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Review

AI Innovations in Liver Transplantation: From Big Data to Better Outcomes

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Abstract: Artificial intelligence (AI) has emerged as a transformative field in computational research with diverse applications in medicine, particularly in the field of liver transplantation (LT) given its ability to analyze and build upon complex and multidimensional data. This literature review investigates the application of AI in LT, focusing on its role in pre-implantation biopsy evaluation, development of recipient prognosis algorithms, imaging analysis, and decision-making support systems, with the findings revealing that AI can be applied across a variety of fields within LT, including diagnosis, organ allocation, and surgery planning. As a result, algorithms are being developed to assess steatosis in pre-implantation biopsies and predict liver graft function, with AI applications displaying great accuracy across various studies included in this review. Despite its relatively recent introduction to transplantation, AI demonstrates potential in delivering cost and time-efficient outcomes. However, these tools cannot replace the role of healthcare professionals, with their widespread adoption demanding thorough clinical testing and oversight.

Keywords: liver transplantation; artificial intelligence; machine learning; living donor liver transplantation; graft evaluation

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1. Introduction

Artificial intelligence (AI) broadly refers to the use of computers to model intelligent behavior with minimal human intervention [1]. AI applications in medicine are divided into two main branches: virtual and physical. The physical category focuses on the mechanical applications of AI in medicine, such as robots and other tangible devices used in healthcare settings [1]. In contrast, the virtual category involves the use of machine learning (ML), also known as deep learning (DL), in developing algorithms applicable in healthcare systems [1]. These virtual applications include decision-making algorithms, electronic record management, and other similar technology [2,3].

Liver transplantation (LT) is a complex procedure, involving numerous preoperative, intraoperative, and postoperative treatment phases [4]. This complexity in combination with the critical decision making that is required in everyday clinical practice makes transplantation the ideal realm for AI integration. AI technologies have shown promising potential in enhancing the decision-making process, improving outcomes, and optimizing resource allocation. Specifically, multiple applications in digital pathology, patient management, and immunosuppression protocols have emerged within the field of LT.

This narrative review aims to provide an overview of the literature about the role AI plays in LT. The structure of this review is organized as follows: The Materials and Methods

Section provides information about the search and collection of the included studies. The Results Section includes the following subcategories: Pre-Transplant Stage, Transplant Operation, and post-transplant monitoring. The Discussion Section provides suggestions for future AI applications in the field of LT. Lastly, Conclusion presents the limitations of our review.

The aim of this narrative review is to provide a comprehensive update on the current applications of AI in LT. Additionally, this review will explore the clinical applicability of these innovations, highlighting their potential to improve patient outcomes and everyday clinical practice overall. Furthermore, this review will provide recommendations for the development of novel AI algorithms and their integration into clinical practice by addressing gaps in the existing technologies and suggesting pathways for future research and implementation.

A summary of the included literature can be found in Table 1. Moreover, Figure 1 provides a visual representation of the numerous applications AI can have in LT.

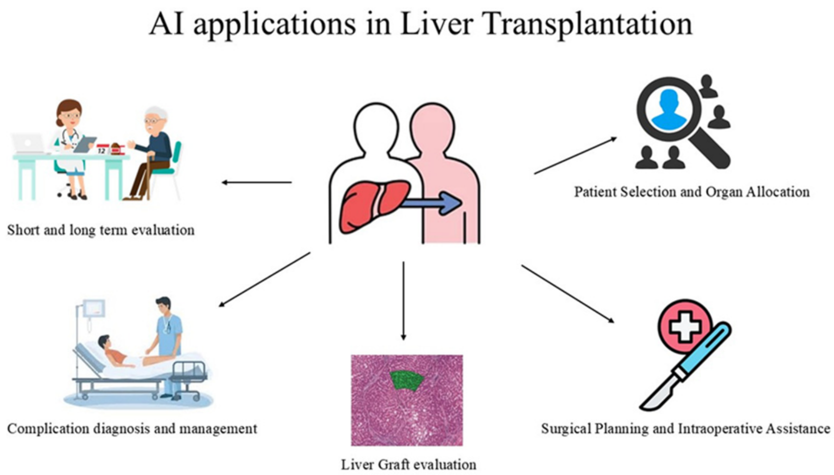

Figure 1. Applications of artificial intelligence (AI) in liver transplantation.

2. Materials and Methods

A comprehensive search of PubMed, ScienceDirect, and Scopus was carried out, restricting the outcomes to studies written in English and published from 2000 until November 2024. The following keywords were used for the search: "Liver transplantation", "Artificial Intelligence", "Machine learning", "Deep Learning", "Digital pathology", and "Organ allocation algorithms". The inclusion criteria included applications of AI in LT and the involvement of human participants. The exclusion criteria included articles in languages other than English, studies that did not involve human participants, and references that did not pertain to applications of AI in LT.

3. Results

AI applications can be involved in all stages of the transplantation process, including patient selection, surgical planning, and post-transplant evaluation, as shown in Figure 1. Additionally, Table 1 presents a comprehensive list of all the studies that employ AI during the different stages of LT.

3.1. Applications of AI During LT

3.1.1. Pre-Transplant Stage

Patient Selection and Organ Allocation

Patient evaluation and transplant listing aims to ensure transparency in the organ allocation process. The primary objective of patient evaluation is to assess their need for urgent transplantation by considering factors like liver disease severity, comorbidities, and overall health [5]. In everyday clinical settings, the MELD (Model for End-Stage Liver Disease) score is central in this process, providing an objective measure of liver disease severity [6]. MELD score predicts short-term mortality risk, with high scores indicating an urgent need for transplantation, directing the organs to those with the greatest risk of death without transplantation. Despite the efficiency of this allocation system, the MELD score still contains certain limitations. Notably, the score does not consider clinical complications related to cirrhosis and portal hypertension, thus underestimating the urgency in approximately 10% of liver failure patients [7,8].

As a result, AI applications have emerged as a crucial way for conducting objective, efficient, and comprehensive patient evaluation and subsequent organ allocation. In the realm of transplantation, AI has been used for various purposes, including assessing the severity of liver disease, which enables the early identification of patients in need of urgent transplantation, while facilitating evidence-based and holistic organ allocation.

Regarding organ allocations, various AI-based algorithms have been developed with results being equal to or even outperforming the MELD score system. Notably, Nagai et al. and Bertsimas et al. have developed ML-based algorithms for the prediction of mortality of patients on the liver transplant list post the 90-day existing mark [9,10]. Nagai et al. developed a neural network (NN) algorithm based on parameters included in the MELD score (bilirubin, serum creatinine, and INR) with additional clinical parameters including ascites and hepatic encephalopathy [10]. While this NN algorithm demonstrated superior performance over the MELD score in predicting mortality and dropout rates due to illness severity, one needs to be mindful of the subjectivity clinical parameters bring when incorporated into the score. Additionally, Bertsimas et al. proposed an ML-based algorithm using optimal classification trees [9]. This method involves several levels of branched decision points (nodes) based on independent feature values until the terminal nodes are reached (leaves). Hence, the algorithm predicting mortality resulted in a reduction in deaths and transplant list patient removal in the 90-day period when compared to the MELD score [9]. Additionally, the vast number of available variables as well as variables not included in the MELD score need to be taken into consideration by any organ allocation algorithm, as was highlighted by Guo et al. [11]. Lastly, hepatocellular carcinoma (HCC) is one of the main causes of urgent LT [12]. Conventional methods for LT with HCC are based on the Milan criteria [13]. Kwong et al. developed an algorithm using 1181 unique variables, applied in a random forest model with Spearman's correlation analyses to successfully predict waitlist dropout among liver transplant candidates with hepatocellular carcinoma [14].

3.1.2. Transplant Operation

Surgical Planning and Intraoperative Assistance

Another application of AI is during living donor LT. It is essential to ensure that the liver graft will have good functioning within the recipient while leaving the donor with enough liver parenchyma for future function and regeneration [15]. Park et al. introduced a DL-assisted CT volumetry method for estimating graft weight, which proved to be less time-consuming than the conventional manual technique, with 70% of the tested grafts not requiring additional corrections, with the remaining 30% requiring only minor alterations by the reviewing radiologists [16]. Furthermore, Giglio et al. developed an ML model trained to predict graft weight based on the somatometric characteristics of the donor as well as the type of graft [17].

Graft Evaluation

Various ML-based algorithms have been developed for evaluating liver pathologies. Liver grafts often exhibit significant steatosis, a condition strongly associated with early allograft dysfunction (EAD) [18]. Therefore, it is imperative to accurately detect and quantify steatosis in pre-implantation liver graft biopsies; however, this can be challenging for less experienced pathologists, leading to misdiagnoses. To address this, Narayan et al. developed an objective computer vision artificial intelligence (CVAI) platform to score donor liver steatosis, providing quantitative and calibrated results [19]. Several researchers, including Sun et al., Pérez-Sanz et al., Jiao et al., and Tang et al., have explored AI's role in steatosis assessment using deep learning convolutional neural network (CNN) and ML [20–23]. Their studies demonstrated great performance, indicating that after overcoming obstacles like validation and inter-observer variability, AI algorithms can be applied in a clinical setting. Pérez-Sanz et al. prioritized sensitivity, specificity, and time efficiency; Jiao et al. introduced an algorithm based on Banff criteria, enabling rapid, objective liver graft assessment; and Tang et al. applied the Segment Anything Model analysis. An additional challenge in the evaluation of steatosis in liver biopsies can be the detection of boundaries of overlapping steatosis, specifically in whole-slide microscopy images of liver biopsies. Roy et al. addressed this obstacle by proposing a deep learning-based region-boundary integrated network named DELINEATE, evaluating both steatosis pixel percentage (DSP%) and isolated steatosis droplet count percentage (DSC%), developing a model potentially applicable in graft evaluation biopsies [24]. Furthermore, non-alcoholic fatty liver disease (NAFLD), a common pathology in the general population and among potential liver donors, can compromise graft quality [25]. Preechathammawong et al. developed a fully automated DL-based method to analyze steatosis and fibrosis in NAFLD, demonstrating a strong correlation with pathologist interpretations while simultaneously incorporating Metavir fibrosis staging [26].

Despite the reliability of biopsies for steatosis evaluation, they remain an invasive procedure regardless of AI involvement [27,28]. Moccia et al. were the first to develop an ML algorithm for steatosis evaluation based on the texture analysis of a smartphone image sample, achieving sensitivity, specificity, and accuracy of 95, 81, and 88%, respectively [29]. Cesaretti et al. further advanced this approach by developing a DL-based AI algorithm that utilizes intraoperative liver graft smartphone images for steatosis evaluation [30]. Their study suggests that the AI-based analysis of intraoperative smartphone images can provide a non-invasive and reliable method for steatosis evaluation, particularly when combined with an eyepiece adaptor to assess for microvascular steatosis [30].

3.1.3. Post-Transplantation

The phase after LT is a critical period that determines the function of the liver graft. After LT, recipients require close monitoring from a multidisciplinary team with the key aspect being the administration of immunosuppressive therapy to prevent graft rejection while minimizing side effects such as infections. Other common aspects of care include the monitoring of the liver graft, with a focus on the recognition of early allograft dysfunction and surgical complications. Numerous AI applications have been reported in the post-LT setting, enhancing patient care and improving everyday clinical practice.

Complication Diagnosis and Management

LT is a complex procedure involving patients who often present with multiple co-morbidities, which can lead to various postoperative complications [31]. Some of the complications that lead to graft failure or patient mortality include vascular abnormalities, biliary strictures, fluid collections, infection, rejection, recurrent or post-transplant malignancy, diabetes, and cardiovascular and renal complications [32]. Due to the complexity and diversity of those complications, there are currently no official guidelines regarding their screening or management. However, the existing AI applications can facilitate early complication identification and intervention, as well as possible prediction.

Based on the Milan criteria, LT is one of the most prominent treatment options for patients with HCC [33]. Despite recent advancements in immunosuppressive treatment and imaging, HCC recurrence following LT remains a significant concern that impacts long-term patient outcomes [34].

Rodriguez-Luna et al. werehe first to investigate the possible application of AI in predicting HCC recurrence, using artificial neural network (ANN) combined with genotyping for microsatellite mutations/deletions (TM-GTP) [35]. Cucchetti et al., He et al., Ivanics et al., and Liu et al. also investigated possible applications in the prediction of HCC recurrence including the development of AI algorithms based on laboratory, clinical, and MRI data from the pretreatment and early post-transplantation period [36–39].

Infections are among the most prevalent complications following LT, impacting patient morbidity and mortality [40]. The types of infections that may develop depend on the time elapsed since the transplantation procedure, the type of immunosuppressive therapy, any pre-existing infections affecting the donor or recipient, and hospital-acquired infections [41]. Therefore, the role of the AI algorithm includes the prediction of occurrence as well as the severity of the most common infections in an LT recipient. Chen et al. have developed ML models able to identify pneumonia based on specific features, including specific laboratory data, intraoperative details including anesthesia time, total fluid transfusion and operation time, and preoperative length of stay [42].

Cardiovascular complications are among the greatest risks in every major operation. Pre-existing cardiovascular conditions, perioperative hemodynamic instability, and long-term metabolic effects of immunosuppressive therapy all increase the risk of those complications [43]. To mitigate these risks, Jain et al. and Soldera et al. developed ML models with increased sensitivity in detecting recipients with a high probability of developing a major cardiovascular event, including stroke, myocardial infarction, and arrhythmias, in the early postoperative period [44,45]. Zaver et al. also developed an AI electrocardiogram for the early detection of cardiovascular complications among LT recipients [46].

Acute kidney injury (AKI) is a frequent multifactorial complication following LT, affecting up to 50% of recipients [47]. AKI is associated with increased morbidity and mortality, as well as the potential progression to chronic kidney failure [48]. Lee et al., He et al., and Zhang et al. have developed algorithms for predicting AKIs using preoperative and intraoperative data as well as laboratory data from the donor [49–51].

Diabetes after LT, often referred to as post-transplant diabetes mellitus (PTDM), is a significant metabolic complication that occurs following LT. PTDM arises from multiple factors, including the adverse effects of immunosuppressive therapy, impaired glucose metabolism related to the liver graft, and both pre-existing and genetic predispositions of the LT recipient. Bhat et al. used random forest methods to investigate the increased probability of diabetes occurrence within 1 year from LT [52].

AI can also assist in the prediction of intraoperative complications. In a multicenter study, Chen et al. utilized fifteen key variables to develop a Categorical Boosting (CatBoost) model capable of forecasting the risk of massive blood transfusion during surgery [53].

Alcohol consumption leading to alcohol-related liver disease has become a leading indication for LT [54]. To qualify for LT, patients must demonstrate a six-month documented abstinence from alcohol [55]. Despite this requirement, certain patients remain at risk of post-transplantation relapses, which can result in irreversible graft damage [56]. There are various risk factors contributing to relapses, including a pre-transplant history of severe or prolonged alcohol use disorder, previous relapses, mental health conditions, inadequate post-transplant follow-up or support, high levels of post-transplant stress, or adjustment difficulties [57]. Lee et al. developed an AI model that uses this psychosocial data to predict harmful alcohol use after LT [58].

Another rare complication that can occur in any type of transplantation is the graft-versus-host disease (GVHD). Cooper et al. used the clinical features of both donors and recipients to develop algorithms able to detect high-risk patients for this rare complication [58].

Lastly, Zabara et al. developed an algorithm to predict post-transplantation complications in patients with hepatitis C, highlighting the impact of the underlying cause of liver failure on LT outcomes [59]. Li et al. also developed a DL model able to predict multiple risk factors, pointing out the multifactorial nature of this operation [60].

Short and Long Term Graft Evaluation

Despite recent advances in surgical techniques and medical management leading to improved outcomes and particularly lowered short-term mortality, a clear improvement in long-term mortality has not been achieved in the last few years [61]. Long-term survival of LT recipients is heterogeneous based on the reason for transplantation and other patient- and donor-related factors [62]. A number of AI algorithms have been developed with the aim of predicting the long-term function of liver grafts. Parmanto et al. were the first to develop an NN-based algorithm in order to predict 90-day graft function based on clinical data [63]. Additionally, researchers including Briceño et al., Dorado-Moreno et al., Lau et al., Guijo-Rubio et al., Ayllon et al., and Börner et al. also developed ML models based on clinical and laboratory data at different time points in addition to donor data to predict short- and long-term graft function up to 9 years post-transplantation [64–69]. The aim of these algorithms is to provide an accurate decision-support model able to assist healthcare professionals in clinical decision making in regard to organ allocation and the personalized management of LT recipients. Lastly, Börner et al. developed an algorithm specifically aimed at predicting in-hospital mortality, as patient mortality is an important factor characterizing LT outcomes [70].

Rejection is one of the major causes of graft failure, occurring due to differences in human leukocyte antigens (HLAs) between the donor and recipient, resulting in an antibody-mediated or T-cell-mediated reaction [71]. Rejection can occur at various time points post-transplantation. This timeframe can be used to categorize the rejection into hyperacute (minutes to hours), acute (5 days–3 months), or chronic (3 months-years). Acute rejection is a manageable complication that can be treated by adjusting the doses of immunosuppressive therapy in combination with high-dose steroid treatment [72]. Various laboratory and clinical data can indicate acute rejection, but a liver biopsy is needed for a definite diagnosis [71]. Liver biopsy is an interventional procedure that carries specific risks, highlighting the need for a screening algorithm. Hughes et al. and Zare et al. developed AI algorithms using clinical and biochemical data either continuously or from specific post-transplantation time points to predict recipients that might face or are at risk of acute rejection [73,74].

Table 1. Study characteristics of studies investigating possible applications of AI in LT.

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Parmanto et al. [63]	2001	NA	Post-Transplant	RNN	Prediction of graft failure based on clinical observations.	Use of RNN to accurately model the temporal sequence of clinical observations	90% correct classification on the learning set and 78% on the test set.
Hughes et al. [73]	2001	117	Post-Transplant	ANN	ML model to monitor and detect acute rejection in LT.	This model uses individual clinical and biochemical variables and can be used for the monitoring of LT recipients in the early post-LT period.	AUROC = 0.902, sensitivity = 80.0% specificity = 90.1%
Rodriguez-Luna et al. [35]	2005	19	Post-Transplant	ANN	ANN analysis performed to prognosticate the risk of HCC recurrence.	The first AI algorithm able to predict the HCC reoccurrence.	This algorithm had a high discriminatory power (17/19, 89.5%), accurately predicting HCC recurrence.
Cucchetti et al. [36]	2010	250	Post-Transplant	ANN and LR	ANN model able to predict tumor grade and MVI.	Preoperative serum alpha-fetoprotein (AFP), tumor number, size, and volume were the used variables.	ANN correctly identified 93.3% of tumor grades and 91% of MVI.
Briceño et al. [64]	2014	1031	Post-Transplant	ANN	ANNs for organ allocation should be based on the concept of survival benefit.	Predicting the 3-month outcome based on donor–recipient matching and 57 variables.	ANNs showed great performance in predicting the probability of graft survival (90.79%) and loss (71.42%).
Dorado-Moreno et al. [66]	2017	1406	Post-Transplant	ANN	ML model for prediction of graft failure.	The model aids healthcare professionals in the donor–recipient matching process.	Accuracy = 73.57%,

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Lau et al. [67]	2017	15,401	Post-Transplant	ANN and RF	ML model for prediction of graft failure.	Identification of 15 significant donor, recipient, and transplant factors influencing graft failure within 30 days post-transplant.	AUC = 0.818
Zare et al. [74]	2017	148	Post-Transplant	ANN	ML model able to monitor and detect acute rejection in LT.	This model can provide efficiency in clinical decision making based on routine laboratory data.	Accuracy = 90%, sensitivity = 87%, and specificity = 90%
Lee et al. [50]	2018	1211	Post-Transplant	DT, RF, GVM, SVM, naïve Bayes, multilayer perceptron, and DBN	ML-based algorithms for prediction of AKI.	An internet-based risk estimator was developed based on the GBM model.	GBM had the best performance with AUROC 0.90
Bhat et al. [52]	2018	61,677	Post-Transplant	RF and LR	Ml algorithm able to identify key predictors and survival outcomes of new-onset diabetes post-LT.	Sirolimus use and Black race were some variables associated with new-onset diabetes.	Various variables were investigated with both models.
Ayllon et al. [68]	2018	822	Post-Transplant	ANN	ANN model for donor–recipient matching.	ANN model demonstrated excellent predictive capabilities for both 3-month and 12-month graft survival, outperforming traditional scoring systems.	3 month predictive capability AUC = 0.94 and 12 month AUC = 0.78
Moccia et al. [29]	2020	40	Transplant Operation	SVM, RF, and MIL	ML algorithm for the analysis of liver graft texture.	This is the first model able to assist surgeons in liver graft assessment inside the OR using RGB images.	Sensitivity = 95, specificity = 81, and accuracy = 88%

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Cesaretti et al. [30]	2020	117	Transplant Operation	SVM-SIL and FCNN	ML algorithm assessing liver steatosis based on smartphone images.	Smartphone cameras are widely available among surgery team members. In the future, better camera quality could lead to better performance of this algorithm.	Automatic liver graft segmentation from smartphone images achieved an accuracy of 98%, whereas the analysis of the liver graft features (cropped picture and donor data) showed an accuracy of 89% in graft classification.
Guo et al. [11]	2021	34,575	Pre-Transplant	DNN, LR, and RF	ML model used for early mortality prediction in patients on LT waiting list.	Variables such as ALP, ALT, and hemoglobin were also top informative features besides the 4 MELD-Na variables.	The performance of models comprising all variables outperformed those with 4 MELD-NA variables for all prediction cases and the DNN model outperformed the LR and RF models.
Pérez-Sanz et al. [21]	2021	20	Transplant Operation	CV ML	ML algorithm for the measurement of steatosis.	The model was able to easily differentiate specific fat staining from artifacts related to the staining procedure.	Accuracy for all classifiers (>0.99) with sensitivity > 0.8 and specificity > 0.9. Regarding speed, KNN and naïve Bayes were the fastest algorithms.

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
He et al. [37]	2021	109	Post-Transplant	DL	ML model able to distinguish post-LT recipients of high recurrence risk.	The variables used included clinical features, MRI images, and pathology images	The combined model showed 80% recall and 89% precision.
Chen et al. [42]	2021	591	Post-Transplant	LR, SVM, RF, ADABoost, XGBoost, and GBM	ML algorithm for prediction of postoperative pneumonia on LT recipients.	Pneumonia was associated with 14 features: INR, HCT, PLT, ALB, ALT, FIB, WBC, PT, serum Na^+, TBIL, anesthesia time, preoperative length of stay, total fluid transfusion, and operation time.	XGBoost model performed best (sensitivity: 52.6%; specificity: 77.5%)
Jain et al. [45]	2021	1459	Post-Transplant	LR, RF, SVM, GBM, and XGBoost	ML model used to predict major adverse cardiovascular events, all-cause mortality, and cardiovascular mortality post-LT.	The top influential factors for postoperative cardiovascular adverse events were age at transplantation, diabetes, serum creatinine, cirrhosis caused by non-alcoholic steatohepatitis, right ventricular systolic pressure, and left ventricular ejection fraction.	GBM model XGBoost achieved the highest performance, with AUROC = 0.71
He et al. [49]	2021	493	Post-Transplant	RF, SVM, CDT, and CIT	ML-based algorithms for the prediction of AKI	RF models can be a useful tool for early clinical intervention of AKI to improve patient survival.	The RF model demonstrated the highest prediction accuracy of 0.79 with an AUC of 0.850
Zhang et al. [51]	2021	780	Post-Transplant	GBM and ADA	ML-based algorithms for early prediction of AKI.	High preoperative indirect bilirubin, low intraoperative urine output, long anesthesia time, low preoperative platelets, and graft steatosis graded 1 were the top predictors for AKI.	The GBM model achieved the highest AUC 0.76

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Guijo-Rubio et al., [69]	2021	39,189	Post-Transplant	MLP, RF, GB, and SVM	ML techniques for donor–recipient matching in LT.	ML methods did not improve liver allocation performance.	LR outperformed several machine learning techniques across all endpoints achieving an AUC of 0.64
Nagai et al. [10]	2022	105,140	Pre-Transplant	NN	NN models that can predict LT waitlist mortality.	The 90-day mortality model specifically identified more waitlist deaths with a higher recall, having the potential to decrease waitlist mortality and lead to more equitable allocation systems	The NN 90-day mortality model outperformed MELD-based models across all the subsets in predicting mortality.
Kwong et al. [14]	2022	18,920	Pre-Transplant	NA	An ML model predicted 3-, 6-, and 12-month waitlist dropouts among patients with HCC.	An online calculator was created for clinical use	This ML model predicted 3-, 6-, and 12-month waitlist dropouts among patients with HCC with a c-statistic of 0.74
Park et al. [16]	2022	581	Transplant Operation	DL	DL-assisted CT volumetry to evaluate graft weight	This algorithm offers a time-efficient graft weight evaluation results derived from the DL model not requiring additional correction in approximately 70% of donors. A graft volume-to-weight conversion formula was also developed.	The CCC for the agreement between the estimated and measured graft weights was 0.834

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Narayan et al. [19]	2022	90	Transplant Operation	CVAI	A CVAI platform able to calculate donor liver steatosis and pred EAD.	The difference in the CVAI steatosis scores between the grafts developing EAD and those that did not was statistically significant.	CVAI steatosis scores were lower than pathologist scores (median 3% vs. 20%, $p < 0.001$).
Sun et al. [20]	2022	91	Transplant Operation	DL CNN	ML model generating steatosis probability map from an input WSI	This algorithm provides fast, accurate, and reproducible donor liver evaluation.	The model had good correlation and agreement with the annotation in both the training set (r = 0.88, ICC = 0.88) and novel input test sets (r = 0.85 and ICC = 0.85).
Chen et al. [53]	2022	1239	Post-Transplant	CatBoost	An ML algorithm for the prediction of intraoperative massive blood transfusion	15 variables were screened out, including age, weight, hemoglobin, platelets, white blood cell count, activated partial thromboplastin time, prothrombin time, thrombin time, direct bilirubin, aspartate aminotransferase, total protein, albumin, globulin, creatinine, and urea.	AUROC: 0.810
Lee et al. [58]	2022	116	Post-Transplant	XGBoost	ML model predicting harmful alcohol use post-LT.	13 psychosocial variables were used.	AUC = 0.692 and positive predictive value = 0.82

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Cooper et al. [75]	2022	1938	Post-Transplant	LR, NN, and GBM	Predictive model for GVHD	Variables used included ABO matching, CMV and EBV, serostatus matching, age differences, and donor race/ethnicity to recipient race/ethnicity matching.	The C5.0 model had the best performance with AUROC 0.86, sensitivity 0.80, and detection prevalence 0.21.
Börner et al. [65]	2022	529	Post-Transplant	DL	ML techniques for donor–recipient matching and survival prediction in LT.	This NN utilizes transparent and easily interpretable data to predict the outcome after LT.	Accuracy = 95.8%, AUC = 0.940, and F1 = 0.899
Giglio et al. [17]	2023	872	Transplant Operation	ML	ML able to predict GW.	The following information was used: donor's age, sex, height, weight, body mass index, graft type, computed tomography estimated graft volume, and total liver volume	MAE value of 50 ± 62 g in predicting GW, with a mean error of 10.3%.
Jiao et al. [22]	2023	88	Transplant Operation	SAM	ML 3-step model able to detect LDF	The AI model is designed to adhere to the Banff consensus recommendations, ensuring clinical relevance and accuracy.	Correlation coefficients between pathologist and computer-assisted manual quantification, between computer-assisted manual quantification and the AI model, and between the AI model and pathologist were 0.94, 0.88, and 0.81, respectively.

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Ivanics et al. [38]	2023	66.059	Post-Transplant	ML	ML-based models for predicting 90-day post-LT mortality across three international registries.	Standardization of registry-based variables could facilitate the added value of MLA-based models.	The best model performance was obtained in Canada (LightGBM: AUROC, 0.42; range, 0.25–0.55) and the US
Liu et al. [39]	2023	315	Post-Transplant	MLP	ML model for the prediction of HCC recurrence	A web calculator based on the MLP model was also developed.	γ-glutamyl transpeptidase (GGT), fibrinogen, neutrophil, aspartate aminotransferase (AST), and total bilirubin (TB) were the top five important factors for the recurrence risk of HCC.
Zaver et al. [46]	2023	300	Post-Transplant	CNN	AI-ECG algorithm in predicting cardiac factors for post-LT cardiovascular complications.	AI-ECG trained to recognize patterns from a standard 12-lead ECG in order to identify the presence of left ventricular systolic dysfunction and atrial fibrillation.	ECG in sinus rhythm had an AUROC = 0.69 for prediction of de novo post-transplant atrial fibrillation.
Zabara et al. [59]	2023	90	Post-Transplant	DL	An ML model to predict postoperative complications following LT in hepatitis C patients.	This model can be used as a tool to guide a more intensive follow-up protocol in high-risk patients.	Accuracy > 99.76%

Table 1. *Cont.*

Authors	Year	N of Patients	Stage of Transplant Process	AI Application	Description	Key Benefits	Results
Tang et al. [23]	2024	95	Transplant Operation	SAM	ML model able to detect LDF hepatocytes in liver biopsies.	Additional algorithms can be applied to filter the false positive results of this model.	The model showed high sensitivity but low specificity due to similarities with other structures.
Soldera et al. [44]	2024	575	Post-Transplant	XGBoost	ML model used to predict major adverse cardiovascular events post-LT.	The modeling dataset included 83 features, encompassing patient and laboratory data, cirrhosis complications, and pre-LT cardiac assessments.	AUROC = 0.89, precision = 0.89, recall = 0.80, and F1-score = 0.84.
Li et al. [60]	2024	160,360	Post-Transplant	DNN	An ML model predicting post-LT risk factors.	The model significantly reduced the task discrepancy by 39%.	Multi-task learning outperform single-task prediction.
Börner et al. [70]	2024	1066	Post-Transplant	DL	This model enables continuous, risk-adjusted monitoring of in-hospital mortality rates after LT.	This approach aims to promptly detect deviations in surgical outcomes, thereby facilitating timely interventions.	DL AUC = 0.857, surpassing traditional risk scores

ADA: adaptive boosting, AFP: alpha-fetoprotein, AKI: acute kidney injury, ALB: albumin, ALT: Alanine Aminotransferase, ANN: artificial neural network, AUC: Area Under the Curve, CCC: Concordance Correlation Coefficient, CatBoost: Categorical Boosting, CDT: Classical Decision Tree, CIT: Conditional Inference Tree, CMV: Cytomegalovirus, CNN: convolutional neural network, CV: computer vision, CVAI: computer vision artificial intelligence, DBN: Deep Belief Network, DL: deep learning, EBV: Epstein–Barr Virus, FCNN: fully convolutional neural network, FIB: fibrinogen, GBM: Gradient Boosting Machine, GVHD: graft-versus-host disease, HCC: hepatocellular carcinoma, HCT: Hematocrit, ICC: Intraclass Correlation Coefficient, INR: International Normalized Ratio, LDF: Large-Droplet Fat, LR: Logistic Regression, LT: liver transplantation, MAE: Mean Absolute Error, MIL: Multiple Instance Learning, ML: machine learning, MLP: multilayer perceptron, MVI: Microscopic Vascular Invasion, MRI: Magnetic Resonance Imaging, NA: Not Applicable, NN: neural network, PLT: platelet, PT: prothrombin time, RF: random forest, RNN: Recurrent Neural Network, SAM: Segment Anything Model, SIL: Single Instance Learning, SVM: Support Vector Machine, TBIL: total bilirubin, WBC: white blood cell, WSI: whole-slide image, XGBoost: Extreme Gradient Boosting.

4. Discussion

In recent years, technological advancements and the digitization of patient records have significantly accelerated the adoption of AI applications across clinical practice, including the field of transplantation [76]. ML and DL have enabled the integration and analysis of vast amounts of patient data, such as laboratory results and medical imaging, providing support to healthcare professionals in decision making and in predicting the outcomes and long-term function of liver grafts. AI also excels at handling large datasets efficiently, making it useful to analyze data related to panels of proteins, omics, and various types of biomarkers from LT recipients and donors, from various types of samples. Additionally, the application of ML and DL algorithms is vital in medical education through simulation-based learning and in research for data extraction and analysis [77].

Liver disease diagnosis is another promising area for AI involvement, with AI applications being reported for the early and precise detection of Wilson's disease and autoimmune liver diseases [78,79]. Since autoimmune liver diseases have a reoccurrence, with risk ranging between 16% and 43% for Autoimmune Hepatitis (AIH), between 9% and 35% for Primary Biliary Cholangitis (PBC), and around 20% for Primary Sclerosing Cholangitis (PSC) [80,81], ML algorithms have been trialed for predicting this risk while also managing patients with autoimmune liver diseases [79].

Acute liver failure remains a major cause of LT, where timely detection is of the highest importance. Drug-induced liver injury (DILI) and herb-induced liver injury (HILI) are significant causes of acute liver failure, potentially resulting in patients needing LT [82]. Roussel Uclaf Causality Assessment Method (RUCAM) is the algorithm used for the severity assessment of DILI and HILI [83]. The structure of the RUCAM algorithm can potentially allow for the addition of ML to facilitate its use in everyday clinical practice [84]. Additionally, AI integration can also facilitate the diagnosis and management of DILI occurring post-LT due to the immunosuppressive medications, with AI being used in early detection, monitoring, and risk stratification [85].

Despite the recent influx of studies highlighting the various applications of AI in LT, its integration into routine clinical practice remains rather limited. A major barrier remains in regard to the lack of AI algorithm transparency. AI systems, particularly those based on ML and DL, often operate as "black boxes", with the resulting decisions or predictions not being backed by an easily interpretable line of reasoning [86]. Additionally, bias is another challenge that needs to be addressed as it can lead to disparities in healthcare outcomes. AI algorithms are trained predominantly on data from one demographic, which may lead to the algorithms underperforming for others. To address these challenges, retrospective studies using large, diverse datasets, potentially involving multicenter collaborations, are desperately needed. Such studies can improve the applicability and reliability of AI algorithms while improving trust among clinicians and researchers.

Since there has been a rapid surge in AI applications in health management, we can expect future AI involvement in the pre-implantation evaluation process, decision making regarding organ allocation, surgical planning, and postoperative management based on algorithms that can reduce cost and be more time efficient compared to conventionally used methods. AI applications in emergency medicine have demonstrated their ability to optimize transfer times [87,88]. Similar technologies could be adapted to enhance the recipient allocation process in the field of LT. Despite the potential benefits applications of AI may provide to the healthcare industry, issues such as accountability in case of errors or adverse outcomes combined with the use of large datasets containing sensitive patient information may hinder future progress. Addressing these issues will require not only technological solutions but also the development of clear regulatory frameworks and ethical guidelines to ensure AI's safe and equitable integration into future clinical practice.

By overcoming these barriers, AI can become indispensable in LT, revolutionizing patient care and improving outcomes.

5. Conclusions

Advancements in AI use for LT should prioritize the development of personalized patient care, including organ allocation algorithms, predictive models for graft function evaluation, and tailored immunosuppressive regimens, as well as algorithms regarding efficient patient education. These advancements could, therefore, potentially improve patient outcomes and transplantation success rates. In comparison to other literature reviews, this review provides the most up-to-date analysis of AI applications in LT, discussing advancements in patient selection, organ allocation, and post-transplantation complications. We acknowledge that there are certain limitations in our review, specifically with the availability of the included studies and the language constraints, which may influence the scope of our analysis. However, we hope this review serves as a foundation to inspire and guide future research, fostering innovation to improve outcomes for LT patients. Future research in the field of AI applications in LT should focus on the integration of ML technology for the optimization of organ allocation and recipient selection. Additionally, more studies should be performed regarding the potential of AI in graft evaluation particularly through smartphone images and digital pathology applications. Lastly, the application of AI could lead to personalized treatment strategies tailored to individual patients.

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