BioMedInformatics

Review

Revolutionizing Kidney Transplantation: Connecting Machine Learning and Artificial Intelligence with Next-Generation Healthcare—From Algorithms to Allografts

Luís Ramalhete [1,2,3,*], Paula Almeida [1], Raquel Ferreira [1], Olga Abade [1], Cristiana Teixeira [1] and Rúben Araújo [2,4]

[1] Blood and Transplantation Center of Lisbon, Instituto Português do Sangue e da Transplantação, Alameda das Linhas de Torres, nº 117, 1769-001 Lisboa, Portugal
[2] NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, 1169-056 Lisbon, Portugal
[3] iNOVA4Health—Advancing Precision Medicine, RG11: Reno-Vascular Diseases Group, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, 1169-056 Lisbon, Portugal
[4] CHRC—Comprehensive Health Research Centre, NOVA Medical School, 1169-056 Lisboa, Portugal
* Correspondence: luis.m.ramalhete@edu.nms.unl.pt

Abstract: This review explores the integration of artificial intelligence (AI) and machine learning (ML) into kidney transplantation (KT), set against the backdrop of a significant donor organ shortage and the evolution of 'Next-Generation Healthcare'. Its purpose is to evaluate how AI and ML can enhance the transplantation process, from donor selection to postoperative patient care. Our methodology involved a comprehensive review of current research, focusing on the application of AI and ML in various stages of KT. This included an analysis of donor–recipient matching, predictive modeling, and the improvement in postoperative care. The results indicated that AI and ML significantly improve the efficiency and success rates of KT. They aid in better donor–recipient matching, reduce organ rejection, and enhance postoperative monitoring and patient care. Predictive modeling, based on extensive data analysis, has been particularly effective in identifying suitable organ matches and anticipating postoperative complications. In conclusion, this review discusses the transformative impact of AI and ML in KT, offering more precise, personalized, and effective healthcare solutions. Their integration into this field addresses critical issues like organ shortages and post-transplant complications. However, the successful application of these technologies requires careful consideration of their ethical, privacy, and training aspects in healthcare settings.

Keywords: kidney transplantation; machine learning; artificial intelligence; precision medicine

check for updates

Citation: Ramalhete, L.; Almeida, P.; Ferreira, R.; Abade, O.; Teixeira, C.; Araújo, R. Revolutionizing Kidney Transplantation: Connecting Machine Learning and Artificial Intelligence with Next-Generation Healthcare—From Algorithms to Allografts. *BioMedInformatics* **2024**, *4*, 673–689. https://doi.org/10.3390/biomedinformatics4010037

Academic Editors: Alexandre G. De Brevern and Carson K. Leung

Received: 29 December 2023
Revised: 14 February 2024
Accepted: 22 February 2024
Published: 1 March 2024

1. Introduction

Kidney transplantation is a vital procedure for patients suffering from end-stage kidney disease [1,2]. While significant progress has been made in refining transplantation techniques and immunosuppressive protocols, the growing demand for transplantable organs, spurred on by an expanding range of therapeutic needs, stands in stark contrast to the ongoing shortage of available donors. This situation highlights the critical necessity of improving and streamlining the entire transplantation process [3–5].

In response to this pressing demand in healthcare, the intersection of medical advancements and technological innovation has heralded the era of 'Next-Generation Healthcare' [6–9]. This transformation is especially evident in the field of kidney transplantation, where the introduction of artificial intelligence (AI) and machine learning (ML) is reshaping the field. These technologies not only address the issue of donor organ scarcity but also enhance the quality and efficiency of transplant procedures, playing a crucial role in improving patient outcomes and optimizing transplant processes [10–12].

The application of these technologies spans a wide range of domains in kidney transplantation, from donor procurement, improving donor–recipient matching and predictive modeling, to enhancing postoperative care and the long-term monitoring of patients [13,14].

Healthcare professionals, empowered by AI and ML algorithms, can now gain deeper insights into patient data, leading to more precise and individualized treatment strategies [15–17]. The impact of these advancements goes beyond surgical procedures, contributing to better pre-transplant patient assessments, refined organ allocation, and improved post-transplant monitoring [18]. As the demand for kidney transplants continues to exceed the supply of available organs, these technological advancements offer a key solution for navigating the complex transplantation process with enhanced precision and efficiency [19].

The objective of this narrative review is to conduct a comprehensive examination of the significant and transformative effects of AI and ML in kidney transplantation. The recent development and rapid advancement of these technologies have ushered in a new era of progress and innovative approaches in this medical field. This review will cover various aspects of kidney transplantation, from donor evaluation to postoperative care, with an emphasis on addressing organ shortages and refining donor–recipient matching processes. Ultimately, this paper aims to present an in-depth and forward-looking perspective on the integration of AI and ML into kidney transplantation, highlighting the potential of these technologies to catalyze a fundamental shift towards more personalized, precise, and effective healthcare solutions in the realm of organ transplantation.

The pressing challenge of organ shortages for kidney transplantation presents a methodological hurdle. AI and ML emerge as pivotal to addressing this, offering innovative approaches to enhance donor–recipient matching and optimize the transplantation process, thereby bridging the gap between the limited supply of and the increasing demand for transplantable organs.

The key contributions of this review are summarized below:

- It introduces AI and ML to enhance donor–recipient matching and address the organ shortage, improving kidney transplant success rates.
- It reviews predictive modeling applications that forecast postoperative complications, aiding in the reduction of organ rejection and the enhancement of patient care.
- It showcases AI advancements in post-transplant monitoring and rehabilitation, leading to personalized and efficient patient recovery.
- It discusses the challenges of integrating AI into healthcare, emphasizing ethical, privacy, and professional training considerations.
- It highlights the potential of AI and ML to revolutionize kidney transplantation through innovation and interdisciplinary collaboration.

2. The Next-Generation Healthcare Paradigm

The healthcare landscape is currently experiencing a significant shift, propelled by the rapid advancements and integration of technology, known as Next-Generation Healthcare (NGH). NGH represents more than just the introduction of new technologies; it is a comprehensive approach that emphasizes real-time data analysis, fostering patient-centric care models. These models are bolstered by AI, ML, and the Internet of Things (IoT), all of which aim to improve health outcomes, enhance efficiency, and reduce costs [14,20–23].

This integration of technology and medicine is transforming healthcare practices, shifting medical care towards a more proactive and predictive system. This shift enables personalized medicine, enhances diagnostic accuracy, and facilitates the development of innovative treatment modalities [24–28].

NGH is instrumental in bringing the concept of personalized care to clinical settings, moving away from the traditional one-size-fits-all approach [29–31]. Patient-centric models, informed by AI-generated insights, customize treatment plans to the unique needs and risk factors of each individual, thereby optimizing patient outcomes and reducing the incidence of adverse events [14].

This approach is particularly beneficial in kidney transplantation, a field that stands to gain immensely from the synergistic combination of NGH and medical expertise. With this paradigm shift, patient outcomes become the primary focus, leading to enhanced success rates, reduced waiting times, and overall improvements in the transplantation process. NGH also holds promise in addressing the issue of organ shortages, whether through refining organ allocation strategies, improving donor–recipient matching, or introducing new tools for donor identification and organ procurement [32–36].

The potential of NGH is particularly noticeable in organ allocation. AI algorithms can analyze complex datasets, including immunological profiles, organ quality information, and geographical considerations, to find the most compatible matches. This not only optimizes graft and patient survival rates but also reduces the risk of rejection and expands patients' access to life-saving transplants. However, the transformative nature of NGH is not without its challenges. Ethical considerations, data security, and the need for healthcare professionals to keep pace with rapidly evolving technologies are essential factors that must be carefully managed for a responsible and effective implementation of NGH.

The transition to NGH introduces methodological challenges in adapting healthcare to a more predictive and personalized model. AI and ML are instrumental in this transition, enabling the shift towards patient-centric care by refining organ allocation strategies and improving the accuracy of donor–recipient matching, thus addressing critical aspects of the organ shortage for kidney transplantation.

3. Machine Learning and Artificial Intelligence in Healthcare

Artificial intelligence and machine learning are becoming increasingly dynamic and indispensable across various sectors, including healthcare [20]. These technologies have enabled a significant transformation in how diagnosis, treatments, and patient care are approached, introducing remarkable innovation and efficiency across the healthcare ecosystem [37,38].

One of the most significant areas in which AI and ML have made groundbreaking contributions is in diagnostics and, consequently, the level of precision achieved by them. Through powerful algorithms that analyze extensive datasets, these technologies aid in early and accurate disease diagnosis. From interpreting medical imaging to scrutinizing pathology reports, AI enhances precision, reduces errors, and ultimately improves patient outcomes. Another growing application is predictive analytics. By extracting patterns and trends from patient data, AI and ML enable healthcare professionals to anticipate disease risks and patient needs, facilitating proactive and preventive healthcare interventions [39].

Further, AI and ML are revolutionizing the customization of treatment plans. By considering a patient's medical history, genetic makeup, and other pertinent data [40], AI models can pinpoint the most effective treatment strategies for individual patients [41]. In drug discovery and development, these technologies expedite the process by identifying new drug targets and predicting the efficacy and safety of potential therapeutics. This not only accelerates the introduction of novel treatments into patient care but also enhances the overall efficiency of pharmaceutical research [27,42], among its numerous other applications.

The significant contributions of AI and ML to diagnostics and treatment planning address the methodological challenge of developing precise, individualized healthcare strategies. By leveraging extensive data analysis, these technologies enable early disease detection and the customization of treatment plans, marking a substantial leap forward in patient care quality.

4. From Algorithms to Allografts: Embracing a Transformative Journey

In the complex field of kidney transplantation, a journey that begins with the altruistic act of organ donation and culminates in the transplantation of the allograft, the role of AI and ML is increasingly pivotal. This journey, marked by the transition from intricate algorithms to life-saving allografts, encapsulates a remarkable process that touches every aspect of transplantation, from donor selection to the patient's final outcome.

As these technologies continue to advance, the field of kidney transplantation is poised to benefit from even more innovative solutions. Examples of such advancements include personalized pre-transplant risk assessment tools, AI-driven therapeutic management systems, and virtual reality-enhanced rehabilitation programs. These innovations exemplify the potential of AI to further elevate patient care and outcomes in kidney transplantation.

The integration of AI into kidney transplantation marks a new era in precision medicine and personalized care. By leveraging the capabilities of AI, the field is set to undergo a transformative change, enhancing patient outcomes, reducing healthcare costs, and broadening access to this vital treatment. The journey from algorithms to allografts is not just a technical evolution but a leap towards a future where technology and medicine converge for the greater good.

The complex journey from algorithms to allografts encapsulates the significant methodological challenges in kidney transplantation. AI and ML technologies provide innovative solutions that enhance the precision and personalization of patient care, thereby transforming the transplantation process, from donor selection to patient recovery.

4.1. Addressing the Organ Shortage

The demand for kidney transplants continually exceeds the supply of donor organs, placing the issue of organ shortage at the forefront of the "Algorithms to Allografts" journey. This challenge is multi-dimensional, calling for a collaborative effort from medical and scientific communities to find innovative solutions to issues like high organ demand, insufficient donor identification, and the discard of organs for various reasons.

Rising organ transplant demand is driven by an increase in chronic diseases such as diabetes and hypertension, an aging population, and the recent medical advancements expanding transplant eligibility [43]. This demand is compounded by a shortage of organs due to factors like cultural barriers, limited awareness or education about donation, inefficiencies in donor identification, and the restrictive legal frameworks in some regions [4,44–47]. Additionally, organs are often discarded due to quality concerns, logistical challenges, or stringent acceptance criteria [48,49].

The intersection of decision modeling, public perception, and policymaking is key to addressing this issue. Studies by Yaghoubi et al. [50] and Boadu et al. [51] delve into healthcare economics and public attitudes towards organ donation. Boadu et al., using ML to analyze survey data from 2017 to 2021, found that approximately 58.8% of people would consider donating to a family member, friend, or stranger, with the key factors influencing this willingness including their support of organ donation, awareness of campaigns, and demographic variables [51]. Khan et al. [52] developed a model that combined ML methods and network science to predict consent outcomes, enhancing detection and potentially increasing organ donation consent rates. Harfouche et al. [53] aimed to improve organ donation processes and reduce illegal trade, offering novel perspectives in understanding consent outcomes. Sauthier et al. [54] utilized ML to enhance the identification of potential organ donors in intensive care units. By employing a neural network model that analyzes clinical data and laboratory time series, their approach showed improved accuracy over traditional logistic regression models in pinpointing potential donors. This method is particularly aimed at addressing the challenge of missed donor identifications, thereby increasing the efficiency of organ donation processes and potentially mitigating the organ shortage issue in kidney transplantation.

In terms of assessing donor–recipient compatibility, ML is redefining this process. Thongprayoon et al. [55] used ML to analyze the outcomes of kidney transplant recipients receiving kidneys from deceased donors with diabetes, identifying distinct clusters with varying post-transplant outcomes. Wies et al. [56] focused on the interpretability of ML models predicting post-transplant survival, particularly regarding donor organ quality. Other researchers have concentrated on predicting allograft or donor discards. Pettit et al. [57] showed the efficacy of the XGBoost model at predicting organ use, while Barah et al. [58] observed random forest's proficiency in identifying kidneys at risk of discard, with Price et al. [59] having developed a kidney discard risk index, identifying 21 factors predictive of organ discard.

Understanding these facets is vital to developing strategies to mitigate organ shortages. This approach involves decision modeling, public perception, AI, ML, precision medicine, and data science, aiming to enhance the transplant process's efficiency and patient outcomes. It ultimately seeks to bridge the gap between organ supply and demand, saving lives and improving the quality of life of transplant recipients. As we integrate advanced algorithms into healthcare, a future can be envisioned where the complexities of organ shortage are met with technological precision, as highlighted by several authors in Table 1.

Table 1. Overview of ML and AI applications to mitigate organ shortage.

Problem	Organ Type	Population	ML AI Models	Results	Ref.
Donor identification	Donor	Potential organ donors (n = 80) Not potential organ donors (n = 564)	Neural networks	AUC-ROC 0.97, sensitivity 0.84, specificity 0.93	[54]
Optimizing the consent rate	Donor	Consent (n = 1461) No consent (n = 2811)	Networked Logistic Regression	Accuracy 99.912, precision 0.999, recall 0.999, F-Measure 0.999	[52]
Donor organ quality	Kidney	Kidney transplants ($n \approx 60{,}000$)	Random forest	VIMP 0.0087	[56]
Donor discard	Liver Kidney	Organ used (n = 167,676) Organ discarded (n = 56,422) Organ used (n = 184,746) Organ discarded (n = 41,965)	XGBoost	AUC-ROC 0.93, AUC-PR 0.87, and F1 statistic 0.76 AUC-ROC 0.95, AUC-PR 0.88, and F1 statistic of 0.79	[57]
Kidney discard	Kidney	Organ used (n = 61,313) Organ discarded (n = 12,510)	Random forest	AUC-ROC 0.90 and balanced accuracy 0.78	[58]
Kidney discard	Kidney	Organ used (n = 79,039) Organ discarded (n = 23,207)	Logistic regression	C statistic 0.89	[59]
Optimizing organ yield	Donor	Donors (n = 89,520)	Tree-based gradient boosting	MAE 0.73, MSE 0.87	[60]
Decision to accept	Kidney	Accepted kidney transplants (n = 36,653)	Neural networks	AUC-ROC 0.81, F1-score 0.66	[61]

AUC-ROC, Receiver operating characteristic curve; VIMP, permutation variable importance; AUC-PR, Precision-Recall Area Under the Curve; MAE, Mean Average Error; MSE, Mean Squared Error.

AI and ML directly tackle the multifaceted challenge of organ shortages. By improving the efficiency of organ donation processes and enhancing donor–recipient compatibility assessments, these technologies offer a methodological breakthrough in addressing one of the most pressing issues in kidney transplantation.

4.2. Predictive Modeling in Kidney Transplantation

Predictive modeling has become an indispensable tool in kidney transplantation, reshaping how healthcare professionals approach various aspects of the process such as donor–recipient matching, risk assessment, and post-transplant management. This approach, employing statistical methods, ML algorithms, and big data analytics, forecasts transplant outcomes with remarkable accuracy by integrating diverse data sources like clinical data, patient medical histories, and genetic information. The enhancement in the probability of successful transplants and the facilitation of individualized patient care, tailored treatment strategies, and the efficient utilization of healthcare resources are direct outcomes of this methodology. The increasing focus on predictive modeling in kidney transplantation, as highlighted in numerous research papers and studies, is laying the groundwork for future advancements that promise to redefine this evolving field.

In kidney transplantation, predictive modeling has been pivotal in several key areas. Donor–recipient matching is one such area, where compatibility is assessed based on factors like blood type, histocompatibility, allosensitization profile, age, and medical history [62]. The objective is not only to find the best match to reduce rejection risks and improve long-term outcomes but also to diminish organ refusal rates. Another crucial area is risk assessment, which evaluates various risks such as organ rejection, infection, and transplant failure, providing tools for personalized risk management and customizing immunosuppressive therapy. Long-term outcomes and survival analysis also play a significant role, in which predictive models estimate graft and patient survival, aiming to optimize long-term results. Lastly, post-transplant monitoring is vital for tracking risks, signs of rejection, infection, or other complications, thus enabling personalized follow-up and timely intervention.

4.2.1. Donor–Recipient Matching and Organ Allocation Strategies

The process of donor–recipient matching and organ allocation in transplant medicine is a crucial element that requires equitable access to and the efficient distribution of organs. This balancing act involves addressing the immediate needs of critically ill patients while also aiming to maximize the long-term success of transplants. The challenge lies in the intricate assessment of compatibility between donors and recipients, factoring in the recipient's medical urgency and waiting time, against a backdrop of clinical, biological, and ethical considerations [63,64].

Innovative approaches are being explored, such as those utilizing data from the Scientific Registry of Transplant Recipients in the United States [insert reference: Scientific Registry of Transplant Recipients (SRTR)]. The Scientific Registry of Transplant Recipients is available online: https://www.srtr.org/ (accessed on 28 December 2023) [65]. Various survival analysis models, including Cox proportional hazards, random survival forests, and advanced artificial neural networks like DeepSurv, DeepHit, and recurrent neural networks (RNNs), have been employed. A study evaluating these models indicated that neural network-based models, particularly the RNN, exhibited superior discriminative abilities (with scores of 0.65, 0.66, and 0.66, respectively) compared to the Cox model and random survival forest model (with scores of 0.65 and 0.64, respectively). The RNN model thus strikes a balance between accurate predictions and practical applicability for healthcare professionals [66].

Furthermore, the study of HLA antigen-level mismatches (Ag-MM) and HLA amino acid-level mismatches (AA-MM) has become increasingly significant. While Ag-MM has traditionally been the focus, AA-MM variability within Ag-MM categories has a substantial impact on allorecognition. The novel Feature Inclusion Bin Evolver for Risk Stratification (FIBERS) system was developed to stratify donor–recipient pairs into low versus high graft survival risk groups based on HLA AA mismatches. FIBERS has proven effective in predicting graft failure risk, even when adjusting for traditional Ag-MMs and donor/recipient characteristics, offering a nuanced understanding of HLA immunogenetics-based risk stratification in kidney graft failure [67].

In terms of living donor kidney transplantation, the development of a living kidney donor profile index (LKDPI) marks a notable advancement in this area. Aligned with the deceased donor, the kidney donor profile index scale, the LKDPI scale, incorporates factors like donor age, BMI, race, smoking habits, and HLA mismatches. The practical application of the LKDPI reveals insightful data: the median LKDPI score is 13 (interquartile range 1–27), with 24.2% of living donors scoring below 0, indicating a lower risk than any deceased donor kidney, and 4.4% scoring above 50, suggesting a higher risk than the median deceased donor kidney. These findings demonstrate the LKDPI's utility in stratifying living donor kidneys, allowing for better comparisons with deceased donor kidneys and informed clinical decision making [68].

The detection of alloreactive anti-HLA antibodies, both pre-transplant and post-transplant, is another critical area of research. Employing multi-beads flow cytometers and unsupervised machine learning techniques like principal component analysis (PCA), Vittoraki et al. [69] observed complex clustering patterns of antibody responses against HLA class I antigens. This study underscores the significance of identifying antigenic targets and cross-reactive groups, aiding in more precise and personalized organ transplantation approaches.

These advancements, as detailed in Table 2, highlight the evolving landscape of kidney transplantation, where technological innovation and detailed immunogenetic analysis are increasingly integral to enhancing patient outcomes. The incorporation of sophisticated models and analytical tools not only improves graft survival predictions but also sheds light on the complex immunological interplay within kidney transplantation.

Table 2. ML and AI approaches to enhancing donor–recipient matching and organ allocation for kidney transplantation.

Problem	Feature/Target	Population	ML AI Models	Results	Ref.
Allocation	Organ donors, recipients, transplant outcomes	180,141 transplants	Neural network	C-index 0.66	[66]
Matching	HLA amino acid mismatch-based risk stratification	166,574 transplants	FIBERS algorithm	hazard ratio 1.09 to 1.11	[67]
Living donor risk index	Donor	69,994 deceased donors 36,025 living donor recipients	Cox regression	Index tool	[68]
Alloreativity	Single antigen beads profile	660 non-transplants 406 transplants	Principal component analysis	--	[69]

4.2.2. Risk Assessment

Risk assessments in kidney transplantation encompass evaluating potential adversities such as allograft rejection, opportunistic infections, the primary non-function of the graft, and graft failure. The accurate prediction or early identification of these events is crucial for guiding clinical decisions for transplant candidates and formulating effective post-transplant management plans.

The risk of allograft rejection involves assessing the likelihood of immunological incompatibility, where the recipient's immune system identifies the transplanted kidney as foreign, leading to potential graft function loss. Contributing factors include HLA compatibility, the patient's allosensitization status [70], patient immune status [71], organ quality [72], and chronic infections, among others.

Infection risk assessment is particularly vital as patients undergo immunosuppressive therapy, increasing their vulnerability to bacterial, viral, fungal, and parasitic infections. This assessment focuses on the intensity of immunosuppression, environmental exposures, and the patient's immunological history, including prior infections and vaccinations [73].

The risk of graft failure is influenced by a range of donor and recipient factors. Donor-related factors such as quality, whether the donor is living or deceased, donor age, and health, as well as HLA compatibility, are considered. Recipient-related factors include comorbid conditions like diabetes mellitus, hypertension, the presence of preformed donor-specific antibodies (DSA), and immunological factors such as antibody-mediated rejection and the patient's immunosuppressive regimen. Technical factors during the transplant surgery and post-transplant care, including adherence to immunosuppressive regimens, also play a role [74–76].

Studies like the ones presented in Table 3 have collectively demonstrated the potential of data-driven approaches in enhancing patient care and transplant success rates.

Jo et al. [77] focused on early subclinical rejection (SCR) prediction post-kidney transplantation. Analyzing data from 2005 to 2020, they identified key risk factors and utilized logistic regression and elastic net models, achieving average AUCs of 0.717 and 0.712, respectively. HLA II mismatch and the induction type were significant variables, with HLA II mismatch having an odds ratio (OR) of 6.77 as a risk factor, and Antithymocyte Globulin (ATG) induction an OR of 0.37 as a favorable factor.

In Brazil, a retrospective study aimed to predict 30-day graft rejection using features from recipient, donor, transplantation, and postoperative data. The XGBoost model was the best performing, with an accuracy of 0.839 and an AUC of 0.715, highlighting important variables such as deceased donor transplantation, glomerulopathy, and the donor's use of vasoactive drugs [78].

Fran et al. [79] employed a quantitative label-free mass spectrometry analysis on biopsies to develop a molecular diagnostic model for T-cell-mediated rejection (TCMR). Their random forest (RF) model achieved an accuracy of 0.80 for TCMR detection and 100% accuracy for stable kidney function in blind tests. The RF model also demonstrated 78.1–82.9% sensitivity and 58.7–64.4% specificity when applied to public transcriptome datasets. Luo et al. [80] evaluated the utility of ML in developing a model for severe pneumonia, with the random forest model showing the best performance, with an AUC of 0.91. Its key predictive features included preoperative pulmonary lesions, reoperation, and recipient age. Konieczny et al. [81] used random forest classifiers and a multi-layer perceptron to predict delayed graft function, achieving an accuracy of 0.94 and an AUC of 0.92. Meanwhile, Quinino et al. [82] developed a XGBoost model to predict immediate graft function (IGF), which showed good predictive performance.

Other studies have focused on supporting clinical decision-making in the immediate post-transplant period, identifying the risks of rejection or rehospitalization. One study on data from 1516 kidney transplant recipients showed AUC scores of 0.83 for rejection and 0.95 for graft failure [83]. Another aimed at predicting the 30-day rehospitalization of 2060 kidney transplant recipients, utilizing structured and unstructured clinical data, achieving an optimal AUC of 0.69 [84].

Table 3. Compilation of ML and AI studies focused on risk stratification in kidney transplantation.

Problem	Feature/Target	Population	ML AI Models	Results	Ref.
Rejection risk	early subclinical rejection	987 transplants	Logistic regression prediction	AUC-ROC 0.72	[77]
Rejection risk	predictive model for 30-day graft rejection	1255 transplant patients	XGBoost	AUC-ROC 0.72; accuracy 0.84; precision 0.90	[78]
Rejection risk	allograft rejection within 1 year	22,687 Afro-American kidney transplant patients	Cluster analysis	odds ratios 1.41–1.76	[85]
Rejection risk	T-cell-mediated rejection	15 transplant patients	Random forest	Accuracy 0.80	[79]
Rejection risk	day 90 day 180 wDay 360	1516 transplants	Gradient-Boosted Regression Trees	AUC-ROC, 0.83	[83]
Rejection infection	Severe Pneumocystis carinii	88 patients	Random forest	AUC-ROC 0.92, F1-Score 0.80, accuracy 0.89, sensitivity 0.82, PPV 0.67, NPV 0.91	[86]

Table 3. *Cont.*

Problem	Feature/Target	Population	ML AI Models	Results	Ref.
Infection	3-year follow-up	863 patients	Least Absolute Shrinkage and Selection Operator (LASSO) regression model	AUC-ROC 0.83, F score 0.76, sensitivity 0.76, specificity 0.88	[87]
Infection	pneumonia, posttransplant hospitalization	519 patients	Random forest	AUC-ROC 0.91, sensitivity 0.67, specificity 0.97	[80]
Graft failure	--	378 transplant patients	Decision tree	AUC-ROC 0.95, accuracy 0.95, sensitivity 0.94, specificity 0.97, F1 score 0.95	[88]
Graft failure	graft failure within 3 years	22,687 Afro-American kidney transplant patients	Cluster analysis	odds ratios 1.93–2.4	[85]
Graft failure/status	1 year 5 years	50,000 transplants	Support vector machine AdaBoost	AUC-ROC 0.82 (1 year), AUC-ROC 0.69 (5 years)	[89]
Immediate graft function	predict immediate graft function	859 transplant patients	XGBoost	AUC-ROC 0.78; sensitivity 0.64; specificity 0.78	[82]
Immediate graft function	delayed graft function	157 transplants	Random forest~ artificial neural network	AUC-ROC 0.84, accuracy 0.84	[81]
Rehospitalization	30-day rehospitalization	2060 transplants	Frequency-inverse document frequency plus logistic regression	AUC-ROC 0.68	[84]

AUC-ROC, Receiver operating characteristic curve.

4.2.3. Predicting Long-Term Outcomes and Survival Analysis

In the context of predicting long-term outcomes and survival following kidney transplantation, the integration of ML represents a significant advancement as data science and medical expertise combine to enhance patient care. ML's ability to process and extract meaningful insights from extensive datasets offers healthcare professionals new perspectives on post-transplant prognostics and management [90].

Traditional approaches, despite their utility, often fall short in capturing the complex nature of transplant outcomes [91]. In contrast, as presented in Table 4, ML algorithms, particularly those employing deep learning (DL) techniques, can integrate diverse data types, including detailed donor and patient characteristics and postoperative care nuances. This comprehensive approach allows for more accurate predictions of graft survival. Research has shown that ML models, with their advanced analytical capabilities, often outperform traditional methods in predicting graft survival rates, thus refining long-term care planning [92]. A case in point; a study by Yi et al. [93] analyzed the baseline and 12-month post-transplant Periodic Acid–Schiff (PAS)-stained slides of kidney donor biopsies. They found that the baseline interstitial and tubular abnormality score predicted early graft damage and 1-year graft loss more effectively than other clinical predictors. Furthermore, 12-month digital features, particularly the Composite Damage Score, were superior predictors of long-term graft loss compared to traditional Banff scores and clinical factors. This demonstrates the potential of artificial intelligence and DL, in transplant pathology, to improve early and long-term graft outcome predictions.

Naqvi et al. [89] tested various ML models across different post-transplantation time frames. Their study reported that the support vector machine (SVM) model achieved an AUC of 0.82 for short-term predictions, while AdaBoost led with an AUC of 0.69 in medium-term predictions and 0.81 in long-term predictions, followed by the SVM with 0.80.

Furthermore, Pan et al. [94] focused on the pre-operative data of kidney transplant recipients from deceased donors, demonstrating their model's good accuracy in predicting post-transplant survival. The significant predictors in their model included biochemical blood indices, recipient age, and donor age, with the model achieving an AUC of 0.69, indicating its moderate predictive accuracy.

Table 4. ML and AI research on predicting the long-term outcomes and survival rates in kidney transplantation.

Problem	Feature/Target	Population	ML AI Models	Results	Ref.
Long-term outcomes	12-month transplantation biopsies	789 transplant biopsies	Region-based Convolutional Neural Networks	AUC-ROC 0.81 (5 yr)	[93]
Long-term outcomes	Graft failure/status	50,000 transplants	AdaBoost	AUC-ROC 0.81 (17 yr)	[89]
Long-term outcomes	Graft survival	3117 transplants	Decision tree	AUC-ROC 0.97 (1 yr), 0.89 (2 yr), 0.79 (3 yr), 0.75 (4 yr), 0.71 (5 yr), 0.71 (6 yr), 0.67 (7 yr), 0.69 (8 yr), 0.67 (9 yr), 0.65 (10 yr)	[95]
Patient survival	Mortality risk	263 transplants	Logistic regression	AUC-ROC 0.69	[94]
Patient survival	Eurotransplant Senior Program	42 transplants	Cox regression analysis	Odds ratio 1.09 (1 yr),1.16 (3 yr), 1.17 (5 yr)	[96]

AUC-ROC, Receiver operating characteristic curve; Yr, Year.

4.2.4. Personalized Post-Transplant Management

The shift towards personalized post-transplant management marks a significant advancement in patient care, with ML and data analytics playing a key role. This approach supports tailored immunosuppression therapy and provides us with tools to predict disease recurrence, steering kidney transplantation towards a more patient-specific model.

Personalized management, particularly in immunosuppression therapy, is crucial. Traditional approaches often rely on standardized protocols, which may not suit every patient due to variations in genetic profiles, lifestyles, and comorbidities. This lack of personalization can contribute to non-adherence, as patients may experience adverse side effects or an insufficient response to the standard regimen. However, ML algorithms can analyze a multitude of factors influencing a patient's response to immunosuppressive drugs. By processing this complex data, these algorithms can predict the most effective regimen for individual patients or tailor a therapy to make it specifically designed for their unique needs.

This personalized approach promises to enhance treatment efficacy by fine-tuning drug types and dosages, thereby maximizing their therapeutic benefits and minimizing their adverse effects. For instance, it could reduce drug toxicity, lower cancer incidence, or prevent graft rejection. Tailored treatments not only improve physical well-being but also serve to alleviate the psychological burdens associated with a generalized approach.

A personalized immunosuppressive therapy could also significantly improve adherence, as when patients experience fewer side effects and better treatment outcomes they are more likely to adhere to their medication regimens. This improves their quality of life

(QOL) and reduces the healthcare system's burden by decreasing the need for additional treatments and hospitalizations related to complications due to non-adherence.

As highlighted in Table 5, several studies have explored optimal dosing and non-adherence. Zhang et al. [97] focused on tacrolimus dosing using the TabNet algorithm, achieving a high R^2 value of 0.824 and minimal prediction errors. Sridharan et al. [98] identified significant predictors useful in optimizing tacrolimus and cyclosporine dosing regimens using various ML algorithms. Zhu et al.'s [99] study on non-adherence found the SVM model to be the most effective, with a sensitivity of 0.59, a specificity of 0.73, and an average AUC of 0.75.

Table 5. ML and AI implementations in the personalized post-transplant management of kidney transplantations.

Problem	Feature/Target	Population	ML AI Models	Results	Ref.
Immunosuppression therapy	Non-adherence	1191 patients	Support vector machine	AUC-ROC 0.75, sensitivity 0.59, specificity 0.73	[99]
Immunosuppression therapy	Tacrolimus daily dose	584 patients	TabNet	R^2 0.824, MAE 0.468, MSE 0.558	[97]
Immunosuppression therapy	optimize tacrolimus and cyclosporine	120 patients	Generalized linear model, support vector machine, artificial neural network	MAE 1.3, 1.3, 1.7 MAEs 93.2, 79.1, 73.7	[98]
Recurrence	Recurrent membranous nephropathy	195 patients	Penalized Cox regression	AUC-ROC 0.91	[100]

AUC-ROC, Receiver operating characteristic curve; MAE, Mean Average Error; MSE, Mean Squared Error.

Monitoring and managing disease recurrence in a transplanted organ is another vital aspect of post-transplant care. For diseases like glomerulonephritis, known for their risk of recurrence, traditional periodic testing may not be sufficient for early detection. ML models can identify patterns in a patient's biomarkers that are indicative of a high recurrence risk, leading to pre-emptive therapy adjustments or more frequent monitoring [100].

Predictive modeling, powered by AI and ML, addresses the methodological challenge of forecasting transplant outcomes and managing post-transplant risks. These advanced tools enable healthcare professionals to make more informed decisions, leading to improved patient care and transplant success rates.

5. Challenges and Future Directions

The landscape of kidney transplantation is evolving rapidly alongside the advancements in AI and ML. While these technologies promise transformative improvements in transplant processes and patient care, they also introduce a set of challenges that require thoughtful navigation.

A primary challenge is the ethical use of patient data and the maintenance of privacy. The efficacy of AI and ML in this field largely relies on their access to extensive, diverse, and highly curated datasets, which include sensitive personal health information. The integration of AI and ML into kidney transplantation, while promising, necessitates a thorough examination of ethical considerations, particularly in the context of data usage and algorithm development. The ethical implications are multifaceted, involving patient privacy, data security, and the potential for bias in AI models.

Ensuring ethical data handling and safeguarding patient privacy are not just legal obligations, as mandated by regulations like the Health Insurance Portability and Accountability Act (HIPAA) [101], but also moral ones. Healthcare institutions and AI developers must implement robust data governance frameworks that prioritize patient consent, data anonymization, and secure data storage and transmission.

Furthermore, addressing potential algorithmic bias is crucial. This bias, where models may unintentionally reinforce healthcare disparities, must be mitigated through diverse data training sets, inclusive practices, and transparent algorithmic procedures [102]. To mitigate this, it is essential to use diverse training datasets that represent various demographics, including age, gender, ethnicity, and socioeconomic status. This diversity in data will certainly help in developing algorithms that are equitable and able to generalize well across different patient populations.

Another hurdle is integrating AI and ML into existing healthcare systems. This integration involves not only the technical aspects of embedding these technologies into existing clinical workflows but also ensuring that healthcare professionals are trained to interpret and utilize the insights that these tools offer. As these tools have become increasingly integrated into kidney transplantation processes, the healthcare sector faces a dual challenge: the technical integration of these technologies into existing systems and the continuous professional development of healthcare providers. Integrating AI and ML into clinical workflows requires more than just embedding new technical systems, as it fundamentally involves preparing healthcare professionals to adeptly navigate and leverage these tools.

Continuous education and training are pivotal for clinicians, nurses, and other healthcare professionals. As technology rapidly advances, the knowledge and skills required to effectively utilize AI and ML in clinical settings evolve correspondingly. This ongoing learning process is essential not only for understanding and interpreting AI and ML outputs accurately but also for applying these insights in a way that complements and enhances healthcare professionals' clinical judgment and decision-making processes.

Maintaining a critical perspective is vital as AI and ML become more prevalent in decision-making processes. Healthcare professionals must ensure that their clinical judgment is not entirely supplanted by algorithmic recommendations. Human oversight remains crucial, particularly in complex medical fields like kidney transplantation, where patient variables are diverse and nuanced.

Adapting to technological advancements is another key aspect of this integration. The field of AI and ML is rapidly evolving, and what is cutting-edge today might become outdated tomorrow. Continuous education ensures that healthcare professionals keep pace with these advancements, allowing them to provide the most current and effective patient care.

Furthermore, with the integration of AI and ML, and, as stated, with new ethical and practical challenges emerging, training and education programs need to address these challenges, providing healthcare professionals with the skills to navigate the ethical implications of AI and ML, such as data privacy, patient consent, and algorithmic bias.

Looking to the future, kidney transplantation in the era of Next-Generation Healthcare is expected to advance towards more personalized and precise patient care. Treatments and monitoring tailored to the individual genetic, lifestyle, and environmental factors of each patient are likely to become the norm. This shift is expected to bring advancements in precision medicine, refined organ matching and allocation processes, and the development of sophisticated predictive models for patient outcomes, which in turn could lead to improved outcomes, reduced instances of graft rejection, and optimized immunosuppression regimes.

However, the success of these advancements depends on the medical community's ongoing adaptation and learning, ensuring that healthcare professionals are well-equipped to effectively utilize these technologies.

To overcome these challenges and fully leverage AI and ML in kidney transplantation, a collaborative approach is essential. This collaboration should involve partnerships between healthcare professionals, data scientists, ethicists, and policymakers. Together, they can work to create frameworks that ensure the responsible use of AI and ML, with a focus on patient safety, privacy, and equitable healthcare resource distribution.

As the ethical integration of AI and ML into kidney transplantation requires collaborative efforts from various stakeholders, including healthcare professionals, AI developers, ethicists, and policymakers, this collaboration should aim to:

Develop Ethical Guidelines: provide clear guidelines for the ethical use of AI in healthcare, focusing on patient consent, data privacy, and algorithm transparency.

Promote Interdisciplinary Dialogues: encourage regular dialogue between technologists, clinicians, and ethicists to address the ethical challenges that arise as AI technologies evolve.

Implement Bias Mitigation Strategies: actively work towards identifying and mitigating biases in AI models through diverse data collection and algorithm testing across different patient groups.

Foster Continuous Learning: plan opportunities for healthcare professionals to engage in lifelong learning about AI and ML advancements, ensuring that their skills remain relevant and their clinical judgment sharp.

The integration of AI and ML in kidney transplantation, while promising, introduces methodological challenges related to ethical considerations, data privacy, and system integration. Addressing these challenges is crucial for the responsible and effective implementation of these technologies, ensuring that they serve to enhance patient outcomes and the efficiency of healthcare.

6. Final Remarks

In conclusion, the integration of AI and ML into the field of kidney transplantation represents a pivotal moment in the evolution of healthcare innovation. While this journey is not without its challenges, the transformative potential of these technologies to enhance patient care and address enduring challenges within the field is substantial.

However, adopting these advancements from a balanced perspective is crucial. This means giving due importance to ethical considerations, safeguarding data privacy, and promoting the continuous education of healthcare professionals. By doing so, the future of kidney transplantation can be steered towards providing care that is not only more precise and personalized, but also available and affordable to the masses.

As we step into this new era, the combined efforts and collaborations of healthcare professionals, biomedical engineers, researchers, and policymakers will be vital. It is through these collaborative endeavors that we can fully realize the promise of Next-Generation Healthcare and set new standards in patient care.

Author Contributions: Conceptualization, L.R. and R.A.; methodology, L.R. and R.A.; writing—original draft preparation, L.R. and R.A.; writing—review and editing, L.R., P.A., R.F., O.A., C.T. and R.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Abecassis, M.; Bartlett, S.T.; Collins, A.J.; Davis, C.L.; Delmonico, F.L.; Friedewald, J.J.; Hays, R.; Howard, A.; Jones, E.; Leichtman, A.B.; et al. Kidney Transplantation as Primary Therapy for End-Stage Renal Disease: A National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQI^{TM}) Conference. *Clin. J. Am. Soc. Nephrol.* **2008**, *3*, 471–480. [CrossRef]
2. Uwumiro, F.E.; Okpujie, V.O.; Oyesomi, A.; Madu, F.C.; Ilelaboye, A.; Shielu, M.L.; Otu, R.C.; Ogunkoya, G.D.; Ezennaya, L.S.; Bojerenu, M.M. Weekend Effect on Mortality, Access to Renal Replacement Therapy, and Other Outcomes Among Patients With End-Stage Renal Disease: A Retrospective Analysis of the Nationwide Inpatient Sample. *Cureus* **2023**, *15*, e34139. [CrossRef] [PubMed]

3. Bastani, B. The Present and Future of Transplant Organ Shortage: Some Potential Remedies. *J. Nephrol.* **2020**, *33*, 277–288. [CrossRef]
4. Lewis, A.; Koukoura, A.; Tsianos, G.-I.; Gargavanis, A.A.; Nielsen, A.A.; Vassiliadis, E. Organ Donation in the US and Europe: The Supply vs Demand Imbalance. *Transplant. Rev.* **2021**, *35*, 100585. [CrossRef] [PubMed]
5. Ahmad, M.U.; Hanna, A.; Mohamed, A.; Schlindwein, A.; Pley, C.; Bahner, I.; Mhaskar, R.; Pettigrew, G.J.; Jarmi, T. A Systematic Review of Opt-out Versus Opt-in Consent on Deceased Organ Donation and Transplantation (2006–2016). *World J. Surg.* **2019**, *43*, 3161–3171. [CrossRef] [PubMed]
6. Manickam, P.; Mariappan, S.A.; Murugesan, S.M.; Hansda, S.; Kaushik, A.; Shinde, R.; Thipperudraswamy, S.P. Artificial Intelligence (AI) and Internet of Medical Things (IoMT) Assisted Biomedical Systems for Intelligent Healthcare. *Biosensors* **2022**, *12*, 562. [CrossRef] [PubMed]
7. Tuli, S.; Tuli, S.; Wander, G.; Wander, P.; Gill, S.S.; Dustdar, S.; Sakellariou, R.; Rana, O. Next Generation Technologies for Smart Healthcare: Challenges, Vision, Model, Trends and Future Directions. *Internet Technol. Lett.* **2020**, *3*, e145. [CrossRef]
8. Parwani, A.V. Next Generation Diagnostic Pathology: Use of Digital Pathology and Artificial Intelligence Tools to Augment a Pathological Diagnosis. *Diagn. Pathol.* **2019**, *14*, 138. [CrossRef]
9. Lee, C.; Luo, Z.; Ngiam, K.Y.; Zhang, M.; Zheng, K.; Chen, G.; Ooi, B.C.; Yip, W.L.J. Big Healthcare Data Analytics: Challenges and Applications. In *Handbook of Large-Scale Distributed Computing in Smart Healthcare*; Springer: Berlin/Heidelberg, Germany, 2017; pp. 11–41. ISBN 9783319582801.
10. Badrouchi, S.; Bacha, M.M.; Hedri, H.; Ben Abdallah, T.; Abderrahim, E. Toward Generalizing the Use of Artificial Intelligence in Nephrology and Kidney Transplantation. *J. Nephrol.* **2022**, *36*, 1087–1100. [CrossRef]
11. Thongprayoon, C.; Kaewput, W.; Kovvuru, K.; Hansrivijit, P.; Kanduri, S.R.; Bathini, T.; Chewcharat, A.; Leeaphorn, N.; Gonzalez-Suarez, M.L.; Cheungpasitporn, W. Promises of Big Data and Artificial Intelligence in Nephrology and Transplantation. *J. Clin. Med.* **2020**, *9*, 1107. [CrossRef]
12. Pullen, L.C. Doctor AI. *Am. J. Transplant.* **2019**, *19*, 1–2. [CrossRef] [PubMed]
13. Peloso, A.; Moeckli, B.; Delaune, V.; Oldani, G.; Andres, A.; Compagnon, P. Artificial Intelligence: Present and Future Potential for Solid Organ Transplantation. *Transpl. Int.* **2022**, *35*, 10640. [CrossRef] [PubMed]
14. Alowais, S.A.; Alghamdi, S.S.; Alsuhebany, N.; Alqahtani, T.; Alshaya, A.I.; Almohareb, S.N.; Aldairem, A.; Alrashed, M.; Bin Saleh, K.; Badreldin, H.A.; et al. Revolutionizing Healthcare: The Role of Artificial Intelligence in Clinical Practice. *BMC Med. Educ.* **2023**, *23*, 689. [CrossRef]
15. Johnson, K.B.; Wei, W.; Weeraratne, D.; Frisse, M.E.; Misulis, K.; Rhee, K.; Zhao, J.; Snowdon, J.L. Precision Medicine, AI, and the Future of Personalized Health Care. *Clin. Transl. Sci.* **2021**, *14*, 86–93. [CrossRef] [PubMed]
16. Vigia, E.; Ramalhete, L.; Ribeiro, R.; Barros, I.; Chumbinho, B.; Filipe, E.; Pena, A.; Bicho, L.; Nobre, A.; Carrelha, S.; et al. Pancreas Rejection in the Artificial Intelligence Era: New Tool for Signal Patients at Risk. *J. Pers. Med.* **2023**, *13*, 1071. [CrossRef] [PubMed]
17. Vigia, E.; Ramalhete, L.; Ribeiro, R.; Barros, I.; Chumbinho, B.; Filipe, E.; Bicho, L.; Nobre, A.; Carrelha, S.; Corado, S.; et al. Predicting Function Delay with a Machine Learning Model: Improve the Long-Term Survival of Pancreatic Grafts. *Pancreat. Disord. Ther.* **2022**, *12*, 231. [CrossRef]
18. Díez-Sanmartín, C.; Sarasa Cabezuelo, A. Application of Artificial Intelligence Techniques to Predict Survival in Kidney Transplantation: A Review. *J. Clin. Med.* **2020**, *9*, 572. [CrossRef]
19. Mudiayi, D.; Shojai, S.; Okpechi, I.; Christie, E.A.; Wen, K.; Kamaleldin, M.; Elsadig Osman, M.; Lunney, M.; Prasad, B.; Osman, M.A.; et al. Global Estimates of Capacity for Kidney Transplantation in World Countries and Regions. *Transplantation* **2022**, *106*, 1113–1122. [CrossRef]
20. Davenport, T.; Kalakota, R. The Potential for Artificial Intelligence in Healthcare. *Future Healthc. J.* **2019**, *6*, 94–98. [CrossRef]
21. Alahi, M.E.E.; Sukkuea, A.; Tina, F.W.; Nag, A.; Kurdthongmee, W.; Suwannarat, K.; Mukhopadhyay, S.C. Integration of IoT-Enabled Technologies and Artificial Intelligence (AI) for Smart City Scenario: Recent Advancements and Future Trends. *Sensors* **2023**, *23*, 5206. [CrossRef] [PubMed]
22. Hood, L.; Flores, M.A.; Brogaard, K.R.; Price, N.D. Systems Medicine and the Emergence of Proactive P4 Medicine. In *Handbook of Systems Biology*; Elsevier: Amsterdam, The Netherlands, 2013; pp. 445–467. ISBN 9780123859440.
23. Martínez-García, M.; Hernández-Lemus, E. Data Integration Challenges for Machine Learning in Precision Medicine. *Front. Med.* **2022**, *8*, 784455. [CrossRef]
24. Ahmed, Z.; Mohamed, K.; Zeeshan, S.; Dong, X. Artificial Intelligence with Multi-Functional Machine Learning Platform Development for Better Healthcare and Precision Medicine. *Database* **2020**, *2020*, baaa010. [CrossRef]
25. Peng, J.; Jury, E.C.; Dönnes, P.; Ciurtin, C. Machine Learning Techniques for Personalised Medicine Approaches in Immune-Mediated Chronic Inflammatory Diseases: Applications and Challenges. *Front. Pharmacol.* **2021**, *12*, 720694. [CrossRef]
26. Fröhlich, H.; Balling, R.; Beerenwinkel, N.; Kohlbacher, O.; Kumar, S.; Lengauer, T.; Maathuis, M.H.; Moreau, Y.; Murphy, S.A.; Przytycka, T.M.; et al. From Hype to Reality: Data Science Enabling Personalized Medicine. *BMC Med.* **2018**, *16*, 150. [CrossRef]
27. Vamathevan, J.; Clark, D.; Czodrowski, P.; Dunham, I.; Ferran, E.; Lee, G.; Li, B.; Madabhushi, A.; Shah, P.; Spitzer, M.; et al. Applications of Machine Learning in Drug Discovery and Development. *Nat. Rev. Drug Discov.* **2019**, *18*, 463–477. [CrossRef]
28. Kessler, R.C.; Bossarte, R.M.; Luedtke, A.; Zaslavsky, A.M.; Zubizarreta, J.R. Machine Learning Methods for Developing Precision Treatment Rules with Observational Data. *Behav. Res. Ther.* **2019**, *120*, 103412. [CrossRef]
29. Goetz, L.H.; Schork, N.J. Personalized Medicine: Motivation, Challenges, and Progress. *Fertil. Steril.* **2018**, *109*, 952–963. [CrossRef]

30. Stefanicka-Wojtas, D.; Kurpas, D. Personalised Medicine—Implementation to the Healthcare System in Europe (Focus Group Discussions). *J. Pers. Med.* **2023**, *13*, 380. [CrossRef] [PubMed]
31. Raghavendran, H.R.B.; Kumaramanickavel, G.; Iwata, T. Editorial: Personalized Medicine—Where Do We Stand Regarding Bench to Bedside Translation? *Front. Med.* **2023**, *10*, 1243896. [CrossRef] [PubMed]
32. Pieterse, A.D.; Huurman, V.A.L.; Hierck, B.P.; Reinders, M.E.J. Introducing the Innovative Technique of 360° Virtual Reality in Kidney Transplant Education. *Transpl. Immunol.* **2018**, *49*, 5–6. [CrossRef] [PubMed]
33. Raynaud, M.; Aubert, O.; Divard, G.; Reese, P.P.; Kamar, N.; Yoo, D.; Chin, C.-S.; Bailly, É.; Buchler, M.; Ladrière, M.; et al. Dynamic Prediction of Renal Survival among Deeply Phenotyped Kidney Transplant Recipients Using Artificial Intelligence: An Observational, International, Multicohort Study. *Lancet Digit. Health* **2021**, *3*, e795–e805. [CrossRef]
34. Thongprayoon, C.; Hansrivijit, P.; Leeaphorn, N.; Acharya, P.; Torres-Ortiz, A.; Kaewput, W.; Kovvuru, K.; Kanduri, S.; Bathini, T.; Cheungpasitporn, W. Recent Advances and Clinical Outcomes of Kidney Transplantation. *J. Clin. Med.* **2020**, *9*, 1193. [CrossRef] [PubMed]
35. Peloso, A.; Naesens, M.; Thaunat, O. The Dawn of a New Era in Kidney Transplantation: Promises and Limitations of Artificial Intelligence for Precision Diagnostics. *Transpl. Int.* **2023**, *36*, 12010. [CrossRef] [PubMed]
36. Díez-Sanmartín, C.; Sarasa-Cabezuelo, A.; Andrés Belmonte, A. The Impact of Artificial Intelligence and Big Data on End-Stage Kidney Disease Treatments. *Expert Syst. Appl.* **2021**, *180*, 115076. [CrossRef]
37. Junaid, S.B.; Imam, A.A.; Balogun, A.O.; De Silva, L.C.; Surakat, Y.A.; Kumar, G.; Abdulkarim, M.; Shuaibu, A.N.; Garba, A.; Sahalu, Y.; et al. Recent Advancements in Emerging Technologies for Healthcare Management Systems: A Survey. *Healthcare* **2022**, *10*, 1940. [CrossRef] [PubMed]
38. Bohr, A.; Memarzadeh, K. The Rise of Artificial Intelligence in Healthcare Applications. In *Artificial Intelligence in Healthcare*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 25–60. ISBN 9780128184387.
39. Badidi, E. Edge AI for Early Detection of Chronic Diseases and the Spread of Infectious Diseases: Opportunities, Challenges, and Future Directions. *Future Internet* **2023**, *15*, 370. [CrossRef]
40. Schork, N.J. Artificial Intelligence and Personalized Medicine. In *Precision Medicine in Cancer Therapy*; Springer: Berlin/Heidelberg, Germany, 2019; pp. 265–283. ISBN 9783030163914.
41. van der Schaar, M.; Alaa, A.M.; Floto, A.; Gimson, A.; Scholtes, S.; Wood, A.; McKinney, E.; Jarrett, D.; Lio, P.; Ercole, A. How Artificial Intelligence and Machine Learning Can Help Healthcare Systems Respond to COVID-19. *Mach. Learn.* **2021**, *110*, 1–14. [CrossRef] [PubMed]
42. Dara, S.; Dhamercherla, S.; Jadav, S.S.; Babu, C.M.; Ahsan, M.J. Machine Learning in Drug Discovery: A Review. *Artif. Intell. Rev.* **2022**, *55*, 1947–1999. [CrossRef] [PubMed]
43. Lim, W.H.; Au, E.; Krishnan, A.; Wong, G. Assessment of Kidney Transplant Suitability for Patients with Prior Cancers: Is It Time for a Rethink? *Transpl. Int.* **2019**, *32*, 1223–1240. [CrossRef]
44. Abouna, G.M. Organ Shortage Crisis: Problems and Possible Solutions. *Transplant. Proc.* **2008**, *40*, 34–38. [CrossRef]
45. Levitt, M. Could the Organ Shortage Ever Be Met? *Life Sci. Soc. Policy* **2015**, *11*, 6. [CrossRef]
46. Li, M.T.; Hillyer, G.C.; Husain, S.A.; Mohan, S. Cultural Barriers to Organ Donation among Chinese and Korean Individuals in the United States: A Systematic Review. *Transpl. Int.* **2019**, *32*, 1001–1018. [CrossRef] [PubMed]
47. Demırkiran, O.; Bozbay, S.; Elmaagac, M.; Agkoç, M. Religious and Cultural Aspects of Organ Donation in the Turkish Population. *Transplant. Proc.* **2019**, *51*, 2158–2162. [CrossRef] [PubMed]
48. Tore Altun, G.; Corman Dincer, P.; Birtan, D.; Arslantas, R.; Kasap Yakin, D.; Ozdemir, I.; Arslantas, M.K. Reasons Why Organs From Deceased Donors Were Not Accepted for Transplantation. *Transplant. Proc.* **2019**, *51*, 2202–2204. [CrossRef] [PubMed]
49. Abdelwahab Elhamahmi, D.; Chaly, T.; Wei, G.; Hall, I.E. Kidney Discard Rates in the United States During American Transplant Congress Meetings. *Transplant. Direct* **2019**, *5*, e412. [CrossRef] [PubMed]
50. Yaghoubi, M.; Cressman, S.; Edwards, L.; Shechter, S.; Doyle-Waters, M.M.; Keown, P.; Sapir-Pichhadze, R.; Bryan, S. A Systematic Review of Kidney Transplantation Decision Modelling Studies. *Appl. Health Econ. Health Policy* **2023**, *21*, 39–51. [CrossRef] [PubMed]
51. Boadu, P.; McLaughlin, L.; Al-Haboubi, M.; Bostock, J.; Noyes, J.; O'Neill, S.; Mays, N. A Machine-Learning Approach to Estimating Public Intentions to Become a Living Kidney Donor in England: Evidence from Repeated Cross-Sectional Survey Data. *Front. Public Health* **2023**, *10*, 1052338. [CrossRef] [PubMed]
52. Khan, M.E.; Tutun, S. Understanding and Predicting Organ Donation Outcomes Using Network-Based Predictive Analytics. *Procedia Comput. Sci.* **2021**, *185*, 185–192. [CrossRef]
53. Tutun, S.; Harfouche, A.; Albizri, A.; Johnson, M.E.; He, H. A Responsible AI Framework for Mitigating the Ramifications of the Organ Donation Crisis. *Inf. Syst. Front.* **2023**, *25*, 2301–2316. [CrossRef]
54. Sauthier, N.; Bouchakri, R.; Carrier, F.M.; Sauthier, M.; Mullie, L.-A.; Cardinal, H.; Fortin, M.-C.; Lahrichi, N.; Chassé, M. Automated Screening of Potential Organ Donors Using a Temporal Machine Learning Model. *Sci. Rep.* **2023**, *13*, 8459. [CrossRef]
55. Thongprayoon, C.; Miao, J.; Jadlowiec, C.C.; Mao, S.A.; Mao, M.A.; Leeaphorn, N.; Kaewput, W.; Pattharanitima, P.; Tangpanithandee, S.; Krisanapan, P.; et al. Differences between Kidney Transplant Recipients from Deceased Donors with Diabetes Mellitus as Identified by Machine Learning Consensus Clustering. *J. Pers. Med.* **2023**, *13*, 1094. [CrossRef]

56. Wies, C.; Miltenberger, R.; Grieser, G.; Jahn-Eimermacher, A. Exploring the Variable Importance in Random Forests under Correlations: A General Concept Applied to Donor Organ Quality in Post-Transplant Survival. *BMC Med. Res. Methodol.* **2023**, *23*, 209. [CrossRef]
57. Pettit, R.W.; Marlatt, B.B.; Miles, T.J.; Uzgoren, S.; Corr, S.J.; Shetty, A.; Havelka, J.; Rana, A. The Utility of Machine Learning for Predicting Donor Discard in Abdominal Transplantation. *Clin. Transplant.* **2023**, *37*, e14951. [CrossRef]
58. Barah, M.; Mehrotra, S. Predicting Kidney Discard Using Machine Learning. *Transplantation* **2021**, *105*, 2054–2071. [CrossRef] [PubMed]
59. Price, M.B.; Yan, G.; Joshi, M.; Zhang, T.; Hickner, B.T.; O'Mahony, C.; Goss, J.; Galván, N.T.N.; Cotton, R.T.; Rana, A. Prediction of Kidney Allograft Discard Before Procurement: The Kidney Discard Risk Index. *Exp. Clin. Transplant.* **2021**, *19*, 204–211. [CrossRef] [PubMed]
60. Marrero, W.J.; Lavieri, M.S.; Guikema, S.D.; Hutton, D.W.; Parikh, N.D. A Machine Learning Approach for the Prediction of Overall Deceased Donor Organ Yield. *Surgery* **2021**, *170*, 1561–1567. [CrossRef] [PubMed]
61. Salaün, A.; Knight, S.; Wingfield, L.; Zhu, T. Interpretable Machine Learning in Kidney Offering: Multiple Outcome Prediction for Accepted Offers. *medRxiv*, 2023; *preprint*. [CrossRef]
62. Papalexopoulos, T.P.; Bertsimas, D.; Cohen, I.G.; Goff, R.R.; Stewart, D.E.; Trichakis, N. Ethics-by-Design: Efficient, Fair and Inclusive Resource Allocation Using Machine Learning. *J. Law Biosci.* **2022**, *9*, lsac012. [CrossRef]
63. Yeung, M.Y.; Coates, P.T.; Li, P.K.-T. Kidney Organ Allocation System: How to Be Fair. *Semin. Nephrol.* **2022**, *42*, 151274. [CrossRef]
64. Caulfield, T.; Murdoch, B.; Sapir-Pichhadze, R.; Keown, P. Policy Challenges for Organ Allocation in an Era of "Precision Medicine". *Can. J. Kidney Health Dis.* **2020**, *7*, 205435812091265. [CrossRef]
65. Scientific Registry of Transplant Recipients Scientific Registry of Transplant Recipients (SRTR). Available online: https://www.srtr.org/ (accessed on 28 December 2023).
66. Paquette, F.-X.; Ghassemi, A.; Bukhtiyarova, O.; Cisse, M.; Gagnon, N.; Della Vecchia, A.; Rabearivelo, H.A.; Loudiyi, Y. Machine Learning Support for Decision-Making in Kidney Transplantation: Step-by-Step Development of a Technological Solution. *JMIR Med. Inform.* **2022**, *10*, e34554. [CrossRef] [PubMed]
67. Dasariraju, S.; Gragert, L.; Wager, G.L.; McCullough, K.; Brown, N.K.; Kamoun, M.; Urbanowicz, R.J. HLA Amino Acid Mismatch-Based Risk Stratification of Kidney Allograft Failure Using a Novel Machine Learning Algorithm. *J. Biomed. Inform.* **2023**, *142*, 104374. [CrossRef] [PubMed]
68. Massie, A.B.; Leanza, J.; Fahmy, L.M.; Chow, E.K.H.; Desai, N.M.; Luo, X.; King, E.A.; Bowring, M.G.; Segev, D.L. A Risk Index for Living Donor Kidney Transplantation. *Am. J. Transplant.* **2016**, *16*, 2077–2084. [CrossRef] [PubMed]
69. Vittoraki, A.G.; Fylaktou, A.; Tarassi, K.; Tsinaris, Z.; Siorenta, A.; Petasis, G.C.; Gerogiannis, D.; Lehmann, C.; Carmagnat, M.; Doxiadis, I.; et al. Hidden Patterns of Anti-HLA Class I Alloreactivity Revealed through Machine Learning. *Front. Immunol.* **2021**, *12*, 670956. [CrossRef] [PubMed]
70. Lim, W.H.; Ho, J.; Kosmoliaptsis, V.; Sapir-Pichhadze, R. Editorial: Future Challenges and Directions in Determining Allo-Immunity in Kidney Transplantation. *Front. Immunol.* **2022**, *13*, 1013711. [CrossRef]
71. Han, H.S.; Lubetzky, M.L. Immune Monitoring of Allograft Status in Kidney Transplant Recipients. *Front. Nephrol.* **2023**, *3*, 1293907. [CrossRef]
72. von Moos, S.; Akalin, E.; Mas, V.; Mueller, T.F. Assessment of Organ Quality in Kidney Transplantation by Molecular Analysis and Why It May Not Have Been Achieved, Yet. *Front. Immunol.* **2020**, *11*, 833. [CrossRef]
73. Chastain, D.B.; Spradlin, M.; Ahmad, H.; Henao-Martínez, A.F. Unintended Consequences: Risk of Opportunistic Infections Associated With Long-Term Glucocorticoid Therapies in Adults. *Clin. Infect. Dis.* 2023; *online ahead of print*. [CrossRef]
74. Pinto-Ramirez, J.; Garcia-Lopez, A.; Salcedo-Herrera, S.; Patino-Jaramillo, N.; Garcia-Lopez, J.; Barbosa-Salinas, J.; Riveros-Enriquez, S.; Hernandez-Herrera, G.; Giron-Luque, F. Risk Factors for Graft Loss and Death among Kidney Transplant Recipients: A Competing Risk Analysis. *PLoS ONE* **2022**, *17*, e0269990. [CrossRef]
75. Betjes, M.G.H.; Roelen, D.L.; van Agteren, M.; Kal-van Gestel, J. Causes of Kidney Graft Failure in a Cohort of Recipients With a Very Long-Time Follow-Up After Transplantation. *Front. Med.* **2022**, *9*, 842419. [CrossRef]
76. Senanayake, S.; Kularatna, S.; Healy, H.; Graves, N.; Baboolal, K.; Sypek, M.P.; Barnett, A. Development and Validation of a Risk Index to Predict Kidney Graft Survival: The Kidney Transplant Risk Index. *BMC Med. Res. Methodol.* **2021**, *21*, 127. [CrossRef]
77. Jo, S.J.; Park, J.B.; Lee, K.W. Prediction of Very Early Subclinical Rejection with Machine Learning in Kidney Transplantation. *Sci. Rep.* **2023**, *13*, 22387. [CrossRef]
78. Minato, A.C.D.S.; Hannun, P.G.C.; Barbosa, A.M.P.; da Rocha, N.C.; Machado-Rugolo, J.; de Almeida Cardoso, M.M.; de Andrade, L.G.M. Machine Learning Model to Predict Graft Rejection After Kidney Transplantation. *Transplant. Proc.* **2023**, *55*, 2058–2062. [CrossRef]
79. Fang, F.; Liu, P.; Song, L.; Wagner, P.; Bartlett, D.; Ma, L.; Li, X.; Rahimian, M.A.; Tseng, G.; Randhawa, P.; et al. Diagnosis of T-Cell-Mediated Kidney Rejection by Biopsy-Based Proteomic Biomarkers and Machine Learning. *Front. Immunol.* **2023**, *14*, 1090373. [CrossRef] [PubMed]
80. Luo, Y.; Tang, Z.; Hu, X.; Lu, S.; Miao, B.; Hong, S.; Bai, H.; Sun, C.; Qiu, J.; Liang, H.; et al. Machine Learning for the Prediction of Severe Pneumonia during Posttransplant Hospitalization in Recipients of a Deceased-Donor Kidney Transplant. *Ann. Transl. Med.* **2020**, *8*, 82. [CrossRef] [PubMed]

81. Konieczny, A.; Stojanowski, J.; Rydzyńska, K.; Kusztal, M.; Krajewska, M. Artificial Intelligence—A Tool for Risk Assessment of Delayed-Graft Function in Kidney Transplant. *J. Clin. Med.* **2021**, *10*, 5244. [CrossRef] [PubMed]
82. Quinino, R.M.; Agena, F.; Modelli de Andrade, L.G.; Furtado, M.; Chiavegatto Filho, A.D.P.; David-Neto, E. A Machine Learning Prediction Model for Immediate Graft Function After Deceased Donor Kidney Transplantation. *Transplantation* **2023**, *107*, 1380–1389. [CrossRef] [PubMed]
83. Roller, R.; Mayrdorfer, M.; Duettmann, W.; Naik, M.G.; Schmidt, D.; Halleck, F.; Hummel, P.; Burchardt, A.; Möller, S.; Dabrock, P.; et al. Evaluation of a Clinical Decision Support System for Detection of Patients at Risk after Kidney Transplantation. *Front. Public Health* **2022**, *10*, 979448. [CrossRef] [PubMed]
84. Arenson, M.; Hogan, J.; Xu, L.; Lynch, R.; Lee, Y.-T.H.; Choi, J.D.; Sun, J.; Adams, A.; Patzer, R.E. Predicting Kidney Transplant Recipient Cohorts' 30-Day Rehospitalization Using Clinical Notes and Electronic Health Care Record Data. *Kidney Int. Rep.* **2023**, *8*, 489–498. [CrossRef] [PubMed]
85. Thongprayoon, C.; Vaitla, P.; Jadlowiec, C.C.; Leeaphorn, N.; Mao, S.A.; Mao, M.A.; Pattharanitima, P.; Bruminhent, J.; Khoury, N.J.; Garovic, V.D.; et al. Use of Machine Learning Consensus Clustering to Identify Distinct Subtypes of Black Kidney Transplant Recipients and Associated Outcomes. *JAMA Surg.* **2022**, *157*, e221286. [CrossRef] [PubMed]
86. Liu, Y.; Qiu, T.; Hu, H.; Kong, C.; Zhang, Y.; Wang, T.; Zhou, J.; Zou, J. Machine Learning Models for Prediction of Severe Pneumocystis Carinii Pneumonia after Kidney Transplantation: A Single-Center Retrospective Study. *Diagnostics* **2023**, *13*, 2735. [CrossRef]
87. Chen, R.-Y.; Zhang, S.; Zhuang, S.-Y.; Li, D.-W.; Zhang, M.; Zhu, C.; Yu, Y.-T.; Yuan, X.-D. A Simple Nomogram for Predicting Infectious Diseases in Adult Kidney Transplantation Recipients. *Front. Public Health* **2022**, *10*, 944137. [CrossRef]
88. Moghadam, P.; Ahmadi, A. A Machine Learning Framework to Predict Kidney Graft Failure with Class Imbalance Using Red Deer Algorithm. *Expert Syst. Appl.* **2022**, *210*, 118515. [CrossRef]
89. Naqvi, S.A.A.; Tennankore, K.; Vinson, A.; Roy, P.C.; Abidi, S.S.R. Predicting Kidney Graft Survival Using Machine Learning Methods: Prediction Model Development and Feature Significance Analysis Study. *J. Med. Internet Res.* **2021**, *23*, e26843. [CrossRef] [PubMed]
90. Chakraborty, C.; Bhattacharya, M.; Pal, S.; Lee, S. From Machine Learning to Deep Learning: Advances of the Recent Data-Driven Paradigm Shift in Medicine and Healthcare. *Curr. Res. Biotechnol.* **2024**, *7*, 100164. [CrossRef]
91. Nankivell, B.J.; Kuypers, D.R. Diagnosis and Prevention of Chronic Kidney Allograft Loss. *Lancet* **2011**, *378*, 1428–1437. [CrossRef] [PubMed]
92. Ravindhran, B.; Chandak, P.; Schafer, N.; Kundalia, K.; Hwang, W.; Antoniadis, S.; Haroon, U.; Zakri, R.H. Machine Learning Models in Predicting Graft Survival in Kidney Transplantation: Meta-Analysis. *BJS Open* **2023**, *7*, zrad011. [CrossRef] [PubMed]
93. Yi, Z.; Salem, F.; Menon, M.C.; Keung, K.; Xi, C.; Hultin, S.; Haroon Al Rasheed, M.R.; Li, L.; Su, F.; Sun, Z.; et al. Deep Learning Identified Pathological Abnormalities Predictive of Graft Loss in Kidney Transplant Biopsies. *Kidney Int.* **2022**, *101*, 288–298. [CrossRef] [PubMed]
94. Pan, J.; Chen, Y.; Ding, H.; Lan, T.; Zhang, F.; Zhong, J.; Liao, G. A Statistical Prediction Model for Survival After Kidney Transplantation from Deceased Donors. *Med. Sci. Monit.* **2021**, *27*, e933559. [CrossRef] [PubMed]
95. Yoo, K.D.; Noh, J.; Lee, H.; Kim, D.K.; Lim, C.S.; Kim, Y.H.; Lee, J.P.; Kim, G.; Kim, Y.S. A Machine Learning Approach Using Survival Statistics to Predict Graft Survival in Kidney Transplant Recipients: A Multicenter Cohort Study. *Sci. Rep.* **2017**, *7*, 8904. [CrossRef]
96. Beetz, N.L.; Geisel, D.; Shnayien, S.; Auer, T.A.; Globke, B.; Öllinger, R.; Trippel, T.D.; Schachtner, T.; Fehrenbach, U. Effects of Artificial Intelligence-Derived Body Composition on Kidney Graft and Patient Survival in the Eurotransplant Senior Program. *Biomedicines* **2022**, *10*, 554. [CrossRef]
97. Zhang, Q.; Tian, X.; Chen, G.; Yu, Z.; Zhang, X.; Lu, J.; Zhang, J.; Wang, P.; Hao, X.; Huang, Y.; et al. A Prediction Model for Tacrolimus Daily Dose in Kidney Transplant Recipients With Machine Learning and Deep Learning Techniques. *Front. Med.* **2022**, *9*, 813117. [CrossRef] [PubMed]
98. Sridharan, K.; Shah, S. Developing Supervised Machine Learning Algorithms to Evaluate the Therapeutic Effect and Laboratory-Related Adverse Events of Cyclosporine and Tacrolimus in Renal Transplants. *Int. J. Clin. Pharm.* **2023**, *45*, 659–668. [CrossRef]
99. Zhu, X.; Peng, B.; Yi, Q.; Liu, J.; Yan, J. Prediction Model of Immunosuppressive Medication Non-Adherence for Renal Transplant Patients Based on Machine Learning Technology. *Front. Med.* **2022**, *9*, 796424. [CrossRef]
100. Chung, E.Y.M.; Blazek, K.; Teixeira-Pinto, A.; Sharma, A.; Kim, S.; Lin, Y.; Keung, K.; Bose, B.; Kairaitis, L.; McCarthy, H.; et al. Predictive Models for Recurrent Membranous Nephropathy After Kidney Transplantation. *Transplant. Direct* **2022**, *8*, e1357. [CrossRef] [PubMed]
101. Centers for Disease Control and Prevention. Available online: https://www.cdc.gov/phlp/publications/topic/hipaa.html (accessed on 28 December 2023).
102. Starke, G.; De Clercq, E.; Elger, B.S. Towards a Pragmatist Dealing with Algorithmic Bias in Medical Machine Learning. *Med. Health Care Philos.* **2021**, *24*, 341–349. [CrossRef] [PubMed]