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Kidney Transplantation and AI Impact: A Narrative Review of Pre- and Post-Transplantation Challenges

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Abstract

This narrative review examines the impact of Artificial Intelligence (AI) on the journey of kidney transplantation (KT), focusing on significance of organ matching, allocation, delayed graft function, rejection, and immunosuppression. KT remains the preferred treatment for end-stage renal disease (ESRD), but its success depends on managing multiple complex variables. The risk factors influencing outcome of KT are grouped into: 1) pre-transplant factors, including donor-recipient matching, organ quality, allocation, and organ shortage; and 2) post-transplant factors, including delayed graft function, rejection episodes, immunosuppression, and immune tolerance. Traditional approaches are compared with AI-driven methods across these stages. Successful transplantation relies heavily on HLA matching, yet

challenges such as genetic heterogeneity, recipient sensitization, health disparities, and organ shortages result in prolonged waiting times and risk of dialysis. While systems like UNOS use advanced matching algorithms, AI through machine learning (ML) and deep learning (DL) technologies can analyze more complex datasets, including genomic variants associated with immunologic responses and clinical variables outside of UNOS datasets unreachable by traditional methods, to improve prediction of post-transplantation complications, optimize therapies, and reduce organ rejection. AI is particularly valuable in computationally complex challenges for solving clinical problems where traditional methods are limited.

Keywords: Artificial intelligence; Human leukocyte antigen (HLA); Immunosuppression; Organ-allocation, Organ-matching; Transplantation

Introduction

This narrative review highlights 1) the major challenges in kidney transplantation as a critical treatment for End-Stage Renal Disease (ESRD), and 2) the potential of Artificial Intelligence (AI) to improve outcomes by addressing issues such as organ allocation, rejection, and personalized immunosuppression.

Kidney Transplantation Challenges, Immunologic Response, and Tolerance

The first successful human kidney transplant between identical twins in 1954 **[1]** laid the foundation for advances in surgical techniques **[2],** immunosuppressive therapy **[3],** and understanding immune responses **[4]** and immunological innovations **[2,5].** Donor-recipient blood type compatibility remains the initial requirement in organ matching. As of January 2026, over 90,000 Americans were on transplant waiting lists, with kidneys being the most needed organ, yet only about 30% of patients received transplants **[6].** Most organs come from deceased donors, while living donors provide shorter waiting times and better-quality grafts, for a longer clinical outcome. However, factors such as brain death and Ischemia-Reperfusion Injury (IRI) during procurement affect organ quality and contribute to Delayed Graft Function (DGF) **[7-9].** Transplantation challenges occur in both pre- and post-transplant phases. Pre-transplant risks include HLA mismatch, recipient pre-sensitization (high panel-reactive antibody), age, and sex, all contributing to organ allocation difficulties **[10,11].** Post-transplant complications include rejection **[12,13],** immunosuppressive therapy complications **[14],** and infection **[15],** which impact graft survival. Five-year survival rates range from 70–80% for deceased donor recipients **[16]** and 80–90% for living donors **[17],** declining thereafter [**18].** Key risk factors for graft loss after one year, include donor and recipient age, HLA mismatch, and DGF **[19-21],** along with comorbidities such as diabetes and cardiovascular disease **[15,20,22].** The immune response to allografts is complex and begins early with IRI, triggering innate immune activation through dendritic cells, macrophages, and Toll-like receptors **[23-25]** recognizing Damage-Associated Molecular Patterns (DAMPs) **[26].** This leads to cytokine release, inflammation, DGF, and potential rejection **[27-29].** Sensitization in transplantation is also a potential for innate allorecognition in kidney transplant **[30]. Figure 1**, shows a graphic presentation of innate and adaptive immune regulatory cells in response to the potential DAMPs associated with allograft **[5].** Acute rejection may occur within weeks via T-Cell Mediated (TCMR) or

Antibody-Mediated (ABMR) mechanisms [31], requiring intensified immunosuppression, tailored to individual characteristics critical to the success of kidney transplantation.

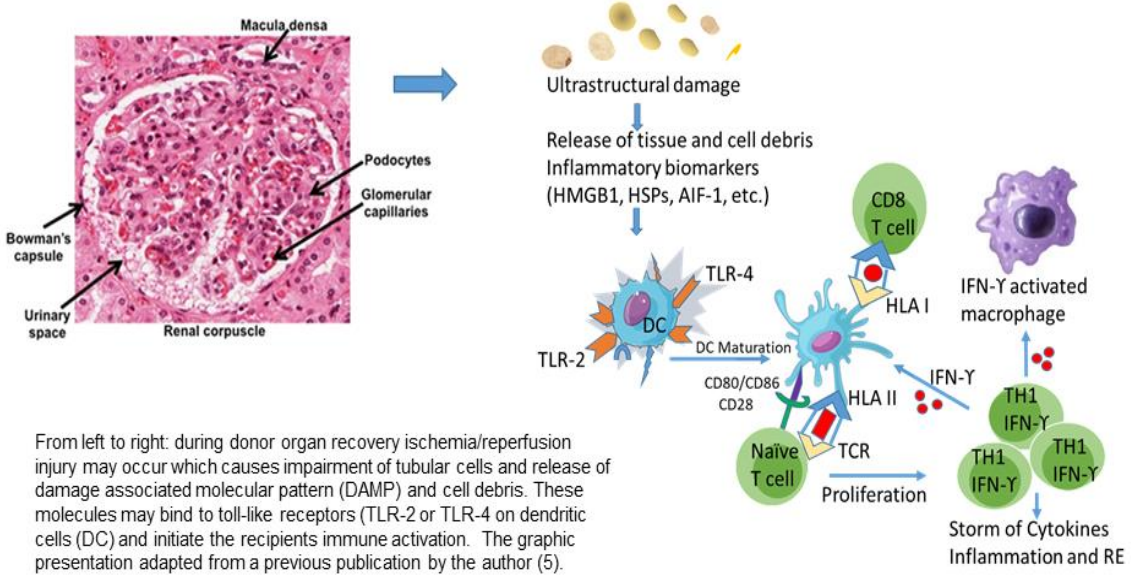

Figure 1: A graphic presentation of innate and adaptive immunity development due to damage to the transplant. Ischemia reperfusion injury (IRI) causes impairment of tubular cells and release of Damage Associated Molecules (DAMP) and cell debris. These molecules bind to TLRs on Dendritic Cells (DC) and initiate the immune activation. Abbreviations: AIF-1, allograft inflammatory factor-1; TLRs: toll-like receptors; HMGB1: high mobility group box1; HSPs: heat shock proteins; HLA: human leukocyte antigen, TH1 T-helper cells; TCR: T-cells receptor; etc. (Adapted from a publication by the author [5].

Long-term graft survival can sometimes occur naturally due to immune tolerance when the recipient recognizes the donor tissue as self, avoiding damaging immune responses, although it involves complex regulatory pathways. However, it is critical from therapeutic standpoint to understand how immune cells stimulate graft tolerance and regulation of alloantigen for a successful transplant [32,34]. AI-driven approaches may help identify potential molecular markers of tolerance through genomic and proteomic analysis. Machine learning can analyze HLA epitopes and *eplets* to reduce donor-specific antibody (*dnDSA*) formation, improve immunologic risk assessment, and enhance clinical outcomes [35,36]. *Eplets* are clusters of amino acids located on the surface of HLA molecules (epitopes) that can induce alloimmune response with the potential for long-term allograft dysfunction. An HLA-Matchmaker algorithm has compatibility at the level of *eplet* identification [59].

Technological Challenges of AI and Machine Learning

AI and Machine Learning (ML) offer significant potential to improve kidney transplantation by addressing organ shortages, reducing rejection, optimizing immunosuppressive therapy, and lowering infection risks. Current systems such as UNOS and Organ Procurement and Transplantation OPTN utilize computerized Kidney Allocation Models (KAS) incorporating HLA high resolution

genotyping [37] and scoring systems like Kidney Donor Profile Index (KDPI) and Expected Post Transplant Survival Score (EPTSS) [38,39], which allow fewer kidney being discarded. While useful, these systems lack real-time adaptability and require continuous refinement. AI can enhance organ allocation by integrating donor-recipient compatibility, clinical history, and genetic data to improve matching efficiency and outcomes [40,41]. AI integration models have shown promise in identifying recipients who may benefit from higher-risk donor kidneys, with shorter waiting time and consideration of all patients factors simultaneously [42], outperforming traditional metrics. ML a subfield of AI uses multiple algorithms known as unsupervised learning (pattern recognition without labels), supervised learning (using known labeled data), and reinforcement learning (decision-making through iterative feedback) [43-46]. Deep Learning (DL), a subset of ML, uses neural networks to analyze multi-layers complex patterns, in kidney transplantation and have the advantage of assessing big databases from population genomics profiles, biopsy imaging, and pharmacogenetics for prediction of clinical complications [47-49]. These technologies are continuously upgraded, thus capable of presenting a real-time data for organ matching and allocation with speed and accuracy, crucial in the maintenance of high-quality organs and significant impact on the outcome of long-term organ survival. As AI systems continue to evolve, they offer prediction of clinical solutions, improved pathological assessment, and personalized immunosuppressive strategies based on metabolic and genetic profiles, for a successful transplantation journey [49,50].

Methods

This narrative review aimed to highlight two key areas: 1) risk factors influencing pre- and post-transplant organ function that may lead to Rejection Episodes (RE) or long-term allograft dysfunction, and 2) the role and advantages of AI technology in successful kidney transplantation.

A literature search was conducted using PubMed (NCBI/NIH), ScienceDirect, and Google for studies published between 2010 and 2025, focusing on organ allocation, transplantation, and AI applications, including Machine Learning (ML) and Deep Learning (DL). Databases from UNOS, OPTN, SRTR, HRSA, and IPD-IMGT/HLA were also included. Emerging AI trends in organ allocation and personalized immunosuppression were reviewed. AI systems build upon traditional data sources such as UNOS and OPTN to support organ allocation modeling [38,39]. In highly sensitized patients, ML can classify recipients with high Panel-Reactive Antibodies (PRA) and improve HLA compatibility assessment [51]. This review integrates key clinical risk factors in transplantation with AI applications to demonstrate an overview of generative AI applications to the clinicians and researchers within the field [41,52].

Only studies specifically addressing kidney transplantation and AI applications were included. Key transplantation variables are summarized in **Table 1.**

Table 1: Application of AI and ML in crucial indicators associated with kidney transplantation.

Indicators	Technology	References
Donor-recipient identification	U-Net/ Random Forest, CNN	UNOS, OPTN, HRSA registry databases [16]
Donor-recipient matching	Random Forest, Neural Network, Gradient boosting	UNOS, OPTN registry databases [16,38,39,67,68]
Donor Organ quality and procurement	Random Forest, OPTN	UNOS, OPTN, [38,39], [78,79,80]
Donor Organ allocation, waiting time and Organ shortage	Linear-based algorithms, XG-Boost, Random Survival Forest	UNOS, OPTN, EPTSS [83,84,86] [72,87]
Delayed graft function (DGF)	Neural Network, Random Forest, Elastic Net (Lasso and Ridge), XG-boosting	UNOS, [90,91,92], [41,49,95,96]
Kidney rejection episodes (REs)	Neural Network, Decision tree, RF, SVM, Hybrid trees, Deep neural networks, XG-Boost	UNOS, [97-100] [78,102-105] [106-109]
Immunosuppression	Tab-Net, XG-Boost, hybrid of tree-based models (DNN)	[111-113], [49,113-116]

A summary of crucial clinical indicators in transplantation, identified through traditional and AI models

The traditional methods are based on linear relationships and known features, and AI techniques use complex algorithms for a multidimensional database for identification of patterns and associated risk factors. Tree-base techniques such as Random Forest (RF) are practical for detection of many aspects of transplantation. The enhanced performance of the RF algorithms was ensembled for hyperspectral image classification at post-transplantation. Similarly, extreme gradient boosting (XG Boost) was used for hyperspectral image classification. Deep Neural Network (DNN) was less popular because of one-dimensional, over the conventional DNN with Multilayer Perception (MLP). The Tab-Net was a deep learning model, designed for tabular data, thus it was useful in transplantation for prediction of immunosuppressant dosing and estimation of graft survival outcome.

Results

Pre-Transplantation Challenges

Donor/Recipient Identification (Traditional and AI): Donor identification is a critical component of transplantation, guided by national policies that match donor organs with recipients based on blood type, demographics, and geographic proximity. Systems such as the UNOS registry store donor-

recipient data within secure, high-resolution databases, including HLA typing, genetic profiles, and clinical variables. These systems, supported by platforms like U-Net, that uses encoders to track every organ donation and transplantation events. The registry incorporate high resolution HLA alleles and haplotypes, Next-Generation Sequencing (NGS) data and epitope-based HLA molecules for accurate labeling the donor-recipient identification [**35,53,54].** AI combines large-scales population genomic and clinical datasets to create comprehensive profiles of donor-recipients identification. Such profiles may not be evident through traditional methods. By integrating ML algorithms such as Random Forest, AI can identify potential risks before transplantation, improving donor-recipient matching and outcomes, particularly in living donor cases **[55-57].** However, their effectiveness depends on data quality and completeness, which remains a challenge in real-time clinical prediction.

Donor-Recipient Matching (Traditional Indicators): HLA genotype matching remains central to transplantation success. Systems like UNOS and OPTN utilize scoring tools such as KDPI and EPTSS **[38,39]** to improve allocation and reduce organ discard **[58].** Advances in genomic testing, including HLA epitope analysis, using the epitope matchmaker and HLA-EpiCheck **[59,60];** predicts the immunogenicity of HLA antigens, T-cell receptor binding sites; the HLA-DQ *eplet* mismatches and the HLA-DQ-dnDSA, better prediction of immunologic risk outcomes **[61,62].** Despite these improvements, outcomes beyond the first year remain affected by rejection and limitations of immunosuppressive therapies. HLA molecules are highly polymorphic, with over 35,000 identified alleles since 2023 **[63-66],** thus, complicating donor-recipients' matching. An HLA classification and alleles are given in **Table 2,** and **Figure 2**. Additionally, *eplet* mismatches often not routinely assessed, can trigger immune responses and contribute to rejection, especially in sensitized patients **[30].** Continuous development of advanced algorithms is required to interpret this genetic complexity.

Table 2: HLA Major Classifications, alleles, subunits and minor antigens at the MHC Class I and Class II Loci.

MHC Class I Locus		MHC Class II Locus			
Major Antigens	NO	Major Antigens	Subunit A1 NO	Subunit B1 NO	Subunit B3-B5 NO
HLA A	1,884	HLA DM	7	13	
HLA B	2,490	HLA DO-	12	13	
HLA C	1,384	HLA DP-	34	155	
Minor Antigens					
HLA E	11	HLA DQ-	47	165	
HLA F	22				
HLA G	49	HLA DR-	7	1,094	92

Table 2, demonstrates number of variant alleles and subunits based on HLA nomenclatures determined by next generation of sequencing presented the during 17th international HLA and Immunogenetics workshop **[64].**

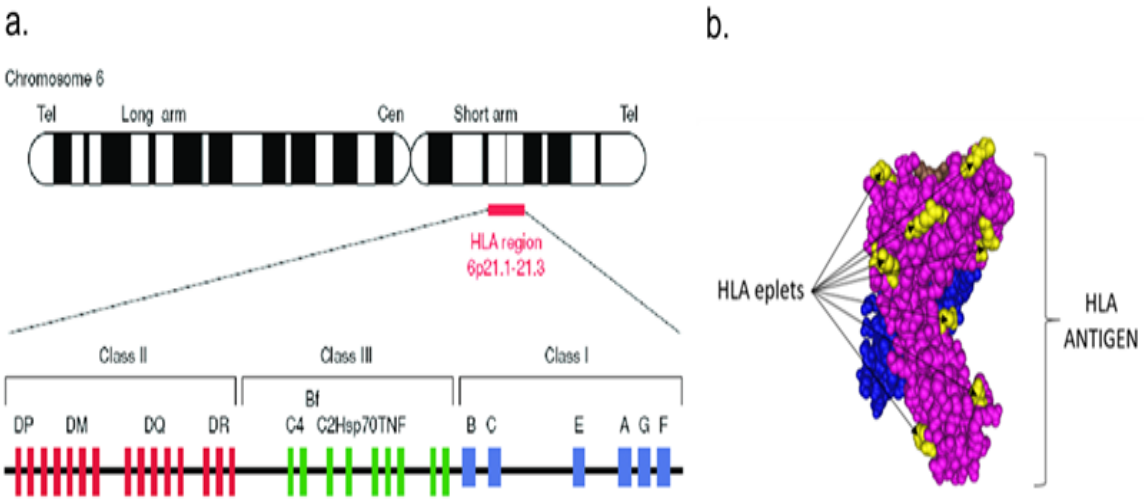

Illustration of genomic map of the human HLA region on chromosome 6 and clusters of *eplets* on HLA molecules. Adapted from Cambridge University free press. a. presents clusters of the HLA loci. b. presents multiple clusters of *eplet* epitopes on the surface of HLA antigen.

Figure 2. The HLA gene map on short arm of chromosome 6.

a. The region is orgnaized into three classes of genes, Class I, -II, -III. The gene product for each class is identified with different gene structure and function. Each plays a significant role in the immune system and transplantation response to allograft.

b. Presents clusters of epletes, which are small structures of polymorphic amino-acides. The eplet mismatches allows increased probability of chronic rejection and graft failure.

Donor-Recipient Matching (AI Approach): AI, particularly ML and Deep Learning (DL), offers advanced solutions for donor-recipient matching by identifying complex patterns beyond traditional statistical models. Techniques such as neural networks and Random Forest algorithms can predict compatibility and identify previously unrecognized variables **[67,68].** Such predictive analysis allows identification of infrequent patterns probably over-looked by the traditional regression models. Integration of multi-omics data (e.g., transcriptomics, proteomics) enhances early detection of rejection biomarkers. For example, integrating high-through put omics technology, such as single RNA sequence and proteomics may provide previously unrecognized biomarkers in association with early rejection episodes **[69].** AI models can also incorporate patient-specific factors (genetics), demographics (age, sex, BMI), comorbidities (hypertension, diabetes, cardiovascular), and drug interactions to enable personalized immunosuppressive strategies, preventing drug toxicity, allograft injury and patient death **[52,70,71].** In this approach AI algorithms cluster high-dimensional donor features into one set

and applied to the recipient features to predict the match [49,71,72]. The system integrates live data from donor—recipient registry and continuous updates, allowing the algorithms to adapt changes for improving allocation accuracy, although they may not always outperform traditional models [41,73].

Donor Organ Quality and Procurement (Traditional Approach): Donor organ quality significantly influences transplant outcomes. The Kidney Donor Profile Index (KDPI) estimates graft longevity, with lower scores indicating better expected survival. Donor age, comorbidities (e.g., diabetes, hypertension), and procurement conditions affect quality. Extended Criteria Donors (ECD) often require biopsy and machine perfusion, which has become a standard method for improving organ preservation and reducing Delayed Graft Function (DGF). However, current organ assessment methods are not standardized and often rely on subjective evaluations, risk scores, and limited biopsy data. Advanced techniques such as omics technologies and imaging are needed to improve organ utilization and reduce discard rates.

Donor Organ Quality and Procurement (AI Technology): AI-based systems are emerging to improve Organ Quality Assessment (OQA) using large datasets of medical images and molecular markers. Deep learning models can analyze imaging data and transcriptome profiles of biopsy samples to detect inflammatory pathways of immune activation at pre- and post-perfusion. These models are trained based on either detection of Mononuclear Leukocytes (MNL) using Convolution Neural Network (CNN), and or tissue segments (U-Net), which is crucial for understanding changes in kidney organ structure associated with susceptibility to DGF or early rejection episodes [74,75]. Biomarkers such as NGAL, KIM-1, and inflammatory gene signatures provide insights into zero- hour kidney injury or during perfusion and procurement [76,77]. Díez-Sanmartín, et al. [78], have used the AI models such as Random Forest specifically, Random survival Forest (RSF), testing donor organ quality, in the context of post-transplant survival rates focusing on Stable Graft Function (SGF) and allograft Rejection Episodes (REs). Furthermore, Fisher et al. [79] have shown Hyperspectral Imaging (HSI) combined with ML algorithms can assess condition of donor kidneys in respect to tissue physiology and compositions, helping in the decision process for organ viability and acceptance or identifying kidneys at risk of discard [79,80,81]. These approaches outperform traditional risk scores by integrating multidimensional data, though further validation is needed.

Donor Organ Allocation, Waiting Time, and Shortage (Traditional Approach): Kidney allocation systems are based on organ quality, urgency, and geographic factors, with viability typically limited to 24–36 hours. Allocation decisions incorporate variables such as comorbidities, dialysis duration, and survival scores (EPTS). Despite sophisticated algorithms, organ shortage and allocation inefficiencies remain major challenges [82]. Programs such as kidney exchange and accelerated placement initiatives (KAPP) aim to improve allocation, including the use of altruistic Non-Directed Donors (NDD) [83,84]. Advances in HIV drug therapy and the Organ Policy Equity-Act, now allow expanded donor pools (e.g., HIV/HCV-positive donors) [85]. However, variability in access and allocation practices continues to limit effectiveness. In accordance with that the OPTN implemented the Kidney Accelerated Placement Program (KAPP) with the goal to improve the utility

of “Hard to Place kidneys” through the organ centers with high acceptance demand **[86].** The organ allocation pathways are numerous. Examples are given in **Figure 3.**

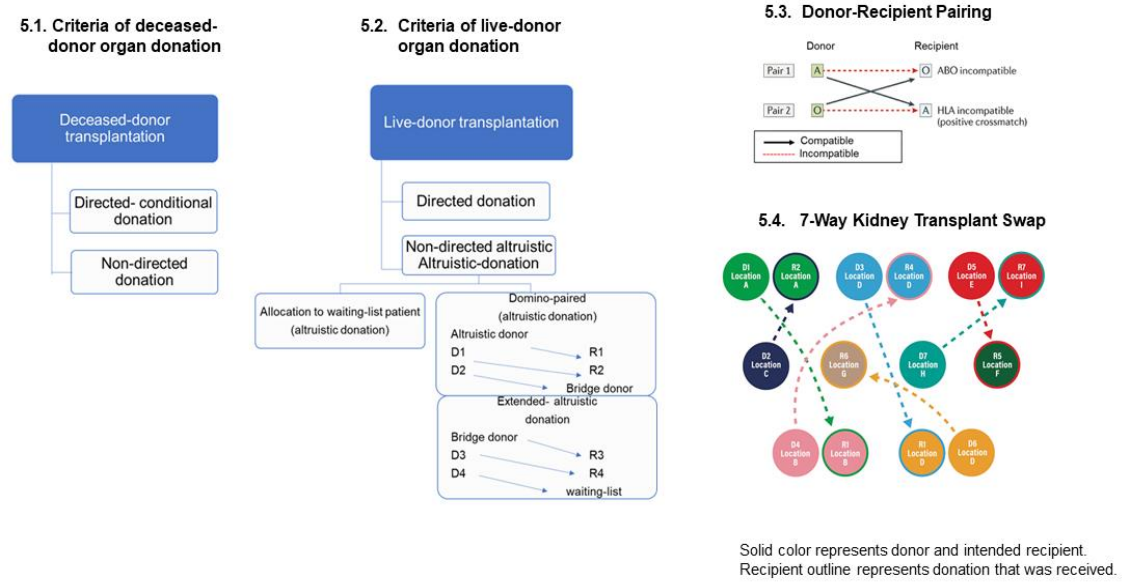

Figure 3: Multiple Traditional and Novel Pathways of donor-recipient selection and organ donation**.**

3.1. In deceased donor transplantation, the directed- conditional donation is between the deceased donor that made a request during life, to be transplanted to a specific recipient in the family member or a friend. In non-directed donation, also known as altruistic donation, the donor and recipient are not known to each other. The organ compatibility (match) is arranged based on medical compatibility between donor-recipient pair.

3.2. In living organ transplantation, the donor makes decision who to donate their organ. The donation is either directed in which the donor selects his/her specific recipient for transplantation. Most often the donation is between 6 antigen matched siblings. Or it is non-directed living donation. As shown here the donated organ either is allocated to a wait-listed patient, or goes toward transplantation chains also called domino-paired donation, which consecutively goes over a limited period donation or an extended altruistic donation chain. During the first period the D2 (donor 2) becomes a bridge donor, if does not have a match, but then matches with R3 (recipient 3) in the extended future run.

3.3. This pattern shows 2 sets of donations between donor-recipient pairs. When the living donors are not compatible with their designated recipients for transplantation but the donor of each pair is compatible with the recipient of the other pair.

3.4. Finding the right match between donors and recipients can be challenging. Kidney swaps can provide a great solution to increase organ allocation and a successful organ transplantation. Here solid color represents donor and intended recipient. Recipient outline represents donation that was received. This is a living-donor chain donation in which more than one pair of living donors are linked with non-directed living donor to form donation chain in order to receive compatible organ.

Donor Organ Allocation, Waiting Time, and Shortage (AI Technology): AI and ML technologies are improving allocation efficiency through data-driven ranking systems and predictive models. Firuzpour, F.; et al. findings indicated techniques such as deep learning and ensemble methods (e.g., XGBoost, Random Survival Forests) outperform traditional scoring systems like KDRI and EPTSS in predicting waitlist and allograft survival outcomes with Concordance-Indices ranging between 0.65-0.72 **[72].** AI integration supports equitable access, reduces waiting times, and improves organ utilization **[40,72,87].** Innovations such as Internet of Things (IoT) devices enable real-time tracking of donor organs, monitoring environmental conditions during transport, and reducing spoilage. Additionally, real-time patient data monitoring allows early detection of complications **[88,89].** Overall, AI-driven systems enhance allocation speed, accuracy, and adaptability, addressing disparities in organ availability and improving transplantation outcomes.

Post-Transplantation Challenges

Delayed Graft Function (DGF) (Traditional Approach): Delayed Graft Function (DGF) is a common complication affecting 20–40% of kidney transplant recipients, particularly with Extended Criteria Donors (ECD). Risk factors include ischemia-reperfusion injury **[90,91],** older donor age, cardiac death prior to donation, and elevated terminal creatinine. Although hypothermic machine perfusion and dopamine infusion may reduce injury, dialysis is often still required upon DGF at post-transplantation. Predicting DGF in advance could improve clinical decision-making and procurement strategies. Emerging approaches, including Next-Generation Healthcare Innovative Technologies (NGHIT), combine with nanotechnology platforms, aim to improve organ quality and reduce complications through advancement in genomic editing and organoid manufacturing **[92].** AI and ML offer advantages in identifying and integrating these risk factors for predictive modeling **[93,94] (Figure 4).**

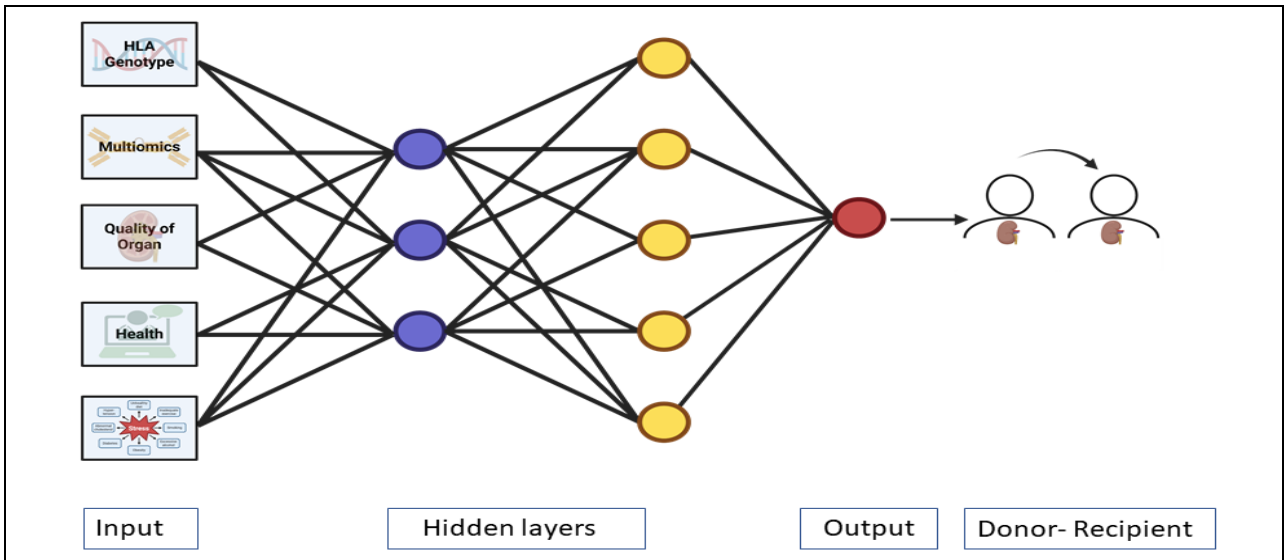

Figure 4: A graphic presentation of the hypothetical neural network model for donor-recipient match. The model comprised of traditional donor-recipient compatibility factors such as HLA genotypes, multi-omics database, quality of organ based on donor age, health and procurement status, immunological condition based on ischemia-reperfusion injury, and stress related factors to assess compatibility on a continuing level for a suitable donor-recipient matching.

Delayed Graft Function (DGF) (AI Approach): ML-based models integrating donor and recipient characteristics can improve prediction of early graft outcomes and may outperform traditional statistical methods like Cox regression models. Models such as Random Forest and XGBoost have demonstrated high accuracy (AUC up to 0.98) in distinguishing Immediate Graft Function (IGF) from DGF, by integrating large sets of donor and recipient clinical and pathological data to predict graft function. Likewise, Artificial Neural Networks (ANN) and Elastic Net algorithms, can integrate clinical, histopathological, and genomic data to accurately predict outcomes such as DGF, RE, and Stable Graft Function (SGF). These models enable early risk stratification and support personalized clinical decision-making to improve long-term outcomes **[95,96].** Furthermore, they out perform traditional statistical approaches by identifying complex, non-linear relationship across multi-dimensional datasets.

Allograft Rejection and Survival Outcomes (Traditional Approach)

Early rejection, particularly within the first two weeks, significantly affects graft survival and requires accurate diagnosis, with biopsy remaining the gold standard. Prognostic factors include cadaveric verses living donor, recipient comorbidities, age, BMI, beneficial to the survival rates in distinct ways. Given the variety and complexity of kidney allograft injury, multiple strategic methods are needed to optimize graft function and preventing the recipients going back to dialysis **[97-99].** While short-term graft survival has improved, long-term outcomes remain limited due to comorbidities, infections (e.g., BK virus, CMV), malignancies, and prolonged immunosuppression and drug toxicity **[100-102].** Improving long-term survival requires predictive tools capable of anticipating complications before clinical manifestation.

Allograft Rejection and Survival Outcomes (AI Approach)

AI tools can analyze clinical, genomic, and biopsy data to predict graft survival over time and identify patients at high risk of allograft dysfunction, preventing them from returning to dialysis **[102,103].** Integration of electronic health records, laboratory data, and genetic profiles enables early detection of complications and supports clinical decision-making for a long-term graft survival. Model performance is assessed using metrics such as accuracy, sensitivity, specificity, and AUC. To predict a 10year kidney allograft survival, advanced models incorporate donor-recipient variables, rejection history (TCMR, ABMR), biopsy classifications (Banff), at different time points and infections data resistance to immunosuppressive regimen to enhance prediction of transplant survival **[104,105].** Techniques such as Random Forest and XG Boost often outperform traditional models, but these tools primarily are research-based and are trained and evaluated for their sensitivity; specificity; accuracy; F1 measures (balance between precision and recall; and area under the curve "AUC" (1.0 indicates perfect, and 0.5 represents random guessing).They are under various stages of development and validation remains ongoing **[102].** AI-driven tools such as Neural Network models can continuously improve prediction outcomes by integrating pre- and post-transplant variables including DGF, GFR, biopsy findings, and immunosuppressant levels through model updates. A Hypothetical example of Neural Network model including input layer for variables, and hidden and output layers to forecast outcomes for organ transplantation is shown in **Figure 5.**

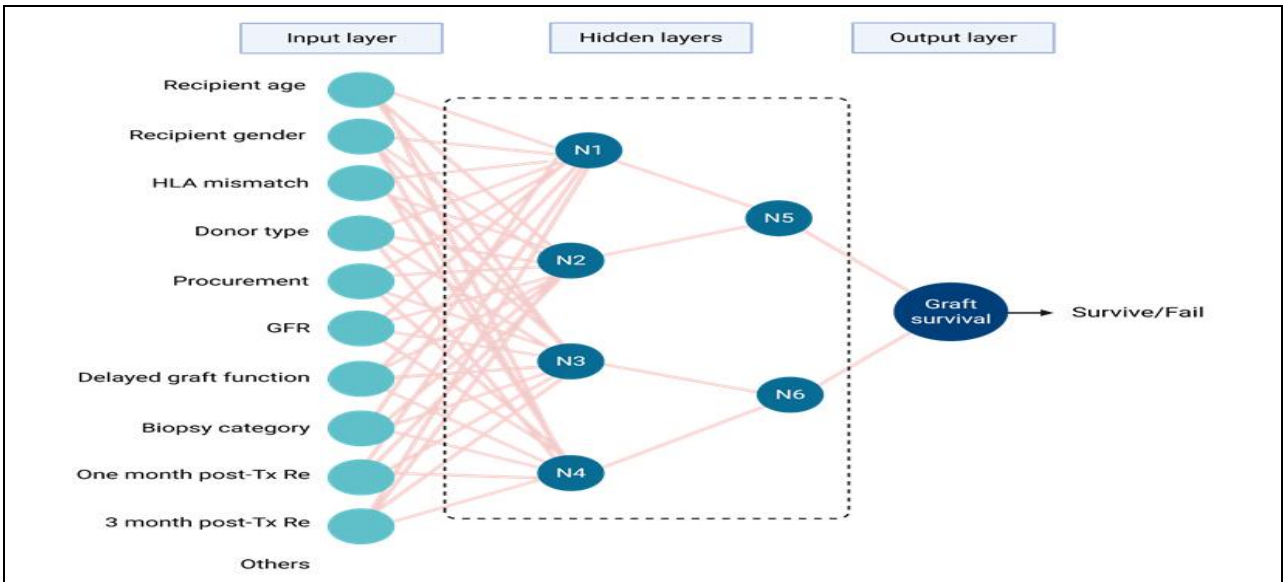

Figure 5: A hypothetical illustration of Neural Network model to Forecast outcomes of kidney transplantation (adapted from AI models).

The model includes three layers of input, hidden and output layer. The model presents donor-recipient's compatibility factors, demographic and clinical characteristics. Additional crucial factors along with the transplantation journey, are data from procurement settings, Glomerular Filtration Rates (GFR), Delayed Graft Function (DGF), Kidney Biopsy Categories, one- and three-month post-transplant rejection episodes and other variables based on immunosuppressive dose ratio of oral vs. plasma concentration analysis.

Studies using combined datasets from pre-transplant factors, post-transplant Glomerular Filtration Rate (GFR), immunosuppressants such as Mycophenolate Mofetil (MMF), 1st month acute rejection and CMV infection have achieved high predictive accuracy (e.g., ~91% for 5-year graft survival), indicating the significance of early post-transplant indicators **[102,106-108].** Some studies explored a wide range of ML models to capture complex multi-omics and clinical data for prediction of kidney allograft outcomes. Badrouchi S, et.al. have proposed 35 models combined of 5 different training algorithms such as Artificial Neural Network (ANN), Decision Trees (DT), Random Forest, Support Vector Machine (SVM), and multiple hybrid trees (extra trees and XG Boost) and multiple datasets based on study feature selections for predicting kidney graft survival. **[78,109].** These models are proposed tool for clinicians to monitor recipient's kidney status, and to determine suitable ways to improve long-term survival rates.

Immunosuppression (Traditional Approach): Effective immunosuppression balances rejection prevention with minimizing infection and toxicity. Dosing remains challenging due to narrow therapeutic windows and variability in drug metabolism **[110].** Genetic polymorphisms, such as CYP3A4/5 and UGT1A9, significantly influence drug response to tacrolimus, cyclosporine, and mycophenolate **[111,112].** Traditional models often struggle to integrate complex genomic and clinical datasets, limiting their ability to predict drug response accurately. Genomics variability across populations (e.g., SNP, *eplets* testing), that traditional models cannot effectively process, further complicates dosing strategies, requiring careful

monitoring to avoid graft rejection or toxicity [112,113].

Immunosuppression (AI Approach): AI and ML enable personalized immunosuppressive therapy by analyzing genomic, metabolic, and clinical variables. These models predict drug response, toxicity, and optimal dosing, improving treatment precision beyond traditional approaches [113,114]. Techniques such as neural networks and advanced models such as TabNet, a deep tabular data learning technique uses a hybrid of tree-based models and Deep Neural Network (DNN) can predict tacrolimus pharmacokinetics, cyclosporine levels, and rejection risk with high accuracy [115]. Integration of multi-omics data allows early detection of adverse effects and supports individualized therapy. By using toxicology resources (e.g., TOXRIC database), and personalized genomics factors in drug development [116], AI predicts individualized drug toxicity, contributes to drug discovery, including prediction of protein structures and donor-specific antibody responses. These innovations enhance precision medicine approaches, improving graft survival while reducing adverse outcomes.

Discussion

This review highlights key challenges in kidney transplantation and evaluates how AI technologies can improve outcomes across the transplant continuum. AI models, including neural networks and ensemble approaches such as Random Forest and XGBoost, demonstrate advantages over traditional methods by analyzing complex, dynamic datasets and enabling real-time, data-driven decision-making providing an optimized allograft survival to the clinical needs [40,41]. A major challenge remains the disparity between organ availability and patient demand, driven by long waiting lists, health inequities, procurement limitations, and organ transport logistics [40,41,117]. Effective communication among transplant team participants is essential, and digital tools such as innovative devices (IoT) [93], which are time sensitive, and mobile applications (e.g., TxpChat) can enhance coordination and improve transplantation rates [88,117]. Since 1984, UNOS has managed the OPTN, providing a national database for transplantation, complemented by genetic registries such as IPD-IMGT/HLA [66]. However, traditional matching approaches often overlook emerging molecular factors, such as RNA-based mutations and *eplet* mismatches, which allows predictability for the de novo Donor Specific Antigens (DSA) and contribute to antibody formation and chronic rejection episodes and graft failure [118,119]. Variability across transplant registries (e.g., UNOS, SRTR, USRDS), heterogeneity in organ transplant records, lack of standardization and complex statistical modeling limit consistency in reporting and predicting long-term outcomes [120,121]. These challenges highlight the need for more robust, integrated data systems. AI introduces opportunities for precision transplantation by integrating complex genetics profile, immunologic and clinical characteristics of donor-recipient pair and tailor immunosuppressive therapies and survival rates to improve donor-recipient matching. AI models can analyze historic databases from patient's registry to forecast donor risk, prioritize candidates, and optimize allocation strategies [49,122], exceeding the capability of traditional methods. For example, UNOS and MIT in recent collaborations have developed AI-driven frameworks to enhance equitable organ allocation and improve access for

high-risk patients. In this model, ML (including Rand Forest, Neural Networks, Logistic Regression, K-nearest Neighbors) have used simultaneously, mathematical algorithms to evaluate all patient's factors into a unique weighted score that corresponds with their risks and medical urgencies priorities the sickest patient **[72].** Machine learning approaches, including supervised and unsupervised methods, enable identification of patterns in donor-recipient characteristics and IRI biomarkers, assisting in risk prediction and clinical decision-making approaches (e.g., organ acceptance, utility of marginal organ and timing) **[41,42].** Models such as XGBoost and Random Forest show high predictive accuracy for graft survival and clinical outcomes, supporting their use in personalized care **[95,109].** AI is also advancing imaging analysis, biopsy interpretation, and integration with emerging technologies such as gene editing (CRISPR/Cas9) **[123**], nanotechnology **[124],** and organoid development **[125].** Innovations such as xenotransplantation and bioengineered kidney organoids offer potential solutions to organ shortages, while AI supports their development and optimization **[125,126].** Although AI remains primarily a supportive tool, it is rapidly becoming an integral component of transplantation. Its ability to process high-dimensional data and continuously update predictive models makes it as a critical driver of improved decision-making in the transplantation journey. Ultimately, integration of AI into clinical practice may enhance donor-recipient matching, optimize immunosuppression, and improve long-term graft survival and patient health.

Conclusions

AI enhances the accuracy and efficiency of organ allocation while offering predictive capabilities for immunosuppressive therapy and long-term allograft outcomes. It improves organ matching and tracking through technologies such as Internet of Things (IoT), enabling real-time monitoring and optimized allocation processes. Despite its promise, AI remains in early stages and requires further validation and clinical implementation to improve transplantation success rates, reduce organ shortage and rejection, and enhance patient survival. Future efforts should focus on integrating AI with emerging technologies such as xenotransplantation and organoid development to advance personalized therapeutics and expand organ availability. AI is particularly valuable in handling complex clinical scenarios where rapid, data-driven decisions are required.

Limitations of Review and Future Direction

This review is not a systematic analysis and does not include quantitative comparisons across studies. However, it highlights the clinical relevance of AI in kidney transplantation. Future advances in AI and ML are expected to improve transplantation by shifting toward personalized, precision medicine. Integration of genomic, clinical, and imaging data can enhance donor-recipient matching, optimize organ allocation, and improve graft survival. AI algorithms are suitable in generating human "3D" kidney-like organoids, (e.g., organoids on Chip), offering novel application of kidney mature structure with cellular heterogeneity suitable models for drug screening **[127]** and kidney disease (e.g., polycystic kidney disease) **[128].** These fully developed organoids potentially have a significant role in translational and therapeutic application and future capability of minimizing current organ shortages. The advances in constructing mature structure organoids through xenotransplantation is a promising approach

to improve inconsistencies in organoid formation, increase accuracy and enhance kidney transplantation. This review integrates key clinical risk factors with AI applications to demonstrate how these technologies can optimize organ allocation, manage rejection, and refine immunosuppressive strategies, offering valuable insights for clinicians and researchers.

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Ethical Considerations

AI in transplantation carries risks, as clinicians may rely on incorrect model recommendations. Therefore, careful evaluation of data quality, ethical implications, and system transparency is essential. Collaborative oversight among healthcare professionals, researchers, and the transplant community is critical to ensure AI improves accuracy, equity, and patient outcomes.

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