictive variables.

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7. Ethical Considerations

- Approved by the SNUH Institutional Review Board (IRB No. H-2205-051-1322).
- Study participants provided informed consent for data usage.