Development of machine learning ensemble model for predicting DSA positivity and immunological risk stratification after kidney transplantation

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INTRODUCTION

Donor-specific antibody (DSA) positivity significantly impacts graft outcomes after kidney transplantation and is strongly associated with antibody-mediated rejection and long-term graft loss. Early identification of patients at risk for DSA development is essential for timely intervention and optimization of immunosuppressive therapy.

However, predicting DSA positivity remains challenging due to the interplay of multiple factors, including immunological sensitization, coagulation status, and renal function. Machine learning approaches offer the ability to integrate such diverse parameters and uncover complex, non-linear patterns that traditional analyses may overlook.

This study aimed to develop a machine learning–based ensemble model to predict DSA positivity and stratify immunological risk by incorporating immunological, clinical, and biochemical data from kidney transplant recipients.

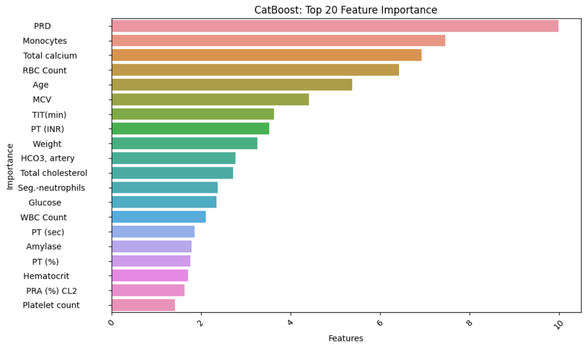

Figure 1: Feature Importance Plot for CatBoost Model in Predicting DSA Positivity in Kidney Transplant Recipients

METHODS

This retrospective study analyzed 45 kidney transplant recipients who underwent mycophenolic acid (MPA) monitoring between May 2023 and March 2025. A total of 382 monitoring events with 120 parameters per event yielded 45,840 data points, covering 23 medications, 86 laboratory tests, and 11 clinical/immunological variables including HLA typing, PRA results, and primary renal disease (PRD). Among the cohort, 5 patients were DSA-positive.

Three models—CatBoost, XGBoost, and multilayer perceptron (MLP)—were trained using stratified 5-fold group cross-validation in an out-of-fold (OOF) manner to prevent patient-level data leakage. The MLP was implemented as a feed-forward neural network with dropout and early stopping to enhance generalization.

Final predictions were generated using a weighted soft voting ensemble (XGBoost 0.5, MLP 0.3, CatBoost 0.2). Model performance was assessed by AUROC, accuracy, precision, recall, and F1-score, and feature importance was evaluated for CatBoost and XGBoost.

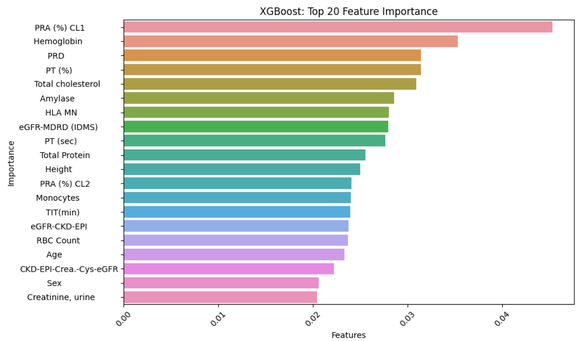

Figure 2: Feature Importance Plot for XGBoost Model in Predicting DSA Positivity in Kidney Transplant Recipients

RESULTS

The ensemble model demonstrated superior predictive performance compared with individual models. It achieved an AUROC of 0.728 and an accuracy of 0.843, with recall, precision, and F1-scores of 0.692, 0.681, and 0.686, respectively. Among individual models, AUROC values were 0.669 for CatBoost, 0.716 for XGBoost, and 0.694 for MLP, confirming that the weighted soft voting ensemble provided the most balanced performance.

Feature importance analyses revealed complementary predictors across models. CatBoost highlighted PRD, monocyte count, total calcium, red blood cell (RBC) count, age, mean corpuscular volume (MCV), PT(INR), and total cholesterol as the most influential factors (Figure 1). These results suggest that comorbid conditions, hematologic indices, and coagulation status are important in predicting DSA positivity.

XGBoost emphasized PRA (%), hemoglobin, PRD, PT(%), total cholesterol, amylase, HLA MN, and eGFR-MDRD as major contributors (Figure 2). PRA and HLA reflected immunological sensitization, while eGFR and hemoglobin captured renal functional reserve and hematologic status.

Taken together, immune-related markers (PRA, HLA typing), coagulation indices (PT, aPTT), and renal function measures (eGFR, creatinine) consistently emerged as dominant predictors. These findings underscore the multifactorial nature of DSA development and demonstrate that integrating immunological, biochemical, and clinical domains provides a robust basis for immunological risk stratification after kidney transplantation.

CONCLUSIONS

This study developed a machine learning–based ensemble model that improved prediction of donor-specific antibody (DSA) positivity and facilitated immunological risk stratification in kidney transplant recipients. The ensemble approach achieved better performance than individual models, underscoring the advantage of integrating boosting methods with deep learning.

Feature importance analyses consistently highlighted immune-related markers, coagulation indices, and renal function parameters as key contributors, reflecting the multifactorial nature of DSA development.

By incorporating multimodal clinical, biochemical, and immunological data, the model may enable early identification of high-risk patients and support optimization of post-transplant immunosuppression strategies. Although the results are promising, validation in larger, multi-center cohorts will be essential to confirm generalizability and assess clinical utility.

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