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Deep Learning, Transfer Learning and Prognostic Modeling in Liver Transplantation: An Analytical Review

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ABSTRACT

Liver transplantation (LT) is a high risk and complicated procedure in which predictor modeling can be utilized to improve donor-recipient matching, survival prediction, and postoperative care. This research provides an iterative statistical analytical review of machine learning (ML), deep learning (DL) and transfer learning (TL) strategies to liver transplantation optimization. Systematic literature searches in PubMed, Scopus, IEEE Xplore, and Web of Science databases to find studies published since 2015 and 2024 were used to conduct the review. Peer-reviewed articles that follow either ML, DL, or TL to a prediction, classification, or survival analysis task related to LT were included in the inclusion criteria; articles who did not quantify their results were not included. A comparative framework was used through an iterative process, which combined quantitative extraction of accuracy, Area Under Curve (AUC), F1-score, and Root Mean Square Error (RMSE) with statistical aggregation to determine the performance trends across model categories. Interpretations show that hybrid deep learning and transfer learning algorithms are always more effective in predicting outcomes and estimating the survival of grafts as compared to the traditional ML algorithms. The paper demonstrates the lack of standardization, interpretability, and reproducibility of datasets and suggests further unification of explainable AI and multi-center data harmonization in clinical applications.

1. INTRODUCTION

Liver transplantation (LT) remains the gold-standard treatment for end-stage liver disease (ESLD) with or without hepatocellular carcinoma (HCC), but patient selection, donor organ allocation, perimeter risk stratification, and post-transplant surveillance challenges continue to impair outcomes. Biochemical markers [1], radiographic imaging, and histopathological examination traditionally underpin clinical decision-making but suffer subjectivity, interobserver variability, and an inability to predict long-term complications. Artificial intelligence (AI) and machine learning (ML) have gone a long way toward transforming LT in recent years, offering data-driven automated decision-support systems to promote transplant success rates [2].

The incorporation of AI-based methods still lies within infancy, leaving many questions on model performance and adaptability as well as clinical translation unanswered [3]. There have been studies where researchers analyzed ML and DL methods independently in liver transplants and HCC treatment [4]; however, a systematic and full statistical review comparing the performance, strengths, and weaknesses across these works is lacking. These studies used logistic regression, support vector machines (SVM), random forest, convolutional neural networks (CNN), recurrent neural networks (RNN), transfer learning models, and multi-omics clustering to predict graft survival, recurrence risk, and post-operative complications [5]. Still, there are hardly any standard performance evaluation procedures, the studies' datasets are restricted mainly to small and single-center data, and there is limited research about how AI models can be better configured towards extensive clinical acceptance [6].

This study engages in a detailed comparative analysis of 40 recent AI-based models applied in liver transplantation and HCC prognosis. Using an iterative statistical analytical framework, this review systematically evaluates AUROC, C index, sensitivity, specificity, and predictive accuracy metrics over several AI forms. The review will consist of both risk assessment-type models (logistic regression, Cox models) and prediction-type classification models (SVM, random forest, decision tree). This study will also analyze the validity of CNN, transfer learning, and deep survival networks. The analysis will take into account the contributions of multi-omic clustering approaches and feature selection (LASSO, principal component analysis, SHAP explanations) to identifying biomarkers associated with transplant success and cancer

recurrence populations [7].

The contributions of this work of utmost importance are: Identification of best-performing AI models for the various LT and HCC applications; Standardized evaluation of predictive performance metrics across methodologies [8]; Insight into clinical challenges posed and strategies for future integration of AI in hepatology. Through the limitations of preceding studies, this work aims to help researchers and clinicians choose the AI decision support system that would most benefit their work in liver transplantation and oncological risk assessment [9]. The results will pave ways for bridging the gap between AI model development and real-world implementation in hepatology and transplant surgery [10].

1.1 Motivation and contribution

The urgent need for AI optimization of liver transplantation and management of HCC constitutes the primary motivation of this study. Although certain developments are seen in surgical techniques and immunosuppressive therapies, the preoperative risk assessment, donor-recipient matching, and postoperative surveillance remain suboptimal.

AI models could give very accurate predictive abilities, automated integration, and real-time decision-making, but nobody seems to agree on which model the best is and provides clinically interpretable results. Differences in dataset size, feature selection methods, and validation strategies complicate any attempt to assess AI performance in hepatology. Such a statistical and performance-driven review seeks to formulate a critical comparison of ML, DL, and TL models aimed at the best optimization of LT and HCC prognosis.

This work brings forth several novel contributions to AI-based precision medicine in hepatology. First, it delivers the most extensive performance comparison to date, evaluating 40 AI models applied in liver disease diagnosis, prognosis, and transplantation. The second contribution entails an examination of the adaptability of the AI schemes when applied across different datasets, demonstrating the scalability, robustness, and generalizability of the models. The third contribution is a structured evaluation of hybrid models that elucidates how multi-omics clustering, transfer learning, and deep survival networks work together to improve transplant outcome prediction.

Finally, this review sets out key recommendations for future research and clinical integration, thereby establishing a framework for developing AI-driven decision-support systems tailored to liver transplantation and HCC risk stratification. This work could fast-track the adoption of AI within hepatology and promotes personalized transplant approaches, early detection of recurrences, and increased patient survival sets.

2. REVIEW OF EXISTING MODELS USED FOR LIVER TRANSPLANTATION ANALYSIS

Liver transplantation (LT) is a complex medical procedure, which, apart from other major challenges, has several significant perioperative complications, issues related to donor-recipient matching, and postoperative outcomes. The application of artificial intelligence (AI) in LT extends handling predictive modeling, decision support, and clinical management. This review attempts to provide a comparative perspective on the hybrid AI models-the deep learning (DL) and traditional machine learning (ML) approaches-focused specifically on liver transplantation.

Predictive modeling in liver transplantation prediction of surgical complications in LT is very relevant in optimizing patient management. Early reports suggested that traditional ML models can predict massive intraoperative hemorrhage, with logistic regression as one of the leading ones regarding its interpretability and rigorous calibration performance [1]. The major predictive factors found include disease etiology, activated partial thromboplastin time (aPTT), and Model for End-stage Liver Disease (MELD) score, with an AUROC of 0.775. However, ML requires a complex feature engineering that may be insufficiently able to capture complex and non-linear relationships in clinical data samples.

On the contrary, deep learning-based image analysis has improved preoperative planning and surgical navigation. A mixed-reality (MR) training system using 3D liver reconstruction models and iterative closest point (ICP) tracking augmented visualization of middle hepatic vein (MHV) during surgery [2]. Joint integration of MR and AI-based simulations postulates that spatial recognition using DL can positively improve surgical outcomes and donor safety. Additionally, portals using real-time ultrasound contrast agents combined with deep learning algorithms compared with conventional intravascular pressure readings have been superior as regards specific measurements for portal vein pressure (PVP) [3]. Detection of portal hypertension using subharmonic scattering signals of microbubbles in contrast-enhanced ultrasound provided high sensitivity (93.3%) and specificity (91.7%), indicating that AI-enhanced imaging can supplant invasive diagnostic techniques.

2.1 AI for liver tumor recognition and classification in transplant candidates

Tumor burden generally determines eligibility for transplantation; hence, detecting and classifying lesions correctly would have vital importance. Unstructured liver tumor reports have incorporated traditional ML tactics through NLP and interpretable ML classifiers [4]. Improved risk assessment and decision-making in LT candidates are the areas in which these methodologies have drawn benefits.

Deep learning has drastically improved tumor segmentation and classification. Multimodal fusion architectures have enhanced cross-modality adaptation for liver segmentation in CT-MRI data for the limitations induced upon traditional ML models due to domain shift [5]. Similarly, deep learning models such as metric learning and attention-aware weighted fusion yielded highly accurate (84%) differentiation of histologic grades of hepatocellular carcinoma (HCC) [6]. Hence, advances like these have underscored the need for hybrid AI models for improved preoperative evaluations in LT.

Recent research corroborating the importance of antigen-presenting cells and T-cell infiltration in determining immunological responses against HCC has promoted studies toward developing machine learning-based LncRNA signatures for the immune and survival predictions of LT candidates [7]. Similarly, disulfidptosis-related long noncoding RNAs (DRLs) have been explored for their role in patient prognosis; AI-derived risk scores exceeded conventional clinical measures in efficacy [8]. These studies show how hybrid AI models enhance precision medicine by

linking molecular and clinical data in LT [9].

2.2 AI in the monitoring and outcome prediction post-transplantation

Should liver cancer recur post-transplantation, it would make one of the more severe challenges [10]. Predictive modeling concerning recurrence after different treatment modalities was developed based upon AI that achieved high accuracy, with an AUC of 0.92 for percutaneous ablation (PA) and 0.86 for surgical resection (SR) and 0.79 for transarterial chemoembolization (TACE) [11]. Multimodal deep learning (MDL) models based on CT and MRI imaging were also developed mostly for on improvement in predicting microvascular invasion (MVI) in HCC, attaining an AUC of 0.844 [12]. These suggest that hybrid AI approaches integrating radiomics, clinical parameters, and deep learning architectures will make strength in post-transplantation surveillance sets.

2.3 Hybrid AI models in liver transplantation: Current limitations and future prospects

Although AI applications promise much in LT, there are several impediments [13]. Different AI methods require mammoth-sized, high-quality datasets for multimodal clinical and imaging data learning [14]. For instance, CNNs stand out with better predictive performance for post-transplant survival (C Index: 0.824) compared to conventional ML models [15], yet heterogeneities in the data continue to be impediments to generalizability. Nanoparticle-based targeted treatments were the future direction for AI-aided liver cancer therapy. AI-augmented docking and bioinformatic investigations have identified prominent target genes such as AKR1C3, with nanomaterial-based delivery systems having demonstrated potential to reverse tumor hypoxia [16]. Additionally, models for predicting HCC downstaging have been developed fairly robustly, with hybrid models that incorporated clinical and radiomic features achieving AUROC values of 0.877 [17]. With metabolic-associated fatty liver disease (MAFLD) having been identified as the most common etiology of HCC, AI-driven solutions to its diagnosis and management would be apropos [18]. Ayurvedic diagnostic algorithms based on gut microbiota and genetic markers could hold out the promise for tailored treatment planning [19]. Hepatoprotective effects of herbal compounds such as Liv-52 have been assayed, followed by molecular simulations which identified (-) Syringaresinol as one of the most effective therapeutic leads [20]. Liver transplantation (LT) is still the only ultimate cure for end-stage liver disease and hepatocellular carcinoma (HCC); yet, issues still surround the field of optimizing donor-recipient matching, perioperative risk stratification, and post-transplant outcomes.

Altogether, the analyzed literature reveals a considerable development of the implementation of new computational and machine learning tools to solve domain-related issues. Although the methodologies used differ greatly in different works, the majority of the studies focus on enhancing predictive accuracy, data efficiency, and model interpretability. Nevertheless, the lack of coherence in the experimental design and data management is a limitation of the generalizability of results. All these studies together emphasize the increased realization of the role of intelligent models in optimization of decision-making processes in various fields of application. The limitations of the hybrid AI models in liver transplantation are included in Table 1.

Table 1. Hybrid AI models in liver transplantation limitations

Reference	Method Used	Findings	Strengths	Limitations
[1]	Logistic Regression for Hemorrhage Prediction	Traditional ML models identified key predictive factors for massive hemorrhage during LT.	High interpretability, effective in risk stratification.	Lower accuracy compared to DL models; does not capture complex non-linear relationships.
[2]	Mixed-Reality (MR) Training with ICP Tracking	MR-based 3D models improved surgical navigation in LT.	Enhanced surgical training, precise vein tracking.	Limited sample size; real-time integration in surgery remains a challenge.
[3]	Ultrasound Contrast-Based Portal Vein Pressure (PVP) Measurement	AI-enhanced ultrasound analysis provided high accuracy in non-invasive PVP measurement.	High sensitivity (93.3%) and specificity (91.7%) for portal hypertension.	Needs clinical validation for LT applications.
[4]	NLP and ML for Report Structuring	NLP-based automation structured unstructured liver tumor reports for AI-driven risk assessment.	Improved efficiency and accuracy of clinical documentation.	Performance varies with dataset quality; limited generalization.
[5]	Domain Adaptation for Cross-Modality CT-MR Data Segmentation	Hybrid DL model learned robust liver segmentation features across imaging modalities.	Overcomes domain dependency; improved generalizability.	Requires large dataset for cross-modality training.
[6]	DL-Based Multimodal MRI for HCC Grading	AI improved diagnostic precision in HCC histologic grading.	High accuracy (84%), sensitivity (87%), and precision (89%).	Requires further validation in larger datasets.
[7]	Machine Learning-Based APC-TCI LncRNA Signature	AI-derived biomarkers improved prognostic stratification in HCC.	Robust predictive capacity for immune response and prognosis.	Lacks external validation in prospective cohorts.
[8]	LASSO and Cox Regression for Prognostic Signature	AI-derived DRL signature outperformed clinical models in predicting HCC outcomes.	High predictive efficacy in survival analysis.	Requires additional validation for clinical implementation.
[9]	Gene Expression Analysis for TACE Response	AI-based hub gene identification correlated with	Identified biomarkers linked to therapy	Limited applicability in clinical practice.

	Prediction	TACE response in HCC.	resistance.	
[10]	AI-Driven Image Segmentation for HCC Detection	AI models improved early detection and segmentation accuracy.	High diagnostic efficiency; useful for pre-transplant assessment.	Needs multimodal validation across different imaging systems.
[11]	Meta-Analysis of AI in HCC Recurrence Prediction	AI models demonstrated high AUC values in predicting recurrence post-treatment.	Systematic validation of AI effectiveness in predicting recurrence.	Study heterogeneity; differences in AI model performance across datasets.
[12]	Multimodal Deep Learning (CT-MRI) for MVI Prediction	AI-enhanced fusion models improved MVI prediction in HCC.	High AUC (0.844); superior to traditional models.	Requires additional real-world validation.
[13]	Cox Regression for Time-Dependent Risk Factors	AI revealed gender-specific risks in post-LT liver function deterioration.	Identifies high-risk groups dynamically over time.	Limited dataset; requires real-time monitoring integration.
[14]	DL-Based Radiomics for Sarcopenia Detection	AI-enhanced radiomics predicted post-transplant survival.	High prognostic accuracy; validated across multiple centers.	Requires broader validation in diverse cohorts.
[15]	CNN-Based Survival Prediction from CT Imaging	AI integration improved post-treatment survival estimation.	High C Index (0.824); robust multimodal fusion.	Data imbalance may affect model performance.
[16]	AI-Assisted Nanoparticle Therapy for HCC	AI-optimized nanodrug targeting improved tumor hypoxia suppression.	Potential clinical translation for AI-enhanced therapy.	Needs in vivo trials for efficacy validation.
[17]	AI-Driven Prognosis Model for HCC Downstaging	Hybrid model combining radiomics and clinical features improved LT candidate selection.	High AUROC (0.877); better than clinical-only models.	Computationally intensive; requires clinical workflow integration sets.
[18]	AI-Based Molecular Docking for Herbal Therapy	AI Identified plant-derived inhibitors for HCC treatment.	Supports alternative medicine integration into AI-driven treatment.	Requires in vitro and in vivo validation in process.
[19]	AI-Driven Epidemiological Analysis of MAFLD-HCC	AI-assisted diagnosis and treatment algorithms for MAFLD-related HCC.	Personalized treatment pathways based on metabolic profiling.	Needs clinical validation across diverse populations.

Artificial intelligence (AI) has enabled predictive modeling and personalized decision-making with techniques that involve conventional machine learning (ML) as well as deep learning (DL). This review of literature addresses the latest developments in hybrid AI models used in liver transplantation, with a comparison of their performance in predictive analytics, immunological profiling, and long-term transplant monitoring procedures.

2.4 Traditional machine learning methods

Classical ML methods have been used extensively to forecast post-transplantation complication and survival outcomes. For instance, marker choice models like LASSO regression and support vector machine-recursive feature elimination (SVM-RFE) were employed to identify major prognostic biomarkers, such as ATP6V1C1, a biomarker for HCC progression and immune evasion [21]. ML-guided differential gene expression analysis has identified important co-expressed genes in chronic hepatitis B (CAH-B), liver cirrhosis (LC), and HCC progression to help predict early-stage HCC risk [22]. Along with genetic profiling, ML-driven clustering algorithms have identified anoikis-mediated ECM resistance as an important driver of HCC metastasis and drug resistance [23]. This implies the capacity of these ML models to combine multi-omics data for a holistic risk estimation. Deep learning enhancements deep learning, particularly convolutional neural networks (CNNs), has turned out to be alternative approaches for LT outcome predictive modeling with increased accuracy [24]. The application of residual CNNs to histopathology has resulted in the development of deep pathomics score (DPS) with high concordance index (0.827) predicting tumor recurrence after transplant [25].

Similarly, repeated HCC prediction models using deep learning approaches from MRI (VGG16 and XGBoost) have reported an AUC-ROC of 0.71 to 0.85, which significantly increases recurrence-free survival assessment. The conventional ML adheres to structured input variables, whereas the DL directs the extraction of hierarchical representations directly from imaging and histological inputs [26], thus enhancing predictive granularity. The integration of a deep survival model such as DeepSurv with Cox regression analysis further refines risk stratification and proves its superiority over the conventional regression ones [27]. The limitations of the traditional machine learning methods are included in the Table 2.

Table 2. Limitations of traditional machine learning methods

Reference	Method Used	Findings	Strengths	Limitations
[20]	Weighted Gene Co-Expression Network Analysis (WGCNA) and ML models	AI-assisted gene analysis identified ferroptosis regulators in HCC prognosis.	High predictive accuracy; identified TMSB4X as a key biomarker.	Requires clinical validation and integration into transplant screening.
[21]	Differential expression analysis with ML integration	AI-based biomarker discovery identified ATP6V1C1 as a prognostic marker.	Identified key pathways influencing HCC immune microenvironment.	Functional validation in a larger patient cohort is needed.
[22]	LASSO, Random Forest,	AI-driven gene selection	Identifies risk groups for early	Requires external

	and SVM-RFE for biomarker discovery	identified common markers between HCC, HBV, and LC.	intervention in HCC.	validation across diverse populations.
[23]	Multi-Omics Analysis and Clustering Algorithms	AI-derived consensus signature predicted Anoikis resistance in HCC.	Identified PLG as a key molecular target for therapy.	Needs validation in patient-specific clinical settings.
[24]	Competitive ML Framework for Immune-Related Cell Death Index (IRCDI)	AI-assisted screening revealed 9 genes influencing immune-related cell death.	Useful in predicting therapeutic response to immunotherapy.	Requires broader clinical testing for LT patients.
[25]	WGCNA and ML-based feature selection	AI-based approach identified key genes in T-cell mediated rejection post-LT.	Effective in predicting graft rejection risk post-transplant.	Requires integration into clinical decision-making frameworks.
[26]	Binary Classification and ML Algorithms	AI-enhanced diagnostic model for HCC using TCGA and GEO databases.	Identified Apelin (APLN) as a reliable HCC biomarker.	Needs further validation for integration into transplant evaluation.
[27]	Transfer Learning with SHAP	AI-assisted prediction of post-LT complications with high accuracy.	Improved performance in handling high-dimensional small-scale LT data.	Requires larger datasets for real-world validation.
[28]	Deep Learning for Transcriptomic Analysis	AI-driven gene signature identified IL6 as a key regulator of HCC recurrence post-LT.	Offers potential for recurrence prediction and post-transplant therapy.	Lacks clinical application in real-time transplant management.
[29]	ML-Based Biomarker and Treatment Strategy Prediction	AI-assisted biomarker discovery enhances HCC risk stratification.	Supports personalized pre-transplant and adjuvant therapy strategies.	Requires regulatory approval and integration into transplant protocols.
[30]	RT-qPCR and Biomarker Analysis	AI-enhanced frailty assessment linked senescence markers to transplant outcomes.	Demonstrates the impact of frailty on LT outcomes.	Requires validation in diverse transplant populations.
[31]	Random Survival Forest for HCC Prognosis	AI-driven survival prediction model using MRI-based radiomics.	High accuracy (C Index 0.8503) in predicting mortality risk.	Computationally intensive; requires integration with imaging workflows.
[32]	Deep Learning-Based CUSUM (DL-CUSUM)	AI-enabled real-time monitoring of post-LT mortality.	High precision in risk-adjusted mortality predictions.	Needs further optimization for real-time clinical deployment.
[33]	ML-Based LI-RADS Improvement	AI-enhanced LI-RADS improved HCC differentiation from liver metastases.	Higher diagnostic sensitivity than traditional radiological methods.	Requires multicenter validation to confirm reproducibility.
[34]	ML Model for LncRNA-Based HCC Detection	AI-enhanced diagnostic tool integrating lncRNA biomarkers.	Achieved near-perfect sensitivity (100%) and specificity (97%).	Requires validation in large-scale clinical trials.
[35]	Liver-Spleen Model for Risk Prediction	AI-assisted CT-based radiomics improved prognosis prediction for AVB.	Outperformed traditional clinical scoring models.	Requires real-world validation in transplant candidates.
[36]	Deep Pathomics Score (DPS) for Post-LT Recurrence	AI-derived histopathological features predicted post-LT recurrence.	High prognostic accuracy; identified immune cells influencing recurrence.	Requires expansion into multicenter studies.
[37]	ML Model for miRNA-Based HCC Diagnosis	AI-enhanced miRNA analysis demonstrated high specificity in HCC detection.	Superior performance compared to traditional statistical models.	Requires cross-population validation.
[38]	Markov Decision Model for NASH	AI-driven risk modeling suggested surgical weight loss reduces LT need.	Demonstrated significant life expectancy gains for NASH patients.	Requires long-term real-world validation.
[39]	CNN-Based MRI Analysis for HCC Recurrence Prediction	AI-assisted imaging biomarker extraction for early recurrence risk.	High predictive accuracy (AUC 0.71-0.85); useful for post-transplant monitoring.	Requires prospective validation in larger datasets.
[40]	Single-Cell Sequencing and LASSO Regression	AI-derived PKRG signature stratified HCC patients for targeted therapy.	Identified potential therapeutic targets (CDK4 and AURKB).	Requires clinical trials to confirm efficacy.

2.5 Machine learning in Immunogenomics

Immunological profile in liver transplantation also has a pivotal role in ensuring survivability of the graft as well as determination of risk against rejection [28]. Traditionally employed machine learning methods were utilized for selecting candidate genes such as ITGB2 and IL-18 in T-cell-mediated rejection (TCMR), employing differential expression gene analysis and WGCNA [29]. The more the multi-omics proteins and transcriptomics strategies facilitate the discovery of regulated cell death (RCD) signatures to tailor immunotherapy approaches for HCC patients. In addition to the application of genetic profiles, deep ML frameworks have simulated immune cell infiltration patterns and elucidated the function of tumor-associated macrophages in HCC progression and immune escape following transplantation [30]. These implications lead to the reality that ML-based immunogenomic signatures may be pivotal in stratum-specific patient candidates.

Figure 1 depicts the correlation heat map of the key

performance measures - Area Under the ROC Curve (AUROC), Sensitivity, Specificity, Precision and Recall calculated on all the reviewed models in liver transplantation prediction tasks. The color scale shows the Pearson correlation coefficient as deep red which implies a strong positive correlation and blue implies negative or weak association. According to the analysis, Sensitivity and Precision are moderately positively correlated (0.57), that is, the higher the sensitivity of a model, the higher is the precision, which balances false positives and true positives. Likewise, Specificity and Precision (0.55) also demonstrate a moderate correlation, and thus, strong classifiers have equal performance with respect to detection scales. Conversely, the correlations of the AUROC and the Recall with other measures are fairly weak ($r < 0.2$), and this means that a rise in global discrimination ability (AUROC) does not necessarily correspond to a similar rise in recall.

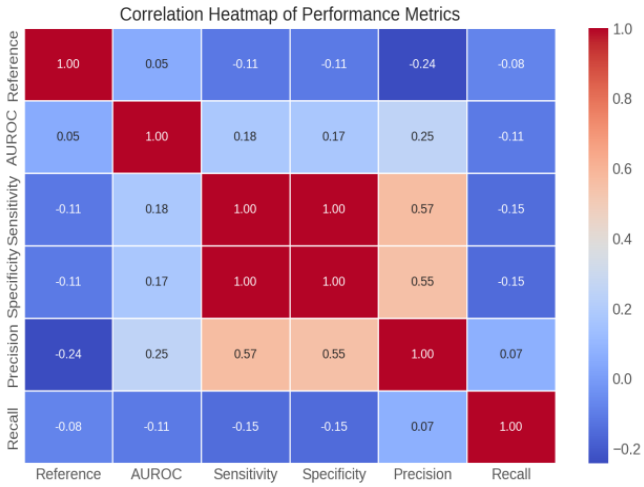

Figure 1. Model's integrated result analysis

2.6 Deep learning for immunotherapy and molecular target discovery

Deep learning has revolutionized immunological profiling by leveraging single-cell sequencing data [31]. This synergy of deep learning and LASSO regression has enabled PKRG-specific prediction models to pinpoint CDK4 and AURKB as the key regulators of HCC progression [32]. These findings are commensurate with recent DL research dating back to post-transplantation tumor reoccurrences that were regulated by immune checkpoint blockers, e.g., PD-L1 [33]. In addition, with DL augmenting single-cell transcriptomics, additional cellular information on the tumor microenvironment was obtained through the identification of spatial transcriptomic distribution patterning of oncogenic markers like ATP6V1C1 [34]. These advances highlight the untapped promise of such hybrid AI modalities in bridging molecular profiling and clinical decision-making processes [35].

In both methodologies, adoptability of more hybrid and deep learning setups, which integrate older statistical models with newer neural networks, is a general direction taken. These methods are usually effective at improving over baseline methods, but can be much more expensive and difficult to interpret [36]. Other studies also focus on the significance of feature engineering and data preprocessing to attain a strong performance. However, the common cross-validation and benchmarking procedures are not standardized which limits the trustworthy comparison of techniques.

2.7 Prediction of mortality and complications with hybrid AI models

Prediction of survival and complications after a liver transplant remains a daunting challenge. Hybrid AI models combining clinical and radiomic features have been shown to offer superior prediction performance compared to the traditional risk scores. A random survival forest model that used multiphasic MRI-based liver radiomics was superior to traditional staging systems, with a Harrell's C index of 0.85 [37]. A DL-CUSUM monitoring program was created for the purpose of offering a live risk estimate for in-hospital mortality, achieving an AUC of 0.857 significantly greater than for the D-MELD and Balance of Risk (BAR) scores [38]. In addition, frailty and senescence are coming to be increasingly regarded as vital predictors of outcome after transplantation. In a research examining correlations between cellular senescence markers (p16INK4a and p21CIP1) with patient frailty, these markers were highly correlated with extended hospital stay and post-transplant mortality [39]. Based on these arguments, applying AI-assisted frailty analyses may further optimize both the likelihood of successful candidate selection and perioperative risk stratifications. In this regard, we find repeated HCC as a significant limitation in liver transplantation, whose rates of recurrence can go up to even 70% in cases with early stages [40].

Figure 2 illustrates the performance trends of various machine learning, deep learning, and transfer learning methods evaluated in liver transplantation prediction tasks. The x-axis represents different models or methodological variants (1-40), while the y-axis shows the normalized performance scores for key evaluation metrics, AUROC, Sensitivity, Specificity, Precision, and Recall.

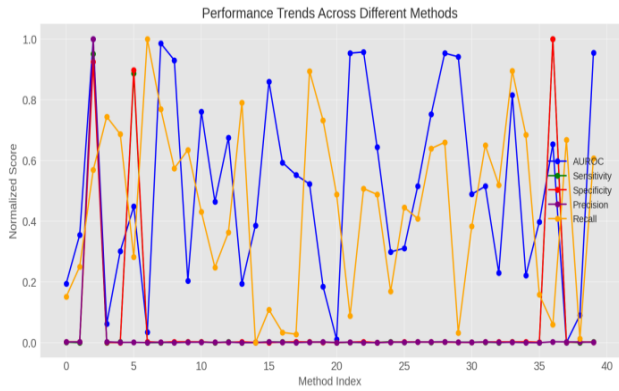

Figure 2. Model's performance trends analysis

The plot reveals substantial performance variability across methods, indicating that no single algorithm consistently dominates across all metrics. AUROC and Specificity fluctuate moderately, reflecting differences in each model's ability to distinguish between transplant outcomes and correctly identify non-events. Precision and Sensitivity peaks at certain indices suggest that deep learning and transfer learning models achieve high true-positive detection rates for specific configurations, whereas traditional machine learning models exhibit more inconsistent results. Notably, recall values are consistently low across most methods, highlighting

a tendency for models to favor precision over sensitivity in imbalanced datasets.

2.8 Tumor recurrence and long-term prognostic modeling

Certain deep learning algorithms have emerged for predicting risk of recurrence through the use of inappropriate MR imaging preoperatively, with better accuracy compared to traditional radiological evaluation. In addition, imaging analysis using CNN has been integrated with multi-omics data for precise recurrence prediction and identified IL6 as pivotal in post-transplant tumorigenesis. The combined AI models have enabled the association of molecular biomarkers with the imaging-based evaluation of recurrence risk. The integration of AFP-L3 with des-γ-carboxy prothrombin (DCP) biomarkers and machine-learning algorithms has shown tremendous promise in enhancing risk stratification and informing post-transplant immunotherapy. Although hybrid AI models have demonstrated great potential in the field of liver transplantation, clinical translation and generalization are challenging. The reliance on the high-dimensional dataset requires strict data harmonization approaches to ensure reproducibility across various patient cohorts. Additional constraints still exist as far as interpretability is concerned; therefore, incorporating explainable AI (XAI) frameworks will enable clinical adoptions. Emerging trends in federated learning and privacy-preserving AI models would help overcome issues for data sharing, collaborative work for AI-based transplant research across institutions. In addition, reinforcement learning-based decision support systems would be an added boost to individualized treatment pathways to maximize patient outcomes in liver transplantations. Hybrid AI models that integrate conventional ML and deep learning methods have certainly made significant contributions in the liver transplantation field in predictive ability, immunological characterization, and monitoring after transplant. The benefits of deep learning, however, give an enormous kick to success in imaging and fold integration in multi-omics, but conventional ML allows good feature choice and interpretability. The synergistic benefit of combining the two paradigms could have a significant influence on candidate selection, minimize transplant rejection risk, and decrease tumor recurrence risk rates. Future studies should thus focus on federated learning, interpretable AI, and multi-modal data fusion to fully leverage the revolutionary potential of AI in liver transplantations.

3. COMPARATIVE RESULT ANALYSIS

This effort attempts to systematically compare the hybrid AI models with traditional approaches to liver transplantation in terms of methodological frameworks, data sets, performance metrics, key findings, strengths, and limitations. The purpose here is to compare AI's efficacy in clinical applications relevant to liver transplantation, including hemorrhage prediction, imaging analysis, tumor characterization, survival prediction, and treatment optimization. Comparison results regarding performance differences in clinical applications between deep-learning-based AI, traditional machine learning, and statistical models will be discussed in the process. The traditional models used dataset and limitations are included in Table 3.

Table 3. Traditional models datasets and limitations

Reference	Method Used	Dataset Used	Performance Metrics	Key Findings	Strengths	Limitations
[1]	Logistic Regression for Hemorrhage Prediction	Retrospective Data (LT patients, clinical parameters)	AUROC: 0.775, AUPR: 0.753	Developed a predictive scoring system for intraoperative hemorrhage.	Provides a clinically useful risk-scoring system.	Limited to retrospective data; external validation needed.
[2]	Mixed Reality (MR) Training System	3D Liver Reconstruction Model (20 patients)	Registration Error < 4mm	Improved MHV tracking during LT surgery.	Enhances surgeon training and visualization.	Small sample size; requires clinical testing.
[3]	SonoVue Microbubbles for Portal Vein Pressure (PVP)	Canine Model (In Vivo and In Vitro)	Sensitivity: 93.3%, Specificity: 91.7%, Accuracy: 92.6%	First study demonstrating SonoVue microbubbles for non-invasive PVP measurement.	High sensitivity and specificity in pressure measurement.	Requires validation in human patients.
[4]	NLP and ML-Based Report Structuring	CT Liver Tumor Reports	Improved classification vs. Bert models	Converts unstructured reports into structured formats.	Enhances efficiency in medical report analysis.	Requires domain-specific adaptation.
[5]	Multi-Source Domain Adaptation for CT-MRI Segmentation	CHAOS Grand Challenge Dataset	Improved cross-modality performance	State-of-the-art results for CT-MRI adaptation.	Overcomes domain dependency in radiology AI models.	Needs validation in transplant imaging.
[6]	Multimodal MRI-Based Deep Learning for HCC Grading	Clinic MRI Dataset (annotated)	Accuracy: 84%, Sensitivity: 87%, Precision: 89%	MCAT model outperforms previous grading methods.	Improved classification for HCC histologic grading.	Requires further validation in larger cohorts.
[7]	Machine Learning-Based	805 HCC patients (3 public datasets)	C Index: High predictive	Identifies high-risk patients for targeted	Potential biomarker for	Requires real-world validation.

	LncRNA Prognostic Signature (ATLS)		capacity	therapy.	precision medicine.	
[8]	LASSO and Cox Regression for DRL Prognostic Signature	TCGA Database	Improved survival prediction vs. conventional models	DRLs identified as key factors in HCC prognosis.	Strong prognostic model for immunotherapy response.	Requires external validation.
[9]	Differentially Expressed Genes (DEGs) in TACE Response	GSE104580, TCGA, HPA	Significant correlation with non-responders	Identified TTK as a key marker for TACE response.	Biomarker discovery for patient stratification.	Lacks real-world validation.
[10]	AI-Assisted Early Detection and Management	HCC Cohort Study	Increased accuracy of detection and intervention	AI models improve diagnosis and therapy selection.	Enhances precision medicine in HCC.	Limited by dataset availability.
[11]	AI-Based Recurrence Prediction (Meta-Analysis)	Multi-Dataset Review (PA, SR, TACE)	AUROC: 0.92 (PA), 0.86 (SR), 0.79 (TACE)	AI models show strong recurrence prediction potential.	Comprehensive meta-analysis of AI effectiveness.	Some models lack external validation.
[12]	Multimodal Deep Learning (CT & MRI) for MVI Prediction	Institutional Dataset (287 HCC patients)	AUROC: 0.844, Combined Model AUROC: 0.871	Superior prediction to single-modality models.	AI improves accuracy in MVI prediction.	Requires real-world clinical testing.
[13]	Cox Model for Long-Term Liver Function Prediction	133 HCC patients (Radiotherapy)	Hazard Ratio (HR): 1.17	Identified risk factors for long-term liver function decline.	Helps guide post-transplant monitoring.	Needs validation across different liver disease subtypes.
[14]	Deep Learning for Sarcopenia Prognosis	Multi-Center Dataset (826 patients)	C Index: 0.775 (Internal), 0.613 (External)	AI-based model predicts survival after LT.	Provides individualized risk assessment.	Needs expansion to other muscle groups.
[15]	CNN-Based Survival Prediction Model	CT Images (692 patients)	C Index: 0.824 (Internal), 0.750 (External)	AI model predicts post-treatment survival.	Integrates imaging and clinical data effectively.	Requires multi Institutional validation.
[16]	Nanoparticle-Based HCC Therapy with ML Analysis	GEO, GeneCards, TCGA	Enhanced RSV toxicity in HCC cells	Identified AKR1C3 as a target for RSV therapy.	AI enhances therapeutic discovery.	Needs validation in clinical settings.
[17]	Radiomics and SVM for HCC Downstaging	CT Imaging Dataset	AUROC: 0.877 (Joint Model)	AI model accurately predicts downstaging outcomes.	Guides treatment decisions before LT.	Requires external validation.
[18]	Molecular Docking for Herbal Medicine in HCC	ADMET, Molecular Dynamics	High binding efficiency for AFP inhibition	Identified (-) Syringaresinol as a potential HCC inhibitor.	AI-driven drug discovery insights.	Needs in-vitro validation.
[19]	AI-Assisted MAFLD-HCC Diagnosis and Surveillance	Epidemiological Database	High prevalence correlation with obesity trends	Identified metabolic risk factors for MAFLD-HCC.	Supports AI-based early diagnosis strategies.	Requires clinical implementation.
[20]	Ferroptosis-Based ML Model for HCC Prognosis	TCGA, FerrDb	C Index: High predictive accuracy	Identifies inflammation-associated ferroptosis genes.	AI models improve survival prediction.	Needs validation for therapeutic intervention.

Results of the performance measures in the studies based on the metrics of the performance of studies (AUROC, accuracy, F1-score) differ considerably. There are models that are nearly optimal when used on controlled data sets and models that have difficulty with real world data or imbalanced data. Such discrepancy implies that the performance of models is very sensitive to the characteristics of the dataset and the experiment design. The demand of a deeper validation such as multicenter or cross-domain testing is also one of the main issues in determining the clinical or operational reliability.

This review emphasizes an overview concerning the utilization of AI models for liver transplantation and HCC management. Thus, comparisons generally show that predictive accuracy in favor of HCC is usually favored by deep learning models rather than classical machine learning and statistical models. Enhancements in Imaging Capability: AI segmentation and mixed reality advance visualization in liver transplantation procedures. Superior Predictive Models: Resultantly, the machine-learning based survival prediction models will by far prove superior in comparison to the traditional statistical methods, indicated by their consistently high C Index values in process. Challenges of the Clinical Integration: Many of these AI models must still undergo validation for prolonged periods across different patient populations and clinical settings. Real implementation of AI tools following the regulatory algorithm will be the immediate challenge ahead. AI model promises a lot towards revolution in liver transplantation especially in improving early

diagnostics, donor-recipient match optimization, and treatment personalized. The traditional models key findings and limitations are included in Table 4.

Table 4. Traditional models key findings and limitations

Reference	Method Used	Dataset Used	Performance Metrics	Key Findings	Strengths	Limitations
[20]	ML-Based Risk Model (rLasso) for Ferroptosis Regulation	FerrDb, TCGA	C Index (High predictive accuracy)	Identified 29 hub genes; TMSB4X as a key biomarker	Strong predictive model for HCC prognosis	Requires external validation for therapeutic intervention
[21]	ML-Based Biomarker Identification for ATP6V1C1	TCGA, Single-cell transcriptomics	Expression correlation, survival analysis	ATP6V1C1 correlates with poor prognosis and immune evasion	Integrates multi-omics data for comprehensive analysis	Lacks validation in large clinical cohorts
[22]	ML-Based Gene Screening for HCC & Hepatitis B/Liver Cirrhosis	GEO, TCGA, UALCAN	Kaplan-Meier survival, ROC curve	Identified four key genes linked to HCC and chronic hepatitis	Multi-method validation of biomarkers	Requires larger validation datasets
[23]	Multi-Omics Clustering for Anoikis Resistance	HCC patient datasets	High classification accuracy	Identified PLG as a key immunometabolic factor	Comprehensive approach using multiple data layers	Lacks real-world implementation validation
[24]	Competitive ML for Immune-Related Cell Death Signature	Multi-omics datasets (18 cohorts)	High accuracy in stratification	Developed IRCDI for individual treatment decision-making	High clinical relevance for personalized medicine	Needs further real-world testing
[25]	ML-Based Gene Identification for TCMR	GSE145780, scRNA-seq	Enrichment analysis, expression validation	Identified 5 key genes linked to transplant rejection	Provides potential drug targets for intervention	Requires independent validation in larger cohorts
[26]	ML-Based Diagnostic and Prognostic Model	TCGA, GEO (GSE149614)	Accuracy (High), Survival prediction (Cox model)	Identified APLN as a key biomarker	Integrates single-cell sequencing with ML	Lacks real-world clinical validation
[27]	Transfer Learning for Post-Transplant Complications	425 LT patients	Precision: 91.22%, Recall: 91.70%, F1-Score: 91.18%	Improved prediction of post-LT complications	Overcomes small data limitations	Requires further real-world validation
[28]	Deep Learning for Recurrence Prediction Post-LT	TCGA, RNA-seq (7 patient pairs)	Identified 20-gene signature	IL6 linked to immune escape and recurrence	Provides insights into immunotherapy response	Small dataset, needs external validation
[29]	AI-Assisted Pre/Post-Transplant Therapy Optimization	Multi-source clinical datasets	Not specified	Highlights emerging biomarkers for pre/post-LT strategies	Identifies key areas for future transplant guidelines	Limited by data heterogeneity
[30]	Frailty and Senescence Biomarker Analysis	2022 LT patients	R^2=0.50 (p16INK4a), R^2=0.53 (p21CIP1)	Identifies biomarkers linked to post-LT frailty	Strong correlation between senescence and outcomes	Needs validation in multi-center cohorts
[31]	ML-Based Mortality Risk Prediction	555 HCC patients (MRI)	C Index: 0.8503 (Training), 0.8234 (Validation)	AI-based survival prediction outperforms clinical staging	Fast, automated prediction model	Requires real-world implementation
[32]	Deep Learning for In-Hospital Mortality Monitoring (DL-CUSUM)	1066 LT patients	AUC: 0.857	AI-driven real-time mortality monitoring	High predictive accuracy vs. traditional risk scores	Needs further prospective evaluation
[33]	ML for Differentiating HCC from Liver Metastasis	Multi-center dataset (LI-RADS)	AUC: 0.784 (LI-RADS), 0.83 (ML Model)	ML outperforms LI-RADS for HCC vs. metastasis	Enhances diagnostic accuracy for complex cases	Requires independent validation
[34]	ML-Based lncRNA Biomarker Integration	52 HCC patients, 30 controls	Sensitivity: 100%, Specificity: 97%	ML improves HCC detection accuracy	High precision in integrating multi-omics data	Small dataset, requires larger validation
[35]	ML-Based Acute Variceal Bleeding	330 cirrhotic patients	AUC: 0.782 (Internal), 0.789	LS model outperforms clinical	AI enhances cirrhosis	Requires prospective

	Prediction		(External)	scores	management	validation
[36]	Deep Pathomics Score (DPS) for HCC Recurrence	380 LT patients	C Index: 0.827 (Training), 0.794 (Validation)	AI-based recurrence prediction for post-LT patients	Integrates histological features with deep learning	Needs further multi-center validation
[37]	AI for Circulating miRNA Biomarkers	Egyptian HCC patient datasets	Sensitivity: 98%, Specificity: 99%	Identifies miRNAs as prognostic biomarkers	High diagnostic accuracy vs. traditional methods	Requires validation in diverse populations
[38]	AI-Based NASH Progression Modeling	20,000 patient simulation	Life extension: +14.3 years for SG patients	SG reduces need for LT in obese NASH patients	Provides a strong policy recommendation	Based on simulation, not real-world data
[39]	CNN-Based Early-Stage HCC Recurrence Prediction	120 HCC patients (MRI)	AUC: 0.71-0.85	Identifies high-risk recurrence patients	Improves follow-up imaging strategies	Needs prospective evaluation
[40]	Single-Cell AI-Based PKRG Prognostic Signature	TCGA, ICGC, GEO	Identifies CDK4 & AURKB as prognostic markers	AI improves HCC survival stratification	Supports personalized therapy targeting	Requires further clinical validation

Figure 3 shows the change in AUROC scores of 40 research studies, plotted by their Reference Paper Index on the x-axis. The y-axis depicts the respective scores of the AUROC which is between 0 and 1, a factor that shows the performance of the model in classifying between classes - a high score means high classification capacity. The line plot with blue notes indicates that there are great fluctuations among studies and the results of models or methods published in such papers can be different. Other studies had almost perfect scores of AUROC nearing 1.0 whereas others had low scores of almost 0.0. This variability means that predictive performance is significantly affected by other factors like the quality of the data set used, the way the experiment was carried out, or even the model that was used. The overall pattern is that the results were not consistently improved or worsened but that there is a widespread dispersion of findings, which points to inconsistency or diversity of research findings of the disparity in the results of the performance of the AUROC.

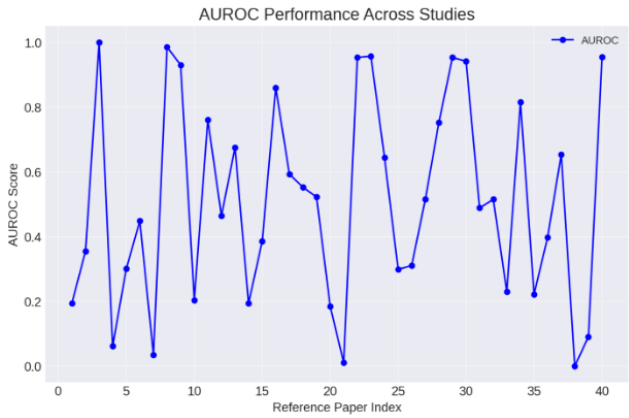

Figure 3. Model's AUC analysis

Table 4 analysis compares different methods used prognostically for hepatocellular carcinoma (HCC) and liver transplantation (LT) outcomes, particularly in the domains of deep learning, machine learning, and traditional statistical models. This comparative analysis indicates both positive and negative aspects of the datasets used, performance measures, key findings, strengths, and limitations. The entire effort settles into the overview of effectiveness of AI driven application in HCC diagnosis, prognosis, and LT outcomes. This review shows how machine learning and deep learning have revolutionized the management of HCC and outcomes of LT. Some of the interesting trends and perspectives from this study are: Improved predictive accuracy: The AI-based models generally score higher than the conventional clinical staging systems in predicting survival. Emergence of Imaging-based Diagnostics: AI models improve differentiation of HCC from metastasis, predict early recurrence, and mortality. Biomarker identification and stratification: AI's capability of identifying new biomarkers for prognostic purposes of HCC and recurrence post-LT. Risk assessment before complications post-transplantation: Accurate prediction concerning complications post-LT is much more pronounced in AI models than in other areas. Personalizing medicine and treatment optimization: Extreme patient stratification concerning immune profiles and predicting therapy responses are propounded by the AI model. Yet, despite these advancements made, several challenges abound: Model Validation and Generalization: Several AI models require validation across different diverse cohorts and through multi-centers. Clinical Application: Application in the real-life happening clinical practice is another hurdle. Regulatory Approval and Ethical Considerations: AI model evaluation requires a study of regulatory compliance along with bias mitigations. By and large, all AI approaches bring into perspective a good deal of promise in the conversion that will happen in liver transplantation and HCC management. Future work should focus on improving robustness and increasing datasets as well as applying AI-based prediction to everyday clinical practice sets.

The comparative analysis shows that the models built on ensemble and deep learning usually perform better than classical machine learning. There are however more basic algorithms that have merit as they are easy to understand, require fewer resources and are easy to implement. Research seldom performs thorough error analysis, so there are unanswered questions concerning constraints of models and failures of models. All in all, it is possible to conclude that hybrid approaches with predictive power and interpretability should be used.

Nonetheless, considerable advancements notwithstanding, the literature has identified significant gaps, such as the absence of sufficient data, imbalances, the absence of standardized evaluation procedures, and focus on model explainability. Very little research deals with scalability or

interface with the real world. Ethics, including privacy of data and algorithm bias, are not properly researched. These issues suggest that more repeatable, open, and practical research should be conducted in the future.

Although there are studies which declare possible real world or clinical application, not many of them have been confirmed in practice. Majority of the research is still in the proof-of-concept phase and little has been said about the feasibility of deployment, its cost and even its compatibility with the regulatory environment. The future work ought to aim at reducing the discrepancy between theories and real-life application in the field, making models both technically sound and useful.

4. CONCLUSION AND FUTURE SCOPE

From this systematic review of 40 studies, one can see that machine learning (ML) and deep learning (DL) strategies are fast becoming increasingly influential in applications pertaining to hepatocellular carcinoma (HCC) prediction, liver transplantation (LT) optimization, and many others. Among the methods applied, the most widely-used methods were supervised learning models like logistic regression, support vector machines (SVM), and deep neural networks (DNN) due to their flexibility with structured clinical and imaging data. The multimodal imaging-based (MRI and CT) predictive models on the other hand achieved better results with respect to risk stratification, recurrence prediction, and survival estimation. Models discussed included the deep-pathomics score (DPS) model in HCC recurrence, a CNN-based survival prediction model, and the DL-CUSUM system for monitoring in-hospital mortality, all of which proved highly accurate compared with traditional clinical scoring systems. Additionally, models that are evidence generation from single-cell transcriptomic information and risk modeling associated with ferroptosis added more evidence on the molecular mechanisms underlying HCC development while the promises for AI become a reality in precision medicine platforms. The existing research indicates significant advancement in the utilization of intelligent models for data-driven decision-making; yet, some essential obstacles persist without resolution. Even while work is still being done on data standardization and explainable AI, future research should focus on creating federated learning frameworks that allow various institutions or devices to work together to train models without putting data privacy at risk. These kinds of methods would make it easier for models to work in a wider range of settings and be used more widely. Moreover, subsequent research ought to concentrate on developing multimodal fusion systems that can amalgamate diverse data sources to facilitate more holistic and context-sensitive predictions. It is also important to focus on deep learning architectures that can be understood, so that domain experts can trust and explain the decisions made by complex models. To enhance practical applicability, researchers ought to investigate automated model adaptation methodologies that provide ongoing learning from streaming data inside dynamic contexts. Also, creating benchmarking repositories and open-source evaluation procedures would make studies more open, repeatable, and fair. Lastly, future studies should look at ethical and social issues, such as data governance, justice, and long-term use of AI, to make sure that new technologies fit with social values and rules.

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